

Evaluation of Production Benchmarks for ^{72}As and ^{211}At Toward Clinical Translation



Doctoral thesis

for

the award of the doctoral degree

of the Faculty of Mathematics and Natural Sciences

of the University of Cologne

submitted by

Lucas Mues

In the year 2026

*“An experiment is a question which science poses to Nature,
and a measurement is the recording of Nature’s answer.”*

—Max Planck¹

¹ Max Planck, „Sinn und Grenzen der exakten Wissenschaft“, 1941; English translation in *Scientific Autobiography and Other Papers*, 1949.

Table of content

Abstract	iii
Kurzzusammenfassung	v
List of Figures	viii
List of Tables.....	xv
List of Abbreviations	xix
1. Introduction.....	1
1.1. From radioactivity to translational radionuclide production	1
1.2. Standard and non-standard radionuclides in nuclear medicine	2
1.3. Nuclear, radiopharmaceutical, and production criteria.....	5
1.4. ^{72}As as a non-standard PET radionuclide	10
1.5. ^{211}At as a therapeutic radionuclide limited by process robustness	15
1.6. Relationship between ^{72}As and ^{211}At	23
2. Aim of this work	25
3. Results & Discussion.....	27
3.1. Nuclear data measurements of $^{72}\text{Se}/^{72}\text{As}$	27
3.1.1. Target preparation and suitability for irradiation.....	27
3.1.2. Excitation functions and production windows	28
3.1.3. Decay characterization and implications for quantitative PET	53
3.2. Production and Processing of ^{211}At	62
3.2.1. Targetry, irradiation performance, and production quality of ^{211}At	62
3.2.2. Recovery, separation, and process optimization of ^{211}At	90
3.2.3. Analytical characterization of processed ^{211}At	125
3.2.4. Chemical usability and proof-of-principle labeling of ^{211}At	151
3.2.5. Waste handling and operational implications of routine ^{211}At work....	164
4. Conclusion.....	168
5. Materials and Methods	173
5.1. General materials and instrumentation.....	173
5.2. Experimental methodologies	175
5.2.1. Irradiation facilities and beamline infrastructure	175
5.2.2. Target preparation	177
5.2.3. Experimental irradiation procedures.....	187
5.2.4. Nuclear data measurements for $^{72}\text{Se}/^{72}\text{As}$	189
5.2.5. Thermal stability investigation for ^{211}At high current targets	192

5.2.6.	Separation of ^{211}At	201
5.2.7.	^{211}At Chemistry and Analysis.....	209
5.3.	Evaluation of experimental data	214
5.4.	Determination of radioactivity	214
5.4.1.	HPGe γ -spectrometry.....	215
5.4.2.	Dose calibrator	218
5.4.3.	Beta-counter.....	219
5.4.4.	Low γ counter.....	221
5.5.	Calculation & Simulation	222
5.5.1.	Normalization of count rates and estimation of uncertainties	222
5.5.2.	SRIM	223
5.5.3.	Stack	224
5.5.4.	TALYS-2.0	225
5.6.	Usage of AI-Based Tools	226
	References	229
	Eidesstattliche Erklärung	Fehler! Textmarke nicht definiert.
	Declaration for the doctoral thesis (unofficial translation)	Fehler! Textmarke nicht definiert.
	Curriculum Vitae	Fehler! Textmarke nicht definiert.
	Acknowledgements	Fehler! Textmarke nicht definiert.
	Appendix.....	241
	Appendix A: Production and decay data measurement of ^{72}As	241
	Appendix B: Production and processing of ^{211}At	267

Abstract

Non-standard radionuclides are often discussed in nuclear medicine because their decay properties appear to fill diagnostic or therapeutic gaps left by established isotopes. Yet their translational value is determined not by nuclear decay properties alone, but by whether production, impurity control, processing, analytical characterization, and downstream radiochemistry can be made experimentally reliable. This thesis addresses this problem through two complementary case studies: ^{72}As , a longer-lived positron emitter whose practical value depends on reliable production and decay-data validation, and ^{211}At , a targeted-alpha-therapy radionuclide whose wider use is constrained by radionuclide availability and robustness of post-production processing.

The first part of this work deals with the production of ^{72}As . Rather than considering half-life and positron emission alone, several charged-particle production routes were evaluated with respect to excitation functions, thick-target yields, accessible energy windows, and impurity formation. Direct production via enriched ^{72}Ge , α -particle-induced production on enriched ^{69}Ga , and indirect formation through ^{72}Se were investigated as complementary routes with different practical limitations. The results show that the relevant production question is not which reaction gives the highest yield in isolation, but which route provides a workable compromise between yield, radionuclidic purity, targetry, and beam-energy control. Particular constraints arise from the formation of ^{71}As in direct ^{72}As production and ^{75}Se in the indirect $^{72}\text{Se}/^{72}\text{As}$ approach. In parallel, complementary radiometric measurements were used to evaluate if the positron-relevant decay data of ^{72}As are sufficiently reliable for PET-imaging. The observed decay was in good agreement with literature data and supported the use of established positron-emission intensities in quantitative considerations.

The second part of this work, dealing with ^{211}At , demonstrates that the translation of a therapeutic α -emitter is not limited by one isolated step, but by the coupling of targetry, energy of α -particles, radiochemical separation, exact analytical measurements, and chemical reactivity of isolated ^{211}At . High-current production on bismuth targets was shown to require careful target preparation, thermal contact of Bi-layer and target

backing, beam geometry, cooling efficiency, and precise α -particle energy. Under suitable conditions, stable production-relevant irradiation was achieved, while the yield-purity balance remained governed by the competition between ^{211}At formation and the energy-dependent production of ^{210}At , the precursor of long-lived ^{210}Po .

Among the investigated separation methods for ^{211}At isolation from the Bi-target, dry distillation emerged as the most robust route under the studied conditions because it combined reproducible transfer, operational simplicity, and chemical reactivity of isolated astatine. Optimized trapping using PTFE-based cooling traps and optimized carrier-gas flow provided an HPGe-based reference recovery of $80.4 \pm 0.4\%$. Alternative liquid–liquid extraction and adsorptive approaches confirmed that ^{211}At can be isolated by different chemical pathways but also demonstrated that recovery alone is an incomplete process metric. Proof-of-principle labeling with 4- $[^{211}\text{At}]$ astato-L-phenylalanine showed that the downstream reactivity of isolated ^{211}At depends strongly on the processing route and chemical history of the astatine fraction. Accurate interpretation of these experiments required careful analytical validation, as common RP-HPLC and TLC methods can give misleading results for unreacted astatine due to adsorption, tailing, redistribution, volatility-related losses, and support-material-dependent retention on TLC plates.

Together, these studies show that non-standard radionuclides require bottleneck-specific validation across the full translational pathway. For ^{72}As , the decisive requirements are reliable production routes, energy windows and decay data for PET interpretation. For ^{211}At , practical implementation depends on reproducible target performance, controlled separation chemistry, validated analytics, labeling compatibility, and operational handling. This thesis thereby argues that emerging medical radionuclides should be evaluated not only by their theoretical nuclear suitability, but by the experimentally demonstrated compatibility of production, purity, processing, characterization, and radiochemical applicability.

Kurzzusammenfassung

Nicht-Standard-Radionuklide werden in der Nuklearmedizin häufig diskutiert, da ihre Zerfallseigenschaften diagnostische oder therapeutische Lücken schließen können, die durch etablierte Radionuklide nur unzureichend abgedeckt werden. Ihre translationale Bedeutung ergibt sich jedoch nicht allein aus günstigen nuklearen Eigenschaften, sondern erst daraus, ob Produktion, Kontrolle radionuklidischer Verunreinigungen, Aufarbeitung, analytische Charakterisierung und nachfolgende Radiochemie experimentell zuverlässig umgesetzt werden können. Diese Arbeit untersucht diese Fragestellung anhand zweier komplementärer Fallbeispiele: ^{72}As als längerlebiger Positronenemitter, dessen praktische Relevanz durch belastbaren Produktions- und Zerfallsdaten zu bestätigen ist, sowie ^{211}At als Radionuklid für die gezielte Alphatherapie, dessen breitere Anwendung bisher vor allem durch die fehlende Robustheit der gesamten Prozesskette begrenzt wird.

Der ^{72}As -Teil untersucht, wie ein vielversprechendes Nicht-Standard PET-Radionuklid bewertet werden muss, bevor ein weitergehender Einsatz sinnvoll diskutiert werden kann. Neben Halbwertszeit und Positronenemission wurden mehrere geladene-Teilchen-induzierte Produktionsrouten hinsichtlich Anregungsfunktionen, integrierte Ausbeuten dicker Targets, zugänglicher Energiefenster und Verunreinigungsbildung untersucht. Die direkte protonen-induzierte Produktion über angereichertes ^{72}Ge , die α -induzierte Produktion an angereichertem ^{69}Ga sowie die indirekte Bildung über ^{72}Se über die $^{75}\text{As}(p,4n)$ -Reaktion wurden als komplementäre Routen mit unterschiedlichen praktischen Einschränkungen bewertet. Die Ergebnisse zeigen, dass nicht die isoliert höchste Ausbeute entscheidend ist, sondern ein praktikabler Kompromiss zwischen Ausbeute, radionuklidischer Reinheit, Targetverfügbarkeit und Kontrolle der Strahlenergie zu gewährleisten ist. Besondere Einschränkungen ergeben sich durch die Bildung von ^{71}As bei der direkten ^{72}As -Produktion sowie von ^{75}Se bei der indirekten $^{72}\text{Se}/^{72}\text{As}$ -Route. Ergänzend wurden radiometrische Methoden eingesetzt, um zu prüfen, ob die für PET-Anwendungen relevanten Zerfallsdaten von ^{72}As mit den bekannten Literaturdaten übereinstimmt. Das beobachtete Zerfallsverhalten stimmte mit den Literatur-bekannten Daten gut überein und unterstützt die Verwendung etablierter Positronenemissionsintensitäten für quantitative Auswertungen.

Der ^{211}At -Teil zeigt, dass die Translation eines therapeutischen α -Emitters nicht durch einen einzelnen Prozessschritt begrenzt wird, sondern durch das Zusammenspiel von Targetry, Strahlenergiekontrolle, radiochemische Abtrennung, analytischer Zuverlässigkeit und chemischer Reaktivität von ^{211}At nach Isolation. Die Produktion von ^{211}At an Bismut-Targets bei hohen Strömen erfordert eine sorgfältige Kontrolle der Targetpräparation, des thermischen Kontakts der Bi-Schicht mit der Targethalterung, der Strahlgeometrie, der Kühlung und der effektiven α -Teilchenenergie. Unter geeigneten Bedingungen konnte eine stabile, produktionsrelevante Bestrahlung erreicht werden, wobei das Verhältnis von Ausbeute und Reinheit weiterhin durch die Konkurrenz zwischen der Bildung von ^{211}At und der energieabhängigen Produktion von ^{210}At , dem Vorläufer des langlebigen ^{210}Po , bestimmt wurde.

Unter den untersuchten radiochemischen Abtrennungsmethoden erwies sich die Trockendestillation unter den gewählten Bedingungen als robustestes Verfahren, da sie reproduzierbaren Transfer, einfache Handhabung und Astat-Fractionen mit hoher chemischer Reaktivität verband. Eine optimierte Abscheidung in PTFE-basierten Kühlfälle unter optimierten Trägergasbedingungen lieferte eine Rückgewinnung von $80,4 \pm 0,4\%$. Alternative kamen die Flüssig-Flüssig-Extraktionen und adsorptive Ansätze zum Einsatz, die bestätigten, dass ^{211}At über verschiedene chemische Wege isoliert werden kann. Diese alternativen Methoden zeigten jedoch auch, dass die Rückgewinnungsausbeute allein kein ausreichendes Maß für die Prozessqualität darstellt. Etablierte RP-HPLC- und DC-Methoden zeigen, dass sich mit diesen Methoden die Menge an nicht reaktivem („freiem“) Astat nicht quantitativ bestimmen lässt. Aufgrund von Adsorption, Tailing, Umverteilung, volatilitätsbedingten Verlusten und nicht geträgertem Verhaltens wurde keine verlässlichen Ergebnisse erhalten. Auch Proof-of-Principle-Markierungen von ^{211}At zu 4- ^{211}At -phenylalanin zeigten darüber hinaus, dass die radiochemische Abtrennungsmethode erheblichen Einfluss auf die Reaktivität des isolierten ^{211}At hatte.

Zusammengefasst zeigen diese Untersuchungen, dass Nicht-Standard-Radionuklide entlang der gesamten Translationskette bottleneck-spezifisch validiert werden müssen. Für ^{72}As sind robuste Produktionsmethoden und präzise Bestimmung der Zerfallsdaten entscheidend für eine breite Anwendung dieses PET-Nuklids in der medizinischen Praxis. Für ^{211}At hängen praktische Implementierung und radiochemische Nutzbarkeit von reproduzierbarer Targetperformance, kontrollierter

Trennchemie, validierter Analytik, Markierungskompatibilität und operationeller Handhabbarkeit ab. Diese Arbeit zeigt damit, dass vielversprechende medizinische Radionuklide nicht nur anhand ihrer theoretischen nuklearen Eignung bewertet werden sollten, sondern anhand der experimentell belegten Vereinbarkeit von Produktion, Reinheit, Aufarbeitung, Charakterisierung und radiochemischer Anwendung.

List of Figures

Figure 1: Translational pathway of a medical radionuclide. Schematic overview of the development path from nuclear properties to clinical implementation. The pathway includes decay properties, production yield, radionuclidic purity, targetry, recovery, analytical characterization, labeling compatibility, radiation protection, and routine feasibility. The main bottlenecks addressed in this thesis are highlighted for ^{72}As and ^{211}At	4
Figure 2: Energy-dependent yield-purity problem in ^{211}At production. Schematic or literature-based excitation functions for the $^{209}\text{Bi}(\alpha,2n)^{211}\text{At}$ and $^{209}\text{Bi}(\alpha,3n)^{210}\text{At}$ reactions. The figure should illustrate that ^{211}At production is governed by an energy-dependent compromise between yield and suppression of $^{210}\text{At}/^{210}\text{Po}$ formation. Experimental cross-section data for the $^{209}\text{Bi}(\alpha,xn)^{211/210}\text{At}$ reactions were compiled from the literature [33, 42–48] and are shown together with TENDL-2025 (TALYS Evaluated Nuclear Data Library) data [49].	7
Figure 3: Slanted target geometry for charged-particle irradiation. Schematic representation of a slanted solid target irradiated by an α -particle beam. The slanted geometry increases the effective beam footprint and can reduce local power density, while also increasing the effective path length through the target material. Both effects must be considered in target design and production-window definition.	10
Figure 4: Comparison of monitor-reaction cross-sections measured in this work with IAEA recommended data. Panels (A) and (B) show proton-induced monitor reactions up to 45 and 70 MeV, respectively, whereas panel (C) shows alpha-induced monitor reactions between 15 and 30 MeV.	30
Figure 5: Experimentally determined cross-section data of the $^{72}\text{Ge}(p,n)^{72}\text{As}$ (left) and $^{72}\text{Ge}(p,2n)^{71}\text{As}$ (right) reaction in comparison to modeled reference data from TENDL-2025 and TALYS-2.0 at default parameters.	31
Figure 6: Direct comparison of the thick target yield for the formation of ^{72}As and ^{71}As via proton induced reaction with ^{72}Ge and the recommended data provided by the IAEA [38].....	32
Figure 7: Illustration of the production window for optimized ^{72}As production with minimal ^{71}As content. The TENDL-2025 fit is added to guide the eyes for easier visualization.	32
Figure 8: Reaction cross-section data of $^{\text{nat}}\text{Ga}(\alpha,x)^{71/72}\text{As}$ reaction (obtained in a cooperative work with Dr. M. Hussain) in comparison to TENDL-2025 and Talys-2.0 modeled reaction data as well as experimental literature data.....	33
Figure 9: Reaction cross-section data of enriched $^{69}\text{Ga}(\alpha,n)^{72}\text{As}$ (left) and $^{69}\text{Ga}(\alpha,2n)^{71}\text{As}$ (right) reaction in comparison to literature known reaction data as well as TENDL-2025 and TALYS-2.0 (default) modeling data.	34
Figure 10: Illustration of the production window for optimized ^{72}As production with minimal ^{71}As content. The TENDL-2025 fit is added to guide the eyes for easier visualization	35
Figure 11: Thick target yield for the formation of ^{72}As and ^{71}As by alpha induced reaction with enriched ^{69}Ga	35
Figure 12: High-purity germanium γ -spectra of the direct measurement of ^{72}Se (Sample 62) (A) and for indirect determination via ^{72}As measurement (Sample 41) (B).	37
Figure 13: Reaction cross-section data of direct formation of ^{72}Se via $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction and the indirect calculation of ^{72}Se by its daughter nuclide ^{72}As . All measurements were performed > 25 days post EOB. The Measured data is compared to literature known results as well as modeling via TENDL-2025 and TALYS-2.0 (default).	38

Figure 14: Reaction cross-section of the competing $^{75}\text{As}(p,n)^{75}\text{Se}$ reaction.	39
Figure 15: Energy window of ^{72}Se production directly compared to the ^{75}Se impurity. The red dotted line indicates a compromise between highest possible ^{72}Se yield with reasonable low ^{75}Se content.	40
Figure 16: Thick-target yields (TTY) of ^{72}Se , determined both directly from the ^{72}Se activity and indirectly from the ingrowth of its daughter nuclide ^{72}As , in comparison with the thick-target yield of the co-produced impurity ^{75}Se . The corresponding $^{75}\text{Se}/^{72}\text{Se}$ thick-target yield ratio is shown to illustrate the energy-dependent impurity contribution relative to the desired generator parent.	40
Figure 17: Comparison of the experimental $^{75}\text{As}(p,4n)^{72}\text{Se}$ excitation function with the TALYS-2.0 default calculation and the literature-based reference curves (Padé fit, TENDL-2025)....	42
Figure 18: TALYS-2.0 single-parameter screening for the $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction: effect of OMP, level-density model, and pre-equilibrium mode.	43
Figure 19: Comparison of the most relevant combined TALYS-2.0 calculations for $^{75}\text{As}(p,4n)^{72}\text{Se}$: <code>ldmodel2_preeqmode3 (ld2-pe3)</code> , <code>ldmodel2_preeqmode3_OMPrv105 (ld2-pe3-rv105)</code> , <code>ldmodel5_preeqmode3 (ld5-pe3)</code> , and <code>ldmodel5_preeqmode3_OMPrv105 (ld5-pe3-rv105)</code> , together with the experimental data and the Padé-based reference fit.	46
Figure 20: Comparison of the experimental excitation function with the TALYS-2.0 default calculation and the two most relevant locally adjusted cases. While the <code>ld2+pe3+rv105</code> case reproduces the peak magnitude more closely, the <code>ld5+pe3+rv105</code> case provides a better description of the peak position. Both calculations still underestimate the high-energy tail. ...	47
Figure 21: Comparison of HPGe spectra of sample 14 (irradiated at ~9 MeV) only containing ^{72}As (A) and sample 1 (irradiated at ~16 MeV) containing both ^{71}As and ^{72}As (B).....	54
Figure 22: Annihilation peak (511 keV) of sample 14 placed inside an annihilation chamber.	55
Figure 23: Decay curve obtained from annihilation measurement of sample 14, showing excellent alignment with the fitted decay curve of ^{72}As ($R^2=0.9998$ & RMSE (root mean square error) = 0.17).	55
Figure 24: X-ray spectrum of a thin ^{72}As sample (sample 16) showing the two main X-ray lines of an arsenic/germanium system at 9.88 keV and 10.98 keV.....	56
Figure 25: Beta-particle gross-count rate of enriched ^{72}Ge sample (sample 14) irradiated with 9.3 MeV protons. Showing the analysis of long-lived and short-lived components.....	57
Figure 26: Plotted the activity of ^{72}As , after correction by the long-lived impurities and the detector efficiency (Section 3.4.3). The data is fitted exponentially and the half-life is calculated.	57
Figure 27: Representative appearance of different bismuth starting materials before and after acid pretreatment. (A) Oxidized bismuth spheres before washing. (B) The same material after pretreatment in 1 M HCl. (C) Three powder batches of the same commercial source showing different surface appearance, consistent with different degrees of oxidation. (D) The same powder batches after mixing and pretreatment. (E) Bismuth pellets before (left) and after oxide removal (right). (F) Fragmented pellets exposing fresh metallic fracture surfaces	63
Figure 28: Photographs of coin targets prepared via sinter target method at medium current irradiation, showing thermal failure at currents below 5 μA_e . These photographs are visually cleaned. The original photographs are shown in the appendix in Figure B-1.	67
Figure 29: Presenting photographs of electrodeposited targets (A) and molten targets (B) after 1 h irradiation showing basically no visible target disintegration. Furthermore, the HPGe	

spectra of electrodeposited- (C) and molten targets (D) is depicted showing the key γ lines emitted by ^{211}At and ^{210}At as well as impurities originating from undesired aluminum irradiation (^{27}Mg , ^{29}Al and ^{66}Ga). For the electrodeposited target, additional impurities (^{60}Cu and ^{61}Cu) are visible.	68
Figure 30: Saturation curve of ^{211}At production in dependence on the irradiation time. The beam current was normalized to 50 μA_e to correct for small current fluctuations.	71
Figure 31: Photograph of a target prepared by melting technique after a 4 h irradiation showing slight abbreviation on the target surface roughly resembling the beam shape footprint. The photograph is edited to increase visually while maintaining radiation protection. The original photograph is shown in the appendix in Figure B-1.	72
Figure 32: Delayed HPGe γ -spectrum of an irradiated molten bismuth target on an AlMg3 backing measured approximately five months after EOB. The spectrum is dominated by characteristic ^{207}Bi γ emissions. The peak at approximately 1460 keV is assigned to an overlap of environmental ^{40}K and weak ^{207}Bi -related emission. Only minor additional peaks were observed, which did not indicate a relevant long-lived γ -emitting activation inventory attributable to the AlMg3 backing.	73
Figure 33: Beam profile for 10% Wobbler intensity. The beam direction is illustrated by the arrow.	76
Figure 34: Beam profile of 20% (A), 30% (B) and 40% (C) wobbler intensities. The apparent differences in signal intensity are attributed to different exposure times of the phosphor imaging plate.	77
Figure 35: Temperature gradient over different measurement points of the Bi/Al test rod prepared analogous to the melting target preparation technique. Showing an overview of the whole experiment as well as an amplified view at the metal interface.	80
Figure 36: Temperature gradient over different measurement points of the Bi/Al test rod prepared analogous to the sinter target preparation technique.	81
Figure 37: Footprint of the alpha beam on the target surface at 6° imposing angle measured via phosphor imager. (A), the bare intensity plot is presented and (B), the plot is segregated into pixel of 1 x1 mm.	82
Figure 38: Depicting a heat map of the calculated target temperature of a 6° -target prepared by melting target method at 10% wobbler intensity.	84
Figure 39: Temperature profile of increasing wobbler activity during irradiation.	85
Figure 40: $^{210}\text{At}/^{211}\text{At}$ ratios measured from March–December 2025, ...	87
Figure 41: Comparison of the calculated thick-target yields of ^{211}At and ^{210}At (A) and the corresponding $^{210}\text{At}/^{211}\text{At}$ activity ratio (B) as a function of projectile energy. Thick-target yields were calculated from IAEA literature data [38].	88
Figure 42: Relative activity loss of ^{210}At and ^{211}At of two irradiated bismuth targets following three successive manual decontamination steps using disposable paper towels (A). Each step consisted of five swipes applied with moderate pressure. Activities were quantified by HPGe spectroscopy. In (B), the corresponding decrease in $^{210}\text{At}/^{211}\text{At}$ ratio is presented.	91
Figure 43: Trapping efficiency of ^{211}At as a function of trapping temperature	96
Figure 44: Showing the Fractions of trapped and over distilled ^{211}At in respect to different capillary materials (*n=3). Tapping over 100 % is due to self-absorption when samples are measured in the dose-calibrator, see text.	98

Figure 45: Recovery rates of ^{211}At over 10 runs (in 40 days) using the same capillary. Recoveries over 100 % are due to self-absorption when samples are measured in the dose-calibrator, see text	99
Figure 46: Influence of carrier gas composition on the trapping efficiency of ^{211}At	100
Figure 47: Showing a bismuth target after irradiation and after dry distillation processing using a vertical oven setup at 570 °C. Photographs is visually cleaned. The original photograph is shown in the Appendix in Figure B-3.	105
Figure 48: Monitoring during dry distillation processing using NaI(Tl) scintillation detectors aiming at the center of the furnace as well as the cold trap.	106
Figure 49: PIN detector compared to NaI positioned at Furnace outlet (left) and at cold trap (right).....	107
Figure 50: Distribution coefficient of selected solvents compared to 0.1, 2 and 6 M HNO_3 . The different distribution coefficients are connected by lines, to guide the eye.	118
Figure 51: Efficiency curves of the HPGe γ -spectroscopy setup used for ^{211}At measurements, presenting the efficiencies for (A) 30 cm detector distance, (B) 30 cm distance with a 1 mm lead filter, and (C) 50 cm distance with a 5 mm lead filter, with corresponding efficiencies of $h_{687\text{ keV}} = 3.19\text{E-}4$, $h_{687\text{ keV}} = 1.84\text{E-}4$, and $h_{687\text{ keV}} = 6.61\text{E-}5$, respectively.	128
Figure 52: Showing a long-time exposure photograph (2 min) of radioluminescence of ^{211}At (~3 GBq) in a V-shaped borosilicate glass vial (right). As comparison, a similar vial without activity is shown right beside (left). The radiation dose measured of this assembly was ~57 mSv h^{-1} contact dose and ~600 $\mu\text{Sv h}^{-1}$ at 30 cm distance (Camera distance). The radiochemical preparation was performed by Lucas Mues (Author) whereas the photograph was taken by Dr. Alexander Haseloer.	130
Figure 53: Long-exposure photographs of ^{211}At -containing V-vials under different gas and solvent conditions. (A) Dried ^{211}At samples under argon, helium, and krypton atmospheres. (B) Corresponding samples after addition of water, chloroform, or diiodomethane. The images show that the visible emission persisted under different atmospheres but decreased markedly after addition of liquid, with the spatial emission pattern depending strongly on the apparent activity distribution (photograph by Dr. Alexander Haseloer).	131
Figure 54: Long-exposure photograph of a ^{211}At -containing vial showing localized blue emission along the vial wall and near residual activity deposits. The spatially localized pattern supports a surface-related radioluminescence contribution rather than a purely homogeneous gas-phase emission. (photograph by Dr. Alexander Haseloer)	132
Figure 55: Exemplary chromatograms showing broad and distorted peaks of free ^{211}At partly washed off the column independently of column material and prepared ^{211}At species. The red graph shows the Waters XBridge column at reducing conditions, the black graph shows the performance of the Merck Chromolith column at reducing conditions and the blue graph shows the PolymerX column with native ^{211}At	137
Figure 56: Exemplary chromatograms of the four different columns (Red: XBridge, Black: Luna C18, Blue: PolymerX and Grey: Chromolith RP-18) under reducing conditions with Water/MeCN + 0.1 % TFA solvent mixture.....	141
Figure 57: Chromatogram of a bypass run for offline control measurement, where every component is precisely the same as the for the online measurement except no stationary phase is connected.	142

Figure 58: Triplicate chromatograms of electrophilic ^{211}At obtained under identical preparation and analytical conditions using a Waters XBridge C18 column and MeCN/water/0.1% TFA as eluent.	143
Figure 59: Representative chromatograms of nucleophilic ^{211}At obtained on a Waters XBridge C18 column using different mobile phases selected to improve astatine recovery according to the results presented in Table 27.	145
Figure 60: Quantification of free ^{211}At in native (A), electrophilic (B) and nucleophilic form (C) using different types of TLC quantified by Cyclone Plus (PerkinElmer)phosphor imager. Different suppliers, types and batches of TLC plates investigated in this study. The plates are numbered as presented in Table 28.	150
Figure 61: UV-HPLC chromatogram of the non-radioactive 4-IPA structural analogue. The main UV-detected peak at 3.42 min was used to define the expected retention region for the corresponding radioastatinated phenylalanine product, 4- ^{211}At]APA, in radio-HPLC analyses.	153
Figure 62: Comparison of the four labeling methods utilizing ^{211}At freshly prepared by dry distillation (DD)-method using PTFE-tube cold trap assembly.	155
Figure 63: Overlay of the radio-HPLC signal recorded with the NaI(Tl) detector (red, left y-axis) and the corresponding UV absorbance trace of the non-radioactive 4-iodo-L-phenylalanine reference compound (4-IPA, black, right y-axis). The product peak assigned to 4- ^{211}At]astato-L-phenylalanine (4- ^{211}At]APA) eluted at 3.35 min, closely matching the UV peak of 4-IPA at 3.37 min. This agreement supports the retention-time-based identification of the labeled product.	156
Figure 64: Representative radio-HPLC chromatograms of four model labeling reactions using ^{211}At purified by LLE with 3-octanone (A) or octanal (B). Destannylation (red) and halogen exchange (green) showed product-associated peaks of the expected retention time of 3.3–3.5 min, whereas the NBS- (black) and KI-mediated reactions (blue) were dominated by formation of an unidentified side product eluting at 2.4 min, especially for the 3-octanone-derived fraction. A slight retention-time shift toward longer retention was observed for the destannylation product peak in the octanal-derived sample. Radioactivity was recorded with the NaI(Tl) detector; chromatograms are vertically offset for clarity.	159
Figure 65: Representative radio-HPLC chromatograms showing the effect of added bismuth on the NBS-mediated (A) and KI-mediated (B) labeling reactions. For each method, chromatograms obtained from a reference sample and from a Bi-spiked sample are overlaid to visualize changes in the radioactive peak pattern. In both cases, ^{211}At was obtained by dry distillation using a PTFE-tube cold-trap assembly. For the Bi-spiked samples, the ^{211}At solution was supplemented with 5 μL $\text{Bi}(\text{NO}_3)_3$ solution (50 mg mL^{-1}) prior to labeling. ^a The indicated chromatogram was multiplied by a factor of 0.8 for activity normalization and visual comparison. ^b The indicated chromatogram was multiplied by a factor of 0.7 for activity normalization and visual comparison.	163
Figure 66: Schematic overview of a sedimentation cell used to prepare thin samples for stack foil irradiations.	179
Figure 67: Photograph of the sedimentation cell used for thin-target preparation, shown disassembled (left) and assembled (right).	179
Figure 68: Photograph of a representative sedimented enriched ^{72}Ge target on an aluminum backing without cover foil (A) and magnified view of the target surface illustrating its homogeneity (B).	179

Figure 69: Schematic illustration of the manual vapor-deposition setup used for the preparation of As ₂ O ₃ targets.	181
Figure 70: Photograph of a representative As ₂ O ₃ target prepared by manual vapor deposition on an aluminum backing (magnified by ~1.5 x (A), ~2 x (B) and ~10 x (C))	181
Figure 71: Schematic illustration of the 6° targets (A) and the coin targets (B) used in this study.	183
Figure 72: Representative bismuth sediments prepared from Bi(OH) ₃ on aluminum backings. The left target shows a thick, compact, and largely homogeneous deposit, whereas the right target exhibits staining indicative of less uniform sedimentation.	187
Figure 73: Photograph of the two Bi/Al test rods used for the experimental determination of the effective thermal contact resistance between bismuth and aluminum for target preparation routes.	194
Figure 74: Schematic illustration of the custom design dry distillation apparatus.	202
Figure 75: Prototype vertical oven assembly used for dry-distillation processing of intact bismuth targets without prior scraping of irradiated bulk material.	204
Figure 76: Schematic illustration of the (2π-) geometry of beta-counting setup.	219
Figure 77: Calibration curve for the “chamber 5” slot of the Berthold multichannel beta counter.	220
Figure A-1: Foil stack for ⁷² As production using ⁷² Ge enriched materials. Irradiated at the C30XP.	256
Figure A-2: Foil stack for ⁷² As production using ⁷² Ge enriched materials. Irradiated at JULIC.	257
Figure A-3: Foil stack for ⁷² As production using ⁷² Ge enriched materials. Irradiated at the BC 1710.	258
Figure A-4: Foil stack 1&2 for ⁷² As production using natural Gallium targets. Irradiated at the C30XP.	259
Figure A-5: Foil stack 1 for ⁷² As production using ⁶⁹ Ge enriched targets. Irradiated at the C30XP.	260
Figure A-6: Foil stack 2 for ⁷² As production using ⁶⁹ Ge enriched targets. Irradiated at the C30XP.	261
Figure A-7: Foil stack for ⁷² Se production using ⁷⁵ As monoisotopic targets. Irradiated at the Injector 2 at PSI.	263
Figure A-8: Monitor reaction fits used for proton-induced irradiation obtained from IAEA [38].	265
Figure A-9: Monitor reaction fits used for α-particle-induced irradiation obtained from IAEA [38].	266
Figure B-1: Original photographs of coin targets prepared by sinter target method irradiated with ~5 μA _e α-beam current presented in Section 3.2.1	267
Figure B-2: Unedited photograph of the target presented in Section 3.2.1, showing a bismuth target prepared by melting technique, irradiated for ~4 h with ~50 μA _e	267
Figure B-3: Original photograph of a bismuth target processed in a vertical oven DD assembly as presented in Section 3.2.2	268
Figure B-4: Photograph of the dry distillation assembly in a glove box environment.	270

Figure B-5: Schematic illustration of the cold trap design applied for dry distillation experiments. This illustration was modified using AI supported tools.	270
Figure B-6: Schematic illustration of the non-cooled packed-bed trap design applied for dry distillation experiments. This illustration was modified using AI supported tools.....	271
Figure B-7: Auxiliary low-cost PIN-diode detector setup used for supplementary qualitative count-rate observations. The detector concept was based on Keller et al. [123], while the Python-based data-acquisition script was provided by a colleague. The setup was not used for traceable absolute activity quantification in this thesis.	272

List of Tables

Table 1: Comparison of selected standard and non-standard radionuclides relevant to molecular imaging and targeted radionuclide therapy. (EC = electron capture, LET = linear energy transfer).....	4
Table 2: Principal production concepts for ^{72}As or its parent ^{72}Se	12
Table 3: Supply and scalability considerations for selected alpha-emitting radionuclides.....	17
Table 4: State of technology and remaining bottlenecks in the production and processing of ^{211}At	22
Table 5: Comparison of the translational bottlenecks discussed for ^{72}As and ^{211}At	24
Table 6: Production-window yields for direct ^{72}As production and indirect ^{72}Se production....	49
Table 7: Example activities obtained from the production-window yields.....	51
Table 8: Time dependent ingrowth of ^{72}As from a separated ^{72}Se parent.	51
Table 9: Radioactivity of ^{72}As (Bq) at EOB via four different techniques used in the three experiments. ^a Absolute decay rates, corrected for emission intensity; ^b Decay rate without correction for emission intensity.....	59
Table 10: Main uncertainty contributions considered for each spectroscopic method used for β^+ emission analysis.....	59
Table 11: Positron emission intensities derived from the three experiments.....	60
Table 12: Production yield of different target preparation methods at 1 μA_e irradiation normalized by integrated current. For thin targets obtained by sedimentation and electrodeposition, a production range normalization is conducted according to the production ratio of the present energy range. Production ratio is calculated using recommended yield data from IAEA [38].	65
Table 13: Saturation Yields determined for irradiation times between 2 and 5 h irradiation times additionally normalized to 50 μA_e current to correct for small current fluctuations.	70
Table 14: Production yield and beam area (~95 % activity) in relation to the wobbler intensity during irradiation.....	76
Table 15: Presenting the absolute difference in temperature at the Bi/Al-metal interface and the corresponding thermal resistance of the rod prepared by melting target method.	81
Table 16: The absolute difference in temperature at the Bi/Al-metal interface and the corresponding thermal resistance of the rod prepared by sinter target method.....	81
Table 17: Parameter for calculations of the convection resistance of the 6° target geometry.	83
Table 18: Conditions used for dry distillation at various research facilities. (FEP = fluorinated ethylene propylene, PEEK = polyether ether ketone PTFE = polytetrafluoroethylene).....	94
Table 19: Melting and boiling points relevant for astatine distillation.	95
Table 20: Fraction of ^{211}At retained at different residence times within a cold trap maintained between -20 °C and -40 °C.....	98
Table 21: Trapping efficiencies of different carrier materials used in packed-bed column trapping of ^{211}At as well as its breakthrough and recovery (*n=1).	102

Table 22: Overview of the distribution coefficient of various solvents tested against 6 M, 2 M and 0.1 M HNO ₃ . Color-coding shows excellent extraction in green whereas low extraction is colored in red.	112
Table 23: Recovery yields and separation parameter of selected solvents.	120
Table 24: Recovery yields and behavior throughout the separation of fabricated resins.	123
Table 25: Approximate refractive indices and corresponding Cherenkov threshold energies for electrons/positrons and α -particles in selected gases, liquids, and borosilicate glass relevant to the ²¹¹ At luminescence experiments. The values were calculated using the Cherenkov condition $\beta > 1/n$. They show that direct Cherenkov emission by α -particles is energetically excluded, while secondary electrons in condensed media could in principle exceed the Cherenkov threshold.	133
Table 26 Recovery of ²¹¹ At [%] from varying HPLC columns in either water/acetonitrile or water/acetonitrile/TFA solvent systems. Radioactivity balance was measured online by post-column injection whereas offline by γ counting was measured of the efflux from the column (online method offline method), (n=3).....	140
Table 27: Astatine recovery from alternative solvents using a Waters XBridge C18 column. Online activity balances were determined by post-column injection, whereas offline balances were determined by γ -ray counting of the collected column effluent. Values are given as online offline balance, n=3. Highlighted entries indicate the parameter varied in the respective experiment. Abbreviations: AA, ascorbic acid; TEAA, triethylammonium acetate; TEA, triethylamine.....	144
Table 28: Recovery rates of ²¹¹ At in different chemical forms are shown (n = 2). ^a High-Performance TLC: Silica gel on a glass backing, omitting UV indicator. ^b Silica gel pre-coated on a polymer-based backing.....	149
Table 29: Radio chemical conversion rates [%] of labeling 4-[²¹¹ At]APA via different labeling methods (DSR, KI or NBS method and halogenic exchange reaction (HAL)). Freshly prepared ²¹¹ At was obtained from different dry distillation processing methods.....	154
Table 30: RCC rates [%] of labeling 4-[²¹¹ At]APA via different labeling methods (DSR, KI or NBS method and halogenic exchange reaction). The freshly prepared ²¹¹ At was obtained from different LLE processing methods. Values represent single experiments (n = 1) and are therefore shown without standard deviation.....	157
Table 31: RCC [%] of labeling 4-[²¹¹ At]APA via different labeling methods using ²¹¹ At obtained from different dry distillation processing methods after a storage period of 2-3 half-lives on the trapping material. Values represent single experiments (n = 1) and are therefore shown without standard deviation.	161
Table 32: RCC [%] of labeling 4-[²¹¹ At]APA via different labeling methods using ²¹¹ At obtained from different LLE processing methods after a storage period of 2-3 half-lives on the packed column after all regular washing steps. Values represent single experiments (n = 1) and are therefore shown without standard deviation.....	162
Table 33: Low-activity solid waste accumulated during 18 months of routine ²¹¹ At work. The table summarizes the mass and measured ²⁰⁷ Bi-specific activity of the individual waste fractions.....	166
Table 34: Target materials used for the preparation of thin activation targets, including irradiation route, chemical form, mass range, and supplier.	178
Table 35: Showing the composition of the Bi(NO ₃) ₃ solution used for electro deposition.....	186

Table 36: Overview of dry distillation conditions used for cold trap assembly studies.	203
Table A-1: Relevant reaction channels for the production of ^{72}As and ^{72}Se . Q -values were obtained from the NNDC Q-Value Calculator [113]. Threshold energies are laboratory-frame kinematic thresholds calculated for endothermic reactions using Eq. A-1. Only radionuclides that remain in the final chemically isolated product fraction were considered relevant for the practical radionuclidic-purity assessment. For direct ^{72}As production, this corresponds primarily to arsenic radioisotopes. For indirect ^{72}Se production, selenium radioisotopes are the relevant impurities, whereas arsenic products formed from ^{75}As are removed during selenium separation.	242
Table A-2: Composition of enriched target material [%] used for sample preparation of ^{72}Ge and ^{69}Ga sediments.	243
Table A-3: Overview of TALYS-2.0 model settings screened in the sensitivity study of the calculated excitation function for the $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction, with individually varied parameter ranges.	250
Table A-4: Combination of selected TALYS-2.0 parameter settings used to assess their combined influence on the calculated excitation function of the $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction.	250
Table A-5: Mass content of the target nuclide in each irradiated sample.	251
Table A-6: Cross-section values for monitor reactions in $^{\text{nat}}\text{Cu}(p,x)$ irradiations. The table lists the effective proton energies, experimentally determined monitor cross-sections, and associated total uncertainties used for beam-current and energy validation in the stacked-foil experiments.	252
Table A-7: Cross-section values for monitor reactions in $^{\text{nat}}\text{Cu}(\alpha,x)$ irradiations. Effective α -particle energies, measured monitor-reaction cross-sections, and total uncertainties are reported for the copper monitor foils used to evaluate the incident beam parameters.	252
Table A-8: Cross-section values for monitor reactions in $^{\text{nat}}\text{Ti}(p,x)$ irradiations. The table summarizes the effective proton energies, monitor cross-sections, and total uncertainties obtained from natural titanium monitor foils.	253
Table A-9: Measured production cross-sections of ^{72}As and ^{71}As from $^{\text{nat}}\text{Ga}(\alpha,x)$ reactions. The table lists the effective α -particle energies, experimentally determined cross-sections, and total uncertainties for arsenic radioisotope formation from natural gallium targets.	253
Table A-10: Measured production cross-sections of ^{72}As and ^{71}As from $^{69}\text{Ga}(\alpha,x)$ reactions. The table gives the effective α -particle energies, cross-sections, and total uncertainties for the formation of ^{72}As and ^{71}As from enriched ^{69}Ga target material.	253
Table A-11: Measured cross-sections for the formation of ^{72}Se (measured directly and indirectly via ^{72}As) and ^{75}Se in proton-induced reactions on ^{75}As . Effective proton energies, experimentally determined production cross-sections, and total uncertainties are listed for the investigated $^{75}\text{As}(p,x)$ reaction channels.	254
Table A-12: Measured cross-sections for the formation of ^{72}As and ^{71}As in $^{72}\text{Ge}(p,x)$ reactions at JULIC. The table summarizes the effective proton energies, production cross-sections, and total uncertainties obtained from the JULIC stacked-foil irradiation.	254
Table A-13: Measured cross-sections for the formation of ^{72}As and ^{71}As in $^{72}\text{Ge}(p,x)$ reactions at the BC1710 cyclotron. Effective proton energies experimentally determined cross-sections, and total uncertainties are reported for the BC1710 irradiation series.	255

Table A-14: Measured cross-sections for the formation of ^{72}As and ^{71}As in $^{72}\text{Ge}(\text{p},\text{x})$ reactions at the C30XP. The table lists the effective proton energies, production cross-sections, and total uncertainties determined from the C30XP irradiation series.	255
Table B-1: Target decontamination study Target 1 (17.12.2025): measured astatine activities, relative activity decrease, and corresponding equivalent α -beam energy.....	269
Table B-2: Target decontamination study Target 2 (11.01.2026): measured astatine activities, relative activity decrease, and corresponding equivalent α -beam energy.....	269
Table B-3: Solvents and their respective supplier and purity used during wet chemical separation and distribution studies. ^a Solid sample dissolved in 1-octanole. ^b Solid sample dissolved in toluene.	273
Table B-4: Comparison of KD values obtained by direct phase measurement and by back-calculation from total activity and upper-phase aliquots.	273
Table B-5: Distribution coefficient of investigated solvents against 0.1 M, 2 M and 6 M HNO_3 . ^{211}At was obtained by dissolving the target material in conc. HNO_3 and diluted. ^a Solid sample dissolved in 1-octanole, ^b Solid sample dissolved in toluene, ^c No clear phase separation was observed.	274
Table B-6: Distribution coefficient of investigated solvents against 0.1, 2 and 6 M HNO_3 . ^{211}At was obtained by DD processing before translation into acid medium.	276
Table B-7: Interpolated NIST mass attenuation coefficients for borosilicate glass (0.5–1 MeV) and derived interaction probabilities for $d = 0.3 \text{ cm}$.”	280
Table B-8: Mean Compton electron energies and the corresponding Cherenkov photons per electron for the three main γ -lines during the decay of ^{211}At decay.....	281
Table B-9: Cost estimation of ^{211}At related waste handling.....	283

List of Abbreviations

AA	ascorbic acid
BC 1710	Baby Cyclotron BC 1710
C30XP	IBA Cyclone® 30XP Cyclotron
CMPO	octyl(phenyl)-N,N-diisobutylcarbamoylmethylphosphine oxide
DD	dry distillation
DGA	diglycolamide resin / DGA resin
DB21C7	dibenzo-21-crown-7 ether
DIPE	diisopropyl ether
DSR	destannylation reaction
EC	electron capture
EOB	end of bombardment
EOP	end of processing
EtOH	ethanol
EXFOR	Experimental Nuclear Reaction Data database
FEP	fluorinated ethylene propylene
FWHM	full width at half maximum
FZJ	Forschungszentrum Jülich
GMP	Good Manufacturing Practice
HAL	halogen-exchange labeling route
HDEHP	bis(2-ethylhexyl)phosphate
HPLC	high-performance liquid chromatography
HPGe	high-purity germanium
HPTLC	high-performance thin-layer chromatography
HR-X	Chroma bond HR-X polymeric reversed-phase resin
IAEA	International Atomic Energy Agency
IBA	Ion Beam Applications
IBM	irradiated bismuth material
IKP	Institute for Nuclear Physics
JULIC	Jülich Isochronous Cyclotron
K _D	distribution coefficient
KI	potassium iodide
LEPS	low-energy photon spectrometer
LET	linear energy transfer
LLE	liquid-liquid extraction
MCA	multichannel analyzer
MeCN	acetonitrile
MeOH	methanol
MIBK	methyl isobutyl ketone
NaI(Tl)	thallium-doped sodium iodide
NBS	N-bromosuccinimide
NCS	N-chlorosuccinimide
NIST	National Institute of Standards and Technology
ODS	octadecylsilane
OMP	optical model potential
PCI	post-column injection

PEEK	polyether ether ketone
PET	positron emission tomography
PIN	p-intrinsic-n diode
PP	polypropylene
PSI	Paul Scherrer Institute
PTB	Physikalisch-Technische Bundesanstalt
PTFE	polytetrafluoroethylene
RCC	radiochemical conversion
R ² / R2	coefficient of determination
RMSE	root mean square error
RP-HPLC	reversed-phase high-performance liquid chromatography
RSD	relative standard deviation
SD	standard deviation
SPECT	single-photon emission computed tomography
SRIM	Stopping and Range of Ions in Matter
STACK	in-house STACK energy-degradation program
TALYS	TALYS nuclear reaction code
TAT	targeted alpha therapy
TBP	tributyl phosphate
TEA	triethylamine
TEAA	triethylammonium acetate
TENDL	TALYS Evaluated Nuclear Data Library
TFA	trifluoroacetic acid
TLC	thin-layer chromatography
TOA	trioctylamine
TODGA	N,N,N',N'-tetraoctyl diglycolamide
TTY	thick target yield
TRUEX	transuranium extraction process
VBA	Visual Basic for Applications
4-[²¹¹ At]APA	4-astato-L-phenylalanine / para-astatophenylalanine
4-BPA	4-borono-L-phenylalanine
4-IPA	4-iodo-L-phenylalanine
4-SPA	4-stannyl-L-phenylalanine

1. Introduction

1.1. From radioactivity to translational radionuclide production

Nuclear medicine has its origins in the late 19th century, closely connected to the discovery of ionizing radiation by Röntgen in 1895 demonstrating the diagnostic relevance of penetrating radiation [1]. At the same time, the recognition emerged that radioactive atoms could be used as tracers of physical, chemical, and biological processes. This was further supported by Marie and Pierre Curie establishing radioactivity as an intrinsic property of certain elements [2], while Rutherford's later investigations of radioactive emissions and the nuclear structure of atoms provided the conceptual basis for describing radioactive decay and nuclear transformations [3, 4].

From these early developments emerged the physical quantities that still define the application of radionuclides today. The half-life $T_{1/2}$, the decay constant λ , the emission probability I , and the reaction cross-section $\sigma(E)$. They determine whether a radionuclide can be produced, measured, purified, transported, incorporated into a radiopharmaceutical, quantified by imaging, and used within a clinically meaningful time window. The relation between half-life and decay constant is given by

$$T_{1/2} = \frac{\ln(2)}{\lambda} \quad (1.1)$$

where λ is the probability per unit time that a radioactive nucleus decays. This relation already illustrates one of the central constraints of nuclear medicine: a radionuclide must live long enough for production, purification, quality control, transport, and biological targeting, but not so long that unnecessary radiation dose, waste, and logistics become dominant limitations.

The medical use of radioactive atoms became conceptually possible through the tracer principle introduced by de Hevesy. The tracer principle showed that radioactive atoms can be used in very small quantities to follow chemical and biological processes without significantly perturbing the system under investigation [5]. This concept remains fundamental to nuclear medicine. However, modern radiopharmaceutical development extends far beyond the mere availability of a radioactive label. A clinically useful radionuclide must combine appropriate nuclear decay properties with reliable

production, sufficient radionuclidic and chemical purity, compatible labeling chemistry, quantitative imaging or dosimetry, radiation protection, logistics, and regulatory feasibility [6–12].

The success of widely used standard radionuclides such as ^{18}F , ^{68}Ga , $^{99\text{m}}\text{Tc}$, ^{177}Lu , and ^{131}I is therefore not only a consequence of favorable decay properties. These radionuclides are routinely applied because their complete translational pathways are well established: production routes are robust, separation and quality-control procedures are validated, clinical workflows are familiar, and supply chains are sufficiently reliable [9, 10]. By contrast, many non-standard radionuclides are physically or medically attractive but remain limited by incomplete nuclear data, uncertain impurity formation, insufficiently robust targetry, difficult recovery chemistry, poorly understood chemical speciation, or limited downstream usability [12–14]. The present thesis deals with two such radionuclides, ^{72}As and ^{211}At , which represent different but complementary challenges in radionuclide translation.

1.2. Standard and non-standard radionuclides in nuclear medicine

A radionuclide may be considered “standard” when its production, processing, quality control, and clinical application have reached a level of routine reliability. This status is not determined by half-life or emission type alone. Instead, it reflects the maturity of the complete process chain. For example, ^{18}F benefits from established cyclotron production and automated radiochemistry, ^{68}Ga from generator availability and convenient coordination chemistry, $^{99\text{m}}\text{Tc}$ from decades of generator-based SPECT (single-photon emission computed tomography) practice, and ^{177}Lu from scalable production, robust chelator chemistry, and increasing clinical use in targeted radionuclide therapy [9, 15, 16].

Non-standard radionuclides occupy a different translational position. They may offer attractive nuclear or chemical properties, but their broader use is still limited by one or more unresolved practical barriers. Such barriers may include incomplete excitation functions, uncertain decay data, low production yields, radionuclidic impurities, expensive enriched targets, insufficient target recovery, problematic separation

chemistry, unstable labeling, adsorption losses, radiolysis, contamination control, or long-lived waste products [12, 14]. The term “non-standard” should therefore not be understood as implying inferior quality. It describes a radionuclide whose full pathway from nuclear production to routine radiopharmaceutical use is not yet sufficiently mature.

This distinction is important because the standard radionuclide set does not cover all clinically relevant situations equally well. Short-lived PET (positron emission tomography) radionuclides such as ^{18}F and ^{68}Ga are highly successful for small molecules and peptides with rapid pharmacokinetics, but they are less suitable for slowly distributing biological vectors such as antibodies or engineered proteins. Established therapeutic β^- -emitters such as ^{177}Lu and ^{131}I are valuable for many applications, but their particle range and linear energy transfer may be suboptimal for microscopic disease, small tumor clusters, or cases in which highly localized energy deposition is required [10, 17–20]. Theranostic concepts also benefit from chemically related radionuclides that allow imaging and therapy to be connected through similar biological or chemical behavior [6, 13, 21].

Selected examples of standard and non-standard radionuclides are summarized in Table 1. The table emphasizes that the translational limitation of a radionuclide is often not a single nuclear property, but the least mature part of the complete process chain.

The two radionuclides considered in this thesis illustrate two different stages of non-standard radionuclide development. For ^{72}As , the central issue is whether the radionuclide can be evaluated as a PET nuclide on the basis of reliable production and decay data. Its half-life is attractive for imaging slower biological processes, but this advantage only becomes practically meaningful if ^{72}As can be produced with sufficient yield and acceptable radionuclidic purity, and if the positron-emission intensity used for PET quantification is sufficiently well known [21–25]. For ^{211}At , the medical motivation is already strong because of its suitability for targeted alpha therapy. The main limitation lies instead in the robustness of the practical process chain: high-current target irradiation, recovery from irradiated bismuth, chemical characterization, downstream labeling compatibility, radiation protection, and waste management [26–35].

Introduction

Table 1: Comparison of selected standard and non-standard radionuclides relevant to molecular imaging and targeted radionuclide therapy. (EC = electron capture, LET = linear energy transfer).

Radionuclide	Half life	Major emission	Typical application	Status	Typical translational limitation
^{18}F	109.8 min	β^+	PET imaging	standard	short half-life for slow biological vectors
^{68}Ga	67.7 min	β^+	PET imaging	standard	short half-life, generator capacity limitations
$^{99\text{m}}\text{Tc}$	6.0 h	γ	SPECT imaging	standard	limited relevance for PET-type quantitative workflows
^{177}Lu	6.7 d	β^+ , γ	targeted radionuclide therapy	standard	lower LET and longer crossfire than α -emitters
^{131}I	8.0 d	β^- , γ	therapy / imaging	standard	high photon burden and dosimetric drawbacks
^{72}As	26.0 h	β^+ , EC	PET imaging / radio arsenic theranostic	non-standard	production-window definition, impurity control, decay-data validation
^{211}At	7.2 h	α , EC	targeted alpha therapy	non-standard	targetry, recovery, analytics, process robustness

As shown schematically in Figure 1, both radionuclides can be viewed along the same translational pathway, but the limiting steps are different. For ^{72}As , production data, impurity formation, and decay-data reliability dominate the evaluation. For ^{211}At , targetry, isolation, analytical control, and downstream usability are the central bottlenecks.

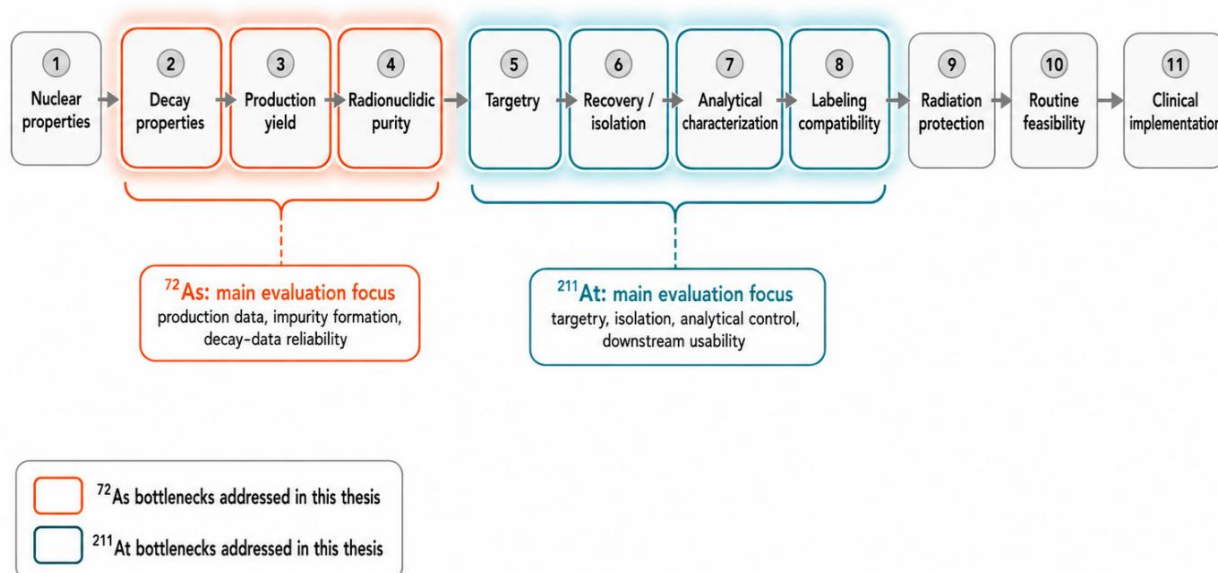


Figure 1: Translational pathway of a medical radionuclide. Schematic overview of the development path from nuclear properties to clinical implementation. The pathway includes decay properties, production yield, radionuclidic purity, targetry, recovery, analytical characterization, labeling compatibility, radiation protection, and routine feasibility. The main bottlenecks addressed in this thesis are highlighted for ^{72}As and ^{211}At

1.3. Nuclear, radiopharmaceutical, and production criteria

Half-life, radiation type, and emission probability

The first criterion in radionuclide selection is the match between the physical half-life of the radionuclide and the biological time scale of the intended application. A radionuclide with a half-life that is too short may decay substantially before synthesis, purification, quality control, transport, and target accumulation are completed. Conversely, a radionuclide with a half-life that is too long may unnecessarily increase absorbed dose to healthy tissue and complicate radiation protection, storage, and waste handling [9, 14].

The second criterion is the type and intensity of emitted radiation. For PET imaging, positron emission is required. The emitted positron loses kinetic energy in tissue and subsequently annihilates with an electron, producing two photons of 511 keV that are emitted approximately back-to-back and detected in coincidence [8]. For SPECT imaging, suitable γ -emission is required. For therapy, β^- -particles, α -particles, or Auger electrons may be selected depending on the desired tissue range, linear energy transfer, and biological target geometry [17–19].

The emission probability I , for example the positron-emission intensity I_{β^+} , is equally important. A radionuclide may decay by a useful emission mode, but if the relevant branching fraction is low, uncertain, or accompanied by interfering radiation, imaging sensitivity, activity calibration, and dosimetric interpretation become more difficult [23, 36]. The usefulness of a radionuclide therefore cannot be inferred from half-life alone. Physical decay, emission intensity, radiation range, detector response, chemical form, biological kinetics, and the intended clinical endpoint must be considered together.

Quantitative PET and non-standard positron emitters

PET is often described as a quantitative imaging modality, but its quantitative character depends critically on accurate radionuclide data. The measured coincidence signal is related to the number of positron annihilation events and therefore depends on the activity present in the field of view, the positron-emission intensity I_{β^+} , the positron

energy spectrum, attenuation, scattering, random coincidences, dead-time effects, and corrections implemented by the scanner and reconstruction software [36, 37]. For routine PET radionuclides such as ^{18}F , the relevant nuclear data are well established and integrated into clinical calibration procedures. For non-standard positron emitters, this assumption must be checked explicitly.

A particular challenge arises for radionuclides with complex decay schemes, competing electron-capture and positron branches, multiple γ -emissions, or limited high-quality experimental branching data. If the positron-emission intensity is uncertain, the inferred activity concentration is also uncertain. Such uncertainty can propagate into standardized uptake values, kinetic modeling, dosimetry, and inter-study comparison. This is especially relevant for radionuclides proposed because their half-life better matches slower biological vectors, such as ^{72}As [22, 25]

For non-standard PET radionuclides, production data and decay data therefore form a coupled basis for evaluation. A radionuclide can only be assessed realistically if it is clear whether it can be produced with sufficient yield and acceptable radionuclidic purity, and whether the measured PET signal can be converted into activity with reliable decay data.

Charged-particle production, excitation functions, and production windows

Many medical radionuclides are produced by charged-particle-induced nuclear reactions using cyclotrons [9, 12]. In such reactions, the reaction cross-section $\sigma(E)$ depends strongly on the projectile energy E , target nuclide, and reaction channel. A desired radionuclide may be formed efficiently only within a limited energy interval, while competing channels open at higher or lower energies and generate radionuclidic impurities [9, 22, 38].

An excitation function describes the energy dependence of the reaction cross-section. It is one of the central experimental tools for production planning, because it shows not only where the desired product is formed, but also where impurities begin to appear. The relevant production question is therefore not simply whether a reaction exists, but

whether an energy interval can be identified in which the desired product yield and radionuclidic purity are simultaneously acceptable.

This energy interval is commonly referred to as the production window. In practice, the production window depends on the excitation functions of the desired and undesired products, the isotopic composition of the target, the energy loss in the target layer, the irradiation time, and the cooling time. For ^{72}As , this means identifying proton-energy intervals on germanium targets or alpha-energy intervals on gallium targets where ^{72}As formation is favorable while radio arsenic impurities such as ^{71}As are controlled [22, 39]. For ^{211}At , this means selecting an α -particle energy high enough for efficient $^{209}\text{Bi}(\alpha,2n)^{211}\text{At}$ production but low enough to suppress $^{209}\text{Bi}(\alpha,3n)^{210}\text{At}$, because ^{210}At decays to the long-lived α -emitter ^{210}Po [40, 41].

Figure 2 illustrates this concept for ^{211}At production. The desired $^{209}\text{Bi}(\alpha,2n)^{211}\text{At}$ channel and the undesired $^{209}\text{Bi}(\alpha,3n)^{210}\text{At}$ channel overlap only partly in energy. The practical irradiation energy must be selected with respect to the complete energy interval covered by the beam in the bismuth layer, not only the incident beam energy.

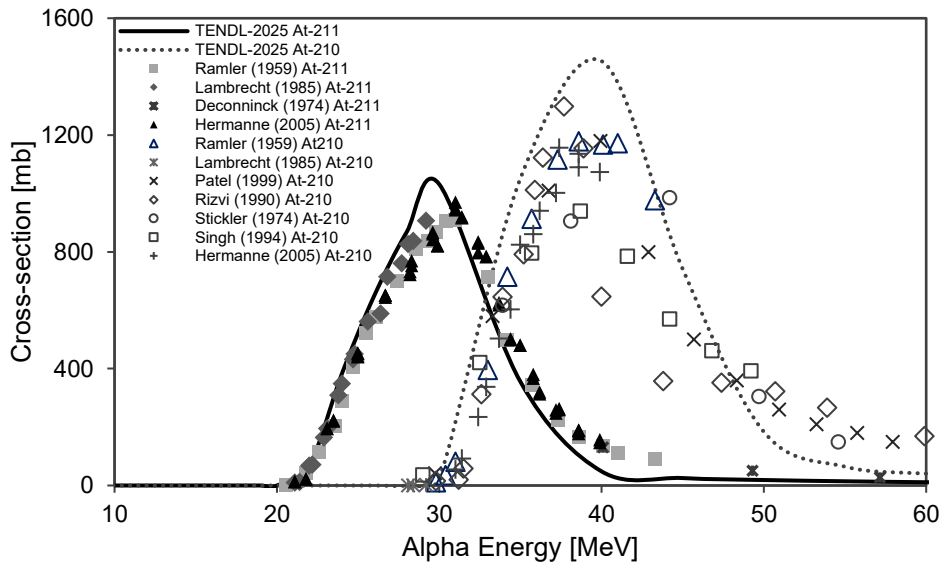


Figure 2: Energy-dependent yield-purity problem in ^{211}At production. Schematic or literature-based excitation functions for the $^{209}\text{Bi}(\alpha,2n)^{211}\text{At}$ and $^{209}\text{Bi}(\alpha,3n)^{210}\text{At}$ reactions. The figure should illustrate that ^{211}At production is governed by an energy-dependent compromise between yield and suppression of $^{210}\text{At}/^{210}\text{Po}$ formation. Experimental cross-section data for the $^{209}\text{Bi}(\alpha,xn)^{211/210}\text{At}$ reactions were compiled from the literature [33, 42–48] and are shown together with TENDL-2025 (TALYS Evaluated Nuclear Data Library) data [49].

Stacked-foil activation, monitor reactions, and thick target yields

Reliable excitation-function measurements require accurate knowledge of both beam current and beam energy. A common experimental method is stacked-foil activation. In this technique, several thin target foils are arranged behind one another, often together with monitor foils and catcher foils. As the charged-particle beam passes through the stack, it continuously loses energy. Each target foil is therefore irradiated with a different effective energy. After irradiation, the induced radioactivity in each foil is measured, usually by γ -ray spectrometry, and the cross-section is calculated from the measured activity, the beam fluence, the number of target atoms, the irradiation time, the decay time, and the relevant decay data [50, 51].

Nominal cyclotron energy is not equal to the effective energy in each foil. Energy losses occur in windows, degraders, monitor foils, target foils, catcher foils, and backing materials. Energy straggling and uncertainties in foil thickness also contribute to the final energy uncertainty. Monitor reactions with recommended cross-sections are used to verify beam energy and beam fluence. They are therefore a central part of activation measurements and help to reduce systematic errors in excitation-function data[38, 52].

Besides differential cross-sections, production-oriented work often uses the thick target yield. The thick target yield connects the excitation function with practical radionuclide production by integrating the cross-section over the energy interval traversed by the beam in the target [53]. In simplified form, the yield depends on

$$Y \propto \int_{E_{\text{out}}}^{E_{\text{in}}} \frac{\sigma(E)}{S(E)} dE \quad (1.2)$$

where E_{in} and E_{out} are the incident and outgoing particle energies in the target, $\sigma(E)$ is the reaction cross-section, and $S(E)$ is the stopping power of the target material. The exact expression additionally depends on irradiation time, decay during irradiation, target composition, and the definition of yield used. Thick target yields are useful because they translate nuclear data into production estimates, but they are sensitive to stopping powers, target thickness, target homogeneity, energy assignment, and impurity formation [53].

Power deposition, local power density, and target stability

At higher beam currents, the limiting factor in radionuclide production is often not the reaction cross-section but the thermal and mechanical stability of the target. Charged particles lose energy while traversing matter, and a significant fraction of this energy is deposited locally as heat. The deposited power can be estimated from the particle rate and the mean deposited energy per particle,

$$P_{\text{dep}} = \dot{N} \Delta E_{\text{dep}} \quad (1.3)$$

where P_{dep} is the deposited power, $\dot{N}$ is the number of incident particles per unit time, and ΔE_{dep} is the mean energy deposited per particle in the target. If the beam is described by an electrical beam current I_b , the particle rate is

$$\dot{N} = \frac{I_b}{ze}, \quad (1.4)$$

where z is the projectile charge state and e is the elementary charge. Thus,

$$P_{\text{dep}} = \frac{I_b}{ze} \Delta E_{\text{dep}}. \quad (1.5)$$

The factor z only enters when converting an electrical current into a particle rate. It does not mean that the deposited energy of a particle with given kinetic energy depends on its charge state in this expression. If the beam intensity is already given as a particle rate, the appropriate expression is simply $P_{\text{dep}} = \dot{N} \Delta E_{\text{dep}}$.

Operationally, the local power density or heat flux is often more important than the total deposited power:

$$q'' = \frac{P_{\text{dep}}}{A_{\text{eff}}}, \quad (1.6)$$

where A_{eff} is the effective beam footprint on the target surface. Melting, delamination, blistering, surface roughening, or local material redistribution can occur when the local heat load exceeds the heat-removal capacity of the target system. Heat removal depends on conduction through the target and backing, thermal contact at interfaces, convective cooling, target geometry, beam profile, and cooling-water conditions [35, 54–57].

These constraints are especially important for solid targets irradiated with intense α -particle beams. Alpha particles deposit substantial energy over relatively short path lengths, which can generate steep thermal gradients and local hot spots. For ^{211}At production, bismuth is particularly challenging because it combines a low melting point of $271.4\text{ }^{\circ}\text{C}$ with a low thermal conductivity of about $7.9\text{ W m}^{-1}\text{ K}^{-1}$ [58, 59]. Slanted target arrangements, optimized backing materials, improved interface quality, efficient water cooling, and beam wobbling are therefore not minor engineering refinements. They directly determine whether a theoretically favorable production window can be used at clinically relevant beam currents [34, 35, 60].

Figure 3 illustrates the role of slanted target geometry. By increasing the effective beam footprint, the local power density can be reduced. At the same time, the beam traverses a longer effective path through the target, which changes the energy degradation and must be considered in the definition of the production window.

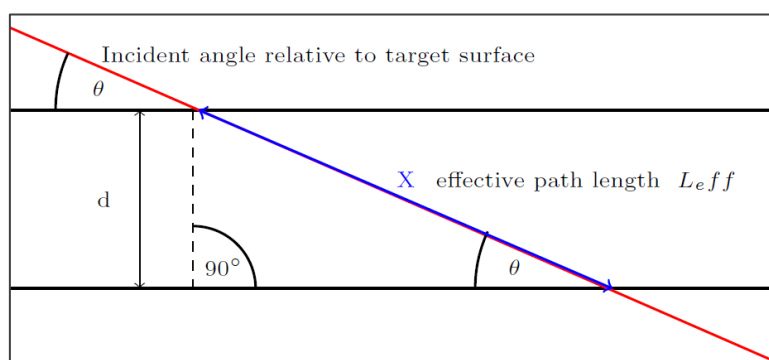


Figure 3: Slanted target geometry for charged-particle irradiation. Schematic representation of a slanted solid target irradiated by an α -particle beam. The slanted geometry increases the effective beam footprint and can reduce local power density, while also increasing the effective path length through the target material. Both effects must be considered in target design and production-window definition.

1.4. ^{72}As as a non-standard PET radionuclide

Medical and nuclear rationale

^{72}As is an emerging positron-emitting radionuclide with a half-life of approximately 26 h [21, 25]. This half-life is substantially longer than those of routine short-lived PET radionuclides such as ^{18}F and ^{68}Ga . It may therefore be better matched to imaging applications involving slower pharmacokinetics, including antibodies, antibody fragments, nanoparticles, or other biological vectors that require many hours to reach

optimal target-to-background ratios. In such applications, short-lived PET radionuclides may decay too rapidly to provide sufficient activity at the biologically relevant imaging time point.

In addition to its half-life, ^{72}As is of interest in the broader context of radio arsenic theranostic. Arsenic offers several radionuclides with potentially complementary properties, including positron-emitting and therapeutic candidates. In particular, the relationship between ^{72}As for imaging and therapeutic radio arsenic isotopes such as ^{77}As has motivated interest in arsenic-based theranostic strategies [21]. However, the potential of ^{72}As cannot be judged by half-life and conceptual theranostic attractiveness alone. A realistic evaluation requires reliable production data, impurity assessment, targetry considerations, separation feasibility, and validated decay data relevant for PET quantification [23]

Production routes and target materials

Several direct and indirect production routes have been discussed for ^{72}As (Table 2). The most relevant direct routes include proton-induced reactions on enriched ^{72}Ge , especially $^{72}\text{Ge}(p,n)^{72}\text{As}$, and alpha-induced production via $^{69}\text{Ga}(\alpha,n)^{72}\text{As}$ [22, 39]. In natural gallium or ^{71}Ga -containing targets, $^{71}\text{Ga}(\alpha,3n)^{72}\text{As}$ may also contribute at higher α -particle energies. Indirect production is possible through the parent radionuclide ^{72}Se , for example via $^{75}\text{As}(p,4n)^{72}\text{Se}$ followed by separation of the daughter ^{72}As in a generator-type system [24, 61].

Direct production on enriched ^{72}Ge is attractive because it can form ^{72}As through proton-induced reactions with a controllable energy window [22]. However, as proton energy increases, competing channels can produce radionuclidic impurities, especially ^{71}As . This impurity is chemically inseparable from ^{72}As after arsenic has been isolated from the target matrix. Its formation must therefore be controlled at the nuclear-production level by beam-energy selection, target thickness, and irradiation conditions.

Introduction

Table 2: Principal production concepts for ^{72}As or its parent ^{72}Se .

Production concept	Target material	Product obtained	Main advantage	Main limitation / Open issue
$^{72}\text{Ge}(\text{p},\text{n})^{72}\text{As}$ and related $^{72}\text{Ge}(\text{p},\text{xn})$ channels	enriched ^{72}Ge	^{72}As	direct production; accessible with proton beams; production window can be optimized	enriched target cost; target recovery; ^{71}As formation at higher proton energies
$^{\text{nat}}\text{Ge}(\text{p},\text{x})^{72}\text{As}$	natural Ge	^{72}As	easier target availability	lower isotopic selectivity; more complex radio arsenic impurity profile
$^{69}\text{Ga}(\alpha,\text{n})^{72}\text{As}$	^{69}Ga -enriched or Ga-containing targets	^{72}As	direct production without enriched Ge target	requires α -beam; target-form and heat-management issues; competing channels
$^{71}\text{Ga}(\alpha,3\text{n})^{72}\text{As}$	^{71}Ga or $^{\text{nat}}\text{Ga}$ contribution	^{72}As	possible contribution in Ga targets at higher energies	higher threshold; more complex impurity pattern
$^{75}\text{As}(\text{p},4\text{n})^{72}\text{Se} \rightarrow ^{72}\text{As}$	arsenic target	parent ^{72}Se for generator-type supply	indirect access; repeated daughter availability possible	requires higher proton energies; $^{72}\text{Se}/^{72}\text{As}$ separation and generator performance
other ^{72}Se routes, e.g. Br- or Ge-based production concepts	target-dependent	^{72}Se	potential generator parent production	facility-dependent; separation and impurity issues

The $^{69}\text{Ga}(\alpha,\text{n})^{72}\text{As}$ route is an important alternative because it provides direct access to ^{72}As without using enriched Germanium. Its practical value depends on the availability of suitable α -particle beams, the excitation function of the desired reaction, the opening of competing (α,xn) channels, and the target chemistry of gallium. If natural gallium is used, both ^{69}Ga and ^{71}Ga contribute to the reaction network, which can increase the complexity of the impurity profile. Gallium targetry also requires attention to target form, thermal behavior, and separation of arsenic from the gallium matrix.

Indirect production via ^{72}Se offers a different strategy. ^{72}Se decays to ^{72}As and may therefore serve as a parent in a generator-type system [24, 61]. This approach can decouple ^{72}As availability from immediate irradiation time and may provide repeated access to the daughter radionuclide. However, it requires efficient production of ^{72}Se , robust separation of selenium and arsenic, control of parent breakthrough, and operation of a chemically reliable generator system. The practical value of this route depends not only on nuclear yield, but also on target processing, generator performance, radionuclidic purity, and compatibility with downstream radiochemistry.

Consequently, no ^{72}As production route can be evaluated solely by its theoretical maximum cross-section. The decisive question is which route provides the best compromise between yield, radionuclidic purity, target availability, target recovery, separation feasibility, and facility-specific beam access.

State of nuclear data and production limitations

The production of ^{72}As requires reliable excitation functions for the desired product and for relevant impurities. For the direct proton-induced route on ^{72}Ge , the excitation functions of $^{72}\text{Ge}(p,xn)^{72,71}\text{As}$ define the useful energy interval for production [22]. The desired product ^{72}As and the impurity ^{71}As are formed through neighboring reaction channels, meaning that small changes in beam energy, target thickness, or energy degradation can significantly affect the final impurity ratio.

The same logic applies to gallium-based production. The $^{69}\text{Ga}(\alpha,n)^{72}\text{As}$ reaction is a direct route to ^{72}As , but the formation of neighboring arsenic, germanium, and gallium radionuclides must be assessed over the relevant α -energy interval [39]. In addition, the isotopic composition of the gallium target determines whether ^{71}Ga -induced channels contribute. For generator-based ^{72}Se production, the relevant limitations shift toward parent production, separation chemistry, generator elution behavior, and radionuclidic purity of the daughter product.

For ^{72}As , the production-related limitations can be summarized as follows:

1. the useful energy interval must suppress chemically inseparable radio arsenic impurities, especially ^{71}As ;
2. enriched ^{72}Ge targets can be expensive and require efficient recovery;
3. gallium-based routes require α -beam access and careful evaluation of target composition and competing channels or enriched target materials (^{69}Ga);
4. generator-based routes require reliable ^{72}Se production and robust selenium/arsenic separation;
5. excitation-function data must be sufficiently accurate for production-window and thick-target-yield calculations.

These points define the technical background needed to understand why production studies for ^{72}As are not only yield measurements. They are evaluations of whether a non-standard PET radionuclide can be produced with predictable activity and radionuclidic composition under realistic irradiation conditions.

Decay data and PET quantification

Even if a suitable production route exists, ^{72}As can only be used quantitatively in PET if its positron-relevant decay data are reliable. The key parameter is the positron-emission intensity I_{β^+} , which specifies the probability that a decay produces a positron. In quantitative PET, the measured annihilation signal is converted into activity by assuming a known relationship between detected coincidence events and the number of decays. If I_{β^+} is inaccurate, the calculated activity is systematically biased [23, 36, 37].

For standard PET radionuclides, such decay data are generally well established and incorporated into routine calibration procedures. For non-standard positron emitters, evaluated data may rely on older measurements, indirect determinations, or incomplete uncertainty budgets. In the case of ^{72}As , evaluated nuclear data exist [25]. The issue is not that ^{72}As lacks any decay-data basis, but that a radionuclide intended for quantitative PET benefits from direct experimental validation of the positron-emission intensity and its uncertainty [23].

This point is especially relevant because the main practical argument for ^{72}As is its longer half-life. Later imaging time points are only useful if the corresponding activity concentrations can be quantified reliably. The production feasibility of ^{72}As and the reliability of its PET-relevant decay data are therefore two connected parts of the same translational assessment.

Summary of open technical questions for ^{72}As

The current scientific and technical question for ^{72}As is not whether the radionuclide is conceptually attractive. Its half-life and positron emission make it a plausible candidate

for imaging slower biological processes, and radio arsenic chemistry provides a possible link to theranostic strategies [21]. The relevant question is more specific: which production route can provide ^{72}As with sufficient yield and radionuclidic purity, and are the positron-relevant decay data sufficiently reliable for quantitative PET?

For this reason, the discussion of ^{72}As must include both nuclear production and decay-data aspects. Excitation functions, production windows, target composition, impurity formation, target recovery, and I_{β^+} are all part of the same evaluation. Without these data, the half-life advantage of ^{72}As remains incomplete as a translational argument.

1.5. ^{211}At as a therapeutic radionuclide limited by process robustness

Medical rationale and supply context of alpha emitters

^{211}At is one of the most compelling radionuclides for targeted alpha therapy. Its half-life of approximately 7.2 h is compatible with many radiochemical procedures and biological targeting vectors, while its α -emission provides high linear energy transfer over a short tissue range [17, 19, 27]. These properties are attractive for treating microscopic disease, small metastases, disseminated tumor cells, and other clinical situations in which localized cytotoxicity is desirable.

Interest in ^{211}At has existed for decades, and recent preclinical and clinical developments have strengthened the case for further translation [27–30, 62–65]. ^{211}At -labeled antibodies, antibody fragments, small molecules, and other targeting agents have been investigated, and early clinical studies have demonstrated that ^{211}At -based therapy is more than a theoretical concept. Recent work on GMP-compliant (Good Manufacturing Practice) ^{211}At solutions and clinical trial infrastructure further illustrates that the field is moving from exploratory radiochemistry toward translational implementation [29, 30].

The practical appeal of ^{211}At is strengthened by its production concept. Unlike several other alpha-emitting radionuclides, ^{211}At can be produced directly in a charged-particle reaction using the monoisotopic target material ^{209}Bi via



This does not mean that ^{211}At production is simple. Suitable α -particle beams, high-current solid-target technology, reliable cooling, recovery chemistry, contamination control, and analytical quality control are required [26, 33–35, 40]. However, the scalability of ^{211}At production is primarily an accelerator-, targetry-, and process-engineering problem. This distinguishes ^{211}At from supply concepts that depend strongly on limited inventories of long-lived parent radionuclides or on irradiation capacities available only at specialized nuclear facilities [12, 66].

The distinction becomes clear when ^{211}At is compared with other alpha emitters. The established generator route to ^{225}Ac is based on ^{229}Th , which is obtained from aged ^{233}U -derived inventories. Such generators can provide high-quality ^{225}Ac , but their output is limited by the available ^{229}Th inventory and the ingrowth rate of ^{225}Ac [66]. Alternative ^{225}Ac production routes, including accelerator production from ^{226}Ra or high-energy proton irradiation of ^{232}Th , are under development, but introduce challenges related to target-material availability, radiochemical separation, long-lived impurities, radiation protection, and radon management [12, 66, 67]. In particular, ^{226}Ra -based production requires handling of a long-lived, radiotoxic target material and careful control of decay-chain products.

Generator-based ^{212}Pb production has its own constraints. ^{212}Pb can be obtained from $^{228}\text{Th}/^{224}\text{Ra}$ -based generator systems, which are attractive for decentralized use, but depend on the availability of suitable parent material and are limited by generator lifetime, breakthrough control, logistics, and quality control. Reactor-based routes for alpha-emitting radionuclides can provide important alternatives, but they require access to suitable neutron fluxes, target materials, and post-irradiation processing capacity. These examples show that radionuclide availability is not determined only by half-life or decay mode, but by the scalability and robustness of the full production chain [66, 68].

In this context, ^{211}At occupies a distinct position. Its main direct production route uses naturally monoisotopic bismuth and can, in principle, be implemented regionally at cyclotron facilities equipped with suitable α -beam and targetry capabilities [26, 33, 39]. The main barriers are not scarcity of the target isotope itself, but robust high-current bismuth targetry, control of the $^{210}\text{At}/^{210}\text{Po}$ impurity pathway, efficient recovery of astatine from irradiated targets, and reproducible analytical characterization of the isolated product.

In Table 3, the different production routes and their advantages and limitations of selected TAT (targeted alpha therapy) nuclides are presented.

Table 3: Supply and scalability considerations for selected alpha-emitting radionuclides.

Radionuclide	Main supply concept	Scalability advantage	Main scalability limitation
^{211}At	direct $^{209}\text{Bi}(\alpha, 2n)^{211}\text{At}$ production	stable monoisotopic Bi target; regional cyclotron production possible	α -beam availability, high-current Bi targetry, $^{210}\text{At}/^{210}\text{Po}$ control, recovery chemistry
^{211}At	$^{211}\text{Rn}/^{211}\text{At}$ generator	distribution time can be extended by parent ^{211}Rn	production of ^{211}Rn ; generator chemistry; ^{207}Po contamination control
^{225}Ac	^{229}Th generator from aged ^{233}U -derived inventories	high-quality generator product	limited ^{229}Th inventory and ingrowth rate
^{225}Ac	accelerator production from ^{226}Ra	potentially scalable accelerator route	^{226}Ra availability, radiotoxicity, radon management, target handling
^{225}Ac	high-energy ^{232}Th spallation	high production potential	complex product mixture, ^{227}Ac impurity concern, high-energy accelerator requirement
^{212}Pb	$^{228}\text{Th}/^{224}\text{Ra}$ generator	generator-based local availability	parent supply, generator lifetime, breakthrough and logistics
reactor-produced alpha emitters	neutron irradiation	established nuclear infrastructure where available	limited access to suitable high-flux irradiation facilities

Direct production of ^{211}At and the yield-purity tradeoff

The clinically most relevant production route for ^{211}At is $^{209}\text{Bi}(\alpha, 2n)^{211}\text{At}$ [33–35, 40]. This route is attractive because it is direct, uses monoisotopic bismuth, and can be

implemented at cyclotrons with suitable α -particle energies. However, the useful energy range is limited by the competing reaction



The product ^{210}At decays to ^{210}Po , a long-lived α -emitting impurity that is undesirable from both product-quality and radiation-protection perspectives [40, 41, 69]. Additional reaction channels, including direct ^{210}Po formation, may also contribute under certain conditions. ^{211}At production is consequently governed by a yield-purity tradeoff: increasing the incident α -particle energy can increase the ^{211}At yield, but it can also increase the formation of ^{210}At and ultimately ^{210}Po [70, 71].

The decisive variable is not only the nominal accelerator energy, but the effective energy interval covered in the bismuth layer. Target thickness, backing material, irradiation angle, energy straggling, windows, degraders, and beam-energy calibration determine which parts of the excitation functions are sampled during irradiation. Figure 2 should therefore be used not only as a reaction scheme, but as an energy-dependent production map: the useful production window is the interval in which ^{211}At yield remains acceptable while ^{210}At formation is suppressed.

A second, less direct route is the $^{211}\text{Rn}/^{211}\text{At}$ generator concept. In this approach, ^{211}Rn is produced first and subsequently decays to ^{211}At . The longer half-life of ^{211}Rn compared with ^{211}At can extend the distribution time and may improve access to ^{211}At away from the production site [26, 72]. However, this route requires production and isolation of ^{211}Rn , generator control, and management of co-produced contaminants such as ^{207}Po . It is therefore an important alternative concept for availability, but it does not remove the need for robust radionuclide production and radiochemical processing.

Bismuth targetry and high-current irradiation

Even if the correct energy window is chosen, high-current production of ^{211}At remains limited by target performance. Bismuth targets must withstand intense α -beam irradiation without melting, delaminating, or developing severe local inhomogeneities. Because the thermal behavior is governed by local power density rather than total

beam power alone, target preparation and the interfacial contact between bismuth and the backing material are decisive parameters [34, 35, 56, 57].

Several target designs have been developed to address these limitations, including external high-current targets, slanted target geometries, improved backing materials, and efficient water cooling [34, 35, 60]. A slanted target geometry increases the effective beam footprint and can reduce local power density. At the same time, it increases the effective path length through the target, which influences energy degradation. Thus, target geometry affects both thermal stability and the nuclear production window.

Targetry for ^{211}At is not only a preparative issue. It is part of the production physics. Interface quality, target thickness, beam profile, irradiation angle, cooling efficiency, and beam homogenization determine whether a theoretically favorable production regime can be realized experimentally. For routine implementation, a target must not only survive a single irradiation but do so reproducibly at beam currents relevant for useful activity levels.

Recovery and separation of ^{211}At from irradiated bismuth

After irradiation, ^{211}At must be recovered from the bismuth target and transferred into a chemical form suitable for radiolabeling. Dry distillation has long been regarded as a classical recovery method because astatine can be volatilized from the irradiated bismuth matrix and collected in a suitable trap or solution [73]. This method can be fast and efficient and has therefore played a central role in ^{211}At production.

Wet-chemical approaches have also been explored, including liquid-liquid extraction, automated dissolution-extraction systems, and extraction chromatography [74–79]. These approaches may offer advantages in automation, integration with target dissolution, or chemical flexibility. At the same time, they introduce constraints such as reagent compatibility, oxidation-state control, radiolysis, phase-transfer efficiency, adsorption losses, and waste-stream complexity.

The success of a recovery route cannot be defined by recovery yield alone. A method may transfer a large fraction of the activity while producing a chemical form that is

difficult to label, unstable during handling, poorly characterized, or incompatible with automation and radiation-protection requirements. Conversely, a process with slightly lower recovery may be more useful if it provides a reproducible product stream with favorable chemical behavior. Recovery and separation must therefore be evaluated together with product quality, analytical interpretability, and downstream radiochemistry.

Analytical control and astatine chemistry

Analytical control of ^{211}At is difficult because astatine chemistry is complex and strongly condition-dependent. Although astatine is a halogen, its chemistry cannot be treated as a simple extension of iodine chemistry. Astatine exhibits distinct redox behavior, hydrolysis, adsorption, solvent interactions, bond-stability characteristics, and metalloid-like behavior [80–87]. These properties make astatine radiochemistry scientifically rich but practically demanding.

Astatine may exist in multiple chemical forms, and its behavior is influenced by redox potential, pH, solvent composition, oxidizing or reducing agents, surfaces, radiolysis, and volatility [88–90]. This creates a challenge for quality control. Methods such as TLC (thin-layer chromatography), reversed-phase HPLC (high-performance liquid chromatography), or extraction-based assays may be affected by adsorption, species interconversion, volatile losses, or interactions with stationary phases and solvents [81, 88–90]. A chromatographic peak or retention factor may therefore not always correspond to a well-defined astatine species unless the method has been validated for the specific chemical system.

For ^{211}At , analytics is part of process development. Different target-processing and recovery methods can only be compared meaningfully if the resulting astatine product streams are characterized by methods that are reproducible and chemically interpretable. This is particularly important when the objective is not only to recover activity, but to produce a radionuclide solution that can be used reliably for radiopharmaceutical synthesis.

Downstream usability, contamination control, and routine implementation

The practical value of a ^{211}At production and isolation route is ultimately determined by downstream usability. The isolated radionuclide must be compatible with representative labeling strategies, provide sufficient activity concentration, maintain chemical reactivity, and support product stability over the relevant time scale. Several labeling approaches have been investigated, including electrophilic astatination, nucleophilic strategies, boron-based precursors, and other methods designed to improve in vivo stability of the astatine-vector bond [32, 80, 91]. The optimal chemical form of recovered ^{211}At may depend strongly on the intended labeling method.

Routine implementation also requires radiation protection and contamination control. Astatine can exhibit volatile behavior under certain chemical conditions, and ^{211}At handling requires specific attention to contamination prevention and monitoring [92, 93]. Production facilities must also consider the long-term consequences of repeated irradiations. Long-lived activation products, including bismuth-derived radionuclides such as ^{207}Bi , can affect waste classification, storage, clearance, and transport procedures [26, 94–98]. Waste and radiation-protection considerations are therefore not external administrative details but part of the practical translation problem.

Recent studies on production, isolation, and shipment of clinically relevant ^{211}At quantities demonstrate that progress is being made toward broader availability [26, 96]. However, many process details remain facility-dependent. The field requires not only proof that ^{211}At can be produced, but robust data on how targetry, recovery, chemical form, analytical control, radiolabeling compatibility, and operational safety interact across the full process chain. An overview of the state of technology and unsolved bottlenecks is presented in Table 4.

Introduction

Table 4: State of technology and remaining bottlenecks in the production and processing of ^{211}At .

Process step	Established or investigated approach	Achieved state	Remaining limitation
direct nuclear production	$^{209}\text{Bi}(\alpha, 2n)^{211}\text{At}$	direct cyclotron production established	narrow energy window; suppression of $^{210}\text{At}/^{210}\text{Po}$
alternative availability concept	$^{211}\text{Rn}/^{211}\text{At}$ generator	demonstrated for preclinical access	^{211}Rn production, generator chemistry, ^{207}Po control
targetry	metallic Bi on backing, external targets, slanted targets, water cooling	high-current target concepts demonstrated	melting, delamination, hotspots, interface quality, reproducibility
energy control	optimized α -energy below strong ^{210}At formation	production-energy principles known	facility-specific energy degradation and target-thickness control
recovery	dry distillation	fast and widely used classical method	product form and downstream compatibility must be verified
wet processing	solvent extraction, automated dissolution, extraction chromatography	promising alternatives demonstrated	reagent compatibility, radiolysis, automation, waste-stream complexity
analytics	TLC, HPLC, γ -spectrometry, α -spectrometry	several methods available	speciation, adsorption, volatility, chromatographic artefacts
labeling	electrophilic and nucleophilic approaches, boron precursors, antibody and small-molecule labeling	extensive preclinical development	in vivo bond stability, dependence on recovered astatine species
routine operation	local production, shipment studies, GMP-oriented work	translational progress visible	availability, contamination control, long-lived waste, regulatory implementation

Summary of open technical questions for ^{211}At

The current state of ^{211}At development is characterized by strong medical motivation and substantial technological progress, but also by unresolved implementation bottlenecks. Direct cyclotron production on bismuth is established in principle, dry distillation and wet-chemical recovery methods exist, and several labeling strategies have been developed. At the same time, high-current target stability, suppression of $^{210}\text{At}/^{210}\text{Po}$, product-stream characterization, downstream compatibility, contamination control, and waste management remain central practical limitations [26, 29, 70].

Thus, the broader implementation of ^{211}At depends less on proving that the radionuclide is medically interesting and more on establishing a reproducible process chain. Production, recovery, analytical characterization, radiochemical usability, and

routine handling must be considered together. In this sense, ^{211}At is a case study for a therapeutically attractive radionuclide whose translational potential is governed by process robustness.

1.6. Relationship between ^{72}As and ^{211}At

At first glance, ^{72}As and ^{211}At represent different areas of radionuclide development. ^{72}As is considered as a non-standard positron emitter for PET imaging and possible radio arsenic-based theranostic concepts, whereas ^{211}At is investigated as an alpha emitter for targeted radionuclide therapy. Their half-lives, radiation types, production routes, target materials, chemical behavior, and intended medical applications differ substantially.

Nevertheless, both radionuclides illustrate the same translational principle: favorable nuclear properties alone are not sufficient for practical application. A radionuclide may be attractive because of its half-life, emission type, or chemical potential, but broader use requires a reliable chain of production, impurity control, separation, analytical characterization, radiochemical usability, and routine-relevant handling.

In the case of ^{72}As , the central translational issue is whether the radionuclide can be evaluated on a sufficiently reliable nuclear-data basis. Its potential as a longer-lived PET radionuclide depends on production yields, radionuclidic purity, and decay data relevant for quantitative PET. In the case of ^{211}At , the central issue is not primarily medical interest, but process robustness. Its broader implementation depends on stable bismuth targetry, controlled irradiation conditions, efficient recovery, chemically meaningful analytical characterization, and downstream usability.

Thus, ^{72}As and ^{211}At provide complementary examples of non-standard radionuclide translation. ^{72}As represents a case in which production and decay data are required to judge the radionuclide realistically, whereas ^{211}At represents a case in which a therapeutically attractive alpha emitter must be transformed into a robustly producible and chemically usable product. Together, both examples show that the path from promising nuclear properties to practical application is governed by the weakest part

of the complete translational chain. In Table 5, the main translation bottlenecks of the two radionuclides ^{72}As and ^{211}At is presented.

Table 5: Comparison of the translational bottlenecks discussed for ^{72}As and ^{211}At .

Radionuclide	Translational role	Main technical question	Key background required for later chapters
^{72}As	non-standard PET radionuclide	Can it be produced with sufficient yield and purity, and can it be quantified reliably in PET?	production routes, excitation functions, impurity formation, I_{β^+} , decay-data validation
^{211}At	targeted alpha therapy radionuclide	Can it be produced, isolated, characterized, and used in a robust process chain?	^{209}Bi targetry, yield-purity tradeoff, $^{210}\text{At}/^{210}\text{Po}$, recovery, analytics, labeling compatibility, waste

2. Aim of this work

The aim of this work was to evaluate the two non-standard radionuclides ^{72}As and ^{211}At with regard to their potential application in nuclear medicine. Although both radionuclides differ considerably in their intended medical utilization, nuclear properties, chemistry, and experimental requirements, both remain limited by practical barriers that prevent broader implementation.

For ^{72}As , this thesis focused on nuclear and decay data required for a realistic assessment of this radionuclide as a non-standard positron emitter. The main objectives were to investigate suitable production routes by measuring excitation functions, to evaluate the associated formation of radionuclidic impurities, and to identify irradiation conditions relevant for practical ^{72}As production. In addition, the decay properties of ^{72}As were studied experimentally, with particular emphasis on positron-emission data relevant for PET quantification. The ^{72}As part of this work therefore aimed to provide experimental input needed to assess the production feasibility, radionuclidic purity, and quantitative PET applicability of this radionuclide.

For ^{211}At , the objective was not to demonstrate the general feasibility of ^{211}At production, which is already well established, but to develop and evaluate a production concept adapted to the technical framework of the IBA (Ion Beam Applications) Cyclone® 30XP cyclotron. A central aim was the design and implementation of an external high-current target system for bismuth irradiations. This included the preparation of suitable bismuth targets, the evaluation of their thermal stability under irradiation, and the establishment of irradiation conditions compatible with reliable ^{211}At production.

Building on this targetry and irradiation work, the thesis further aimed to establish a reproducible processing routine for the isolation of ^{211}At from irradiated bismuth targets. The isolated radionuclide was analytically characterized with regard to parameters relevant for subsequent radiochemical application, including recovery, radionuclidic and radiochemical purity. In addition, selected labeling experiments were performed as proof-of-principle studies to evaluate whether the processed ^{211}At product was suitable for subsequent radiochemical use.

Aim of this work

The two parts of this thesis therefore address different, but closely related, stages of radionuclide translation. The ^{72}As study focuses on the experimental data needed to evaluate a non-standard PET radionuclide realistically, whereas the ^{211}At study focuses on establishing a production, separation, characterization, and proof-of-principle labeling workflow for a therapeutically attractive alpha emitter under the technical conditions of the IBA Cyclone® 30XP cyclotron. Taken together, both parts show that practical implementation depends not only on favorable nuclear properties, but also on reliable production routes, controlled impurity formation, robust targetry, efficient separation procedures, and quality-control methods suitable for routine-relevant radiochemical work.

3. Results & Discussion

The ^{72}As -related part of this work combines production-oriented and decay-oriented experiments. Cross-section measurements define the relevant reaction channels, their usable energy ranges, and the associated impurity constraints. The spectrometric studies address the decay data needed for quantitative PET-related use. Together, these results allow ^{72}As to be assessed on the basis of experimental evidence rather than theoretical suitability alone.

3.1. Nuclear data measurements of $^{72}\text{Se}/^{72}\text{As}$

The cross-sections for the production of ^{72}As and ^{72}Se were determined using stacked-foil activation technique employing both natural and enriched target materials. Irradiations were performed with proton and α -particle beams to investigate relevant production routes over a broad energy range. The induced activities were quantified by high-resolution γ -ray spectrometry, allowing reliable identification of the reaction products and assessment of their formation cross-sections. In the case of the enriched target material, this approach additionally enabled a more differentiated evaluation of the individual reaction channels, in particular the contribution of unwanted conformation of ^{71}As or ^{75}Se . These measurements provide the experimental basis for the evaluation of excitation functions, production yields, and the suitability of the investigated reactions for practical radionuclide production.

3.1.1. Target preparation and suitability for irradiation

For the ^{72}As -related activation experiments, thin solid targets were prepared using different approaches depending on the respective material and irradiation purpose. Enriched elemental ^{72}Ge and $^{69}\text{Ga}_2\text{O}_3$ were mainly processed by sedimentation onto thin aluminum backings, whereas natural As_2O_3 targets were prepared by manual vapor deposition. In both cases, the aim was to obtain mechanically stable and sufficiently homogeneous thin layers suitable for stacked-foil irradiation and

subsequent activity quantification. Visual inspection, gravimetric evaluation, and, where applicable, light-microscopic control showed that the applied preparation methods provided targets of adequate quality for the low-current irradiations used in this work. No pronounced target failure was observed under the applied irradiation conditions. Thus, target preparation did not represent the main limitation of the ^{72}As studies but rather served as the experimental basis for the subsequent cross-section and decay-data investigations.

With this experimental basis established, the following sections focus on the key question for practical ^{72}As production, namely which reaction channels and energy windows provide the most favorable balance between yield and radionuclidic purity.

3.1.2. Excitation functions and production windows

This chapter discusses which of the investigated reaction routes are suitable for the production of ^{72}As . The main points considered are which reactions allow access to ^{72}As , how high the production cross-sections are, in which energy ranges acceptable radionuclidic purity can be achieved, and how strongly competing reaction channels restrict practical production. The relevant product- and impurity-forming reaction channels, including their Q-values and kinematic threshold energies, are summarized in Appendix Table A-1. Numerical values of all reaction cross-section data determined experimentally during this study are presented in the Appendix A-7.

Monitoring

Before discussing the measured excitation functions themselves, the reliability of the underlying beam-current and energy assignment has to be considered, since any practical interpretation of the cross-section data depends directly on the accuracy of this monitoring procedure.

The monitor reactions for proton as well as alpha induced reactions employed in this study are presented in Figure 4 validating the elaborated flux and energy region by monitor foil technique.

Figure 4(A) shows the monitor reaction data calculated for the proton induced reactions at the Jülich Isochronous Cyclotron (JULIC), Baby Cyclotron BC 1710 and IBA Cyclone® 30XP (C30XP) cyclotrons up to proton energies of 45 MeV whereas (B) shows the monitor reaction data used for the irradiation at Injector 2 at the Paul Scherrer Institute (PSI) up to 70 MeV proton energy. For alpha induced reactions at the C30XP cyclotron, the applied monitor reactions are presented in Figure 4(C). All are set in relation to the reference cross-section data obtained by the IAEA (International Atomic Energy Agency) [38],

Generally, all applied monitor reactions showed acceptable precision, with almost no deviation beyond the calculated uncertainties presented in the graphs. For α -induced reactions, it should be noted that the formation of ^{67}Cu via the $^{\text{nat}}\text{Cu}(\alpha, x)^{67}\text{Cu}$ reaction is possible. Since its half-life (61.8 h) and emitted γ -radiation energies (184.6 keV (48.7%), 93.3 keV (16.2%), and 300.2 keV (0.8%)) are quite similar to those of ^{67}Ga , ^{67}Cu may interfere with the quantification of ^{67}Ga . However, the maximum reaction cross-section of the $^{\text{nat}}\text{Cu}(\alpha, x)^{67}\text{Cu}$ reaction is very low ($\sigma_{\text{max}} \approx 0.5 \text{ mb}$) [99] and lies within the uncertainty range of the literature data; hence, ^{67}Cu formation was neglected in the quantification of ^{67}Ga .

Taken together, the monitor reactions confirmed the consistency of the beam-current and energy assignment used for the evaluation.

Results & Discussion

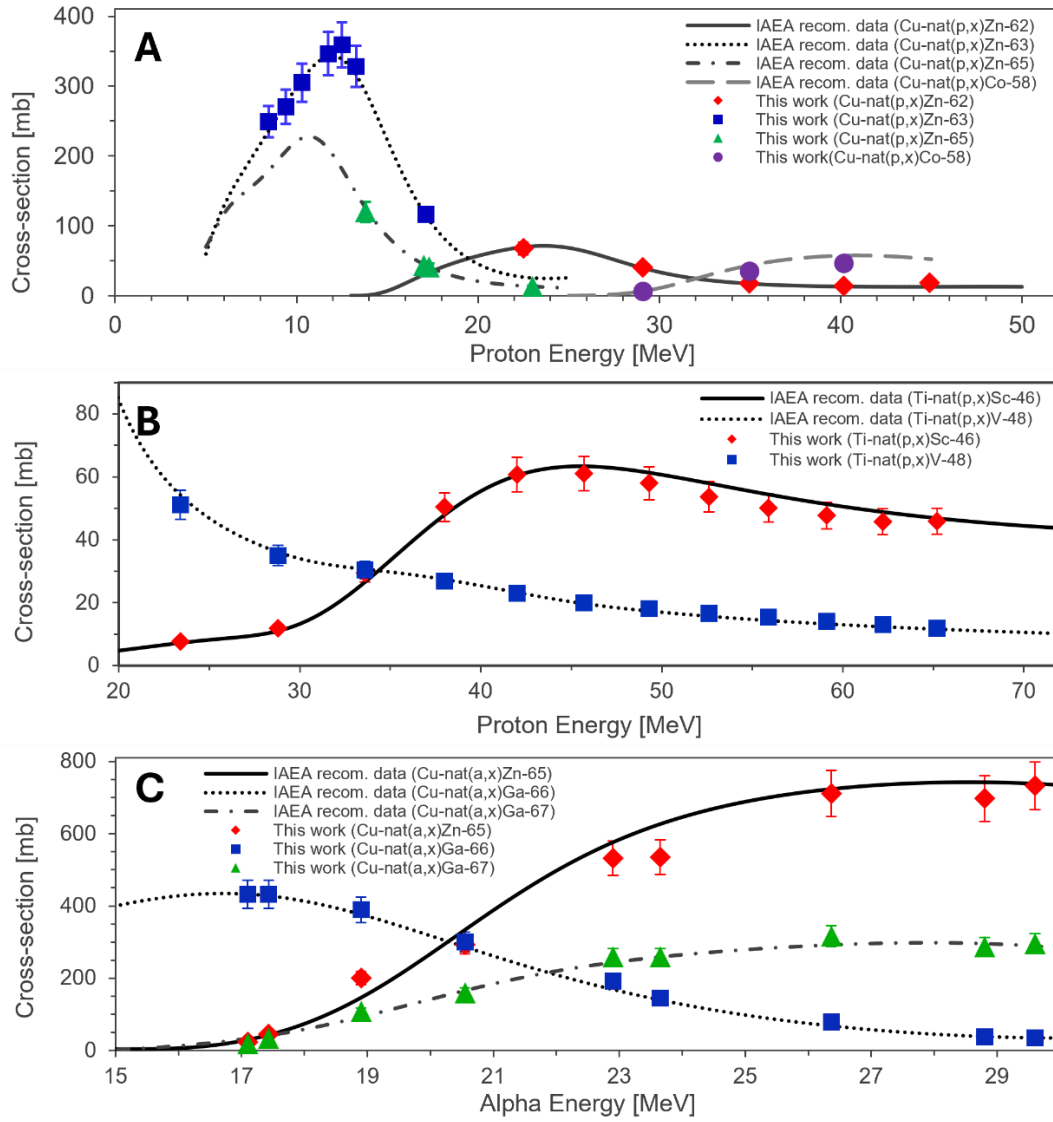
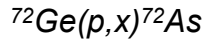


Figure 4: Comparison of monitor-reaction cross-sections measured in this work with IAEA recommended data. Panels (A) and (B) show proton-induced monitor reactions up to 45 and 70 MeV, respectively, whereas panel (C) shows alpha-induced monitor reactions between 15 and 30 MeV.

Direct production of ^{72}As

With the monitor reactions providing internal consistency for beam current and energy assignment, the experimental excitation functions can now be discussed with respect to their practical implications for ^{72}As production.

For practical radionuclide production, the main formation channel cannot be considered in isolation. The competing production of ^{71}As is particularly relevant, since it directly constrains the usable energy window for radionuclidically acceptable ^{72}As production.

Proton induced reactions

This section presents the experimentally determined excitation functions for the reactions $^{72}\text{Ge}(p,n)^{72}\text{As}$ and $^{72}\text{Ge}(p,2n)^{71}\text{As}$ on a highly enriched germanium target over the proton energy range from threshold to ~45 MeV in a comparative study of three cyclotrons: JULIC, BC1710 and C30XP. The underlying goal is to establish production-relevant cross-sections for the non-standard PET radionuclide ^{72}As , and to quantify the competing ^{71}As channel that drives radio nuclidic impurity once the (p,2n) threshold is exceeded. The resulting datasets are then used to compute thick-target yields (in MBq $\mu\text{Ae}^{-1} \text{h}^{-1}$) and to identify energy windows that maximize ^{72}As yield while minimizing co-production of arsenic isotopic impurities.

In Figure 5, the experimentally determined reaction cross-section of the $^{72}\text{Ge}(p,n)^{72}\text{As}$ reaction (A) and the side reaction $^{72}\text{Ge}(p,2n)^{71}\text{As}$ (B) are presented in comparison to previous publications of Levkovskii (1991)² [101] and modeled reference data obtained TENDL-2025 [99] as well as TALYS-2.0 simulation [22].

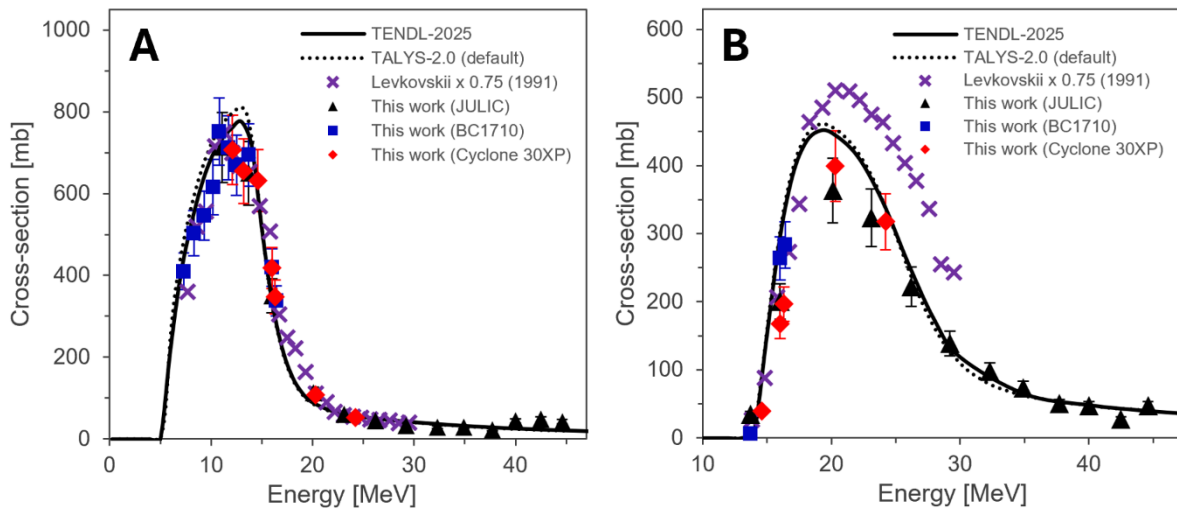


Figure 5: Experimentally determined cross-section data of the $^{72}\text{Ge}(p,n)^{72}\text{As}$ (left) and $^{72}\text{Ge}(p,2n)^{71}\text{As}$ (right) reaction in comparison to modeled reference data from TENDL-2025 and TALYS-2.0 at default parameters.

The experimental data demonstrates that the desired ^{72}As production via the (p,n) channel can be described well by TALYS-2.0 default values, while TENDL-2025 also provides a satisfactory overall representation of the excitation function.

² Reaction cross-section data originating from the work of Levkovskii, the numerical values presented here were obtained via EXFOR (Experimental Nuclear Reaction Data database) Entry: A0510 [100].

The fitted experimental cross-sections shown in Figure 5 were used as the basis for the integrated thick-target yield calculations presented in Figure 6. The thick-target yield calculated based on the measurements presented in this work are compared to evaluated literature data presented by IAEA [38] showing reasonable concordance over the investigated energy ranges.

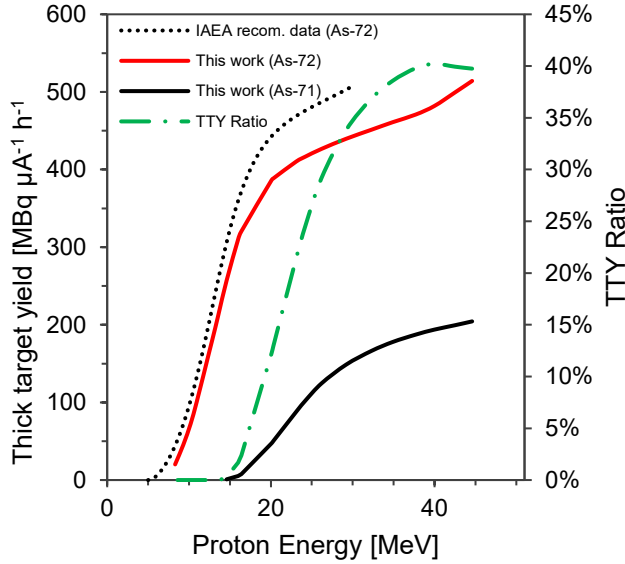


Figure 6: Direct comparison of the thick target yield for the formation of ^{72}As and ^{71}As via proton induced reaction with ^{72}Ge and the recommended data provided by the IAEA [38].

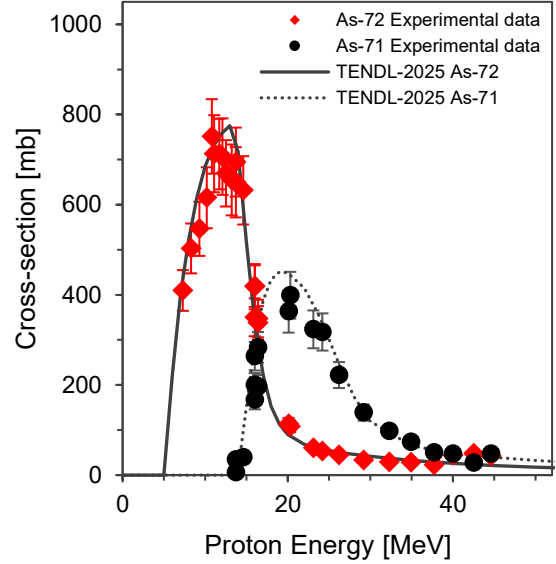
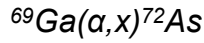


Figure 7: Illustration of the production window for optimized ^{72}As production with minimal ^{71}As content. The TENDL-2025 fit is added to guide the eyes for easier visualization.

These presented results further indicate that the integral yield of ^{72}As is higher than that of ^{71}As throughout the investigated energy range. From a practical production perspective, a low proton-energy window of approximately 14–7 MeV is particularly favorable, since the $^{72}\text{Ge}(p,2n)^{71}\text{As}$ channel is not yet open in this range, enabling radionuclidically purer ^{72}As production (Figure 7). At higher proton energies, larger absolute yields of ^{72}As can be achieved, but at the expense of increasing co-production of ^{71}As and other longer-lived arsenic impurities, further indicated by the TTY ratio presented in Figure 6. The results therefore highlight the trade-off between maximizing production yield and maintaining high radionuclidic purity.

Alpha induced reactions

Production of ^{72}As via α -particle irradiation of gallium was investigated as an alternative route to the more established $^{72}\text{Ge}(p, n)^{72}\text{As}$ reaction. In particular, the $^{69}\text{Ga}(\alpha, n)^{72}\text{As}$ reaction is attractive because it allows direct cyclotron production of ^{72}As from a stable gallium target material. At the same time, the competing $^{69}\text{Ga}(\alpha, 2n)^{71}\text{As}$ channel has to be considered, since the co-production of ^{71}As directly limits the achievable radionuclidic purity and therefore defines the practically useful energy window.

To assess this production route, excitation functions for the formation of ^{72}As and ^{71}As were measured using both natural gallium and highly enriched ^{69}Ga targets over an α -

particle energy range from threshold up to approximately 30 MeV. All irradiation was performed at the C30XP at the Forschungszentrum Jülich (FZJ). Since literature data for this route remain comparatively scarce and rather unreliable, particularly for Ga_2O_3 targets and in the energy range relevant for practical radionuclide production, the present measurements provide

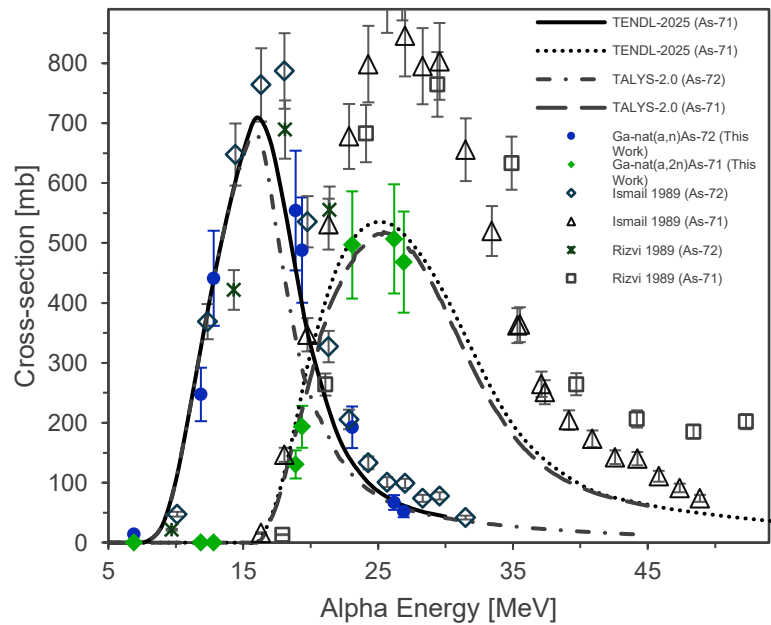


Figure 8: Reaction cross-section data of $^{nat}\text{Ga}(\alpha, x)^{71/72}\text{As}$ reaction (obtained in a cooperative work with Dr. M. Hussain) in comparison to TENDL-2025 and Talys-2.0 modeled reaction data as well as experimental literature data.

production-relevant cross-section data, $\sigma(E_\alpha)$, for the evaluation of ^{72}As production and impurity formation.

The cross-sections obtained from natural gallium targets are shown in Figure 8 for the formation of ^{72}As and ^{71}As . The corresponding data measured with enriched ^{69}Ga targets are presented in Figure 9 for the $^{69}\text{Ga}(\alpha, n)^{72}\text{As}$ and $^{69}\text{Ga}(\alpha, 2n)^{71}\text{As}$ reactions. Overall, the data obtained from natural and enriched targets show good agreement, supporting the internal consistency of the measurements. As expected, the ^{72}As production channel dominates at lower α -particle energies, whereas the onset of the

$^{69}\text{Ga}(\alpha,2n)^{71}\text{As}$ reaction becomes increasingly relevant at higher energies. This behavior clearly illustrates the yield-purity trade-off that has to be considered when selecting an irradiation energy for practical ^{72}As production.

In addition, the measured excitation functions are generally well reproduced by TENDL-2025 and TALYS-2.0 default calculations, particularly with respect to the overall energy dependence and the position of the main reaction maxima. This agreement is observed for both the natural and enriched gallium datasets. In contrast, comparison with previously published experimental data for natural gallium, especially those reported by Ismail 1989 [102] and Rizvi 1989 [103], reveals substantial deviations in the absolute cross-section values, most notably for ^{71}As formation. The present results are closer to the model calculations than to these earlier datasets. This may indicate systematic differences between the present and previous measurements, although the underlying cause cannot be resolved within the scope of this work.

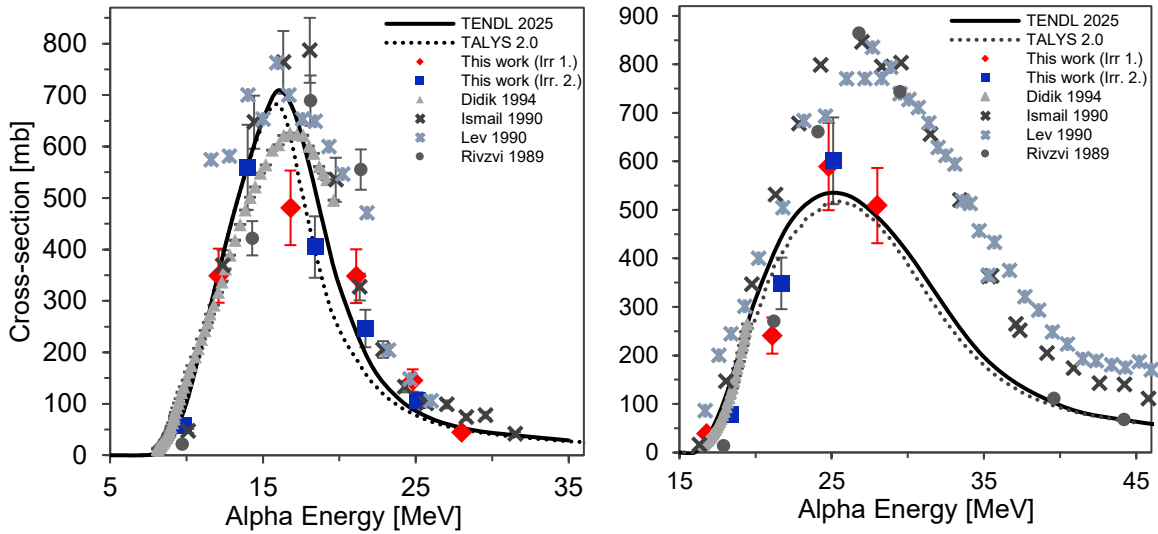


Figure 9: Reaction cross-section data of enriched $^{69}\text{Ga}(\alpha,n)^{72}\text{As}$ (left) and $^{69}\text{Ga}(\alpha,2n)^{71}\text{As}$ (right) reaction in comparison to literature known reaction data as well as TENDL-2025 and TALYS-2.0 (default) modeling data.

In Figure 10, the cross-section data for both ^{71}As and ^{72}As are presented in order to identify a suitable energy range for the production of ^{72}As with high radionuclidic purity for diagnostic applications. To avoid co-production of ^{71}As , the incident α -particle energy must remain below the threshold of the $^{69}\text{Ga}(\alpha,2n)^{71}\text{As}$ reaction, which opens at approximately $E_\alpha \approx 17$ MeV as confirmed by the experimentally determined data presented in this section. Above this threshold, the production cross-section of ^{71}As

increases rapidly and reaches a maximum at around 28 MeV. Accordingly, an optimal production energy window for maximum yield with high-purity ^{72}As is suggested in the range from 7–17 MeV. The corresponding thick-target yields of ^{71}As and ^{72}As , derived from the cross-section data determined in this work, are shown in Figure 11 further illustrating the steep increase in the ^{71}As fraction above the reaction threshold.

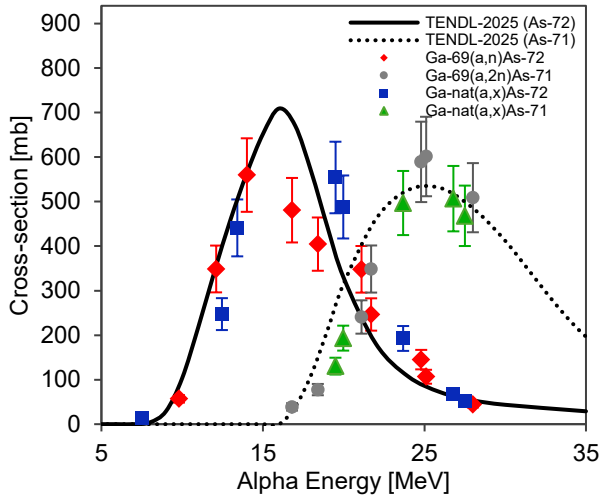


Figure 10: Illustration of the production window for optimized ^{72}As production with minimal ^{71}As content. The TENDL-2025 fit is added to guide the eyes for easier visualization

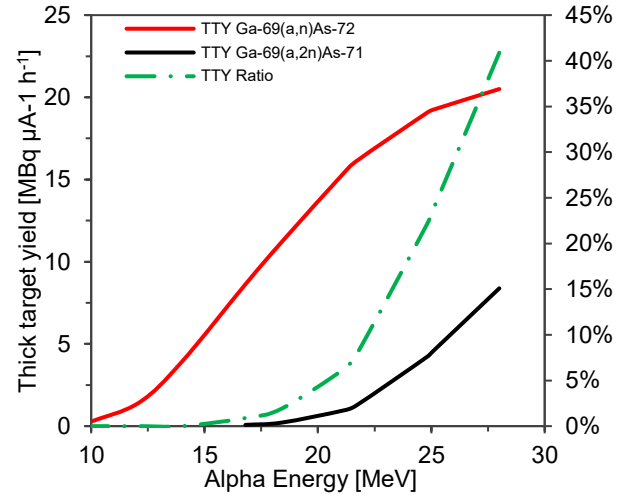


Figure 11: Thick target yield for the formation of ^{72}As and ^{71}As by alpha induced reaction with enriched ^{69}Ga .

For the $^{69}\text{Ga}(\alpha,n)^{72}\text{As}$ production route, the available literature appears to be very limited and is essentially restricted to experimental excitation-function studies. The older works [102–104] provide cross-section data for α -induced reactions on gallium, but do not report thick-target yields or integral yields in a production-oriented sense. This is also evident from the way the data are presented, i.e., as excitation functions and tabulated cross-sections (mb) rather than activity-based yields. Consequently, these studies are useful for evaluating reaction behavior and for benchmarking model calculations, but not as a source of experimentally determined thick target yields for $^{69}\text{Ga}(\alpha,n)^{72}\text{As}$. The more recent study by Rahman and Amin [39] should therefore be interpreted primarily as a model-based production-route evaluation rather than as an experimental yield study. In that work, TALYS-1.96 calculations using different level-density models were compared with experimental EXFOR cross-sections, adjusted where necessary, and the integral yields were then calculated from the best-fitting

models. Accordingly, the reported value of $7.94 \text{ MBq } \mu\text{Ae}^{-1} \text{ h}^{-1}$ at 20 MeV for $^{69}\text{Ga}(\alpha, n)^{72}\text{As}$ represents a calculated best-fit estimate and not an experimentally measured physical yield. More recent experimental studies on α -irradiated gallium oxide demonstrated the practical production and chemical separation of $^{72,71}\text{As}$, but these works do not provide a channel-specific experimental thick-target yield for the $^{69}\text{Ga}(\alpha, n)^{72}\text{As}$ route. Overall, the literature therefore suggests that this reaction is supported by experimental cross-section data, but that its yield assessment still relies mainly on theoretical or semi-empirical treatment rather than on direct experimental thick-target yield measurements.

Indirect production of ^{72}As

Beyond the direct production routes, the indirect $^{72}\text{Se}/^{72}\text{As}$ pathway offers an additional production concept, shifting the focus from immediate product formation toward delayed availability and potential generator-based use. ^{72}As can be obtained indirectly through the electron-capture decay of ^{72}Se ($T_{1/2} = 8.5 \text{ d}$). This parent–daughter system may therefore represent an attractive alternative, particularly with regard to centralized production logistics and prolonged or delayed application. The following chapter addresses the production of ^{72}Se and evaluates its potential as an indirect route to ^{72}As .

$^{75}\text{As}(p, x)^{72}\text{Se}$

In this study, the excitation functions for the production of ^{72}Se as generator parent for ^{72}As via proton irradiation of monoisotopic ^{75}As is presented. Incident energies from reaction threshold up to $E_p = 70 \text{ MeV}$ are covered utilizing the injector 2 cyclotron at the PSI, Switzerland. Because ^{72}Se decays by EC to ^{72}As , the practical feasibility of a $^{72}\text{Se}/^{72}\text{As}$ generator is governed primarily by how efficiently and cleanly the parent nuclide can be produced on target. Accordingly, we quantify the energy dependence of the dominant multi-neutron emission pathway (notably $^{75}\text{As}(p, 4n)^{72}\text{Se}$) and track competing channels that generate selenium co-products, with particular attention to longer-lived impurities such as ^{75}Se from $^{75}\text{As}(p, n)^{75}\text{Se}$ that can degrade parent

radionuclidic purity and impact generator performance. Long living arsenic impurities are neglected for this study since they can easily be removed chemically.

Figure 13 presents the experimentally determined reaction cross-sections for ^{72}Se production. The ^{72}Se cross-section was determined directly by measuring its 45.9 keV γ -line. In addition, the ^{72}Se production cross-section was independently derived from the ingrowth of its daughter nuclide ^{72}As . The daughter-based measurement was performed 25 days after end of bombardment (EOB) to ensure that directly produced ^{72}As had fully decayed. Exemplary spectra of two selected samples for the direct and indirect measurement are presented in Figure 12. The cross-sections obtained by the two methods differ slightly but remain consistent within the experimental uncertainties. Both datasets show good agreement with previously reported experimental data from Fox (2021) [105] and Mushtaq (1988) [106]. By contrast, the TALYS-2.0 default calculation and TENDL-2025 prediction deviate substantially from the experimental data obtained in this study and from the literature data.

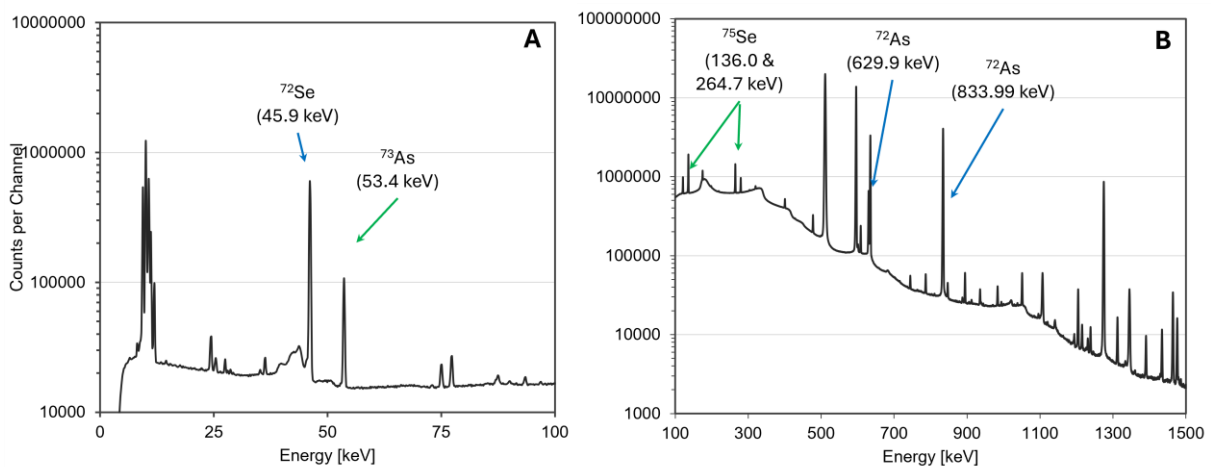


Figure 12: High-purity germanium γ -spectra of the direct measurement of ^{72}Se (Sample 62) (A) and for indirect determination via ^{72}As measurement (Sample 41) (B).

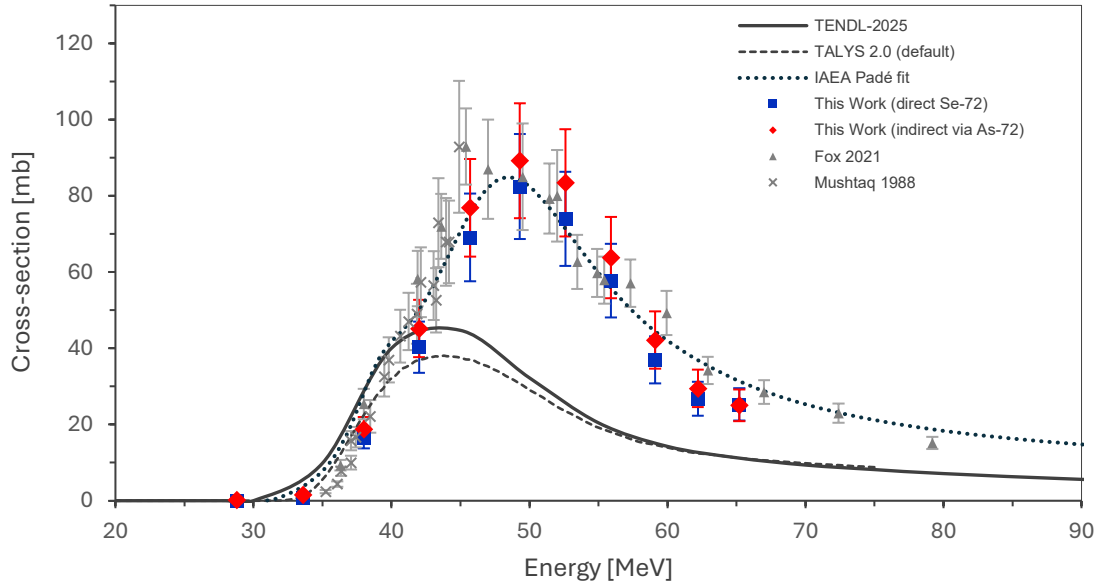


Figure 13: Reaction cross-section data of direct formation of ^{72}Se via $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction and the indirect calculation of ^{72}Se by its daughter nuclide ^{72}As . All measurements were performed > 25 days post EOB. The Measured data is compared to literature known results as well as modeling via TENDL-2025 and TALYS-2.0 (default).

Figure 14 shows the determined reaction cross-section for the unwanted side product ^{75}Se . The cross-section data are compared with experimental data from Fox (2021) [105], Musthaq (1988) [106] and with TENDL-2025 and TALYS-2.0 model predictions. Overall, the present data show good agreement with reference data, although they lie slightly below the literature values at lower proton energies.

In contrast to the previously discussed direct production routes, the indirect production pathway via ^{72}Se is characterized by an important difference in impurity formation. In the direct production of ^{72}As , the main unwanted by-product, predominantly ^{71}As , is formed mainly at higher projectile energies than ^{72}As . Therefore, as shown in Figure 7 and Figure 10, the formation of ^{71}As can be largely suppressed by reducing the projectile energy below its reaction threshold.

For ^{72}Se production, however, the main selenium impurity is ^{75}Se , whose reaction threshold lies below that of ^{72}Se . Although the cross-section of the $^{75}\text{As}(p,n)^{75}\text{Se}$ reaction decreases with increasing projectile energy, ^{72}Se will inevitably be co-produced. This represents an intrinsic limitation to the achievable radionuclidic purity and must be considered when evaluating the generator route.

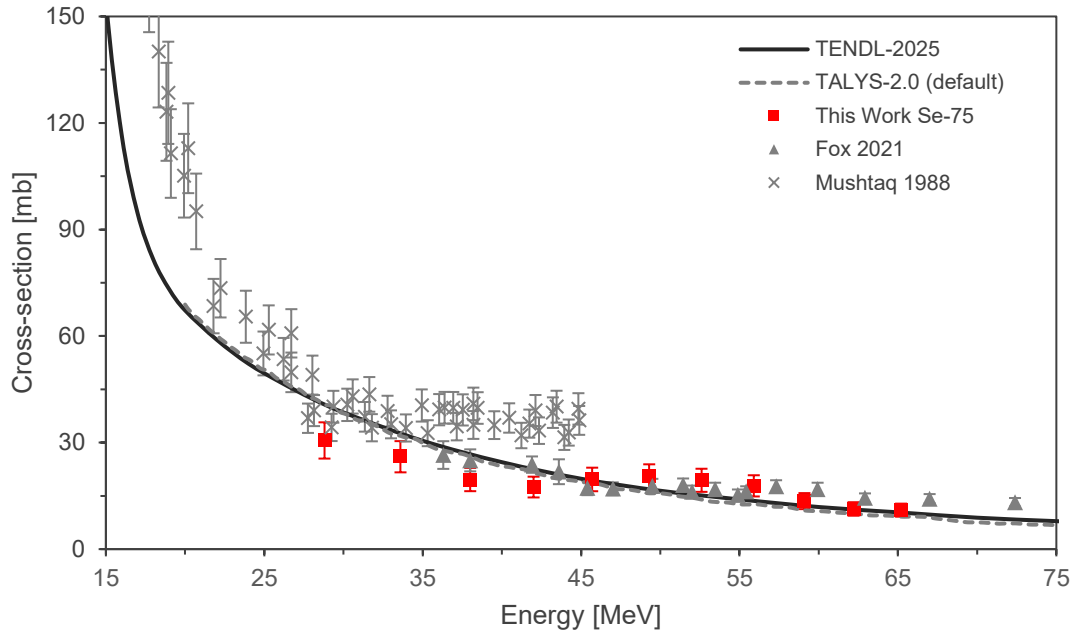


Figure 14: Reaction cross-section of the competing $^{75}\text{As}(p,n)^{75}\text{Se}$ reaction.

Nevertheless, a favorable production window can be identified by minimizing the ^{75}Se content while maximizing the production yield of ^{72}Se , as shown in Figure 15. Within the energy range investigated in this study, higher proton energies are generally beneficial for reducing the $^{75}\text{Se}/^{72}\text{Se}$ ratio. This trend is more clearly visible in

Figure 16, which presents the thick-target yields of ^{72}Se and ^{75}Se and the $^{75}\text{Se}/^{72}\text{Se}$ TTY ratio. The yield ratio decreases rapidly to below 10% above approximately 45 MeV and approaches a plateau of about 3% between 55 MeV and 65 MeV. Based on these results, a proton energy range of approximately 40–65 MeV can be regarded as favorable for ^{72}Se production, with higher energies within this interval providing improved suppression of ^{75}Se relative to ^{72}Se .

Results & Discussion

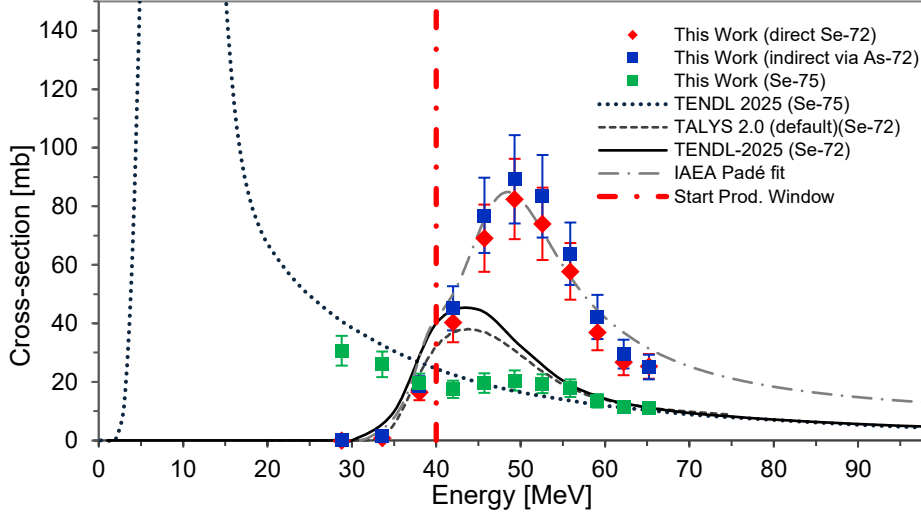


Figure 15: Energy window of ^{72}Se production directly compared to the ^{75}Se impurity. The red dotted line indicates a compromise between highest possible ^{72}Se yield with reasonable low ^{75}Se content.

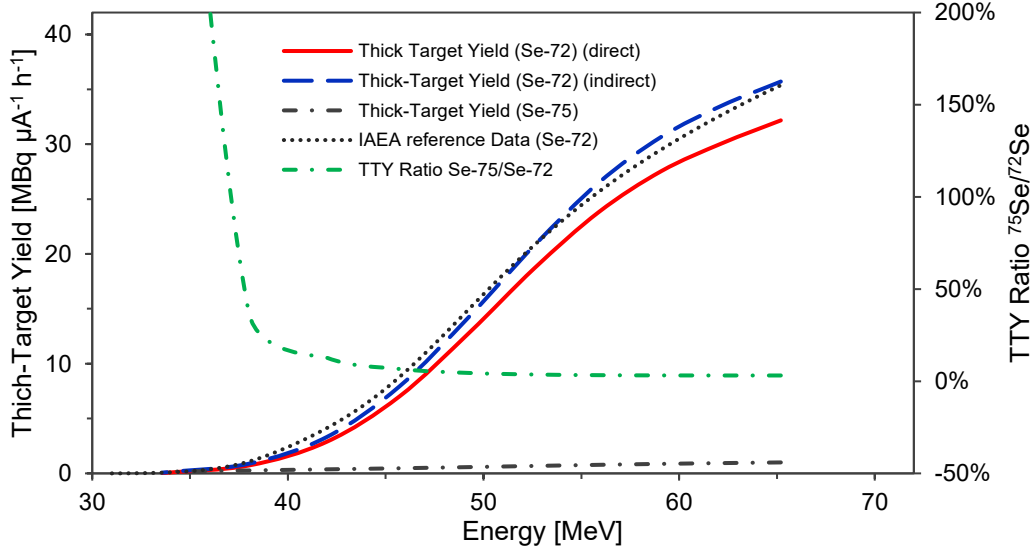


Figure 16: Thick-target yields (TTY) of ^{72}Se , determined both directly from the ^{72}Se activity and indirectly from the ingrowth of its daughter nuclide ^{72}As , in comparison with the thick-target yield of the co-produced impurity ^{75}Se . The corresponding $^{75}\text{Se}/^{72}\text{Se}$ thick-target yield ratio is shown to illustrate the energy-dependent impurity contribution relative to the desired generator parent³.

The experimental excitation-function data and the derived thick-target yields demonstrate that the $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction is a viable route for producing ^{72}Se as generator parent of ^{72}As , particularly in the energy range where the $^{75}\text{Se}/^{72}\text{Se}$ yield ratio is minimized. At the same time, the comparison with TALYS-2.0 and TENDL-2025

³ The reference thick-target yields used for comparison were taken from the evaluated IAEA dataset [61], rather than directly from a single publication. The recommended excitation function was obtained by critically selecting the available experimental data and fitting the retained points with a nine-parameter Padé function using a χ^2 -based optimization.

reveals a pronounced discrepancy between model predictions and experimental data, especially with respect to the magnitude and shape of the ^{72}Se excitation function. Since this reaction is central to the proposed indirect production route, the origin of this model deficiency was investigated in more detail. The following section therefore presents a TALYS-2.0 sensitivity analysis of the $^{75}\text{As}(p,4n)^{72}\text{Se}$ excitation function, focusing on the influence of the optical model potential, level-density description, and pre-equilibrium treatment.

TALYS-2.0 sensitivity analysis of the $^{75}\text{As}(p,4n)^{72}\text{Se}$ excitation function

After the benchmark systems $^{72}\text{Ge}(p,x)^{71,72}\text{As}$ and $^{69}\text{Ga}(\alpha,x)^{72}\text{As}$ had been found to be reproduced reasonably well by TALYS/TENDL, the $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction was selected as the main problem case for a more detailed model analysis. This choice was further supported by the evaluation of Amjed et al., who likewise reported only fair agreement of TALYS and EMPIRE with the $^{75}\text{As}(p,4n)^{72}\text{Se}$ excitation function up to about 45 MeV, followed by an underestimation at higher energies, while TENDL-2025 showed no satisfactory agreement over the full energy range [107].

The aim of this study was not to derive an unrestricted best fit, but rather to identify which physically meaningful model ingredients are primarily responsible for the observed discrepancy between calculated and experimental excitation functions. For this purpose, the TALYS-2.0 description was examined in a stepwise sensitivity analysis by varying the proton optical model potential (OMP), the level-density treatment, and the pre-equilibrium prescription. To allow a compact comparison of the resulting excitation functions, four characteristic quantities were extracted from each calculation: the effective threshold energy E_{thr} , the maximum cross-section σ_{max} , the energy of the maximum E_{max} , and the cross-section at 70 MeV, $\sigma(70 \text{ MeV})$, as a simple descriptor of the high-energy tail. A summary of those points of interest is presented in Table A-3 and Table A-4 in the Appendix.

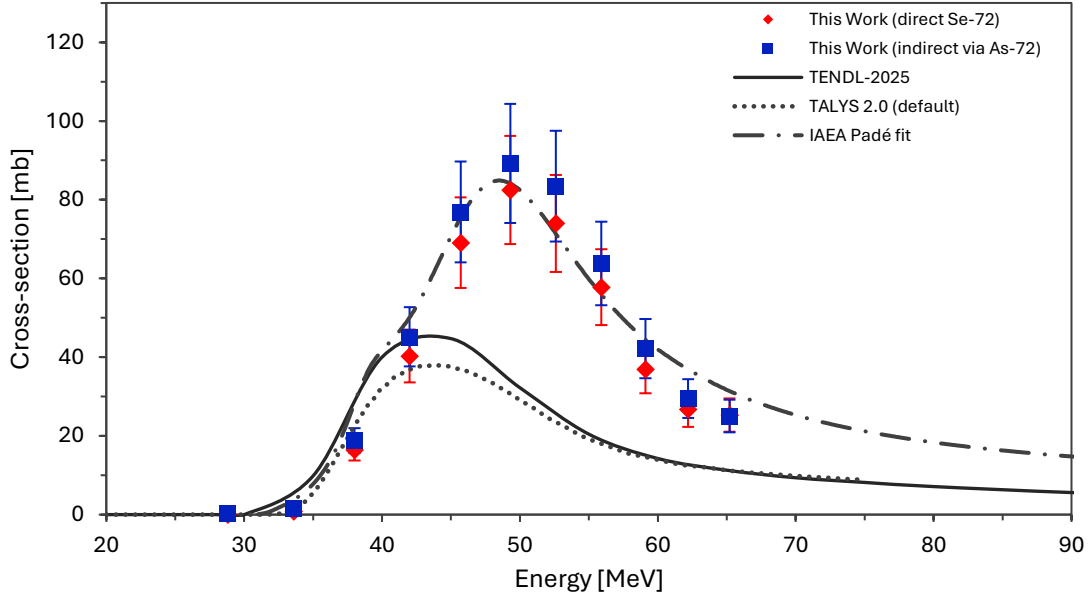


Figure 17: Comparison of the experimental $^{75}\text{As}(p,4n)^{72}\text{Se}$ excitation function with the TALYS-2.0 default calculation and the literature-based reference curves (Padé fit, TENDL-2025).

The default TALYS-2.0 calculation already reproduced the threshold region reasonably well. An effective threshold energy of 31.0 MeV was obtained, which is in excellent agreement with the Padé-based reference value of 31 MeV. This is an important first observation, since it shows that the main deficiency of the default calculation is not the onset of the reaction itself. The discrepancy becomes apparent only once the excitation function develops above threshold. The default calculation reached a maximum cross-section of only 38.1 mb at 36.9 MeV and decreased to 9.8 mb at 70 MeV. In comparison, the Padé-based reference curve showed a maximum of 84.9 mb at 48.4 MeV and still 25.3 mb at 70 MeV. Thus, the default TALYS-2.0 calculation underestimated the peak cross-section by more than a factor of two, placed the maximum too low in energy by more than 11 MeV, and also failed to reproduce the magnitude of the high-energy tail. A similar tendency was seen for the TENDL-2025 prediction, which remained low in magnitude and reached its maximum even earlier. Taken together, this indicates that the main problem is not the threshold energy, but the shape and strength distribution of the excitation function over the full energy range. An overview of the modeled excitation functions is presented in Figure 18.

The first parameter family considered was the proton optical model potential. Small local variations of the real-volume radius parameter were tested using *rvadjust p 0.95*

(rv095) and *rvadjust p 1.05* (rv105). These changes had only a limited effect on the calculated excitation function. The threshold energy remained unchanged at 31.0 MeV, and the maximum cross-section changed only slightly from 38.1 mb in the default calculation to 39.3 mb for *rvadjust p 0.95* and 38.0 mb for *rvadjust p 1.05*. A somewhat clearer effect was observed in the energy of the maximum, which shifted from 36.9 MeV to 43.9 MeV for both OMP variations, and in the high-energy tail, where σ (70 MeV) changed from 9.8 mb to 9.3 mb and 10.5 mb, respectively. These results show that the proton OMP mainly modifies the detailed shape of the excitation function, in particular the peak location and the high-energy tail, but does not resolve the pronounced underestimation of the peak height. The OMP is therefore not the dominant source of discrepancy, at least not through small local variations of the radius parameter alone.

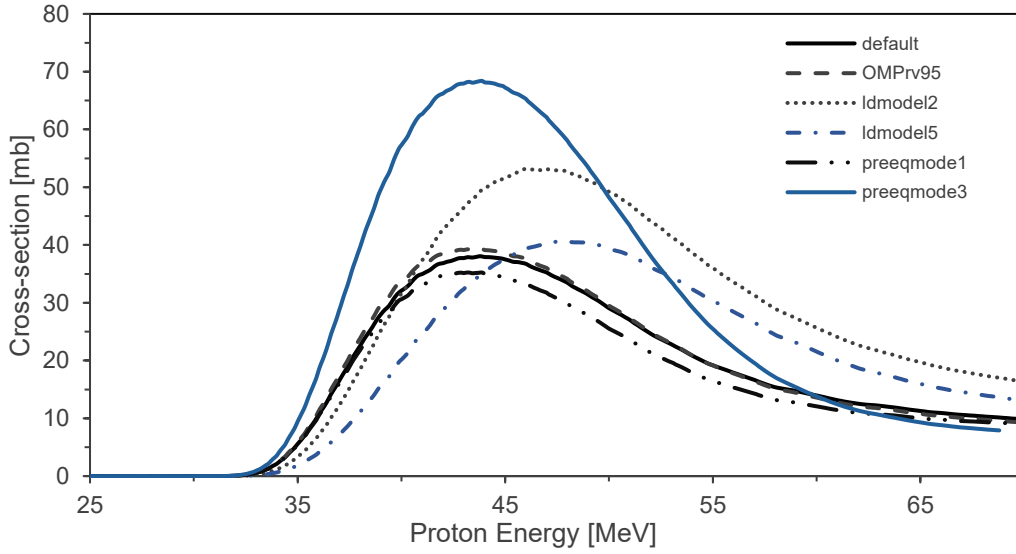


Figure 18: TALYS-2.0 single-parameter screening for the $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction: effect of OMP, level-density model, and pre-equilibrium mode.

A much stronger effect was obtained when the level-density model was changed. The use of *ldmodel 2* (ld2) increased the maximum cross-section to 53.2 mb and shifted the maximum to 46.0 MeV, while at the same time increasing σ (70 MeV) to 16.3 mb. In contrast, *ldmodel 5* (ld5) resulted in only a moderate increase of the maximum cross-section to 40.7 mb but shifted the peak to 48.0 MeV and increased the 70 MeV cross-section to 13.1 mb. Both alternative level-density descriptions therefore improved the

default TALYS-2.0 result, but in different ways. *ldmodel 2* clearly provided the strongest increase in peak height and high-energy yield, whereas *ldmodel 5* reproduced the peak position more closely. This behavior is physically plausible, since the level-density model does not primarily open or close reaction channels in a formal sense, but changes the statistical population of energetically accessible final states and therefore the balance between competing (p,xn) channels. In the present case, the sensitivity to the adopted level-density prescription was substantially stronger than the sensitivity to the OMP radius variation, indicating that the statistical decay description is a key factor for the $^{75}\text{As}(p,4n)^{72}\text{Se}$ channel.

The pre-equilibrium treatment also had a pronounced influence, although with a different signature. *preeqmode 1* (pe1) lowered the maximum cross-section to 35.2 mb and therefore worsened the description relative to the default case. By contrast, *preeqmode 3* (pe3) increased the maximum cross-section markedly to 68.0 mb, while keeping the threshold at 31.0 MeV. However, this increase in peak height was accompanied by a less favorable high-energy behavior, with $\sigma(70 \text{ MeV})$ decreasing to 8.0 mb. The pre-equilibrium treatment therefore appears to control primarily the amount of flux feeding the peak region, whereas the high-energy tail is not improved in the same way. This again suggests that the different model ingredients affect different parts of the excitation function. In the present case, the level-density model and the pre-equilibrium treatment act as the two dominant levers, but they do not improve the same observables to the same extent.

Based on these screening results, a small number of combined calculations were carried out in order to test whether the favorable single-parameter effects could be combined. The obtained excitation functions are presented in Figure 19. The most relevant case was the combination of *ldmodel 2* and *preeqmode 3*. This immediately brought the calculated maximum cross-section into the correct order of magnitude. For *ldmodel 2*, *preeqmode 3*, a maximum of 96.3 mb was obtained at 46.0 MeV, with a threshold of 31.1 MeV. Thus, the threshold remained realistic, and the peak cross-section now approached the Padé-based reference much more closely than any single-parameter calculation. The remaining discrepancy was mainly shifted to the position of the maximum and to the high-energy tail, since the peak still occurred about 2.4 MeV too early and $\sigma(70 \text{ MeV})$ remained low at 11.4 mb. Adding a small OMP

variation on top of this combination changed the peak height only minimally but increased the tail systematically. The best case in this subgroup was the combination of *ldmodel 2*, *preeqmode 3* and OMP rv105, which gave 96.9 mb at 46.0 MeV and increased $\sigma(70 \text{ MeV})$ to 14.7 mb. Even in this most favorable case, however, the high-energy tail remained clearly below the Padé-based reference value of 25.3 mb.

A second combination block was used to test whether the beneficial effect of *preeqmode 3* also persisted with a different level-density model. In the *ld5+pe3* calculation, the peak was shifted to 47.8 MeV, which is very close to the Padé-based reference value of 48.4 MeV, but the maximum cross-section reached only 72.9 mb and the tail remained weak at 9.2 mb. A modest improvement was obtained for *ld5+pe3+rv105*, which yielded 76.3 mb at 47.8 MeV and 12.5 mb at 70 MeV. This confirms that the favorable effect of *preeqmode 3* is not restricted to *ldmodel 2*, but it also shows that the level-density prescription remains decisive for how strongly the peak is populated. In other words, *ldmodel 5* is advantageous with respect to the peak position, whereas *ldmodel 2* is clearly more effective in raising the peak cross-section itself.

Finally, a control block with *ldmodel 2* combined with *preeqmode 1* was used to separate the individual contributions more clearly. In this case, the maximum cross-section remained low, with values of 47.7–48.9 mb depending on the additional OMP variation, while the peak stayed at 46.0 MeV. The 70 MeV cross-sections were somewhat higher than in *ld2+pe3*, ranging from 12.8–15.2 mb, but the decisive increase of the peak region was absent. This control set therefore demonstrates that the improvement seen in *ld2+pe3* does not arise from *ldmodel 2* alone. Rather, the strong increase of the peak height is specifically linked to the combination of *ldmodel 2* with *preeqmode 3*, whereas the OMP variation again acts mainly as a secondary shape correction.

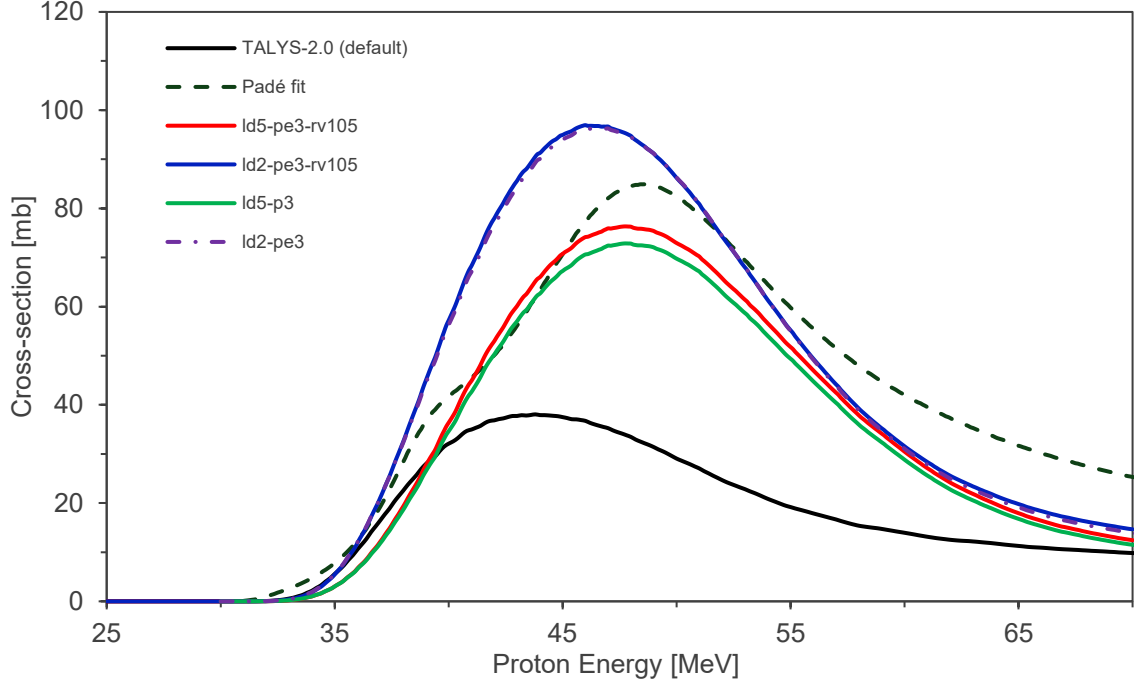


Figure 19: Comparison of the most relevant combined TALYS-2.0 calculations for $^{75}\text{As}(p,4n)^{72}\text{Se}$: *ldmodel2_preeqmode3* (ld2-pe3), *ldmodel2_preeqmode3_OMPrv105* (ld2-pe3-rv105), *ldmodel5_preeqmode3* (ld5-pe3), and *ldmodel5_preeqmode3_OMPrv105* (ld5-pe3-rv105), together with the experimental data and the Padé-based reference fit.

Based on these results (Figure 19), the most relevant adjusted TALYS-2.0 cases were finally compared directly with the experimental excitation function and the literature-based reference curve in order to illustrate the remaining trade-off between peak magnitude, peak position, and high-energy behavior. A direct comparison of the excitation functions obtained by ld2+pe3+rv105 and the ld5+pe3+rv105 combinations against the experimental data as well as the IAEA Padé-fit is presented in Figure 20.

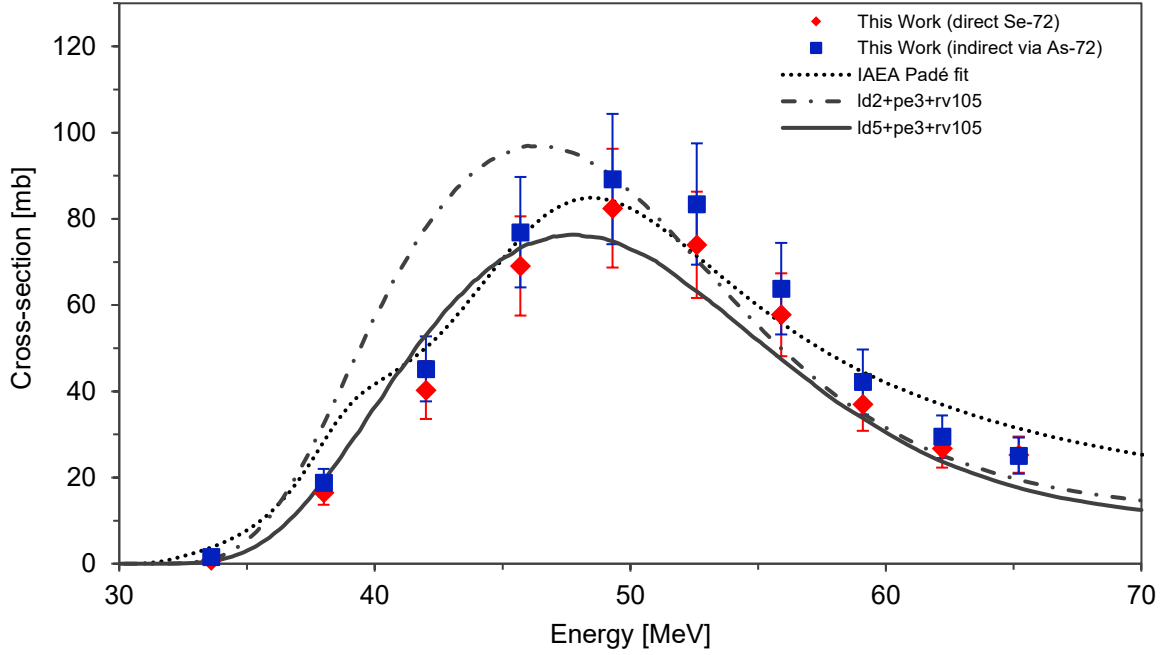


Figure 20: Comparison of the experimental excitation function with the TALYS-2.0 default calculation and the two most relevant locally adjusted cases. While the $ld2+pe3+rv105$ case reproduces the peak magnitude more closely, the $ld5+pe3+rv105$ case provides a better description of the peak position. Both calculations still underestimate the high-energy tail.

Taken together, the TALYS-2.0 sensitivity study shows that the disagreement for the $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction is not caused by a single isolated deficiency. The threshold energy is already reproduced well by the default calculation, and small OMP variations affect mainly the detailed shape of the curve rather than its overall magnitude. The dominant deficiencies lie instead in the description of the peak region and the high-energy tail, which are strongly influenced by the level-density and pre-equilibrium treatments. Among the tested single-parameter variations, *ldmodel 2* gave the clearest overall improvement, while *preeqmode 3* provided the strongest isolated increase in peak height. Their combination, particularly in $ld2+pe3+rv105$ and $ld5+pe3+rv105$, yielded the best overall agreement obtained in the present study and showed that a local, physically guided modification of the TALYS-2.0 input can reduce the discrepancy substantially. At the same time, the persistent underestimation of the high-energy tail and the slightly too low peak energy indicate that the remaining mismatch is not removed completely. The $^{75}\text{As}(p,4n)^{72}\text{Se}$ channel therefore remains a genuine challenge for the TALYS-2.0 description, even after targeted local adjustments. This is consistent with the earlier evaluation of Amjed et al., who also identified this reaction

as a difficult case for TALYS-based modeling and ultimately based the recommended excitation function on a fit to the experimental data rather than on an explicitly documented TALYS parameter set [107].

The sensitivity studies highlight the limitations of the theoretical description of the $^{75}\text{As}(p,4n)^{72}\text{Se}$ excitation function. However, the production assessment is ultimately based on the experimentally determined production windows. Therefore, the following section evaluates the integrated yields within these windows and compares the indirect $^{75}\text{As}(p,4n)^{72}\text{Se}$ route with the direct $^{72}\text{Ge}(p,x)^{72}\text{As}$ and $^{69}\text{Ga}(\alpha,x)^{72}\text{As}$ production routes.

Production-window yields and achievable ^{72}As activities

The excitation functions discussed in the previous sections define the energy dependence of the individual production channels. For a practical assessment, however, the maximum cross-section alone is not sufficient. Instead, the relevant quantity is the activity that can be obtained within an energy interval in which the desired radionuclide is produced with acceptable radionuclidic purity. Therefore, the selected production windows were translated into integral production-window yields. This allows a direct comparison of the direct ^{72}As production routes with the indirect $^{72}\text{Se}/^{72}\text{As}$ generator approach.

The yield comparison was restricted to radionuclidic impurities that are expected to remain in the chemically isolated product fraction and therefore directly affect the usability of the final product. For direct ^{72}As production, the most relevant impurity is ^{71}As , since arsenic isotopes cannot be separated chemically from ^{72}As . For the indirect ^{72}Se route, the corresponding long-term limitation is ^{75}Se , because selenium isotopes remain in the isolated ^{72}Se parent fraction. Other possible reaction channels were considered but not included explicitly in the main yield table. Radiative-capture reactions such as (p,γ) or (α,γ) were neglected because their cross-sections are expected to be small compared with the dominant neutron-emission channels in the selected production windows. In the $^{75}\text{As}(p,x)$ case, arsenic products such as ^{74}As or ^{73}As , formed for example through (p,pn) - or $(p,p2n)$ -type channels, are chemically separated from the selenium product together with the bulk arsenic target material. ^{73}Se may be co-produced at EOB, but it was not considered the long-term limiting

selenium impurity because of its comparatively short half-life of approximately 7 h. A cooling period of three days corresponds to about ten half-lives of ^{73}Se and reduces its activity to approximately 10^{-3} of the EOB value, while about 78% of the ^{72}Se parent activity remains. In contrast, ^{75}Se is long-lived and therefore represents the more relevant radionuclidic-purity constraint for the $^{72}\text{Se}/^{72}\text{As}$ generator parent fraction. A summary of the reaction channels considered and the rationale for their inclusion or exclusion is given in Table A-1.

The production-window yield $Y_{\text{win}}(E_{\text{in}}, E_{\text{out}})$ is given in $\text{MBq } \mu\text{A}^{-1} \text{ h}^{-1}$. It represents the yield integrated over the selected projectile-energy interval from E_{in} to E_{out} , and is therefore distinct from a point-wise cross-section or from a full thick-target yield curve extending over the complete stopping range. For a given integrated beam charge $Q = I \cdot t_{\text{irr}}$, the corresponding end-of-bombardment activity can be estimated as

$$A_{\text{EOB}} \approx Y_{\text{win}}(E_{\text{in}}, E_{\text{out}}) \cdot Q \quad (3.1)$$

where I is the beam current and t_{irr} is the irradiation time. For longer irradiations, radioactive decay during production must be considered explicitly using the activity build-up term.

$$A_{\text{EOB}}(t_{\text{irr}}) = A_{\text{sat}}(1 - e^{-\lambda t_{\text{irr}}}), \quad (3.2)$$

where A_{sat} is the saturation activity and λ is the decay constant of the produced radionuclide that is described in Eq. (1.1). This correction is particularly relevant for long irradiations or products with a short half-life. In Table 6, the production window and the corresponding integral yields for each production route are presented.

Table 6: Production-window yields for direct ^{72}As production and indirect ^{72}Se production.

Production route	Product	Energy interval [MeV]	Desired product yield [$\text{MBq } \mu\text{A}^{-1} \text{ h}^{-1}$]	Relevant impurity	Impurity yield [$\text{MBq } \mu\text{A}^{-1} \text{ h}^{-1}$]	Impurity ratio [%]
$^{72}\text{Ge}(p,n)^{72}\text{As}$	^{72}As	5–14	231.0	^{71}As	0	0
$^{69}\text{Ga}(\alpha,n)^{72}\text{As}$	^{72}As	7–16	7.3	^{71}As	0	0
$^{75}\text{As}(p,4n)^{72}\text{Se}$	^{72}Se	42–65	31.5	^{75}Se	0.7	2.3
$^{75}\text{As}(p,4n)^{72}\text{Se}$	^{72}Se	46–65	29.3	^{75}Se	0.6	2.2
$^{75}\text{As}(p,4n)^{72}\text{Se}$	^{72}Se	50–65	25.2	^{75}Se	0.5	2.1

Among the direct production routes, the $^{72}\text{Ge}(\text{p},\text{n})^{72}\text{As}$ reaction provides by far the highest yield within the selected low-energy window. In the 5–14 MeV interval, an integral yield of 231.0 MBq $\mu\text{Ae}^{-1} \text{ h}^{-1}$ is obtained, while the formation of ^{71}As remains negligible within this energy window. This makes the enriched germanium route the most efficient direct route for producing ^{72}As with high radionuclidic purity at small- to medium-sized medical cyclotrons.

The $^{69}\text{Ga}(\alpha,\text{n})^{72}\text{As}$ route is also radionuclidically clean with respect to ^{71}As when restricted to the 7–16 MeV interval, below the relevant onset of the $(\alpha,2\text{n})$ channel. However, the calculated yield of 7.3 MBq $\mu\text{Ae}^{-1} \text{ h}^{-1}$ is substantially lower than for the proton-induced reaction on enriched ^{72}Ge . Although the selected energy interval is favorable with respect to radionuclidic purity, the lower yield and the requirement for an alpha-particle beam make this route less attractive for routine production.

For the indirect route, ^{72}Se is produced via the $^{75}\text{As}(\text{p},4\text{n})^{72}\text{Se}$ reaction. Three possible production windows were evaluated between 42 MeV and 65 MeV, 46 MeV and 65 MeV, and between 50 MeV and 65 MeV. The widest interval, 42–65 MeV, gives the highest ^{72}Se yield of 31.5 MBq $\mu\text{Ae}^{-1} \text{ h}^{-1}$, accompanied by a ^{75}Se yield of 0.7 MBq $\mu\text{Ae}^{-1} \text{ h}^{-1}$, corresponding to a $^{75}\text{Se}/^{72}\text{Se}$ activity ratio of approximately 2%. Narrowing the lower energy boundary to 46 MeV or 50 MeV reduces both the ^{72}Se and ^{75}Se yields, while the relative $^{75}\text{Se}/^{72}\text{Se}$ ratio remains approximately constant at about 2%. Thus, within the evaluated intervals, reducing the target thickness does not substantially improve the relative radionuclidic purity, but decreases the obtainable ^{72}Se activity.

For practical comparison, Table 7 gives example activities expected from the selected yield values for representative integrated charges. These values illustrate the production scale rather than a fixed optimized production protocol.

The direct $^{72}\text{Ge}(\text{p},\text{n})^{72}\text{As}$ route therefore provides the highest immediate ^{72}As activity per unit charge. Even moderate integrated charges result in GBq-scale ^{72}As activities, provided that enriched ^{72}Ge targets and suitable targetry are available. In contrast, the gallium alpha route gives substantially lower activities under otherwise comparable integrated-charge conditions.

Results & Discussion

Table 7: Example activities obtained from the production-window yields.

Production route	Product	Yield [MBq $\mu\text{Ae}^{-1} \text{h}^{-1}$]	Activity after 10 $\mu\text{Ae} \text{h}$	Activity after 100 $\mu\text{Ae} \text{h}$	Activity after 500 $\mu\text{Ae} \text{h}$
$^{72}\text{Ge}(\text{p},\text{n})^{72}\text{As}$	^{72}As	231.0	2.31 GBq	23.1 GBq	115.5 GBq
$^{69}\text{Ga}(\alpha,\text{n})^{72}\text{As}$	^{72}As	7.3	72.8 MBq	727.9 MBq	3.64 GBq
$^{75}\text{As}(\text{p},4\text{n})^{72}\text{Se}$, 42–65 MeV	^{72}Se	31.5	315 MBq	3.15 GBq	15.75 GBq
$^{75}\text{As}(\text{p},4\text{n})^{72}\text{Se}$, 46–65 MeV	^{72}Se	29.3	293 MBq	2.93 GBq	14.65 GBq
$^{75}\text{As}(\text{p},4\text{n})^{72}\text{Se}$, 50–65 MeV	^{72}Se	25.2	252 MBq	2.52 GBq	12.60 GBq

The indirect ^{72}Se route has to be evaluated differently. Its immediate product is not ^{72}As but the longer-lived parent ^{72}Se . After chemical separation of ^{72}As from ^{72}Se , daughter activity grows in again according to the parent-daughter relationship

$$A_{72\text{As}}(t) = A_{72\text{Se}}(t) \cdot \frac{\lambda_{72\text{As}}}{\lambda_{72\text{As}} - \lambda_{72\text{Se}}} (1 - e^{-(\lambda_{72\text{As}} - \lambda_{72\text{Se}})t}), \quad (3.3)$$

where $A_{72\text{As}}(t)$ is the daughter activity, $A_{72\text{Se}}(t)$ is the parent activity at the same time, and $\lambda_{72\text{As}}$ and $\lambda_{72\text{Se}}$ are the decay constants of ^{72}As and ^{72}Se , respectively. Because ^{72}Se has a substantially longer half-life than ^{72}As , the system approaches transient equilibrium. At transient equilibrium, the ^{72}As activity is approximately 1.15 times the remaining ^{72}Se activity:

$$A_{72\text{As}} \approx 1.15 \cdot A_{72\text{Se}} \quad (3.4)$$

The corresponding ingrowth fractions are shown in Table 8.

Table 8: Time dependent ingrowth of ^{72}As from a separated ^{72}Se parent.

Ingrowth time after ^{72}As separation	Activity ratio $A(^{72}\text{As})/A(^{72}\text{Se})$
24 h	0.49
48 h	0.77
72 h	0.93
96 h	1.02
120 h	1.08
transient Equilibrium	1.15

Thus, a $^{72}\text{Se}/^{72}\text{As}$ generator does not provide the full daughter activity immediately after separation. Instead, a substantial fraction of the available ^{72}As is regenerated within one to three days. For example, 1 GBq of ^{72}Se corresponds to approximately 0.49 GBq of ^{72}As after 24 h, 0.77 GBq after 48 h, and 0.93 GBq after 72 h. At transient equilibrium, the same parent activity corresponds to approximately 1.15 GBq of ^{72}As .

Concluding, the direct $^{72}\text{Ge}(p,n)^{72}\text{As}$ route is the most favorable option for high-yield direct production of ^{72}As in the investigated energy range. The $^{69}\text{Ga}(\alpha,n)^{72}\text{As}$ route is radionuclidically clean in the selected threshold window but limited in yield. The indirect $^{75}\text{As}(p,4n)^{72}\text{Se}$ route provides lower immediate activity per unit charge than the germanium route but offers the advantage of producing a longer-lived parent radionuclide from which ^{72}As can be repeatedly obtained after ingrowth. Its main radionuclidic-purity limitation is the co-production of ^{75}Se , which is chemically inseparable from ^{72}Se and cannot be sufficiently reduced by practical cooling times. Therefore, the direct and indirect routes address different production scenarios: immediate high-activity ^{72}As production is best served by the enriched germanium route, whereas the $^{72}\text{Se}/^{72}\text{As}$ approach is more relevant for generator-based availability and temporal decoupling of production from applications.

Altogether, the experimental excitation functions, thick-target yield and production yield estimates, and TALYS-2.0 sensitivity analysis establish the relevant production windows for ^{72}As or its ^{72}Se generator parent, while also clarifying the associated limitations in yield, radionuclidic purity, and model reliability. However, optimized production conditions alone are not sufficient for quantitative PET-related applications. Reliable decay data are equally essential, since quantities such as half-life and emission probabilities directly affect activity determination, image quantification, dosimetry, and the associated uncertainty budget. Therefore, the following chapter addresses the decay properties of ^{72}As and evaluates their relevance for its application as a PET radionuclide.

3.1.3. Decay characterization and implications for quantitative PET

While the previous section addressed how ^{72}As can be produced with suitable radionuclidic purity, the present section addresses the complementary question of how this radionuclide can be characterized quantitatively after production. In particular, the focus lies on decay properties that are relevant for interpreting positron-related signals in PET applications.

Quantitative PET applications require accurate positron emission data, therefore, the decay of ^{72}As was re-investigated using a dedicated multi-technique approach. In contrast to standard PET nuclides, ^{72}As exhibits a more complex decay scheme with multiple γ -rays and several positron branches, making precise characterization of the β^+/EC contributions non-trivial [8, 14, 21, 24, 25, 108]. For this reason, radio nuclidic pure ^{72}As produced via the $^{72}\text{Ge}(\text{p},\text{n})^{72}\text{As}$ reaction was analyzed by combining high-resolution γ & X-ray spectroscopy, annihilation-radiation analysis, and gross beta counting [23]. The central aim of this decay analysis was to determine the positron emission intensity experimentally and more reliably, to provide improved decay data for quantitative imaging applications.

Because meaningful decay analysis requires a well-defined radionuclide composition, the discussion first considers the extent to which the investigated ^{72}As samples can be regarded as sufficiently pure for subsequent annihilation, β -counting, and X-ray-based evaluation.

For decay analysis, it is of major importance, that a radionuclidically pure sample is used for other nuclides not to interfere with the quantification. Therefore, for decay analysis study, enriched ^{72}Ge samples are used for the production of ^{72}As via $^{72}\text{Ge}(\text{p},\text{n})^{72}\text{As}$ reaction resented in Section 3.1.2. To ensure a pure ^{72}As sample, only samples irradiated below the threshold energy of ^{71}As ($E_{\alpha} \approx 14 \text{ MeV}$) are used. Three samples employed for cross-section measurements are therefore suitable for decay analysis studies. These samples had been irradiated at proton energies of $9.3 \pm 0.3 \text{ MeV}$ (Sample 14), $8.3 \pm 0.3 \text{ MeV}$ (Sample 15), and $7.3 \pm 0.4 \text{ MeV}$ (Sample 16), respectively, at the Baby Cyclotron 1710 (BC1710).

The radionuclidic purity was confirmed by HPGe (high-purity germanium) γ -spectroscopy measurements of the samples. The γ -spectrum of a sample irradiated at

9.3 MeV proton energy is presented in Figure 21(A) in direct comparison to a spectrum of an unsuited target irradiated at 16 MeV (B). Most importantly, isotopic impurities like ^{71}As , ^{73}As and ^{74}As might cause unwanted X-ray distribution originating from excited germanium daughter nuclides as well as unwanted β -particle emission interfering with direct beta counting and annihilation studies. While ^{71}As and ^{74}As can be quantified by HPGe, readily, ^{73}As only possesses a low energy γ -line (53.4 keV) and is therefore challenging to quantify only using γ -spectroscopy with Fig. 21 not including this low energy region. However, since the half-life of ^{73}As (80.3 d) is reasonable long in comparison to ^{72}As combined with low (p, γ) cross-section (cs_{max} (5 MeV) = 16.7 mb) [49], its activity contribution is < 1% at irradiations above 7 MeV and is therefore within the margin of error estimated for X-ray spectroscopy.

Comparative activities of the three samples were determined using HPGe γ -spectrometry to quantify the positron emission probability.

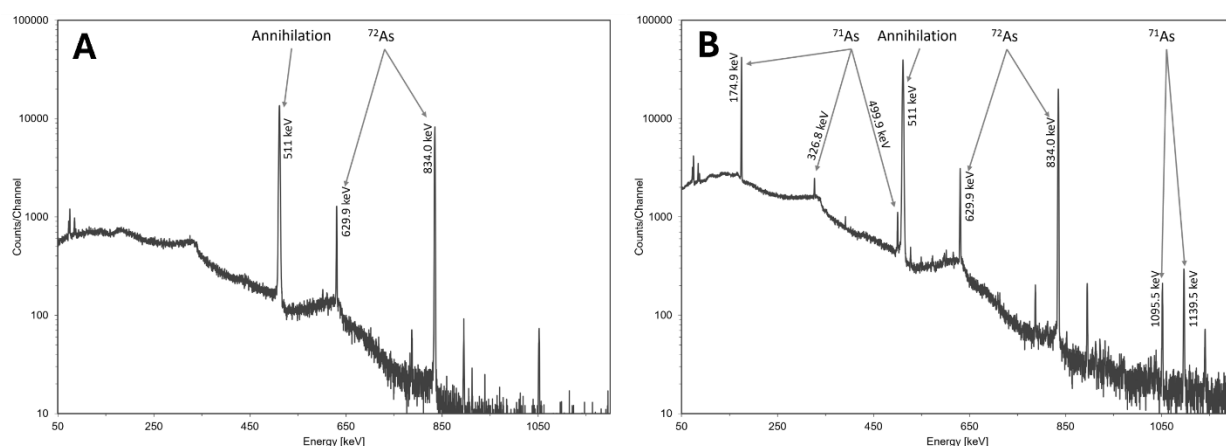


Figure 21: Comparison of HPGe spectra of sample 14 (irradiated at ~9 MeV) only containing ^{72}As (A) and sample 1 (irradiated at ~16 MeV) containing both ^{71}As and ^{72}As (B).

Annihilation measurements

For quantitative PET, the key question is not only how the decay scheme of ^{72}As looks in general, but which experimentally accessible observables can be used to relate the measured annihilation radiation to the total positron emission.

For this reason, the 511 keV annihilation signal was evaluated to confirm the positron-emitting origin of the produced activity and to assess whether the signal could be assigned predominantly to ^{72}As . The broad 511 keV peak and the manually selected integration regions are shown in Figure 22.

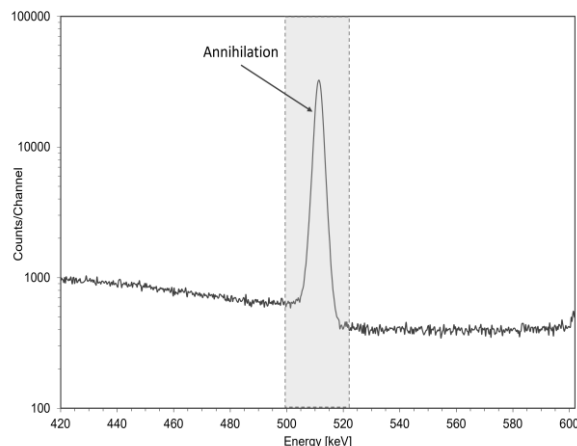


Figure 22: Annihilation peak (511 keV) of sample 14 placed inside an annihilation chamber.

After correcting for the minor contribution of ^{74}As from the small ^{74}Ge content in the target material (0.145%), the decay curve of the annihilation signal yielded a half-life of 26.0 ± 0.2 h. This agrees very well with the literature value and shows that the measured annihilation signal was dominated by ^{72}As . The resulting decay curve is shown in Figure 23. The annihilation-based activities at EOB were 212.8 kBq, 138.3 kBq, and 148.2 kBq for samples 14, 15, and 16, respectively.

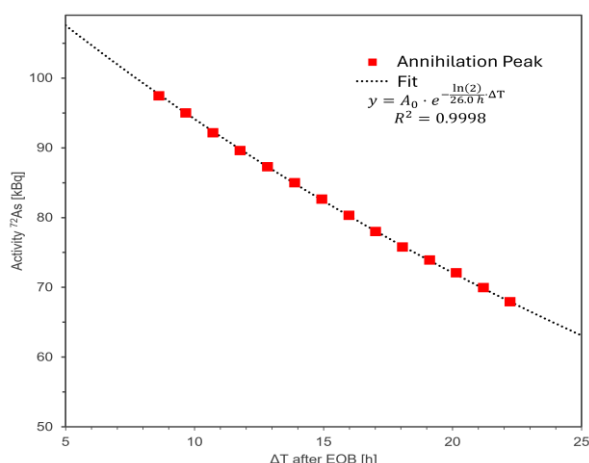


Figure 23: Decay curve obtained from annihilation measurement of sample 14, showing excellent alignment with the fitted decay curve of ^{72}As ($R^2=0.9998$ & RMSE (root mean square error) = 0.17).

X-ray measurements

A typical X-ray spectrum obtained from the samples investigated is shown in Figure 24. The spectrum exhibits the characteristic germanium K_α and K_β X-ray lines resulting

from the decay of ^{72}As to ^{72}Ge . The corresponding literature energies are 9.88 keV for the K_α group and 10.98 keV for the K_β group of germanium, with individual component intensities of $K_{\alpha 1} = 9.886$ keV (3.83%), $K_{\alpha 2} = 9.855$ keV (1.97%), $K_{\beta 1} = 10.982$ keV (0.49%), and $K_{\beta 3} = 10.975$ keV (0.25%), yielding a summed Ge K -X-ray intensity of 6.54% [109]. A weak peak observed at 23.4 keV was attributed to

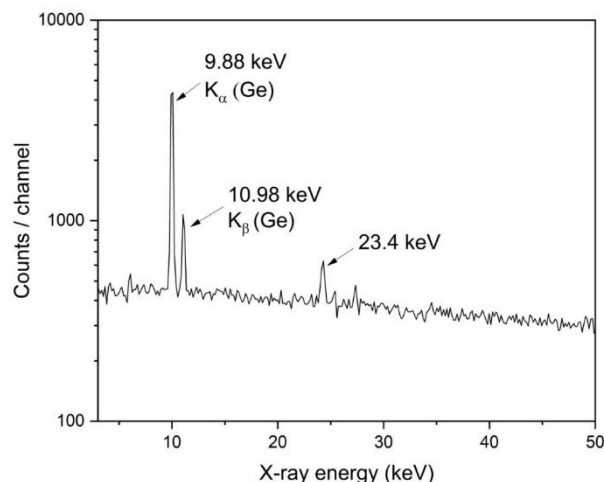


Figure 24: X-ray spectrum of a thin ^{72}As sample (sample 16) showing the two main X-ray lines of an arsenic/germanium system at 9.88 keV and 10.98 keV.

background noise. The EC-related activities at EOB derived from X-ray spectroscopy were 30.1 kBq, 20.7 kBq, and 22.8 kBq for samples 14, 15, and 16, respectively.

Beta-counting

The beta-counting data was evaluated to identify the different activity components contributing to the measured decay signal after EOB. In particular, decay-curve analysis allowed the ^{72}As contribution to be separated from longer-lived radionuclidic impurities.

The gross activity measured in the proportional counter decreased with decay time as shown in Figure 25. Analysis of the decay curve revealed the presence of a long-lived component with a fitted half-life of ~ 80 d, which was attributed to ^{73}As . After subtraction of this contribution, the remaining activity followed a significantly shorter half-life of 26.0 h, consistent with the decay of ^{72}As , as shown in Figure 26.

Although ^{74}As is also a positron emitter and may in principle contribute to the measured decay curve, its concentration in the present samples was too low to allow reliable quantification. Its contribution was therefore estimated to be below 1% relative to the ^{72}As activity. It should further be noted that ^{73}As decays exclusively by EC and does not emit positrons. Nevertheless, it was detected with very low efficiency in the

proportional counter, most likely due to ionization caused by its 53.4 keV γ -ray. Based on the calculated production from the $^{72}\text{Ge}(p,\gamma)$ reaction, the ^{73}As activity at EOB was expected to amount to about 0.2% of the ^{72}As activity, whereas the experimentally observed contribution was only about 0.01% due to low efficiency for weak γ irradiation.

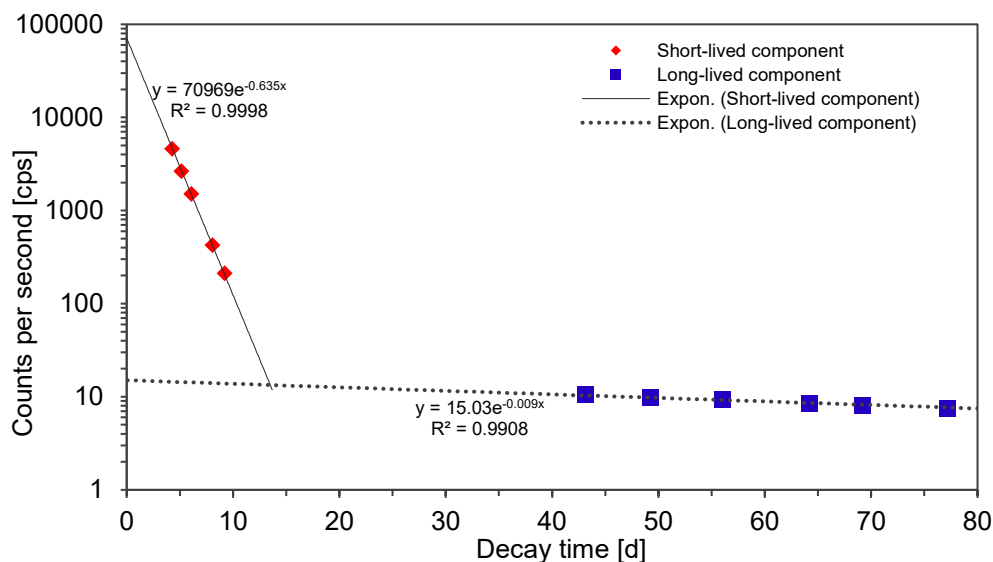


Figure 25: Beta-particle gross-count rate of enriched ^{72}Ge sample (sample 14) irradiated with 9.3 MeV protons. Showing the analysis of long-lived and short-lived components.

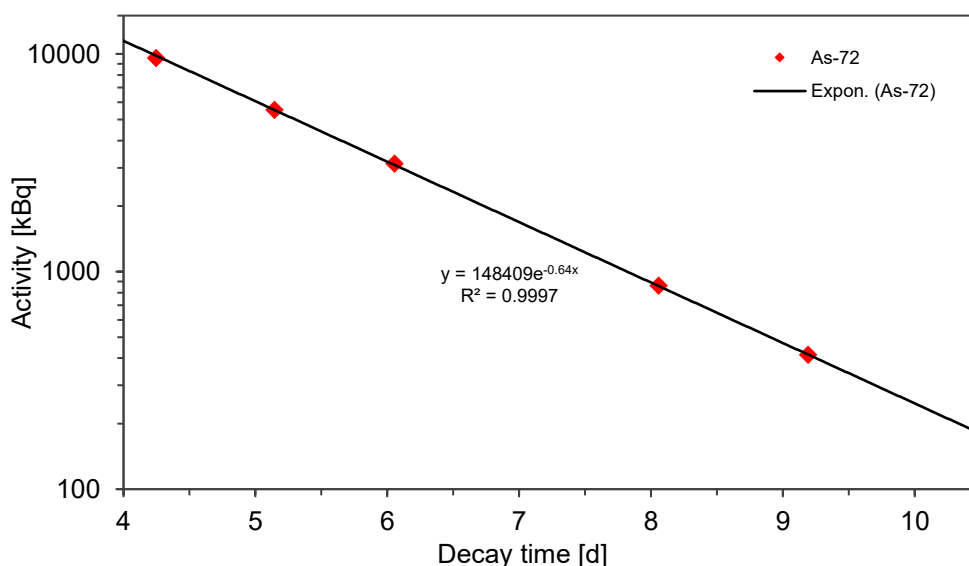


Figure 26: Plotted the activity of ^{72}As , after correction by the long-lived impurities and the detector efficiency (Section 3.4.3). The data is fitted exponentially and the half-life is calculated.

The fitted data in Figure 26 yielded an exponential equation $y = 148409 \cdot e^{-0.64 \cdot x}$. Using these equations, the half life of the plotted data can be calculated following Eq. (3.5–3.6):

$$y(x) = a \cdot e^{-b \cdot x} \quad (3.5)$$

$$T_{1/2} = \frac{\ln(2)}{b} \quad (3.6)$$

Here, a is the y -intercept, b is the decay constant λ in $1/d$ and x is the decay time in days.

The half-life of the measured ^{72}As was pinpointed to 26.0 h, perfectly matching the literature value [109]. From the y -intercept the EOB activity of the sample can be directly read out. This method, however, is prone to highly sensitive plotting of the data points. Therefore, the EOB activity was calculated manually using the previously determined detector efficiency. The data was then plotted using the calculated EOB activity as fixed y -intercept allowing a double check of the EOB activity via regression models like R^2 .

The activities at EOB derived from gross beta counting were 204.6 kBq, 136.1 kBq, and 148.4 kBq for samples 14, 15, and 16, respectively.

Decay data evaluation:

The values reported in the following are based on a re-evaluation of the original spectra. This re-analysis led to minor deviations from some previously published intermediate and final values reported by Hussain et al. [23]. For the present thesis, only results that could be reproduced consistently from the original spectra and the applied correction scheme were used. The overall conclusions, however, remain unchanged.

The positron emission probability of ^{72}As was determined from three enriched ^{72}Ge samples irradiated with protons at different energies using three independent counting approaches, namely beta counting, X-ray spectroscopy, and γ -spectrometric analysis of the annihilation radiation. The corresponding activities obtained at EOB are summarized in Table 9. The main method-specific uncertainty contributions considered

in the evaluation are summarized in Table 10. These contributions were considered in the propagation of the sample-specific uncertainties reported in Table 9. Error propagation for the final derived quantities was performed as described in Section 5.5.1.

Table 9: Radioactivity of ^{72}As (Bq) at EOB via four different techniques used in the three experiments. ^aAbsolute decay rates, corrected for emission intensity; ^bDecay rate without correction for emission intensity.

Experiment	Sample 14	Sample 15	Sample 16
Projectile Energy [MeV]	9.3 ± 0.3	8.3 ± 0.3	7.3 ± 0.4
γ -spectrometry [kBq] ^a	239.6 ± 10.2	157.8 ± 6.7	169.3 ± 7.2
Annihilation activity [kBq] ^b	212.8 ± 12.9	138.3 ± 8.4	148.2 ± 9.0
X-ray spectroscopy [kBq] ^b	30.1 ± 2.2	20.7 ± 1.5	22.8 ± 1.6
Beta-particle counting [kBq] ^b	204.6 ± 14.1	136.1 ± 9.4	148.4 ± 10.2

Table 10: Main uncertainty contributions considered for each spectroscopic method used for β^+ emission analysis.

Experiment	Peak area analysis %	Intensity of radiation counted (%)	Efficiency of the detector (%)	Absorption corrections (%)
γ -ray spectroscopy	1	1	4	<0.1
Annihilation counting	2	3.6	4	2
Beta-particle counting	2	3.7	5	3
X-ray spectroscopy	2	3.8	5	2

The absolute ^{72}As activity at EOB was obtained independently by γ -spectrometry using the 630 keV and 834 keV lines. The activities derived from annihilation counting, X-ray spectroscopy, and gross-beta counting were then related to this γ -based reference activity in order to determine the relative contributions of the β^+ and EC decay branches. The resulting positron emission probabilities are summarized in Table 11.

Results & Discussion

Table 11: Positron emission intensities derived from the three experiments.

Experiment	Sample 14 (9.3 MeV)	Sample 15 (8.3 MeV)	Sample 16 (7.3 MeV)	Weighted average
Annihilation activity	88.8 ± 6.6	87.7 ± 6.5	87.5 ± 6.5	88.0 ± 3.8
X-ray spectroscopy	87.4 ± 1.1	86.9 ± 1.1	86.4 ± 1.1	87.0 ± 0.6
Beta-particle counting	85.3 ± 6.9	86.3 ± 7.0	87.7 ± 7.1	86.4 ± 4.0
Overall representative value				87.1 ± 5.6
Abriola And Sonzogni (evaluated) [25]				87.8 ± 2.2

The positron activities derived from gross-beta counting and from analysis of the 511 keV annihilation radiation are in good agreement for all three samples, indicating good internal consistency of the applied approach. For the X-ray-based evaluation, the corrected K_α and K_β signal was converted to an EC-related activity by accounting for the fluorescence yield of germanium and the probability of EC from the K shell. Comparison of this EC-related activity with the absolute ^{72}As activity obtained by γ -spectrometry yielded an average EC contribution of about 13%, consistent with the corresponding β^+ branching derived independently from the positron-based methods.

The positron emission probabilities obtained from the three independent approaches agree well overall. For each counting method, a weighted average of the sample-wise branching ratios was used as a first estimate of the method-specific mean value. The resulting method-specific averages were $88.0 \pm 3.8\%$ for annihilation counting, $87.0 \pm 0.6\%$ for X-ray spectroscopy, and $86.4 \pm 4.0\%$ for beta counting. Since part of the uncertainty is common to all samples of a given method, these values should be regarded primarily as method-specific summary values. As an overall representative result across the three approaches, a mean positron branching ratio of $87.1 \pm 5.6\%$ was obtained, where the quoted uncertainty reflects the spread between methods rather than a full combined absolute uncertainty. This value is in good agreement with the evaluated literature value of $87.8 \pm 2.2\%$ [30]. Taken together, these results confirm the accepted β^+ and EC branching ratios of ^{72}As and provide an independent experimental verification based on direct measurement of the emitted radiation rather than solely on evaluation of the decay scheme.

Accurate branching data are directly relevant for quantitative PET, because of the conversion of measured annihilation events into activity scales with the adopted positron emission probability. In the case of ^{72}As , the present measurements confirm that this source of systematic uncertainty is small and remains at approximately the percent level. Nevertheless, for applications requiring more accurate dosimetry, the present measurements provide additional confidence in the decay data of this radionuclide.

Overall, the present results confirm the accepted β^+ and EC branching ratios of ^{72}As and provide an independent experimental verification based on direct measurement of the emitted radiation. Together with the production data discussed above, they establish the basis required for a realistic assessment of ^{72}As as a non-standard positron emitter. The following part of this thesis therefore shifts to a different but complementary translational challenge, namely the production-oriented handling of ^{211}At , from irradiated target material to a chemically usable product.

3.2. Production and Processing of ^{211}At

In the case of ^{211}At , the central limitations are not primarily related to decay characterization, but to the establishment of robust target preparation, irradiation stability, processing, and product control under production-relevant conditions. The following sections therefore focus on the practical evaluation of ^{211}At production and handling.

3.2.1. Targetry, irradiation performance, and production quality of ^{211}At

The ^{211}At -related discussion starts with the production itself. The key questions are whether the investigated target concepts remain stable under irradiation, how relevant local heat deposition becomes for target performance, and which production conditions influence the balance between yield and radionuclidic purity.

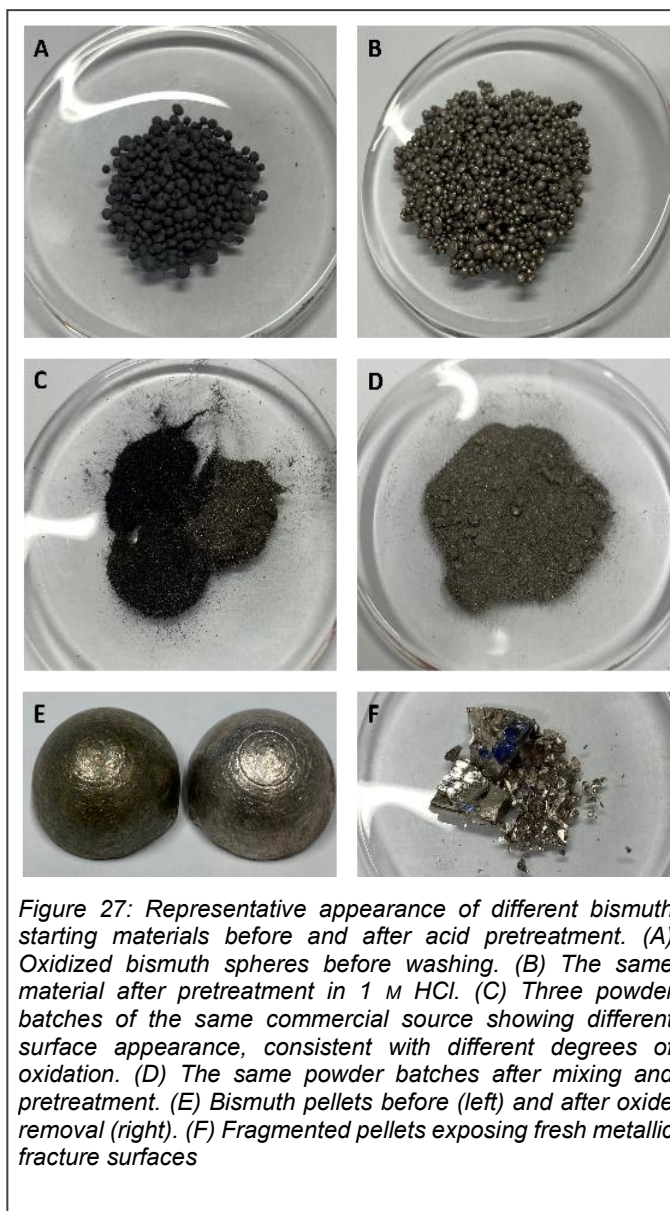
Target material pretreatment

Prior to target preparation, noticeable differences in the appearance of the starting bismuth material were observed, particularly for powders and small beads, indicating varying degrees of surface oxidation. This effect was much less pronounced for compact pellets and was not relevant for target preparations including commercially available foils, electrodeposition and sedimentation, comprising dissolution of bismuth or bismuth(III)-nitrate.

A brief washing step in 1 M HCl reproducibly removed the dull oxide layer and restored the metallic appearance of the material, as illustrated in Figure 27. The associated mass loss depended strongly on the morphology of the starting material and was highest for bismuth powder (ca. 6 mg per 100 mg), followed by spheres (ca. 2 mg per 100 mg), while compact pellets showed only minor losses (<1 mg per 100 mg). These observations are consistent with the expected increase in oxide fraction with increasing

specific surface area. The pretreatment was therefore particularly relevant for powder-based pressed- and molten target preparation, whereas for larger chunks used in later pressing and melting experiments, surface oxidation became less critical because the material was either crushed immediately before use or melted directly and the oxide-rich slag could be removed mechanically.

After oxide removal, the sample stayed visibly free of surface oxide for at least one month stored under air atmosphere before showing slight return of color shift of bismuth powder.



Target production

For target production, the first aspect to be addressed is the target concept itself, since the achievable production performance depends not only on the nuclear reaction but also on whether the bismuth layer remains mechanically and thermally stable during irradiation.

Several target preparation routes were investigated in order to identify a suitable approach for the production of bismuth targets for ^{211}At production. The evaluated methods covered both rather simple strategies that are often suitable for first feasibility tests layers as sedimentation or the use of commercially available foil, and more

application-oriented concepts such as pressed or sintered targets, molten bismuth layers, and electrodeposited layer. In principle, all five approaches allowed the preparation of targets that were sufficiently stable to be tested in first irradiation experiments. At the same time, clear differences became apparent with regard to achievable areal density, mechanical stability, reproducibility, ease of preparation, and the expected behavior under beam load. To obtain an initial comparison under controlled conditions, all target types were therefore first subjected to low-current irradiation before moving on to more demanding production experiments.

Low current irradiation:

As a first screening step, all five target preparation methods were irradiated under low-current conditions (1 μA_e , 5–20 min). The purpose of these measurements was to establish a common basis for comparing production yield and basic thermal stability, while keeping the thermal load sufficiently low to avoid immediate exclusion of otherwise promising target concepts. In this way, pronounced weaknesses could already be identified before entering the actual scale-up stage.

The results of these low-current irradiations are summarized in Table 12. With the exception of the sedimentation target, all target types gave production yields in a comparatively similar range between 17.8 and 32.4 MBq $\mu\text{A}_e^{-1} \text{ h}^{-1}$. The sedimentation target, in contrast, reached only 0.6 MBq $\mu\text{A}_e^{-1} \text{ h}^{-1}$. However, this direct comparison must be interpreted with some caution, since both the sedimentation and the electrodeposition targets were substantially thinner than the other target types. As a result, only part of the available energy window of the $^{209}\text{Bi}(\alpha, 2n)^{211}\text{At}$ reaction was effectively used in these two cases. For the sedimentation and electrodeposition targets, the accessible energy intervals were only about 1.1 MeV and 2.4 MeV, respectively, whereas the melted, sintered, and foil targets covered the full relevant depth⁴. Using these reduced energy intervals, the corresponding literature integral yields were calculated to be approximately 8.8 MBq $\mu\text{A}_e^{-1} \text{ h}^{-1}$ for 30–29 MeV and 23.7

⁴ For bismuth targets irradiated with α particles of up to 30 MeV, the effective production window is limited to approximately 30–20 MeV, where the lower boundary corresponds to the threshold of the $^{209}\text{Bi}(\alpha, 2n)^{211}\text{At}$ reaction.

MBq $\mu\text{A}_e^{-1} \text{h}^{-1}$ for 30–27.5 MeV. Based on these values, the experimentally obtained yields of the sedimentation and electrodeposited targets can be roughly extrapolated by correcting for the reduced production fraction of the covered energy range (22% and 58%, respectively). This results in approximate normalized yields of 2.8 MBq $\mu\text{A}_e^{-1} \text{h}^{-1}$ for the sedimentation target and 37.6 MBq $\mu\text{A}_e^{-1} \text{h}^{-1}$ for the electrodeposited target, which should be understood as orientation values corrected for the covered energy interval rather than as strictly comparable absolute production yields. Even after such correction, the sedimentation target remains clearly inferior to the other preparation routes. This is in line with the expected limitations of this target type, since the deposited material is comparatively soft and porous and, due to the use of $\text{Bi}(\text{OH})_3$, also contains a lower effective bismuth density.

Table 12: Production yield of different target preparation methods at 1 μA_e irradiation normalized by integrated current. For thin targets obtained by sedimentation and electrodeposition, a production range normalization is conducted according to the production ratio of the present energy range. Production ratio is calculated using recommended yield data from IAEA [38].

Target	Energy range [MeV]	Production ratio(E) [%]	Int. current [$\mu\text{A}_e\text{h}$]	A(^{211}At) EOB [MBq]	Yield [MBq $\mu\text{A}_e^{-1}\text{h}^{-1}$]	Corrected yield [MBq $\mu\text{A}_e^{-1}\text{h}^{-1}$]
Electro plated	30–27.6	50	0.17	3.2	18.8	37.6
Sediment	30–28.9	22	0.33	0.2	0.6	2.8
Foil	30–0	100	0.17	4.8	28.2	28.2
Melting target	30–0	100	0.17	5.5	32.4	32.4
Sinter	30–0	100	0.08	1.4	17.8	17.8

A second important observation from this first screening concerned the commercially available foil target. Although its measured yield was within the range of the other compact target types, visible surface melting was already observed after low-current irradiation. This behavior is likely not primarily a consequence of the bismuth material itself, but rather of the chosen holder geometry and cooling arrangement. In contrast to the other target concepts, the foil target and the sedimentation target were irradiated in a 90° copper target holder with indirect water cooling. In this design, heat first had to be transferred from the target material into the holder before it could be removed by the cooling water. Additional thermal contact resistance at this interface likely reduced the overall cooling efficiency. Moreover, the foil was considerably thicker than required for the relevant production depth. The excess bismuth layer therefore did not contribute

to ^{211}At formation, but instead likely increased the thermal resistance of the assembly because of the comparatively poor thermal conductivity of bismuth.

Taken together, the low-current screening has already narrowed down the number of practically relevant target concepts. Based on the observed production performance and the first indications of thermal behavior, only the electrodeposited, sintered, and molten targets were selected for the subsequent high-current irradiation studies.

Production scale-up

After this initial screening, the three remaining target concepts were evaluated under increasingly demanding irradiation conditions. For this purpose, irradiation times of 5–10 min were used while the beam current was gradually increased up to 50 μA_e . The electrodeposited and molten targets were tested in the established 6° target configuration, whereas the sintered targets had to be mounted in a coin-type geometry because the pressing procedure was limited to simple pellet shapes. Since these geometries differed substantially in their irradiated area, the applied beam current was normalized to the target surface and is therefore discussed in terms of $\mu\text{A}_e \text{ cm}^{-2}$. As a practical indicator of target integrity during irradiation, the vacuum stability of the cyclotron was monitored. Pronounced vacuum deterioration was taken as a sign of thermally induced target degradation, for example due to local melting, decomposition, or release of gaseous species.

Under these conditions, both the electrodeposited and the molten targets remained stable up to the maximum tested current of 50 μA_e , corresponding to about 2.5 $\mu\text{A}_e \text{ cm}^{-2}$. The sintered targets behaved very differently. In this case, irradiation had to be stopped already above 5 μA_e ($\sim 1.6 \mu\text{A}_e \text{ cm}^{-2}$) because of strong vacuum deterioration. The corresponding post-irradiation appearance is shown in Figure 28. This behavior points toward insufficient thermal robustness of the sintered target assembly.

A plausible explanation is an increased thermal contact resistance between the aluminum backing and the pressed bismuth pellet. Since the pellet was introduced as a mechanically pre-formed body, microscopic voids and incomplete surface contact are very likely to remain at the interface. In this respect, the sintered target resembles

the previously discussed foil target, where inefficient heat transfer also appeared to limit the usable irradiation conditions. Such an interpretation is well in line with the general literature on metallic interfaces, where mechanically pressed, dry contacts are known to exhibit significantly higher thermal contact resistance than metallurgically bonded interfaces. In contrast, reflowed metallic layers or well-developed sintered joints usually allow more efficient heat transfer across the interface [110–112]. In addition, the sintered pellets could not simply be made arbitrarily thin, since a minimum thickness of roughly 200–300 μm was needed to retain sufficient mechanical stability during preparation and mounting. This additional inactive bismuth thickness likely further increased the thermal resistance of the target system.

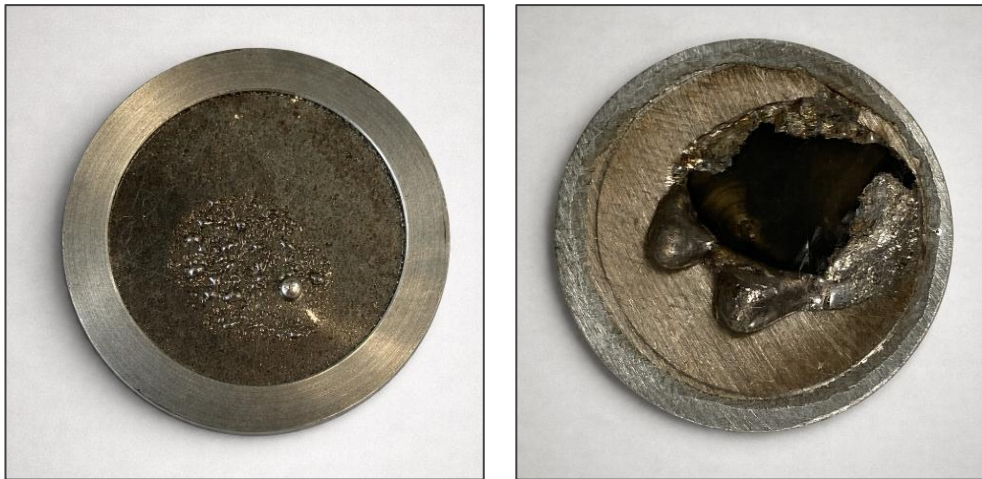


Figure 28: Photographs of coin targets prepared via sinter target method at medium current irradiation, showing thermal failure at currents below 5 μA_e . These photographs are visually cleaned. The original photographs are shown in the appendix in Figure B-1.

In principle, these limitations might be improved by refining the preparation route, for example by applying higher pressing forces, enabling thinner, yet mechanically stable pellets, introducing hot pressing, or further optimizing the sintering parameters. However, such modifications would have required considerable additional technical development and were outside the scope of the present work. For this reason, the sintered target approach was not pursued further in the subsequent production scale-up.

A more practical comparison between the two remaining target concepts, namely electrodeposited and molten targets, was therefore extended beyond simple current endurance and included post-irradiation handling, dry-distillation behavior, and practical target recovery. Both target types were examined visually for macroscopic defects and were additionally characterized by HPGe γ -spectrometry with regard to radionuclidic purity. In both cases, the bismuth layer thickness was determined gravimetrically to be approximately 30 μm . At an incident angle of 6° , this thickness should in principle be sufficient to stop the incoming alpha particles completely within the bismuth layer. A direct comparison of both target types is shown in Figure 29, where the photographs of the targets are presented in Figure 29 (A, B) and the corresponding HPGe γ -spectra in Figure 29 (C, D). On visual inspection, both targets appeared largely intact and homogeneous. No obvious signs of local melting, delamination, or cracking were observed. The γ -spectra, however, revealed a clear difference between the two preparation routes.

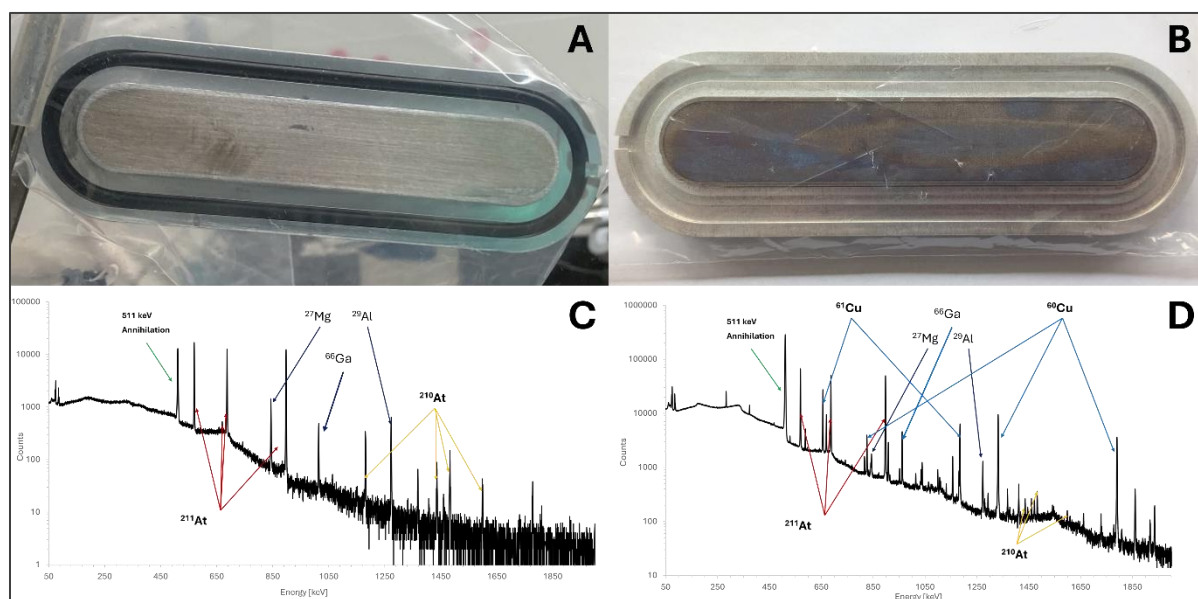


Figure 29: Presenting photographs of electrodeposited targets (A) and molten targets (B) after 1 h irradiation showing basically no visible target disintegration. Furthermore, the HPGe spectra of electrodeposited- (C) and molten targets (D) is depicted showing the key γ lines emitted by ^{211}At and ^{210}At as well as impurities originating from undesired aluminum irradiation (^{27}Mg , ^{29}Al and ^{66}Ga). For the electrodeposited target, additional impurities (^{60}Cu and ^{61}Cu) are visible.

For the electrodeposited target, activation products originating from the nickel underlayer were clearly visible, most prominently ^{60}Cu and ^{61}Cu . If the stopping power

calculations are correct, such radionuclides should not be formed in appreciable amounts, since the alpha beam should be fully stopped within the bismuth layer. Their presence therefore strongly suggests that at least part of the incident beam reached the nickel strike layer. The most direct explanation would be local thickness variations in the bismuth deposit, producing thin regions through which alpha particles could partially penetrate. This interpretation appears particularly plausible for ^{61}Cu , since the threshold of the $^{58}\text{Ni}(\alpha, p)^{61}\text{Cu}$ reaction is only 3.3 MeV, and additional cumulative formation of ^{61}Cu may occur via short-lived ^{61}Zn produced in $^{58}\text{Ni}(\alpha, n)$ reactions. The observation of ^{60}Cu is more difficult to explain in this way, since the relevant reaction thresholds are considerably higher, namely 15.7 MeV for $^{58}\text{Ni}(\alpha, pn)^{60}\text{Cu}$ and 13.4 MeV for $^{58}\text{Ni}(\alpha, d)^{60}\text{Cu}$ [113]. Its formation would therefore require either even thinner effective bismuth regions or an additional mechanism that places nickel closer to the irradiated surface.

One possible explanation, although not proven by the present data, could be partial intermixing at the Bi/Ni interface during electrodeposition [114]. From a chemical point of view, this would not be implausible, since the Ni-Bi system is known to form intermetallic phases, and interdiffusion as well as NiBi_3 formation have been reported for Bi/Ni interfaces [115]. Still, the present results do not allow direct proof of such a mixed interfacial layer, and this interpretation therefore remains tentative.

Besides the purity aspect, these impurities also had a direct practical consequence for handling. The additional activation products noticeably increased the radiation exposure associated with the electrodeposited targets. Measured 20 min after EOB, the dose rate at a distance of 30 cm was approximately 1.2 mSv h^{-1} for the electrodeposited target, compared with $260 \mu\text{Sv h}^{-1}$ for the molten target. At contact, the corresponding values were about 9.8 mSv h^{-1} and 3.2 mSv h^{-1} , respectively. These results show that electrodeposited targets can indeed perform well with respect to apparent thermal stability and projected yield but also illustrate that the overall target concept still requires substantial optimization regarding radionuclidic purity and radiation safety. Although promising, the electrodeposition route was therefore not taken further into the later production scale-up of the present study.

The molten targets, in contrast, showed no visible degradation after irradiation and produced only minor additional activation products in the HPGe spectra. These were

mainly assigned to the aluminum backing including miniscule copper-traces of the target assembly (^{27}Mg , ^{29}Al , ^{66}Ga), rather than to the target concept itself. Based on this combination of thermal robustness, practical handling, and radionuclidic purity, the molten-target approach was selected for the subsequent scale-up work.

This scale-up was then explored over a period of approximately one year using close to 100 irradiations with the molten-target design. Irradiation times ranged from only 3 min up to full 4 h production runs, corresponding to integrated beam charges of 3.8–212.9 μAe h. Across this range, reproducible production values between 25–36 MBq $\mu\text{Ae}^{-1} \text{ h}^{-1}$ were obtained. Using short irradiations below 8 min, the thick-target yield was determined to be 32.9 MBq $\mu\text{Ae}^{-1} \text{ h}^{-1}$. From this value, a saturation yield of approximately 342 MBq μAe^{-1} was estimated, corresponding to a saturation activity of about 17.1 GBq for irradiation at 50 μAe . This is in reasonable agreement with literature data. Lebeda et al. [116] reported an average of 395 ± 24 MBq μAe^{-1} saturation yield for an internal target system, whereas Gagnon et al. [35] reported saturation yields of up to 241 ± 17 MBq μAe^{-1} at 29.0 MeV for an external target system. In view of the target configuration and beam energy applied in the present work (29.3 ± 0.3 MeV), the obtained values are therefore in overall good agreement with literature reports.

On this basis, theoretical production values for longer irradiations (> 30 min) were calculated and compared with the experimentally measured activities after correction for beam-current fluctuations. The comparison is shown in Figure 30, while the corresponding experimental ^{211}At activities are summarized in Table 13.

Table 13: Saturation Yields determined for irradiation times between 2 and 5 h irradiation times additionally normalized to 50 μAe current to correct for small current fluctuations.

Duration [h]	Integrated current [μAe h]	Average current [μAe]	Activity EOB [GBq]	Activity (Corr. For 50 μAe) [GBq]
2.1	100	48.4	2.87	2.97
3.6	150	42.3	4.18	4.95
4.6	200	43.8	5.68	6.48
5.0	200	40.3	5.37	6.67
4.1	160	38.9	4.20	5.40
4.2	213	51.1	5.65	5.52
3.9	200	50.9	5.43	5.34

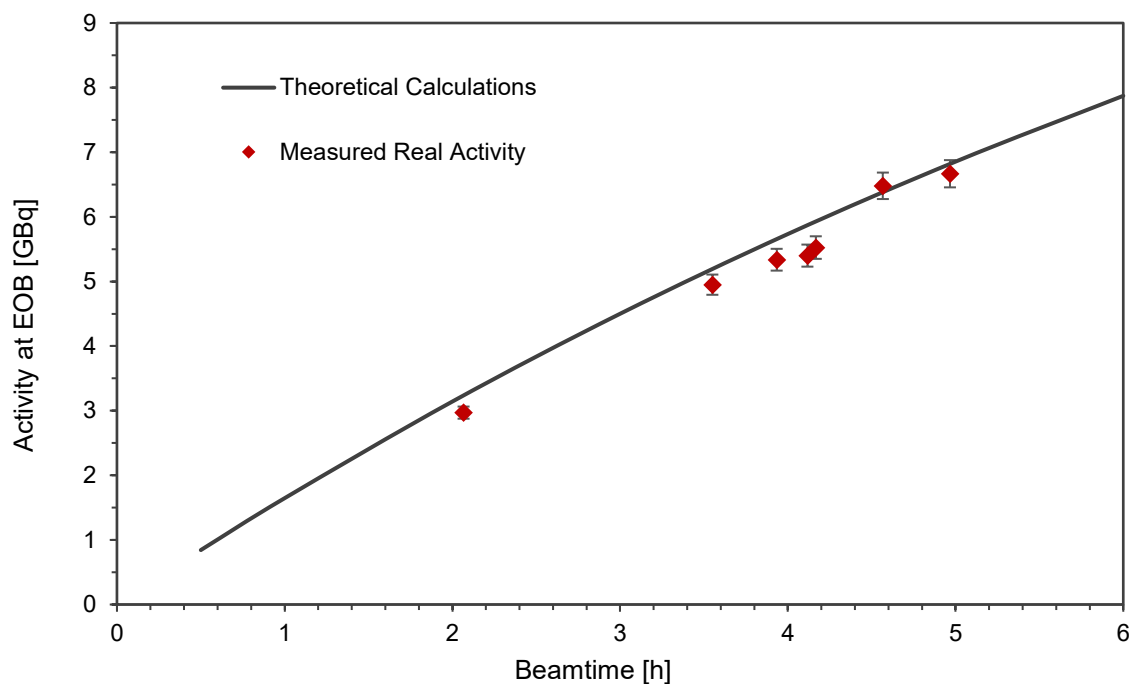


Figure 30: Saturation curve of ^{211}At production in dependence on the irradiation time. The beam current was normalized to $50\ \mu\text{A}_e$ to correct for small current fluctuations.

Overall, the agreement between predicted and measured activities was good. None of the experimental values deviated by more than 8% from the theoretical expectation. Even so, the measured activities were in most cases slightly lower than the calculated values. This systematic tendency suggests that, besides the expected influence of saturation and decay during longer irradiations, an additional minor loss mechanism may be present. One plausible explanation would be the partial evaporation of volatile ^{211}At species during beam exposure. In addition, Figure 31 shows slight beam-patterned abrasion after 4 h irradiation, which indicates some localized surface loss in the irradiated area and may point toward beam-induced erosion or sputtering-related effects. However, since the deviations remained small throughout the investigated operating range, these effects do not challenge the general suitability of the molten-target concept.



Figure 31: Photograph of a target prepared by melting technique after a 4 h irradiation showing slight abbreviation on the target surface roughly resembling the beam shape footprint. The photograph is edited to increase visually while maintaining radiation protection. The original photograph is shown in the appendix in Figure B-1.

Since the molten target concept was based on an AlMg3 backing rather than on high-purity aluminum, an additional question was whether the alloying constituents could give rise to relevant long-lived activation products. This aspect is particularly relevant for routine production workflows, since residual long-lived activation products in the spent target assemblies would directly affect post-irradiation handling, interim storage and radioactive-waste management. Prompt post-irradiation spectra had already shown minor short-lived activation products, mainly assigned to ^{29}Al , ^{27}Mg and ^{30}P . These radionuclides are expected from irradiation of aluminum- and magnesium-containing backing material or associated target components, but their half-lives are only in the range of a few minutes. Consequently, they affect mainly the immediate post-EOB dose situation and early handling but are not expected to contribute significantly to long-term residual activity.

To experimentally verify this assumption, one irradiated molten target on an AlMg3 backing was remeasured by HPGe γ -spectrometry approximately five months after irradiation. The resulting spectrum is shown in Figure 32. At this delayed time point, the previously observed short-lived radionuclides had fully decayed within the practical sensitivity of the measurement. The spectrum was dominated by γ -emissions attributable to ^{207}Bi , while no relevant additional long-lived γ -emitting activation products assignable to the AlMg3 backing were observed above background.

The delayed spectrum should therefore be interpreted as a practical radiation-safety screening rather than as a complete activation analysis. Within this scope, the residual activity was dominated by ^{207}Bi associated with the irradiated bismuth target material,

while no additional long-lived γ -emitting products from the AlMg3 backing were detected at a level that would be expected to affect handling or storage.

This result supports the interpretation that the use of AlMg3 as backing material does not introduce a significant long-lived γ -emitting impurity inventory under the irradiation conditions applied in this work. The observation is also consistent with the prompt spectra, where backing-related products were mainly short-lived and therefore relevant only during the early handling phase after EOB. It should be noted, however, that the delayed HPGe measurement does not exclude all possible activation products in an absolute sense. In particular, radionuclides without sufficiently intense γ emissions, very low-level activities below the detection sensitivity, or pure alpha/beta emitters would not be fully assessed by this approach. Nevertheless, for the practical question addressed here, namely whether AlMg3 gives rise to measurable long-lived γ -emitting activation products that would complicate target handling, storage or radiation protection, the delayed measurement provides no indication of a relevant additional contribution.

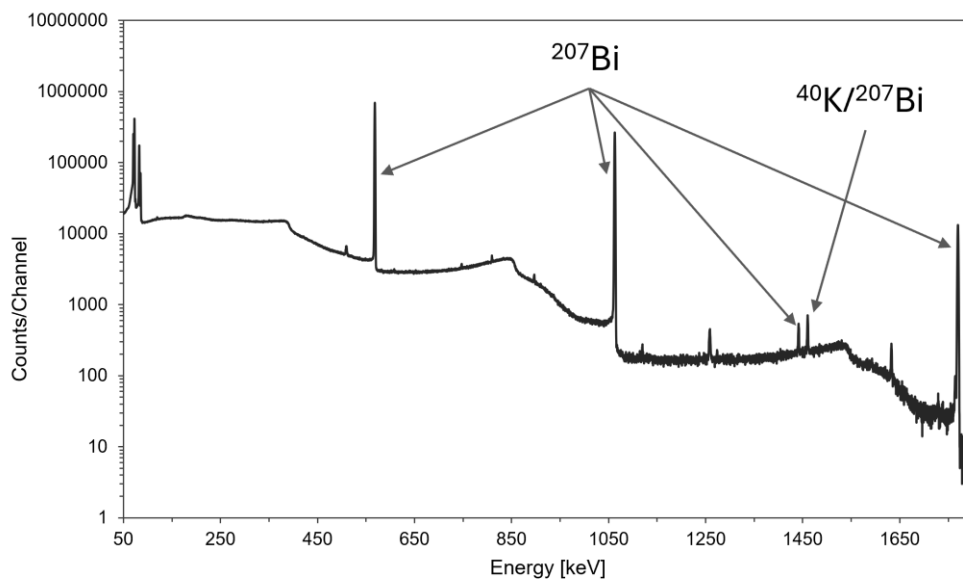


Figure 32: Delayed HPGe γ -spectrum of an irradiated molten bismuth target on an AlMg3 backing measured approximately five months after EOB. The spectrum is dominated by characteristic ^{207}Bi γ emissions. The peak at approximately 1460 keV is assigned to an overlap of environmental ^{40}K and weak ^{207}Bi -related emission. Only minor additional peaks were observed, which did not indicate a relevant long-lived γ -emitting activation inventory attributable to the AlMg3 backing.

In combination with the low post-irradiation dose rates observed for molten targets, the absence of detectable long-lived backing-derived γ -emitters further supports the suitability of the AlMg3-backed molten bismuth target design for repeated high-current ^{211}At production.

In summary, the molten target approach enabled reliable production scale-up of ^{211}At to clinically relevant activity levels. Activities of up to about 5.6 GBq ^{211}At at EOB were obtained in 4 h irradiations, while the targets remained sufficiently stable under the applied irradiation conditions.

Beam profile and Wobbler tests

Optimization of production yield and thermal stability does not depend solely on the target composition. The beam footprint and the intensity distribution across the target surface are equally important. An inhomogeneous beam intensity distribution may create local hot spots, thereby substantially increasing the local target temperature. Likewise, a strongly focused beam reduces the effective irradiated area and increases the local power density, counteracting the advantage of the shallow beam incidence angle and the enlarged artificial surface area. In contrast, an excessively broad beam may extend beyond the actual target area and irradiate parts of the adjacent aluminum ring, resulting in beam loss and, consequently, a reduced production yield. For this reason, a beam profile analysis was carried out using the molten target assembly.

After decay of ^{211}At to negligible levels, i.e. one week after EOB, the target activity is dominated by ^{207}Bi in the range of a few kBq. This activity level is well suited for investigation by phosphor imaging, providing a spatial distribution of the residual activity that can be used as a proxy for the relative EOB activity distribution.

The beam profile measured for a 1 h irradiation at $50\text{ }\mu\text{A}_e$ and 10% wobbler intensity is shown in Figure 33. The beam-affected area was approximated using the 80% intensity contour (red ellipse) and projected onto the actual target area (grey). Based on this approximation, a beam area of 9.75 cm^2 was calculated, corresponding to an area length of 73 mm and a width of 17 mm.

Notably, the beam footprint is slightly shifted toward the beam-facing side of the target. This shift originates from a modified backing geometry introduced to improve mechanical stability. Under the present irradiation conditions, the effect is considered minor, since the beam footprint remains well within the active target area. Its relevance increases, however, for broader beam profiles at higher wobbler intensities.

In the original target design, using a backing thickness of 0.5 mm instead of the modified 1.0 mm, the high cooling-water pressure ($\sim 20\text{ bar}$) caused deformation of the aluminum backing, thereby compromising the integrity of the bismuth layer deposited on top.

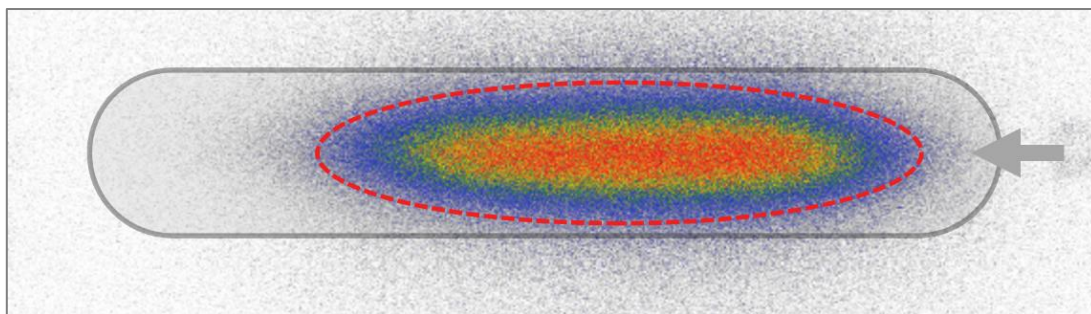


Figure 33: Beam profile for 10% Wobbler intensity. The beam direction is illustrated by the arrow.

The beam area, as well as the spatial intensity distribution, can be manipulated by applying artificial beam wobbling. In this study, the influence of this beam manipulation on both the beam profile and the production yield was investigated. Beam profiles and production yields from 1 h irradiations at 50 μA_e using 20–40% wobbler intensities were compared with nominal standard wobbler intensity of 10%. The corresponding production yields and beam areas as a function of wobbler intensity are summarized in Table 14.

The irradiation performed at 40% wobbler intensity exhibited comparatively poor beam stability, resulting in a significantly lower average beam current of only $\sim 38 \mu\text{A}_e$. Notably, even after normalizing the production yield to the beam current, the irradiation at 40% wobbler intensity still showed a distinctly lower yield, indicating that additional beam loss mechanisms are likely involved.

Table 14: Production yield and beam area ($\sim 95\%$ activity) in relation to the wobbler intensity during irradiation.

Wobbler [%]	Beam time [min]	Avg. beam current [μA_e]	Production yield [$\text{MBq } \mu\text{A}_e^{-1} \text{ h}^{-1}$]	Beam area [cm^2]
10	61	50.0	31.4	9.8
20	61	50.8	29.5	10.1
30	63	50.0	28.8	11.5
40	60	37.5	21.6	13.5

Figure 34 shows the beam footprints obtained at 20–40% wobbler intensity. With increasing wobbler intensity, the beam shape becomes progressively more distorted, changing from a roughly elliptical profile to a pattern resembling two partially overlapping ellipses at 20% and 30%. At 40%, the beam footprint expands further in

length and appears to exceed the actual target area, which is consistent with additional beam spill-over and a corresponding loss in production efficiency.

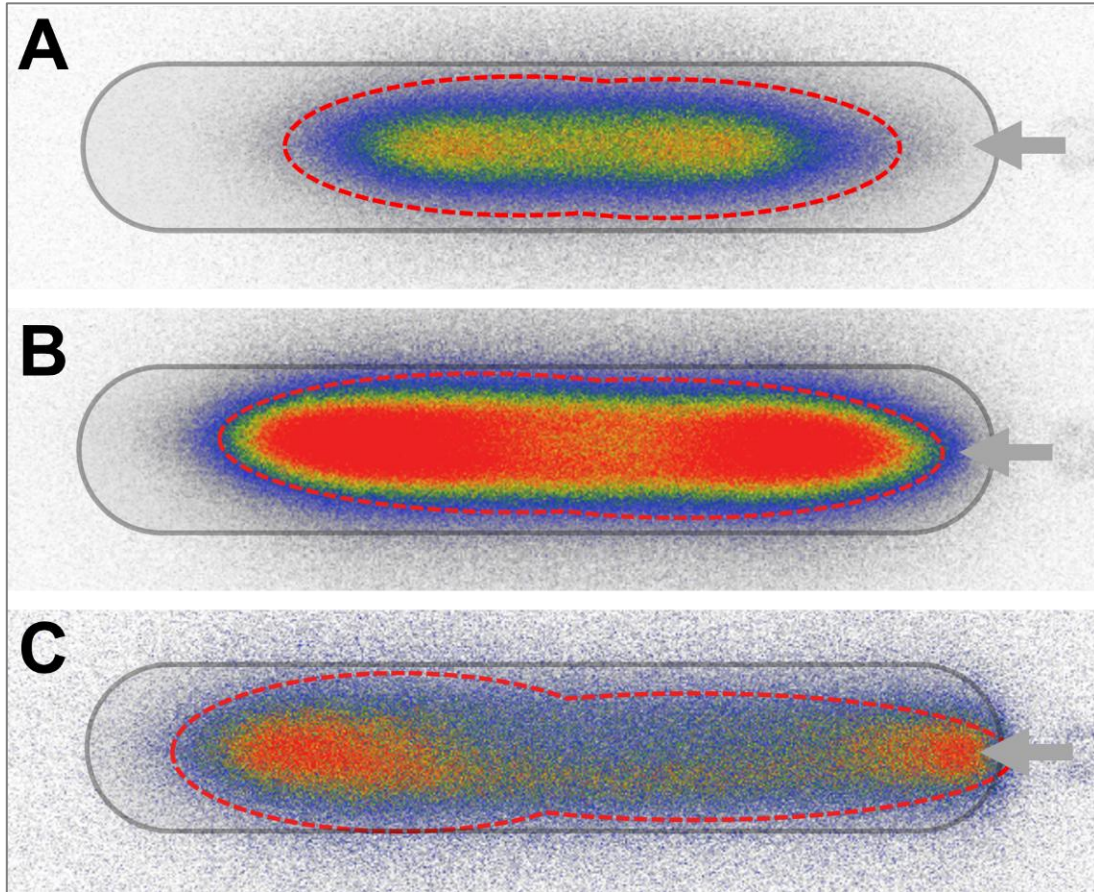


Figure 34: Beam profile of 20% (A), 30% (B) and 40% (C) wobbler intensities. The apparent differences in signal intensity are attributed to different exposure times of the phosphor imaging plate.

Although the beam area increases with increasing wobbler intensity, which would be expected to reduce the local power density q'' , the production yield decreases continuously. Within the investigated parameter range, this indicates that beam broadening and partial beam spill-over have a stronger influence on the production yield than any benefit arising from a reduced local power density. A more detailed thermal interpretation is discussed in the following section.

Thermal calculations

To interpret the observed target behavior more mechanistically, the thermal coupling between bismuth and aluminum has to be considered explicitly, since poor interface contact is expected to enhance local overheating and thereby promote target failure.

The thermal stability of the investigated bismuth targets was evaluated by combining experimentally determined interfacial heat-transfer properties with spatially resolved post-irradiation activity distributions. In this way, the influence of beam shaping, local power density, and heat removal on the resulting temperature profile could be assessed under irradiation-relevant conditions. The following section presents the experimentally derived thermal boundary conditions, the reconstructed power-density distributions, and their implications for target stability.

Thermal contact resistance measurements

The thermal contact resistance was evaluated for two target preparation routes, i.e. molten and pressed/sintered Bi/Al assemblies, using in-house manufactured test rods prepared analogously to the corresponding target fabrication methods⁵. The resistance was derived from spatially resolved temperature measurements along the rod axis. For each sample, the temperature profiles in the aluminum and bismuth sections were fitted separately by linear regression and extrapolated to the interface position. The resulting temperature offset at the interface was taken as the geometric representation of the interfacial temperature drop and was used to calculate the corresponding thermal contact resistance. An example of this evaluation procedure for a molten sample is shown in Figure 35, where panel (A) displays the complete temperature profile and panel (B) a magnified view of the interface region, revealing a temperature discontinuity of approximately 2.28 K.

Repeated measurements at different cooling powers yielded comparatively consistent interface temperature drops for the molten samples, ranging from 1.26 to 3.87 K with

⁵ For the other three target preparation methods investigated in this study, comparable test rods could not be fabricated. Consequently, thermal contact resistance could not be measured for these methods using the present technique.

an average of 2.6 K (Table 15). This corresponds to an effective thermal contact resistance of $3.9 \cdot 10^{-5} \pm 0.9 \cdot 10^{-5} \text{ K m}^2 \text{ W}^{-1}$. In contrast, the pressed/sintered targets showed a much larger average temperature discontinuity of 33.7 K, corresponding to an effective thermal resistance of $5.0 \cdot 10^{-4} \pm 3.4 \cdot 10^{-5} \text{ K m}^2 \text{ W}^{-1}$ (Figure 36 and Table 16). Thus, the molten targets exhibited approximately one order of magnitude lower effective interface resistance than the pressed/sintered variants.

This pronounced difference is in good qualitative agreement with the irradiation experiments, in which the molten targets also showed superior thermal stability. The lower effective resistance of the molten Bi/Al assemblies therefore strongly suggests a more efficient heat-transfer path across the interface, consistent with improved interfacial conformity and thermal coupling compared to the pressed/sintered targets.

At the same time, the absolute values should be interpreted with appropriate caution. Literature values for optimized low-melting metallic interface systems can be considerably lower; for example, thermal resistances as low as $1.7 \cdot 10^{-6} \text{ K m}^2 \text{ W}^{-1}$ have been reported for indium–bismuth–tin coated copper interfaces [117]. However, such values strongly depend on surface roughness, planarity, wetting behavior, and substrate condition, and are therefore not directly comparable to the present target-like Bi/Al assemblies. The values reported here are thus best understood as effective interface-related thermal resistances under target-relevant preparation conditions rather than intrinsic material constants.

In addition, the present measurement approach is highly sensitive to experimental uncertainties, particularly in the case of the molten targets, where the interfacial temperature drop is small by nature. This is reflected in the comparatively large relative standard deviation (SD) of about 33%, which should be interpreted in the context of the low absolute temperature offset rather than as an indication of random behavior. Under these conditions, even small deviations in probe positioning, thermal insulation, or fitted slope can noticeably influence the extrapolated interface temperature difference. A further indication of residual systematic uncertainty is given by the heat-balance comparison: the nominal electrical heating power was 35.2 W, whereas the conductive heat flow estimated from the aluminum temperature gradient averaged 33.2 W and the calorimetrically determined heat uptake of the cooling water was 30.8 W. Together with the geometric limitations of the test rods and borehole

arrangement, this suggests that unwanted heat losses were not fully suppressed. The resulting values should therefore be regarded as effective target-related thermal resistance rather than high-precision intrinsic interface properties. Additionally, a further limitation results from the temperature dependence of the thermal conductivity of both aluminum and bismuth. By applying linear fits to the measured temperature profiles, the present evaluation implicitly assumes constant k within the investigated temperature range. Any deviation from this assumption may slightly affect the extrapolated interface temperature discontinuity and thus the absolute thermal resistance.

Nevertheless, these limitations primarily affect the absolute accuracy of the derived resistance values, whereas the relative difference between the two preparation routes remains large and consistent. The present study was therefore not intended to establish a reference-grade thermal contact resistance for Bi/Al interfaces, but rather to provide an experimentally grounded comparison between two target preparation methods. Within this scope, the results suggest that the molten targets exhibit more favorable thermal coupling under the tested conditions, while also providing a reasonable effective input parameter for subsequent thermal modelling.

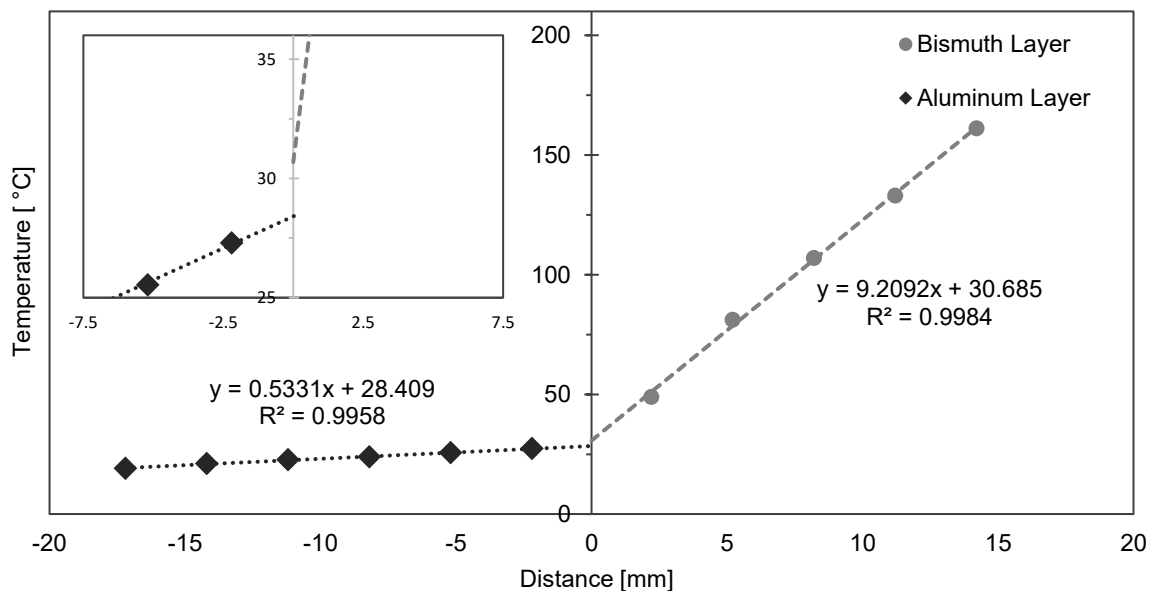


Figure 35: Temperature gradient over different measurement points of the Bi/Al test rod prepared analogous to the melting target preparation technique. Showing an overview of the whole experiment as well as an amplified view at the metal interface.

Results & Discussion

Table 15: Presenting the absolute difference in temperature at the Bi/Al-metal interface and the corresponding thermal resistance of the rod prepared by melting target method.

Coolant flow rate [L min ⁻¹]	ΔT [K]	Contact resistance (dt/q) [K W ⁻¹]
0.8	3.07	4.56E-05
0.8	1.96	2.91E-05
0.8	2.28	3.38E-05
0.6	3.87	5.75E-05
0.6	2.67	3.97E-05
0.4	1.26	1.87E-05
0.2	3.27	4.86E-05
Mean	2.63	3.90E-05
SD	0.88	1.30E-05

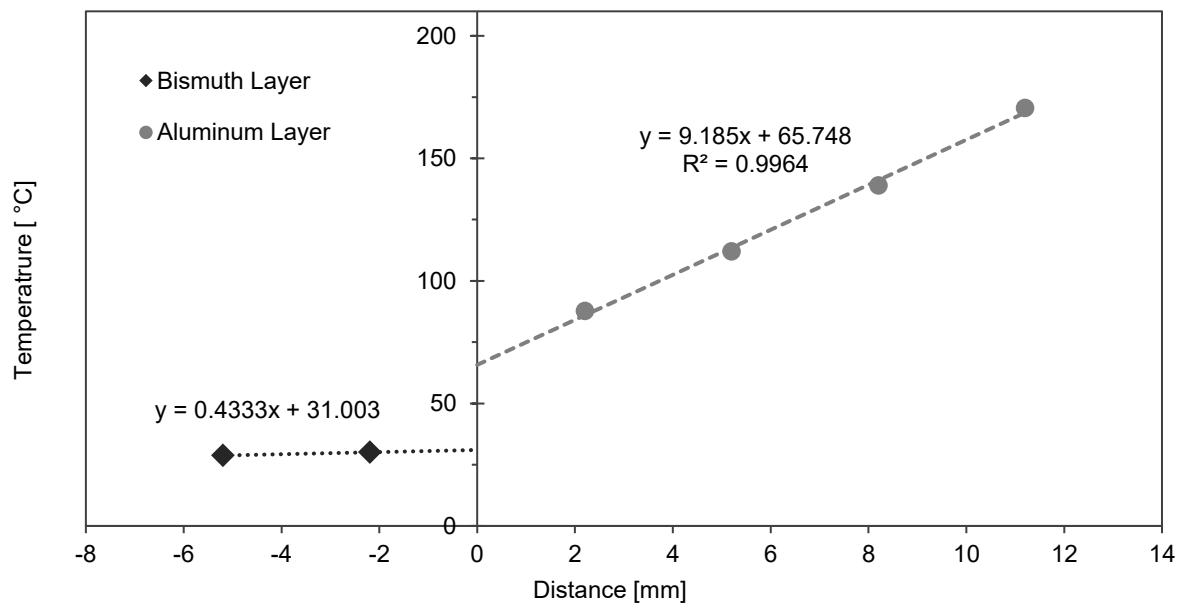


Figure 36: Temperature gradient over different measurement points of the Bi/Al test rod prepared analogous to the sinter target preparation technique.

Table 16: The absolute difference in temperature at the Bi/Al-metal interface and the corresponding thermal resistance of the rod prepared by sinter target method.

Coolant flow rate [L min ⁻¹]	ΔT [K]	Contact resistance (dt/q) [K W ⁻¹]
0.8	34.75	5.16E-04
0.6	31.02	4.61E-04
0.4	36.36	5.40E-04
0.2	32.80	4.87E-04
Mean	33.73	5.01E-04
SD	2.32	3.44E-05

Target temperature modelling

The contact-resistance measurements alone do not yet indicate the thermal behavior of the target under beam conditions. They therefore served as effective input parameters for a simplified steady-state reconstruction of the temperature field during irradiation. As described in the previous chapter, the measurements provide an experimentally derived estimate of the thermal coupling between bismuth and aluminum for both target preparation routes. Although the absolute values remain associated with non-negligible uncertainty, they are sufficiently robust for use in a simplified thermal model. In the following, these parameters were combined with the intrinsic conductive contributions of the target materials, the convective boundary condition, and the spatially resolved local power-density distribution to estimate the target temperature field under irradiation.

Figure 37, shows an exemplary beam footprint recorded with a phosphor imager after a 1 h irradiation using 10% wobbler intensity. The image is shown both as the original delayed activity distribution (A) and after discretization into $1 \times 1 \text{ mm}^2$ pixels (B). This rasterized activity map was used to determine the local power density q_i'' for each pixel according to Eq. (5.10), followed by the corresponding local temperature increase ΔT_i following Eq. (5.11).

Assuming a total deposited beam power of 750 W (based on Eq. (5.6)), the highest reconstructed local power density reached 1.12 W m^{-2} , corresponding to 1.12 MW m^{-2} .

The delayed phosphor image was used as a robust surrogate for the spatial activity distribution and, consequently, for the relative beam footprint. However, detector- and radiation-induced signal spreading may smooth sharp local intensity gradients. Therefore, image-derived peak values are interpreted as conservative estimates rather than exact point maxima.

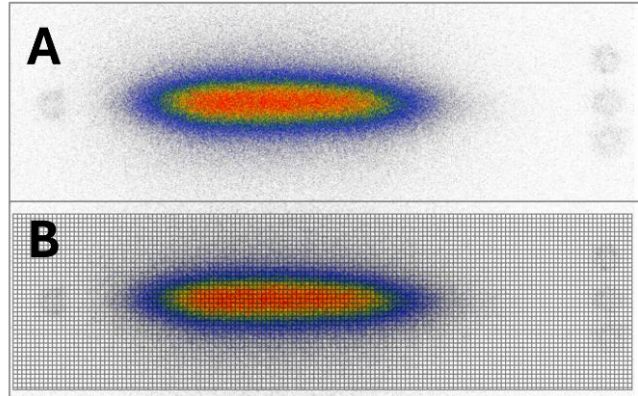


Figure 37: Footprint of the alpha beam on the target surface at 6° imposing angle measured via phosphor imager. (A), the bare intensity plot is presented and (B), the plot is segregated into pixel of $1 \times 1 \text{ mm}$.

The applicability of the local one-dimensional approximation was assessed by estimating the thermal healing length using Eq. (5.17). The resulting healing length of 0.131 mm was significantly smaller than the applied pixel size of 1 mm. This indicates that lateral heat spreading within the bismuth layer occurs over a length scale below the spatial resolution of the reconstructed activity map, justifying neglect of three-dimensional lateral heat spreading.

The convective contribution entering Eq. (5.11) was determined from the area-specific convective thermal resistance R''_{conv} according to Eq. (5.13), with the heat-transfer coefficient h derived from Eq. (5.14)–(5.16). The parameters used for this calculation are summarized in Table 17, resulting in a convective thermal resistance of $R_{\text{conv}} = 6.92 \cdot 10^{-6} \text{ m}^2 \text{ K W}^{-1}$ for the present cooling geometry and flow conditions.

Table 17: Parameter for calculations of the convection resistance of the 6° target geometry.

Parameter	Value
Hydraulic diameter D_h	$3.33 \cdot 10^{-3} \text{ m}$
Flow $\dot{V}$	48 L min^{-1}
Raynolds number Re	$1.5 \cdot 10^5$

In addition, the area-specific conductive thermal resistances of the target layers were calculated as $3.75 \cdot 10^{-6} \text{ m}^2 \text{ K W}^{-1}$ for a 30 μm bismuth layer and $7.69 \cdot 10^{-6} \text{ m}^2 \text{ K W}^{-1}$ for the 1 mm aluminum backing (according to Eq. (5.5)). Together with the experimentally determined Bi/Al contact resistance, these contributions were combined in Eq. (5.11) to obtain the local temperature increase ΔT_i . The absolute local target temperature T_i was then obtained from Eq. (5.12).

The resulting temperature distribution is shown in Figure 38 as a three-dimensional surface plot. The reconstructed temperature field exhibits a relatively broad maximum of approximately $\sim 90^\circ\text{C}$. This value remains far below the melting point of bismuth and therefore indicates that, under the investigated irradiation conditions, the molten target preparation route is thermally stable at the expected steady-state equilibrium. This interpretation is consistent with the visual post-irradiation inspection, which showed no indication of target failure.

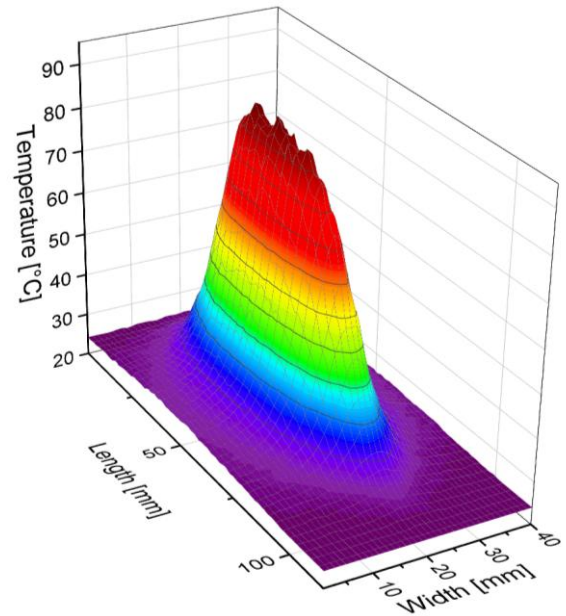


Figure 38: Depicting a heat map of the calculated target temperature of a 6°-target prepared by melting target method at 10% wobbler intensity.

As a separate plausibility check, the possible contribution of radiative heat loss was estimated using the Stefan–Boltzmann relation given in Eq. (5.18). Even under an upper-bound scenario evaluated at the hottest modelled position, the resulting radiative heat flux ranged only from $30.7 - 178.9 \text{ W m}^{-2}$ for emissivity of 0.06 and 0.34 [118], representing polished and roughened bismuth surfaces, respectively. Compared with the reconstructed local heat fluxes, this corresponds to a relative contribution of less than 0.1% in both cases. Radiative heat transfer was therefore neglected in the primary temperature reconstruction, which is justified by its negligible contribution relative to conductive and convective heat removal.

The calculated maximum temperature is somewhat higher than the value reported by Gagnon et al. (2012) [35] for a comparable target configuration, where a temperature of approximately 56°C was obtained. Nevertheless, both values remain of the same order of magnitude. The observed difference is plausible, given the strong sensitivity of the overall thermal response to small variations in contact resistance, target preparation, beam-shape assumptions, and cooling conditions. A more detailed quantitative comparison would therefore require a closer parameter-level alignment between the two models than is possible within the scope of the present work.

Using the same temperature-modelling approach, the beam profiles obtained in the previously presented wobbler-intensity studies were also evaluated in order to assess the thermal effects of alpha-beam wobbling. The beam profiles recorded at wobbler intensities of 20–40% and the corresponding thermal calculations are shown in Figure 39. A slight decrease in the maximum reconstructed target temperature was observed with increasing wobbling, from approximately ~90 °C at 10% intensity to about ~84 °C at 30% intensity. At the same time, however, the beam homogeneity deteriorated with increasing wobbler intensity, as already discussed in a previous section. At 40% intensity, the beam became unstable, preventing continuous irradiation.

Figure 39 therefore illustrates that moderate beam wobbling can slightly reduce local thermal maxima, but this effect is limited by the simultaneous loss of beam stability and homogeneity at higher wobbling intensities.

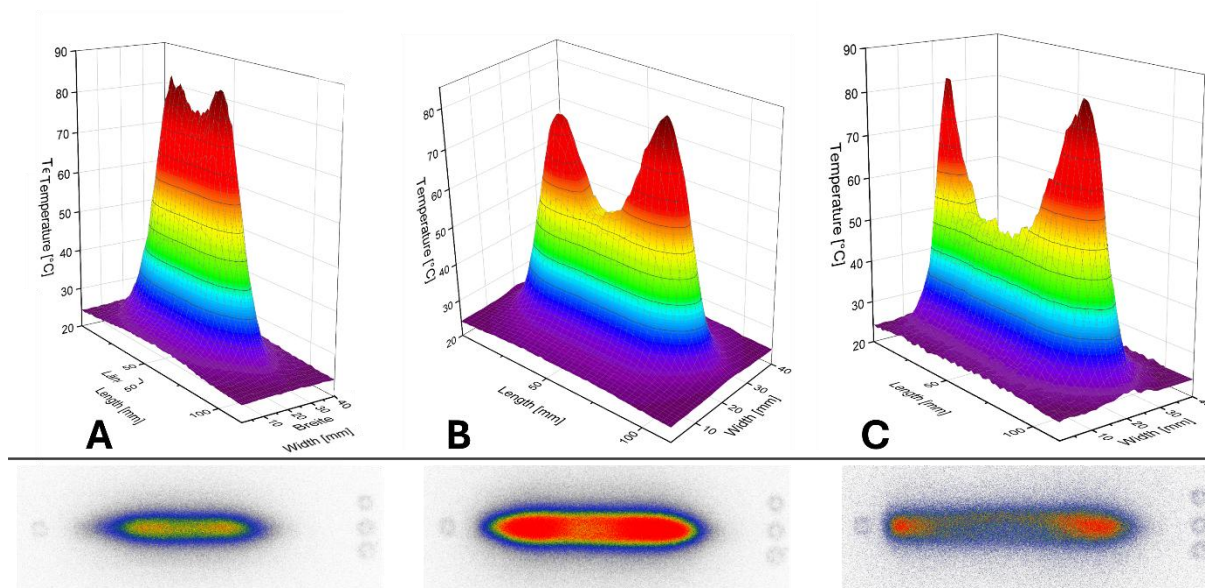


Figure 39: Temperature profile of increasing wobbler activity during irradiation.

Overall, these results show that target integrity depends strongly on local heat deposition as well as on the thermal coupling within the target assembly.

At the same time, practical ^{211}At production is not only limited by target stability, but also by radionuclidic purity. The irradiation results therefore need to be discussed not only in terms of target survival and production yield, but also with regard to the

formation of ^{210}At . The following section focuses on this aspect under production-relevant irradiation conditions.

Radio nuclidic impurities

Besides achieving the required activity levels, radionuclidic purity after processing is of equal importance. In the production of ^{211}At via the $^{209}\text{Bi}(\alpha,2n)^{211}\text{At}$ reaction, particular attention must be paid to the co-produced isotopic impurity ^{210}At . Since ^{210}At and ^{211}At are isotopes of the same element, they cannot be separated from one another by conventional chemical processing. This impurity is of special concern because ^{210}At decays to ^{210}Po , a long-lived and highly radiotoxic α -emitting daughter nuclide that is unsuitable for medical applications [29].

In the present work, ^{210}At activity was quantified by HPGe γ -spectrometry and related to the corresponding ^{211}At activity. An average $^{210}\text{At}/^{211}\text{At}$ EOB ratio of 20 ± 9 ppm ($n=46$) was determined (Figure 40). This corresponds to a calculated maximum ^{210}Po activity after 70.5 h (t_{max}) of 2.6–7.0 Bq per 100 MBq ^{211}At . These values indicate that the selected production conditions provide a reasonable compromise between production yield and radionuclidic purity. In this approximation, directly produced ^{210}Po via the $^{209}\text{Bi}(\alpha,p2n)^{210}\text{Po}$ reaction was not considered explicitly, as the estimate focuses on delayed ^{210}Po ingrowth from co-produced ^{210}At since ^{210}Po is expected to be efficiently removed during target processing using for example dry distillation or solid supported liquid-liquid extraction [40, 71].

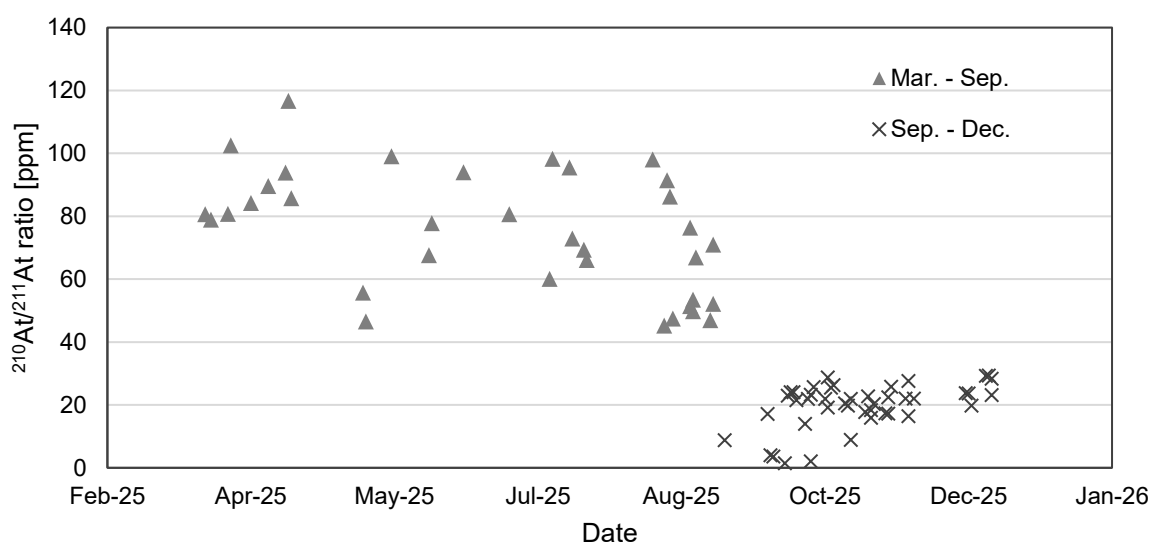


Figure 40: $^{210}\text{At} / ^{211}\text{At}$ ratios measured from March–December 2025,

Because the residual $^{210}\text{At}/^{211}\text{At}$ ratio cannot be reduced by conventional chemical separation alone, its control relies primarily on the irradiation conditions. Additional post-irradiation treatment of the target may further reduce directly formed ^{210}Po but cannot isotope-selectively remove ^{210}At from ^{211}At . The most effective strategy to suppress ^{210}At formation is therefore to limit the α -particle energy on target to the onset region of the competing $^{209}\text{Bi}(\alpha,3n)^{210}\text{At}$ reaction. However, this inevitably reduces the achievable ^{211}At yield and introduces a direct trade-off between production yield and radionuclidic purity. This relationship is illustrated by the calculated thick-target yields of ^{211}At and ^{210}At , as well as the resulting $^{210}\text{At}/^{211}\text{At}$ activity ratio, as a function of α -particle energy (Figure 41). While the ^{211}At yield increases with increasing energy, the relative formation of ^{210}At rises disproportionately, resulting in a pronounced increase in the $^{210}\text{At}/^{211}\text{At}$ ratio at higher α -particle energies.

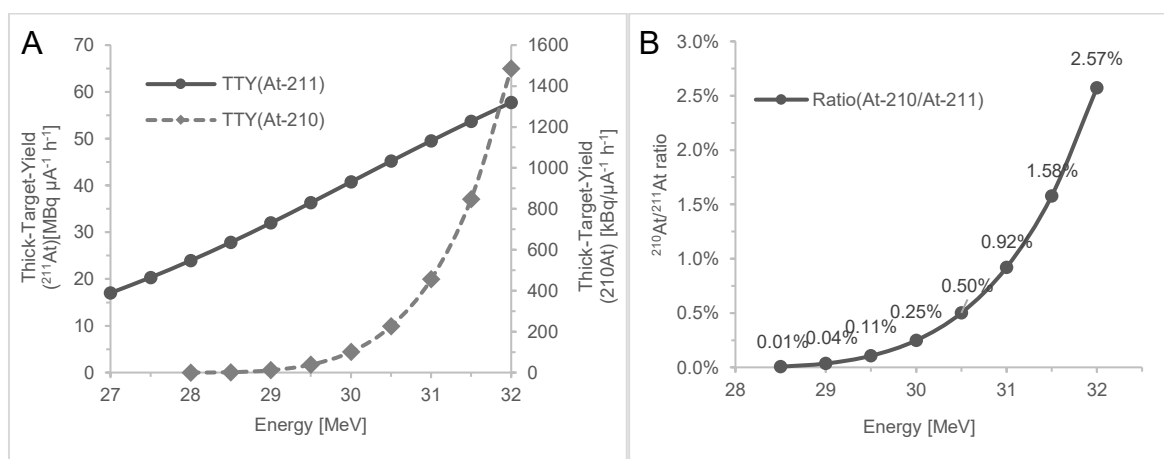


Figure 41: Comparison of the calculated thick-target yields of ^{211}At and ^{210}At (A) and the corresponding $^{210}\text{At}/^{211}\text{At}$ activity ratio (B) as a function of projectile energy. Thick-target yields were calculated from IAEA literature data [38].

This strong energy dependence explains why even small changes in the effective α -particle energy deposited in the target can markedly affect radionuclidic purity. In this work, ^{211}At was produced using a nominal α -particle energy of 29.3 ± 0.3 MeV. Prior to September 2025, the average $^{210}\text{At}/^{211}\text{At}$ ratio was approximately 76 ppm ($n = 34$), whereas after cyclotron maintenance the average ratio decreased to 20 ppm ($n = 46$) (Figure 40). This change is attributed to a slight, millimeter-scale rearrangement of the deflector, reducing the effective α -particle energy at the target.

Because of the close relationship between α -particle energy and the $^{210}\text{At}/^{211}\text{At}$ production ratio, the measured activity ratios can be used as an additional indicator of the effective α -particle energy by comparison with the calculated energy dependence shown in Figure 41 (B). Before September 2025, the average ratio of 76 ppm corresponds to an estimated α -particle energy of approximately 28.7 MeV. During the same period, the average ^{211}At production yield was $35.5 \text{ MBq } \mu\text{Ae}^{-1} \text{ h}^{-1}$, which independently corresponds to an energy of about 29.2 MeV according to Figure 41 (A). After September 2025, the reduced $^{210}\text{At}/^{211}\text{At}$ ratio of approximately 20 ppm indicates an α -particle energy of about 28.5 MeV. The simultaneously observed production yield of $32.9 \text{ MBq } \mu\text{Ae}^{-1} \text{ h}^{-1}$ corresponds to approximately 28.9 MeV. Although the absolute energy estimates derived from the activity ratios are systematically lower by approximately 0.4–0.5 MeV than those inferred from the production yields, both approaches indicate a comparable small decrease in the effective α -particle energy after the maintenance-related deflector adjustment.⁶

Altogether, these observations underline that optimization of the effective α -particle energy at the target is the key parameter for balancing ^{211}At production yield against radionuclidic purity. For fixed-energy cyclotrons in particular, this may require the use of beam degraders or corresponding adaptations of the target design to suppress ^{210}At formation as far as reasonably achievable.

Overall, these results define the production-side boundary conditions for the subsequent ^{211}At processing workflow. After target stability, thermal limitations, production yield, and radionuclidic purity had been evaluated, the next step was to assess how efficiently the produced astatine could be recovered from the irradiated target and transferred into a chemically usable form.

⁶ The energy values derived from Figure 41 were re-evaluated after the defense. The previously stated values of 29.6, 29.4, 28.9, and 29.0 MeV were corrected to 28.7, 29.2, 28.5, and 28.9 MeV, respectively. This correction does not affect the conclusion that both indicators support a small decrease in the effective α -particle energy after the cyclotron maintenance.

3.2.2. Recovery, separation, and process optimization of ^{211}At

Following irradiation, the decisive question is no longer whether ^{211}At was formed, but whether it can be recovered reproducibly, purified sufficiently, and transferred into a form suitable for further handling. The present section therefore follows the processing chain from target-associated post-irradiation measures to thermochemical and extraction-based separation approaches.

The produced ^{211}At has to be recovered from the activated bismuth target and transferred into a form suitable for downstream application. Besides recovery, the processing step also influences radionuclidic purity, chemical purity, processing time, and practical handling under highly radioactive conditions. In this work, further post-production processing was investigated by target decontamination as a possible way to reduce the residual $^{210}\text{At}/^{211}\text{At}$ ratio, as well as by dry distillation and liquid–liquid extraction for separation of ^{211}At from the target material. Particular focus was placed on the applicability, robustness, and limitations of these approaches under the irradiation and target conditions used in this study.

Target decontamination

The first issue considered here is whether post-irradiation treatment of the target surface can further improve radionuclidic purity, especially in cases where the effective α -particle energy on target cannot be adjusted more precisely during irradiation.

Although the $^{210}\text{At}/^{211}\text{At}$ ratios obtained under the selected production conditions were low, more stringent radionuclidic purity requirements may still call for a further reduction of the residual ^{210}At content. Because conventional chemical processing does not allow selective separation of ^{210}At from ^{211}At , the most effective way to limit later ^{210}Po ingrowth is usually control of the α -particle energy during irradiation [12, 26, 40]. However, in fixed-energy cyclotron systems this option may be limited, and additional post-irradiation measures can therefore become relevant. As previously discussed, the formation of ^{210}At rises strongly with increasing α -particle energy, whereas the increase in ^{211}At yield is more gradual (Figure 41). Consequently, highest concentration and therefore the highest ratio of $^{210}\text{At}/^{211}\text{At}$ should be in the outermost target fraction, which

is exposed to the highest projectile energies. Partial removal of this surface layer should therefore lower the residual $^{210}\text{At}/^{211}\text{At}$ ratio in the remaining target material, analogous in outcome, though not in mechanism, to lowering the effective beam energy on target, albeit at the expense of some ^{211}At yield.

To further elaborate this hypothesis, irradiated bismuth targets were subjected to a manual decontamination procedure by wiping the activated target surface with a disposable paper towel. One decontamination step consisted of five swipes with one paper towel, applying moderate pressure, after which the target was re-measured by HPGe γ -spectrometry. This procedure was repeated for three consecutive steps. The resulting $^{210}\text{At}/^{211}\text{At}$ activities are shown in Figure 42. A clear stepwise decrease in the residual ratio was observed. Starting from an initial value of 24 ppm, the first wiping step reduced the ratio by approximately 7 ppm, corresponding to a relative decrease of 29%. The second step produced a further reduction of 4 ppm (22%), while the third step still lowered the ratio by an additional 2 ppm (18%). These results demonstrate that partial post-irradiation removal of the bismuth surface can indeed decrease the residual $^{210}\text{At}/^{211}\text{At}$ ratio in the remaining target material.

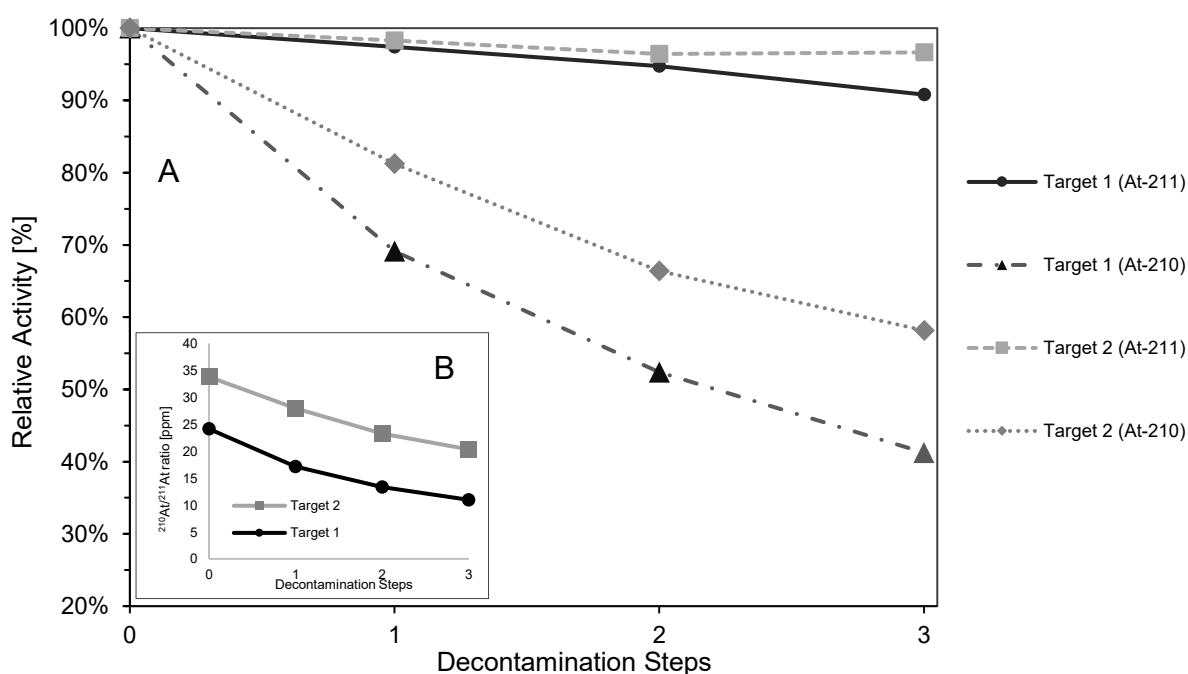


Figure 42: Relative activity loss of ^{210}At and ^{211}At of two irradiated bismuth targets following three successive manual decontamination steps using disposable paper towels (A). Each step consisted of five swipes applied with moderate pressure. Activities were quantified by HPGe spectroscopy. In (B), the corresponding decrease in $^{210}\text{At}/^{211}\text{At}$ ratio is presented.

This interpretation is supported by the activity ratios measured in the paper towels used for decontamination. In all cases, the removed material exhibited markedly elevated $^{210}\text{At}/^{211}\text{At}$ ratios, ranging from approximately 100 to 220 ppm, and was therefore substantially more enriched in ^{210}At than the residual target. This finding indicates that the wiped material originated mainly from the outer target surface, which is expected to be more enriched in ^{210}At than the deeper target layers. At the same time, it should be emphasized that this procedure does not constitute isotopic separation in the strict sense, since both ^{210}At and ^{211}At are removed together with the wiped target material. Rather, it represents a selective adjustment of the residual isotopic ratio by controlled removal of the most contaminated target fraction or alternatively seen as a post irradiation alpha beam energy decrease.

An inherent drawback of this approach is the associated loss of ^{211}At activity. Nevertheless, this loss can, in principle, be regarded as reflecting the same general trade-off encountered when the α -particle energy is reduced during irradiation: improved radionuclidic purity is achieved at the expense of production yield [26, 40].

To quantify this effect, the reduction in ^{211}At activity caused by the post-irradiation target decontamination method presented in this study was converted into an equivalent loss in production yield and, subsequently, into an equivalent α -particle energy. For the two investigated targets, the production yield decreased from 32.1 MBq $\mu\text{Ae}^{-1} \text{ h}^{-1}$ before decontamination to 29.2 MBq $\mu\text{Ae}^{-1} \text{ h}^{-1}$ and 31.0 MBq $\mu\text{Ae}^{-1} \text{ h}^{-1}$, respectively, after three cleaning cycles. According to the reference yield–energy relationship, these values correspond approximately to α -particle energies of 28.6 MeV and 28.8 MeV. The discussed results are presented in full in Table B-1 and Table B-2 in the appendix.

This interpretation is consistent with the isotope ratios shown in Figure 41(B) and the ^{210}At content presented in Figure 42(B). The approximately 10 ppm ^{210}At content observed for Target 1 agrees well with the nominal value expected at about 28.6 MeV, whereas the approximately 20 ppm observed for Target 2 is consistent with the reference value at about 28.8 MeV.

In this respect, post-irradiation target decontamination may be regarded as a practical corrective measure when optimization of the α -particle beam energy is not feasible, or when an additional reduction of the $^{210}\text{At}/^{211}\text{At}$ ratio is desired after irradiation. From an operational perspective, however, adjustment of the effective α -particle energy on

target remains the preferable primary strategy, since manual treatment of open irradiated targets inevitably introduces additional radiation-protection and handling concerns.

Dry distillation

Once the limits of surface decontamination had been assessed, the main focus shifted to the actual isolation of ^{211}At from the irradiated target matrix. Dry distillation was investigated first, since it offers a direct thermochemical route from bulk target material to an isolated astatine fraction.

Thermochemical isolation of ^{211}At by dry distillation

In the present work, dry distillation was evaluated as a thermochemical route for the isolation of ^{211}At from irradiated bismuth target material. While the general combination of a heated volatilization step with downstream trapping is well established in the astatine literature, the specific operating conditions differ substantially between research groups. A comparison of representative literature procedures is given in Table 18. Despite the widespread use of dry distillation for nearly four decades, a systematic assessment of how individual process parameters affect the isolation of ^{211}At remains limited. The aim of this study was therefore not merely to reproduce literature procedures, but to identify which parameters most strongly govern the release, transport, trapping, and recovery of ^{211}At under practically relevant conditions.

For this purpose, > 100 distillation experiments were performed using a custom-built setup consisting of a tube furnace, a controlled carrier-gas stream, and a downstream trapping assembly. The liberated ^{211}At was either collected in a cooled capillary trap or, in selected experiments, in a non-cooled packed-bed retention column. The parameter screening focused on four major aspects: trapping temperature, gas residence time in the trapping zone, trapping surface material, and carrier-gas composition. Furnace temperature was investigated primarily with respect to the release of ^{211}At from the irradiated bismuth material (IBM), rather than the trapping efficiency itself.

Results & Discussion

Table 18: Conditions used for dry distillation at various research facilities. (FEP = fluorinated ethylene propylene, PEEK = polyether ether ketone PTFE = polytetrafluoroethylene).

Institution	Gas flow rate [mL min ⁻¹]	Carrier gas / atmosphere	Furnace temperature [°C]	Cold-trap temperature [°C]	Transfer line / tubing material	Recovery yield [%]
Osaka University Hospital	20 for drying; 6 He + 10 O ₂ during distillation	He/O ₂ atmosphere, dried over molecular sieves	850	-3	Polymer tubing; material not further specified	40 ± 3 at EOS
Osaka University	20	He/O ₂ mixture; moisture content specified by the authors	840	0 to -5; ice-water cooling	PTFE	80–90
Duke University Medical Center	50–110	Ar	700	-77	PTFE tubing, 1/16 inch; PEEK used in earlier setup	55–65
University of Gothenburg	20–50	N ₂ under reduced pressure, approximately -0.3 to -0.4 bar	not specified	< -40	FEP tubing, 1/16 inch	89 ± 2
National Cancer Center Japan	40	30% O ₂ in N ₂	850	not specified	PTFE tubing, 2 mm inner diameter	65 ± 5
Research Center Jülich	35	Synthetic air, 20% O ₂ / 80% N ₂	800	-20	PTFE tubing, 1/16 inch inner diameter, 50 cm length	80 ± 1

A full factorial optimization of all relevant process variables was not feasible within the scope of this work. Therefore, individual parameters were investigated in a targeted manner while the remaining conditions were kept as constant as possible.

A central experimental challenge throughout this study was the reliable quantification of separation yield. Large fluctuations in apparent recovery were observed, which were traced predominantly to self-absorption effects in the scraped bismuth target material. Because of the high atomic number and density of bismuth, larger fragments strongly attenuate the low-energy X-rays emitted by ²¹¹At, causing the activity introduced into the furnace to be underestimated when measured with a dose calibrator. Since self-absorption is much less pronounced in the isolated astatine fraction, determined recoveries may be artificially inflated and can even exceed complete recovery (> 100%). Such values therefore do not indicate super-quantitative separation, but rather a measurement artefact caused by matrix-dependent attenuation. Averaging

over multiple experiments was used to reduce sample-dependent scatter, although the systematic bias caused by self-absorption remains inherent to dose-calibrator-based quantification of the starting material.

Rather than treating dry distillation as a single fixed procedure, the following discussion examines which process parameters most strongly determine release, transport, trapping, and apparent recovery.

The first parameter investigated was the furnace temperature, since efficient release of ^{211}At from the IBM is a prerequisite for any subsequent trapping strategy. At the same time, the upper temperature range is constrained by the risk of co-distillation of unwanted species, most importantly ^{210}Po . This nuclide is either formed directly in the $^{209}\text{Bi}(\alpha, x)^{210}\text{Po}$ reaction or indirectly via decay of ^{210}At , and its high radiotoxicity makes its transfer into the final astatine fraction highly undesirable for in-vivo applications. Additional non-radioactive contaminants such as bismuth or aluminum residues may likewise interfere with subsequent processing or labeling steps. Table 19 summarizes the melting and boiling points of the most relevant materials. Although the boiling point of polonium is 962 °C, evaporation below the boiling point must still be expected, as for all liquids [119]. Consequently, furnace temperature must be regarded as a compromise between fast and complete release of ^{211}At and minimization of co-volatilization of contaminants.

Table 19: Melting and boiling points relevant for astatine distillation.

Element / complex	T_m (°C)	T_b (°C)
At	302	337
Bi	271	1564
Bi_2O_3	817–820	1890
Po	254	962
Al	660	2519
Mg	650	1090

The release of ^{211}At from bismuth bulk material was therefore investigated at oven set-points of 700 °C, 750 °C, and 800 °C. Since the furnace control is based on the temperature measured outside the fused silica tube, the actual temperature at the sample position was slightly lower; a small offset of approximately 20–30 °C was

observed in the relevant temperature range. For consistency, all temperatures reported in this work refer to the furnace set-point. At 700 °C, astatine release increased gradually over 25 min, indicating comparatively slow volatilization. In contrast, 95% and 98% of the activity were released within 10 min at 750 °C and 800 °C, respectively. These results show that the transition from 700 °C to 750 °C and 800 °C changes the process from a slow-release regime to a practically complete and rapid volatilization. On this basis, 800 °C was selected for subsequent experiments, as it minimized processing time while maintaining efficient release.

Once efficient liberation from the IBM had been established, the trapping temperature emerged as the most important parameter controlling recovery in the cold-trap configuration. The trapping efficiency was therefore studied between ambient temperature (~ 25 °C) and -40 °C, while breakthrough was quantified by the activity retained on a downstream activated carbon filter. As shown in Figure 43, the retained fraction increased strongly with decreasing trap temperature. At room temperature, only about half of the ^{211}At was captured. Around 0 °C, retention increased to approximately 80%, and below about -20 °C near-quantitative trapping was achieved. The breakthrough fraction displayed the expected inverse behavior and decreased correspondingly. These results clearly identify the cooled capillary as a temperature-driven trapping process and show that sub-zero operation is essential for high recovery in this setup.

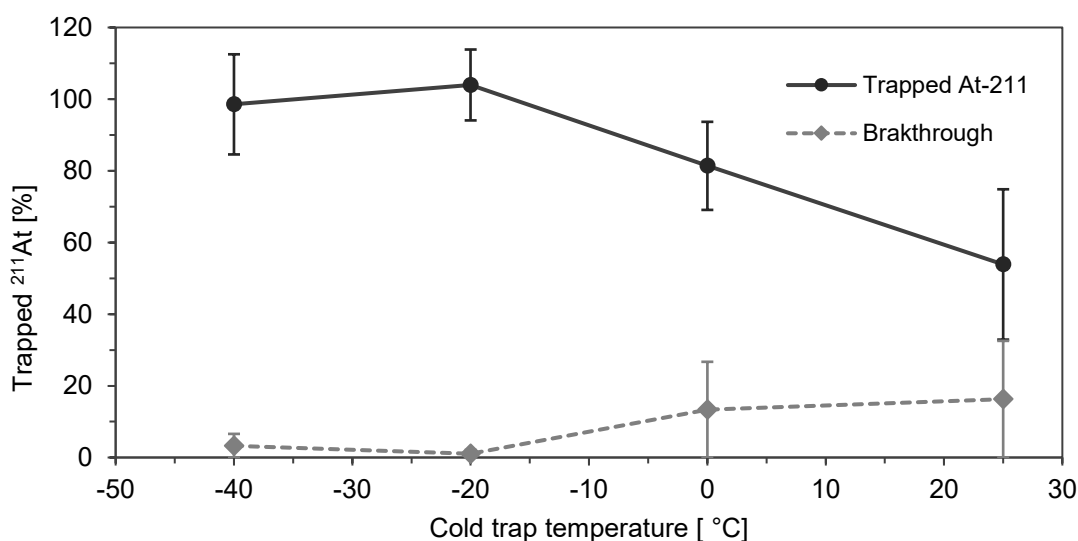


Figure 43: Trapping efficiency of ^{211}At as a function of trapping temperature

Operation at low temperature, however, introduces moisture as an additional practical limitation. Even trace water in the carrier gas may condense or freeze in the cold zone and thereby block the gas flow or even rinse previously trapped ^{211}At from the capillary wall. This effect is particularly relevant when cold traps are operated in non-ideal glovebox atmospheres or under conditions where ingress of ambient moisture cannot be completely excluded. In the present work, this problem was mitigated by thorough gas drying using molecular sieve and phosphorus pentoxide columns, combined with pre-drying of the entire setup by flushing for at least 10 min at flow rates above 50 mL min^{-1} . These observations show that efficient low-temperature trapping requires thorough drying of the carrier gas to avoid condensation-related losses.

In addition to temperature, the residence time of gaseous astatine in the cold trap was expected to influence recovery. Residence time is governed by the flow rate, inner diameter, and length of the capillary. In the present setup, a flow rate of $30\text{--}40\text{ mL min}^{-1}$ corresponds to a linear gas velocity of about 1.2 m s^{-1} in a capillary with 0.8 mm inner diameter, giving residence times as short as $0.17\text{--}1.72\text{ s}$ for lengths between 20 cm and 2 m . At first sight, such short contact times could be expected to limit the cooling and deposition of ^{211}At . However, the data summarized in Table 20 show that trapping remained essentially unchanged throughout this residence-time window when the capillary was operated at $-20\text{ }^{\circ}\text{C}$ to $-40\text{ }^{\circ}\text{C}$. Even at the shortest residence time of 0.17 s , trapping was already close to quantitative. Within the experimentally accessible range, the process was therefore not residence-time limited. This is an important result, indicating that once sufficiently low temperatures are reached, the deposition of ^{211}At occurs rapidly relative to transport through the trap. Moderate variations in flow rate or trap geometry within this range are therefore of secondary importance compared with other factors such as surface interactions or gas-phase chemistry.

The importance of surface interactions became evident when different capillary materials were compared. Polymer-based capillaries (PEEK, PTFE, PP, and FEP) as well as metallic tubing (stainless steel and titanium) were evaluated using the same trapping concept. As shown in Figure 44, most materials provided near-quantitative retention of ^{211}At . The main exception was stainless steel, which gave a markedly reduced trapping yield of only about 60% and the highest breakthrough fraction. This behavior suggests material-dependent interactions between volatile astatine species and the tubing wall, possibly related to differences in adsorption behavior or surface-

mediated speciation [120]. In contrast, PTFE, FEP, and PP showed consistently high trapping efficiencies and were also advantageous from a practical perspective. Among these, PTFE was selected as the preferred material because it combined quantitative trapping with flexibility, simple handling, and moderate cost.

Table 20: Fraction of ^{211}At retained at different residence times within a cold trap maintained between $-20\text{ }^{\circ}\text{C}$ and $-40\text{ }^{\circ}\text{C}$.

Length [cm]	Inner diameter [mm]	Flow rate [mL min ⁻¹]	Residence time [s]	Trapped ^{211}At [%]	Over distillation [%]
20	0.8	35	0.17	96.5 ± 7.5	2.9 ± 5.9
50	0.8	45	0.34	98.8 ± 13.5	2.4 ± 4.7
50	0.8	35	0.43	98.8 ± 22.7	2.7 ± 4.5
50	0.8	25	0.60	103.1 ± 9.4	1.6 ± 1.5
100	0.8	35	0.86	85.8 ± 14.9	4.8 ± 7.7
50	1.6	35	1.72	97.7 ± 11.0	0.6 ± 0.7

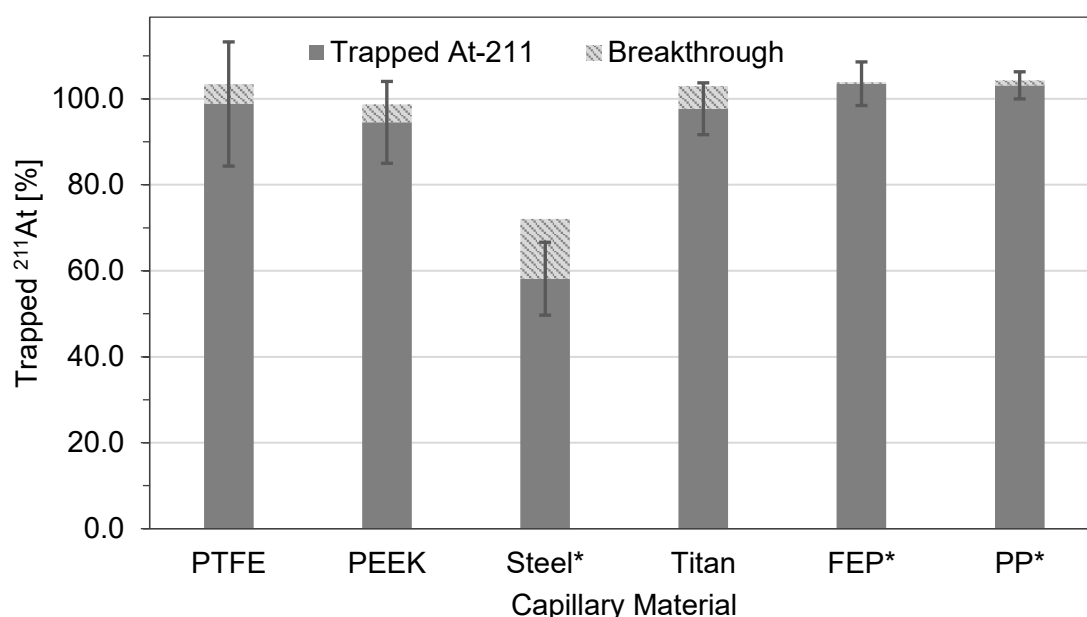


Figure 44: Showing the Fractions of trapped and over distilled ^{211}At in respect to different capillary materials (*n=3). Tapping over 100 % is due to self-absorption when samples are measured in the dose-calibrator, see text.

One potential drawback of polymer capillaries is their susceptibility to radiation-induced degradation. To address this, repeated distillations were performed with the same PTFE capillary using activities between 120 and 210 MBq of ^{211}At , with a total process

time of less than 30 min per run. Over 10 cycles spanning 40 days, no systematic decrease in trapping efficiency or increase in breakthrough was observed (Figure 45). Thus, under the conditions tested here, PTFE did not show any measurable loss of functional performance. Visual inspection revealed only slight brown discoloration near the capillary segment closest to the furnace outlet and at the connector to the fused silica tubing. Since this discoloration did not affect performance, it was not considered a limiting factor, although it remains unclear whether it originated from radiation exposure, local thermal stress, or both. As a precaution, the capillary tip was trimmed before reused in subsequent runs. Overall, these results indicate that PTFE tubing is sufficiently robust for repeated use in the applied activity range and therefore represents a practical choice for routine operation.

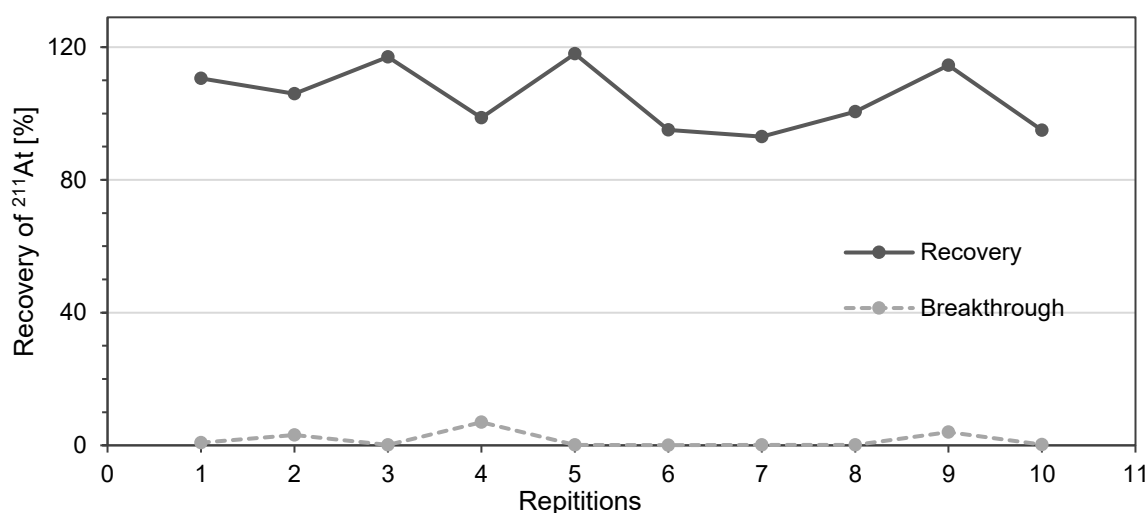


Figure 45: Recovery rates of ^{211}At over 10 runs (in 40 days) using the same capillary. Recoveries over 100% are due to self-absorption when samples are measured in the dose-calibrator, see text

Besides the trap material itself, the gas-phase environment strongly influenced the outcome of the separation. The transport behavior of astatine is likely influenced by its chemical form in the gas phase [121]. To assess this effect, three atmospheres were compared: argon, synthetic air (20% O_2 , 80% N_2), and an Ar/CO_2 mixture originating from open dry-ice-based cooling concepts. As shown in Figure 46, the use of an oxygen-free atmosphere led to a pronounced deterioration in performance. In pure argon, the recovery in the cold trap fell below 50%, while roughly one third of the activity

passed through to the downstream carbon filter. The Ar/CO₂ mixture performed somewhat better, with approximately 60% recovery, but still remained clearly inferior to the oxygen-containing atmosphere, which gave near-quantitative trapping. These findings demonstrate that the carrier gas does not merely serve as a transport medium but actively affects the chemical state and therefore the trapping behavior of ²¹¹At.

Notably, the sum of the trapped and breakthrough fractions under inert or weakly oxidizing conditions often remained below 100%. This incomplete mass balance indicates additional hold-up losses within the system, most likely due to deposition in connectors or in the capillary itself from which the activity could no longer be quantitatively recovered. Since breakthrough activity was captured in the downstream activated carbon filter, loss by simple escape from the system appears unlikely. The missing fraction is therefore more likely explained by internal hold-up within the setup. Literature reports show that high trapping efficiencies can also be achieved under inert atmospheres when colder cryotrap conditions, for example around $-78\text{ }^{\circ}\text{C}$, and optimized trap geometries are used [122]. Such experiments were not part of the present work. The current data therefore don't imply that oxidizing atmospheres are universally required for dry distillation of ²¹¹At, but they clearly show that under the specific conditions investigated here an oxygen-containing carrier gas was decisive for reliable and efficient trapping.

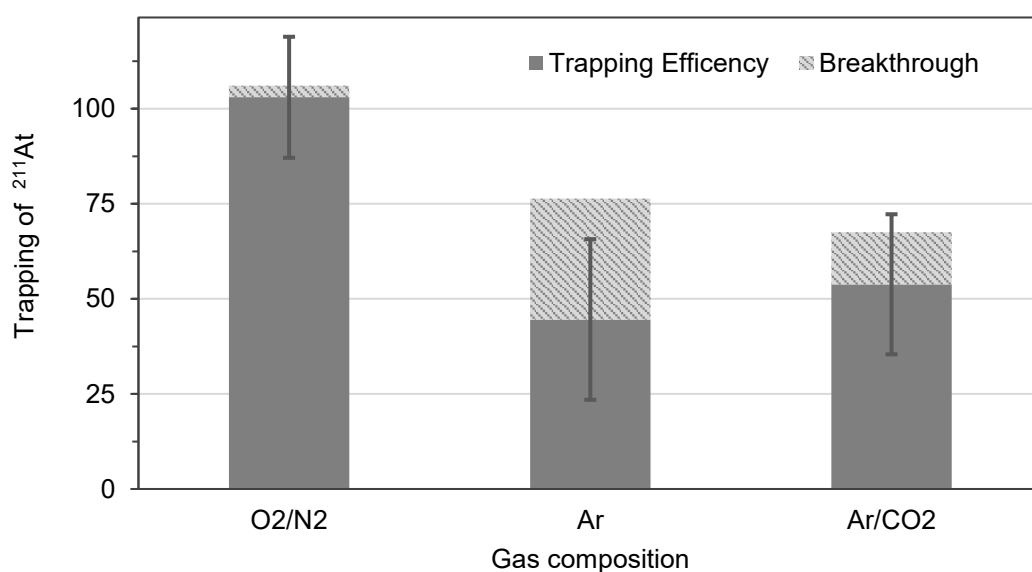


Figure 46: Influence of carrier gas composition on the trapping efficiency of ²¹¹At.

Because the cooled-capillary concept is operationally effective but also associated with practical limitations such as moisture condensation and the need for active cooling, an alternative room-temperature trapping strategy was explored. In this approach, the cooled capillary was replaced by a packed-bed column filled with inert, radiation-resistant solid materials such as ceramics, glass, carbon, or metals. The rationale was that a large accessible surface area at ambient temperature might provide sufficient retention of volatile astatine while simplifying handling and potentially offering a format better suited for transport or intermediate storage. To minimize premature deposition before the absorber bed, the column was connected directly to the furnace tubing via ground-glass joints omitting any polymer components. Recovery was assessed by counter-flow elution with 1 mL MeOH (methanol), and breakthrough was again quantified using downstream activated carbon filters.

As summarized in Table 21, the best room-temperature trapping was achieved with coiled graphite foil (~69%) and with fused silica insulation, glass beads, and zirconia beads (all around 64–66%). These values are comparable to those obtained with the capillary trap operated at room temperature, but clearly below the performance observed for the cooled capillary below $-20\text{ }^{\circ}\text{C}$. Quartz wool and gold beads performed less favorably, with trapping efficiencies of only about 37% and 50%, respectively. Breakthrough behavior did not fully mirror the retention data, and the overall activity balance was again often incomplete. Since the activated carbon filter retained breakthrough activity quantitatively, losses due to undetected breakthrough can be excluded. The missing activity is therefore more likely caused by internal hold-up within the system or by geometry/composition effects during measurement. The latter is especially plausible for dense materials such as gold beads, where strong self-attenuation of the low-energy astatine X-rays is expected to cause underestimation of the retained activity.

Results & Discussion

Table 21: Trapping efficiencies of different carrier materials used in packed-bed column trapping of ^{211}At as well as its breakthrough and recovery ($n=1$).

Material	Trapping [%]	Breakthrough [%]	Overall Recovery [%]
Fused silica insulation	64.0 ± 14.4	16.1 ± 16.7	50.9 ± 22.8
Glass beads (3 mm)	64.3 ± 12.3	1.2 ± 0.9	66.6 ± 24.8
Fused silica wool	37.2 ± 0.1	13.2 ± 17.0	36.1 ± 14.6
Gold beads (1 mm)	50.7 ± 1.4	8.7 ± 5.4	0.5 ± 0.1
Graphite coil*	69.3	17.4	29.9
Zirconia beads (5 mm)	65.7 ± 5.6	0.7 ± 0.2	45.4 ± 16.8

The elution behavior of the room-temperature trapping materials provided an additional and practically important distinction between them. Although several materials showed moderate to good trapping, quantitative release of the collected ^{211}At was achieved only for selected packings. Fused silica insulation and glass beads gave the best recoveries after elution, with zirconia performing somewhat less favorably. Recovery from fused silica wool and graphite foil was lower, while essentially no elution was observed from gold beads. These results emphasize that trapping efficiency alone is not a sufficient criterion for evaluating thermochemical separation concepts. Any practically useful trap must also permit rapid and quantitative recovery of the collected astatine into a small solvent volume suitable for downstream radiochemistry. In this respect, the packed-bed concept is promising, but still not competitive with the cooled PTFE capillary under the optimized conditions established in this work.

Overall, the present study shows that dry distillation of ^{211}At is governed by a combination of rapid release from the irradiated bismuth matrix, efficient low-temperature deposition, surface-dependent interactions in the trapping zone, and gas-phase speciation controlled by the carrier atmosphere. Among the investigated variables, trap temperature and carrier-gas composition had the strongest impact on recovery, whereas residence time within the tested range was of minor importance once sufficiently low trap temperatures were reached. PTFE-based cold trapping in an oxidizing atmosphere provided the best balance between separation efficiency, handling, and robustness. Based on these results, the reference conditions used in this work were defined as a furnace temperature of 800 °C, a 50 cm PTFE capillary operated at -20 °C to -40 °C, a carrier-gas flow of approximately 35 mL min⁻¹, and synthetic air mixture (20% O₂, 80% N₂) as carrier gas. When the recovery under these

reference conditions was quantified by HPGe spectroscopy, thereby avoiding dose-calibrator artefacts arising from self-absorption, an overall recovery of $80.4 \pm 0.4\%$ ($n=9$) was obtained. This value represents the most reliable performance metric of the dry-distillation procedure established in the present work.

Vertical oven Setup: Alternatives to target scrapings

Although the tube-furnace approach proved suitable for scraped target material, it still required mechanical removal of the activated layer. The following experiments therefore explored whether direct processing of intact targets could reduce manual handling without fundamentally compromising recovery.

Mechanical removal of the irradiated bismuth layer from the aluminum backing is a common preparatory step in dry distillation of ^{211}At . However, this step has repeatedly been discussed critically in literature because it increases direct handling of activated target material and may therefore raise radiation-safety concerns. In the present work, direct distillation of the intact target was investigated as a possible alternative, with the aim of reducing manual processing steps prior to separation.

Direct application of this concept in the established tube-furnace setup was not possible, since the dimensions of the bismuth targets used for irradiation exceeded the size limitations of the available furnace. To address this limitation, a prototype vertical oven setup was developed that could be adapted more flexibly to larger target geometries.

The vertical oven setup was evaluated using three irradiated bismuth targets under a synthetic air atmosphere at a heating temperature of $570\text{ }^{\circ}\text{C}$ and a flow rate of 40 mL min^{-1} . Under these conditions, an average recovery of $81 \pm 4\%$ was obtained, while $25 \pm 2\%$ of the activity remained on the target after cooling, decay-corrected to end of bombardment. The sum of both fractions exceeds 100%, indicating that activity quantification was affected by measurement uncertainty and/or self-absorption effects, similar to the effects already discussed for the tube-furnace distillation experiments. Accordingly, the corresponding recovery values are interpreted in comparative terms between experimental conditions and should not be understood as exact absolute

recoveries. Nevertheless, the achieved recovery clearly demonstrates that direct dry distillation of ^{211}At from the intact target is feasible in principle.

Compared with dry distillation of scraped IBM in the tube furnace, processing in the vertical oven required longer heating times of approximately 30 to 60 min. This indicates slower release of ^{211}At under applied conditions and is most likely related to the lower operating temperature. In contrast to the tube-furnace setup, the temperature in the vertical oven was limited by the melting point of the aluminum backing and by the thermal stability of the borosilicate glass components. While this restricted the attainable process temperature and likely reduced the release rate, the overall concept still provided recoveries in a range comparable to the established scraping-based approach.

From a practical perspective, the longer heating time must therefore be weighed against the reduced number of manual preparation steps and the omission of the scraping procedure. In applications where minimization of direct handling of activated target material is a priority, this trade-off may favor the vertical oven concept despite the slower processing.

A likely limitation of the present prototype is the oxidizing atmosphere used during heating. Under oxygen-rich conditions, bismuth may oxidize to Bi_2O_3 , forming solid slag-like structures on the target surface, as shown in Figure 47. Such oxide formation may hinder mass transfer and thereby slow or partially inhibit the release of ^{211}At from the target layer. In this respect, the current recovery values may not yet reflect the full potential of the vertical oven concept. Improved performance may be achievable by using materials that permit higher operating temperatures and by further optimizing the gas atmosphere and heating geometry.

Overall, the results show that direct dry distillation of ^{211}At from intact bismuth targets is technically feasible and can provide recoveries in the range of established scraping-based procedures. Although the present prototype is not yet optimized with respect to processing time or release efficiency, it demonstrates a viable pathway toward simplified and potentially safer target processing without prior mechanical removal of the irradiated layer.



Figure 47: Showing a bismuth target after irradiation and after dry distillation processing using a vertical oven setup at 570 °C. Photographs is visually cleaned. The original photograph is shown in the Appendix in Figure B-3.

Process monitoring during dry distillation

Because global recovery values alone do not reveal where activity is released, retained, or lost within the system, additional detector-based process monitoring was used to obtain a more time-resolved view of the separation process.

Monitoring ^{211}At during the dry distillation process was crucial for identifying the progress of the separation and potential weak points of the setup. The two most relevant monitoring positions were the furnace region, providing information on the release of ^{211}At from the IBM, and the cold trap region, indicating the arrival and trapping of transported activity. Additional detector positions, such as the rear end of the furnace or the charcoal trap assembly, were temporarily used during setup development to identify possible activity losses or unintended deposition sites.

For process monitoring, two 1-inch thallium-doped sodium iodide (NaI(Tl)) scintillation detectors (Radhound, LabLogic) were shielded with several layers of 1 mm lead foil and installed inside the glovebox. These detectors provided a highly sensitive and robust means of tracking the presence of activity within the distillation assembly and were therefore well suited for general process observation.

In practice, however, their comparatively large detection volume and high sensitivity proved disadvantageous for local signal assignment within the confined distillation geometry. Once ^{211}At had left the furnace, the NaI(Tl) detectors responded to its presence over a relatively broad section of the capillary system, such that the recorded signal mainly reflected the general presence of activity in the setup rather than its exact

position. Only minor changes in count rate were observed when the activity entered the copper cooling block, where shielding and absorption partially reduced the detected signal. The use of collimation in combination with precise detector positioning proved difficult under glovebox conditions due to limited space, shielding, and handling constraints. A representative activity profile of the ^{211}At dry distillation process obtained with 1 cm diameter circular collimation is shown in Figure 48.

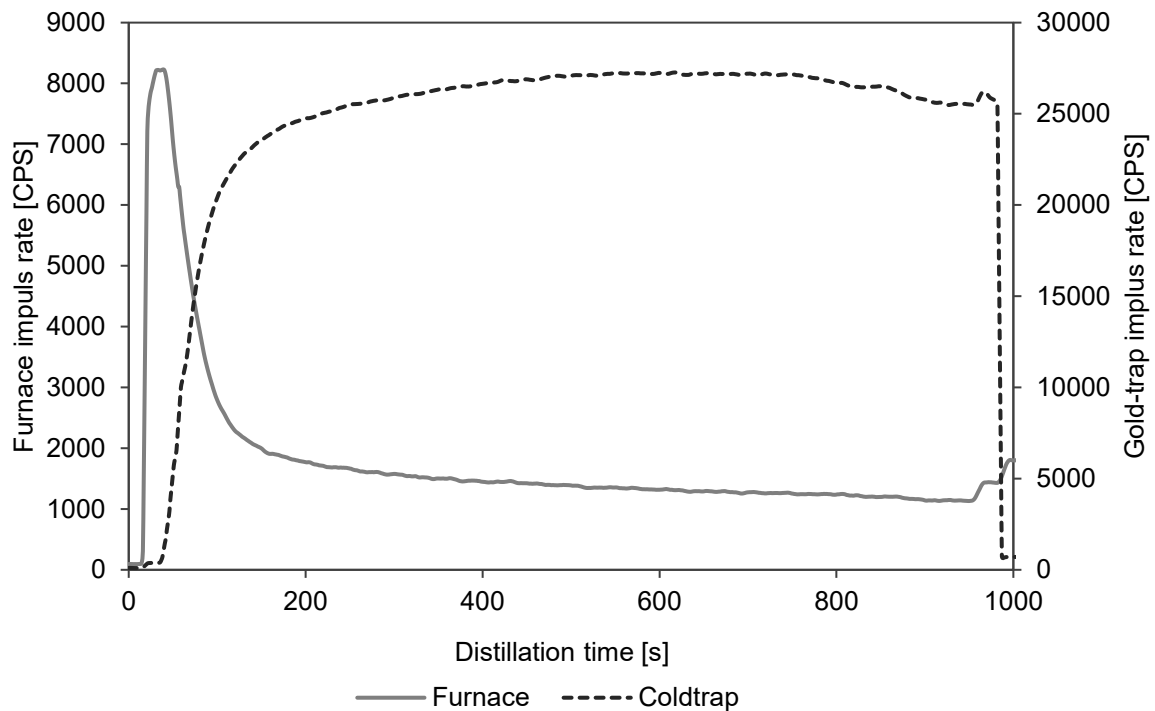


Figure 48: Monitoring during dry distillation processing using NaI(Tl) scintillation detectors aiming at the center of the furnace as well as the cold trap.

To address this limitation, a compact PIN (p-intrinsic-n diode)-diode-based detector module was introduced for localized monitoring at selected positions of the transfer line. The detector concept and signal processing were based on a design by Keller et al. [123], and were slightly adapted for the present setup. In this application, the lower absolute efficiency of the PIN detector proved beneficial. In contrast to the NaI(Tl) detectors, their response was more strongly dominated by activity in the immediate vicinity of the detector position, thereby enabling a more localized interpretation of the signal without the need for additional shielding or collimation.

When mounted directly at the furnace outlet, the PIN detector showed a distinct decrease in signal once no further activity emerged from the furnace, thereby providing a practical indication of the effective end of the release step (Figure 49A). When placed near the cooling trap, the detector exhibited a delayed signal increase compared with the NaI(Tl) detector, consistent with the time required for volatile ^{211}At species to traverse the approximately 10–15 cm long room-temperature capillary section before reaching the cold region (Figure 49B).

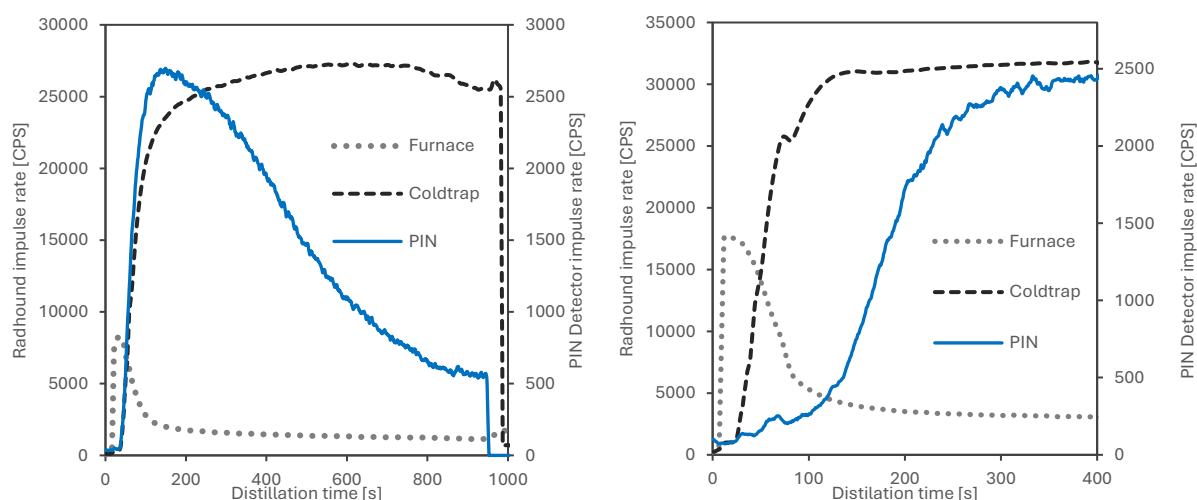


Figure 49: PIN detector compared to NaI positioned at Furnace outlet (left) and at cold trap (right).

These observations show that the NaI(Tl) detectors were well suited for sensitive overall monitoring of the distillation process, whereas the compact PIN detector provided superior local process information under the given geometric constraints. The combination of both approaches therefore proved particularly useful: NaI-based monitoring enabled reliable detection of activity within the setup, while the PIN detector allowed improved assignment of transport progression and distillation endpoint. In addition, the PIN-based detector concept is economically attractive, with low material costs, making it a practical option for distributed multi-point monitoring in shielded radiochemical environments. Such compact and position-sensitive detector elements may therefore be of interest for future semi-automated or automated ^{211}At processing modules.

The delayed rise of the PIN signal at the cooling trap, relative to the NaI response, further suggests that local detector positioning can provide qualitative information on the temporal progression of ^{211}At transport through the capillary system. However, as no dedicated transport study was conducted, this observation should be regarded as qualitative only and was not interpreted quantitatively in the present work.

Solvent extraction

Dry distillation was not the only separation route evaluated in this work. As an alternative wet-chemical strategy, liquid–liquid extraction was investigated with the aim of comparing thermochemical and solvent-based processing in terms of recovery, purity, and practical handling.

Implementation of solid supported liquid-liquid extraction method

Solvent extraction, as well as its implementation in solid-supported liquid–liquid extraction systems for the separation of ^{211}At , has previously been described in detail by several groups, including Burns et al. [76]. In order to assess the suitability of this approach for potential later clinical application, the method reported by Burns et al. [76, 96, 124] was adapted with minor modifications and established at Forschungszentrum Jülich.

As a first step, the activity quantification used for the extraction experiments was evaluated by comparing dose calibrator measurements with HPGe-based γ -spectrometry. For this purpose, three samples were measured by HPGe, applying decay correction to account for the longer acquisition times, and eight additional samples were quantified using the dose calibrator. Overall, both methods showed satisfactory agreement for the intended purpose. Based on these measurements, the extraction procedure using 3-octanone resulted in a recovery of $88 \pm 6\%$ ($n=11$), suggesting that the method performed reproducibly within the scope of the investigated experiments.

In addition to the immediate recovery, the retrieval of ^{211}At from the 3-octanone phase after prolonged residence time on the column was also investigated, as this aspect is relevant when considering delayed processing or a possible shipment of ^{211}At -loaded columns. For this purpose, the recovery was re-evaluated after several hours, corresponding to approximately two half-lives of ^{211}At . Under these conditions, a moderate decrease in recovery was observed, with the decay-corrected recovery dropping to $69 \pm 4\%$ ($n=3$). A substantial fraction of the remaining activity was found to remain associated with the column material. This behavior is in slight disagreement

with the observations reported by McIntosh et al. (2023) [96], who described no notable decrease in recovery beyond the inherent radioactive decay of ^{211}At . Possible explanations for the reduced recovery after prolonged residence time include stronger retention of ^{211}At on the stationary phase, slow changes in astatine speciation, or time-dependent redistribution processes within the extraction system. However, these possibilities were not investigated further in the present work. The observed decrease in recovery is therefore reported here as an empirical finding, while its mechanistic origin remains unresolved.

When interpreting these recovery data, it should also be considered that activity quantification was performed using two different measurement approaches, namely HPGe γ -spectrometry and dose calibrator measurements. Although both methods showed overall satisfactory agreement within the scope of this study, they are based on different measurement principles and are associated with different sources of uncertainty. In particular, HPGe measurements required time and slight decay correction because of the longer acquisition times, whereas dose calibrator readings allowed faster routine quantification but may be more sensitive to geometry- or matrix-related effects. The observed agreement between both methods supports the general validity of the reported recovery values, but small systematic deviations cannot be fully excluded. This is particularly relevant when comparing immediate and delayed recovery measurements. Since the decrease observed after prolonged storage on the column is moderate rather than drastic, part of the apparent difference may lie within the combined uncertainty arising from decay correction, counting geometry, and routine sample handling. Nevertheless, the consistent trend toward lower recovery after extended residence time suggests that the effect is unlikely to be solely an artefact of activity quantification.

Besides astatine recovery, the carry-over of bismuth during the separation was also investigated, since residual bismuth may be relevant for subsequent processing steps. For this purpose, extraction experiments were carried out under comparable conditions using a ^{207}Bi -containing solution in the absence of ^{211}At , and the transferred bismuth fraction was quantified by low- γ counting. For the 3-octanone-based procedure, a carry-over of approximately 2% ($n=1$) of the initial bismuth activity was observed. Although this fraction appears small at first glance, its chemical relevance should not be judged from the percentage alone. In dissolved target solutions, bismuth is typically

present in a very large excess compared to ^{211}At . Consequently, even a minor fractional transfer may still correspond to a considerable absolute amount of bismuth on a molar scale. This may become relevant because subsequent processing or labeling steps are governed by chemical stoichiometry rather than by radioactive activity alone. At the same time, the practical relevance of this residual bismuth for subsequent labeling chemistry cannot be concluded from the extraction experiment alone. This aspect was therefore addressed separately in dedicated labeling experiments and is discussed in Section 3.2.4.

Motivated by these findings, the search for alternative organic phases expanded beyond 3-octanone. In particular, solvent systems previously discussed in the literature, such as MIBK (methyl isobutyl ketone), as well as additional candidate solvents, were considered. As an initial screening step, a distribution study of ^{211}At in a broader range of organic solvents was therefore carried out in order to identify promising alternatives for subsequent extraction experiments.

Distribution Coefficient

To assess the suitability of different organic solvents for the extraction of ^{211}At from nitric acid media, the distribution coefficients (K_D) of 20 organic systems were determined under otherwise identical experimental conditions. The investigated aqueous phases comprised 6 M, 2 M, and 0.1 M HNO_3 , allowing a direct comparison of solvent performance as a function of acidity. As described in Section 5.2.6, K_D values were calculated from direct activity measurements of both phases, since this approach showed better consistency in preliminary method comparisons. The corresponding preliminary comparison is provided in Appendix Table B-4. The K_D values determined in this study are summarized in Table 22. A more detailed presentation of these results can be found in the appendix in Table B-5.

To aid interpretation of the measured distribution coefficients, it should be noted that for equal phase volumes the fraction of activity transferred to the organic phase is given by:

$$f_{\text{org}} = \frac{K_D}{K_D + 1} \quad (3.7)$$

Accordingly, the value of $K_D = 10$ already corresponds to an organic-phase recovery of 90.9%, while $K_D = 300$ corresponds to 99.7%. Although the numerical difference between these two K_D values appear very large, the absolute difference in transferred activity is only about 8.8% of absolute activity. The practical distinction is therefore mainly reflected in the much lower residual activity remaining in the aqueous phase at very high K_D values.

Table 22: Overview of the distribution coefficient of various solvents tested against 6 M, 2 M and 0.1 M HNO_3 . Color-coding shows excellent extraction in green whereas low extraction is colored in red.

Org. Solvent	6 M HNO_3	2 M HNO_3	0.1 M HNO_3
1-Octanole	9.73	2.75	5.93
3-Octanone	33.55	20.64	12.64
Cinnamaldehyde	74.22	43.50	33.23
Tributyl phosphate	59.42	40.57	5.49
di-isopropyl ether	5.48	4.82	6.25
Tri octylamine	187.89	234.31	37.94
Toluol	0.35	0.94	0.32
Methyl isobutyl ketone	87.11	129.59	118.95
2-Hexanone	34.31	34.13	36.99
Octanal	301.99	271.46	114.63
2,4-Nonadione	182.06	130.17	92.99
CMPO	2.84	0.13	0.09
DB21C7 (0.1 M)	0.79	3.25	1.16
Cyclohexanone	x	45.37	106.24
Di(2-ethylhexyl) phosphoric acid	56.13	65.29	72.27
Oleic Acid	24.76	9.55	16.14
Diocetyl sulfide	72.58	33.93	14.82
Dodecane thiol	27.43	26.74	15.79
Dodecanal	105.22	81.66	17.62
1-Dodecanol	6.22	2.07	6.34

Overall, the screening revealed a pronounced solvent dependence of the distribution behavior of ^{211}At . The measured K_D values covered nearly three orders of magnitude, ranging from values well below unity ($K_D = 1$) for poorly extracting systems such as toluene (0.3), CMPO (n-octyl(phenyl)-N,N-diisobutylcarbamoylmethylphosphine oxide) (0.1), and DB21C7 (dibenzo-21-crown-7 ether) (0.8), up to values above 300 for octanal in 6 M HNO_3 . This wide range demonstrates that the partitioning of ^{211}At is

governed strongly by the chemical nature of the organic phase and cannot be explained by hydrophobicity alone. This is particularly evident from the very poor extraction observed for toluene, which served as a “non-coordinating” reference solvent. Despite its high hydrophobicity, toluene showed K_D values of only 0.4, 0.9, and 0.3 in 6 M, 2 M, and 0.1 M HNO_3 , respectively, further suggesting that non-specific transfer into a non-polar, non-coordinating organic phase is negligible under the investigated conditions.

Among the simple oxygen-containing solvents, the weakest extraction was observed for 1-octanol and diisopropyl ether (DIPE), which yielded only modest K_D values in the range of approximately 3–10. Although these systems performed better than toluene, their extraction efficiency remained limited compared with carbonyl-containing solvents. In contrast, ketones and aldehydes showed markedly enhanced distribution coefficients across all acidities, indicating that neutral oxygen donor functionality is highly favorable for the transfer of ^{211}At into the organic phase. In particular, 2-hexanone displayed consistently high and remarkably stable K_D values of 34.3, 34.1, and 37.0 for 6 M, 2 M, and 0.1 M HNO_3 , respectively. This nearly acid-independent behavior, combined with very low relative standard deviation (RSD) values, identifies 2-hexanone as one of the most robust and reproducible systems in the present screening. A similar but overall stronger behavior was observed for methyl isobutyl ketone (MIBK), which yielded K_D values of 87.1, 129.6, and 119.0, making it one of the best-performing solvents over the entire acidity range. Within the ketone series, however, the observed differences cannot be attributed to alkyl chain length alone, since branching, carbonyl position, and ring structure are superimposed on any chain-length effects. The present data therefore don't support a simple monotonic relationship between increasing hydrophobicity and extraction efficiency. These findings indicate that ketone-based systems are particularly promising candidates for further astatine extraction studies.

The favorable performance of the ketone-based solvents observed here is in broad qualitative agreement with previous work by Burns and co-workers [125], who reported ^{211}At distribution ratios of up to 69 ± 4 for 3-octanone and 95 ± 6 for MIBK in 1–3 M HNO_3 , and likewise identified ketones as particularly effective media for astatine extraction from nitric acid. While the absolute values obtained in the present study differ, especially in the case of 3-octanone, both datasets consistently rank MIBK

among the strongest conventional solvents tested. Direct numerical comparison is limited, however, because the experimental conditions were not identical.

The only ether investigated in the present screening, DIPE, showed only modest extraction. This is broadly consistent with previous studies on DIPE, for which Burns and co-workers reported a distribution ratio of 11.3 ± 0.6 in nitric acid media [125], still clearly below the values obtained for MIBK and 3-octanone. In a mechanistic study, Alliot et al. [74] further showed that astatine extraction into DIPE is, at a given pH, largely independent of the counter-ion present in the aqueous phase, while the nature of the organic solvent itself has a strong influence on the observed distribution behavior. Taken together, these findings are consistent with the present observation that ether-based systems are extractive, but clearly less favorable than the best ketone-based solvents.

An even stronger extraction behavior was observed for aldehydes. Octanal exhibited the highest K_D values of all investigated solvents, reaching 302.0 in 6 M HNO_3 , 271.5 in 2 M HNO_3 and 114.6 in 0.1 M HNO_3 . Dodecanal also performed very well at higher acid concentration, with K_D values of 105.2 and 81.7 in 6 M and 2 M HNO_3 , respectively, but decreased more strongly to 17.6 in 0.1 M HNO_3 . Cinnamaldehyde followed the same general trend, although at lower absolute values (74.2, 43.5 & 33.2 at 6, 2 and 0.1 M HNO_3 , respectively). Within the aliphatic aldehydes, octanal consistently showed higher K_D values than dodecanal, indicating that increasing alkyl chain length alone does not necessarily improve ^{211}At extraction. This further supports the conclusion that lipophilicity is not the sole factor governing the observed distribution behavior. The particularly high extraction into aliphatic aldehydes, compared with aromatic cinnamaldehyde, further suggests that both donor functionality and molecular environment affect the observed partitioning behavior. The aldehyde series therefore represents one of the most effective solvent classes identified in this work, with octanal standing out as the strongest overall candidate.

The diketone 2,4-nonadione also showed outstanding extraction performance, with K_D values of 182.1, 130.2, and 93.0 for 6 M, 2 M, and 0.1 M HNO_3 , respectively. Its consistently high performance across all acidities places it among the most promising systems investigated. Compared with the simple ketones, the higher distribution coefficients of 2,4-nonadione may indicate stronger or more favorable interactions with

the extracted astatine species. However, as the present experiments were limited to solely activity-based distribution measurements, solid conclusions regarding partitioning mechanisms can't be drawn from these data.

The organophosphorus extractants displayed distinctly different behaviors depending on their functional group. Tributyl phosphate (TBP) showed good extraction in concentrated nitric acid, with K_D values of 59.4 and 40.6 in 6 M and 2 M HNO_3 , respectively, but dropped sharply to 5.5 in 0.1 M HNO_3 . This pronounced decrease indicates a strong dependence on the composition of the aqueous phase and suggests that TBP favors species formed in nitrate-rich and strongly acidic media. In contrast, bis(2-ethylhexyl)phosphate (HDEHP) remained an efficient extractant over the full acidity range and even showed slightly improved performance toward lower acidities, with K_D values of 56.1, 65.3, and 72.3 in 6 M, 2 M and 0.1 M HNO_3 , respectively. The bifunctional organophosphorus extractant CMPO, despite its established relevance in other extraction systems [126], performed unexpectedly poorly in the present study, yielding K_D values of only 2.8, 0.1, and 0.1 for 6 M, 2 M, and 0.1 M HNO_3 , respectively. However, this result should be interpreted with caution, as the applied CMPO system differed substantially from classical TRUEX (transuranium extraction process)-type formulations in which additives like TBP or n-dodecane contributes significantly to the overall solvent properties [127]. In contrast, CMPO was used here as a 0.1 M solution in toluene without further modifier. Since the present experiments were carried out at trace-level ^{211}At activities, the poor extraction performance is unlikely to result from insufficient ligand concentration in a stoichiometric sense. Rather, the low K_D values suggest that the applied CMPO/toluene formulation did not provide a favorable organic environment for efficient partitioning under the investigated conditions. The present data therefore indicates poor extraction for the tested CMPO system but should not be taken as evidence that CMPO-based extraction systems in general are inherently unsuitable for astatine.

Within the organophosphorus group, HDEHP therefore appears considerably more suitable for ^{211}At extraction than TBP or the tested CMPO/toluene system under the investigated conditions.

Tri-octylamine showed exceptionally high distribution coefficients in strongly and moderately acidic media, with values of 187.9 in 6 M HNO_3 and 234.3 in 2 M HNO_3 , but

significantly dropped to 37.9 in 0.1 M HNO₃. These values place tri-octylamine among the most powerful extractants identified in this work. However, visual observations during the experiments showed formation of a white precipitate in the tri-octylamine system at 2 M and 0.1 M HNO₃, whereas no precipitation was observed in 6 M HNO₃. This suggests that the system was more complex than a simple partitioning between two liquid phases. The precipitate may reflect the formation of a protonated amine salt, an amine nitrate-associated phase, or another poorly soluble intermediate species, but was not further investigated. Consequently, the measured K_D values for tri-octylamine at lower acidities should be interpreted with caution, with some part of the activity may have been associated with a solid or interfacial phase rather than being truly dissolved in the organic phase. This observation may also explain the comparatively elevated scatter observed for the tri-octylamine measurements, particularly at 2 M HNO₃ (RSD = 21%). Although tri-octylamine clearly exhibits a strong affinity for ²¹¹At under certain conditions, its practical applicability may be limited by phase instability and precipitation phenomena under the elaborated conditions.

The sulfur-containing extractants, dioctyl sulfide and dodecane thiol, showed consistently good, yet not outstanding extraction behavior. Dioctyl sulfide yielded K_D values of 72.6, 33.9, and 14.8, while dodecane thiol gave 27.4, 26.7, and 15.8 for 6 M, 2 M, and 0.1 M HNO₃, respectively. Both systems clearly outperformed non-coordinating solvents such as toluene and structural analogous weak oxygen donors such as 1-octanole or DIPE, indicating that sulfur donor functionality is indeed favorable for astatine partitioning. Nevertheless, neither sulfur-containing solvent surpassed the best performing aldehydes, ketones, or tri-octylamine. This suggests that soft donor interactions alone are not sufficient to guarantee maximum extraction efficiency under the present nitric acid conditions.

A comparison of all solvent systems also shows that the influence of nitric acid concentration is strongly solvent-dependent. No universal trend can be identified across the full dataset. Instead, several distinct classes of behavior are observed. Solvents such as TBP, octanal, dodecanal, cinnamaldehyde, dioctyl sulfide, dodecane thiol, and 2,4-nonadione generally showed higher K_D values in more concentrated nitric acid, indicating that strongly acidic and nitrate-rich conditions promote extraction in these systems. In contrast, HDEHP and cyclohexanone performed best at lower acid concentration, while 2-hexanone remained nearly unaffected by the acid

concentration. Such solvent-specific acid dependence strongly suggests that the extraction behavior is influenced by changes in astatine speciation in the aqueous phase. Although the exact chemical forms of astatine present in the investigated nitric acid solutions cannot be identified from the current data alone, the observed trends clearly indicate that different solvents preferentially interact with different astatine species or extraction-relevant equilibria.

With respect to analytical quality, most solvent systems showed acceptable to very good reproducibility. In particular, 2-hexanone, dioctyl sulfide, dodecane thiol, and 2,4-nonadione were characterized by low relative standard deviations across most acidities, indicating reliable phase separation and stable partitioning behavior. In contrast, larger scatters were observed for some weaker systems, such as 1-octanol and DIPE, as well as for selected cases including tri-octylamine and dodecanal at low acid concentration. In these cases, minor differences in phase disengagement, sampling, or interfacial retention may have contributed to the observed variability. An additional source of uncertainty may also have arisen from preparation of the aqueous stock solutions. Since the ^{211}At tracer was introduced in a small volume of highly concentrated nitric acid, minor volumetric deviations during dilution would have a proportionally greater effect on the final acid concentration in the 0.1 M HNO_3 system than in the 2 M or 6 M systems. As a result, the low-acid samples were likely more susceptible to small concentration shifts during preparation, which may have contributed to the increased scatter observed in some measurements. Nevertheless, the overall ranking of the solvents remained sufficiently clear to identify the most promising candidates for further investigation.

Taken together, the present screening demonstrates that ^{211}At extraction from nitric acid is highly sensitive to the functionality of the organic phase. Non-coordinating hydrocarbons and weak oxygen donors showed only limited extraction, whereas carbonyl-containing solvents, especially aldehydes and selected ketones, displayed substantially improved partitioning. Octanal emerged as the strongest overall solvent in the present study, while MIBK, 2,4-nonadione, 2-hexanone, HDEHP, and tri-octylamine also showed highly favorable distribution behavior. At the same time, the precipitation observed for tri-octylamine at lower acidities highlights the importance of considering not only high K_D values but also phase stability and practical handling. The K_D values of those extractants are presented in Fig. 47. The sulfur-containing solvents

dioctyl sulfide and dodecane thiol likewise showed consistently favorable, although not outstanding, extraction behavior, indicating that soft sulfur donor functionality may also promote ^{211}At transfer into the organic phase. In view of the strong performance of several carbonyl-containing solvents and the generally favorable response of sulfur donor systems, thiocarbonyl-containing extractants may represent an interesting direction for future studies, although their practical applicability may be limited by the lower stability and higher reactivity often associated with simple thiocarbonyl compounds [128, 129]. From a process-development perspective, octanal, MIBK, 2,4-nonadione, HDEHP, and 2-hexanone appear to be the most promising candidates for further extraction and back-extraction studies.

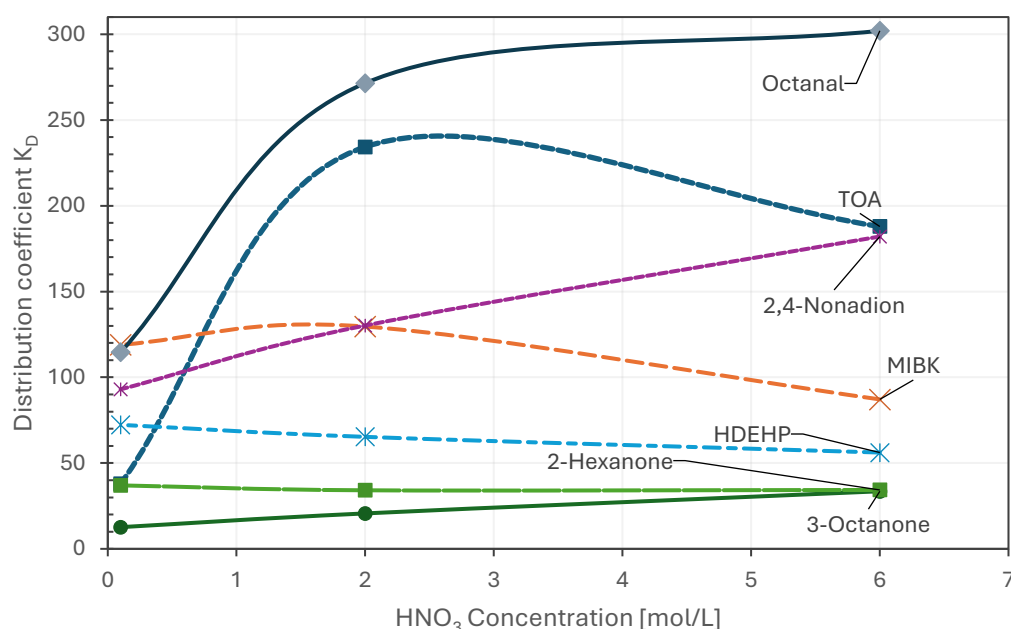


Figure 50: Distribution coefficient of selected solvents compared to 0.1, 2 and 6 M HNO_3 . The different distribution coefficients are connected by lines, to guide the eye.

To assess whether the preparation route of the ^{211}At tracer solution influences the measured distribution coefficients, a limited second screening series was performed using ^{211}At isolated by dry distillation, transferred into chloroform, evaporated to dryness, and subsequently redissolved directly in the respective nitric acid solutions. The investigated solvents and the respective distribution coefficients are presented in the appendix in Table B-6. The resulting K_D values differed substantially from those

obtained using the primary stock solution route based on concentrated nitric acid. While weak donors such as 1-octanol remained poor extractants in both approaches, several other solvent systems showed pronounced shifts in both absolute extraction strength and acid dependence. In particular, 3-octanone, cinnamaldehyde, and TBP exhibited markedly higher K_D values in the alternative approach, especially at lower acidities, whereas octanal showed substantially reduced extraction compared with the primary dataset. These differences are too large to be explained by normal experimental scatter alone and instead suggest that the measured distribution behavior depends strongly on the chemical pre-history of the ^{211}At tracer.

A plausible explanation is that the two preparation routes generated different astatine species or different distributions of extraction-relevant species prior to phase contact. In the primary procedure, ^{211}At was handled in strongly oxidizing nitric acid from the outset, whereas in the alternative route the tracer underwent dry distillation, transfer into chloroform, solvent evaporation, and only then redissolution in the target acid concentration. Such changes in chemical environment are likely to affect astatine speciation and may therefore alter the subsequent partitioning behavior. Although the present data do not allow direct identification of the underlying species, they clearly demonstrate that the measured K_D values are influenced not only by solvent identity and aqueous acidity, but also by tracer pre-treatment.

Since the direct nitric acid stock solution route more closely reflected the intended experimental workflow of the present study, it was retained as the primary basis for solvent evaluation and comparison. The alternative dataset is nevertheless of clear mechanistic interest, as it highlights the pronounced sensitivity of astatine extraction behavior to prior chemical handling.

Recovery of alternative extractants

Distribution studies of ^{211}At indicated that several organic phases may represent suitable alternatives to 3-octanone. Based on these screening experiments, selected candidates were further evaluated under the same extraction protocol as used for the

3-octanone-based separation (Table 23). In addition to liquid organic phases, commercially available extraction chromatographic resins were included in order to assess whether a more directly applicable off-the-shelf separation approach could be identified. The results of these experiments are summarized in Table 24, including the ^{211}At recovery, the corresponding bismuth carry-over, the ^{211}At lost by washing and breakthrough and the residual activity on the column. For the resin-based experiments, the distribution of ^{211}At between breakthrough, recovered eluate, and residual column activity additionally allowed a first qualitative assessment of whether the limiting factor was insufficient retention, incomplete elution, or both.

To assess non-specific losses unrelated to the actual separation chemistry, a control experiment using blank carrier material was included in the evaluation of the wet separation procedure. This experiment showed that a fraction of the initial ^{211}At activity could remain associated with the carrier/support material after processing even in the absence of the intended separation system. Although this observation is based on a single control and therefore does not allow derivation of a general correction factor, it nevertheless demonstrates that incomplete overall recovery cannot necessarily be attributed to the extraction chemistry alone. This interpretation is consistent with the activity balance observed in the liquid-liquid extraction (LLE)-based separation experiments, where loading and washing of the column were generally associated with only minor activity losses, whereas reduced recovery became apparent mainly during elution (Table 23). Accordingly, at least part of the missing activity is likely related to incomplete release of previously retained ^{211}At from the carrier material and/or other surfaces of the experimental setup.

Table 23: Recovery yields and separation parameter of selected solvents.

Extractant	^{211}At recovery [%]	Breakthrough [%]	^{211}At Washed out [%]	Residual ^{211}At [%]	Bi carry-over [%]
3-Octanone	82 ± 2	2 ± 1	3 ± 1	8 ± 2	2
Cinnamon aldehyde	80 ± 7	2 ± 3	5 ± 4	12 ± 3	2
TOA	60 ± 12	2	11 ± 4	29 ± 2	12
Octanal	89 ± 1	5 ± 2	4 ± 2	11 ± 1	1.5

Among the liquid organic phases, aldehyde-type solvents showed particularly promising behavior. Octanal afforded a recovery of $89 \pm 1\%$ ($n = 5$), whereas cinnamaldehyde yielded $80 \pm 7\%$ ($n = 3$). The high recovery observed for octanal is in good agreement with its favorable distribution behavior discussed in the previous section and suggests that octanal may represent a viable alternative to 3-octanone under the investigated conditions. Cinnamaldehyde likewise enabled effective recovery of ^{211}At , although the extraction efficiency was somewhat lower than expected from its distribution coefficient alone. This indicates that a favorable equilibrium distribution does not necessarily translate directly into improved performance under practical column conditions, where loading, washing, and re-elution behavior contribute to the overall recovery.

A further notable observation was made for delayed re-elution after storage on the column. In a single experiment using cinnamaldehyde, a recovery of 87% was obtained after approximately two half-lives of ^{211}At , indicating no obvious deterioration in back-extraction efficiency under these conditions. A similarly adverse time-dependent effect, as previously observed for 3-octanone, was likewise not apparent in the limited delayed-elution experiment performed with octanal. In contrast, 3-octanone had shown a tendency toward increased residual activity on the column after prolonged residence times, in some cases approaching about 25% of the initial activity after approximately two half-lives. This may point toward time-dependent changes in astatine speciation or strengthening of non-specific interactions during prolonged storage on the column. However, since no dedicated long-term blank control was available, this observation should be regarded as indicative rather than conclusive.

With respect to bismuth carry-over, both aldehyde systems remained in the same general range as the 3-octanone-based procedure. In single experiments, bismuth carry-over values of approximately 2% and 1.5% were observed for cinnamaldehyde and octanal, respectively. These results indicate that the improvement in ^{211}At recovery obtained for octanal was not associated with a substantial penalty in terms of bismuth transfer. From a practical point of view, this makes octanal particularly attractive among the tested liquid phases, as it combined high astatine recovery with bismuth carry-over comparable to the previously established procedure, while no obvious deterioration was observed in the limited delayed-elution experiment performed here.

Although tri-octylamine had shown precipitation tendencies during the preceding distribution-coefficient experiments, it was nevertheless included in the recovery study in order to evaluate whether usable separation performance could still be achieved under column conditions. Recovery values of $61 \pm 9\%$ ($n = 3$) were obtained, indicating that extraction was possible in principle. During the washing steps, most of the precipitate appeared to be removed; however, the final eluate still showed slight turbidity. Even though the overall recovery was not negligible, the persistent precipitation and reduced optical clarity of the final solution suggest that tri-octylamine is less suitable from a practical handling perspective, particularly for workflows requiring a clean and well-defined product solution for subsequent processing or labeling.

To further explore the practical applicability of solid-supported liquid extraction, several commercially available resins were screened as ready-to-use alternatives to the in-house packed HR-X columns (Chroma bond HR-X polymeric reversed-phase resin). The investigated materials comprised TBP Resin, ZR Resin, and DN Resin. According to the manufacturer, TBP Resin consists of tributyl phosphate supported on an inert matrix, ZR Resin is based on a hydroxamate functionality, and DN Resin is a TODGA-based (N,N,N',N'-tetraoctyl diglycolamide) DGA resin (DGA normal / diglycolamide resin). Since these resin experiments were performed primarily as an initial feasibility screen, the results should be interpreted as comparative observations rather than optimized process data.

Among the tested resins, DN Resin gave the most favorable screening result, with a ^{211}At recovery of 76% in a single experiment, together with an initial breakthrough of 10% and a residual activity fraction of 11% remaining on the column after elution. In comparison, TBP Resin and ZR Resin yielded lower recoveries of 55% and 51%, respectively, and both showed comparatively high initial breakthrough values of 18% and 20%. These data suggest that the reduced performance of TBP and ZR Resin cannot be attributed solely to incomplete retention during sample loading but also reflects incomplete recovery of the retained ^{211}At during elution. This interpretation is further supported by the substantial residual activity fractions observed on the columns after elution, amounting to 23% for TBP Resin and 11% for ZR Resin (Table 24). Accordingly, the present data point not only to insufficient capture in some cases, but also to non-negligible retention of ^{211}At on the solid phase.

Results & Discussion

Table 24: Recovery yields and behavior throughout the separation of fabricated resins.

Resin	^{211}At recovery [%]	Breakthrough [%]	^{211}At Washed out [%]	Residual ^{211}At [%]	Bi carry-over [%]
TBP Resin	55	18	10	23	11
ZR Resin	51	20	3	11	24
DN Resin	76	10	9	11	25

At first glance, the elevated initial breakthrough observed for TBP and ZR Resin could suggest that a larger resin amount might improve separation performance. However, the simultaneously increased fraction of residual ^{211}At remaining on the column after elution indicates that such an optimization may not necessarily lead to improved overall recovery. A higher resin mass could reduce breakthrough but may also increase irreversible or poorly reversible interaction of ^{211}At with the stationary phase. Within the scope of the present screening experiments, this question could not be resolved further and would require dedicated optimization of resin mass, conditioning, and elution conditions.

A more critical limitation of all three commercially available resins was the comparatively high bismuth carry-over. Bismuth transfer ranged from 11% to 25%, which is approximately one order of magnitude higher than the values observed for the in-house prepared HR-X columns combined with 3-octanone or octanal. Even though DN Resin showed the most promising ^{211}At recovery among the tested ready-to-use materials, this advantage must be weighed against the substantially increased transfer of bismuth into the final fraction. The observed bismuth carry-over was regarded as a potentially relevant process impurity. Since its influence on subsequent ^{211}At labeling could not be inferred from the separation data alone, this aspect was addressed in dedicated labeling experiments discussed later in Section 3.2.4. Consequently, any further evaluation of these resin-based approaches should not only focus on improving astatine recovery, but also on clarifying whether the associated bismuth excess can be tolerated in subsequent labeling or formulation steps.

Overall, the present screening experiments suggest that the most promising alternatives to the previously established 3-octanone system were found among the tested aldehyde solvents, particularly octanal. In contrast, the commercially available resins demonstrated that ^{211}At can in principle be recovered using ready-to-use

extraction chromatographic materials, but their present performance remained limited by incomplete recovery, elevated breakthrough, and substantial bismuth carry-over. At the current stage, these resin systems should therefore be regarded as exploratory candidates rather than immediately competitive alternatives to the optimized solvent-based procedure.

High recovery by itself did not guarantee that the isolated ^{211}At was analytically well defined or straightforward to use in later steps. For this reason, the next part does not focus on yield alone, but on how the processed astatine can readily be analyzed or behaves in routine analytical systems and whether free astatine can be quantified reliably after separation.

Taken together, the separation experiments show that high apparent recovery alone is not sufficient to identify the most suitable processing route for ^{211}At . Rather, the decisive question is whether the recovered activity is transferred into a product stream that is not only isolated efficiently but can also be quantified reliably and interpreted in chemically meaningful terms. For this reason, the following section examines the analytical behavior of processed ^{211}At and the limitations of common routine methods.

.

3.2.3. Analytical characterization of processed ^{211}At

The separation studies established how ^{211}At can be recovered from irradiated targets, yet they did not resolve how reliably the resulting product can be quantified and chemically interpreted. Any comparison between different separation routes remains incomplete unless the isolated ^{211}At fraction can also be quantified reliably and evaluated with respect to free astatine, process-related artefacts, and chemical state. Thus, the aim of the following section is to examine the processed ^{211}At under analytically relevant conditions, with particular attention to recovery, and possible misinterpretation by common chromatographic methods.

Shielded HPGe detection for ^{211}At quantification

Since all later process comparisons depend on activity determination, the discussion first considers the measurement geometries and analytical constraints relevant for reliable quantification of ^{211}At over a broad activity range.

One major challenge when working with ^{211}At is its reliable quantification. The emitted α -particles can only be detected using dedicated alpha detectors, which require short source-to-detector distances and essentially barrier-free measurement geometries. Such conditions are often difficult to realize in routine production settings. In addition, ^{211}At exhibits only a low total abundance of γ -emission, below 1%, while simultaneously emitting intense X-rays in the energy range of approximately 70–90 keV. This combination creates both analytical difficulties and practical opportunities. Without these X-rays, rapid direct quantification using proportional counters or dose calibrators would hardly be feasible. However, quantification based on X-ray emission is inherently highly geometry- and matrix-dependent, such that even small changes in sample positioning or composition may cause substantial deviations in the apparent activity. At the same time, the intense low-energy X-rays complicate more accurate quantification by HPGe γ -spectrometry, as they strongly increase the total count rate, detector background, and dead time. This effect is further enhanced because the 70–90 keV range typically coincides with a region of high intrinsic efficiency of HPGe detector crystals.

To address both the pronounced geometry dependence of low-energy measurements and the excessive background contribution from X-rays, an HPGe-based detection method employing external lead shielding was established in this work. Lead sheets of 1 or 5 mm thickness were used in combination with adapted source-to-detector distances. A detailed description of the efficiency calibration procedure is given separately in the Methods section; in the present section, only the consequences of the modified detector geometry for ^{211}At quantification are discussed.

The resulting calibration curves for the most relevant detector assemblies are shown in Figure 51 and demonstrate a pronounced shift of the efficiency maximum toward higher energies with increasing shielding, accompanied by an overall reduction in absolute efficiency. Without lead shielding at a distance of 30 cm, the efficiency maximum was approximately $9.26 \cdot 10^{-4}$ at 142 keV (A). With 1 mm lead shielding at the same distance, mounted between two 5 mm acrylic glass plates, the maximum efficiency decreased to $2.43 \cdot 10^{-4}$ and shifted to approximately 400 keV (B). An even stronger effect was observed for the 5 mm lead configuration at 50 cm distance, where the maximum efficiency further decreased to $6.69 \cdot 10^{-5}$ and shifted to around 610 keV (C). This energy range lies close to the principal γ -lines of ^{211}At at 569.7, 687.0, and 897.8 keV.

Although the 569.7 and 897.8 keV γ -lines can also be observed in ^{211}At measurements, the 687.0 keV line was preferred for routine quantification, as it is well accessible in the shielded detector geometries as well as the direct characteristic γ -line of ^{211}At , while the other two lines originate from its short-lived daughter ^{211}Po . At this energy, the full-energy peak efficiency decreased by approximately a factor of five, from $3.19 \cdot 10^{-4}$ for the unshielded 30 cm geometry to $6.61 \cdot 10^{-5}$ for the 5 mm lead-shielded configuration at 50 cm. In return, the low-energy region below approximately 300 keV was effectively suppressed.

This enabled measurement of freshly irradiated targets as well as samples from large-scale processing without exceeding approximately 20% detector dead time. This threshold should not be understood as a strict physical limit, but rather as a practical compromise: it kept dead-time and pile-up effects sufficiently moderate for robust quantification, while still providing adequate count rates in the relevant high-energy γ -region. In contrast to a simple increase in source-to-detector distance, shielding suppresses predominantly the undesired low-energy contribution without relying solely

on geometric dilution of the entire spectrum. Consequently, higher count rates at the relevant ^{211}At γ -lines could be maintained, allowing shorter acquisition times without major loss of statistical quality. Overall, the use of lead shielding transformed the HPGe setup from a strongly X-ray-dominated measurement geometry into a configuration better suited for robust high-activity ^{211}At quantification via its higher-energy γ -lines. A potential drawback of additional lead shielding is that it can alter spectral background and apparent peak shape, for example by increasing backscatter-related contributions [130, 131]. In the present work, however, this was not considered a major limitation, since ^{211}At quantification was based on the isolated 687.0 keV γ -line and peak areas were determined by manual integration. Inference: such area-based evaluation is expected to be less sensitive to moderate deviations between measured and calibrated peak shape than strictly model-dependent peak fitting [132]. More critical sources of uncertainty were considered to be geometry- and matrix-dependent effects as well as potential peak overlap, which are recognized sources of systematic error in γ -spectrometry [130].

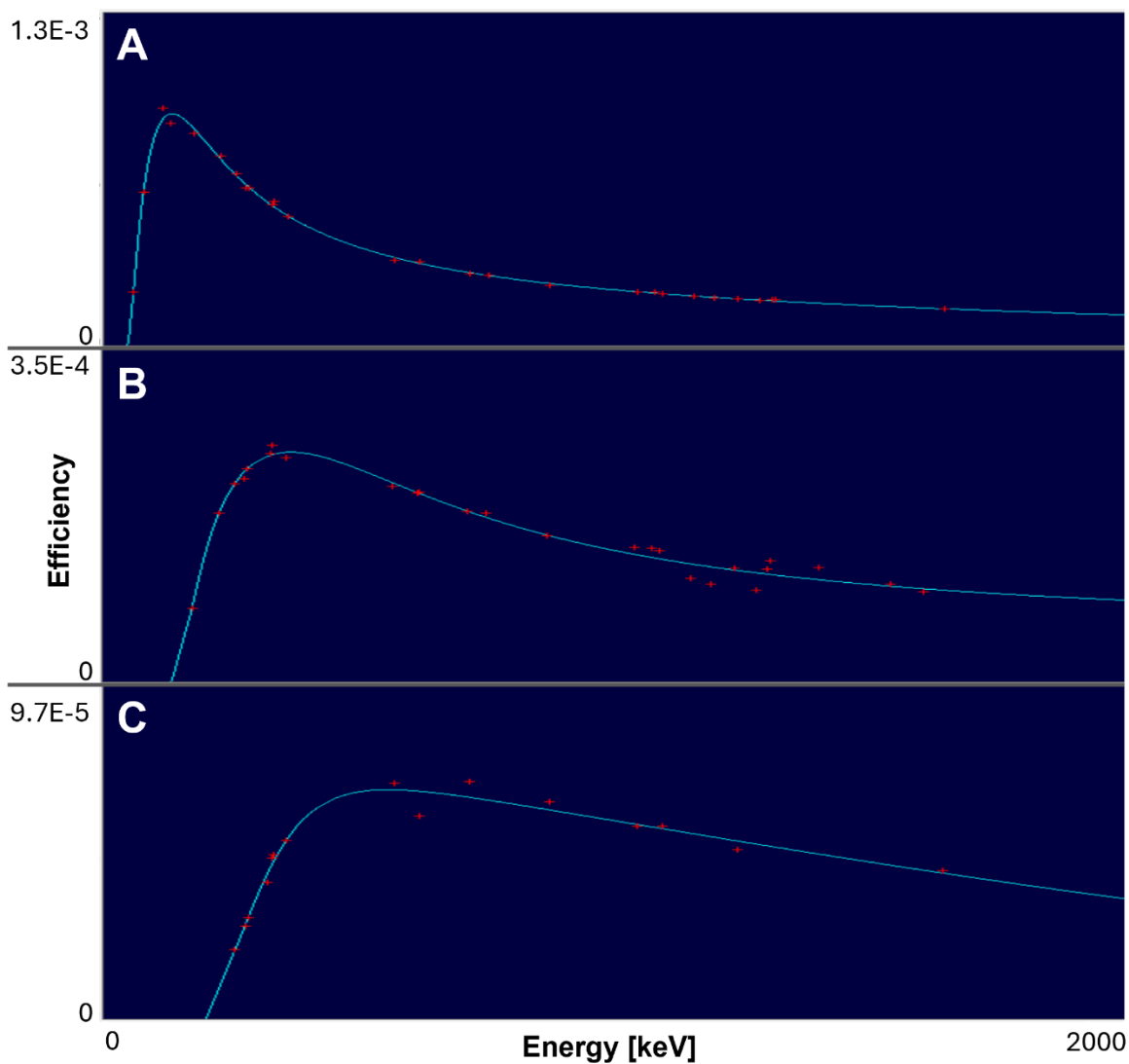


Figure 51: Efficiency curves of the HPGe γ -spectroscopy setup used for ^{211}At measurements, presenting the efficiencies for (A) 30 cm detector distance, (B) 30 cm distance with a 1 mm lead filter, and (C) 50 cm distance with a 5 mm lead filter, with corresponding efficiencies of $h_{687 \text{ keV}} = 3.19\text{E-}4$, $h_{687 \text{ keV}} = 1.84\text{E-}4$, and $h_{687 \text{ keV}} = 6.61\text{E-}5$, respectively.

Visible radioluminescence from concentrated ^{211}At samples

Beyond routine activity quantification, an additional side observation concerned the faint visible emission of highly active ^{211}At samples. Although not central to the processing workflow, this phenomenon provided useful insight into the physical origin of the observed luminescence.

Well-known photographs of concentrated ^{225}Ac and ^{224}Ra preparations showing a faint blue glow have become a recognizable visual motif in targeted alpha therapy and radionuclide production contexts [133, 134]. The exact origin of such optical emission depends on the geometry, medium, and radiation field, and may include Cherenkov light, radioluminescence of air or surrounding materials, or a combination of these processes. Inspired by these benchmarks, we explored the visible appearance of ^{211}At produced at Forschungszentrum Jülich and assessed under which practical conditions its preparations yield a detectable optical signal.

For this experiment, ^{211}At was obtained by a 4 h irradiation under standard production conditions and quantified by HPGe γ -spectrometry yielding 4.6 GBq ^{211}At at EOB. The ^{211}At obtained was processed using dry distillation method and collected in 100 μL CHCl_3 in a 4 mL V-shaped borosilicate glass vial. The sample was dried under argon and subsequently adjusted to a nitrogen atmosphere. The post processing activity was determined to be 3.3 GBq ^{211}At using HPGe γ -spectroscopy.

At this activity, a very faint blue luminescence could already be observed with bare eyes under ordinary laboratory lighting conditions during the gas exchange. Under darkened conditions, the luminescence became clearly visible to the unaided eye and remained detectable even after substantial decay of the sample. A photograph of two minutes exposure time was taken right after processing (Figure 52). The picture shows two V-vials, one containing the ^{211}At sample and the other being a reference vial with no added activity. The sample vial was surrounded in a faint blue glow originating from the tip of the V-shape. Furthermore, several localized bright spots were visible along the inner wall of the vial. These most likely originated from small residual CHCl_3 droplets formed during transfer of the astatine solution and fixed in place after solvent evaporation. Their visibility suggests that localized blue emission may already occur at substantially lower local ^{211}At activities than the total activity investigated here. This observation was further supported by a later inspection of the sample (1.5 half-lives

later). When approximately 1 GBq ^{211}At remained in the vial, the blue glow was still visible with the naked eye.

To the best of our knowledge, comparable photographic documentation of visible luminescence from a GBq-scale ^{211}At sample has not been reported before.



Figure 52: Showing a long-time exposure photograph (2 min) of radioluminescence of ^{211}At (~3 GBq) in a V-shaped borosilicate glass vial (right). As comparison, a similar vial without activity is shown right beside (left). The radiation dose measured of this assembly was $\sim 57 \text{ mSv h}^{-1}$ contact dose and $\sim 600 \mu\text{Sv h}^{-1}$ at 30 cm distance (Camera distance). The radiochemical preparation was performed by Lucas Mues (Author) whereas the photograph was taken by Dr. Alexander Haseloer.

To further investigate the origin of this luminescence effect, subsequent experiments were conducted investigating the behavior of ^{211}At under different gas atmospheres present or whether the sample is in a dry or submerged/dissolved in liquid.

A second ^{211}At sample was produced in a 2.5 h irradiation under otherwise unchanged conditions. After processing analogous to the first experiment, the product was

subdivided into three fractions, transferred into comparable V-shaped vials, dried, and subsequently exposed to different gas atmospheres, argon, helium and krypton gas (Figure 53(A) from left to right respectively). Thereafter, the three samples were placed next to each other inside the cabinet and a photo was taken with two minutes exposure time. Beside the total activity of the combined vial was significantly lower than for the first experiment (639, 1270 & 924 MBq end of processing (EOP)) due to the shorter irradiation time and then further subdivided into three, the blue glow was still visible by the bare eye, yet significantly more faint than for the first experiment.

The three vials showed slight differences in the intensity of the glow, originating from uneven partitioning of the activity into the three vials, yet the color and appearance of the glow was all the same and comparable to the first experiment containing N₂ atmosphere, too. Within the limitations of incomplete gas exchange and unequal activity partitioning, no major qualitative change in color or spatial emission pattern was observed between argon, helium, krypton, and nitrogen atmospheres.



Figure 53: Long-exposure photographs of ^{211}At -containing V-vials under different gas and solvent conditions. (A) Dried ^{211}At samples under argon, helium, and krypton atmospheres. (B) Corresponding samples after addition of water, chloroform, or diiodomethane. The images show that the visible emission persisted under different atmospheres but decreased markedly after addition of liquid, with the spatial emission pattern depending strongly on the apparent activity distribution (photograph by Dr. Alexander Haseloer).

The vials were subsequently filled with water, chloroform, or diiodomethane (Figure 53(B)) to assess whether the visible emission persisted under liquid-covered conditions. Upon addition of liquid, the visible emission decreased markedly and was no longer visible without long-exposure photography. However, the solvent experiment did not isolate refractive-index effects, because the activity distribution differed strongly

between solvents. In water and diiodomethane, activity appeared to remain localized near the vial tip, whereas in chloroform a more homogeneous blue shimmer was observed (Figure 54). Thus, the experiment mainly indicates that the spatial distribution of ^{211}At relative to the glass surface strongly affects the visible emission. The persistence of a weak optical signal under liquid-covered conditions further suggests that gas-phase radioluminescence is not the dominant mechanism.



Figure 54: Long-exposure photograph of a ^{211}At -containing vial showing localized blue emission along the vial wall and near residual activity deposits. The spatially localized pattern supports a surface-related radioluminescence contribution rather than a purely homogeneous gas-phase emission. (photograph by Dr. Alexander Haseloer)

Radioluminescence presented for ^{225}Ac or ^{224}Ra is sometimes described as Cherenkov radiation most prominently known from pictures of nuclear reactors. The key requirement for Cherenkov radiation to occur is the emission of a charged particle with high enough energy to traverse a medium faster than the speed of light in the same medium. For light charged particles like electrons/positrons this happens at reasonable low energy, depending on the medium and can be readily calculated by the equations 3.8–3.10 [135]:

$$\beta \equiv \frac{v}{c} > \frac{1}{n} \rightarrow \beta_t = \frac{1}{n} \quad (3.8)$$

With the prerequisite for Cherenkov radiation β , the particle velocity v in a certain medium and the speed of light c in vacuum ($c \approx 3 \cdot 10^8 \frac{m}{s}$) and n^7 is the refractive index of the medium forming then the Cherenkov threshold β_t .

$$\gamma = \frac{1}{\sqrt{1-\beta^2}} \rightarrow \gamma_t = \frac{1}{\sqrt{1-\frac{1}{n^2}}} \quad (3.9)$$

$$T = (\gamma - 1)mc^2 \rightarrow T_t = (\gamma_t - 1)mc^2 \quad (3.10)$$

This is then substituted into the relativistic Lorentz factor γ , forming the threshold factor γ_t . That further forms the kinetic energy T in dependence of the particle mass m (for electrons and positrons $m_e c^2 = 0.511 \text{ MeV}$)

However, for larger charged particles like alpha particles (~ 8000 times heavier than electrons $m_\alpha c^2 \cong 3727 \text{ MeV}$), the energy required to generate Cherenkov radiation increases drastically.

In Table 25, the required energies for charged particles present in this experiment at different media are listed.

Table 25: Approximate refractive indices and corresponding Cherenkov threshold energies for electrons/positrons and α -particles in selected gases, liquids, and borosilicate glass relevant to the ^{211}At luminescence experiments. The values were calculated using the Cherenkov condition $\beta > 1/n$. They show that direct Cherenkov emission by α -particles is energetically excluded, while secondary electrons in condensed media could in principle exceed the Cherenkov threshold.

Medium	n^8	β_t	γ_t	$T_t(m_e)[\text{MeV}]$	$T_t(m_\alpha)[\text{GeV}]$
Water	1.333	0.75	1.51	0.26	1.91
Chloroform	1.435	0.70	1.39	0.20	1.47
Diiodomethane	1.743	0.57	1.22	0.11	0.82
Air	1.00027	0.99973	43.04	21.48	156.71
Argon	1.00028	0.99972	42.27	21.09	153.82
Borosilicate glass	1.473	0.68	1.36	0.18	1.35

This table strongly underlines that alpha particles originating from decay reactions are orders of magnitude from reaching enough energy to produce Cherenkov radiation.

⁷ The refractive index is dependent on the photon wavelength. For visible Cherenkov light, the sake of simplicity, refractive index for the standard reference 589 nm (Sodium-D line) is chosen in this study.

⁸ Refractive indices are approximate literature values used for order-of-magnitude Cherenkov threshold estimates. Liquid values are given as n_D^{20} , i.e. at 20 °C and the sodium D-line, $\lambda = 589.3 \text{ nm}$, unless stated otherwise. Gas refractive indices depend on pressure, temperature, humidity, and wavelength; therefore, standard-condition values were used only for qualitative comparison. Refractive-index data were taken from Harvey for water [136], Kedenburg et al. for chloroform [137], CRC/Vogel for diiodomethane [138], Ciddor for air [139], Larsén/RefractiveIndex.INFO for argon [140], and SCHOTT BOROFLOAT® for borosilicate glass [141]

Beta particles on the other hand readily possess energies higher than 260 keV producing Cherenkov radiation at least in medium. Yet even decay electrons/positrons would have a hard time producing Cherenkov radiation in gaseous medium like air or argon. So at least in liquid medium the presence of Cherenkov radiation is possible as denoted by Ackerman and Graves [142] explaining Cherenkov radiation for ^{225}Ac and ^{224}Ra since both emitting multiple beta particle during their decay chain. For ^{211}At itself, no relevant prompt β -emission is available to drive Cherenkov light directly. ^{211}At decays either by EC to short-lived ^{211}Po , followed by α -emission, or by α -emission to long-lived ^{207}Bi . The latter mainly decays by EC on a time scale of decades. Therefore, any direct β -contribution from the ^{211}At decay chain is negligible under the conditions of the present experiment. Only secondary electrons generated by photon interactions, especially Compton scattering in the vial material, remain a plausible Cherenkov-related contribution.

In the following, only a plausibility estimate is given as to whether Cherenkov radiation could contribute measurably to the observed blue glow of ^{211}At samples. Detailed derivations and estimation steps are provided in Appendix B-4. Since the same optical effect was observed under gaseous as well as liquid conditions, the borosilicate glass vial was considered the most likely common medium in which the relevant light-generating process occurs. Accordingly, the Cherenkov threshold for electrons in borosilicate glass was taken as the relevant benchmark for further assessment [143].

Direct Cherenkov generation by α -particles can be excluded to a good approximation, since the α -particle energies present in the ^{211}At decay chain are far below the threshold required in borosilicate glass. Indirect generation of Cherenkov light by secondary electrons is, in principle, possible. In particular, γ -induced Compton electrons from the major photon emissions of the ^{211}At decay series can reach energies above the electron threshold in glass. However, the corresponding order-of-magnitude estimates indicate only a comparatively small visible photon yield. Thus, while Cherenkov emission from secondary electrons cannot be ruled out mathematically, it is unlikely to account for the pronounced blue glow observed experimentally.

This interpretation is also supported by the spatial appearance of the emission. If Cherenkov light generated by photon interactions in the glass were the dominant mechanism, a more homogeneous light distribution across the vial wall would be

expected. Instead, the luminescence appeared strongly localized, particularly at the rim and at small residual deposits on the inner glass surface, including regions where the local activity was presumably well below the GBq range. The observed pattern therefore argues against Cherenkov light as the dominant source of the visible emission.

A more plausible explanation is localized radioluminescence of the borosilicate glass induced by α -particle energy deposition near the surface. If ^{211}At is present as a dry deposit adhering to the inner wall of the vial, a substantial fraction of emitted α -particles enters the glass in 2π geometry. The deposited power is small in absolute terms, yet confined to a very thin near-surface region and therefore associated with high local excitation density. Under such conditions, radiative recombination and defect-related luminescence in the glass matrix provide a more consistent explanation for the observed blue glow than Cherenkov emission [144, 145]. This interpretation is also in line with the marked decrease in visible glow after dissolving the activity in chloroform, where the activity is no longer concentrated at the glass surface [146].

Taken together, the observations are more consistent with localized radioluminescence of the borosilicate glass than with Cherenkov radiation as the dominant mechanism [142, 144, 145].

Radio-HPLC for ^{211}At analytics

Simple activity quantification, however, is not sufficient for downstream radiochemistry. Reliable quantification of free ^{211}At by RP-HPLC is as important for the analytical evaluation of astatine radiolabeling reactions, since incomplete detection of unreacted astatine may directly affect parameters such as radiochemical conversion and radiochemical purity. In the present study, the recovery of free astatine was therefore assessed systematically with regard to both stationary phase and mobile phase composition. The aim was not only to compare different chromatographic conditions, but also to determine whether limited recovery of free astatine reflects a specific column-related effect or a more general analytical limitation of RP-HPLC.

Initial recovery assessment was based on the online radiotrace recorded with a flow-through radiation detector, as commonly used in routine radiopharmaceutical analysis. To provide a reference independent of column retention, post-column injection (PCI) method was employed [147, 148]. In this approach, the astatine solution was injected downstream of the analytical column and therefore passed only through the remaining HPLC flow path and the detector, but not through the stationary phase itself. This allowed online evaluation of the detector response independently of possible retention on the column.

During the first measurements, it became clear that free astatine often produced broad and tailing radiotracers, in marked contrast to the sharp and well-defined peaks generally obtained for astatine-labeled organic compounds and for the post-column injection control. Under these conditions, signal integration became increasingly uncertain, since the beginning and end of the peak could not always be defined reproducibly. Exemplary chromatograms are presented in Figure 55. This made it necessary to differentiate between a purely signal-related integration problem and a genuine loss of ^{211}At due to incomplete elution from the column.

Notably, PCI did not always result in sharp and symmetrical signals. In several cases, pronounced tailing was still observed, indicating that the distorted peak shape of free ^{211}At cannot be attributed to column retention alone. Instead, extra-column effects such as band broadening or non-specific interaction with downstream components of the HPLC system are likely to contribute as well.

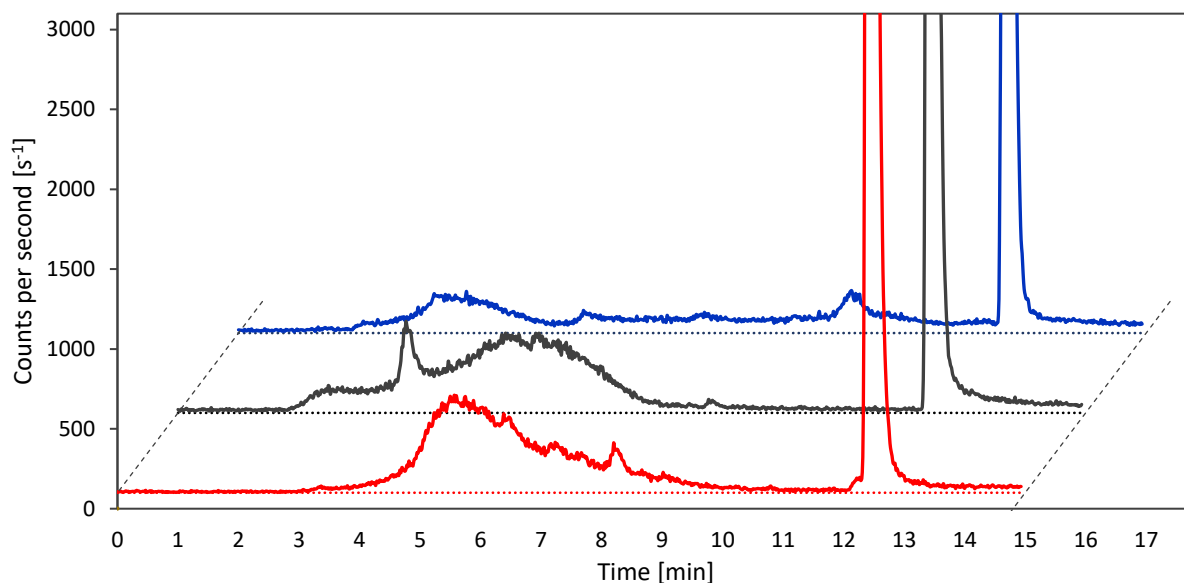


Figure 55: Exemplary chromatograms showing broad and distorted peaks of free ^{211}At partly washed off the column independently of column material and prepared ^{211}At species. The red graph shows the Waters XBridge column at reducing conditions, the black graph shows the performance of the Merck Chromolith column at reducing conditions and the blue graph shows the PolymerX column with native ^{211}At .

To address this, the online detector-based evaluation was complemented by offline recovery measurements. For this purpose, the complete column effluent was collected and quantified using a low level γ -counter. In addition, a reference measurement was performed under otherwise comparable conditions without the analytical column, so that the same activity passed through the HPLC system and collection procedure without being exposed to the stationary phase. In this way, losses related specifically to column retention could be assessed more reliably. While this procedure is not practical for routine quality control, it allowed quantification of the total eluted activity independently of peak shape and also improved counting statistics because the full sample could be measured for a longer time. Since the main photon emissions of ^{211}At are low-energy X-rays, therefore, sample volume and geometry were kept as constant as possible in order to minimize self-absorption effects during offline counting.

The chromatographic comparison itself was performed in two steps. In a first series, four reversed-phase columns with distinctly stationary-phase chemistries were tested under two broadly relevant solvent systems, namely water/acetonitrile and water/acetonitrile containing 0.1% TFA (trifluoroacetic acid). In the second series, the mobile phase was varied further in order to identify conditions that improved astatine

recovery. Since free astatine may occur in chemically different forms depending on the preceding labeling chemistry, three representative astatine formulations were included.

Astatine sample composition

To assess the chromatographic behavior of free astatine under practically relevant conditions, three representative astatine formulations were included in this study: an electrophilic, a nucleophilic, and a native formulation without deliberate adjustment of the oxidation state. This distinction was chosen to reflect the two principal classes of astatine labeling chemistry while also covering free astatine that may occur outside deliberately controlled labeling conditions [32, 149].

Electrophilic labeling approaches are generally based on oxidized astatine, whereas nucleophilic methods rely on astatide. Consequently, unreacted astatine can be present in chemically different forms depending on the labeling route and is therefore not necessarily expected to show uniform chromatographic behavior.

In the present study, electrophilic astatine was prepared by oxidation with *N*-chlorosuccinimide, whereas nucleophilic astatine was generated by reduction with ascorbic acid. In addition, astatine resolved without further redox treatment was included as a native formulation in order to mimic free astatine potentially formed by deastatination. This case was considered particularly relevant, since release of astatine from the labeled vector remains one of the main limitations in the development of ^{211}At radiopharmaceuticals [32, 91, 149].

The three formulations were therefore not intended to represent all conceivable inorganic astatine species, but rather to cover the most relevant practical situations in which free astatine may be encountered during radiolabeling studies or as a result of bond instability. This was considered sufficient to evaluate whether chromatographic recovery of free astatine is robust across chemically distinct but practically meaningful sample types.

Stationary and mobile phase considerations

Because the behavior of free astatine already appeared to be strongly condition-dependent, several stationary phases were tested rather than optimizing only one column from the start. Although all reversed-phase columns provide a comparatively non-polar environment, their detailed surface properties can differ considerably depending on the support material, ligand chemistry, endcapping, and residual silanol activity [150]. Such differences can strongly affect problematic inorganic analytes, as has also been reported for n.c.a. [^{18}F]fluoride [151].

The four columns selected for this study were chosen to cover a broad range of stationary-phase chemistry. The Luna C18(2) represents a rather conventional silica-based ODS (octadecylsilane) column and can be considered a typical first choice in RP-HPLC method development. The Waters XBridge C18 was included because its hybrid particle design offers increased pH stability and reduced silanol activity. A PolymerX column was tested as a silica-free alternative based on a polystyrene-divinylbenzene copolymer, thereby excluding classical silanol interactions altogether. Finally, the Merck Chromolith RP-18 was included because it had previously shown low retention for n.c.a. [^{18}F]fluoride.

Before comparing solvent systems in detail, one practical issue had to be addressed first. Once astatine had been retained on a column, part of it could reappear in subsequent runs by slowly “bleeding-off” and thereby falsify the apparent recovery. Waiting for full decay was not realistic, since this would require about ten half-lives, i.e. roughly 72 h. Therefore, a regeneration procedure was established. Based on the approach reported by Guérard and co-workers [152], reducing solutions were tested for removal of retained astatine. Injection of sodium sulfite through a small loop proved insufficient, since substantial residual activity was still released afterwards. More reliable cleaning was achieved by prolonged elution with sodium thiosulfate solution using a manually operated HPLC pump. This solution was less alkaline than sodium sulfite, hence it was considered more suitable for repeated use on the silica-based columns, especially the Chromolith RP-18. A minimum of five column volumes of 0.5% freshly prepared sodium thiosulfate was sufficient to remove residual activity and enabled repeated measurements on the same day.

Results & Discussion

The first comparative results are summarized in Table 26, which compiles the recovery of ^{211}At from the four HPLC columns under neutral water/acetonitrile conditions and under acidic water/acetonitrile/0.1% TFA conditions. Recoveries derived from the online chromatographic signal are complemented by offline values obtained from the collected eluent, allowing a more robust assessment whenever distorted peak shapes limited the reliability of peak integration. Exemplary chromatograms of recovery measurements of the four tested columns operated with acetonitrile (MeCN) / water solvent mixture are presented in Figure 56.

Table 26 Recovery of ^{211}At [%] from varying HPLC columns in either water/acetonitrile or water/acetonitrile/TFA solvent systems. Radioactivity balance was measured online by post-column injection whereas offline by γ counting was measured of the efflux from the column (online method | offline method), (n=3).

MeCN / Water				
Column	Electrophilic At	Nucleophilic At	Native At	Avrg. over all samples
Phenomeenex Luna C18(2)	33 $\pm$ 10 29 $\pm$ 9	40 $\pm$ 18 41 $\pm$ 4	41 $\pm$ 21 50 $\pm$ 11	38 40
Waters Xbridge C18	63 $\pm$ 4 49 $\pm$ 7	60 $\pm$ 12 30 $\pm$ 12	43 $\pm$ 10 60 $\pm$ 12	55 46
Phenomenex Polymer X	24 $\pm$ 13 24 $\pm$ 8	28 $\pm$ 12 36 $\pm$ 18	39 $\pm$ 11 39 $\pm$ 14	30 33
Merck Chromolith	80 $\pm$ 20 73 $\pm$ 14	89 $\pm$ 26 66 $\pm$ 11	68 $\pm$ 13 68 $\pm$ 4	79 69
Avrg. over all columns	53 47	54 43	47 54	

MeCN / Water / 0.1% TFA				
Column	Electrophilic At	Nucleophilic At	Native At	Avrg. over all samples
Phenomeenex Luna C18(2)	16 $\pm$ 5 22 $\pm$ 9	44 $\pm$ 24 43 $\pm$ 19	8 $\pm$ 4 14 $\pm$ 5	23 26
Waters Xbridge C18	37 $\pm$ 13 37 $\pm$ 15	71 $\pm$ 16 42 $\pm$ 10	14 $\pm$ 4 16 $\pm$ 5	40 32
Phenomenex Polymer X	9 $\pm$ 2 12 $\pm$ 4	31 $\pm$ 2 30 $\pm$ 13	7 $\pm$ 14 12 $\pm$ 4	16 18
Merck Chromolith	18 $\pm$ 2 25 $\pm$ 5	68 $\pm$ 8 47 $\pm$ 13	21 $\pm$ 1 18 $\pm$ 3	36 30
Avrg. over all columns	19 24	54 41	13 15	

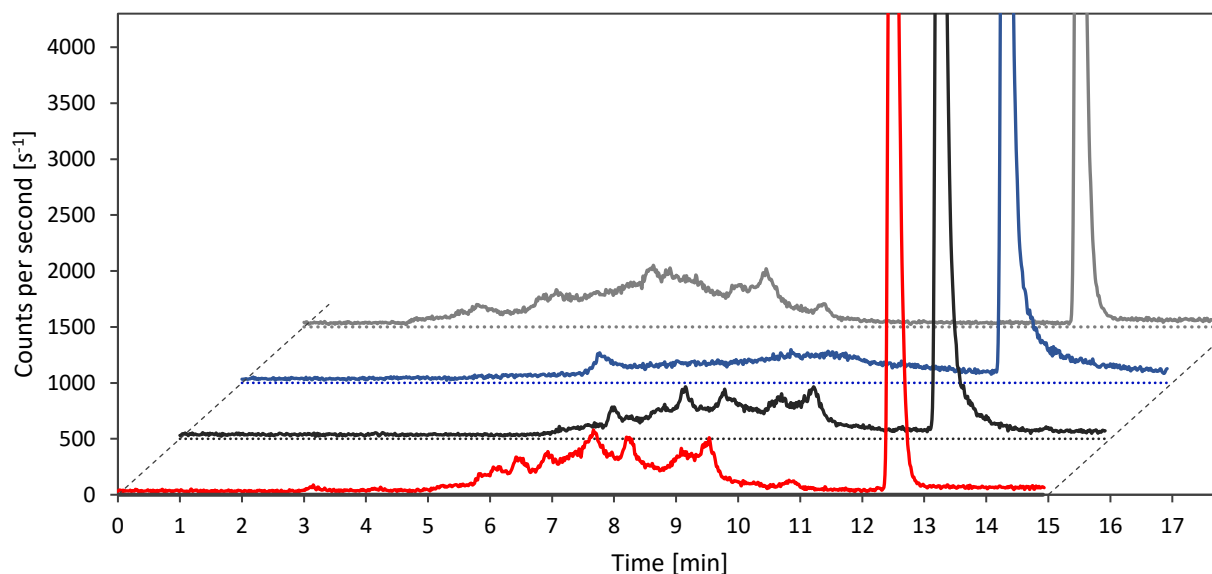


Figure 56: Exemplary chromatograms of the four different columns (Red: XBridge, Black: Luna C18, Blue: PolymerX and Grey: Chromolith RP-18) under reducing conditions with Water/MeCN + 0.1% TFA solvent mixture.

Under neutral conditions, incomplete recovery was observed for all columns. Averaged over the three astatine formulations, the lowest recovery was found for the PolymerX column (30%), followed by Luna C18(2) (38%) and XBridge C18 (55%). The highest apparent recovery was obtained with the Chromolith RP-18 (79%). At first glance, this might suggest that the Chromolith is clearly superior. However, this interpretation is weakened by the offline data. In particular, the comparatively high online recovery observed for the nucleophilic sample under neutral conditions was associated with a large standard deviation and was not confirmed by offline counting, where only 66% of the activity was recovered. This suggests that at least part of the apparent advantage resulted from distorted peak integration rather than from genuinely better chromatographic performance. In addition, PCI chromatograms of free ^{211}At as well as chromatograms taken without column (reference measurements) occasionally still showed pronounced tailing, indicating that the distorted signal shape cannot be attributed to interaction with the stationary phase alone (Figure 57). Extra-column effects within the HPLC system, such as dispersion and/or non-specific interaction with downstream components, are therefore also likely to contribute.

Furthermore, similar discrepancies were also seen for other strongly distorted chromatograms. In some cases, online integration even yielded apparent recoveries above 100%, reaching up to 120%, which clearly indicates an artefact caused by broad and tailing signals rather than true quantitative elution[148, 153].

A further important observation was the pronounced variability between nominally identical samples. Even when prepared according to the same protocol, replicate samples often gave visibly different chromatograms, as shown in Figure 58. This affected not only the apparent peak area, but in some cases also the number of peaks observed. The relatively large standard deviations listed in Table 26 reflect the same effect. These findings indicate that free astatine should not be viewed as a single, uniform analyte. Instead, its chromatographic behavior appears to depend strongly on the exact species distribution present in solution, which is in line with the known complexity of astatine chemistry [87, 154, 155].

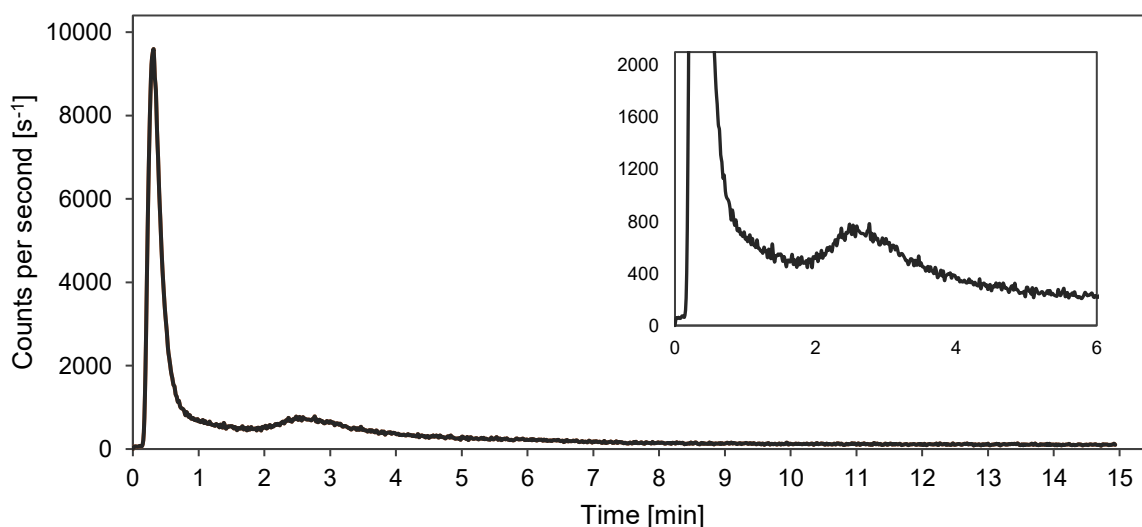


Figure 57: Chromatogram of a bypass run for offline control measurement, where every component is precisely the same as the for the online measurement except no stationary phase is connected.

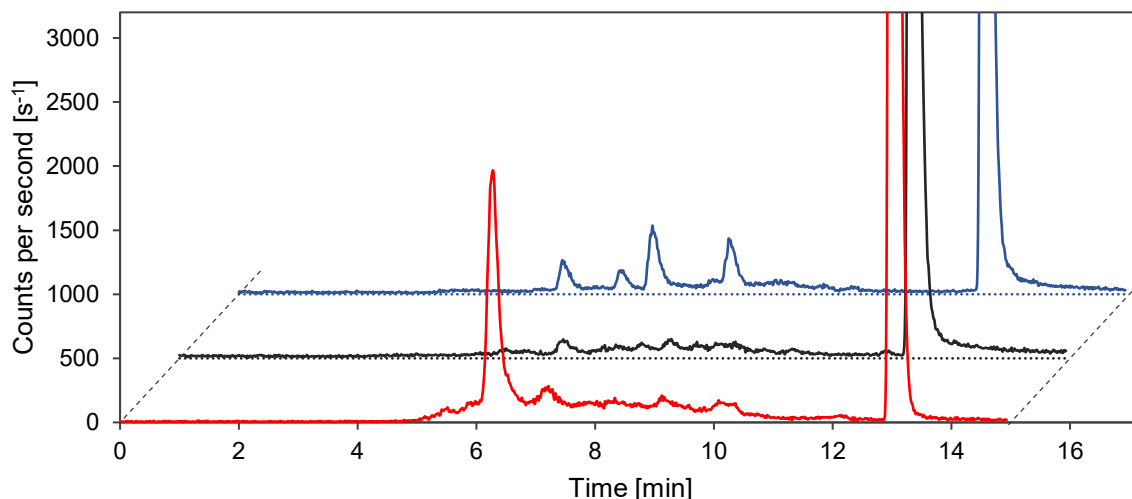


Figure 58: Triplicate chromatograms of electrophilic ^{211}At obtained under identical preparation and analytical conditions using a Waters XBridge C18 column and MeCN/water/0.1% TFA as eluent.

In a second step, the same columns were tested with water/acetonitrile containing 0.1% TFA, (Table 26) since this is one of the most common RP-HPLC solvent systems in radiopharmaceutical analysis. Under these acidic conditions, the recovery of the electrophilic and native astatine formulations dropped significantly on all columns. In several cases, the decrease was approximately threefold compared with the corresponding neutral system. Only the nucleophilic formulation was less strongly affected and remained in a range of about 30% to 68%, depending on the column. A reasonable explanation is that acidic conditions shift the astatine speciation toward more strongly retained oxidized forms, whereas reduced astatine is somewhat less affected. From a practical perspective, this identifies TFA-containing RP-HPLC systems as particularly unfavorable for reliable quantification of free astatine.

Since neither the neutral nor the acidic standard systems gave sufficiently robust recovery, additional solvent optimization was carried out on a single column. For this purpose, the Waters XBridge C18 was selected. Although its initial average recovery was not the highest, its broad pH stability made it the most suitable platform for further method development. The results of this second series are shown in Table 27.

Changing the organic modifier from acetonitrile to MeOH had only a minor effect and did not substantially improve recovery. Likewise, the addition of low concentrations of ascorbic acid did not lead to a meaningful improvement, despite the expectation that a

more reducing environment might favor astatide formation. A clearer benefit was obtained with triethylammonium acetate (approximately pH 7.5), which increased the recovery to 75–91% depending on the astatine formulation. The best overall results were finally achieved with a strongly basic mobile phase containing triethylamine at pH 10.5. Under these conditions, all three formulations showed markedly improved recoveries in the range of 88–98%. An illustration of representative chromatograms of free ^{211}At under reducing or basic environmental conditions is presented in Figure 59.

Table 27: Astatine recovery from alternative solvents using a Waters XBridge C18 column. Online activity balances were determined by post-column injection, whereas offline balances were determined by γ -ray counting of the collected column effluent. Values are given as online | offline balance, $n=3$. Highlighted entries indicate the parameter varied in the respective experiment. Abbreviations: AA, ascorbic acid; TEAA, triethylammonium acetate; TEA, triethylamine

Solvent	Electrophilic ^{211}At	Nucleophilic ^{211}At	Native ^{211}At	Avrg. over all samples
MeCN/Water	63 $\pm$ 4 49 $\pm$ 7	60 $\pm$ 12 30 $\pm$ 12	43 $\pm$ 10 60 $\pm$ 12	55 46
MeOH/Water	53 $\pm$ 4 55 $\pm$ 3	52 $\pm$ 5 49 $\pm$ 7	52 $\pm$ 7 64 $\pm$ 7	52 56
MeCN/Water + 0.1% AA	56 $\pm$ 23 62 $\pm$ 21	47 $\pm$ 6 52 $\pm$ 4	35 $\pm$ 2 46 $\pm$ 2	46 53
MeCN/Water + 10 mM TEAA	75 $\pm$ 6 71 $\pm$ 6	91 $\pm$ 3 92 $\pm$ 2	82 $\pm$ 5 86 $\pm$ 2	83 83
MeCN/Water + 0.4% TEA	98 $\pm$ 9 79 $\pm$ 9	88 $\pm$ 16 95 $\pm$ 8	98 $\pm$ 4 103 $\pm$ 3	95 92
MeCN/Water + 0.4% TEA + 0.1% Na ₂ SO ₃	84 $\pm$ 17 75 $\pm$ 12	74 $\pm$ 5 74 $\pm$ 8	72 $\pm$ 6 71 $\pm$ 7	77 73
MeCN/Water + 0.4% TEA + 0.1% Na ₂ S ₂ O ₃	78 $\pm$ 9 74 $\pm$ 3	87 $\pm$ 7 84 $\pm$ 8	78 $\pm$ 4 74 $\pm$ 10	81 77

This basic triethylamine system therefore represents the most useful condition identified in the present work. At the same time, its limitations should be kept in mind. The standard deviations show that variability was reduced yet not eliminated. In addition, such highly basic eluents require alkaline-stable stationary phases and are therefore not universally transferable to any RP-HPLC setup. For certain analytes, especially those bearing acidic functional groups, high pH may also lead to a major loss of retention.

Finally, combining high pH with additional reducing salt did not improve the method further. On the contrary, mixtures of triethylamine with sulfite- or thiosulfate-containing

additives led to lower reproducibility and lower overall recovery. This indicates that retention of free astatine is not governed by redox state alone, but rather by a more complex interplay of speciation, pH, and secondary interactions at the stationary phase.

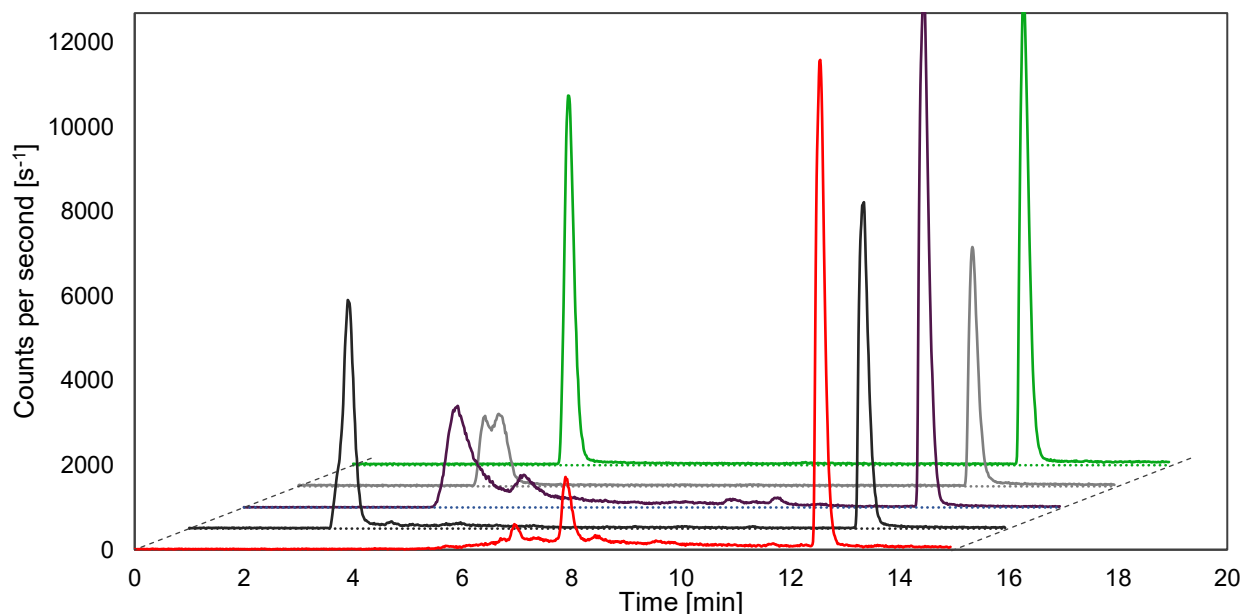


Figure 59: Representative chromatograms of nucleophilic ^{211}At obtained on a Waters XBridge C18 column using different mobile phases selected to improve astatine recovery according to the results presented in Table 27.

The practical relevance of incomplete astatine recovery became particularly evident when chromatograms from actual radiolabeling experiments were evaluated. In selected cases, the conventional online chromatogram suggested nearly quantitative conversion, whereas inclusion of PCI-based recovery assessment reduced the apparent conversion substantially. This indicates that incomplete recovery of free astatine is not merely a chromatographic inconvenience but can directly influence the interpretation of labeling performance.

Summarizing, the present study shows that free ^{211}At behaves problematically under many otherwise standard RP-HPLC conditions. Rather than eluting as a compact and readily integrable signal, it frequently gives broad and tailing radiotracers, and a considerable fraction may remain on the stationary phase. As a result,

chromatographic evaluation based on the eluted activity alone can underestimate the amount of free astatine present in a sample.

This effect was observed across all four columns tested and was especially pronounced for acidic TFA-containing mobile phases. Among the conditions investigated, the most practical improvement was achieved with a strongly basic triethylamine-containing mobile phase on the alkaline-stable XBridge C18 column, where recoveries of 88–98% were obtained. These conditions appear suitable for applications such as reaction screening or labeling optimization, but they do not fully remove the underlying variability and are not compatible with every chromatographic system. Overall, the results underline that free astatine cannot simply be expected to behave like radioiodine in RP-HPLC analysis [86, 156], and retention effects should be considered routinely in ^{211}At radiochemistry.

Radio-TLC for ^{211}At analytics

Because the RP-HPLC results revealed substantial retention and recovery artefacts, a second analytical approach was examined in the form of radio-TLC. The following results show, however, that TLC introduces a different set of limitations rather than providing a universally simpler solution.

In the present experiments, the main limitation of radio-TLC for ^{211}At was not the readout of the stationary phase itself, but the instability of astatine during plate development. Several studies indicate that ^{211}At can be lost from the TLC plate during development, either by transfer into the liquid phase or by volatilization of reactive astatine species. Nishinaka et al. reported that redox conversion of astatine species on silica may lead to formation of volatile At^0 , which is released from the thin layer during development [157]. Likewise, Aneheim et al. observed substantial losses of activity when aqueous mobile phases were used, and noted that large fractions of the activity appeared to volatilize under these conditions [146]. Their reported TLC data furthermore included a separate liquid fraction, indicating that activity was not exclusively retained on the plate after development. Taken together, these findings show that radio-TLC of ^{211}At must be interpreted primarily as a balance between chromatographic migration, volatilization, and redistribution of activity during development. Against this background, differences between TLC brands, batches, and backing materials should be considered an additional source of variability rather than the principal limitation of the method.

As shown in Figure 60, the migration pattern of ^{211}At was not only dependent on the redox treatment of the sample solution, but also on TLC type and even batch. Under native conditions, all plates showed comparable overall migration behavior, but also a characteristic activity pattern toward the plate edges. This observation is consistent with partial volatilization of astatine during development followed by re-deposition on cooler or less solvent-wetted regions of the plate. In contrast, this edge-associated redistribution was markedly reduced for the oxidized and reduced preparations, suggesting that the species formed under these conditions were less prone to volatilization under the selected development conditions.

Semi-quantitative comparison of the activity remaining on the developed plate with the corresponding post-development reference spot further supported these trends. Native

^{211}At showed recoveries of approximately 50% across all investigated plate types, indicating substantial activity loss or redistribution during development. Oxidized ^{211}At generally showed much higher recoveries, mostly around 90% or above, and comparatively low variability. Reduced ^{211}At also exhibited overall higher apparent recoveries than native ^{211}At , but with markedly larger scatter between replicate measurements. This larger variation suggests that reduced astatine species may be particularly sensitive to minor differences in spotting, local plate structure, or development behavior.

Importantly, several recoveries observed exceeded 100% (complete recovery). These values clearly show that the present approach is not suitable for absolute quantification and should instead be regarded as a semi-quantitative comparison of trends. Most likely, these deviations arise from the combined influence of pipetting uncertainty at 1 μL spotting volume, local heterogeneity in spot geometry, differences in signal integration between diffuse and compact spots, and potentially also matrix- or backing-dependent differences in detector response. Accordingly, the recovery values shown in Table 28 should not be interpreted as absolute chemical recoveries, but rather as an indicator of relative plate-to-plate and condition-to-condition behavior.

A notable observation was made for the polymer-backed Macherey-Nagel plates, which showed high apparent recoveries for oxidized ^{211}At together with a more compact and visually better-defined spot morphology than most other tested materials. Since the HPTLC (high-performance thin-layer chromatography) plate with glass backing and without UV indicator did not show a similarly pronounced deviation, the observed differences are unlikely to arise solely from the silica phase itself. Instead, the data suggests that additional plate properties such as backing material, binder composition, or plate microstructure contribute measurably to the chromatographic behavior of astatine. This is in line with the general observation made throughout this work that ^{211}At exhibits strong and often difficult-to-predict interactions with solid surfaces.

Results & Discussion

Table 28: Recovery rates of ^{211}At in different chemical forms are shown ($n = 2$). ^aHigh-Performance TLC: Silica gel on a glass backing, omitting UV indicator. ^b Silica gel pre-coated on a polymer-based backing.

TLC Plate	Position	Native ^{211}At	Oxidized ^{211}At	Reduced ^{211}At
Supelco HPTLC ^a	1	$48.9 \pm 3.1\%$	$93.7 \pm 3.4\%$	$65.3 \pm 21.5\%$
Supelco Bactch HX45586554	2	$34.6 \pm 18.2\%$	$88.5 \pm 5.7\%$	$51.2 \pm 21.5\%$
Merck Batch HX57758354	3	$52.5 \pm 2.9\%$	$96.1 \pm 6.6\%$	$108.9 \pm 46.8\%$
Meck Batch HX888581	4	$44.3 \pm 13.6\%$	$93.9 \pm 3.8\%$	$104.9 \pm 26.5\%$
Machery-Nagel ALUGRAM [®]	5	$53.5 \pm 21.4\%$	$88.8 \pm 14.4\%$	$81.4 \pm 19.9\%$
Machery-Nagel POLYGRAM ^{®b}	6	$52.0 \pm 6.0\%$	$128.8 \pm 0.2\%$	$132.3 \pm 5.5\%$

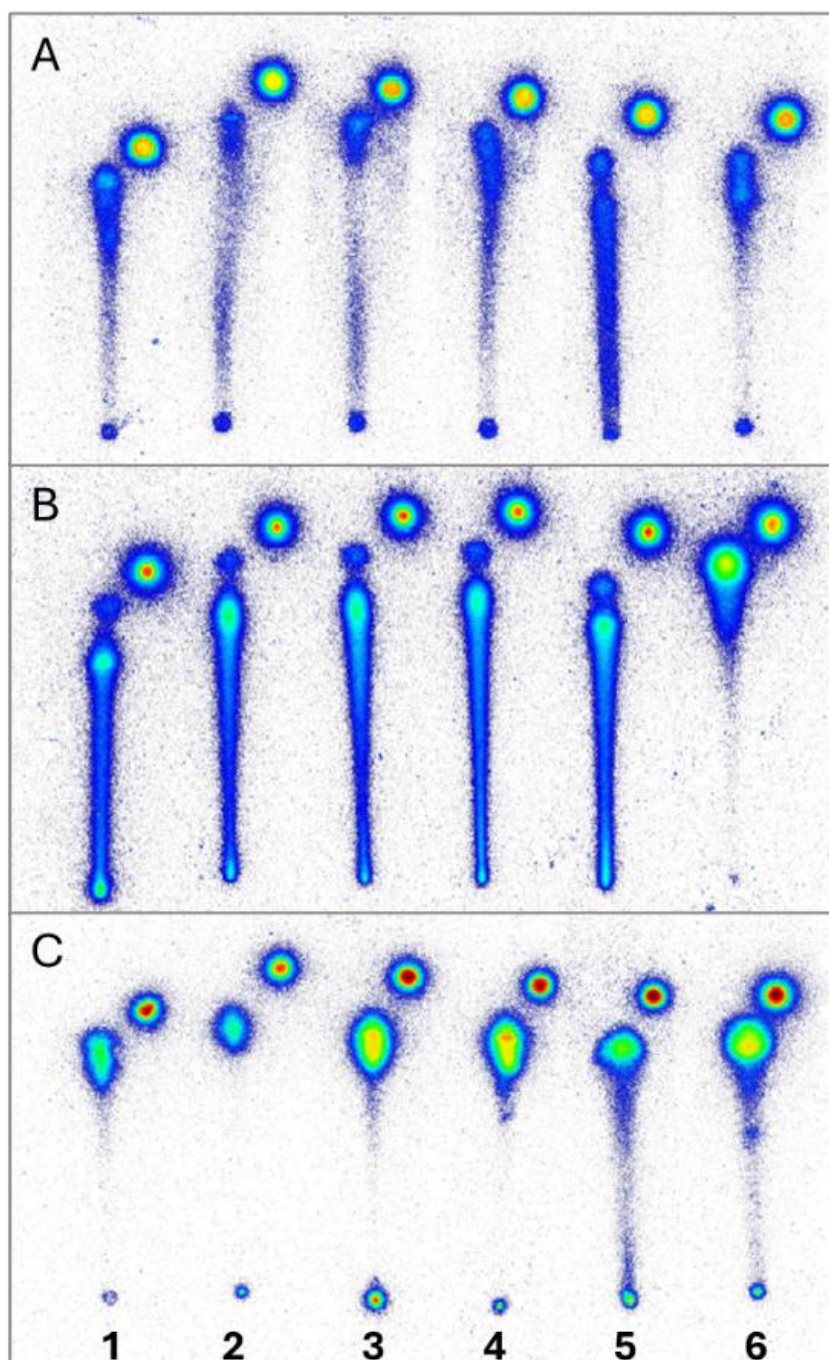


Figure 60: Quantification of free ^{211}At in native (A), electrophilic (B) and nucleophilic form (C) using different types of TLC quantified by Cyclone Plus (PerkinElmer) phosphor imager. Different suppliers, types and batches of TLC plates investigated in this study. The plates are numbered as presented in Table 28

Overall, these findings highlight a fundamental limitation of TLC for ^{211}At analysis. In addition to longitudinal migration along the development axis, in-depth penetration into the silica layer and plate-specific retention effects may influence both apparent mobility and detector response. Such effects are particularly relevant for astatine, because

volatilization, adsorption, and possible re-deposition may occur simultaneously during development. Consequently, TLC can provide useful comparative information on astatine behavior, but only if the results are interpreted in a strictly system-specific manner and not transferred uncritically between different plate materials or development conditions. For robust quantitative analysis of ^{211}At species, independent orthogonal methods remain necessary.

Summarizing, these analytical results show that the quality of a processed ^{211}At fraction cannot be inferred from nominal recovery alone and that common chromatographic methods may bias the interpretation of free astatine. These findings directly affect the evaluation of subsequent labeling experiments and therefore motivate the chemistry section that follows.

3.2.4. Chemical usability and proof-of-principle labeling of ^{211}At

After production, separation, and analytical characterization, the remaining question was whether the isolated ^{211}At could still be used efficiently in radiolabeling chemistry. To test this directly, selected proof-of-principle labeling experiments were carried out with ^{211}At obtained from different processing routes. The purpose was not to optimize the individual syntheses, but to assess downstream chemical usability under chemically relevant conditions.

Radiolabeling of Phenyl Alanine

Validation of separation methods by model labeling of 4-[^{211}At]APA

To assess whether the developed separation methods provided ^{211}At in a chemically usable form, the isolated activity was subjected to a series of model radiolabeling reactions using 4-astatophenylalanine (4-[^{211}At]APA) as reference compound. The aim of this study was not to optimize radiochemical conversion (RCC) of the individual labeling reactions, but rather to evaluate whether ^{211}At obtained from the different processing routes remained suitable for subsequent synthetic application. In this way,

the labeling experiments served as practical proof of principle for downstream usability of the isolated radionuclide.

Several routes toward non-protected 4-[^{211}At]APA were investigated, including direct destannylation reaction (DSR) of 4-SPA, boronic-acid-based substitution approaches of 4-BPA inspired by potassium iodide (KI)- and NBS (N-bromosuccinimide)-mediated protocols presented by Shirakami et al.[158], as well as halogen exchange using 4-IPA following Meyer et al.[159]. The different labeling routes were intentionally applied as comparative test reactions rather than as individually optimized syntheses. Consequently, the observed RCCs primarily reflect the chemical compatibility of the isolated ^{211}At fraction with the respective reaction system rather than the maximum achievable performance of each method.

Beyond the precursor structure itself, the labeling routes investigated differed fundamentally in the chemical conditions under which the astatination was performed. The chloramine-T-mediated labeling of 4-SPA was carried out under short, acidic, oxidizing conditions and is consistent with an electrophilic astatodestannylation pathway, derived from established radioiododestannylation procedures described by Israel et al. and Vaidyanathan et al. [160, 161]. The boronic-acid-based routes of Shirakami et al. likewise represent electrophilic substitution approaches, but involves different reactive astatine intermediates depending on the additive used: under NBS conditions, an N-astatosuccinimide-type intermediate has been proposed, whereas KI is thought to promote the formation of reactive interhalogen species such as AtI and/or AtI_2^- [158]. In contrast, the labeling route based on p-iodophenylalanine according to Meyer et al. represents a distinct Cu^+ -assisted nucleophilic halogen exchange chemistry in the presence of Sn(II) and therefore probes a markedly different reaction environment than the oxidative substitution-based approaches. Taken together, the applied test reactions do not only compare different precursor classes but also challenge the isolated ^{211}At fraction under clearly different redox-chemical and speciation-dependent labeling conditions.

Product analysis was performed using the same HPLC method throughout the study, ensuring direct comparability between experiments. Consequently, observed differences in product formation could be attributed mainly to the applied separation route and resulting chemical matrix rather than to changes in analytical conditions.

The retention time of the desired product was assigned using the non-radioactive structural analogue 4-IPA as a reference, since no stable isotope of astatine exists for this purpose. The UV-HPLC chromatogram of 4-IPA showed a main peak at 3.42 min (Figure 61), which was used as chromatographic reference for assigning the corresponding radioactive product peak to 4-[^{211}At]APA.

The initial comparison focused on whether the isolated ^{211}At fractions obtained by different processing routes performed similarly in direct downstream labeling or whether route-dependent differences in astatine speciation became apparent.

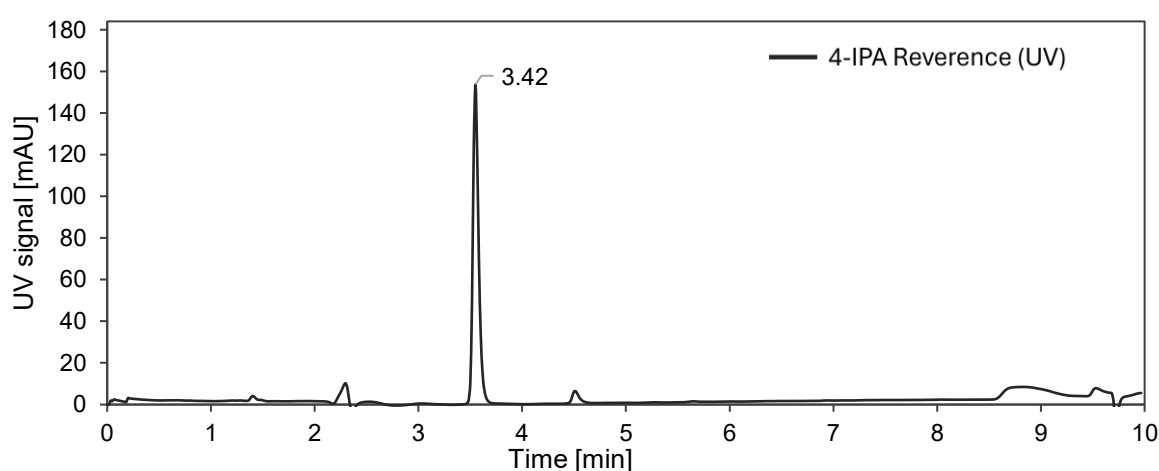


Figure 61: UV-HPLC chromatogram of the non-radioactive 4-IPA structural analogue. The main UV-detected peak at 3.42 min was used to define the expected retention region for the corresponding radioastatinated phenylalanine product, 4-[^{211}At]APA, in radio-HPLC analyses.

Compatibility of dry-distillation-derived ^{211}At with model labeling

The first group of validation experiments was performed using ^{211}At recovered by dry distillation in detail described in Section 3.2.2. Two cooled capillary-based trapping approaches were evaluated, employing either a polymer-based PTFE capillary or a titanium capillary as trapping segment. The titanium configuration was included as a potentially more radiolysis-stable long-term reusable and chemically inert alternative to PTFE. In addition, labeling was in one case performed directly from a PTFE dry-distillation loop, thereby minimizing intermediate handling steps.

Beyond the cooled trapping setups, a non-cryogenic alternative based on adsorption of volatilized ^{211}At on fused silica insulation foam at room temperature was tested. After elution from the foam material, the recovered activity was subjected to model labeling. This approach was of particular interest as it is a simplified separation concept avoiding active cooling in combination with a radiolysis stable collecting material like fused silica or gold beads, while still allowing direct assessment of whether the resulting ^{211}At fraction remained suitable for subsequent synthetic use.

Overall, the dry-distillation-derived fractions showed good compatibility with the model labeling reactions (Table 29). In particular, the stannyl precursor route, “KI”-method and halogenic exchange yielded high 70–90% RCC for the cooled capillary approaches. The fused silica “non-cooling” alternative showed almost comparable results between 69% and 75% for the mentioned labeling methods. The radio labeling via N-astatosuccinimide-type intermediate showed overall the lowest conversion rates, yet constantly > 50% RCC, supporting the feasibility of all three processing methods for astatination using all four labeling approaches. Exemplary chromatograms of the four labeling methods are presented in Figure 62.

Table 29: Radio chemical conversion rates [%] of labeling 4- ^{211}At]APA via different labeling methods (DSR, KI or NBS method and halogenic exchange reaction (HAL)). Freshly prepared ^{211}At was obtained from different dry distillation processing methods.

Method	PTFE	Titanium	Fused silica	Gold	FEP
DSR	82	83	75	0	70
KI	90	80	74	0	-
NBS	69	72	54	0	-
HAL	72	83	69	57	-

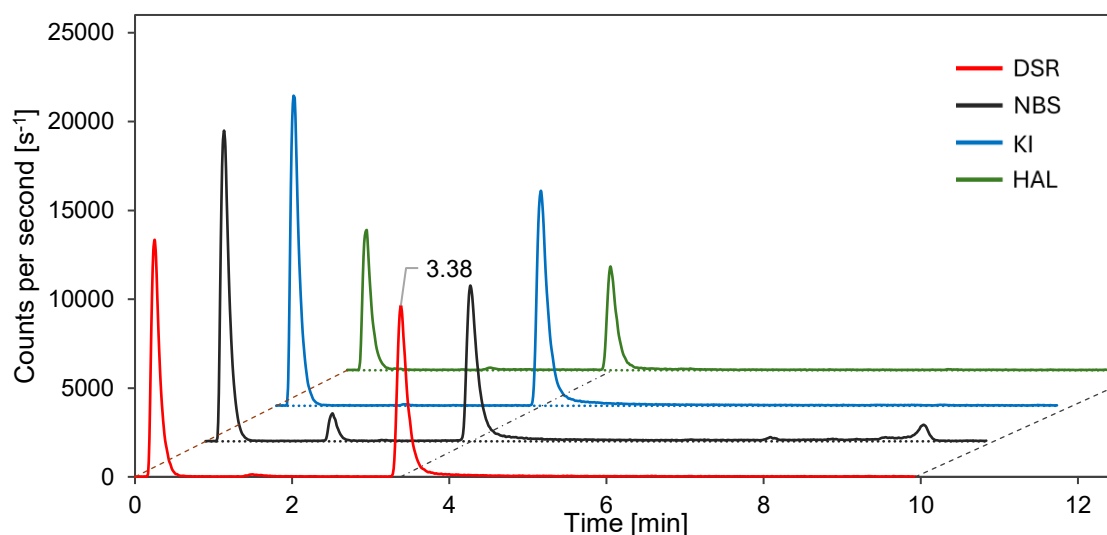


Figure 62: Comparison of the four labeling methods utilizing ^{211}At freshly prepared by dry distillation (DD)-method using PTFE-tube cold trap assembly.

While Figure 62 summarizes the radiochemical performance of the four labeling strategies, the halogen-exchange approach also provided an additional analytical advantage. The separate UV-HPLC analysis of the non-radioactive structural analogue 4-IPA had previously established its retention region under the applied chromatographic conditions (Figure 61). Since the reference 4-IPA was used directly as precursor in the halogen-exchange reaction, the remaining UV-detectable precursor peak could serve as an internal retention-time reference during radio-HPLC analysis. In the overlay chromatogram shown in Figure 63, the product peak eluted at 3.35 min and closely matched the UV-detected 4-IPA peak at 3.37 min. This agreement supports the assignment of the radioactive peak to 4- ^{211}At]APA and illustrates an additional analytical advantage of the halogen-exchange strategy.

As described previously (Section 3.2.2), the use of gold beads as adsorption material resulted in almost no apparent recovery of ^{211}At after trapping. To nevertheless assess whether the trapped activity remained chemically accessible, the ^{211}At -loaded gold beads were directly transferred into the respective reaction solutions while otherwise following the same labeling protocols. Under these conditions, successful labeling was observed only for the halogen-exchange approach based on a Cu^+ -assisted nucleophilic pathway, yielding 57% RCC.

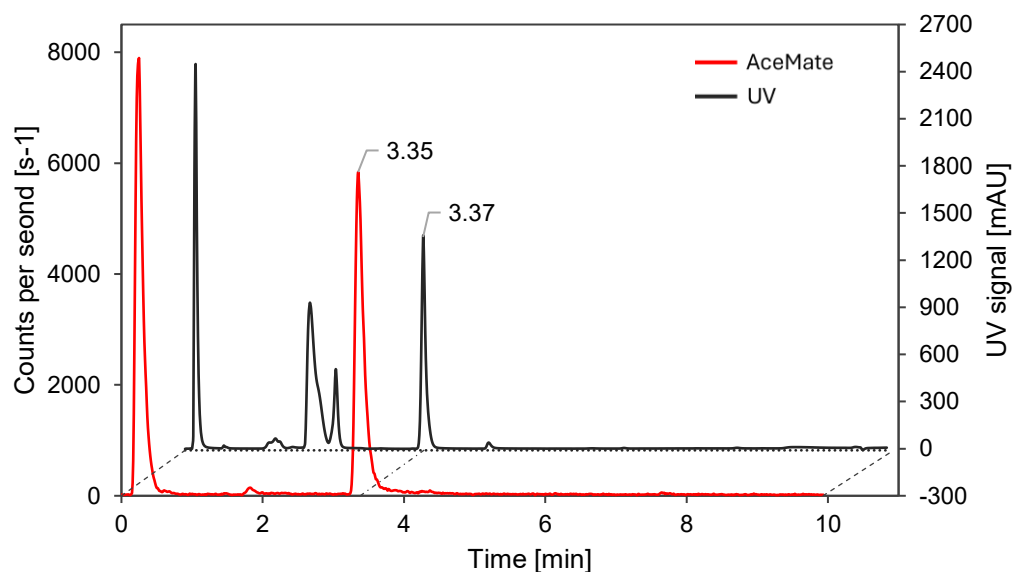


Figure 63: Overlay of the radio-HPLC signal recorded with the NaI(Tl) detector (red, left y-axis) and the corresponding UV absorbance trace of the non-radioactive 4-iodo-L-phenylalanine reference compound (4-IPA, black, right y-axis). The product peak assigned to 4-[^{211}At]astato-L-phenylalanine (4-[^{211}At]APA) eluted at 3.35 min, closely matching the UV peak of 4-IPA at 3.37 min. This agreement supports the retention-time-based identification of the labeled product.

The fact that successful labeling was only observed for the Cu^+ -assisted halogen-exchange reaction indicates that the astatine retained on the gold beads was not completely chemically inaccessible but required sufficiently activating conditions to participate in the reaction. This may be explained by the comparatively harsh reaction conditions of the halogen-exchange protocol, which was performed at 120 °C for 60 min, in contrast to the other room-temperature labeling approaches. Elevated temperature may have promoted desorption or redistribution of astatine species from the gold surface. Moreover, the reducing/nucleophilic reaction environment may have been more suitable for mobilizing or converting adsorbed astatine into a reactive form, whereas the electrophilic/oxidizing conditions of the other labeling strategies were apparently insufficient. The observed 57% RCC therefore most likely reflects a combination of partial release from the gold surface and favorable astatine speciation under the halogen-exchange conditions, rather than quantitative recovery of the trapped activity.

Direct labeling of a stannyl precursor was performed by flushing the PTFE capillary directly with precursor solution, following a concept inspired by Koziorowski and Weinreich [162]. This approach allowed rapid radiolabeling without an additional reformulation step. Across all experiments ($n = 3$), an average RCC of $62 \pm 18\%$ was

obtained. No clear influence of the residence time in the capillary was observed, as labeling immediately after separation resulted in $59 \pm 22\%$ RCC, while labeling after approximately 14 h gave $67 \pm 15\%$ RCC. Despite the considerable scatter, the results show that dry-distilled ^{211}At can be used directly for downstream labeling, indicating that at least part of the isolated activity is present in a reactive form.

Compatibility of solvent-extracted ^{211}At with model labeling

In a second series of experiments, ^{211}At obtained by liquid-liquid extraction was investigated. The main purpose was to determine whether extraction into an organic phase and subsequent reformulation affected the model radiolabeling. The tested extractants included TBP, 3-octanone, octanal, cinnamaldehyde, and to a limited extent trioctylamine (TOA). For the latter, no complete dataset was obtained, as precipitation effects and additional handling problems repeatedly interfered with the experiments. The RCCs obtained from LLE experiments are presented in Table 30.

Table 30: RCC rates [%] of labeling 4- ^{211}At]APA via different labeling methods (DSR, KI or NBS method and halogenic exchange reaction). The freshly prepared ^{211}At was obtained from different LLE processing methods. Values represent single experiments ($n = 1$) and are therefore shown without standard deviation.

Method	None	3-Octanone	Octanal	TOA	TBP	Cinnamaldehyde
DSR	61	87	75	53	85	83
KI	25	5	52	16	14	12
NBS	13	9	22	-	44	5
HAL	63	88	52	-	77	61

Compared to dry-distillation-derived fractions, the solvent-extracted samples showed a more pronounced dependence on the subsequent labeling chemistry. In particular, the boronic-acid-based labeling routes using KI or NBS performed poorly across all extraction solvents tested. The conversion rate of deboronation was generally below 25% only with two exceptions employing octanal as extractant using the KI based labeling method (52% RCC) or using TBP resin under NBS based labeling conditions (44% RCC). This suggests that the low RCC did not arise from a single extractant but rather reflected a more general incompatibility between the recovered ^{211}At species

and the present reaction conditions. In contrast, both destannylation as well as halogenic exchange showed high conversion – consistently > 50% RCC – under all tested conditions. This indicates that the downstream usability of extracted ^{211}At strongly depends on the type of processing method and that the different labeling approaches differ substantially in their tolerance toward residual isolation and reformulation conditions.

Figure 64 shows representative radio-HPLC chromatograms of the four exemplary labeling approaches performed with ^{211}At fractions purified by LLE using either 3-octanone (A) or octanal (B) as extraction solvent (Table 30). For both extraction systems, the destannylation and halogen-exchange approaches showed clearly distinguishable product-associated peaks of the expected retention time around 3.3–3.5 min. In contrast, the NBS- and KI-mediated reactions behaved differently, particularly for the 3-octanone-derived fraction. In these chromatograms, no clearly resolved product-associated peak was observed, instead, the main peak eluted at approximately 2.4 min.

This main peak was also present for all other extractants presented in Table 30, although less pronounced for the octanal-derived samples compared to 3-octanone. The observation that this signal occurred in both the NBS- and KI-mediated reactions indicates that it cannot be attributed exclusively to NBS-specific chemistry. Rather, it suggests the formation or stabilization of an unidentified, more weakly retained radioactive side product under these labeling and preparation conditions. Since no reference compound or structural analysis was available for this species, it was not assigned to a defined chemical identity.

The comparison therefore indicates that 3-octanone- and octanal-based LLE fractions are most suited for destannylation and halogen-exchange labeling approaches, whereas the side product formation was significant for NBS- and KI-mediated reactions. In addition, the destannylation reaction using the octanal-derived fraction resulted in a product peak of later retention time compared with the corresponding 3-octanone-derived sample, most likely reflecting matrix-dependent chromatographic effects rather than necessarily indicating formation of a different product.

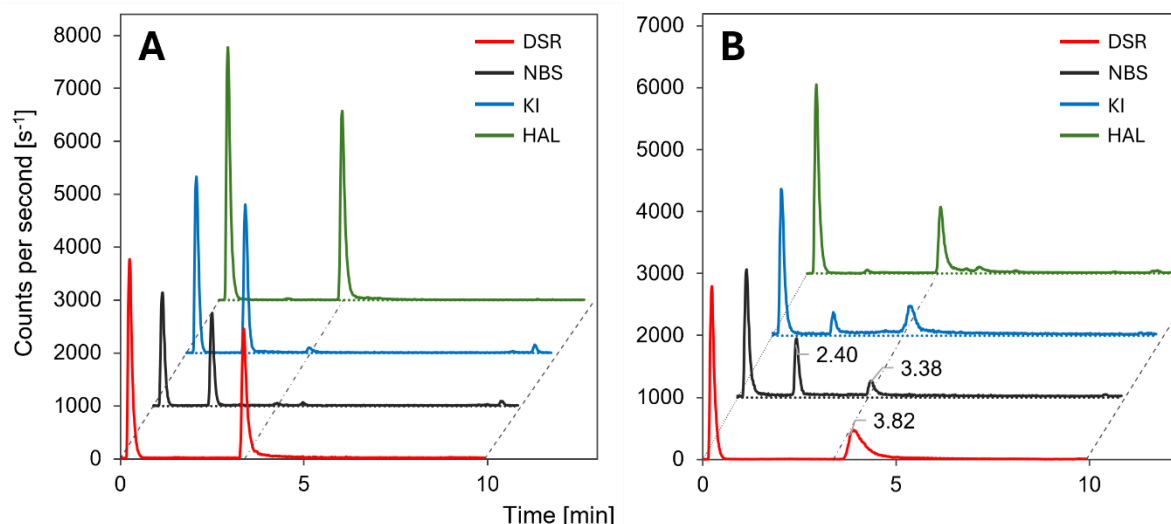


Figure 64: Representative radio-HPLC chromatograms of four model labeling reactions using ^{211}At purified by LLE with 3-octanone (A) or octanal (B). Destannylation (red) and halogen exchange (green) showed product-associated peaks of the expected retention time of 3.3–3.5 min, whereas the NBS- (black) and KI-mediated reactions (blue) were dominated by formation of an unidentified side product eluting at 2.4 min, especially for the 3-octanone-derived fraction. A slight retention-time shift toward longer retention was observed for the destannylation product peak in the octanal-derived sample. Radioactivity was recorded with the NaI(Tl) detector; chromatograms are vertically offset for clarity

A slight retention-time shift was observed for the destannylation-derived product peak in the octanal-derived sample compared with the corresponding 3-octanone-derived fraction. Since the overall chromatographic profile and peak shape remained consistent with the expected product, this shift was not interpreted as evidence for formation of a different product. Rather, it is most plausibly explained by minor matrix-dependent chromatographic effects, such as residual extraction solvent, slight variations in the injected sample composition, or differences in solvent strength between the reaction mixture and the HPLC mobile phase. Such effects can alter analyte–stationary phase interactions and result in small retention-time deviations, particularly for radioactive tracer analyses performed in complex reaction matrices.

Control experiments addressing extractant-related interference

To clarify whether the poor performance of the KI- and NBS-mediated labeling routes originated mainly from residual extractant, additional control experiments were performed using ^{211}At retained on bare HR-X material, washed with ethanol (EtOH), and subsequently used for labeling without the presence of an extraction solvent.

Despite the absence of the respective extractants, both boronic-acid-based approaches again showed only limited product formation of 25% and 13% for KI and NBS method respectively. This observation argues against residual extractant alone as the dominant cause of failure and instead suggests that the chemical state of the recovered ^{211}At in combination with the intrinsic sensitivity of these labeling systems plays the more decisive role.

Influence of activity level and decay time on labeling performance

Immediate labeling performance alone, however, does not fully reflect practical usability. Since isolated ^{211}At may have to be stored or transferred before application, the temporal stability of the processed fractions was investigated.

To elaborate the influence of radiolysis under practically relevant activity conditions, the most promising labeling conditions were tested both shortly after isolation, typically within 20 min, and again after approximately two half-lives stored in the trapping material at activity levels of 200–500 MBq. This activity level was chosen to simulate a more demanding dose regime and to assess whether prolonged storage measurably affected subsequent product formation.

In general, the comparison between immediate and delayed labeling provided a first indication of the radiolytic or chemical robustness of the isolated ^{211}At fractions as well as the tolerance of the respective precursor systems. Since the experiments were not intended as a detailed RCC optimization study, these results should primarily be interpreted qualitatively, i.e. in terms of retained labeling feasibility rather than absolute synthetic performance.

^{211}At isolated by dry distillation processing routine showed basically no decrease in conversion yield for the cooled capillary trapping using PTFE or Titanium capillaries with $\geq 69\%$ RCC over all labeling methods. The silica-based trapping at room temperature however showed slight labeling decrease to 54–38% RCC for KI, NBS and halogenic exchange (Table 31).

A cautious interpretation of these findings is that the observed waiting-time effect was governed by a change in the chemical state of the trapped ^{211}At fraction. While this

effect appeared negligible for the cooled PTFE and titanium capillary traps, it became noticeable for the silica-based trapping approach. Because ^{211}At is known to react with hydroxylated silica surfaces [121], the reduced RCC after storage may reflect a surface-induced shift in astatine speciation. This would be particularly relevant for labeling routes that depend on specific reactive astatine intermediates, such as the KI- and NBS-based boronic acid substitution methods and the Cu-mediated halogen exchange route. For the boronic acid approaches, AtI and/or AtI_2^- have been proposed as reactive species in the KI-mediated pathway, whereas the NBS-mediated route has been linked to an astatosuccinimide-type intermediate [158]. By contrast, the chloramine-T-mediated destannylation of the stannyl precursor appeared largely unaffected, possibly because the oxidative reaction conditions sufficiently re-establish a reactive electrophilic astatine species at the start of the labeling step.

Table 31: RCC [%] of labeling 4- ^{211}At]APA via different labeling methods using ^{211}At obtained from different dry distillation processing methods after a storage period of 2-3 half-lives on the trapping material. Values represent single experiments ($n = 1$) and are therefore shown without standard deviation.

Method	PTFE	Titanium	Fused silica
DSR	79	78	78
KI	84	72	54
NBS	63	72	41
HAL	78	79	38

For LLE-based delayed labeling studies, a similar trend was observed to that seen for dry-distillation-derived ^{211}At . The conversion rates obtained are summarized in Table 32 presenting an overall markable RCC decrease over the waiting period. The highest deviation was observed for ^{211}At extracted with 3-octanone and subsequently labeled via destannylation, where the RCC decreased from 87% to 45%. In contrast, destannylation using ^{211}At obtained from extraction with octanal showed essentially no decrease in conversion under the same conditions. The boronic-acid-based labeling approaches were more severely affected across all tested extraction systems, in some cases decreasing to levels at which no labeled product could be detected (11–0%).

Table 32: RCC [%] of labeling 4- ^{211}At APA via different labeling methods using ^{211}At obtained from different LLE processing methods after a storage period of 2-3 half-lives on the packed column after all regular washing steps. Values represent single experiments ($n = 1$) and are therefore shown without standard deviation.

Method	3-Octanone	Octanal	Cinnamaldehyde
DSR	45	84	31
KI	6	11	0
NBS	4	9	7
HAL	72	32	32

Influence of bismuth carry-over

In addition to astatine speciation itself, residual impurities from target processing may interfere with labeling chemistry. The following experiments therefore examine whether the bismuth carry-over observed for some extraction systems affects RCC.

As suggested in Section 3.2.2, the LLE methods showed non negligible carryover of bismuth target material during separation. To investigate possible interference by residual bismuth, labeling of ^{211}At solutions, obtained by cooled capillary based dry distillation was examined supplemented with 5 μL of a 50 mg mL^{-1} Bi solution, artificially increasing the metal impurity content. The experiments were carried out for both the KI- and NBS-mediated boronic-acid approach. In both cases, no relevant change in labeling performance was observed compared to the corresponding reference experiments without added bismuth. The obtained HPLC chromatograms are depicted in Figure 65. The reference labeling reactions showed 72% and 49% for the KI and NBS approach respectively, whereas the labeling with the spiked solution yielded 62% and 49% RCC. Within the limits of this simplified challenge experiment, bismuth carry-over therefore did not appear to be the dominant factor controlling reaction outcome.

Taken together, the model labeling experiments show that successful isolation of ^{211}At cannot be judged solely from recovery performance but must also be evaluated with respect to downstream synthetic compatibility. While several separation routes yielded ^{211}At that remained suitable for subsequent labeling, the RCC strongly depended on the reaction type. In particular, the destannylation proved to be comparatively robust, whereas the boronic-acid-based methods were markedly more sensitive to the origin and chemical history of the isolated ^{211}At fraction, showing rather poor labeling behavior for LLE processed ^{211}At .

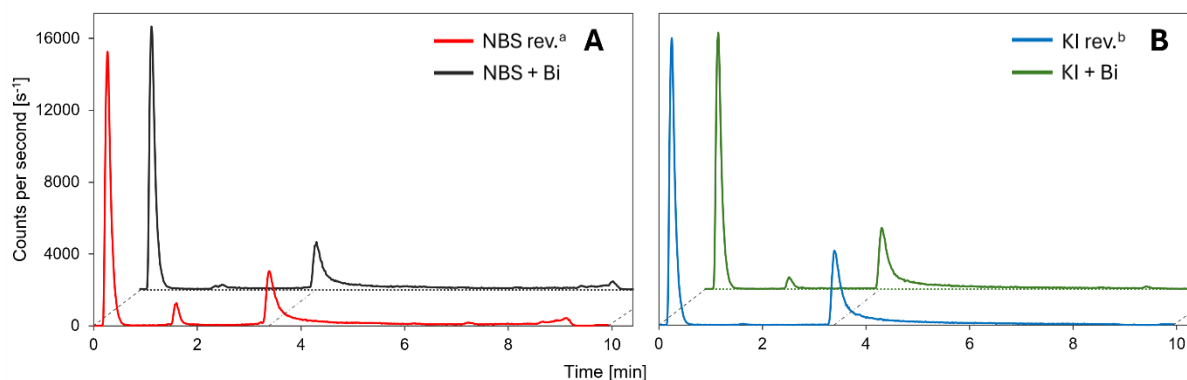


Figure 65: Representative radio-HPLC chromatograms showing the effect of added bismuth on the NBS-mediated (A) and KI-mediated (B) labeling reactions. For each method, chromatograms obtained from a reference sample and from a Bi-spiked sample are overlaid to visualize changes in the radioactive peak pattern. In both cases, ^{211}At was obtained by dry distillation using a PTFE-tube cold-trap assembly. For the Bi-spiked samples, the ^{211}At solution was supplemented with $5\ \mu\text{L Bi}(\text{NO}_3)_3$ solution ($50\ \text{mg mL}^{-1}$) prior to labeling. ^aThe indicated chromatogram was multiplied by a factor of 0.8 for activity normalization and visual comparison. ^bThe indicated chromatogram was multiplied by a factor of 0.7 for activity normalization and visual comparison.

This distinction is important, since the present experiments were not designed to establish optimized labeling protocols for 4- ^{211}At]APA, but rather to benchmark the practical usability of ^{211}At obtained from different processing routes. Under these conditions, the labeling reactions served as an indicator of radionuclide quality. The results therefore suggest that dry distillation currently provides the more generally robust stream, whereas LLE and adsorptive recovery approaches may require more careful matching to the intended downstream chemistry.

The present labeling experiments indicate that the value of a isolation method is defined not only by recovery and radionuclide transfer, but also by the combination of recovery, analytical interpretability, and downstream reactivity. Yet even this does not fully define routine applicability. Repeated ^{211}At work also creates long-term operational consequences through daughter nuclide accumulation, waste segregation, and disposal effort, which are addressed in the following section.

3.2.5. Waste handling and operational implications of routine ^{211}At work

At this point, the discussion leaves the immediate product stream and turns to the operational boundary conditions of routine implementation. For ^{211}At , these are determined not only by the short-lived parent nuclide itself, but by the cumulative formation of the long-lived daughter, ^{207}Bi and its implications for waste classification, disposal effort, and practical scalability.

For single applications, this is generally of limited relevance, since the resulting ^{207}Bi activity is strongly diluted, particularly in the context of patient administration. In laboratories where ^{211}At is processed repeatedly, however, the situation is different, as the daughter activity accumulates over time and therefore becomes relevant for waste management. The decay of 1 MBq of ^{211}At yields 10.9 Bq of ^{207}Bi . Consequently, the exemption activity of 1 MBq for ^{207}Bi corresponds to 91.7 GBq of processed ^{211}At . Even though this represents a comparatively large amount of ^{211}At , the cumulative formation of ^{207}Bi must be considered once production and processing become routine. Waste handling is therefore not treated here as a purely administrative side issue, but as a practical component of implementing repeated ^{211}At production and processing.

In practical considerations, freshly generated waste benefits from an initial decay period before final classification. After approximately 10 half-lives of ^{211}At , corresponding to about 3 days, the astatine activity has decayed to a negligible level and the remaining radiological inventory is dominated by the long-lived daughter products, most importantly ^{207}Bi , simplifying further waste assessment (neglecting all α -radiation) and making subsequent disposal decisions more robust.

To assess the relevance of this issue under realistic laboratory conditions, the following evaluation is based not on a single production campaign, but on waste generated over an extended period of continuous ^{211}At work.

To evaluate the relevance of this issue under realistic operating conditions, all waste arising over 18 months of continuous ^{211}At work was collected, segregated, and classified. During this period, production averaged 2–3 irradiations per week, and a total of approximately 78.9 GBq of ^{211}At was processed. Waste was separated into low-activity and high-activity fractions. The high-activity fraction was further divided into

combustible and non-combustible waste, whereas the low-activity fraction was differentiated by material type in order to identify the dominant contributors and possible points for reduction.

Over the investigated period, a total of 98.2 kg of solid waste was generated, consisting of 64.9 kg low-activity and 33.3 kg high-activity waste. In addition, approximately 30 L of low-activity and 60 L of high-activity liquid waste were collected. The low-activity solid fraction consisted mainly of gloves, protective sleeves, packaging material, and paper tissues. As summarized in Table 33, 62.2 kg of this material showed a specific ^{207}Bi activity below the clearance limit of 0.1 Bq g^{-1} . Only one waste bag, containing 2.6 kg of disposable paper tissues, exceeded this limit.

This result indicates that the low-activity stream was largely classified correctly and that the overall waste concept worked well. At the same time, it also shows how strongly the final classification can be influenced by only a small number of misplaced highly contaminated items. The elevated activity in the affected waste bag is most plausibly explained by one or two incorrectly discarded tissues. In principle, such items can be identified by subsequent manual screening. In practice, however, this approach is time-consuming and only sufficiently reliable under low-background conditions. Although additional sorting did allow some contaminated gloves or sleeves to be identified and removed, retrospective correction is clearly less efficient than careful segregation at the time the waste is generated.

The quantitative distribution of ^{207}Bi supports this interpretation. Roughly 4 kBq of ^{207}Bi was found in approximately 65 kg of low-activity solid combustible waste, whereas a total of 271 kBq was associated with only 33 kg of high-activity waste. Thus, the great majority of the long-lived bismuth inventory was successfully concentrated in the intentionally separated high-activity fraction, while the low-activity stream retained only a minor residual share. This is an important finding, as it shows that routine ^{211}At work does not inevitably convert the full waste output into problematic long-term radioactive waste, provided that segregation is performed consistently.

The 33.3 kg of high-activity solid waste consisted of 20.1 kg combustible and 13.2 kg non-combustible material. The combustible fraction was mainly composed of polymer-based laboratory consumables such as syringes, reaction vials, and paper tissues,

whereas the non-combustible fraction largely comprised glass vials and aluminum target residues.

The radiological classification of the waste stream is only one side of the problem. From an operational point of view, the distribution between combustible and non-combustible fractions also directly affects disposal effort and cost.

Table 33: Low-activity solid waste accumulated during 18 months of routine ^{211}At work. The table summarizes the mass and measured ^{207}Bi -specific activity of the individual waste fractions.

Waste components	Weight [g]	Specific activity [Bq g⁻¹]
Sleeves	1185	0.048
Sleeves	3058	0.018
Gloves	9962	0.043
Gloves	8825	0.055
Gloves	8369	0.014
Gloves	12704	0.053
Gloves	2412	0.027
Packaging Material	1924	0.055
Packaging Material	3541	0.077
Packaging Material	2766	0.062
Paper Towles	2628	0.296
Paper Towles	2838	0.067
Mixed	4640	0.084
Sum/ Weighted Avrg.	64852	0.0584

For the period investigated here, the total disposal cost was estimated to be on the order of 3400 € (a more differentiated cost assessment is present in the appendix in Table B-9). The largest share originated from combustible high-activity solid waste, whereas non-combustible solids and high-activity liquid waste contributed to a lesser extent. These values are inherently dependent on the local disposal infrastructure and should therefore be understood as a case-specific example rather than a universally transferable estimate. Nevertheless, they illustrate that waste handling already represents a noticeable practical and economic factor at the scale of research and

development work, where typical daily handled activities were in the range of 100–500 MBq for purification studies, analytical procedures and radiolabeling experiments.

Summarizing, the present results show that waste handling in routine ^{211}At work is determined less by the short-lived parent nuclide itself than by the cumulative formation of ^{207}Bi and by the consistency of waste segregation. Most of the low-activity solid waste remained below clearance limits, while the overwhelming fraction of the long-lived activity was concentrated in a comparatively small high-activity waste stream. This indicates that the long-term waste burden associated with ^{211}At can be kept manageable when a strict and well-structured waste concept is applied. At the same time, the observed disposal effort and associated costs underline that waste handling should be considered an integral part of process design, particularly when moving from exploratory research towards larger-scale routine production and application.

Overall, the results of this thesis show that the practical implementation of ^{211}At depends not only on successful production and processing, but also on the ability to manage the long-term operational consequences in a controlled and economically realistic manner.

4. Conclusion

This thesis evaluated the non-standard radionuclides ^{72}As and ^{211}At by addressing the experimental bottlenecks that determine whether their nuclear-medical potential can be translated into practical use. For ^{72}As , the objective was to establish experimentally grounded production and decay data for its realistic assessment as a non-standard positron emitter. For ^{211}At , the aim was to develop robust production, separation, characterization, and proof-of-principle radiochemical workflow under the technical conditions of the C30XP cyclotron. Although the two radionuclides differ markedly in application, chemistry, half-life, and production requirements, both cases demonstrate that implementation depends on verified production routes, controlled impurity formation, reliable analytical methods, and process conditions compatible with routine radiochemical work.

For ^{72}As , three production concepts were investigated: the direct $^{72}\text{Ge}(\text{p},\text{n})^{72}\text{As}$ route, the direct $^{69}\text{Ga}(\alpha,\text{n})^{72}\text{As}$ route, and the indirect generator-based $^{75}\text{As}(\text{p},4\text{n})^{72}\text{Se}$ route. Route selection cannot be based on formation yield alone, but must combine excitation-function data, usable energy window, integral yield, radionuclidic impurities, target availability, beam requirements, and intended supply concept.

Among the direct routes, enriched $^{72}\text{Ge}(\text{p},\text{n})^{72}\text{As}$ provided the most favorable compromise. It offers a low-energy proton window of approximately 5 to 14 MeV and an integral yield of $231.0 \text{ MBq } \mu\text{Ae}^{-1} \text{ h}^{-1}$. This energy range is compatible with small to medium-sized medical cyclotrons and allows efficient production with good impurity control, if the proton energy remains below about 14 MeV, suppressing the competing $^{72}\text{Ge}(\text{p},2\text{n})^{71}\text{As}$ channel. Although enriched ^{72}Ge is required, the combination of low-energy accessibility, favorable yield, and manageable impurity formation identifies $^{72}\text{Ge}(\text{p},\text{n})^{72}\text{As}$ as the most practical direct production pathway investigated in this work.

The $^{69}\text{Ga}(\alpha,\text{n})^{72}\text{As}$ route was technically feasible but clearly less attractive for routine-oriented production. Despite a high peak cross-section, the integral yield was only $7.3 \text{ MBq } \mu\text{Ae}^{-1} \text{ h}^{-1}$, mainly because of the restricted useful energy interval, higher stopping power of α -particles, and lower number of incident projectiles per unit charge

Conclusion

compared with proton irradiation. Together with the need for α -beam capability and enriched ^{69}Ga , this route remains a possible fallback rather than a preferred strategy.

The generator-based $^{75}\text{As}(p,4n)^{72}\text{Se}$ route represents a complementary concept. Instead of producing ^{72}As directly, it produces the longer-lived parent ^{72}Se , which decays to ^{72}As . In the proton energy range of approximately 42 to 65 MeV, an integral ^{72}Se yield of $31.5 \text{ MBq } \mu\text{A}^{-1} \text{ h}^{-1}$ was obtained. Although this yield is lower than for $^{72}\text{Ge}(p,n)^{72}\text{As}$, the 8.5 d half-life of ^{72}Se enables prolonged irradiation, delayed processing, transport of the generator nuclide, and repeated access to ^{72}As after daughter ingrowth. This route may therefore support decentralized ^{72}As availability even when production itself requires a high-energy cyclotron.

The main limitation of $^{75}\text{As}(p,4n)^{72}\text{Se}$ is impurity control. Formation of ^{75}Se occurs in a lower-energy window and cannot be fully avoided. However, within the investigated 42 to 65 MeV production window, the measured ^{75}Se impurity ratio was only 2.3% relative to ^{72}Se . For a generator application, this is less critical than for direct product use, provided that ^{72}As elution from ^{72}Se is sufficiently selective and selenium radionuclides remain retained in the generator matrix. Other impurities can be mitigated by decay or chemical separation; for example, decay of short-lived ^{73}Se before processing converts it into ^{73}As , which can then be removed during separation of selenium from the arsenic target matrix. Thus, $^{75}\text{As}(p,4n)^{72}\text{Se}$ remains promising despite its higher energy requirement and more complex impurity profile.

Overall, the best ^{72}As route depends on the intended use scenario. For local or regional direct production, enriched $^{72}\text{Ge}(p,n)^{72}\text{As}$ is most attractive, combining low-energy proton irradiation, a favorable production window, high yield, and manageable impurity control. For centralized production and distribution, $^{75}\text{As}(p,4n)^{72}\text{Se}$ offers a generator strategy that compensates for the high-energy requirement through the longer-lived ^{72}Se parent and repeated daughter elution. In contrast, $^{69}\text{Ga}(\alpha,n)^{72}\text{As}$ is feasible but practically limited. This shows that ^{72}As cannot be evaluated as a PET radionuclide by half-life and positron emission alone; its practical value depends on matching the production route to cyclotron infrastructure, impurity tolerance, target availability, and supply concept.

Conclusion

In addition to production data, the decay properties of ^{72}As were investigated using complementary measurement approaches. Particular attention was given to the β^+ branching ratio, as it directly affects PET quantification, activity determination, and comparison with other positron-emitting radionuclides. The experimentally determined representative β^+ branching ratio of $87.1 \pm 5.6\%$ agrees with the literature value of $87.8 \pm 2.2\%$. This agreement was supported by HPGe-based annihilation-radiation measurements, direct β -particle measurements with a β -counter, and X-ray measurements to assess the electron-capture contribution and infer the total emission balance. These results strengthen confidence in the decay-data basis of ^{72}As and support its quantitative assessment for PET-related applications. Thus, the relevance of ^{72}As is not only a consequence of its favorable half-life and high positron-emission probability, but of experimentally defined production and decay-data conditions.

The ^{211}At part of this thesis addressed a different translational barrier. Here, the objective was not to demonstrate the general feasibility of ^{211}At production, which is already established, but to develop a production concept adapted to the C30XP cyclotron. This required an external high-current target system for bismuth irradiation, including metallic bismuth target preparation, thermal-stability evaluation, and irradiation conditions compatible with reliable ^{211}At production. Stable high-current irradiation was feasible when target preparation, mechanical contact, interface quality, beam shaping, and thermal load were controlled appropriately. Target robustness alone is insufficient: the effective α -particle energy on target remains the key parameter controlling the balance between ^{211}At yield and radionuclidic purity. Practical ^{211}At production therefore requires simultaneous control of target stability, thermal load, beam properties, and effective particle energy, particularly for reproducible routine operation.

Following production, several strategies for ^{211}At recovery from irradiated bismuth targets were investigated, including dry distillation, solvent-based approaches, and adsorptive methods. Dry distillation was identified as the most robust and reproducible route. The best-performing configuration combined oxidizing carrier-gas conditions with PTFE-based cold trapping and yielded an HPGe-determined overall ^{211}At recovery of $80.4 \pm 0.4\%$ under optimized reference conditions. Direct distillation of intact targets in a prototype vertical oven further demonstrated a promising route toward reduced

Conclusion

manual handling and streamlined processing. Solvent-based and adsorptive approaches confirmed that ^{211}At can be transferred by several chemical routes, but they did not provide the same balance of recovery, robustness, reproducibility, and practical handling.

A major outcome of the ^{211}At work is that isolated ^{211}At cannot be judged by nominal recovery alone. Analytical characterization was essential but challenging. Free ^{211}At did not behave as a routine radiohalogen species in standard chromatographic systems. In RP-HPLC, it frequently produced broad and tailing radiotracers, and a relevant activity fraction could remain associated with the stationary phase. Acidic TFA-containing mobile phases were particularly unfavorable, whereas a strongly basic triethylamine-containing mobile phase on an alkaline-stable XBridge C18 column provided the most useful improvement within the investigated conditions. Radio-TLC showed limitations including volatility, redistribution, and plate-dependent behavior. Chromatographic quality control of ^{211}At therefore requires system-specific validation and cannot be transferred uncritically from radioiodine chemistry or other radiohalogen systems.

The downstream labeling experiments showed that a processing route must ultimately be judged by functional radiochemical usability. The proof-of-principle studies were not intended to optimize 4- ^{211}At]APA synthesis itself, but to test whether ^{211}At obtained from different separation routes remained suitable for subsequent radiochemistry. Under the investigated conditions, dry-distillation-derived ^{211}At was the more generally compatible product stream. The stannyl precursor route appeared comparatively robust, whereas boronic-acid-based approaches were more sensitive to the origin and chemical history of the isolated astatine fraction. These experiments served as a functional test of product quality and demonstrated that separation chemistry directly affects subsequent labeling performance.

Finally, the thesis evaluated the accumulation and disposal of long-lived ^{207}Bi during repeated ^{211}At work. Over 18 months of continuous operation, during which approximately 78.9 GBq of ^{211}At were processed, most of the long-lived bismuth inventory was concentrated in a comparatively small high-activity waste fraction, while most low-activity solid waste remained below clearance limits. These findings show

Conclusion

that the long-term waste burden can remain manageable when strict waste segregation is implemented from the beginning, but the disposal effort and associated costs also show that waste management must be treated as an integral part of process design rather than an administrative afterthought.

Overall, this thesis demonstrates that practical implementation of non-standard radionuclides depends on bottleneck-specific experimental evidence. For ^{72}As , the decisive elements were production-route selection, excitation-function measurements, impurity assessment, production-window definition, and experimentally verified β^+ decay data. For ^{211}At , they extended beyond production yield and included target robustness, controlled α -particle energy, reproducible recovery from bismuth, reliable analytical characterization, preservation of radiochemical reactivity, and management of ^{207}Bi -containing waste.

The two radionuclides therefore illustrate complementary aspects of radionuclide translation. For ^{72}As , this work defines the production- and decay-data constraints that determine whether it can be realistically considered as a non-standard PET radionuclide. For ^{211}At , it establishes a coherent C30XP-based workflow linking high-current bismuth targetry, dry-distillation-based recovery, chromatographic characterization, proof-of-principle labeling, and ^{207}Bi waste management. Thus, the thesis does not merely discuss the theoretical attractiveness of ^{72}As and ^{211}At but identifies the practical conditions under which these radionuclides can be produced, evaluated, processed, and moved toward nuclear-medical application.

5. Materials and Methods

5.1. General materials and instrumentation

Unless stated otherwise, all chemicals were obtained from commercial suppliers and used without further purification. Ultrapure water was freshly prepared using an ELGA PURELAB water purification system and had an operational resistivity of 16.2–18.0 M Ω ·cm. Aqueous solutions were prepared using this water. Mineral acids, bases, and inorganic salts were of analytical or reagent grade unless specified otherwise, while organic solvents used for chromatographic applications were of HPLC grade. For procedures in which reagent purity, acid concentration, solvent composition, or material composition directly influenced the experimental outcome, the respective details are given in the corresponding method sections.

Bismuth metal used for target preparation was obtained from Strategic Elements, Deggendorf, Germany, with a stated purity of 99.99%. Further materials that were critical for specific experiments, including enriched target materials, backing materials, precursor compounds, extraction media, chromatographic columns, resins, reference materials, and calibration sources, are described together with the respective experimental procedures.

pH measurements were performed using a WTW MultiCal[®] pH 526 pH meter. Heating and temperature-controlled procedures were carried out using a Präzitherm[®] PZ28-3T high-precision heating plate, unless stated otherwise. Routine activity measurements were performed with a Comcer dose calibrator equipped with a VIK-type ionization chamber. Storage phosphor imaging was performed using a PerkinElmer Storage Phosphor System Cyclone[®] Plus and, where applicable, a FUJIFILM BAS-5000 imaging plate reader. Instrument-specific settings, calibration procedures, geometries, and acquisition parameters are provided in the respective method sections when relevant for data evaluation.

Chromatographic measurements were carried out on an AZURA P6.1L gradient HPLC system equipped with two Rheodyne 7725i injection valves positioned before and after the chromatographic column, enabling post-column injection for activity balance

determination [148]. Radioactivity detection was performed using a 3" NaI(Tl) well-type scintillation detector combined with a polypropylene flow cell. Sample injection was performed by full-loop injection using 20 μ L loops, and data were acquired using ClarityChrom software.

5.2. Experimental methodologies

5.2.1. Irradiation facilities and beamline infrastructure

Over the course of this work, irradiations were performed at four different cyclotrons, each providing different projectile types, energy ranges, and beamline conditions. This made it possible to investigate several production routes for the formation of ^{72}Se and ^{72}As , as well as the production of ^{211}At . A brief overview of the irradiation facilities relevant to this work is given below.

JULIC

The Jülich Isochronous Cyclotron (JULIC), located at the Institute for Nuclear Physics (IKP), **Forschungszentrum Jülich**, is a long-established accelerator equipped with an external target station and an adapter system for different target holders. For proton irradiation, beam energies of up to $E_p = 45$ MeV can be provided, while beam currents typically range from the nA regime to low- μA values, depending on the experimental requirements. Owing to its flexible target station and well-established operation, JULIC was particularly suitable for activation experiments and nuclear data measurements.

BC 1710

The Baby Cyclotron 1710, operated at FZJ, is a compact fixed-energy two-particle isochronous cyclotron. It accelerates protons to approximately $E_p \approx 17$ MeV and deuterons to $E_d \approx 10$ MeV. During irradiations, beam currents in the range of approximately $I = 1\text{--}15$ μA_e can be achieved. Due to its stable operation and well-defined beam characteristics, the BC1710 was used primarily for low-current activation and cross-section measurements.

IBA Cyclone® 30 XP

The IBA Cyclone® 30XP at INM-5, FZJ, is a multi-particle variable-energy isochronous cyclotron capable of accelerating protons, deuterons, and α -particles. Its nominal beam energies are $E_p = 15\text{--}30$ MeV, $E_d = 7.5\text{--}15$ MeV, and $E_\alpha = 30$ MeV, with the α -particle energy being fixed. The cyclotron combines high-current capability with flexible irradiation infrastructure and was therefore particularly important for both research-scale irradiation and production-oriented experiments. For the ^{211}At studies presented in this work, the availability of intense α -particle beams were essential.

Injector 2 Cyclotron

The Injector 2 cyclotron at the **Paul Scherrer Institute (PSI)**, Villigen, Switzerland, is a 72 MeV four-sector separated-sector cyclotron serving as a pre-accelerator for the PSI Ring Cyclotron. A fraction of the beam can be diverted for radioisotope production and activation experiments. Owing to its high beam energy and high beam quality, Injector 2 was used in this work for irradiations requiring an extended proton energy range beyond that accessible at the cyclotrons available at Forschungszentrum Jülich.

5.2.2. Target preparation

Targets for ^{72}As Production Studies

Sedimentation:

Sedimentation was used to prepare thin target layers for stacked-foil activation experiments. In this method, the target material in fine powder form was suspended either in toluene or in a 1:1 mixture of toluene and 2-propanol containing 0.5–1.0 mg mL⁻¹ Levapren-450® (Arlanxeo, Dormagen, Germany). Levapren-450® acted as an adhesive binder and improved the mechanical stability of the final sediment layer.

For sedimentation, the suspension was thoroughly homogenized and transferred into a custom-built sedimentation cell (Figure 66). The cell consisted of two cylindrical Teflon discs, each 10 mm thick, clamped around a centrally positioned aluminum foil of precisely known mass. Depending on the experiment, aluminum foils of 10–50 µm thickness and 13 mm diameter were used. The foils were obtained from Goodfellow (purity: 99.0%). The upper Teflon disc contained a cylindrical cavity with a diameter of 10 mm, corresponding to a sedimentation volume of 0.785 mL above the foil.

After loading, the sedimentation cell was placed in a drying oven at 60–80 °C overnight in order to allow slow solvent evaporation without disturbing the uniform settling of the suspended particles. Complete dryness was confirmed by the absence of dark or glossy spots within the deposited layer. The cell was then carefully disassembled, and the aluminum backing carrying the sediment was removed. Each target was inspected visually and under a light microscope, and only mechanically stable and sufficiently homogeneous sediments were selected for irradiation. Representative examples are shown in Figure 68.

To improve mechanical robustness during handling and irradiation, the sedimented layer was covered with a circular aluminum foil of 15 mm diameter and 5 or 10 µm thickness, previously weighed to known mass. The final target assembly was weighed again, and the mass as well as the areal density of the deposited target layer were calculated gravimetrically.

In this work, several target materials were prepared by sedimentation. An overview of the materials used, the corresponding net mass ranges, and their suppliers is given in

Table 34. For experiments involving enriched material, in particular ^{72}Ge and ^{69}Ga , the isotopic compositions are summarized in the appendix in Table A-2

Table 34: Target materials used for the preparation of thin activation targets, including irradiation route, chemical form, mass range, and supplier.

Irradiation experiment	Target material	Mass range [mg]	Supplier
$^{72}\text{Ge}(\text{p},\text{n})^{72}\text{As}$	^{72}Ge (enriched)	1.8–7.5	Chemotrade GmbH, Germany
$^{\text{nat}}\text{Ga}(\text{a},\text{n})^{72}\text{As}$	$^{\text{nat}}\text{Ge}$	2.8–15.0	Merck KGaA
$^{69}\text{Ga}(\text{a},\text{n})^{72}\text{As}$	^{69}Ga (enriched)	1.4–5.2	Trace Sciences International
$^{75}\text{As}(\text{p},\text{x})^{72}\text{Se}$	$^{\text{nat}}\text{As}$	13.4–28.5	Merck KGaA

Conversion of ^{69}Ga to $^{69}\text{Ga}_2\text{O}_3$

Since the enriched ^{69}Ga was supplied as metallic solid material, it could not be used directly for sedimentation and was first converted into $^{69}\text{Ga}_2\text{O}_3$. Therefore, 96 mg of ^{69}Ga -metal were dissolved overnight in a mixture of 400 μL HCl (12 M) and 600 μL HNO_3 (16 M) in a 50 mL Falcon tube. The solution was then adjusted to pH 7.8 by addition of 1 M NaOH, causing precipitation of white $^{69}\text{Ga}(\text{OH})_3$. The suspension was centrifuged for 3 min (8000 rpm), and the supernatant was carefully decanted. The precipitate was washed with 15 mL Milli-Q water and shaken it for 5 min before centrifuged again. The supernatant was removed and washing procedure was repeated three-fold. The washed $^{69}\text{Ga}(\text{OH})_3$ was then transferred quantitatively into a fused-silica Petri dish and dried overnight at 85 °C in a drying cabinet.

After drying, the material was heated at 460 °C for 6 h in order to convert $^{69}\text{Ga}(\text{OH})_3$ into $^{69}\text{Ga}_2\text{O}_3$. In the end, 89% of the initial ^{69}Ga mass was recovered. The resulting $^{69}\text{Ga}_2\text{O}_3$ powder was subsequently used for sedimentation as described above.

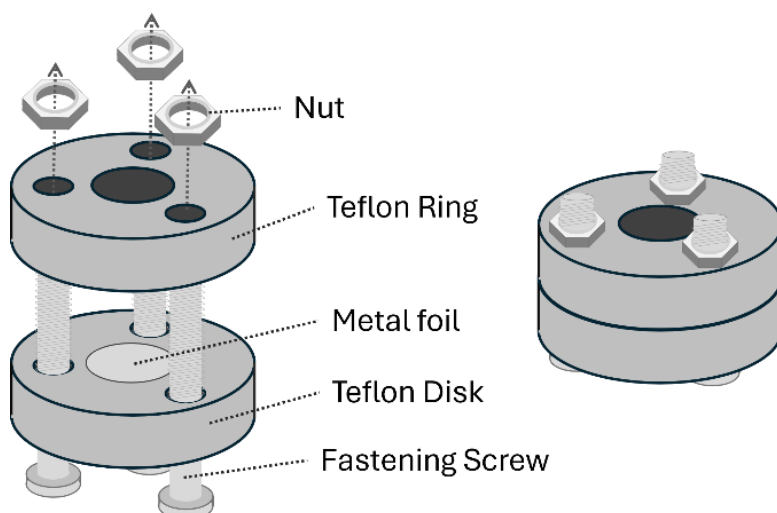


Figure 66: Schematic overview of a sedimentation cell used to prepare thin samples for stack foil irradiations.



Figure 67: Photograph of the sedimentation cell used for thin-target preparation, shown disassembled (left) and assembled (right).

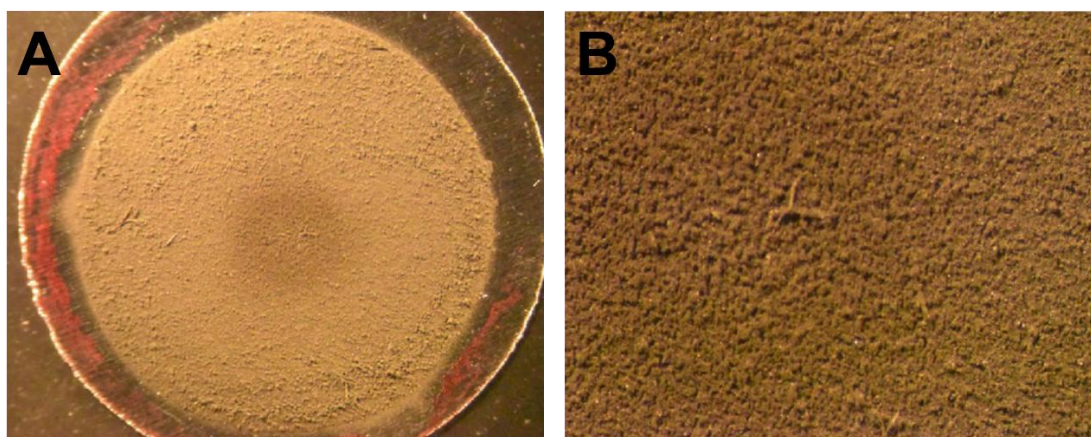


Figure 68: Photograph of a representative sedimented enriched ^{72}Ge target on an aluminum backing without cover foil (A) and magnified view of the target surface illustrating its homogeneity (B).

Vapor deposition

Target preparation for thin, natural arsenic targets was conducted utilizing small-scale, economical, manually operated vapor deposition. In this configuration (Figure 69), a fused silica glass plate was positioned upon a high-precision heating plate. Superimposed on this fused silica plate, a fused silica tube, 10 mm high, with an inner diameter of 12 mm and a wall strength of 2 mm was situated. The upper and lower end of the tube were polished to the greatest extent, feasible to create an airtight connection between the two silica components. In the center of the tube, As_2O_3 powder (20–60 mg) was introduced as target material. Subsequently, an aluminum foil of 50–100 μm thickness was weighed and placed atop of the tubing to seal the sample chamber. The aluminum foil was thermally regulated from the upper side with a vessel filled with ice water to maintain its temperature significantly lower than that of the remaining surfaces within the chamber. The entire assembly was heated to 465 °C resulting in the evaporation of As_2O_3 from the base of the chamber and its subsequent condensation on the cooled aluminum foil at the apex. After 5 min consistent heating at 465 °C, when all the As_2O_3 powder evaporated, the heating was turned off, and the apparatus was disassembled carefully. The aluminum foil was covered with roughly 50% of the added As_2O_3 in a robust, stable and fine crystalline layer which could even endure minor abrasions from plastic forceps. Every sample was subjected to visual control validating the homogeneity and integrity of every target. In Figure 70, images of a representative target and its enlarged surface architecture are illustrated. Thereafter, the deposited layer was covered with a 16 mm wide, 5 μm thick aluminum foil, the rims of the foil were folded over to further protect the As_2O_3 layer and to avert contamination arising from evaporating arsenic gas during irradiation. The entire assembly was weighed, and the mass and area density of the target surface was computed. A complete overview of all applied targets and their corresponding net masses is provided in Table A-5 in the Appendix.

Materials and Methods

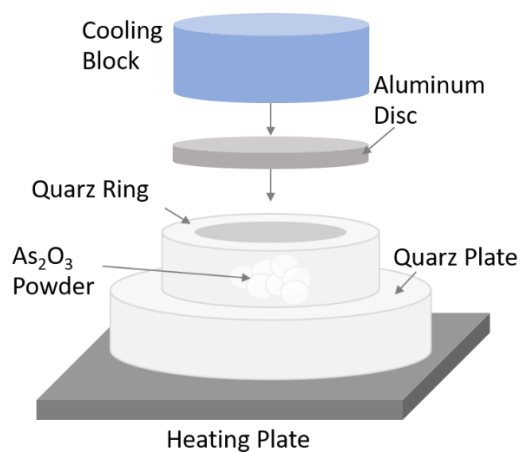


Figure 69: Schematic illustration of the manual vapor-deposition setup used for the preparation of As₂O₃ targets.



Figure 70: Photograph of a representative As₂O₃ target prepared by manual vapor deposition on an aluminum backing (magnified by ~1.5 x (A), ~2 x (B) and ~10 x (C))

Bismuth Targets for ^{211}At Production

Target Layouts

To produce ^{211}At , different target designs were employed, exploiting different benefits of the respected target layout.

The target design by IBA employed a rectangular target of 132 x 42 mm and a target area of 110 x 20 mm with smoothened edges. The target area was framed with a thin 100 μm high 500 μm thick rim. The target fits inside an automated shuttle delivery system with a fixed 6° beam incident angle for a large beam surface area and corresponding target cooling area. This target setup provides excellent properties for high current irradiation, due to its inherent dose decrease due to the automated delivery system as well as maximized thermal conductivity.

Alternatively, a coin target system of 25 mm diameter was designed with a 20 mm mold of 1–2 mm in the middle. This target can either be mounted onto a 20° angled slanted beam target holder, or onto an 90° aluminum holder. This target design offers an in-between solution for robust and practical geometry suitable for harsh target preparation or versatile preparation trials.

An illustration of the two target layouts is depicted in Figure 71.

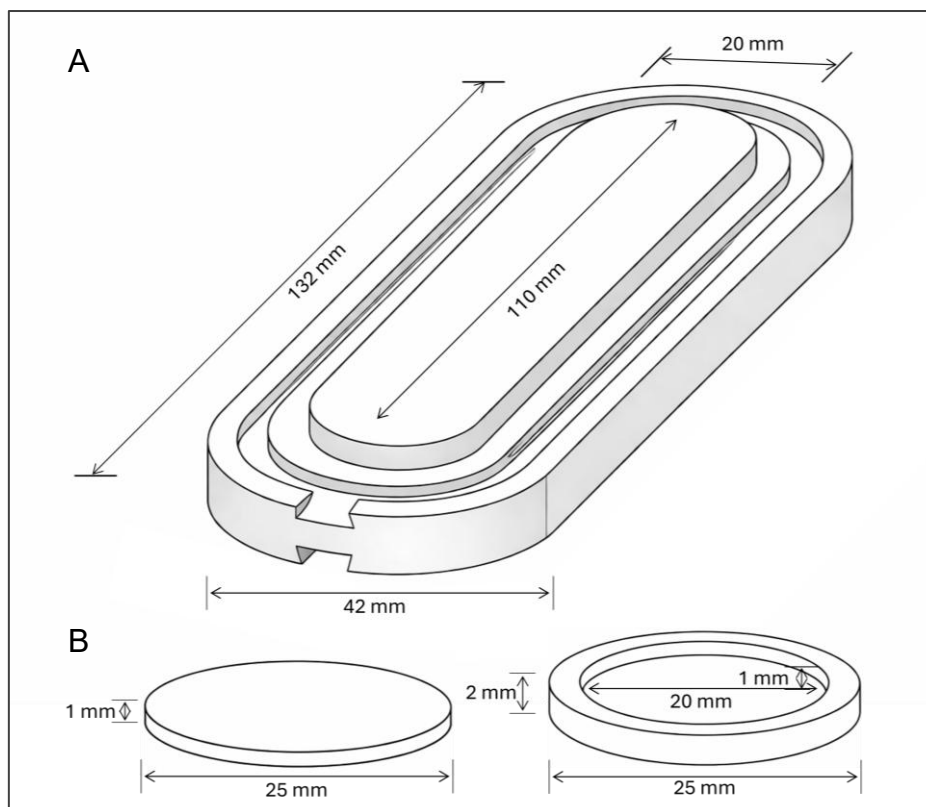


Figure 71: Schematic illustration of the 6° targets (A) and the coin targets (B) used in this study.

Delayed γ -spectrometric screening of irradiated AlMg3-backed targets

In addition to the routine post-irradiation γ -spectrometric characterization, a delayed measurement was performed to assess whether the use of AlMg3 rather than high-purity aluminum as target backing resulted in measurable long-lived activation products. For this purpose, an irradiated molten bismuth target on an AlMg3 backing, originally irradiated in mid-December 2025, was remeasured by HPGe γ -spectrometry approximately five months after EOB. At this time point, short-lived radionuclides previously observed in prompt post-irradiation spectra, such as ^{29}Al , ^{27}Mg and ^{30}P , had decayed by many orders of magnitude and therefore no longer contributed to the spectrum.

The target was measured in a fixed counting geometry using the same HPGe detector setup as described above. Peak identification was based on the observed γ -ray energies and the expected decay behavior of radionuclides formed during alpha irradiation of the target system. A background spectrum was recorded under

comparable detector conditions and used to distinguish target-related photopeaks from environmental or detector-background contributions. The delayed measurement was used as a qualitative screening for persistent γ -emitting activation products rather than as a full quantitative activation inventory. Therefore, radionuclides not observed above the background level are discussed as not detectable within the sensitivity of the applied measurement conditions.

Pretreatment of target material

For powder- and granule-based target preparation, bismuth starting materials were subjected to a brief pretreatment step prior to target preparation in order to remove pre-existing surface oxide layer. This was particularly relevant for fine powder and small grain size, for which surface oxidation is more pronounced due to the higher surface area ratio. To minimize further oxidation before use, these materials were cleaned shortly before target preparation or stored under inert atmosphere.

For pretreatment, the bismuth was immersed in 1 M HCl and stirred for 2–5 min, depending on sample mass and particle size. It was then rinsed thoroughly with water and followed by 2-propanol before being dried. After drying, the material was either used directly for target preparation or stored under argon until further use.

Molten targets

Molten bismuth targets were mainly prepared in the 6° IBA target. To start, pretreated bismuth pellets were crushed into chunks of 20–500 mg. The chunks were visually checked for any green stains left on the surface originating from Bi_2O_3 contamination. Then, the aluminum target backings were cleaned with 2-propanol in an ultra-sonic bath for 5–10 minutes, before heating the target backings to 330 °C. Roughly 150 mg of the bismuth chunks (2–4 pieces) were placed on the hot surface inside the target area melt. To ensure proper connection of the bismuth with the aluminum surface, the bismuth was spread over the aluminum using a 330 °C solder iron. During that process, the bismuth changes color and goes from a drop like inert corpus to a smooth spreading liquid. With that method, the whole target area is covered with a very thin

film of silvery shining bismuth. During this process, sludge formation is visible. The formed sludge is thoroughly removed with the solder iron to not disturb the aluminum-bismuth layer formation. Afterwards, further bismuth chunks are placed onto the framed target area completely filling it with bismuth, continuously removing formed slag from the liquid bismuth. Afterwards, the target is slowly cooled down to room temperature before manually machined down to a surface mass of approximately 30 mg cm^{-2} using sandpaper with different grits.

Press & Sinter targets

Target pressing was performed into the more versatile 25 mm coin targets. For sinter targets, cleaned bismuth chunks were freshly ground down into a fine powder. The powder was weighed and portions of 500–1500 mg were filled into a press (20 mm diameter) and pressed into pellets using 15 tons of pressure (4.8 tons cm^{-2}). The pressure was kept up for 20–25 minutes before the press was disassembled and the coin was removed. The prepressed bismuth coin was then placed into a 20 mm diameter 500 μm deep mold inside the aluminum target backing and pressed a second time at 6–7 tons pressure into the aluminum casket forming a strong connection of bismuth onto aluminum. Afterwards, the pressed target was heated to 210°C , added a weight on top and left sintering for 5 h under inert gas atmosphere to strengthen the bismuth layer. Every target was thoroughly tested for any signs of detachment.

Electroplated targets

For the electroplated targets, both 6° targets and coin targets were used. For a firm connection of the bismuth to the aluminum backing, the aluminum was first thoroughly cleaned in an ultrasonic bath containing 0.5 M NaOH solution at 50°C before further conditioning with a thin zinc film by submerging it into a zincate bath containing 20 g L^{-1} ZnO in 3 M NaOH solution and shaking for 5 minutes. Afterwards, a secondary thin layer of nickel was electroplated on the tin surface (cathode) by “Nickel-Strike” reaction [163] using a nickel anode and a NiCl_2 bath containing 125 g L^{-1} $\text{NiCl}_2 \cdot 6 \text{ H}_2\text{O}$ dissolved in 1 M HCl solution, deposited at 10 mA cm^{-2} for 2 minutes. Afterwards, the target was

thoroughly rinsed with water, dried and weighed. Thereafter, bismuth is deposited onto the nickel surface using a $\text{Bi}(\text{NO}_3)_3$ solution at 2.5 mA cm^{-2} for 1.5 h. The target was thoroughly cleaned, dried and weighed again to calculate the weight of the bismuth layer. The detailed composition of the $\text{Bi}(\text{NO}_3)_3$ solution is presented in Table 35: Showing the composition of the $\text{Bi}(\text{NO}_3)_3$ solution used for electro deposition. 35.

Table 35: Showing the composition of the $\text{Bi}(\text{NO}_3)_3$ solution used for electro deposition.

Chemicals	Concentration	Amount in 200 mL
$\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$	0.15 M	14.6 g
Glycerol	1.4 M	20.5 mL
KOH	1.2 M	13.5 g
Tartaric acid	0.3 M	9 g
HNO_3 (65 %)	1.8 M	25 mL

Sedimentation

For bismuth targets, sedimentation was employed analogously to those for the production of ^{72}As using the same sedimentation cells. For the suspension, metallic bismuth was dissolved in 5 M HNO_3 and precipitated as white fluffy, slightly gel like $\text{Bi}(\text{OH})_3$ by addition of 20% NH_4OH solution. After filtration it was washed with H_2O and let rest over night at 80°C to reach complete dryness. Afterwards, 200–300 mg of fine $\text{Bi}(\text{OH})_3$ powder was suspended in 10–15 mL of Levapren-450[®] solution as prepared earlier this chapter and stirred thoroughly. The suspension was then filled into the prepared sedimentation containing a 50 μm thick, cleaned, weighted aluminum foil and let drying at $60\text{--}80^\circ\text{C}$ until next day. The targets were checked visually for any stained spots indicating inhomogeneous sedimentation. Passing the quality assessment, the sediments were covered with a 10 μm thick aluminum foil of know mass. The finished sandwich is weighed again, and the mass of the sediment is calculated. A picture of an average $\text{Bi}(\text{OH})_3$ sediment is shown in Figure 72.

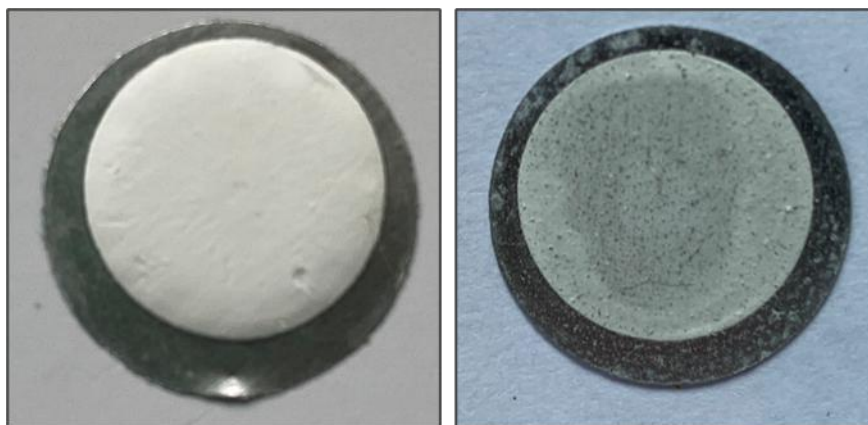


Figure 72: Representative bismuth sediments prepared from $\text{Bi}(\text{OH})_3$ on aluminum backings. The left target shows a thick, compact, and largely homogeneous deposit, whereas the right target exhibits staining indicative of less uniform sedimentation.

5.2.3. Experimental irradiation procedures

The irradiation procedures differed significantly between the $^{72}\text{Se}/^{72}\text{As}$ -related nuclear data experiments and the production studies of ^{211}At . Therefore, the experimental approaches are described separately in the following sections.

Irradiation procedure for ^{72}Se and ^{72}As

Nuclear cross-section and decay-data measurements related to the formation of ^{72}Se and ^{72}As were carried out using different projectile types and beam energies at a total of four cyclotrons located at Forschungszentrum Jülich and PSI. These experiments were generally performed at low beam currents of approximately $I \approx 1 \mu\text{A}_e^9$ in order to ensure controlled activation conditions and to keep thermal loading of the targets low. Typical irradiation times were in the range of 30–60 min. The use of different irradiation facilities allowed the accessible energy range to be adapted to the respective reaction under investigation.

⁹ For proton irradiation: $\mu\text{A} = \mu\text{A}_e$ since the proton number of protons $z_p=1$

Irradiation procedure for ^{211}At

The production of ^{211}At was carried out exclusively at the C30XP at Forschungszentrum Jülich, since this radionuclide was produced via α -particle induced reactions. Two different beamlines were employed depending on the experimental objective.

Low-current irradiations, typically below $I < 10 \mu\text{A}_e$, were performed at the experimental beamline. This beamline provided flexible target stations and was therefore particularly suitable for the investigation of different target geometries and target preparation methods. However, the available cooling water flow rate was comparatively low, typically below $\sim 1.3 \text{ L min}^{-1}$, which limited the applicable beam current and consequently the maximum tolerable thermal load.

Upscaling experiments and high-current irradiations were performed at a high current beamline, which is equipped with an automatic target transfer system and is designed for high-power irradiation. This setup reduced radiation exposure during handling of highly activated targets and enabled production-oriented irradiation conditions. The high current beamline is operated with a cooling water flow rate of approximately 48 L min^{-1} . In combination with a shallow beam incidence angle of 6° , this provided substantially improved target cooling and allowed irradiation currents of up to approximately $I \approx 50 \mu\text{A}_e$. Depending on the aim of the experiment, irradiation times between $t = 3$ and 300 min were applied.

5.2.4. Nuclear data measurements for $^{72}\text{Se}/^{72}\text{As}$

Determination of particle flux and energy

The reaction cross-sections were determined using the stacked-foil technique [22, 23, 51, 51, 164–167]. In this approach, target foils and auxiliary foils of known areal density, such as monitor, degrader, and catcher foils, were arranged in a defined sequence and irradiated simultaneously. After irradiation, the foil stack was carefully disassembled and the individual foils were analyzed, primarily by HPGe γ -ray spectrometry. The activities measured in the individual foils were then used to calculate the reaction cross-sections for the corresponding production routes.

Beam energy and particle flux determination

The calculation of the reaction cross-section requires a precise determination of both the incident particle flux and the beam energy at the position of the target material. Although most cyclotrons allow online readout of the beam current using beam integrators, this approach is often associated with significant uncertainty, since it is difficult to distinguish between charge deposited on the target foil itself and charge intercepted by the rim of the target holder or other surrounding components. Therefore, beam monitoring is commonly performed using well-established monitor reactions with recommended excitation functions [38].

In stacked-foil irradiations, the incident particle energy E_0 decreases continuously while the beam passes through entrance windows, monitor foils, degrader foils, catcher foils, and target layers. Consequently, the particle energy in a given foil is not a single value, but an interval between the entrance energy E_{in} and the exit energy E_{out} . Effective energies were initially assigned as the midpoint between E_{in} and E_{out} . For foils spanning regions of steeper excitation-function gradients, this assignment was checked and, where necessary, refined by comparison with the monitor-reaction data. The resulting energy uncertainty was propagated into the final cross-section uncertainty. The corresponding energy loss ($E_{in}-E_{out}$) was calculated from stopping-power data using SRIM [168] or tabulated libraries [169] yielding the energy-degradation profile throughout the entire foil stack.

For a given particle energy, the particle flux ϕ (particles s^{-1}) or the integrated beam current can be derived from the measured activity of a monitor nuclide produced via a recommended monitor reaction with known cross-section σ . In addition to current standardization, monitor reactions can also be used to refine the beam-energy assignment within the foil stack. Starting from the activation equation [9], the ratio of two monitor products formed in the same foil can be expressed as follows:

$$A_{\text{EOB},i} = N_{T,i} \Phi \sigma_i(E) (1 - e^{-\lambda_i t_{\text{irr}}}) \quad (5.1)$$

$$\frac{\sigma_1(E)}{\sigma_2(E)} = \frac{A_{\text{EOB},1}}{A_{\text{EOB},2}} \cdot \frac{N_{T,2}}{N_{T,1}} \cdot \frac{1 - e^{-\lambda_2 t_{\text{irr}}}}{1 - e^{-\lambda_1 t_{\text{irr}}}} \quad (5.2)$$

where $A_{\text{EOB},i}$ is the end-of-bombardment activity of monitor product i , $N_{T,i}$ is the corresponding number of target atoms, λ_i is the decay constant, and t_{irr} is the irradiation time.

By comparing the experimentally determined cross-section ratio with recommended reference data, the effective beam energy in the respective monitor foil can be calculated. Therefore, monitor reactions can serve both as a standard for beam-current determination as well as confirmation check for the beam-energy assigned to the monitor. This procedure is particularly important in activation experiments, since even small deviations in beam position, degrader thickness, or homogeneity may propagate into noticeable errors in the assigned cross-sections.

Consequently, the final uncertainty of the experimental cross-section therefore depended not only on counting statistics or detector efficiency, but on the accuracy of the beam-current determination, foil thicknesses, decay data, irradiation time, and the energy assignment within the stack as well.

Decay data measurements of ^{72}As

To investigate the decay data of ^{72}As , a comparative study combining conventional HPGe γ -spectrometry, annihilation measurements using a dedicated annihilation chamber, β -counting, and low-energy X-ray spectrometry was performed [23].

Materials and Methods

The annihilation chamber consists of a copper capsule, tightly encapsulating the sample foil, causing annihilation to occur quantitatively in proximity of the target foil due to the high material density of copper compared to environmental air. Therefore, the geometry stays similar. However, due to attenuation effects caused by the copper chamber, an additional calibration through the annihilation chamber is required.

5.2.5. Thermal stability investigation for ^{211}At high current targets

The thermal stability of the target assembly was investigated by combining two complementary approaches: (i) an experimental determination of the effective Bi/Al thermal contact resistance using target-like test rods and (ii) an activity-based reconstruction of the local power-density distribution in irradiated targets. The experimentally derived interface resistances were subsequently used as input parameters for a simplified steady-state thermal model to estimate the temperature distribution in the target under irradiation-relevant conditions. In this model, the target was treated as a sequence of dominant thermal resistances along the heat-flow path, including heat conduction through the bismuth layer and aluminum backing, the experimentally determined Bi/Al contact resistance, and convective heat removal at the water-cooled rear side. The approach was intended as an engineering-level estimate of the temperature field and hotspot formation rather than as a fully resolved transient or computational fluid dynamics model.

Determination of thermal contact resistance

Preparation of test rods

To determine the effective thermal contact resistance between bismuth and aluminum, composite test rods consisting of an aluminum base and a bismuth section were prepared. The rods were fabricated as closely as possible to the corresponding target preparation routes in order to preserve target-relevant interface properties. Because the measurement concept required a sufficiently extended axial temperature profile, only molten and pressed/sintered Bi/Al assemblies were investigated. Electrodeposited layers were not included in this part of the study, since the achievable bismuth thickness was insufficient for the preparation of suitable rod geometries (Figure 73).

For the pressed/sintered rod, an aluminum cylinder of 25 mm diameter and 10 mm height was prepared. The aluminum piece was cleaned in an ultrasonic bath containing 0.1 M NaOH for 5 min, rinsed with water, and placed in a 25 mm press die. The die was filled with freshly prepared and pretreated fine bismuth powder. The powder was

compacted for 25 min at a load of 15 tons, corresponding to approximately 3 tons cm⁻². The resulting composite rod was removed carefully and inspected for mechanical integrity. To improve cohesion of the bismuth section, the rod, with a total height of approximately 35 mm, was placed in an argon-filled metal container, heated to 210 °C, loaded with a defined weight, and sintered for 5 h. After cooling to room temperature, measurement boreholes of 12.5 mm depth and 1.5 mm diameter were drilled along the rod axis at defined distances in order to accommodate the temperature probes. The borehole positions were chosen such that separate linear temperature gradients could be determined in the aluminum and bismuth sections and extrapolated toward the interface.

For the molten rod, an aluminum rod segment of 25 mm length was prepared, processed analogously, and cleaned in the same manner. A casting mold was then formed around the rod using a rectangular sheet of graphite foil as an inner anti-adhesion layer and a copper sheet as an outer stabilizing layer. The mold was additionally covered with fused silica insulation to reduce uncontrolled heat loss and to promote more homogeneous heating. The entire assembly was placed on a heating plate and heated to 350 °C. A small amount of pretreated bismuth was first introduced and spread across the aluminum surface using a soldering iron at 330 °C in order to establish complete wetting of the interface. After the first layer had formed, additional bismuth was added until a bismuth column of approximately 30 mm height was obtained. During this process, oxide-rich slag was removed repeatedly. After cooling to room temperature, the rod was machined to the final geometry and measurement boreholes of 12.5 mm depth and 1.5 mm diameter were drilled analogously to the pressed/sintered rod. Representative photographs and a schematic overview of the borehole arrangement are shown in Figure 73.



Figure 73: Photograph of the two Bi/Al test rods used for the experimental determination of the effective thermal contact resistance between bismuth and aluminum for target preparation routes.

Thermal contact resistance measurement

The aim of the following measurement was to determine the effective interface-related thermal resistance between the aluminum and bismuth sections under steady-state heat-flow conditions.

To determine the effective thermal contact resistance, the axial temperature profile along each composite rod was measured under stationary heat-flow conditions. The rods were placed with the aluminum side on a water-cooled aluminum block. A cylindrical copper heating block (25 mm diameter, 20 mm height) was placed on the bismuth side of the rod in direct contact. The heating block contained a 6 mm borehole for an electrical cartridge heater (ARCELI Reprap 24 V, 40 W ceramic heating cartridge) and a second 1 mm borehole for a resistance thermometer. All contacting

surfaces were coated with thermal paste to minimize unwanted contact resistances outside the Bi/Al interface of interest. The full assembly was wrapped in high-temperature fused silica insulation and fixed with metal wire to reduce convective heat losses to the surroundings. The heater cartridge was connected to a power supply, adjusting the core heating block temperature to 150–250 °C. After a stabilization period of 30–60 min, the temperatures at all probe positions were recorded for 5 min each.

The heat flux through the rod was estimated independently by calorimetry of the cooling water. For this purpose, the coolant temperature was measured immediately before and after the cooling block using an electrically insulated high-precision resistance thermometer. From the coolant mass flow $\dot{m}$, the specific heat capacity of water c_p , and the measured coolant temperature rise ΔT_{water} , the removed heat flow $\dot{Q}$ was calculated according to Eq. (5.3). Division by the cross-sectional area A of the rod yielded the corresponding area-specific heat flux q'' according to Eq. (5.4).

$$\dot{Q} = \dot{m} \cdot c_p \cdot \Delta T \quad (5.3)$$

$$q'' = \frac{\dot{Q}}{A}, \quad \text{with} \quad (5.4)$$

Here, $\dot{Q}$ is the heat flow in W, $\dot{m}$ is the coolant mass flow in kg s⁻¹, c_p is the specific heat capacity of water in J kg⁻¹ K⁻¹, ΔT_{water} is the coolant temperature increase in K, A is the rod cross-sectional area in m², and q'' is the resulting area-specific heat flux in W m⁻².

As an independent consistency check, the heat flux was also estimated from the measured axial temperature gradient within the aluminum section of the rod by applying Fourier's law of heat conduction. Using the thermal conductivity of the employed aluminum alloy, k_{AlMg3} (~150 W m⁻¹ K⁻¹), and the temperature difference ΔT_{Al} between two known axial positions separated by the distance Δy , the corresponding heat flux was calculated according to Eq. (5.5):

$$q''_{\text{cond}} = -k_{\text{AlMg3}} \cdot \frac{dT}{dx} \quad (5.5)$$

Here, q''_{cond} is the conductive heat flux in W m⁻², k_{Al} is the thermal conductivity of aluminum in W m⁻¹ K⁻¹, ΔT_{Al} is the temperature difference in K, and Δy is the axial spacing between the two probe positions in m.

The nominal electrical heating power of the cartridge heater was calculated from the applied voltage and current and used only as an external consistency check for the experimentally determined heat fluxes, not as a direct correction factor.

$$P_{el} = U \cdot I \quad (5.6)$$

Here, P_{el} is the nominal electrical heating power in W, U is the applied voltage in V, and I is the electrical current in A.

For each rod, the temperature profiles in the aluminum and bismuth sections were fitted separately by linear regression and extrapolated to the nominal interface position ($x = 0$). The resulting interfacial temperature discontinuity ΔT_{int} was interpreted as the effective temperature drop across the Bi/Al interface. The corresponding area-specific thermal contact resistance was then calculated according to Eq. (5.7):

$$R''_{tc} = \frac{\Delta T_{int}}{q''} \quad (5.7)$$

where R''_{tc} is the area-specific thermal contact resistance in $\text{m}^2 \text{K W}^{-1}$, ΔT_{int} is the extrapolated interfacial temperature discontinuity in K, and q'' is the heat flux through the rod in W m^{-2} .

Irradiation conditions for thermal stability tests

Thermal stability under irradiation was investigated using 6° high-current target systems prepared by the molten-target method described above (Section 5.2.2). The bismuth loading of the investigated targets was adjusted to approximately 30 mg cm^{-2} . Prior to irradiation, all targets were inspected visually for cracks, delamination, or macroscopic surface inhomogeneities. Irradiation was performed at an α -particle beam current of $50 \mu\text{A}_e$ and an irradiation time of 1 h. In order to investigate the influence of beam homogenization on local thermal load, the target stability was compared at wobbler intensities between 10% and 40%.

Activity-based reconstruction of local power density and target temperature

For the thermal model, two types of experimental information were combined: the total ^{211}At production yield determined by HPGe γ -ray spectrometry and the spatially resolved delayed activity distribution of residual ^{207}Bi obtained by phosphor imaging after complete decay of ^{211}At . The ^{207}Bi distribution was used as an experimental surrogate for the spatial beam footprint and thus for the relative local power deposition during irradiation. For this purpose, irradiated targets were allowed to decay for at least one week and were then measured using a phosphor imager.

The obtained image was discretized into a raster of $1 \times 1 \text{ mm}^2$ pixel. For each pixel, the integrated signal intensity was determined and normalized to the pixel area. A background correction was performed by subtracting the mean signal of the outermost image region from all pixels. The resulting corrected signal map was then used for the relative redistribution of the deposited beam power over the target surface.

The total deposited beam power P_{dep} was calculated from the incident particle rate $\dot{N}$ and the deposited energy per incident α particle, ΔE_{dep} , according to Eq. (5.8):

$$P_{\text{dep}} = \dot{N} \cdot \Delta E_{\text{dep}} \quad (5.8)$$

The particle rate was obtained from the electrical beam current I according to Eq. (5.9):

$$\dot{N} = \frac{I}{z e} \quad (5.9)$$

Here, P_{dep} is the deposited beam power in W, $\dot{N}$ is the particle rate in s^{-1} , ΔE_{dep} is the deposited energy per particle in J, I is the beam current in A, z is the projectile charge number, and e is the elementary charge.

As a first-order approximation, the corrected rasterized ^{207}Bi signal distribution was taken to represent the relative spatial distribution of deposited beam power. Each pixel i was therefore assigned a fraction of the total deposited power proportional to its relative signal contribution. For a constant pixel area A_{pix} , the local power density q_i'' was calculated according to Eq. (5.10):

$$q_i'' = \frac{P_{\text{dep}}}{A_{\text{pix}}} \frac{S_i}{\sum_j S_j} \quad (5.10)$$

Here, q_i'' is the local power density of pixel i in $W\ m^{-2}$, S_i is the corrected signal intensity of pixel i , $\sum_j S_j$ is the summed signal of all pixels, P_{dep} is the total deposited beam power, and A_{pix} is the area of one pixel.

The local power-density map served as the input for a steady-state thermal-resistance model. For each pixel, the temperature increases relative to the coolant temperature, ΔT_i , was calculated as the product of the local power density and the sum of the area-specific thermal resistances along the dominant heat-flow path, according to Eq. (5.11):

$$\Delta T_i = q_i'' \cdot \left(R_{conv}'' + R_{tc}'' + \frac{d_{Bi}}{k_{Bi}} + \frac{d_{Al}}{k_{Al}} \right) \quad (5.11)$$

The corresponding absolute local target temperature was then obtained from Eq. (5.12):

$$T_i = T_{coolant} + \Delta T_i \quad (5.12)$$

Here, R_{conv}'' is the area-specific convective thermal resistance at the coolant interface in $m^2\ K\ W^{-1}$, R_{tc}'' is the experimentally determined area-specific Bi/Al contact resistance in $m^2\ K\ W^{-1}$, d_{Bi} and d_{Al} are the thicknesses of the bismuth and aluminum layers in m, k_{Bi} and k_{Al} are their thermal conductivities in $W\ m^{-1}\ K^{-1}$, $T_{coolant}$ is the coolant temperature, and T_i is the local absolute target temperature.

The area-specific convective thermal resistance at the coolant interface was calculated from the convective heat-transfer coefficient h according to Eq. (5.13):

$$R_{conv}'' = \frac{1}{h} \quad (5.13)$$

The heat transfer coefficient was estimated by using the Gnielinski correlation according to Eq. (5.14):

$$h = \frac{Nu \cdot k_f}{D_h}, \quad (5.14)$$

The Nusselt number Nu was calculated according to the Gnielinski relation:

$$Nu = \frac{(f/8) \cdot (Re_{Dh} - 1000) \cdot Pr}{1 + 12.7 \cdot \left(\frac{f}{8}\right)^{1/2} (Pr^{2/3} - 1)} \quad (5.15)$$

For smooth channels, the Darcy friction factor f was estimated using the Petukhov relation:

$$f = (0.79 \ln(Re) - 1.64)^{-2} \quad (5.16)$$

Where, k_f is the thermal conductivity of the coolant in $W\ m^{-1}\ K^{-1}$, D_h is the hydraulic diameter of the cooling channel in m, Nu is the Nusselt number, Re is the Reynolds number, Pr is the Prandtl number, and f is the Darcy friction factor.

Thus, the convective boundary condition was fully defined by the coolant properties, the hydraulic diameter, and the flow-dependent dimensionless numbers.

Radiative heat transfer was not included in the primary temperature reconstruction. Instead, its possible contribution was estimated separately as a plausibility check, since conduction through the target stack and forced convection at the coolant interface were expected to dominate heat removal under the applied irradiation conditions.

To assess whether lateral heat spreading within the bismuth layer had to be considered explicitly, the thermal healing length was estimated according to Eq. (5.17) and compared with the spatial discretization used for the activity-based reconstruction. If the estimated healing length was smaller than the applied spatial discretization, the model was treated as locally one-dimensional with respect to the dominant heat-flow path.

$$L_H = \sqrt{\frac{k_{Bi}\ d_{Bi}}{g_{sink}}}, \quad (5.17)$$

Here, L_h is the thermal healing length in m, k_{Bi} is the thermal conductivity of bismuth, d_{Bi} is the bismuth thickness, and g_{sink} is the heat sink conductance toward the underlying cooling path.

As an additional plausibility check, the possible magnitude of radiative heat loss from the target surface was estimated using the Stefan–Boltzmann equation:

$$q''_{rad,i} = \varepsilon \sigma_B (T_s^4 - T_{amb}^4) \quad (5.18)$$

Here, q''_{rad} is the radiative heat flux in $W\ m^{-2}$, ε is the surface emissivity, σ is the Stefan–Boltzmann constant in $W\ m^{-2}\ K^{-4}$, T_s is the surface temperature in K, and T_{amb} is the ambient temperature in K.

For an upper-bound estimate, q''_{rad} was evaluated at the hottest modelled target position using representative emissivity values for polished and roughened bismuth surfaces. This comparison was used only to assess the order of magnitude of radiative heat loss relative to the conductive and convective heat fluxes and not as part of the primary temperature reconstruction.

Overall, the model was intended as a first-order steady-state estimate of target temperature under irradiation-relevant conditions and primarily served to compare the thermal consequences of the experimentally observed power-density distributions using target-relevant interface parameters.

5.2.6. Separation of ^{211}At

Dry distillation

Implementation and optimization of distillation procedure

Dry distillation for the separation of ^{211}At from irradiated target bulk material and accompanying side products was performed in a sealed environment inside an MBraun Labmaster[®] glovebox using a custom-built distillation apparatus. After irradiation, the activated surface layer was manually scraped from the aluminum target backing using a chisel and collected in a sample container. Depending on the activity required for the respective experiment, the recovered IBM was either used as a whole or divided into aliquots.

The distillation setup consisted of a fused silica glass tube positioned inside a tube furnace and connected downstream to a capillary-based trapping system. Capillaries of different materials, inner diameters, and lengths were evaluated, depending on the specific experimental series. The capillary was connected to the tube using a polymer chromatographic fitting and wrapped around a copper cooling block coupled to a thermoelectric cooling (TEC) assembly. The cooling unit comprised a Peltier element mounted on a water-cooled heat sink operated at 0.5 ± 0.2 °C. The Peltier element was powered by an adjustable power supply and regulated via the applied current, while the voltage was allowed to vary. Downstream of the capillary trap, a two-stage activated carbon filter system was installed, consisting of a small filter (~25 mg carbon) followed by a larger safety filter (~2000 mg carbon), in order to retain any ^{211}At passing the trapping zone. The filter assembly was connected to an adjustable vacuum pump to generate the carrier-gas flow.

At the upstream side, the fused silica tube was connected to a gas-flow monitor and a gas-drying assembly. The latter consisted of three serial drying/purification columns filled with activated carbon, molecular sieve, and phosphorus pentoxide, respectively, to remove traces of organic vapors and moisture from the incoming gas stream before it entered the distillation apparatus. Prior to each distillation, the furnace was pre-heated to the desired operating temperature in the range of 600–800 °C, the full setup

was assembled, and the internal atmosphere was dried by flushing the system with conditioned gas at a flow rate of at least 50 mL min^{-1} for 10 min.

For distillation, the radioactive sample was transferred into a fused silica sample holder. To avoid suction of ambient moist air during loading, the vacuum pump was temporarily stopped, and the gas flow was adjusted to 0 mL min^{-1} . The front connection of the fused silica tube was then briefly opened, the sample holder was placed in the center of the heated zone of the furnace, and the apparatus was immediately re-sealed. Subsequently, the carrier-gas flow was re-established and adjusted to $15\text{--}45 \text{ mL min}^{-1}$, thereby initiating the directed transport. Distillation times between 5 min and 35 min were applied, depending on the experimental objective and furnace temperature. Transport of radioactivity through the system was monitored online using external radiation detectors positioned at defined locations along the apparatus.

A schematic representation of the dry distillation setup is shown in Figure 74. The capillary materials, dimensions, furnace temperatures, and cooling conditions used in the individual experiments are summarized in Table 36.

An illustration of the cold trap as well as the packed-bed non-cooled trap design is presented in Appendix B-2 in Figure B-5 and Figure B-6.

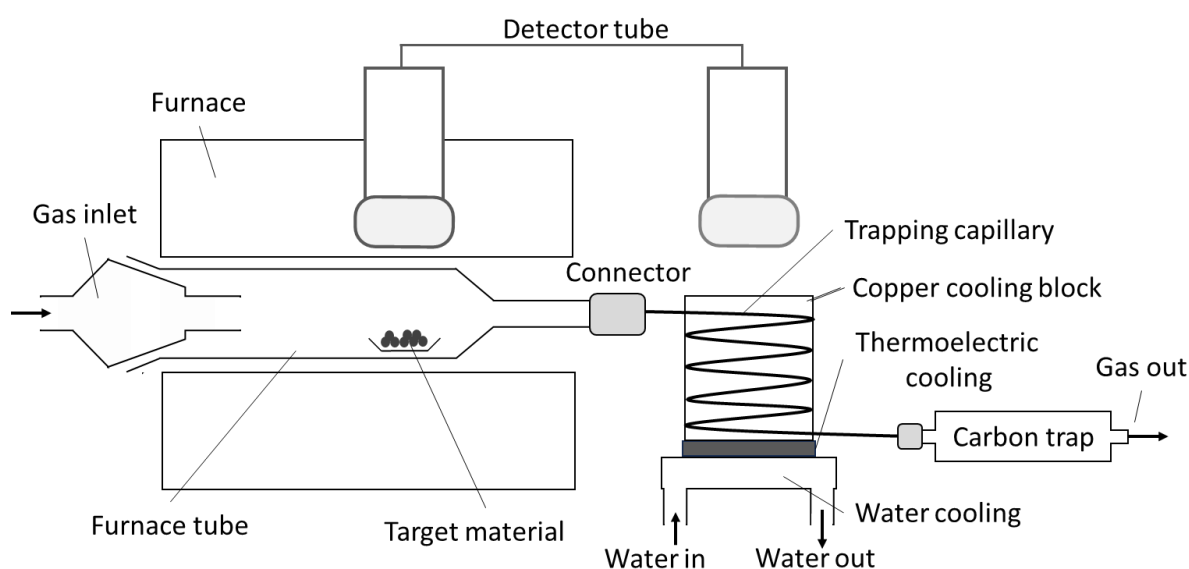


Figure 74: Schematic illustration of the custom design dry distillation apparatus.

Table 36: Overview of dry distillation conditions used for cold trap assembly studies.

Operational parameter	Applied values
Oven temperature	600–800 °C
Cold-trap temp.	+25 °C–80 °C
Capillary material	PTFE, PEEK, PP, FEP, Titanium, Stainless Steel,
Capillary length	20–200 cm
Capillary diameter	0.7–1.6 mm
Cas flow	10–45 mL min ⁻¹
Atmosphere	Argon (100%), Argon (saturated with CO ₂), Synthetic air (80% N ₂ , 20% O ₂)

Vertical oven setup

To investigate scraping-free dry distillation of ²¹¹At, a prototype vertical oven setup was constructed for direct processing of intact irradiated bismuth targets. In contrast to the tube-furnace setup used for distillation of scraped irradiated bulk material, the vertical configuration was designed to accommodate larger target geometries and thereby omit the mechanical removal step prior to separation.

The setup consisted of a vertically arranged heating chamber connected to a glass riser and a downstream capillary-based cold-trap assembly. The heating zone was restricted in size by a glass disc supporting the target position and connected to the outlet tubing via a vertical glass pipe. Downstream of the heating chamber, volatilized ²¹¹At was transferred into a capillary cold trap analogous to the trapping concept used for the tube-furnace experiments. A schematic illustration of the prototype is shown in Figure 75.

For the experiments, intact irradiated bismuth targets were introduced directly into the vertical oven assembly without prior scraping of the activated surface layer. Distillation was performed under a synthetic air atmosphere at a gas flow rate of 40 mL min⁻¹. The oven setpoint was 570 °C, resulting in an estimated glass surface temperature of approximately 525 °C. This condition was chosen as the practical upper operating limit of the prototype, constrained by the aluminum backing and the borosilicate glass components. Distillation times ranged from 30 min to 60 min, depending on target behavior and apparent completion of activity transfer.

After completion of the distillation, the activity recovered in the trapping system as well as the residual activity remaining on the target were quantified. The residual target activity was determined after cooling and decay-corrected to EOB.

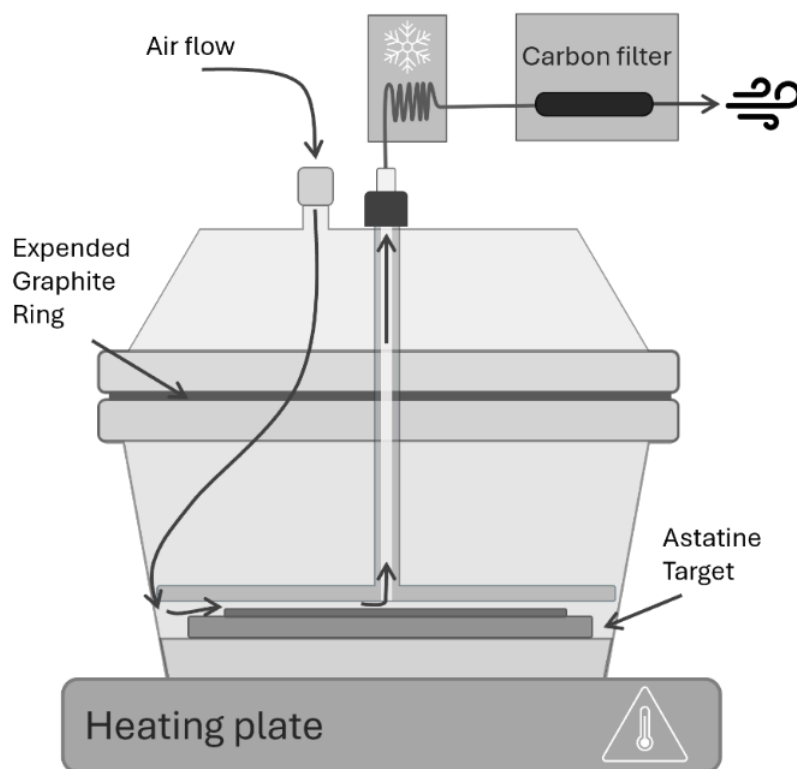


Figure 75: Prototype vertical oven assembly used for dry-distillation processing of intact bismuth targets without prior scraping of irradiated bulk material.

Detector-assisted monitoring of dry distillation

Online monitoring of the ^{211}At dry distillation process was performed using detector systems placed at selected positions of the distillation setup inside the glovebox. Monitoring focused mainly on the furnace region, to observe the release of volatile activity, and on the cooling trap region, to follow the arrival of transported ^{211}At . Additional positions were temporarily monitored during setup development to identify possible weak points or undesired activity deposition.

For general activity detection, two 1-inch NaI(Tl) scintillation detectors (Radhound. LabLogic) were used. The detectors were shielded with several layers of 1 mm lead foil and, in selected measurements, equipped with 1 cm diameter circular lead

collimators. They served as sensitive detectors for qualitative monitoring of activity changes during distillation.

To obtain more localized information along the transfer line, a compact PIN-diode-based detector module was additionally employed. The detector concept followed the design and signal processing approach reported by Keller et al. [123], with slight modifications for the present application, including a stacked PIN-diode arrangement to moderately increase the detection probability. The module was positioned directly at relevant sections of the capillary system, particularly near the furnace outlet and cooling trap.

The PIN detector was used exclusively for relative and time-resolved process monitoring and was not calibrated for absolute activity quantification. Detector signals were recorded as count-rate profiles and used to compare detector response at different process positions during dry distillation.

Liquid-liquid extraction

Implementation of solvent extraction

The liquid -liquid extraction method was inspired by Burns et al. [76, 125] with minor modifications. After irradiation, the bismuth target material was scraped off the aluminum backing inside a negative-pressure glove box in order to minimize contamination by bismuth splinters or volatilized ^{211}At . The collected scrapings were packed, transferred to a fume hood, and their activity was measured. The material was then carefully transferred into a 5 mL V-shaped glass vial.

The vial was sealed with a septum-containing lid and connected to a CO_2 -cooled cold trap followed by an activated carbon trap. Subsequently, 1 mL of 10 M HNO_3 was added through the septum. The vial was left to stand for 5–10 min to allow complete dissolution of the bismuth. Any gas formed during dissolution was directed through the trap assembly. Afterwards, 2 mL of 6 M HNO_3 was added to adjust the nitric acid concentration of the solution to approximately 6 M.

Columns containing 40 mg HR-X resin (45 μm particle size) were conditioned with the respective organic extractant and soaked for at least 24 h prior to use. Before sample

loading, the columns were drained to remove excess extractant. The dissolved bismuth solution was then loaded onto the column. Subsequently, the column was washed once with 600 μL of 6 M HNO_3 , twice with 600 μL of 2 M HNO_3 , and twice with 600 μL of H_2O in order to remove residual bismuth and ^{210}Po . After completion of the washing steps, the retained ^{211}At was re-eluted using the respective organic solvent. Unless stated otherwise, the procedure was kept identical for all investigated solvents, with only the organic extractant used for column conditioning and ^{211}At elution being varied.

Recovery values were determined from activity measurements of the initial sample and the collected fractions and/or final eluate. Depending on sample type and activity level, measurements were performed using either a dose calibrator or HPGe γ -spectrometry. Where required, activities were decay-corrected to a common reference time.

For the bismuth carry-over experiments, ^{207}Bi was used as a radiotracer. The ^{207}Bi stock solution was prepared by dissolving previously irradiated bismuth target material after decay of ^{211}At for at least one week. Based on the approximate amount of dissolved target material, the stock solution contained about 500 mg mL^{-1} target-derived bismuth and approximately 10 kBq mL^{-1} ^{207}Bi . An aliquot of 100 μL of this stock solution, corresponding to a nominal bismuth amount of about 50 mg and approximately 1 kBq of ^{207}Bi , was diluted to 1 mL prior to use in the extraction procedure. Bismuth carry-over was quantified as the fraction of ^{207}Bi activity recovered in the respective eluate relative to the initially applied ^{207}Bi activity.

Distribution Coefficient

The distribution coefficient was determined using a small amount of bismuth, manually scraped from the central region of a freshly irradiated bismuth target. Only a few milligrams of material were collected out of the beam center area in order to obtain a high specific ^{211}At activity in a very small bismuth mass, targeting a total activity of approximately 100 $\text{MBq } ^{211}\text{At}$. The collected bismuth sample was dissolved in 50 μL of 10 M HNO_3 .

Approximately 10 MBq of this solution was subsequently diluted to about 10 mL using HNO₃ solutions of different concentrations (6 M, 2 M, and 0.1 M), yielding aqueous stock solutions with an activity concentration of approximately 1 MBq mL⁻¹.

For each distribution experiment, 500 µL of the aqueous stock solution was mixed with 500 µL of the investigated organic solvent in a 1.5 mL V-shaped polymer centrifugation vial. The mixture was thoroughly agitated for 20 min and subsequently centrifuged for 20 min to ensure complete phase separation. It has to be noted, that the organic solvents were not saturated with aqueous phase before, to keep the experimental setup as close as possible to the liquid-liquid extraction setup, defining the process-relevant conditions of this experiment.

After centrifugation, a 250–300 µL aliquot was withdrawn from both phases. The upper phase was sampled first using an analytical pipette. The lower phase was then sampled carefully through the side of the vial using a cannula with an outer diameter of 0.9 mm, taking care not to disturb the upper phase. From each collected aliquot, 100 µL was transferred for activity measurement.

Although back-calculation based on the total activity and an aliquot of the upper phase would have been experimentally simpler, preliminary tests gave less consistent results with this approach. Direct measurement of both phases was therefore used throughout, as it provided more robust K_D values under the investigated conditions. A direct comparison of both methods is presented in the Appendix in Table B-4.

The activity of each sample was quantified using a HIDEX AMG Automatic Gamma Counter (model 425-601, Turku, Finland) and decay-corrected to the start of counting. The distribution coefficient was then calculated according to Eq. 5.19:

$$K_D = \frac{A_{\text{org}}/V_{\text{org}}}{A_{\text{aq}}/V_{\text{aq}}} = \frac{A_{\text{org}} \cdot V_{\text{aq}}}{A_{\text{aq}} \cdot V_{\text{org}}} \quad (5.19)$$

A total of 20 organic solvents were screened for distribution coefficient measurements under otherwise identical conditions, including phase volume, temperature, mixing time, centrifugation time, and aqueous phase composition. The complete list of investigated solvents, including supplier and stated purity, is provided in Appendix B-3 Table B-3.

In addition to the main screening approach based on direct dilution of a ^{211}At stock solution in concentrated nitric acid, a limited set of comparative experiments was performed using an alternative tracer preparation route. For this purpose, ^{211}At was isolated by dry distillation, transferred into chloroform, evaporated to dryness, and subsequently redissolved directly in 6 M, 2 M, or 0.1 M HNO_3 . The resulting aqueous stock solutions were adjusted to approximately 1.5 MBq mL^{-1} and used for selected distribution coefficient measurements under otherwise identical conditions. These experiments were performed for exploratory comparison and were not used as the primary basis for solvent selection.

Alternative extractants

To evaluate potential alternatives to 3-octanone, selected solvents identified in the preceding distribution studies were investigated in the same extraction setup described above. Unless stated otherwise, only the extractant used for column conditioning and ^{211}At re-elution was varied, while the overall loading and washing procedure was kept unchanged. In addition, commercially available tributyl phosphate resin (TBP), zirconium resin (ZR), and DN resins were included as exploratory ready-to-use alternatives and assessed based on ^{211}At recovery, breakthrough, residual column activity, and bismuth carry-over. For selected systems, delayed elution after extended residence time on the column was further examined.

5.2.7. ^{211}At Chemistry and Analysis

Radiolabeling with ^{211}At

To evaluate the applicability of isolated ^{211}At for downstream radiochemistry, labeling studies were performed by synthesis of [^{211}At]4-astato-L-phenylalanine (4-[^{211}At]APA) using different labeling strategies. The investigated approaches comprised (1) direct labeling of 4-stannyl-L-phenylalanine (4-SPA), (2) labeling via a boronic acid derivative [158] and (3) copper-mediated halogenic exchange [159]. For all labeling reactions, the radiochemical conversion (RCC) was determined by high-performance liquid chromatography (HPLC).

HPLC analysis was performed using a MultoKrom 100-3 C18 AQ reversed-phase column, via a solvent system consistent of Solvent A: 90% ultrapure water and 10% HPLC-grade acetonitrile containing $0.3\text{ g L}^{-1}\text{ NH}_4\text{Ac}$, and Solvent B: 100% HPLC-grade acetonitrile. Separations were performed at a constant flow rate of 1.5 mL min^{-1} using a 10 min gradient. The gradient started at 90% A and 10% B and was linearly changed to 10% A and 90% B over 7.0 min. The high-B condition was held until 8.0 min, after which the system was returned to the initial composition of 90% A and 10% B at 8.02 min and re-equilibrated until 10.0 min. Chromatograms were evaluated using ClarityChrom version 8.2 (KNAUER GmbH).

Since astatine has no stable isotopes, peak assignment was supported by comparison with the structurally analogous non-radioactive 4-iodo-L-phenylalanine (4-IPA) as reference. The retention time of 4-IPA was determined by UV-HPLC under identical chromatographic conditions and used to estimate the expected retention time for 4-APA in the corresponding radio-HPLC chromatograms.

Astatination of 4-stannyl-phenylalanine

The radiolabeling of 4-SPA with ^{211}At to produce 4-astato-L-phenylalanine (4-[^{211}At]APA) was performed according to a modified radioiodination approach for 4-iodo-L-phenylalanine described by Israel et al. and Vaidyanathan et al. [160, 161]. The 4-SPA was synthesized in house, dried and stored at $-20\text{ }^{\circ}\text{C}$. Solutions of $0.8\text{ nmol per }10\text{ }\mu\text{L}$ in water were freshly prepared prior to each radiolabeling.

For labeling, 2–20 MBq ^{211}At in 10 μL EtOH (or directly from HCCl_3) was adjusted to pH 1–2 by addition of 10 μL 0.1 M HCl. 10 μL precursor solution was added. The reaction was started by addition of 10 μL chloramine-T solution (0.8 nmol) in methanol. The reaction took place at room temperature for 1 minute.

Astatination of 4-borono-L-phenylalanine

Two different methods were employed for the radiolabeling of 4-borono-L-phenylalanine (4-BPA) both described by Shirakami et al. 2021 [158].

The “NBS-Method” containing N-bromosuccinimide (NBS) as oxidating agent was performed by mixing 100 μL of 1 mg mL^{-1} 4-BPA solution in 7% (w/v) HNaCO_3 with 2–20 MBq (5–60 μL) of ^{211}At in EtOH. Then, 30 μL of 0.4 mg mL^{-1} NBS solution was added. The reaction took place for 30 min at room temperature. Thereafter, 100 μL of 30 mg mL^{-1} ascorbic acid (AA) solution in water was added to the mixture to quench the reaction.

The “KI-Method” applies potassium iodide and proceeds via an inter-halogenic species [158] which further reacts with the aryl boronic acid. For the reaction, 100 μL of 1 mg mL^{-1} 4-BPA solution in 7% (w/v) HNaCO_3 in water was mixed with 2–20 MBq (5–60 μL) of ^{211}At in EtOH. 60 μL KI solution (0.1 M in water) was added. The mixture was allowed to stand for 30 min at room temperature.

Astatination of 4-iodo-L-phenylalanine

For Cu(I)-mediated synthesis of 4- ^{211}At]APA from 4-iodo-L-phenylalanine (4-IPA), 1 mg 4-IPA was added to a 2 mL V-shaped glass vial. A reaction mixture of SnSO_4 (1 mg mL^{-1}), gentisic acid (2.5 mg mL^{-1}) and citric acid (5.0 mg mL^{-1}) in 500 μL H_2O was added to the 4-IPA. Then, 28 μL of CuSO_4 (13 μM) in water was added. 2–20 MBq ^{211}At was diluted in 500 μL MeOH and added to the mixture. The vial was then heated to 120 $^\circ\text{C}$ for 60 min [159].

HPLC Recovery

To investigate whether free inorganic ^{211}At can be reliably quantified by reversed-phase HPLC, recovery studies were performed using representative astatine formulations and different chromatographic conditions. Particular attention was given to non-specific retention of free astatine on the stationary phase, as this may lead to misestimation of radiochemical conversion or radiochemical purity.

Freshly purified and dried ^{211}At , utilizing dry distillation procedure, was reconstituted in three different formulations intended to represent common forms of unreacted astatine encountered in radiolabeling studies: an electrophilic formulation prepared in 1 mg mL^{-1} N-chlorosuccinimide in methanol, a nucleophilic formulation prepared in 100 mg mL^{-1} ascorbic acid in acetonitrile/water, and a native formulation prepared in acetonitrile/water without deliberate redox adjustment [149]. The activity concentration was adjusted to approximately 3 MBq mL^{-1} . Samples were allowed to equilibrate for at least 20 min before analysis. All measurements were performed in triplicate using freshly prepared samples from freshly purified astatine.

Four reversed-phase columns with different stationary phase chemistries were examined: a silica-based C18 column (Phenomenex Luna C18(2); $5\text{ }\mu\text{m}$, $100\text{ }\text{\AA}$, $250 \times 4.6\text{ mm}$ (Phenomenex Ltd. Deutschland, Aschaffenburg, Germany=), a hybrid-silica C18 column (Waters XBridge BEH C18; $5\text{ }\mu\text{m}$, $130\text{ }\text{\AA}$, $250 \times 4.6\text{ mm}$ (Waters GmbH, Eschborn, Germany)), a polymer-based reversed-phase column (Phenomenex PolymerX; $5\text{ }\mu\text{m}$, $100\text{ }\text{\AA}$, $250 \times 4.6\text{ mm}$ (Phenomenex Ltd. Deutschland)), and a monolithic silica-based RP-18 column (Merck Chromolith Performance RP-18 endcapped, $100 \times 4.6\text{ mm}$ (Merck KGaA)). For all solvent systems, the same gradient was applied: 0–1 min 5% B, 1–6 min 5–100% B, and 6–15 min 100% B at a flow rate of 1 mL min^{-1} . Water and acetonitrile were used as base solvents, and selected experiments included modifiers such as TFA, ascorbic acid, triethylammonium acetate, triethylamine, sodium sulfite, and sodium thiosulfate.

Recovery of ^{211}At was determined by two complementary approaches. First, online recovery was measured using post-column injection method [148]. After elution of the sample from the primary injector, an identical aliquot was injected via the second valve directly after the column to provide a reference signal corresponding to the total injected activity. Recovery was calculated from the decay-corrected ratio of the

chromatographic peak area to the post-column peak area. Second, offline recovery was determined by collecting the entire effluent over 12 min and quantifying the activity in a γ counter. For this purpose, measurements were performed both with and without the column in the flow path, and recovery was calculated from the decay-corrected ratio of eluted activities.

Because retained astatine caused carry-over between successive runs, columns were washed after analysis using a reducing eluent. Prolonged flushing with at least five column volumes of 0.5% sodium thiosulfate solution was found to be sufficient to remove residual activity quantitatively inspired by [152].

TLC Analysis

To evaluate whether thin-layer chromatography (TLC) is suitable for analyzing chemically different forms of processed ^{211}At , several silica-based TLC plates from different manufacturers and production batches were comparatively screened. Since previous observations indicated that astatine shows pronounced material-dependent interactions during chromatographic analysis, the influence of TLC substrate and plate composition was investigated under otherwise identical development conditions.

^{211}At was freshly isolated by dry distillation, collected in CHCl_3 , and dried under a gentle argon stream. The activity was subsequently reconstituted under three different solution conditions intended to generate operationally distinct astatine species: (i) oxidizing conditions using 1 mg mL^{-1} N-chlorosuccinimide (NCS) in methanol, (ii) reducing conditions using 100 mg mL^{-1} ascorbic acid in $\text{MeCN}/\text{H}_2\text{O}$, and (iii) untreated conditions in $\text{MeCN}/\text{H}_2\text{O}$ without additional redox reagent, referred to here as native ^{211}At .

The activity concentration was adjusted to 3 MBq mL^{-1} . After preparation, solutions were allowed to equilibrate for at least 20 min under continuous agitation before application.

For each condition, $1 \mu\text{L}$ aliquots were spotted on six different TLC plates. As an internal qualitative reference for possible activity loss during development, an

additional 1 μL aliquot of the same sample solution was applied to each plate after chromatographic development. Plates originating from the same astatine solution were developed simultaneously in a shared chamber in order to minimize chamber-to-chamber variation. All experiments were performed in duplicate.

Chromatographic development was carried out using a mobile phase adapted from Palagyi and Zaduban [170], consisting of methanol, 25% NH_4OH , water, and 10% acetic acid in a volume ratio of 9:1:1:0.5. This eluent was selected because it has previously been reported to separate different iodine species and was therefore explored as a potentially suitable system for astatine screening. After development, TLC plates were dried and analyzed by phosphor imaging. The qualitative distribution of radioactivity on the plate surface was compared between TLC types, while semi-quantitative recovery was estimated by relating the total signal remaining on the developed TLC plate to the signal intensity of the post-development reference spot. The TLC plates investigated in this study included different silica gel 60 stationary phases, suppliers, and batches, including both glass-backed and polymer-backed materials. Unless stated otherwise, plates contained a fluorescent UV_{254} indicator.

5.3. Evaluation of experimental data

All results reported in this study are given as arithmetic mean $\pm$ standard deviation, with n referring to the number of independent experiments, unless stated otherwise.

As experiments with ^{211}At are rarely trivial to repeat, some datasets are based on only a small number of repetitions. These results are therefore mainly intended to show general trends and reproducibility. Data from single experiments are given as individual values.

5.4. Determination of radioactivity

Due to the diverse nature of the investigations conducted in this study, different qualitative and quantitative methods had to be applied.

For the production and processing of ^{211}At , γ -ray spectroscopy was applied using high purity germanium detectors (HPGe) for proper quantification. A more rapid, less accurate quantification was done using a dose calibrator. For low activity studies containing large number of samples, a low- γ counter was applied.

The quantification of ^{72}As as well as its by-products for reaction cross-section analysis was quantified using HPGe, too. For the investigation of the decay properties of ^{72}As , beside HPGe for annihilation studies, the emission of β -particles was directly measured using a beta-counter. The analysis of X-ray emission was performed using a low energy photon spectrometer (LEPS)

5.4.1. HPGe γ -spectrometry

High-resolution γ -ray spectrometry was performed using a high-purity germanium (HPGe) detector (Ortec) operated with GammaVision for acquisition and analysis. Energy ranges across ~35 keV–2000 keV, enabling reliable nuclide identification and activity quantification. The detector was cooled using liquid nitrogen (LN₂) 77 K and housed in a graded shield composited of a 5 cm thick lead shielding layered by a 2 mm copper frame and a 4 mm polymer sheet to suppress laboratory background and decrease the potential for Bremsstrahlung.

Energy and absolute peak efficiency calibrations were established for the measurement geometry using certified reference sources: ¹⁵²Eu, ²²⁶Ra, ¹³⁷Cs, ⁵⁷Co, ⁶⁰Co, ²⁴¹Am and ¹³³Ba purchased from (Eckert & Ziegler) with activities traceable to national standards (PTB(Physikalisch-Technische Bundesanstalt), Germany). Energy calibration used ²⁴¹Am, ¹³³Ba ⁶⁰Co & ¹³⁷Cs sources employing prominent lines 59.5, 661.7, 1173.2 and 1332.5 keV to fit a linear channel-to-energy relation. Efficiency $\varepsilon(E)$ was derived from net peak counts N_P , counting time t_m , the death time correction C_{tot} , emission probability I_γ , and decay-corrected activity $A(t) = A_0 e^{-\lambda(t-t_0)}$:

$$\varepsilon(E) = \frac{N_P}{t_m A(t) I_\gamma C_{tot}} \quad (5.20)$$

The various energy dependent efficiencies were fitted polynomial, employing the software internal calibration tool.

The total activity A was calculated using HPGe γ -spectrometry according to Eq. (5.21):

$$A = \frac{N_P}{\varepsilon(E) T_L I_\gamma} \quad (5.21)$$

Facilitating the γ emission probabilities I_γ provided by IAEA [109], the live time T_L containing a dead time correction and the detector efficiency $\varepsilon(E)$. To correct the decay during measurement, the integrated, corrected peak counts C_P recorded over a measurement time t_m were corrected using the decay law to obtain the activity A_0 at the start of counting.

$$C_P = \varepsilon(E) I_\gamma \int_0^{t_m} A_0 e^{-\lambda t} dt = \varepsilon I_\gamma \frac{A_0}{\lambda} (1 - e^{-\lambda t_m}) \quad (5.22)$$

$$A_0 = \frac{\lambda C}{\varepsilon(E)I_\gamma(1-e^{-\lambda t_m})} \quad (5.23)$$

Shielded HPGe geometries for ^{211}At quantification

For ^{211}At quantification, additional shielded HPGe measurement geometries were established to reduce the contribution of intense low-energy X-rays and to enable measurement of high-activity samples. External lead absorbers of 1 mm or 5 mm thickness were placed between sample and detector. In the 1 mm configuration, the absorber was mounted between two 5 mm acrylic glass plates for foil stability and reproducible positioning. Depending on sample activity, different source-to-detector distances were applied.

As absorber thickness and detector distance affected the full-energy peak efficiency, separate efficiency calibrations were established for each shielding-distance configuration. Calibration was performed analogously to the general HPGe procedure described above, using identical absorber arrangement and source positioning as later applied for sample measurements.

Quantification of ^{211}At was primarily based on the 687.0 keV γ -line. Shielded detector geometries were used preferentially for freshly irradiated targets and high-activity process samples.

Annihilation measurement:

Positron emission from ^{72}As was quantified indirectly via measurement of the 511 keV annihilation radiation using HPGe γ -ray spectrometry. Positron annihilation ideally produces two 511 keV γ -quanta emitted in opposite directions (180°), allowing coincidence-based detection. In contrast to a conventional nuclear photopeak, the 511 keV annihilation line however is intrinsically broadened due to the non-zero momentum of the electron-positron pair during annihilation, which causes Doppler shifts of the emitted photons [171]. As a result, automated peak-fitting procedures may yield unsatisfactory results, and the peak area was therefore evaluated manually using predefined integration limits [36, 172, 173].

For the measurements, each sample was placed in a copper chamber (annihilation chamber) consisting of two copper disks, one containing a 1 mm deep groove of 13 mm diameter perfectly accommodating the sample. A total chamber thickness of 5 mm was selected to ensure complete stopping and annihilation of the emitted positrons ($\bar{E}_{\beta^+} \cong 1.1$ MeV) within a well-defined and reproducible geometry close to the sample position. This minimizes geometry-dependent variations in the detection efficiency of the 511 keV annihilation radiation and allows reliable correction for attenuation related effects. Detector efficiency was corrected for the γ -attenuation caused by the copper chamber.

To obtain the net annihilation count rate, the natural background in the region of the 511 keV peak was subtracted. Additional corrections were applied for in-flight annihilation, attenuation effects of the copper chamber, and minor contributions to the 511 keV signal arising from pair production and from co-produced positron-emitting radionuclides. Contributions from ^{71}As , ^{74}As , and ^{69}Ge were estimated on the basis of irradiation conditions, isotopic composition of the enriched target material, and nuclear-model calculations. The corrected annihilation count rates were subsequently normalized and used for further analysis.

X-ray analysis:

To quantify the electron-capture (EC) branch of ^{72}As , the three selected samples described above were analyzed by X-ray spectroscopy. Measurements were performed with a well-shielded LEPS detector equipped with a 300 μm Be window (ORTEC), optimized for low-energy photon detection. The detector resolution was 330 eV at the 5.9 keV X-ray line and 540 eV at the 122 keV γ -line of ^{57}Co (FWHM (full width at half maximum)). Detector efficiency in the low-energy region was established using calibrated ^{55}Fe (5.89 keV) and $^{93\text{m}}\text{Nb}$ (16.58 and 18.70 keV) standards, and the efficiency at the relevant germanium X-ray energies was obtained by interpolation. In addition, the efficiency curve across the wider energy range of interest was checked using ^{57}Co , ^{210}Pb , ^{133}Ba , and ^{241}Am point sources. All spectra were acquired at a source-to-detector distance of 10 cm. During counting, the 10 μm Al-covered side of the germanium sediment was always oriented toward the detector in order to minimize

attenuation of the low-energy X-rays in the cover material. Absorption losses in the sample and in the Al cover were estimated to be approximately 0.5% and 0.3%, respectively.

The net peak areas of the K_α and K_β X-ray lines of the daughter nuclide ^{72}Ge were determined separately after background subtraction. Since the detector efficiency differed slightly at the respective X-ray energies, both contributions were corrected individually before summation. The corrected X-ray rate was then converted to the electron capture related activity by accounting for the fluorescence yield of germanium, $\omega_K = 0.54$, and the probability of EC from the K-shell, $P_K = 0.89$ [25, 174]. In this way, the EC contribution was derived directly from the measured X-ray signal rather than from evaluated X-ray branching data. The resulting EC-related activity was subsequently compared with the absolute ^{72}As activity obtained independently by HPGe γ -ray spectrometry using the 630 keV and 834 keV lines.

5.4.2. Dose calibrator

For activity measurements a Comcer radionuclide dose calibrator (“curimeter”; well-type ionization chamber) was used. Samples in sealed vials were lowered reproducibly to a fixed depth in the well using the supplied dipper. For each nuclide a setting containing a specific calibration factor was selected. The calibration factor was determined by fractionating a HPGe measurement of a radio-nuclidic pure sample to its dose calibration measurement. Background activity was measured with an empty container and subtracted.

5.4.3. Beta-counter

The emission of β^+ -particles originating from ^{72}As was measured using a multi-channel anticoincidence gas-flow proportional counter Berthold, Multi-Logger LB 5310. As counting gas, P-10 gas was employed, a basic counting gas which consists of 90% Argon and 10% Methane. Due to the anticoincidence array¹⁰ of the detector, a large fraction of background noise is filtered reducing the background activity to ≈ 5 counts per minute (cpm). The background radiation was subtracted manually from the measured activities. An illustration of the 2π geometry present in this type of proportional counter is depicted in Figure 76.

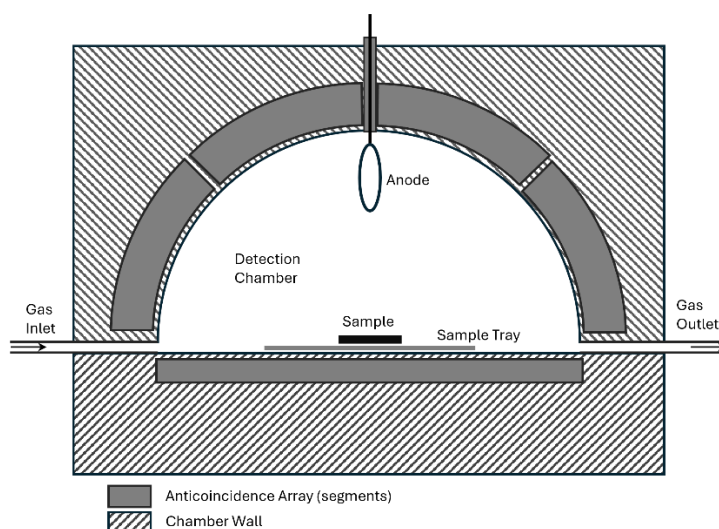


Figure 76: Schematic illustration of the (2π -) geometry of beta-counting setup.

The 2π arrangement of the gas-flow proportional counter inherently comes with a high maximum efficiency of $\approx 50\%$ where all radiation moving into the chamber direction is eventually captured. Until that point an energy calibration must be performed similar to HPGe. In Figure 77, the experimentally determined efficiency of the three measuring chambers used (Chamber 5). The counting efficiency of the proportional counter was determined using calibrated β -emitting standards, namely ^{14}C , ^{36}Cl , $^{90}\text{Sr}/^{90}\text{Y}$, and ^{99}Tc (NEN, USA). For the $^{90}\text{Sr}/^{90}\text{Y}$ standard, secular equilibrium between parent and

¹⁰ An anticoincidence array consists of one or more guard detectors assembled around the detector chamber. Any signal recognized in coincidence of those guard detectors with the sample -detector, is filtered out.

daughter nuclides was assumed, and the total activity was distributed between both emitters according to their respective β -particle energies. The resulting efficiency curve was used to interpolate detector efficiency for the mean positron energy of ^{72}As . For the three sample positions used in the detector, efficiencies of 0.49, 0.48, and 0.48 were obtained for the mean positron energy of 1170 keV.

Each counting position adjacent to the sample was intentionally left empty in order to minimize mutual interference between neighboring sample positions. Counting times were chosen such that at least 20,000 counts were accumulated for each measurement, corresponding to a statistical uncertainty below 1%.

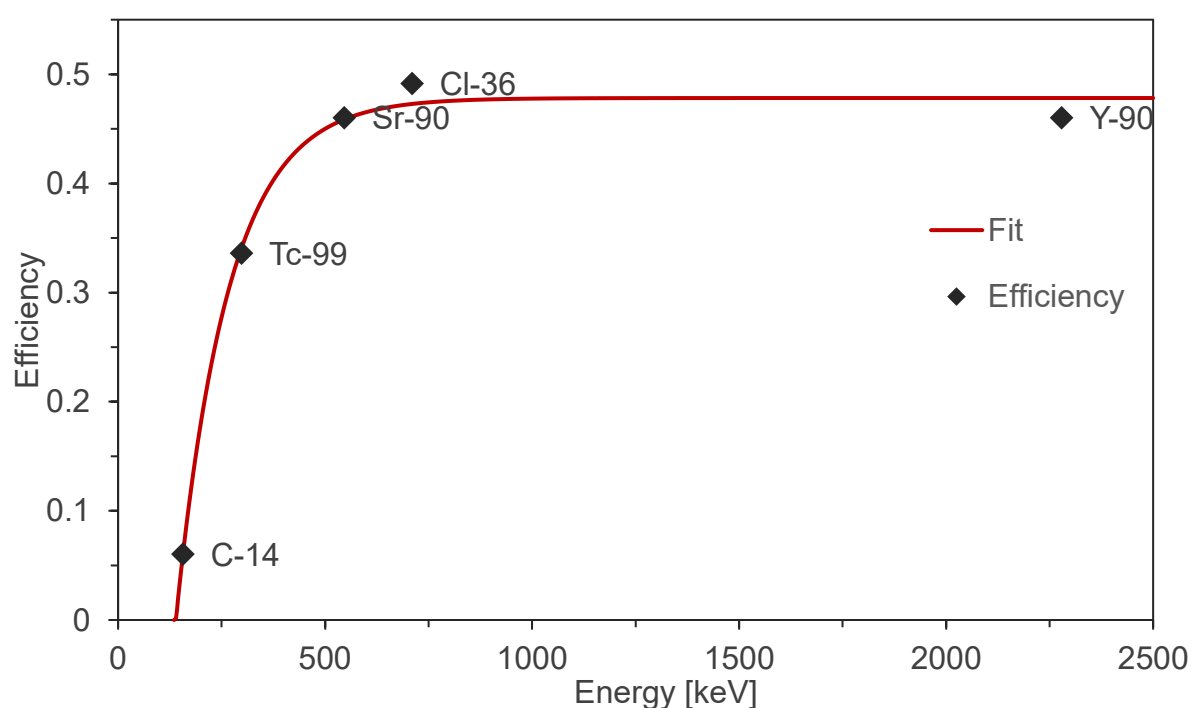


Figure 77: Calibration curve for the "chamber 5" slot of the Berthold multichannel beta counter.

5.4.4. Low γ counter

Low activity γ -spectrometry was performed using a Hidex low-background γ counter (Hidex AMG; Turku, Finland) equipped with a 3" NaI(Tl) detector and 4π Pb shielding with an inner Cu liner. The system includes an integrated multichannel analyzer (MCA) covering photon energies up to ≈ 4 MeV. Samples were measured in scintillation vials ($\varnothing$ 13 mm or $\varnothing$ 28 mm; maximum height 95 mm). The counting time per sample was 60 s.

Energy calibration was performed using ^{137}Cs ($E_\gamma = 661.7$ keV) source; the full-energy peak efficiency was determined with multi-gamma standards (^{57}Co : 122 keV; ^{137}Cs : 662 keV; ^{60}Co : 1173/1332 keV) certified by PTB, Germany. An automated background correction is included in every data acquisition.

5.5. Calculation & Simulation

5.5.1. Normalization of count rates and estimation of uncertainties

For each measurement, the observed net count rate of ^{72}As was first corrected for the measurement time and thereafter decay-corrected to EOB. The activity was then corrected for detector efficiency and for all relevant method-specific effects. Depending on the counting method, these included absorption and self-absorption in the sample and cover materials, as well as corrections for coincidence losses, pile-up, and, in the case of annihilation counting, a correction for in-flight annihilation of positrons was estimated using the approach of Dolley et al. [37], based on the positron energy distribution of the radionuclide and the corresponding annihilation probability in copper as a function of positron energy. For the present counting geometry, this resulted in a correction factor of 1.047 (4.7%).

The normalized count rate was then converted into an absolute disintegration rate using the emission intensity of the counted radiation. In the present context, this term refers to the evaluated emission probability of the radiation used for quantification, i.e. the number of photons, positrons or characteristic X-rays emitted per 100 decays of the parent nuclide, and not to the experimentally observed peak area itself [175]. In simplified form, the activity A can therefore be expressed as

$$A = \frac{N}{\varepsilon f_{\text{corr}} I_{\text{rad}}}, \quad (5.24)$$

where N is the net count rate, ε the detector efficiency, f_{corr} the product of all relevant correction factors, and I_{rad} the emission intensity of the counted radiation.

The combined uncertainty was estimated from the individual uncertainty contributions by standard error propagation [176, 177]. In relative form, this can be written as

$$u_{\text{rel}}^2(A) = u_{\text{rel}}^2(N) + u_{\text{rel}}^2(\varepsilon) + u_{\text{rel}}^2(f_{\text{corr}}) + u_{\text{rel}}^2(I_{\text{rad}}). \quad (5.25)$$

Here, the uncertainty of the net count rate mainly reflects peak-area evaluation and counting statistics, whereas detector efficiency, absorption-related corrections and adopted decay-data parameters contribute primarily as systematic input quantities [176]. In the case of X-ray counting, normalization may additionally include atomic parameters such as the fluorescence yield and shell-dependent vacancy probabilities.

Accordingly, the uncertainty assigned to the emission intensity term may represent the combined uncertainty of several evaluated quantities rather than that of a single tabulated line intensity.

For the final cross-section values, additional uncertainty contributions from beam current determination, target areal density, decay data, and time corrections were included. The combined standard uncertainty u_c was obtained by quadratic summation of the individual independent components according to the law of propagation of uncertainty [176, 178]:

$$u_c = \sqrt{\sum_i u_i^2}. \quad (5.26)$$

This treatment corresponds to the standard approach for independent uncertainty components in activation and nuclear analytical measurements [177]. Possible correlations between selected input quantities, such as common detector-efficiency calibrations, monitor-reaction data, or shared decay-data inputs, were not treated explicitly in this simplified approach. A full treatment would require covariance terms, as discussed by Otuka et al. [52].

5.5.2. SRIM

The stopping and range of ions in matter (SRIM) code [168] was used to simulate the interaction of energetic α particle (He^{2+} -ions) with target material bismuth. SRIM uses Monte-Carlo implementation of the binary collision approximation, which describes the path of the incoming ions as a series of individual collisions with atoms in the target material. In this way, both nuclear and electronic stopping can be considered, allowing estimation of the particle range, energy loss, and broadening of the ion distribution within the target.

Simulations were carried out for He^{2+} ions in the energy range from 30 MeV to 0 MeV, corresponding to the conditions relevant for this work. The target material was treated as a homogeneous amorphous bismuth layer with a density of $\rho = 9.8 \text{ g cm}^{-3}$. At least 10^4 ions were simulated in each run. Calculations were performed using the “Detailed

calculation with full damage cascade” option in SRIM to include not only the primary ion trajectories, but also secondary atomic displacements. The main outputs considered were the depth profiles and range distributions.

5.5.3. Stack

The incident particle energies at each foil position were determined using the in-house STACK program developed at Forschungszentrum Jülich. STACK is implemented as an Excel workbook with VBA (Virtual Basic for Application) macros and is routinely used in stacked-foil activation experiments to propagate the beam energy through complex multilayer targets and degraders [22, 23, 164, 165]. Starting from the nominal primary energy E_0 (exiting the cyclotron), the code tracks the energy loss sequentially through the stack using the areal density of each layer (ρx), together with tabulated or parameterized stopping power data. The calculation follows an iterative Bethe-type [179] treatment of electronic stopping and employs a range–energy formalism [169] to ensure stable conversion between residual range and particle energy across different materials.

For each foil i , STACK provides the entrance and exit energies $E_{\text{in},i}$ and $E_{\text{out},i}$, as well as an effective mean energy $E_{\text{eff},i}$ (for “thin” samples typically approximated by the mid-point energy unless a different weighting is specified)¹¹. The corresponding energy interval $\Delta E_i = E_{\text{in},i} - E_{\text{out},i}$ is used to assign the measured activities to well-defined energy bins. In addition, the tool supports sensitivity checks against uncertainties in foil thickness, density, and initial energy, enabling a consistent estimate of the systematic contribution to the energy scale. The resulting energy profile served as the basis for the cross-section evaluation and for the consistency assessment with monitor reactions.

The STACK files created for each target stack are presented in the Appendix in Figure A-1-Figure A-7.

¹¹ For targets with “complex” chemical structures like oxides etc. a sample layer system is created, layering the sample according to its composition and molar ratios (e.g.: $\text{Al}_2\text{O}_3 \square [\text{O}/\text{Al}/\text{O}/\text{Al}/\text{O}]$)

5.5.4. TALYS-2.0

Nuclear reaction model calculations were performed using TALYS-2.0 in order to compare the experimentally determined excitation functions with model predictions and to assess the sensitivity of the calculated cross-sections to selected model ingredients. The calculations covered the p - and α -induced reactions relevant to this work. Particular emphasis was placed on the $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction, for which the default calculations showed a pronounced discrepancy with the experimental data. In contrast, the benchmark systems $^{72}\text{Ge}(p,x)^{71,72}\text{As}$ and $^{69}\text{Ga}(\alpha,x)^{72}\text{As}$ were described reasonably well by TALYS/TENDL (TALYS Evaluated Nuclear Data Library) and were therefore used mainly as validation cases.

All calculations were carried out with text-based TALYS input files in a Linux/WSL environment. For each run, the projectile, target nuclide, and incident energy grid were defined explicitly. Excitation functions $\sigma(E)$, with E denoting the incident projectile energy and σ the reaction cross-section, were calculated on equidistant energy grids. For the $^{75}\text{As}(p,4n)^{72}\text{Se}$ case, the final calculations were performed from 30 to 70 MeV with $\Delta E = 0.1$ MeV in order to describe the threshold region and peak shape with sufficient resolution. Channel-resolved and residual-production cross-sections were written separately using the TALYS-2.0 options “*channels y*” and “*fileresidual y*”. For direct comparison with experimental data, the exclusive (p,4n) channel was used.

The modeling approach was intentionally kept limited and transparent. Rather than performing an unrestricted fit, a controlled sensitivity analysis was carried out for the $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction. Based on the first comparison runs, three parameter families were examined in more detail: the proton optical model potential, the level-density description, and the pre-equilibrium treatment. These quantities were varied stepwise to identify which model components have the strongest influence on the calculated excitation function. The quality of the description was assessed not only visually but also using characteristic observables such as the effective threshold energy E_{thr} , the maximum cross-section σ_{max} , the energy of the maximum E_{max} , and the cross-section at 70 MeV, $\sigma(70 \text{ MeV})$. Since the Ge and Ga benchmark systems were already reproduced reasonably well by the default calculations, no extensive local optimization was carried out for these reactions. Instead, they served as internal reference cases

showing that the disagreement observed for $^{75}\text{As}(p,4n)^{72}\text{Se}$ reflects a channel-specific modeling limitation rather than a general failure of TALYS-2.0 [180, 181]. A more detailed explanation of the varied model parameter of TALYS-2.0 is presented in Appendix A-4.

5.6. Usage of AI-Based Tools

For the preparation of this work, AI-based tools, including DeepL, ChatGPT (OpenAI), Gemini (Google) and Microsoft Word spelling and grammar checking features were used as auxiliary tools. These tools were used throughout selected parts of the manuscript for literature research support, image editing, translation support, and rephrasing and language editing for the improvement of clarity and readability of author-written text.

AI-based tools were not used as primary sources of scientific information. All statements obtained by those tools were independently verified and finalized by the author.

*“For a successful technology, reality must take precedence over public relations,
for nature cannot be fooled.”*

—Richard P. Feynman¹²

¹² Richard P. Feynman, *Personal Observations on Reliability of Shuttle*, Appendix F to the Rogers Commission Report, 1986.

References

1. Röntgen WC (1895) Ueber eine neue Art von Strahlen. Sitzungsberichte Phys-Med Ges Zu Würzburg 29:132–141
2. Curie P, Curie M (1900) Les nouvelles substances radioactives et les rayons qu'elles émettent. Gauthier Villars, Paris, pp 79–114
3. Rutherford E (1899) Uranium Radiation and the Electrical Conduction Produced by It. Philos Mag 47:109–163
4. Rutherford E (1911) The Scattering of α and β Particles by Matter and the Structure of the Atom. Philos Mag 21:669–688
5. Hevesy G de, Paneth F (1913) Die Löslichkeit des Bleisulfids und Bleichromats. Z Für Anorg Chem 82:323–328. <https://doi.org/10.1002/zaac.19130820125>
6. Baum RP, Kulkarni HR (2012) THERANOSTICS: From Molecular Imaging Using Ga-68 Labeled Tracers and PET/CT to Personalized Radionuclide Therapy - The Bad Berka Experience. Theranostics 2:437–447. <https://doi.org/10.7150/thno.3645>
7. Murud KM, Larsen RH, Hoff P, Zalutsky MR (1999) Synthesis, purification, and in vitro stability of ^{211}At - and ^{125}I -labeled amidobisphosphonates. Nucl Med Biol 26:397–403. [https://doi.org/10.1016/S0969-8051\(98\)00119-X](https://doi.org/10.1016/S0969-8051(98)00119-X)
8. Qaim SM, Scholten B, Spahn I, Neumaier B (2019) Positron-emitting radionuclides for applications, with special emphasis on their production methodologies for medical use. Radiochim Acta 107:1011–1026. <https://doi.org/10.1515/ract-2019-3154>
9. Qaim SM (2019) Medical Radionuclide Production: Science and Technology. De Gruyter, Berlin/Boston
10. Müller C, Van Der Meulen NP, Benešová M, Schibli R (2017) Therapeutic Radiometals Beyond ^{177}Lu and ^{90}Y : Production and Application of Promising α -Particle, β^- -Particle, and Auger Electron Emitters. J Nucl Med 58:91S–96S. <https://doi.org/10.2967/jnumed.116.186825>
11. Qaim SM, Coenen HH (2005) Produktion pharmazeutisch relevanter Radionuklide: An Reaktoren und Zyklotronen. Pharm Unserer Zeit 34:460–466. <https://doi.org/10.1002/pauz.200500143>
12. International Atomic Energy Agency (2021) Alternative Radionuclide Production with a Cyclotron. International Atomic Energy Agency, Vienna
13. Qaim SM, Scholten B, Neumaier B (2018) New developments in the production of theranostic pairs of radionuclides. J Radioanal Nucl Chem 318:1493–1509. <https://doi.org/10.1007/s10967-018-6238-x>
14. Qaim SM (2011) Development of novel positron emitters for medical applications: nuclear and radiochemical aspects. Radiochim Acta 99:611–625. <https://doi.org/10.1524/ract.2011.1870>
15. Lewis JS, Windhorst AD, Zeglis BM (2019) Radiopharmaceutical chemistry, 1st ed. Springer, Cham
16. International Atomic Energy Agency (2018) Quality Control in the Production of Radiopharmaceuticals. International Atomic Energy Agency, Vienna
17. Kim Y-S, Brechbiel MW (2012) An overview of targeted alpha therapy. Tumor Biol 33:573–590. <https://doi.org/10.1007/s13277-011-0286-y>

References

18. Kassis AI (2004) The Amazing World of Auger Electrons. *Int J Radiat Biol* 80:789–803. <https://doi.org/10.1080/09553000400017663>
19. Eychenne R, Chérel M, Haddad F, et al (2021) Overview of the Most Promising Radionuclides for Targeted Alpha Therapy: The “Hopeful Eight.” *Pharmaceutics* 13:906. <https://doi.org/10.3390/pharmaceutics13060906>
20. Maingueneau C, Berdal M, Eychenne R, et al (2022) ²¹¹At and ¹²⁵I-Labeling of (Hetero)Aryliodonium Ylides: Astatine Wins Again. *Chem – Eur J* 28:e202104169. <https://doi.org/10.1002/chem.202104169>
21. Sanders VA, Cutler CS (2021) Radioarsenic: A promising theragnostic candidate for nuclear medicine. *Nucl Med Biol* 92:184–201. <https://doi.org/10.1016/j.nucmedbio.2020.03.004>
22. Hussain M, Mues genannt Koers L, Spahn I, et al (2024) Excitation functions of ⁷²Ge(p,xn)^{72,71}As reactions from threshold up to 45 MeV for production of the non-standard positron emitter ⁷²As. *Sci Rep* 14:16724. <https://doi.org/10.1038/s41598-024-67319-9>
23. Hussain M, Mues genannt Koers L, Spahn I, et al (2025) Positron emission intensity in the decay of ⁷²As for use in PET studies. *Radiochim Acta* 113:601–609. <https://doi.org/10.1515/ract-2025-0005>
24. Feng Y, Phipps MD, Phelps TE, et al (2019) Evaluation of ⁷²Se/⁷²As generator and production of ⁷²Se for supplying ⁷²As as a potential PET imaging radionuclide. *Appl Radiat Isot* 143:113–122. <https://doi.org/10.1016/j.apradiso.2018.10.026>
25. Abriola D, Sonzogni AA (2010) Nuclear Data Sheets for A = 72. *Nucl Data Sheets* 111:1–140. <https://doi.org/10.1016/j.nds.2009.12.001>
26. Feng Y, Zalutsky MR (2021) Production, purification and availability of ²¹¹At: Near term steps towards global access. *Nucl Med Biol* 100–101:12–23. <https://doi.org/10.1016/j.nucmedbio.2021.05.007>
27. Guérard F, Gestin J-F, Brechbiel MW (2013) Production of [²¹¹At]-Astatinated Radiopharmaceuticals and Applications in Targeted α -Particle Therapy. *Cancer Biother Radiopharm* 28:1–20. <https://doi.org/10.1089/cbr.2012.1292>
28. Albertsson P, Bäck T, Bergmark K, et al (2023) Astatine-211 based radionuclide therapy: Current clinical trial landscape. *Front Med* 9:1076210. <https://doi.org/10.3389/fmed.2022.1076210>
29. Lindegren S, Albertsson P, Bäck T, et al (2020) Realizing Clinical Trials with Astatine-211: The Chemistry Infrastructure. *Cancer Biother Radiopharm* 35:425–436. <https://doi.org/10.1089/cbr.2019.3055>
30. Naka S, Ooe K, Shirakami Y, et al (2024) Production of [²¹¹At]NaAt solution under GMP compliance for investigator-initiated clinical trial. *EJNMMI Radiopharm Chem* 9:29. <https://doi.org/10.1186/s41181-024-00257-z>
31. Guérard F, Maingueneau C, Liu L, et al (2021) Advances in the Chemistry of Astatine and Implications for the Development of Radiopharmaceuticals. *Acc Chem Res* 54:3264–3275. <https://doi.org/10.1021/acs.accounts.1c00327>
32. Gao J, Li M, Yin J, et al (2024) The Different Strategies for the Radiolabeling of [²¹¹At]-Astatinated Radiopharmaceuticals. *Pharmaceutics* 16:738. <https://doi.org/10.3390/pharmaceutics16060738>
33. Lambrecht RM, Mirzadeh S (1985) Cyclotron isotopes and radiopharmaceuticals—XXXV astatine-211. *Int J Appl Radiat Isot* 36:443–450. [https://doi.org/10.1016/0020-708X\(85\)90207-8](https://doi.org/10.1016/0020-708X(85)90207-8)

References

34. Zalutsky MR, Pruszyński M (2011) Astatine-211: Production and Availability. *Curr Radiopharm* 4:177–185. <https://doi.org/10.2174/1874471011104030177>
35. Gagnon K, Risler R, Pal S, et al (2012) Design and evaluation of an external high-current target for production of ²¹¹At. *J Label Compd Radiopharm* 55:436–440. <https://doi.org/10.1002/jlcr.2968>
36. Qaim SM, Bisinger T, Hilgers K, et al (2007) Positron emission intensities in the decay of ⁶⁴Cu, ⁷⁶Br and ¹²⁴I. *Radiochim Acta* 95:67–73. <https://doi.org/10.1524/ract.2007.95.2.67>
37. Dolley SG, Steyn GF, Van Rooyen TJ, et al (2017) Concurrent spectrometry of annihilation radiation and characteristic gamma-rays for activity assessment of selected positron emitters. *Appl Radiat Isot* 129:76–86. <https://doi.org/10.1016/j.apradiso.2017.07.057>
38. Hermanne A, Ignatyuk AV, Capote R, et al (2018) Reference Cross Sections for Charged-particle Monitor Reactions. *Nucl Data Sheets* 148:338–382. <https://doi.org/10.1016/j.nds.2018.02.009>
39. Rahman AKMR, Amin MdN (2023) Production routes analysis of PET agent ⁷²As from alpha and proton induced reaction using different level density models. *AIP Adv* 13:095121. <https://doi.org/10.1063/5.0169903>
40. Henriksen G, Messelt S, Olsen E, Larsen RH (2001) Optimisation of cyclotron production parameters for the ²⁰⁹Bi(α ,2n)²¹¹At reaction related to biomedical use of ²¹¹At. *Appl Radiat Isot* 54:839–844. [https://doi.org/10.1016/S0969-8043\(00\)00346-8](https://doi.org/10.1016/S0969-8043(00)00346-8)
41. Schultz MK, Hammond M, Cessna JT, et al (2006) Assessing the ²¹⁰At impurity in the production of ²¹¹At for radiotherapy by ²¹⁰Po analysis via isotope dilution alpha spectrometry. *Appl Radiat Isot* 64:1365–1369. <https://doi.org/10.1016/j.apradiso.2006.02.046>
42. Ramler WJ, Wing J, Henderson DJ, Huizenga JR (1959) Excitation Functions of Bismuth and Lead. *Phys Rev* 114:154–163. <https://doi.org/10.1103/PhysRev.114.154>
43. Deconninck G, Longrée M (1974) Fonctions d'excitation des réactions induites par particules alpha sur ²⁰⁹Bi entre 40 et 100 MeV. *Ann Société Sci Brux* 88:341
44. Hermanne A, Tárkányi F, Takács S, et al (2005) Experimental study of the cross-sections of alpha-particle induced reactions on ²⁰⁹Bi. *Appl Radiat Isot* 63:1–9. <https://doi.org/10.1016/j.apradiso.2005.01.015>
45. Patel HB, Shah DJ, Singh NL (1999) Study of (alpha,xn) reactions on ¹⁶⁹Tm, ¹⁸¹Ta and ²⁰⁹Bi up to 70 MeV. *Il Nuovo Cimento A* 112:1439–1452
46. Rizvi IA, Bhardwaj MK, Ansari MA, Chaubey AK (1990) Non-equilibrium reaction mechanism in alpha-particle induced excitation function for ²⁰⁹Bi up to 60 MeV. *Int J Rad Appl Instrum [A]* 41:215–219. [https://doi.org/10.1016/0883-2889\(90\)90112-T](https://doi.org/10.1016/0883-2889(90)90112-T)
47. Stickler JD, Hofstetter KJ (1974) Comparison of ³He-, ⁴He-, and ¹²C-induced nuclear reactions in heavy-mass targets at medium excitation energies. I. Experimental cross sections. *Phys Rev C* 9:1064–1071. <https://doi.org/10.1103/PhysRevC.9.1064>
48. Singh NL, Mukherjee S, Somayajulu DRS (1994) Non-equilibrium analysis of (alpha,xn) reactions on heavy nuclei. *Il Nuovo Cimento A* 107:1635–1645. <https://doi.org/10.1007/BF02780697>
49. Koning AJ, Rochman D (2025) TENDL-2025: TALYS-based Evaluated Nuclear Data Library. In: TENDL-2025. https://tendl.imperial.ac.uk/tendl_2025/tendl2025.html. Accessed 15 May 2026

References

50. Uddin MdS, Chakraborty AK, Spellerberg S, et al (2017) Excitation functions of proton induced nuclear reactions on natFe up to 16 MeV, with emphasis on radiochemical determination of low cross sections. *Radiochim Acta* 105:985–992. <https://doi.org/10.1515/ract-2017-2818>
51. Uddin MS, Scholten B, Basunia MS, et al (2020) Accurate determination of production data of the non-standard positron emitter ⁸⁶Y via the ⁸⁶Sr(p,n)-reaction. *Radiochim Acta* 108:747–756. <https://doi.org/10.1515/ract-2020-0021>
52. Otuka N, Lalremruata B, Khandaker MU, et al (2017) Uncertainty propagation in activation cross section measurements. *Radiat Phys Chem* 140:502–510. <https://doi.org/10.1016/j.radphyschem.2017.01.013>
53. Otuka N, Takács S (2015) Definitions of radioisotope thick target yields. *Radiochim Acta* 103:1–6. <https://doi.org/10.1515/ract-2013-2234>
54. Bird RB, Stewart WE, Lightfoot EN (2017) *Transport Phenomena*, 3rd ed. John Wiley & Sons, Hoboken, NJ
55. Bergman TL, Lavine AS, Incropera FP, DeWitt DP (2017) *Fundamentals of Heat and Mass Transfer*, 8th ed. John Wiley & Sons, Hoboken, NJ
56. International Atomic Energy Agency (2008) *Cyclotron Produced Radionuclides: Principles and Practice*. International Atomic Energy Agency, Vienna
57. International Atomic Energy Agency (2004) *Standardized High Current Solid Targets for Cyclotron Production of Diagnostic and Therapeutic Radionuclides*. International Atomic Energy Agency, Vienna
58. Ho CY, Powell RW, Liley PE (1972) Thermal Conductivity of the Elements. *J Phys Chem Ref Data* 1:279–421. <https://doi.org/10.1063/1.3253100>
59. Holleman AF, Wiberg N (2016) *Holleman • Wiberg Anorganische Chemie: Set Band 1+2, 103., grundlegend überarbeitete Auflage*. De Gruyter, Berlin/Boston
60. Helmeke H-J, Mahnke E, Schaardt U, Knapp WH (2004) External targets for the production of ²¹¹At – Review and status of the target development at the Hannover cyclotron. *Z Für Med Phys* 14:195–199. <https://doi.org/10.1078/0939-3889-00213>
61. International Atomic Energy Agency (2022) Recommended experimental data for ⁷⁵As(p,4n)⁷²Se reaction. In: IAEA Nucl. Data Serv. Med. Isot. Data Portal. <https://nds.iaea.org/medical/asp72se0.html>. Accessed 12 Apr 2026
62. Andersson H, Cederkrantz E, Bäck T, et al (2009) Intraperitoneal α -Particle Radioimmunotherapy of Ovarian Cancer Patients: Pharmacokinetics and Dosimetry of ²¹¹At-MX35 F(ab')₂ — A Phase I Study. *J Nucl Med* 50:1153–1160. <https://doi.org/10.2967/jnumed.109.062604>
63. Choi J, Vaidyanathan G, Koumarianou E, et al (2018) Astatine-211 labeled anti-HER2 5F7 single domain antibody fragment conjugates: radiolabeling and preliminary evaluation. *Nucl Med Biol* 56:10–20. <https://doi.org/10.1016/j.nucmedbio.2017.09.003>
64. El Fakiri M, Ayada N, Müller M, et al (2024) Development and Preclinical Evaluation of [²¹¹At]PSA_t-3-Ga: An Inhibitor for Targeted α -Therapy of Prostate Cancer. *J Nucl Med* 65:593–599. <https://doi.org/10.2967/jnumed.123.267043>
65. Mease RC, Kang CM, Kumar V, et al (2022) An Improved ²¹¹At-Labeled Agent for PSMA-Targeted α -Therapy. *J Nucl Med* 63:259–267. <https://doi.org/10.2967/jnumed.121.262098>
66. Radchenko V, Morgenstern A, Jalilian AR, et al (2021) Production and Supply of α -Particle-Emitting Radionuclides for Targeted α -Therapy. *J Nucl Med* 62:1495–1503. <https://doi.org/10.2967/jnumed.120.261016>

References

67. Higashi T, Nagatsu K, Tsuji AB, Zhang M-R (2022) Research and Development for Cyclotron Production of ^{225}Ac from ^{226}Ra --The Challenges in a Country Lacking Natural Resources for Medical Applications. *Processes* 10:1215. <https://doi.org/10.3390/pr10061215>
68. Kokov KV, Egorova BV, German MN, et al (2022) ^{212}Pb : Production Approaches and Targeted Therapy Applications. *Pharmaceutics* 14:189. <https://doi.org/10.3390/pharmaceutics14010189>
69. Azzam A, Alharby AA (2020) Comparative study and TALYS 1.6 code calculations for the excitation functions of P and α -induced reactions on Bi target with special attention to the medical radioisotope ^{211}At . *Eur Phys J Plus* 135:192. <https://doi.org/10.1140/epjp/s13360-020-00223-z>
70. Sevenois MBC, Miller BWM, Jensen HJ, et al (2023) Optimized cyclotron production of ^{211}At : The challenge of ^{210}Po -characterization. *Radiat Phys Chem* 212:111155. <https://doi.org/10.1016/j.radphyschem.2023.111155>
71. Sevenois M (2024) Optimised ^{211}At production: understanding the impact of the $^{210}\text{At}/^{210}\text{Po}$ contaminant on radiation protection and dosimetry. PhD Thesis, Vrije Universiteit Brussel
72. Crawford JR, Yang H, Kunz P, et al (2017) Development of a preclinical $^{211}\text{Rn}/^{211}\text{At}$ generator system for targeted alpha therapy research with ^{211}At . *Nucl Med Biol* 48:31–35. <https://doi.org/10.1016/j.nucmedbio.2017.01.011>
73. Lindegren S, Bäck T, Jensen HJ (2001) Dry-distillation of astatine-211 from irradiated bismuth targets: a time-saving procedure with high recovery yields. *Appl Radiat Isot* 55:157–160. [https://doi.org/10.1016/S0969-8043\(01\)00044-6](https://doi.org/10.1016/S0969-8043(01)00044-6)
74. Alliot C, Chérel M, Barbet J (2009) Extraction of astatine-211 in diisopropylether (DIPE). *Radiochim Acta* 97:161–165. <https://doi.org/10.1524/ract.2009.1590>
75. Balkin E, Hamlin D, Gagnon K, et al (2013) Evaluation of a Wet Chemistry Method for Isolation of Cyclotron Produced [^{211}At]Astatine. *Appl Sci* 3:636–655. <https://doi.org/10.3390/app3030636>
76. Burns JD, Tereshatov EE, Avila G, et al (2021) Rapid recovery of At-211 by extraction chromatography. *Sep Purif Technol* 256:117794. <https://doi.org/10.1016/j.seppur.2020.117794>
77. Ekberg C, Jensen H, Mezyk SP, et al (2017) Extraction of ^{211}At from nitric acid solutions into various organic solvents for use as an α -source for radiation chemistry studies. *J Radioanal Nucl Chem* 314:235–239. <https://doi.org/10.1007/s10967-017-5364-1>
78. O'Hara MJ, Krzysko AJ, Niver CM, et al (2017) An automated flow system incorporating in-line acid dissolution of bismuth metal from a cyclotron irradiated target assembly for use in the isolation of astatine-211. *Appl Radiat Isot* 122:202–210. <https://doi.org/10.1016/j.apradiso.2017.02.001>
79. O'Hara MJ, Krzysko AJ, Hamlin DK, et al (2019) Development of an autonomous solvent extraction system to isolate astatine-211 from dissolved cyclotron bombarded bismuth targets. *Sci Rep* 9:20318. <https://doi.org/10.1038/s41598-019-56272-7>
80. Eychenne R, Alliot C, Gustin J-F, Guérard F (2022) Radiolabeling chemistry with heavy halogens iodine and astatine. In: *Nuclear Medicine and Molecular Imaging*. Elsevier, Oxford, pp 121–132
81. Rössler K, Tornau W, Stöcklin G (1974) Rapid separation of carrier-free inorganic and organic compounds of radioiodine and astatine by high-pressure liquid chromatography. *J Radioanal Chem* 21:199–209. <https://doi.org/10.1007/BF02520862>

References

82. Berdal M, Gouard S, Eychenne R, et al (2021) Investigation on the reactivity of nucleophilic radiohalogens with arylboronic acids in water: access to an efficient single-step method for the radioiodination and astatination of antibodies. *Chem Sci* 12:1458–1468. <https://doi.org/10.1039/D0SC05191H>
83. Ayed T, Pilmé J, Tézé D, et al (2016) ²¹¹At-labeled agents for alpha-immunotherapy: On the in vivo stability of astatine-agent bonds. *Eur J Med Chem* 116:156–164. <https://doi.org/10.1016/j.ejmech.2016.03.082>
84. Champion J, Sabatié-Gogova A, Bassal F, et al (2013) Investigation of Astatine(III) Hydrolyzed Species: Experiments and Relativistic Calculations. *J Phys Chem A* 117:1983–1990. <https://doi.org/10.1021/jp3099413>
85. Champion J, Alliot C, Renault E, et al (2010) Astatine Standard Redox Potentials and Speciation in Acidic Medium. *J Phys Chem A* 114:576–582. <https://doi.org/10.1021/jp9077008>
86. Archimandritis SC, Potamianos S, Varvarigou AD (2002) Optimization of synthesis and quality control procedures for the preparations of ¹⁸F and ¹²³I labelled peptides. In: Optimization of synthesis and quality control procedures for the preparation of ¹⁸F and ¹²³I labelled peptides for nuclear medicine. International Atomic Energy Agency, Vienna, pp 105–116
87. Liu L, Maurice R, Galland N, et al (2022) Pourbaix Diagram of Astatine Revisited: Experimental Investigations. *Inorg Chem* 61:13462–13470. <https://doi.org/10.1021/acs.inorgchem.2c01918>
88. Pozzi OR, Zalutsky MR (2007) Radiopharmaceutical Chemistry of Targeted Radiotherapeutics, Part 3: α -Particle-Induced Radiolytic Effects on the Chemical Behavior of ²¹¹At. *J Nucl Med* 48:1190–1196. <https://doi.org/10.2967/jnumed.106.038505>
89. Pozzi OR, Zalutsky MR (2017) Radiopharmaceutical chemistry of targeted radiotherapeutics, part 4: Strategies for ²¹¹At labeling at high activities and radiation doses of ²¹¹At α -particles. *Nucl Med Biol* 46:43–49. <https://doi.org/10.1016/j.nucmedbio.2016.11.009>
90. Nishinaka I, Hashimoto K (2021) Separation of astatine from irradiated lead targets based on dry distillation in a glass test tube. *J Radioanal Nucl Chem* 327:869–875. <https://doi.org/10.1007/s10967-020-07546-2>
91. Müller M, Pedersen NB, Shalgunov V, et al (2026) Astatine-211—Towards In Vivo Stable Astatine-211 Labeled Radiopharmaceuticals and Their (Pre)Clinical Applications. *Med Res Rev* 46:203–237. <https://doi.org/10.1002/med.70008>
92. Ohnuki K, Yoshimoto M, Haba H, et al (2022) Protection from contamination by ²¹¹At, an enigmatic but promising alpha-particle-emitting radionuclide. *EJNMMI Phys* 9:39. <https://doi.org/10.1186/s40658-022-00469-9>
93. Ohnuki K, Takenaka Y, Yoshimoto M, Fujii H (2022) The safe handling of ²¹¹At compounds. *Ann Nucl Med* 36:842–843. <https://doi.org/10.1007/s12149-022-01778-w>
94. Craig Allison J., Taprogge J, Flux GD, Murray I (2023) Radiation protection aspects for alpha therapies. *Q J Nucl Med Mol Imaging* 67:4–13. <https://doi.org/10.23736/S1824-4785.22.03501-4>
95. Council of the European Union (2006) Council Directive 2006/117/Euratom of 20 November 2006 on the supervision and control of shipments of radioactive waste and spent fuel
96. McIntosh LA, Burns JD, Tereshatov EE, et al (2023) Production, isolation, and shipment of clinically relevant quantities of astatine-211: A simple and efficient approach to

References

- increasing supply. Nucl Med Biol 126–127:108387. <https://doi.org/10.1016/j.nucmedbio.2023.108387>
97. Newton D, Talbot RJ, Priest ND (2001) Human biokinetics of injected bismuth-207. *Hum Exp Toxicol* 20:601–609. <https://doi.org/10.1191/096032701718890586>
98. Buijs WC, Corstens FH, Beentjes LB (1985) Long-term retention of ²⁰⁷Bi in the human body after injection of ²⁰⁶Bi. *Health Phys* 49:1267–1269
99. Koning AJ, Rochman D, Sublet J-Ch, et al (2019) TENDL: Complete Nuclear Data Library for Innovative Nuclear Science and Technology. *Nucl Data Sheets* 155:1–55. <https://doi.org/10.1016/j.nds.2019.01.002>
100. International Atomic Energy Agency EXFOR: Experimental Nuclear Reaction Data. <https://nds.iaea.org/exfor/>. Accessed 15 Mar 2026
101. Levkovskii VN (1991) The Cross-Sections of Activation of Nuclides of Middle-Range Mass (A=40-100) by Protons and Alpha Particles of Middle Range Energies (E=10-50 MeV). Inter-Vesti, Moscow
102. Ismail M (1990) Measurement and analysis of the excitation function for alpha-induced reactions on Ga and Sb isotopes. *Phys Rev C* 41:87–108. <https://doi.org/10.1103/PhysRevC.41.87>
103. Rizvi IA, Bhardwaj MK, Ansari MA, Chaubey AK (1989) Nonequilibrium effects in α -particle induced reactions on gallium isotopes. *Can J Phys* 67:870–875. <https://doi.org/10.1139/p89-150>
104. Didik VA, Malkovich RSh, Skoryatina EA, Kozlovskii VV (1994) Experimental determination of the cross sections of nuclear reactions by the method of analysis of the concentration profiles of transmutation nuclides. *At Energy* 77:570–572. <https://doi.org/10.1007/BF02408219>
105. Fox MB, Voyles AS, Morrell JT, et al (2021) Measurement and modeling of proton-induced reactions on arsenic from 35 to 200 MeV. *Phys Rev C* 104:064615. <https://doi.org/10.1103/PhysRevC.104.064615>
106. Mushtaq A, Qaim SM, Stöcklin G (1988) Production of ⁷³Se via (p,3n) and (d,4n) reactions on arsenic. *Int J Rad Appl Instrum [A]* 39:1085–1091. [https://doi.org/10.1016/0883-2889\(88\)90146-3](https://doi.org/10.1016/0883-2889(88)90146-3)
107. Amjed N, Aslam MN, Hussain M, Qaim SM (2021) Evaluation of nuclear reaction cross section data of proton and deuteron induced reactions on ⁷⁵As, with particular emphasis on the production of ⁷³Se. *Radiochim Acta* 109:525–537. <https://doi.org/10.1515/ract-2021-1018>
108. George KJH, Borjani S, Cross MC, et al (2021) Expanding the PET radioisotope universe utilizing solid targets on small medical cyclotrons. *RSC Adv* 11:31098–31123. <https://doi.org/10.1039/D1RA04480J>
109. International Atomic Energy Agency (IAEA) — Nuclear Data Section (2013) Isotope Browser (mobile app)
110. Qin Y, Albano B, Spencer J, et al (2023) Thermal management and packaging of wide and ultra-wide bandgap power devices: a review and perspective. *J Phys Appl Phys* 56:093001. <https://doi.org/10.1088/1361-6463/acb4ff>
111. Salerno LJ, Kittel P (1997) Thermal Contact Conductance. National Aeronautics and Space Administration, Ames Research Center, Moffett Field, CA
112. Dhuley RC (2019) Pressed copper and gold-plated copper contacts at low temperatures – A review of thermal contact resistance. *Cryogenics* 101:111–124. <https://doi.org/10.1016/j.cryogenics.2019.06.008>

References

113. National Nuclear Data Center Q-Value Calculator (QCalc). <https://www.nndc.bnl.gov/qcalc/>. Accessed 10 Mar 2026
114. Sant'ana G, Möckli D, Viegas ADC, et al (2024) Ni/Bi bilayers: The effect of thickness on the superconducting properties. *J Appl Phys* 135:043905. <https://doi.org/10.1063/5.0182758>
115. Vaughan M, Satchell N, Ali M, et al (2020) Origin of superconductivity at nickel-bismuth interfaces. *Phys Rev Res* 2:013270. <https://doi.org/10.1103/PhysRevResearch.2.013270>
116. Lebeda O, Jiran R, Ráliš J, Štursa J (2005) A new internal target system for production of ²¹¹At on the cyclotron U-120M. *Appl Radiat Isot* 63:49–53. <https://doi.org/10.1016/j.apradiso.2005.02.006>
117. Hill RF, Strader JL (2006) Practical utilization of low melting alloy thermal interface materials. IEEE, Dallas, TX, USA, pp 23–27
118. OMEGA Engineering Table of Total Emissivity. <https://www.omegaengineering.cn/temperature/Z/pdf/z088-089.pdf>. Accessed 24 May 2026
119. Neuhausen J, Köster U, Eichler B (2004) Investigation of evaporation characteristics of polonium and its lighter homologues selenium and tellurium from liquid Pb-Bi-eutecticum. *Radiochim Acta* 92:917–923. <https://doi.org/10.1524/ract.92.12.917.55105>
120. Serov A, Aksenov NV, Bozhikov GA, et al (2011) Adsorption interaction of astatine species with quartz and gold surfaces. *Radiochim Acta* 99:593–600. <https://doi.org/10.1524/ract.2011.1850>
121. Dietzel D, Yakushev A, Düllmann ChE (2025) Reactivity and volatility of astatine in a quartz column. *J Radioanal Nucl Chem* 334:6959–6972. <https://doi.org/10.1007/s10967-025-10335-4>
122. Vaidyanathan G, Pozzi OR, Choi J, et al (2020) Labeling Monoclonal Antibody with α -emitting ²¹¹At at High Activity Levels via a Tin Precursor. *Cancer Biother Radiopharm* 35:511–519. <https://doi.org/10.1089/cbr.2019.3204>
123. Keller O, Benoit M, Müller A, Schmeling S (2019) Smartphone and Tablet-Based Sensing of Environmental Radioactivity: Mobile Low-Cost Measurements for Monitoring, Citizen Science, and Educational Purposes. *Sensors* 19:4264. <https://doi.org/10.3390/s19194264>
124. Yennello SJ, McIntosh LA, Burns JD, et al (2021) Advances in ²¹¹At production at Texas A&M University. *EPJ Web Conf* 252:03002. <https://doi.org/10.1051/epjconf/202125203002>
125. Burns JD, Tereshatov EE, McCarthy MA, et al (2020) Astatine partitioning between nitric acid and conventional solvents: indication of covalency in ketone complexation of AtO⁺. *Chem Commun* 56:9004–9007. <https://doi.org/10.1039/D0CC03804K>
126. Law JD (2018) *Aqueous Reprocessing of Used Nuclear Fuel*. World Scientific, Hackensack, New Jersey
127. Horwitz EP, Schulz WW (1991) The TRUEX Process: A Vital Tool for Disposal of U.S. Defense Nuclear Waste. In: Cecille ML, Casarci M, Pietrelli L (eds) *New Separation Chemistry Techniques for Radioactive Waste and Other Specific Applications*. Springer, Dordrecht, pp 21–29
128. Bingham NM, Abousalman-Rezvani Z, Collins K, Roth PJ (2022) Thiocarbonyl chemistry in polymer science. *Polym Chem* 13:2880–2901. <https://doi.org/10.1039/D2PY00050D>

References

129. Usov VA, Timokhina LV, Voronkov MG (1990) The synthesis and properties of thioaldehydes. *Russ Chem Rev* 59:378–395. <https://doi.org/10.1070/RC1990v059n04ABEH003531>
130. Badawy I, El-Gammal W (2001) Estimation of the self-attenuation correction factor for gamma rays emission from nuclear materials. In: *Symposium on International Safeguards: Verification and Nuclear Material Security*. International Atomic Energy Agency, Vienna, Austria
131. Kanisch G, Mundschenk H, Schkade U-K, Wershofen H (2019) Interferences in gamma spectrometry. Federal Ministry for the Environment, Nature Conservation and Nuclear Safety
132. International Atomic Energy Agency (1998) *Software for Nuclear Spectrometry*. International Atomic Energy Agency, Vienna
133. Burgoyne AR (2022) 17 mCi Ac-225(NO₃)₃ at ORNL by Dr Andrew R Burgoyne. In: *Wikimedia Commons*. [https://commons.wikimedia.org/wiki/File:17_mCi_Ac-225\(NO₃\)₃_at_ORNL_by_Dr_Andrew_R_Burgoyne.jpg](https://commons.wikimedia.org/wiki/File:17_mCi_Ac-225(NO3)3_at_ORNL_by_Dr_Andrew_R_Burgoyne.jpg). Accessed 15 May 2026
134. Burgoyne AR (2023) Ra-224 nitrate (21.4 mCi) - Photo by Dr Andrew R. Burgoyne - Oak Ridge National Laboratory. In: *Wikimedia Commons*. [https://commons.wikimedia.org/wiki/File:Ra-224_nitrate_\(21.4_mCi\)_-_Photo_by_Dr_Andrew_R._Burgoyne_-_Oak_Ridge_National_Laboratory.jpg](https://commons.wikimedia.org/wiki/File:Ra-224_nitrate_(21.4_mCi)_-_Photo_by_Dr_Andrew_R._Burgoyne_-_Oak_Ridge_National_Laboratory.jpg). Accessed 15 May 2026
135. Kratz J-V, Lieser KH (2013) *Nuclear and Radiochemistry: Fundamentals and Applications*, 3rd ed. Wiley-VCH, Weinheim
136. Harvey AH (2024) Index of Refraction of Liquid Water. In: *NIST Chem. WebBook CRC Handb. Chem. Phys.* <https://www.nist.gov/publications/index-refraction-liquid-water>. Accessed 24 Apr 2026
137. Kedenburg S, Vieweg M, Gissibl T, Giessen H (2012) Linear refractive index and absorption measurements of nonlinear optical liquids in the visible and near-infrared spectral region. *Opt Mater Express* 2:1588–1611. <https://doi.org/10.1364/OME.2.001588>
138. *Surface Tension Components and Parameters of Liquids: Diiodomethane*. <https://www.surface-tension.de/LIQUIDS/Diiodomethane3.htm>. Accessed 24 Apr 2026
139. Ciddor PE (1996) Refractive index of air: new equations for the visible and near infrared. *Appl Opt* 35:1566–1573. <https://doi.org/10.1364/AO.35.001566>
140. Argon: Larsén 1934 refractive index data. In: *RefractiveIndex.INFO*. <https://refractiveindex.info/?book=Ar&page=Larsen&shelf=main>. Accessed 24 Apr 2026
141. SCHOTT AG BOROFLOAT 33: Optical Properties. SCHOTT AG, Mainz
142. Ackerman NL, Graves EE (2012) The potential for Cerenkov luminescence imaging of alpha-emitting radionuclides. *Phys Med Biol* 57:771–783. <https://doi.org/10.1088/0031-9155/57/3/771>
143. Zyla PA, Particle Data Group (2020) Review of Particle Physics. *Prog Theor Exp Phys* 2020:083C01. <https://doi.org/10.1093/ptep/ptaa104>
144. Girard S, Kuhnhehn J, Gusarov A, et al (2013) Radiation Effects on Silica-Based Optical Fibers: Recent Advances and Future Challenges. *IEEE Trans Nucl Sci* 60:2015–2036. <https://doi.org/10.1109/TNS.2012.2235464>
145. Yamamoto S, Horita R, Toshito T, Komori M (2018) Imaging of the scintillation light of float and silica glasses during irradiation of radiations. *J Instrum* 13:P10021–P10021. <https://doi.org/10.1088/1748-0221/13/10/P10021>

References

146. Aneheim E, Palm S, Jensen H, et al (2019) Towards elucidating the radiochemistry of astatine – Behavior in chloroform. *Sci Rep* 9:15900. <https://doi.org/10.1038/s41598-019-52365-5>
147. Humpert S, Mues L, Pedersen NB, et al (2026) Reconsidering astatine-211 analytics: Retention effects in reversed-phase HPLC. *J Pharm Biomed Anal* 278:117547. <https://doi.org/10.1016/j.jpba.2026.117547>
148. Humpert S, Hoffmann C, Neumaier F, et al (2023) Validation of analytical HPLC with post-column injection as a method for rapid and precise quantification of radiochemical yields. *J Chromatogr B* 1228:123847. <https://doi.org/10.1016/j.jchromb.2023.123847>
149. Vanermen M, Ligeour M, Oliveira M-C, et al (2024) Astatine-211 radiolabelling chemistry: from basics to advanced biological applications. *EJNMMI Radiopharm Chem* 9:69. <https://doi.org/10.1186/s41181-024-00298-4>
150. Cruz E, Euerby MR, Johnson CM, Hackett CA (1997) Chromatographic classification of commercially available reverse-phase HPLC columns. *Chromatographia* 44:151–161. <https://doi.org/10.1007/BF02466449>
151. Ory D, Van den Brande J, de Groot T, et al (2015) Retention of [18F]fluoride on reversed phase HPLC columns. *J Pharm Biomed Anal* 111:209–214. <https://doi.org/10.1016/j.jpba.2015.04.009>
152. Maingueneau C, Eychenne R, Gestin J-F, Guérard F (2022) Preparation of ²¹¹At-labeled aromatic compounds from thioarylprecursors. *Nucl Med Biol* 108–109:S43–S44. [https://doi.org/10.1016/S0969-8051\(22\)00124-X](https://doi.org/10.1016/S0969-8051(22)00124-X)
153. Lindegren S, Jensen H, Jacobsson L (2014) A radio-high-performance liquid chromatography dual-flow cell gamma-detection system for on-line radiochemical purity and labeling efficiency determination. *J Chromatogr A* 1337:128–132. <https://doi.org/10.1016/j.chroma.2014.02.043>
154. Visser GWM (1989) Inorganic Astatine Chemistry: Part II: The Chameleon Behaviour and Electrophilicity of At-species. *Radiochim Acta* 47:97–104. <https://doi.org/10.1524/ract.1989.47.23.97>
155. Wilbur DS (2013) Enigmatic astatine. *Nat Chem* 5:246–246. <https://doi.org/10.1038/nchem.1580>
156. Taşdelen B, Kam E, Asliyukse H (2014) Quality control of iodine-131-labeled metaiodobenzylguanidine. *Nucl Med Commun* 35:95–98. <https://doi.org/10.1097/MNM.000000000000016>
157. Nishinaka I, Hashimoto K, Suzuki H (2018) Thin layer chromatography for astatine and iodine in solutions prepared by dry distillation. *J Radioanal Nucl Chem* 318:897–905. <https://doi.org/10.1007/s10967-018-6088-6>
158. Shirakami Y, Watabe T, Obata H, et al (2021) Synthesis of [211At]4-astato-L-phenylalanine by dihydroxyboryl-astatine substitution reaction in aqueous solution. *Sci Rep* 11:12982. <https://doi.org/10.1038/s41598-021-92476-6>
159. Meyer GJ, Walte A, Sriyapureddy SR, et al (2010) Synthesis and analysis of 2-[211At]-l-phenylalanine and 4-[211At]-l-phenylalanine and their uptake in human glioma cell cultures in-vitro. *Appl Radiat Isot* 68:1060–1065. <https://doi.org/10.1016/j.apradiso.2009.12.043>
160. Israel I, Brandau W, Farmakis G, Samnick S (2008) Improved synthesis of no-carrier-added p-[124I]iodo-L-phenylalanine and p-[131I]iodo-L-phenylalanine for nuclear medicine applications in malignant gliomas. *Appl Radiat Isot* 66:513–522. <https://doi.org/10.1016/j.apradiso.2007.10.004>

References

161. Vaidyanathan G, McDougald D, Grasfeder L, et al (2011) An alternative and expedient synthesis of radioiodinated 4-iodophenylalanine. *Appl Radiat Isot* 69:1401–1406. <https://doi.org/10.1016/j.apradiso.2011.05.004>
162. Koziorowski J, Weinreich R (1997) Simple preparation of ^{76}Br , ^{123}I and ^{211}At labeled 5-halo-2'-deoxyuridine. *J Radioanal Nucl Chem* 219:127–128. <https://doi.org/10.1007/BF02040279>
163. Nickel Institute (2023) Nickel Plating Handbook. Nickel Institute
164. Spahn I, Steyn GF, Kandil SA, et al (2007) New nuclear data for production of ^{73}As , ^{88}Y and ^{153}Sm : important radionuclides for environmental and medical applications. In: International Conference on Nuclear Data for Science and Technology 2007. EDP Sciences, Nice, France, pp 1363–1366
165. Spahn I, Steyn GF, Nortier FM, et al (2007) Excitation functions of $\text{natGe}(p,xn)^{71,72,73,74}\text{As}$ reactions up to 100 MeV with a focus on the production of ^{72}As for medical and ^{73}As for environmental studies. *Appl Radiat Isot* 65:1057–1064. <https://doi.org/10.1016/j.apradiso.2007.04.012>
166. Uddin MS, Basunia MS, Sudár S, et al (2022) Excitation functions of proton-induced nuclear reactions on ^{86}Sr , with particular emphasis on the formation of isomeric states in ^{86}Y and ^{85}Y . *Eur Phys J A* 58:67. <https://doi.org/10.1140/epja/s10050-022-00714-w>
167. Dragoun A, Spahn I, Hussain M, et al (2025) Cross-section measurements of the $^{93}\text{Nb}(p,n)^{93m}\text{Mo}$ reaction up to 17 MeV. *J Radioanal Nucl Chem* 334:5149–5154. <https://doi.org/10.1007/s10967-025-10178-z>
168. Ziegler JF, Ziegler MD, Biersack JP (2010) SRIM – The stopping and range of ions in matter (2010). *Nucl Instrum Methods Phys Res Sect B* 268:1818–1823. <https://doi.org/10.1016/j.nimb.2010.02.091>
169. Williamson CF, Boujot JP, Picard J (1966) Tables of Range and Stopping Power of Chemical Elements for Charged Particles of Energy 0.5 to 500 MeV. Commissariat à l'Énergie Atomique (CEA), Saclay, France
170. Palágyi Š, Zaduban M (1969) Separation of Radioiodide, Radioiodate and Radioperiodate by Thin-Layer Chromatography. *Chem Zvesti* 23:876–880
171. Charlton M, Humberston JW (2000) Positron Physics. Cambridge University Press, Cambridge
172. Papini D Doppler Broadening of 511 keV Annihilation Gamma Ray. https://nucleus.iaea.org/sites/connect/RRIHpublic/CompendiumDB/Shared%20Documents/Netherlands/Lab%20templates/Lab_Protocol_compendium_Positron.pdf. Accessed 15 May 2026
173. Gribakin GF, Young JA, Surko CM (2010) Positron-molecule interactions: Resonant attachment, annihilation, and bound states. *Rev Mod Phys* 82:2557–2607. <https://doi.org/10.1103/RevModPhys.82.2557>
174. Krause MO (1979) Atomic radiative and radiationless yields for K and L shells. *J Phys Chem Ref Data* 8:307–327. <https://doi.org/10.1063/1.555594>
175. National Nuclear Data Center Nuclear Data Sheets: General Policies - Presentation of Data. <https://www.nndc.bnl.gov/nds/docs/NDSPolicies.pdf>. Accessed 17 Apr 2026
176. Joint Committee for Guides in Metrology (2008) Evaluation of measurement data - Guide to the expression of uncertainty in measurement. Bureau International des Poids et Mesures (BIPM), Sèvres, France
177. International Atomic Energy Agency (2004) Quantifying uncertainty in nuclear analytical measurements. International Atomic Energy Agency, Vienna, Austria

References

178. Joint Committee for Guides in Metrology (2008) Evaluation of measurement data - Supplement 1 to the "Guide to the expression of uncertainty in measurement" - Propagation of distributions using a Monte Carlo method. Bureau International des Poids et Mesures (BIPM), Sèvres, France
179. Bethe HA (1930) Zur Theorie des Durchgangs schneller Korpuskularstrahlen durch Materie. *Ann Phys* 5:325–400. <https://doi.org/10.1002/andp.19303970304>
180. Koning AJ, Hilaire S, Goriely S (2023) TALYS: modeling of nuclear reactions. *Eur Phys J A* 59:. <https://doi.org/10.1140/epja/s10050-023-01034-3>
181. Koning AJ, Hilaire S, Duijvestijn MC (2007) TALYS-1.0. In: ND2007. EDP Sciences, Nice, France, p 058
182. Sudár S, Qaim SM (2018) Mass number and excitation energy dependence of the $\Theta_{\text{eff}}/\text{Orig}$ parameter of the spin cut-off factor in the formation of an isomeric pair. *Nucl Phys A* 979:113–142. <https://doi.org/10.1016/j.nuclphysa.2018.09.039>
183. Sui Z, Qian S, Niu L, et al (2025) Glass scintillator: A window to future high-energy radiation detection. *Innov Camb* 6:100878. <https://doi.org/10.1016/j.xinn.2025.100878>
184. Hubbell JH, Seltzer SM (1995) Tables of x-ray mass attenuation coefficients and mass energy-absorption coefficients 1 keV to 20 MeV for elements $Z = 1$ to 92 and 48 additional substances of dosimetry interest. National Institute of Standards and Technology, Gaithersburg, MD
185. Klein O, Nishina Y (1929) Über die Streuung von Strahlung durch freie Elektronen nach der neuen relativistischen Quantendynamik von Dirac. *Z Für Phys* 52:853–868. <https://doi.org/10.1007/BF01366453>
186. Frank IM, Tamm IE (1937) Coherent visible radiation of fast electrons passing through matter. *C R Acad Sci USSR* 14:109–114
187. Berger MJ, Seltzer SM (1982) Stopping powers and ranges of electrons and positrons. National Bureau of Standards, Washington, DC
188. Hecht S, Schlaer S, Pirenne MH (1942) Energy, Quanta, and Vision. *J Gen Physiol* 25:819–840. <https://doi.org/10.1085/jgp.25.6.819>
189. Stavsetra L, Hult EA, Omtvedt JP (2005) Real-time gain shift correction for on-line alpha-liquid scintillation spectroscopy. *Nucl Instrum Methods Phys Res Sect Accel Spectrometers Detect Assoc Equip* 551:323–329. <https://doi.org/10.1016/j.nima.2005.06.045>

Appendix

Appendix A: Production and decay data measurement of ^{72}As

Appendix A-1: Reaction Channels, Q-values and Impurity threshold energies

Reaction Q-values were obtained using the National Nuclear Data Center Q-Value Calculator (QCalc). For endothermic reactions ($Q > 0$), laboratory-frame threshold energies were calculated from the corresponding Q-values according to

$$E_{\text{thr}} \approx -Q \left(1 + \frac{m_a}{m_A} \right) \quad (\text{A-1})$$

where m_a is the projectile mass and m_A is the target mass. The small relativistic correction term was neglected. The listed threshold energies therefore represent kinematic channel-opening energies and should not be interpreted as the onset of practically relevant production yields.

Appendix

Table A-1: Relevant reaction channels for the production of ^{72}As and ^{72}Se . Q -values were obtained from the NNDC Q-Value Calculator [113]. Threshold energies are laboratory-frame kinematic thresholds calculated for endothermic reactions using Eq. A-1. Only radionuclides that remain in the final chemically isolated product fraction were considered relevant for the practical radionuclidic-purity assessment. For direct ^{72}As production, this corresponds primarily to arsenic radioisotopes. For indirect ^{72}Se production, selenium radioisotopes are the relevant impurities, whereas arsenic products formed from ^{75}As are removed during selenium separation.

Target material	Reaction channel	Product	Role in this work	Q-value [MeV]	E_{thr} [MeV]
^{72}Ge	$^{72}\text{Ge}(p,n)^{72}\text{As}$	^{72}As	desired product	-5.138	5.210
^{72}Ge	$^{72}\text{Ge}(p,2n)^{71}\text{As}$	^{71}As	arsenic impurity	-13.546	13.736
^{72}Ge	$^{72}\text{Ge}(p,3n)^{70}\text{As}$	^{70}As	high-energy arsenic impurity	-25.177	25.530
^{69}Ga	$^{69}\text{Ga}(\alpha,n)^{72}\text{As}$	^{72}As	desired product	-6.744	7.135
^{69}Ga	$^{69}\text{Ga}(\alpha,2n)^{71}\text{As}$	^{71}As	arsenic impurity	-15.153	16.031
^{69}Ga	$^{69}\text{Ga}(\alpha,3n)^{70}\text{As}$	^{70}As	high-energy arsenic impurity	-26.783	28.335
^{75}As	$^{75}\text{As}(p,n)^{75}\text{Se}$	^{75}Se	selenium side product	-1.647	1.669
^{75}As	$^{75}\text{As}(p,2n)^{74}\text{Se}$	^{74}Se	stable selenium side product	-9.675	9.804
^{75}As	$^{75}\text{As}(p,3n)^{73}\text{Se}$	^{73}Se	selenium impurity	-21.732	22.022
^{75}As	$^{75}\text{As}(p,4n)^{72}\text{Se}$	^{72}Se	desired generator parent	-30.162	30.564
^{75}As	$^{75}\text{As}(p,5n)^{71}\text{Se}$	^{71}Se	high-energy selenium impurity	-42.955	43.528
^{75}As	$^{75}\text{As}(p,pn)^{74}\text{As} /$ $^{75}\text{As}(p,d)^{74}\text{As}$	^{74}As	target-derived arsenic impurity	-10.245 / - 8.021	10.383 / 8.129
^{75}As	$^{75}\text{As}(p,p2n)^{73}\text{As} /$ $^{75}\text{As}(p,dn)^{73}\text{As} /$ $^{75}\text{As}(p,t)^{73}\text{As}$	^{73}As	target-derived arsenic impurity	-18.220 / - 15.995 / - 9.738	18.465 / 16.210 / 9.869

Appendix

Appendix A-2: Enriched target material

Table A-2: Composition of enriched target material [%] used for sample preparation of ^{72}Ge and ^{69}Ga sediments.

Germanium	Enrichmetn	Gallium	Enrichment
^{70}Ge	0.49	^{69}Ga	99.81
^{72}Ge	96.42	^{71}Ga	0.19
^{73}Ge	2.94		
^{74}Ge	0.15		
^{76}Ge	0.01		

Appendix A-3: Evaluation of the X-ray data and derivation of the EC branch

For the X-ray-based analysis, the total K X-ray signal was taken as the sum of the background-corrected net peak areas of the K_α and K_β regions:

$$N_{KX} = N_{K\alpha} + N_{K\beta}, \quad (\text{A2})$$

where $N_{K\alpha}$ and $N_{K\beta}$ denote the respective net peak areas after background subtraction.

Because the detector efficiency was slightly different at the two X-ray energies, both components were corrected separately. The emitted K X-ray rate at EOB was therefore calculated as

$$A_{KX,EOB} = \left(\frac{N_{K\alpha}}{t_m \varepsilon_{K\alpha}} + \frac{N_{K\beta}}{t_m \varepsilon_{K\beta}} \right) \cdot C_{\text{decay}} \cdot C_{\text{abs}}, \quad (\text{A3})$$

where t_m is the live counting time, $\varepsilon_{K\alpha}$ and $\varepsilon_{K\beta}$ are the detector efficiencies at the respective X-ray energies, C_{decay} accounts for decay during counting and decay correction to EOB, and C_{abs} accounts for self-absorption in the sample and absorption in the Al cover. In the present case, C_{abs} thus includes both the attenuation in the thin germanium sediment and the attenuation in the 10 μm Al cover.

The EC-related activity was then obtained from the corrected K X-ray rate according to

$$A_{EC} = \frac{A_{KX,EOB}}{\omega_K \cdot P_K}, \quad (\text{A4})$$

with $\omega_K = 0.54$ for the K-shell fluorescence yield of Germanium and $P_K = 0.89$ for the probability of EC from the K shell in the decay of ^{72}As . Unlike the γ -ray-based activity determination, no γ -line emission probability enters at this stage. Instead, the factors ω_K and P_K provide the link between the experimentally observed K X-rays and the underlying EC decay rate.

Finally, the EC branching ratio was obtained by comparison with the absolute ^{72}As activity determined independently from γ -ray spectrometry:

$$I_{EC} = \frac{A_{EC}}{A_{\gamma,EOB}} \cdot 100 \quad (\text{A5})$$

and the positron branching ratio was derived by difference:

Appendix

$$I_{\beta^+} = 100 - I_{EC}. \quad (\text{A6})$$

This procedure is consistent with the evaluation scheme used in the draft, in which the summed K_{α} and K_{β} signal was corrected for efficiency, fluorescence yield, and K-shell capture probability, and then compared with the independently determined γ -based activity of ^{72}As .

Appendix A-4: Physical explanation of the varied TALYS-2.0 parameters

The TALYS-2.0 parameter variations used in the present work were not intended as arbitrary tuning of the calculated excitation functions. Instead, only a small number of model ingredients with a clear physical meaning were varied in a controlled manner. These quantities affect different parts of the reaction calculation and are therefore suitable for a sensitivity analysis of the $^{75}\text{As}(p,4n)^{72}\text{Se}$ excitation function. In the following, E^* denotes the excitation energy of the residual system and $\rho(E^*, J, \pi)$ the level density as a function of excitation energy E^* , spin J , and parity π . Here, the term accessible final states refer to the energetically and quantum-mechanically allowed excited states of the residual nucleus that can be populated after particle emission. Their number and distribution are governed by the adopted level-density description and directly affect the statistical competition between neighboring reaction channels. The TALYS-2.0 level-density options used here correspond to different physical descriptions of these state densities, while the pre-equilibrium and optical-model options affect the reaction dynamics before and during particle emission.

Proton optical model potential: rvadjust

The optical model potential describes the interaction between the incoming projectile and the target nucleus and therefore controls the entrance-channel transmission coefficients. In TALYS-2.0, the keyword *rvadjust* acts as a multiplicative factor on the OMP parameter r_V , i.e. the radius parameter of the real volume term of the optical model. For protons, the default global value of r_V is given in TALYS-2.0 by an A -dependent expression, and *rvadjust* $p \times$ scales this value by the factor x . Thus, the variation of *rvadjust* does not rescale the final cross-section directly but modifies the underlying transmission probabilities in a physically interpretable way. In the present study, only small local variations around the default value were considered. Such changes are expected to influence primarily the overall reaction probability and the detailed shape of the excitation function, especially in the threshold and high-energy tail regions, while the exact direction of the effect remains channel dependent.

Level-density model 1: ldmodel 1

In TALYS-2.0, *ldmodel 1* corresponds to the Constant Temperature + Fermi gas model (CTM). In this approach, the excitation-energy region is divided into a lower-energy part, where a constant-temperature law is used, and a higher-energy part, where a Fermi-gas description is applied above a matching energy E_M . This model represents the TALYS-2.0 default and provides a smooth phenomenological description of the state density over a broad energy range. Physically, it may be viewed as a compromise model that connects the low-energy discrete-level region to the higher-energy statistical continuum. As a result, *ldmodel 1* often provides a robust baseline description, but it does not necessarily give the most favorable statistical weighting for a specific multiple-neutron emission channel.

Level-density model 2: ldmodel 2

ldmodel 2 corresponds to the Back-shifted Fermi gas model (BFM). In this model, the level density is described by a Fermi-gas approach over the full excitation-energy range. Pairing effects are not treated by switching to a different low-energy description but are included through a back-shift of the available excitation energy. The main model parameters are therefore the level-density parameter a and the back-shift parameter δ .

In the present calculations, these parameters were not manually adjusted. The TALYS-2.0 default implementation of *ldmodel 2* was used, meaning that the nucleus-specific values of a and δ were taken from the internal TALYS-2.0 parameter set or from the implemented systematics. The same applies to the spin-cut-off description. In this context, Sudár and Qaim [182] discuss the parameter

$$\eta = \frac{\theta_{eff}}{\theta_{rig}} \quad (A7)$$

with θ_{eff} being the effective moment of inertia and θ_{rig} the rigid-body moment of inertia. This parameter mainly affects the spin distribution of the populated states and is therefore especially relevant when isomeric cross-section ratios are investigated. Since the present work does not evaluate isomeric ratios, total production cross-sections, η was not treated as an additional fit parameter.

The use of *ldmodel 2* should therefore be understood as a change of the underlying TALYS-2.0 level-density prescription rather than as an individually optimized parameter set. For the $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction, this can still affect the calculated excitation function, because the level density influences the competition between the different particle-emission channels and thus the calculated population of ^{72}Se relative to neighboring residual nuclei.

Level-density model 5: ldmodel 5

ldmodel 5 is fundamentally different from *ldmodel 1* and *ldmodel 2*. It corresponds to Skyrme-Hartree-Fock-Bogolyubov combinatorial level densities from numerical tables. TALYS-2.0 classifies *ldmodel 5* as a microscopic option and states that the combinatorial model provides energy-, spin- and parity-dependent level densities based on a detailed microscopic calculation of the intrinsic state density. In addition, the corresponding TALYS-2.0 options indicate that parity-dependent tabulated level densities are explicitly available for *ldmodel 5*. Thus, the transition from *ldmodel 1* or *ldmodel 2* to *ldmodel 5* is not merely a change of fit parameters, but a change from a phenomenological effective description to a microscopic tabulated one. In practical terms, this does not mean that fewer channels are opened. Rather, the relative statistical population of competing channels is redistributed because the underlying state densities are described differently.

Pre-equilibrium model 1: preeqmode 1

In TALYS-2.0, *preeqmode 1* corresponds to the Exciton model with analytical transition rates and an energy-dependent matrix element. This means that pre-equilibrium emission is described within the exciton framework, but the transition rates between exciton configurations are handled analytically. Physically, this affects the probability that particles are emitted before the system reaches full compound-nuclear equilibration. Since the $^{75}\text{As}(p,4n)^{72}\text{Se}$ channel lies in an energy range where pre-equilibrium contributions can become important, changing the pre-equilibrium prescription can alter both the peak region and the high-energy side of the excitation function.

Pre-equilibrium model 3: preeqmode 3

preeqmode 3 is also an exciton-model approach, but TALYS-2.0 defines it as the Exciton model with numerical transition rates and optical model for collision probability. Relative to *preeqmode 1*, this represents a more elaborate treatment of the transition dynamics, since the collision probability is linked more directly to optical-model information. In physical terms, *preeqmode 3* can therefore change how strongly the reaction flux is shifted into pre-equilibrium particle emission before statistical equilibration is reached. For higher-energy multiple-neutron channels, this may have a marked influence on the peak height and on the competition between neighboring (p,x) channels.

Practical interpretation for the present study

The parameter changes used in this work should therefore not be understood as arbitrary modifications of the calculated cross-sections. The OMP variation probes the sensitivity of the entrance-channel transmission coefficients, the level-density variation probes the statistical population of energetically accessible final states in the competing residual nuclei, and the pre-equilibrium variation probes the extent to which particle emission occurs before full compound-nuclear equilibration. The observed changes in the calculated $^{75}\text{As}(p,4n)^{72}\text{Se}$ excitation function can therefore be interpreted in physical terms, even though the resulting improvement remains local and reaction specific.

Appendix

Sensitivity Studies – Experimental values

Table A-3: Overview of TALYS-2.0 model settings screened in the sensitivity study of the calculated excitation function for the $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction, with individually varied parameter ranges.

Parameter	Threshold [MeV]	Max CS [mb]	E_{max} [MeV]	$\text{CS}_{70\text{MeV}}$ [mb]
Default	31.0	38.1	36.9	9.8
rvomp0.95	31.0	39.3	43.9	9.3
rvomp1.05	31.0	38.0	43.9	10.5
ldmodel2	31.2	53.2	46	16.3
ldmodel5	31.3	40.7	48	13.1
preeqmode1	31.0	35.2	43.2	9.0
preeqmode3	31	68	44	8
Parade-fit	31	84.9	48.4	25.3
TENDL-2025	35.0	44.7	33.7	9.4

Table A-4: Combination of selected TALYS-2.0 parameter settings used to assess their combined influence on the calculated excitation function of the $^{75}\text{As}(p,4n)^{72}\text{Se}$ reaction.

Fit	Threshold [MeV]	Max CS [mb]	E_{max} [MeV]	$\text{CS}_{70\text{MeV}}$ [mb]
ld2_preeq3	31.1	96.3	46.0	11.4
ld2_preeq3_rv095	31.1	96.2	46.0	13.2
ld2_preeq3_rv105	31.1	96.9	46.0	14.7
ld5_preeq3	31.2	72.9	47.8	9.2
ld5_preeq3_rv095	31.2	72.7	47.7	8.6
ld5_preeq3_rv105	31.2	76.3	47.8	12.5
ld5_preeq3_rv110	31.3	64.9	47.8	8.9
ld2_preeq1	31.2	47.7	46.0	12.8
ld2_preeq1_rv095	31.2	48.9	46.0	13.4
ld2_preeq1_rv105	31.2	46.9	46.0	15.2

Appendix

Appendix A-5: Target masses

Table A-5: Mass content of the target nuclide in each irradiated sample.

$^{72}\text{Ge}(\text{p},\text{x})^{72}\text{As}$		$^{\text{nat}}\text{Ga}(\alpha,\text{x})^{72}\text{As}$		$^{69}\text{Ga}(\alpha,\text{x})^{72}\text{As}$		$^{75}\text{As}(\text{p},\text{x})^{72}\text{Se}$	
Sample	Weight [g]	Sample	Weight [g]	Sample	Weight [g]	Sample	Weight [g]
1	0.0022	1	0.0031	1	0.0039	4	0.0218
2	0.0018	3	0.0036	2	0.0014	21	0.0240
3	0.0031	4	0.0028	3	0.0037	31	0.0170
4	0.0033	5	0.0031	4	0.0052	32	0.0145
5	0.0035	8	0.0031	5	0.0020	33	0.0142
6	0.0032	11	0.0150	6	0.0029	41	0.0173
7	0.0028	12	0.0118	7	0.0033	42	0.0134
11	0.0031	13	0.0150	8	0.0034	43	0.0158
12	0.0023	14	0.0149	9	0.0022	44	0.0245
13	0.0021			10	0.0031	51	0.0236
14	0.0026					53	0.0285
15	0.0020					54	0.0194
16	0.0027					62	0.0171
17	0.0075						
18	0.0068						

Appendix

Appendix A-6: Cross-section data

Table A-6: Cross-section values for monitor reactions in $^{nat}\text{Cu}(p,x)$ irradiations. The table lists the effective proton energies, experimentally determined monitor cross-sections, and associated total uncertainties used for beam-current and energy validation in the stacked-foil experiments.

^{65}Zn		^{63}Zn		^{62}Zn		^{58}Co	
Energy [MeV]	CS [mb]	Energy [MeV]	CS [mb]	Energy [MeV]	CS [mb]	Energy [MeV]	CS [mb]
17.3 ± 0.3	41.0 ± 3.7	17.1 ± 0.3	116.5 ± 10.5	44.9 ± 0.2	18.6 ± 1.7	40.2 ± 0.2	46.6 ± 4.2
13.8 ± 0.4	120.0 ± 10.8	13.3 ± 0.4	328.4 ± 29.6	40.2 ± 0.2	13.9 ± 1.3	35.0 ± 0.3	35.3 ± 3.2
17.0 ± 0.3	43.6 ± 3.9	12.5 ± 0.4	359.1 ± 32.3	35.0 ± 0.3	18.0 ± 1.6	29.1 ± 0.3	6.5 ± 0.6
23.0 ± 0.3	12.9 ± 1.2	11.8 ± 0.5	346.4 ± 31.2	29.1 ± 0.3	40.6 ± 3.7		
		10.3 ± 0.5	305.1 ± 27.5	22.5 ± 0.4	67.5 ± 6.1		
		9.4 ± 0.5	270.4 ± 24.3				
		8.5 ± 0.5	248.8 ± 22.4				

Table A-7: Cross-section values for monitor reactions in $^{nat}\text{Cu}(\alpha,x)$ irradiations. Effective α -particle energies, measured monitor-reaction cross-sections, and total uncertainties are reported for the copper monitor foils used to evaluate the incident beam parameters.

Energy [MeV]	CS (^{65}Zn) [mb]	CS (^{66}Ga) [mb]	CS (^{67}Ga) [mb]
29.6 ± 0.3	732.7 ± 65.9	34.6 ± 3.1	296.5 ± 26.7
28.8 ± 0.3	697.4 ± 62.8	37.3 ± 3.4	287.2 ± 25.8
26.4 ± 0.3	711.5 ± 64.0	78.4 ± 7.1	317.2 ± 28.5
23.7 ± 0.4	534.8 ± 48.1	144.5 ± 13.0	259.1 ± 23.3
22.9 ± 0.4	531.9 ± 47.9	192.1 ± 17.3	258.8 ± 23.3
20.6 ± 0.4	293.5 ± 26.4	300.1 ± 27.0	159.5 ± 14.4
18.9 ± 0.5	200.3 ± 18.0	389.7 ± 35.1	108.5 ± 9.8
17.4 ± 0.5	45.1 ± 4.1	432.9 ± 39.0	33.6 ± 3.0
17.1 ± 0.5	23.1 ± 2.1	432.1 ± 38.9	18.9 ± 1.7

Appendix

Table A-8: Cross-section values for monitor reactions in $^{nat}\text{Ti}(p,x)$ irradiations. The table summarizes the effective proton energies, monitor cross-sections, and total uncertainties obtained from natural titanium monitor foils.

Energy [MeV]	CS (^{46}Sc) [mb]	CS (^{48}V) [mb]
65.2 ± 0.3	45.9 ± 4.1	11.8 ± 1.2
62.3 ± 0.3	45.8 ± 4.1	13.1 ± 1.3
59.2 ± 0.3	47.7 ± 4.3	14.1 ± 1.4
56 ± 0.3	50.1 ± 4.6	15.4 ± 1.4
53 ± 0.4	53.7 ± 4.8	16.5 ± 1.5
49.6 ± 0.4	58.0 ± 5.3	18.0 ± 1.6
46.2 ± 0.4	61.0 ± 5.6	20.0 ± 1.8
42.2 ± 0.4	60.8 ± 5.6	23.1 ± 2.1
38.6 ± 0.5	50.4 ± 4.5	26.8 ± 2.4
34.2 ± 0.5	29.4 ± 2.6	30.4 ± 2.7
29.3 ± 0.5	11.9 ± 1.3	35.0 ± 3.2
24.0 ± 0.5	7.6 ± 0.8	51.2 ± 4.6

Table A-9: Measured production cross-sections of ^{72}As and ^{71}As from $^{nat}\text{Ga}(\alpha,x)$ reactions. The table lists the effective α -particle energies, experimentally determined cross-sections, and total uncertainties for arsenic radioisotope formation from natural gallium targets.

Energy [MeV]	CS (^{72}As) [mb]	CS (^{71}As) [mb]
27.5 ± 0.3	51.9 ± 6.8	468.2 ± 61.8
26.8 ± 0.3	67.0 ± 8.8	506.7 ± 66.9
23.7 ± 0.3	192.6 ± 25.4	496.9 ± 65.6
20.0 ± 0.4	488.0 ± 64.4	193.4 ± 25.5
19.5 ± 0.4	554.3 ± 73.2	130.4 ± 17.2
13.4 ± 0.4	441.0 ± 58.2	-
12.5 ± 0.4	247.3 ± 32.6	-

Table A-10: Measured production cross-sections of ^{72}As and ^{71}As from $^{69}\text{Ga}(\alpha,x)$ reactions. The table gives the effective α -particle energies, cross-sections, and total uncertainties for the formation of ^{72}As and ^{71}As from enriched ^{69}Ga target material.

Energy [MeV]	CS (^{72}As) [mb]	CS (^{71}As) [mb]
28 ± 0.3	44.2 ± 6.7	508.9 ± 77.7
25.1 ± 0.3	106.6 ± 15.7	601.4 ± 89.3
24.8 ± 0.3	145.1 ± 21.9	589.3 ± 90.3
21.7 ± 0.3	246.5 ± 36.3	348.6 ± 52.9
21.1 ± 0.3	348.0 ± 52.4	240.8 ± 37.5
18.4 ± 0.4	404.6 ± 59.9	77.7 ± 12.7
16.8 ± 0.4	480.8 ± 72.5	38.8 ± 8.2
14 ± 0.4	559.7 ± 82.6	-
12.1 ± 0.5	348.7 ± 52.6	-
9.8 ± 0.5	57.0 ± 8.5	-

Appendix

Table A-11: Measured cross-sections for the formation of ^{72}Se (measured directly and indirectly via ^{72}As) and ^{75}Se in proton-induced reactions on ^{75}As . Effective proton energies, experimentally determined production cross-sections, and total uncertainties are listed for the investigated $^{75}\text{As}(p,x)$ reaction channels.

Energy [MeV]	CS (^{72}Se (direct)) [mb]	CS (^{72}Se (indirect via ^{72}As)) [mb]	CS (^{75}Se) [mb]
65.2 ± 0.3	25.3 ± 4.2	25.1 ± 4.2	11.0 ± 1.8
62.3 ± 0.3	26.7 ± 4.5	29.5 ± 4.9	11.3 ± 1.9
59.2 ± 0.3	37.0 ± 6.2	42.2 ± 7.5	13.5 ± 2.3
56 ± 0.3	57.8 ± 9.6	63.8 ± 10.6	17.8 ± 3.0
53 ± 0.4	74.0 ± 1.2	83.4 ± 14.1	19.4 ± 3.3
49.6 ± 0.4	82.5 ± 1.4	89.2 ± 15.1	20.5 ± 3.4
46.2 ± 0.4	69.1 ± 1.2	76.9 ± 12.8	19.6 ± 3.3
42.2 ± 0.4	40.3 ± 6.7	45.2 ± 7.5	17.5 ± 2.9
38.6 ± 0.5	16.5 ± 2.8	18.8 ± 3.2	19.6 ± 3.3
34.2 ± 0.5	0.8 ± 1.4	1.6 ± 0.3	26.0 ± 4.4
29.3 ± 0.5	-	0.2 ± 0.1	30.6 ± 5.1

Table A-12: Measured cross-sections for the formation of ^{72}As and ^{71}As in $^{72}\text{Ge}(p,x)$ reactions at JULIC. The table summarizes the effective proton energies, production cross-sections, and total uncertainties obtained from the JULIC stacked-foil irradiation.

Energy [MeV]	CS (^{72}As) [mb]	CS (^{71}As) [mb]
44.6 ± 0.3	42.4 ± 5.5	47.2 ± 6.1
42.5 ± 0.3	48.1 ± 6.2	27.5 ± 3.6
40.0 ± 0.3	44.2 ± 5.3	47.3 ± 6.1
37.7 ± 0.3	22.7 ± 2.7	50.2 ± 6.5
34.9 ± 0.4	28.6 ± 3.4	73.8 ± 9.6
32.3 ± 0.4	29.3 ± 3.5	97.8 ± 12.7
29.2 ± 0.4	33.2 ± 4.0	138.8 ± 18.0
26.24 ± 0.4	44.5 ± 5.3	222.0 ± 28.8
23.1 ± 0.5	60.6 ± 7.3	323.4 ± 42.0
20.1 ± 0.5	113.4 ± 13.6	363.3 ± 47.2
16.0 ± 0.5	350.1 ± 42.0	200.4 ± 26.0
13.7 ± 0.5	649.7 ± 77.9	34.5 ± 4.5
11.1 ± 0.5	713.0 ± 85.5	

Appendix

Table A-13: Measured cross-sections for the formation of ^{72}As and ^{71}As in $^{72}\text{Ge}(p,x)$ reactions at the BC1710 cyclotron. Effective proton energies experimentally determined cross-sections, and total uncertainties are reported for the BC1710 irradiation series.

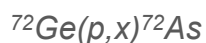
Energy [MeV]	CS (^{72}As) [mb]	CS (^{71}As) [mb]
16.4 ± 0.3	337.8 ± 37.2	283.5 ± 34.0
16.0 ± 0.3	419.3 ± 46.1	263.8 ± 31.6
13.7 ± 0.3	694.5 ± 76.4	6.6 ± 0.8
12.5 ± 0.3	669.5 ± 73.6	
11.7 ± 0.3	712.2 ± 78.3	
10.8 ± 0.4	751.4 ± 82.6	
10.2 ± 0.4	615.3 ± 67.7	
9.3 ± 0.4	546.4 ± 60.1	
8.3 ± 0.4	502.9 ± 55.3	
7.3 ± 0.4	409.7 ± 45.1	

Table A-14: Measured cross-sections for the formation of ^{72}As and ^{71}As in $^{72}\text{Ge}(p,x)$ reactions at the C30XP. The table lists the effective proton energies, production cross-sections, and total uncertainties determined from the C30XP irradiation series.

Energy [MeV]	CS (^{72}As) [mb]	CS (^{71}As) [mb]
24.2 ± 0.3	52.8 ± 6.3	317.6 ± 41.3
20.3 ± 0.3	108.1 ± 12.9	399.1 ± 51.9
16.4 ± 0.3	347.3 ± 41.7	196.5 ± 25.5
16.0 ± 0.3	418.0 ± 50.2	167.8 ± 21.8
14.6 ± 0.4	631.8 ± 75.8	39.8 ± 5.2
13.2 ± 0.4	654.9 ± 78.6	
12.1 ± 0.4	706.6 ± 84.8	

Appendix

Appendix A-7: STACK calculation tables



Projectile data					
Name	Proton number	Molar mass	Incident energy		No. of foils
	opr	upr	startenergy	precision	
H	1	1.0079	25	100	16

Target-Daten											
No.:	Target	protons target	Mass	Weight	Diameter	Description	Area density	average energy	incident energy	Exit energy	Energy absorption
			[g/mol]	[g]	[mm]		[g/cm ²]	[MeV]	[MeV]	[MeV]	[MeV]
		otrg	utrg	weight	dfole		flweight		energy_in	energy_out	
1	Cu	29	63.546	0.0289	13.0	Monitor 1	1	2.177E-02	24.85	25.00	0.30
2	Al	13	26.98154	0.00540	15.0	Cover 17	2	3.056E-03	24.68	24.70	0.05
3	Ge	32	72	0.00750	10.0	Sample 17	2	9.549E-03	24.59	24.65	0.13
4	Al	13	26.98154	0.0183	13.0	Backing	2	1.379E-02	24.41	24.52	0.23
5	Ti	22	47.9	0.0155	13.0	Monitor 2	3	1.168E-02	24.20	24.29	0.17
6	Cu	29	63.546	0.2883	13.0	Degrader	4	2.172E-01	22.51	24.12	3.21
7	Al	13	26.98154	0.00540	15.0	Cover 18	5	3.056E-03	20.88	20.91	0.06
8	Ge	32	72	0.00680	10.0	Sample 18	5	8.658E-03	20.79	20.85	0.13
9	Al	13	26.98154	0.0182	13.0	Backing	5	1.371E-02	20.59	20.72	0.27
10	Cu	29	63.546	0.2372	13.0	Degrader	6	1.787E-01	18.95	20.46	3.01
11	Cu	29	63.546	0.0291	13.0	Monitor 3	7	2.192E-02	17.25	17.45	0.40
12	Al	13	26.98154	0.00492	15.0	Cover 1	8	2.784E-03	17.02	17.05	0.06
13	Ge	32	72	0.00224	10.0	Sample 1	8	2.852E-03	16.97	16.99	0.05
14	Al	13	26.98154	0.0187	13.0	Backing	8	1.409E-02	16.78	16.94	0.32
15	Al	13	26.98154	0.00491	15.0	Cover 2	9	2.778E-03	16.59	16.62	0.06
16	Ge	32	72	0.00182	10.0	Sample 2	9	2.317E-03	16.54	16.56	0.04
17	Al	13	26.98154	0.0188	13.0	Backing	9	1.416E-02	16.35	16.52	0.33
18	Cu	29	63.546	0.0588	13.0	Degrader	10	4.430E-02	15.76	16.19	0.86
19	Al	13	26.98154	0.00492	15.0	Cover 3	11	2.784E-03	15.30	15.33	0.07
20	Ge	32	72	0.00308	10.0	Sample 3	11	3.922E-03	15.23	15.26	0.07
21	Al	13	26.98154	0.018	13.0	Backing	11	1.356E-02	15.02	15.19	0.34
22	Cu	29	63.546	0.0588	13.0	Degrader	12	4.430E-02	14.39	14.85	0.92
23	Al	13	26.98154	0.00493	15.0	Cover 6	13	2.790E-03	13.90	13.94	0.07
24	Ge	32	72	0.00320	10.0	Sample 6	13	4.074E-03	13.82	13.86	0.08
25	Al	13	26.98154	0.0179	13.0	Backing	13	1.349E-02	13.60	13.78	0.36
26	Cu	29	63.546	0.0292	13.0	Monitor 4	14	2.200E-02	13.18	13.42	0.49
27	Al	13	26.98154	0.00492	15.0	Cover 7	15	2.784E-03	12.89	12.93	0.08
28	Ge	32	72	0.00281	10.0	Sample 7	15	3.578E-03	12.82	12.86	0.08
29	Al	13	26.98154	0.018	13.0	Backing	15	1.356E-02	12.59	12.78	0.39
30	Ni	28	58.7	1.1823792	13.0	Beam dump	16	8.908E-01	6.20	12.39	12.39

Figure A-1: Foil stack for ^{72}As production using ^{72}Ge enriched materials. Irradiated at the C30XP.

Appendix

Projectile data													
Name	Proton number	Molar mass			Incident energy		No. of foils						
	opr	upr			startenergy	precision							
H	1	1.0079			44	100	34						

Target-Daten												
No.:	Target	protons target	Mass	Weight	Diameter	Description		Area density	average energy	incident energy	Exit energy	Energy absorption
			[g/mol]	[g]	[mm]			[g/cm ²]	[MeV]	[MeV]	[MeV]	[MeV]
		otrg	utrg	weight	dfolie			flweight		energy_in	energy_out	
1	Cu	29	63.546	0.0295	13.0	Monitor 1	1	2.223E-02	43.90	44.00	43.80	0.20
2	Al	13	26.98154	0.00491	15.0	Cover 1	2	2.778E-03	43.79	43.80	43.77	0.03
3	Ge	32	72	0.00224	10.0	Sample 1	2	2.852E-03	43.76	43.77	43.75	0.02
4	Al	13	26.98154	0.0187	13.0	Backing	2	1.409E-02	43.67	43.75	43.59	0.15
5	Cu	29	63.546	0.2868	13.0	Degrader	3	2.161E-01	42.61	43.59	41.62	1.98
6	Al	13	26.98154	0.00491	15.0	Cover 2	4	2.778E-03	41.60	41.62	41.58	0.03
7	Ge	32	72	0.00182	10.0	Sample 2	4	2.317E-03	41.57	41.58	41.56	0.02
8	Al	13	26.98154	0.0188	13.0	Backing	4	1.416E-02	41.48	41.56	41.41	0.16
9	Cu	29	63.546	0.2857	13.0	Degrader	5	2.152E-01	40.38	41.41	39.35	2.05
10	Cu	29	63.546	0.0301	13.0	Monitor 2	6	2.268E-02	39.24	39.35	39.13	0.22
11	Al	13	26.98154	0.00492	15.0	Cover 3	7	2.784E-03	39.12	39.13	39.10	0.03
12	Ge	32	72	0.00308	10.0	Sample 3	7	3.922E-03	39.08	39.10	39.06	0.04
13	Al	13	26.98154	0.018	13.0	Backing	7	1.356E-02	38.98	39.06	38.90	0.16
14	Cu	29	63.546	0.2867	13.0	Degrader	8	2.160E-01	37.82	38.90	36.74	2.16
15	Al	13	26.98154	0.00494	15.0	Cover 4	9	2.795E-03	36.73	36.74	36.71	0.03
16	Ge	32	72	0.00334	10.0	Sample 4	9	4.253E-03	36.69	36.71	36.67	0.04
17	Al	13	26.98154	0.0179	13.0	Backing	9	1.349E-02	36.58	36.67	36.50	0.17
18	Cu	29	63.546	0.2901	13.0	Degrader	10	2.186E-01	35.35	36.50	34.20	2.30
19	Cu	29	63.546	0.03	13.0	Monitor 3	11	2.260E-02	34.08	34.20	33.96	0.24
20	Al	13	26.98154	0.00494	15.0	Cover 5	12	2.795E-03	33.94	33.96	33.92	0.04
21	Ge	32	72	0.00346	10.0	Sample 5	12	4.405E-03	33.90	33.92	33.87	0.05
22	Al	13	26.98154	0.018	13.0	Backing	12	1.356E-02	33.78	33.87	33.70	0.18
23	Cu	29	63.546	0.2882	13.0	Degrader	13	2.171E-01	32.48	33.70	31.26	2.43
24	Al	13	26.98154	0.00493	15.0	Cover 6	14	2.790E-03	31.24	31.26	31.22	0.04
25	Ge	32	72	0.00320	10.0	Sample 6	14	4.074E-03	31.20	31.22	31.18	0.05
26	Al	13	26.98154	0.0179	13.0	Backing	14	1.349E-02	31.08	31.18	30.99	0.19
27	Cu	29	63.546	0.2894	13.0	Degrader	15	2.180E-01	29.68	30.99	28.37	2.62
28	Cu	29	63.546	0.0301	13.0	Monitor 4	16	2.268E-02	28.23	28.37	28.09	0.28
29	Al	13	26.98154	0.00492	15.0	Cover 7	17	2.784E-03	28.07	28.09	28.05	0.04
30	Ge	32	72	0.00281	10.0	Sample 7	18	3.578E-03	28.03	28.05	28.00	0.04
31	Al	13	26.98154	0.018	13.0	Backing	19	1.356E-02	27.90	28.00	27.80	0.21
32	Cu	29	63.546	0.287	13.0	Degrader	20	2.162E-01	26.38	27.80	24.96	2.83
33	Al	13	26.98154	0.00516	15.0	Cover 11	21	2.920E-03	24.94	24.96	24.91	0.05
34	Ge	32	72	0.00307	10.0	Sample 11	21	3.909E-03	24.89	24.91	24.86	0.05
35	Al	13	26.98154	0.0182	13.0	Backing	21	1.371E-02	24.75	24.86	24.63	0.23
36	Cu	29	63.546	0.2379	13.0	Degrader	22	1.792E-01	23.35	24.63	22.06	2.58
37	Cu	29	63.546	0.0302	13.0	Monitor 5	23	2.275E-02	21.89	22.06	21.71	0.34
38	Al	13	26.98154	0.00530	15.0	Cover 12	24	2.999E-03	21.69	21.71	21.66	0.06
39	Ge	32	72	0.00230	10.0	Sample 12	24	2.928E-03	21.64	21.66	21.62	0.04
40	Al	13	26.98154	0.018	13.0	Backing	24	1.356E-02	21.49	21.62	21.36	0.25
41	Cu	29	63.546	0.2381	13.0	Degrader	25	1.794E-01	19.91	21.36	18.45	2.91
42	Al	13	26.98154	0.00530	15.0	Cover 13	26	2.999E-03	18.42	18.45	18.39	0.06
43	Ge	32	72	0.00213	10.0	Sample 13	26	2.712E-03	18.37	18.39	18.35	0.04
44	Al	13	26.98154	0.0182	13.0	Backing	26	1.371E-02	18.20	18.35	18.05	0.29
45	Cu	29	63.546	0.2383	13.0	Degrader	27	1.795E-01	16.37	18.05	14.68	3.37
46	Cu	29	63.546	0.0301	13.0	Monitor 6	28	2.268E-02	14.45	14.68	14.21	0.47
47	Al	13	26.98154	0.00520	15.0	Cover 14	29	2.943E-03	14.18	14.21	14.14	0.08
48	Ge	32	72	0.00256	10.0	Sample 14	29	3.259E-03	14.10	14.14	14.07	0.07
49	Al	13	26.98154	0.0181	13.0	Backing	29	1.364E-02	13.89	14.07	13.71	0.36
50	Cu	29	63.546	0.1191	13.0	Degrader	30	8.973E-02	12.69	13.71	11.67	2.04
51	Al	13	26.98154	0.00533	15.0	Cover 15	31	3.016E-03	11.63	11.67	11.58	0.09
52	Ge	32	72	0.00197	10.0	Sample 15	31	2.508E-03	11.55	11.58	11.52	0.06
53	Al	13	26.98154	0.0181	13.0	Backing	31	1.364E-02	11.31	11.52	11.10	0.42
54	Cu	29	63.546	0.1193	13.0	Degrader	32	8.988E-02	9.87	11.10	8.64	2.46
55	Al	13	26.98154	0.00526	15.0	Cover 16	33	2.977E-03	8.58	8.64	8.53	0.11
56	Ge	32	72	0.00267	10.0	Sample 16	33	3.400E-03	8.48	8.53	8.43	0.10
57	Al	13	26.98154	0.0183	13.0	Backing	33	1.379E-02	8.15	8.43	7.88	0.55
58	Ni	28	58.7	1.1823792	13.0	Beam dump	34	8.908E-01	3.94	7.88	0.00	7.88

Figure A-2: Foil stack for ⁷²As production using ⁷²Ge enriched materials. Irradiated at JULIC.

Appendix

Projectile data					
Name	Proton number	Molar mass	Incident energy		No. of foils
	opr	upr	startenergy	precision	
H	1	1.0079	17.4	100	20

Target-Daten											
No.:	Target	protons target	Mass	Weight	Diameter	Description	Area density	average energy	incident energy	Exit energy	Energy absorption
			[g/mol]	[g]	[mm]		[g/cm ²]	[MeV]	[MeV]	[MeV]	[MeV]
		otrg	utrg	weight	dfolie		flweight		energy_in	energy_out	
1	Cu	29	63.546	0.01168	13.0	Monitor 1	1	8.800E-03	17.32	17.40	0.16
2	Al	13	26.98154	0.00491	15.0	Cover 1	2	2.778E-03	17.21	17.24	0.06
3	Ge	32	72	0.00224	10.0	Sample 1	2	2.852E-03	17.15	17.18	0.05
4	Al	13	26.98154	0.0187	13.0	Backing	2	1.409E-02	16.97	17.13	0.32
5	Al	13	26.98154	0.00491	15.0	Cover 2	3	2.778E-03	16.78	16.81	0.06
6	Ge	32	72	0.00182	10.0	Sample 2	3	2.317E-03	16.73	16.75	0.04
7	Al	13	26.98154	0.0188	13.0	Backing	3	1.416E-02	16.55	16.71	0.32
8	Cu	29	63.546	0.11876	13.0	Degrader	4	8.947E-02	15.51	16.38	1.75
9	Al	13	26.98154	0.00492	15.0	Cover 3	5	2.784E-03	14.60	14.63	0.07
10	Ge	32	72	0.00308	10.0	Sample 3	5	3.922E-03	14.52	14.56	0.08
11	Al	13	26.98154	0.018	13.0	Backing	5	1.356E-02	14.31	14.49	0.35
12	Al	13	26.98154	0.00494	15.0	Cover 4	6	2.795E-03	14.10	14.14	0.07
13	Ge	32	72	0.00334	10.0	Sample 4	6	4.253E-03	14.02	14.07	0.09
14	Al	13	26.98154	0.0179	13.0	Backing	6	1.349E-02	13.80	13.98	0.36
15	Cu	29	63.546	0.01198	13.0	Monitor 2	7	9.026E-03	13.53	13.62	0.20
16	Al	13	26.98154	0.00494	15.0	Cover 5	8	2.795E-03	13.39	13.43	0.08
17	Ge	32	72	0.00346	10.0	Sample 5	8	4.405E-03	13.31	13.35	0.09
18	Al	13	26.98154	0.018	13.0	Backing	8	1.356E-02	13.07	13.26	0.37
19	Cu	29	63.546	0.01195	13.0	Monitor 3	9	9.003E-03	12.78	12.89	0.20
20	Al	13	26.98154	0.00493	15.0	Cover 6	10	2.790E-03	12.64	12.68	0.08
21	Ge	32	72	0.00320	10.0	Sample 6	10	4.074E-03	12.56	12.60	0.09
22	Al	13	26.98154	0.0179	13.0	Backing	10	1.349E-02	12.32	12.51	0.39
23	Cu	29	63.546	0.01211	13.0	Monitor 4	11	9.124E-03	12.02	12.12	0.22
24	Al	13	26.98154	0.00492	15.0	Cover 7	12	2.784E-03	11.87	11.91	0.08
25	Ge	32	72	0.00281	10.0	Sample 7	12	3.578E-03	11.78	11.82	0.08
26	Al	13	26.98154	0.018	13.0	Backing	12	1.356E-02	11.54	11.74	0.41
27	Al	13	26.98154	0.00516	15.0	Cover 11	13	2.920E-03	11.29	11.33	0.09
28	Ge	32	72	0.00307	10.0	Sample 11	13	3.909E-03	11.19	11.24	0.09
29	Al	13	26.98154	0.0182	13.0	Backing	13	1.371E-02	10.93	11.15	0.43
30	Cu	29	63.546	0.012	13.0	Monitor 5	14	9.041E-03	10.59	10.71	0.24
31	Al	13	26.98154	0.00520	15.0	Cover 14	15	2.943E-03	10.43	10.48	0.10
32	Ge	32	72	0.00256	10.0	Sample 14	15	3.259E-03	10.34	10.38	0.08
33	Al	13	26.98154	0.0181	13.0	Backing	15	1.364E-02	10.07	10.30	0.46
34	Cu	29	63.546	0.01178	13.0	Monitor 6	16	8.875E-03	9.71	9.84	0.25
35	Al	13	26.98154	0.00533	15.0	Cover 15	17	3.016E-03	9.54	9.59	0.11
36	Ge	32	72	0.00197	10.0	Sample 15	17	2.508E-03	9.45	9.48	0.07
37	Al	13	26.98154	0.0181	13.0	Backing	17	1.364E-02	9.17	9.42	0.50
38	Cu	29	63.546	0.01168	13.0	Monitor 7	18	8.800E-03	8.79	8.92	0.26
39	Al	13	26.98154	0.00526	15.0	Cover 16	19	2.977E-03	8.60	8.66	0.11
40	Ge	32	72	0.00267	10.0	Sample 16	19	3.400E-03	8.50	8.55	0.10
41	Al	13	26.98154	0.0183	13.0	Backing	19	1.379E-02	8.17	8.45	0.55
42	Ni	28	58.7	1.1823792	13.0	Beam dump	20	8.908E-01	3.95	7.90	7.90

Figure A-3: Foil stack for ⁷²As production using ⁷²Ge enriched materials. Irradiated at the BC 1710.

Appendix

$^{nat}\text{Ga}(\alpha, x)^{72}\text{As}$

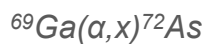
Projectile data					
Name	Proton number	Molar mass	Incident energy		No. of foils
	opr	upr	startenergy	precision	
He	2	4.0026	30	100	10

Target-Daten											
No.:	Target	protons target	Mass	Weight	Diameter	Description	Area density	average energy	incident energy	Exit energy	Energy absorption
			[g/mol]	[g]	[mm]		[g/cm ²]	[MeV]	[MeV]	[MeV]	[MeV]
		otrg	utrg	weight	dfolie		flweight		energy_in	energy_out	
1	Cu	29	63.546	0.0123	13.0	Monitor 1	1	9.267E-03	29.37	30.00	1.26
2	Al	13	26.98154	0.00350	13.0	Spacer	2	2.637E-03	28.51	28.74	0.46
3	Al	13	26.98154	0.00540	16.0	Cover 1	3	2.686E-03	28.04	28.28	0.48
4	Ga	31	69.72	0.00310	10.0	Sample 1	3	3.947E-03	27.53	27.80	0.54
5	Al	13	26.98154	0.0189	13.0	Backing	3	1.424E-02	25.92	27.27	2.69
6	Al	13	26.98154	0.00560	16.0	Cover 2	4	2.785E-03	24.30	24.57	0.55
7	Ga	31	69.72	0.00360	10.0	Sample 3	4	4.584E-03	23.68	24.02	0.69
8	Al	13	26.98154	0.0179	13.0	Backing	4	1.349E-02	21.88	23.33	2.89
10	Al	13	26.98154	0.00560	16.0	Cover 3	5	2.785E-03	20.12	20.43	0.64
11	Ga	31	69.72	0.00280	10.0	Sample 4	5	3.565E-03	19.49	19.80	0.62
12	Al	13	26.98154	0.0179	13.0	Backing	5	1.349E-02	17.47	19.18	3.42
	Al	13	26.98154	0.00360	13.0	Spacer	6	2.712E-03	18.86	19.18	0.65
13	Cu	29	63.546	0.0121	13.0	Monitor 4	7	9.116E-03	14.76	15.76	1.99
	Al	13	26.98154	0.00350	13.0	Spacer	8	2.637E-03	18.20	18.53	0.65
14	Al	13	26.98154	0.00550	16.0	Cover 4	9	2.735E-03	13.34	13.77	0.85
15	Ga	31	69.72	0.00310	10.0	Sample 5	9	3.947E-03	12.46	12.92	0.92
16	Al	13	26.98154	0.0180	13.0	Backing	9	1.356E-02	9.28	12.00	5.43
14	Al	13	26.98154	0.00550	16.0	Cover 4	10	2.735E-03	5.81	6.56	1.50
15	Ga	31	69.72	0.00310	10.0	Sample 8	10	3.947E-03	4.21	5.06	1.69
16	Al	13	26.98154	0.0180	13.0	Backing	10	1.356E-02	1.68	3.37	3.37

Target-Daten											
No.:	Target	protons target	Mass	Weight	Diameter	Description	Area density	average energy	incident energy	Exit energy	Energy absorption
			[g/mol]	[g]	[mm]		[g/cm ²]	[MeV]	[MeV]	[MeV]	[MeV]
		otrg	utrg	weight	dfolie		flweight		energy_in	energy_out	
1	Cu	29	63.546	0.0119	13.0	Monitor 1	1	8.965E-03	29.39	30.00	1.21
2	Al	13	26.98154	0.00360	13.0	Spacer	2	2.712E-03	28.55	28.79	0.48
3	Al	13	26.98154	0.00540	16.0	Cover 12	3	2.686E-03	28.07	28.31	0.48
4	Ga	31	69.72	0.01180	10.0	Sample 12	3	1.502E-02	26.79	27.83	2.08
5	Al	13	26.98154	0.0107	13.0	Backing	3	8.061E-03	24.97	25.75	1.57
6	Cu	29	63.546	0.012	13.0	Monitor 2	4	9.041E-03	23.46	24.18	1.44
7	Al	13	26.98154	0.00370	13.0	Spacer	5	2.788E-03	22.45	22.74	0.59
8	Al	13	26.98154	0.00540	16.0	Cover 14	6	2.686E-03	21.87	22.16	0.58
9	Ga	31	69.72	0.01490	10.0	Sample 14	6	1.897E-02	19.97	21.58	3.23
10	Al	13	26.98154	0.0108	13.0	Backing	6	8.137E-03	17.31	18.35	2.08
13	Al	13	26.98154	0.00550	16.0	Cover 1	7	2.735E-03	15.90	16.27	0.74
14	Ga	31	69.72	0.01500	10.0	Sample 11	7	1.910E-02	13.41	15.53	4.24
15	Al	13	26.98154	0.0108	13.0	Backing	7	8.137E-03	9.71	11.29	3.16
18	Al	13	26.98154	0.00550	16.0	Cover 3	8	2.735E-03	7.50	8.13	1.27
19	Ga	31	69.72	0.01500	10.0	Sample 13	8	1.910E-02	3.43	6.86	6.86
20	Al	13	26.98154	0.0107	13.0	Backing	8	8.061E-03	0.00	0.00	0.00

Figure A-4: Foil stack 1&2 for ^{72}As production using natural Gallium targets. Irradiated at the C30XP.

Appendix



Projektil-Daten					
Name	O-zahl Projektil	Molmasse	Anfangs- energie	Genauig-keit	Folien- zahl
He	opr	upr	startenergy	precision	
He	2	4.0026	30.2	100	15

Target-Daten												
Nr.:	Target	O-Zahl Target	Molmasse	Gewicht	Durchmesser	Beschreibung	Kenng.	Flächen- gewicht	mittlere Energie	Eintritts- energie	Austritts-energie	Energie- absorption
		otrg	[g/mol] utrg	[g] weight	[mm] dfole			[g/cm ²] flweight	[MeV]	[MeV] energy in	[MeV] energy out	[MeV]
1	Cu	29	63.546	0.012	13.0	Monitor 1	1	9.041E-03	29.59	30.20	28.98	1.22
2	Al	13	26.98154	0.0018	13.0	Spacer	2	1.356E-03	28.86	28.98	28.74	0.24
3	Al	13	26.98154	0.0027	16.0	Sample_Cover1	3	1.343E-03	28.63	28.74	28.51	0.24
4	O	8	15.9994	0.0007	13.0	Sample 1	3	5.274E-04	28.46	28.51	28.40	0.11
5	Ga	31	69.72	0.0019	13.0	Sample 1	3	1.462E-03	28.31	28.40	28.21	0.19
6	O	8	15.9994	0.0007	13.0	Sample 1	3	5.274E-04	28.15	28.21	28.10	0.11
7	Ga	31	69.72	0.0019	13.0	Sample 1	3	1.462E-03	28.00	28.10	27.90	0.20
8	O	8	15.9994	0.0007	13.0	Sample 1	3	5.274E-04	27.85	27.90	27.80	0.11
9	Al	13	26.98154	0.0037	13.0	Sample Backing 1	3	2.788E-03	27.54	27.80	27.29	0.50
10	Cu	29	63.546	0.0120	13.0	Monitor 2	4	9.041E-03	26.64	27.29	25.98	1.31
11	Al	13	26.98154	0.0018	13.0	Spacer	5	1.356E-03	25.85	25.98	25.72	0.26
12	Al	13	26.98154	0.0027	16.0	Sample_Cover 3	6	1.343E-03	25.59	25.72	25.47	0.26
13	O	8	15.9994	0.0007	13.0	Sample 3	6	5.274E-04	25.41	25.47	25.35	0.12
14	Ga	31	69.72	0.0018	13.0	Sample 3	6	1.386E-03	25.25	25.35	25.15	0.20
15	O	8	15.9994	0.0007	13.0	Sample 3	6	5.274E-04	25.09	25.15	25.03	0.12
16	Ga	31	69.72	0.0018	13.0	Sample 3	6	1.386E-03	24.93	25.03	24.83	0.20
17	O	8	15.9994	0.0007	13.0	Sample 3	6	5.274E-04	24.77	24.83	24.71	0.12
18	Al	13	26.98154	0.0037	13.0	Sample Backing 3	6	2.788E-03	24.44	24.71	24.16	0.55
19	Cu	29	63.546	0.012	13.0	Monitor 3	7	9.041E-03	23.44	24.16	22.72	1.44
20	Al	13	26.98154	0.0018	13.0	Spacer	8	1.356E-03	22.58	22.72	22.44	0.28
21	Al	13	26.98154	0.0024	16.0	Sample_Cover 4	9	1.194E-03	22.31	22.44	22.19	0.25
22	O	8	15.9994	0.0007	13.0	Sample 4	9	5.274E-04	22.12	22.19	22.06	0.13
23	Ga	31	69.72	0.0026	13.0	Sample 4	9	1.944E-03	21.90	22.06	21.75	0.31
24	O	8	15.9994	0.0007	13.0	Sample 4	9	5.274E-04	21.68	21.75	21.62	0.13
25	Ga	31	69.72	0.0026	13.0	Sample 4	9	1.944E-03	21.46	21.62	21.30	0.31
26	O	8	15.9994	0.0007	13.0	Sample 4	9	5.274E-04	21.23	21.30	21.17	0.13
27	Al	13	26.98154	0.0035	13.0	Sample Backing 4	9	2.637E-03	20.87	21.17	20.58	0.59
28	Cu	29	63.546	0.0120	13.0	Monitor 4	10	9.041E-03	19.77	20.58	18.96	1.62
29	Al	13	26.98154	0.0018	13.0	Spacer	11	1.356E-03	18.80	18.96	18.64	0.33
30	Al	13	26.98154	0.0027	16.0	Sample_Cover_5	12	1.343E-03	18.47	18.64	18.31	0.33
31	O	8	15.9994	0.0005	13.0	Sample 5	12	3.767E-04	18.25	18.31	18.20	0.11
32	Ga	31	69.72	0.0010	13.0	Sample 5	12	7.685E-04	18.13	18.20	18.06	0.14
33	O	8	15.9994	0.0005	13.0	Sample 5	12	3.767E-04	18.01	18.06	17.95	0.11
34	Ga	31	69.72	0.0010	13.0	Sample 5	12	7.685E-04	17.88	17.95	17.81	0.14
35	O	8	15.9994	0.0005	13.0	Sample 5	12	3.767E-04	17.76	17.81	17.70	0.11
36	Al	13	26.98154	0.0035	13.0	Sample Backing 5	12	2.637E-03	17.37	17.70	17.03	0.67
37	Cu	29	63.546	0.0120	13.0	Monitor 5	13	9.041E-03	16.10	17.03	15.17	1.86
38	Al	13	26.98154	0.0018	13.0	Spacer	14	1.356E-03	14.97	15.17	14.78	0.39
39	Al	13	26.98154	0.0027	16.0	Sample_Cover 6	15	1.343E-03	14.59	14.78	14.39	0.39
40	O	8	15.9994	0.0006	13.0	Sample 6	15	4.520E-04	14.31	14.39	14.24	0.15
41	Ga	31	69.72	0.0015	13.0	Sample 6	15	1.092E-03	14.12	14.24	14.00	0.23
42	O	8	15.9994	0.0006	13.0	Sample 6	15	4.520E-04	13.92	14.00	13.84	0.16
43	Ga	31	69.72	0.0015	13.0	Sample 6	15	1.092E-03	13.72	13.84	13.61	0.24
44	O	8	15.9994	0.0006	13.0	Sample 6	15	4.520E-04	13.52	13.61	13.44	0.16
45	Al	13	26.98154	0.0036	13.0	Sample Backing 6	15	2.712E-03	13.02	13.44	12.59	0.85

Figure A-5: Foil stack 1 for ^{72}As production using ^{69}Ge enriched targets. Irradiated at the C30XP.

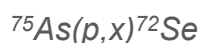
Appendix

Projekttil-Daten					
Name	O-zahl Projekttil	Molmasse			
	opr	upr			
He	2	4.0026	Anfangs- energie	Genauig-keit	Folien- zahl
			startenergy	precision	
			29.55	100	15

Target-Daten												
Nr.:	Target	O-Zahl Target	Molmasse	Gewicht	Durchmesser	Beschreibung	Kenng.	Flächen- gewicht	mittlere Energie	Eintritts- energie	Austritts-energie	Energie- absorption
		otrg	[g/mol] utrg	[g] weight	[mm] dfolie			[g/cm ²] flweight	[MeV]	[MeV] energy in	[MeV] energy out	[MeV]
1	Cu	29	63.546	0.0120	13.0	Monitor 6	1	9.041E-03	28.93	29.55	28.31	1.24
2	Al	13	26.98154	0.0180	13.0	Spacer	2	1.356E-02	27.07	28.31	25.83	2.48
3	Al	13	26.98154	0.0027	16.0	Sample Cover 7	3	1.343E-03	25.70	25.83	25.58	0.26
4	O	8	15.9994	0.0006	13.0	Sample 7	3	4.520E-04	25.53	25.58	25.48	0.10
5	Ga	31	69.72	0.0017	13.0	Sample 7	3	1.258E-03	25.39	25.48	25.30	0.18
6	O	8	15.9994	0.0006	13.0	Sample 7	3	4.520E-04	25.25	25.30	25.20	0.10
7	Ga	31	69.72	0.0017	13.0	Sample 7	3	1.258E-03	25.10	25.20	25.01	0.18
8	O	8	15.9994	0.0006	13.0	Sample 7	3	4.520E-04	24.96	25.01	24.91	0.10
9	Al	13	26.98154	0.0035	13.0	Sample Backing 7	3	2.637E-03	24.65	24.91	24.39	0.52
10	Cu	29	63.546	0.0120	13.0	Monitor 7	4	9.041E-03	23.68	24.39	22.97	1.43
11	Al	13	26.98154	0.0018	13.0	Spacer	5	1.356E-03	22.83	22.97	22.68	0.28
12	Al	13	26.98154	0.0027	16.0	Sample Cover 8	6	1.343E-03	22.54	22.68	22.40	0.28
13	O	8	15.9994	0.0006	13.0	Sample 8	6	4.520E-04	22.35	22.40	22.29	0.11
14	Ga	31	69.72	0.0017	13.0	Sample 8	6	1.296E-03	22.19	22.29	22.09	0.20
15	O	8	15.9994	0.0006	13.0	Sample 8	6	4.520E-04	22.03	22.09	21.98	0.11
16	Ga	31	69.72	0.0017	13.0	Sample 8	6	1.296E-03	21.87	21.98	21.77	0.21
17	O	8	15.9994	0.0006	13.0	Sample 8	6	4.520E-04	21.71	21.77	21.66	0.11
18	Al	13	26.98154	0.0038	13.0	Sample Backing 8	6	2.863E-03	21.34	21.66	21.03	0.63
19	Cu	29	63.546	0.012	13.0	Monitor 8	7	9.041E-03	20.23	21.03	19.44	1.59
20	Al	13	26.98154	0.0018	13.0	Spacer	8	1.356E-03	19.28	19.44	19.12	0.32
21	Al	13	26.98154	0.0027	16.0	Sample Cover 9	9	1.343E-03	18.96	19.12	18.80	0.32
22	O	8	15.9994	0.0005	13.0	Sample 9	9	3.767E-04	18.74	18.80	18.69	0.10
23	Ga	31	69.72	0.0011	13.0	Sample 9	9	8.363E-04	18.62	18.69	18.54	0.15
24	O	8	15.9994	0.0005	13.0	Sample 9	9	3.767E-04	18.49	18.54	18.44	0.11
25	Ga	31	69.72	0.0011	13.0	Sample 9	9	8.363E-04	18.36	18.44	18.29	0.15
26	O	8	15.9994	0.0005	13.0	Sample 9	9	3.767E-04	18.23	18.29	18.18	0.11
27	Al	13	26.98154	0.0035	13.0	Sample Backing 9	9	2.637E-03	17.85	18.18	17.52	0.66
28	Cu	29	63.546	0.0120	13.0	Monitor 9	10	9.041E-03	16.61	17.52	15.69	1.82
29	Al	13	26.98154	0.0018	13.0	Spacer	11	1.356E-03	15.51	15.69	15.32	0.38
30	Al	13	26.98154	0.0027	16.0	Sample Cover 10	12	1.343E-03	15.13	15.32	14.94	0.38
31	O	8	15.9994	0.0006	13.0	Sample 10	12	4.520E-04	14.86	14.94	14.79	0.15
32	Ga	31	69.72	0.0015	13.0	Sample 10	12	1.160E-03	14.67	14.79	14.55	0.24
33	O	8	15.9994	0.0006	13.0	Sample 10	12	4.520E-04	14.47	14.55	14.39	0.15
34	Ga	31	69.72	0.0015	13.0	Sample 10	12	1.160E-03	14.27	14.39	14.15	0.25
35	O	8	15.9994	0.0006	13.0	Sample 10	12	4.520E-04	14.07	14.15	13.99	0.16
36	Al	13	26.98154	0.0036	13.0	Sample Backing 10	12	2.712E-03	13.57	13.99	13.16	0.83
37	Cu	29	63.546	0.0120	13.0	Monitor 10	13	9.041E-03	12.03	13.16	10.90	2.26
38	Al	13	26.98154	0.0018	13.0	Spacer	14	1.356E-03	10.65	10.90	10.41	0.49
39	Al	13	26.98154	0.0027	16.0	Sample Cover 2	15	1.343E-03	10.16	10.41	9.90	0.51
40	O	8	15.9994	0.0003	13.0	Sample 2	15	2.260E-04	9.85	9.90	9.80	0.10
41	Ga	31	69.72	0.0006	13.0	Sample 2	15	4.520E-04	9.74	9.80	9.68	0.12
42	O	8	15.9994	0.0003	13.0	Sample 2	15	2.260E-04	9.63	9.68	9.57	0.10
43	Ga	31	69.72	0.0006	13.0	Sample 2	15	4.520E-04	9.51	9.57	9.45	0.12
44	O	8	15.9994	0.0003	13.0	Sample 2	15	2.260E-04	9.40	9.45	9.34	0.11
45	Al	13	26.98154	0.0037	13.0	Sample Backing 2	15	2.788E-03	8.76	9.34	8.18	1.16

Figure A-6: Foil stack 2 for ⁷²As production using ⁶⁹Ge enriched targets. Irradiated at the C30XP.

Appendix



Projektil-Daten		
Name	O-zahl Projektil	Molmasse
H	opr	upr
1	1	1.01

Anfangs- energie	Genauig- keit	Folien- zahl
startenergy	precision	
66.5	100	58

Target-Daten												
Nr.:	Target	O-Zahl Target	Molmasse	Gewicht	Durchmesser	Dicke/Masse	Kenng.	Flächen- gewicht	mittlere Energie	Eintritts- energie	Austritts-energie	Energie- absorption
			[g/mol]	[g]	[mm]			[g/cm²]	[MeV]	[MeV]	[MeV]	[MeV]
		otrg	utrg	weight	dfolie			flweight		energy_in	energy_out	
1	Al	13	26.98	0.18	13.0	Top Cover	1	1.356E-01	65.96	66.50	65.43	1.07
2	Ti	22	47.90	0.015	13.0	Monitor 1	2	1.130E-02	65.39	65.43	65.35	0.08
3	Al	13	26.98	0.0024	13.0	Sam_Cover_4	3	1.808E-03	65.34	65.35	65.33	0.01
4	O	8	16.00	0.00230	13.0	Sample_4	3	1.733E-03	65.33	65.33	65.32	0.02
5	As	33	74.92	0.01092	13.0	Sample_4	3	8.227E-03	65.29	65.32	65.27	0.05
6	O	8	16.00	0.00230	13.0	Sample_4	3	1.733E-03	65.26	65.27	65.25	0.02
7	As	33	74.92	0.01092	13.0	Sample_4	3	8.227E-03	65.22	65.25	65.20	0.05
8	O	8	16.00	0.00230	13.0	Sample_4	3	1.733E-03	65.19	65.20	65.18	0.02
9	Al	13	26.98	0.08830	13.0	Backing_4	3	6.652E-02	64.92	65.18	64.65	0.53
10	W	74	183.85	0.512	13.0	Degrader	4	3.857E-01	63.66	64.65	62.67	1.98
13	Al	13	26.98	0.018	13.0	Spacer	5	1.356E-02	62.62	62.67	62.56	0.11
14	Ti	22	47.90	0.015	13.0	Monitor 2	6	1.130E-02	62.52	62.56	62.48	0.08
15	Al	13	26.98	0.018	13.0	Spacer	7	1.356E-02	62.42	62.48	62.37	0.11
16	Al	13	26.98	0.0024	13.0	Sam_Cover_21	8	1.808E-03	62.36	62.37	62.35	0.01
17	O	8	16.00	0.00266	13.0	Sample_21	8	2.004E-03	62.34	62.35	62.34	0.02
18	As	33	74.92	0.012	13.0	Sample_21	8	9.041E-03	62.31	62.34	62.28	0.06
19	O	8	16.00	0.00266	13.0	Sample_21	8	2.004E-03	62.27	62.28	62.26	0.02
20	As	33	74.92	0.012	13.0	Sample_21	8	9.041E-03	62.23	62.26	62.20	0.06
21	O	8	16.00	0.00266	13.0	Sample_21	8	2.004E-03	62.19	62.20	62.18	0.02
22	Al	13	26.98	0.08830	13.0	Backing_21	8	6.652E-02	61.90	62.18	61.63	0.55
23	W	74	183.85	0.512	13.0	Degrader	9	3.857E-01	60.61	61.63	59.58	2.04
26	Al	13	26.98	0.018	13.0	Spacer	10	1.356E-02	59.53	59.58	59.47	0.12
27	Ti	22	47.90	0.015	13.0	Monitor 3	11	1.130E-02	59.43	59.47	59.38	0.09
28	Al	13	26.98	0.018	13.0	Spacer	12	1.356E-02	59.33	59.38	59.27	0.12
29	Al	13	26.98	0.0024	13.0	Sam_Cover_31	13	1.808E-03	59.26	59.27	59.25	0.02
30	O	8	16.00	0.00210	13.0	Sample_31	13	1.582E-03	59.24	59.25	59.24	0.02
31	As	33	74.92	0.00852	13.0	Sample_31	13	6.419E-03	59.22	59.24	59.19	0.04
32	O	8	16.00	0.00210	13.0	Sample_31	13	1.582E-03	59.19	59.19	59.18	0.02
33	As	33	74.92	0.00852	13.0	Sample_31	13	6.419E-03	59.16	59.18	59.13	0.04
34	O	8	16.00	0.00210	13.0	Sample_31	13	1.582E-03	59.13	59.13	59.12	0.02
35	Al	13	26.98	0.08810	13.0	Backing_31	13	6.637E-02	58.83	59.12	58.55	0.57
36	W	74	183.85	0.512	13.0	Degrader	14	3.857E-01	57.49	58.55	56.43	2.12
39	Al	13	26.98	0.018	13.0	Spacer	15	1.356E-02	56.37	56.43	56.31	0.12
40	Ti	22	47.90	0.015	13.0	Monitor 4	16	1.130E-02	56.26	56.31	56.22	0.09
41	Al	13	26.98	0.018	13.0	Spacer	17	1.356E-02	56.16	56.22	56.10	0.12
42	Al	13	26.98	0.0024	13.0	Sam_Cover_62	18	1.808E-03	56.09	56.10	56.08	0.02
43	O	8	16.00	0.00130	13.0	Sample_62	18	9.794E-04	56.08	56.08	56.07	0.01
44	As	33	74.92	0.00855	13.0	Sample_62	18	6.442E-03	56.05	56.07	56.03	0.05
45	O	8	16.00	0.00130	13.0	Sample_62	18	9.794E-04	56.02	56.03	56.02	0.01
46	As	33	74.92	0.00855	13.0	Sample_62	18	6.442E-03	55.99	56.02	55.97	0.05
47	O	8	16.00	0.00130	13.0	Sample_62	18	9.794E-04	55.97	55.97	55.96	0.01
48	Al	13	26.98	0.08770	13.0	Backing_62	18	6.607E-02	55.66	55.96	55.37	0.59
49	W	74	183.85	0.512	13.0	Degrader	19	3.857E-01	54.26	55.37	53.16	2.21
51	Al	13	26.98	0.018	13.0	Spacer	20	1.356E-02	53.10	53.16	53.04	0.13
52	Ti	22	47.90	0.015	13.0	Monitor 5	21	1.130E-02	52.99	53.04	52.94	0.09
53	Al	13	26.98	0.018	13.0	Spacer	22	1.356E-02	52.88	52.94	52.82	0.13
54	Al	13	26.98	0.0024	13.0	Sam_Cover_41	23	1.808E-03	52.81	52.82	52.80	0.02
55	O	8	16.00	0.00246	13.0	Sample_41	23	1.853E-03	52.79	52.80	52.78	0.02
56	As	33	74.92	0.00863	13.0	Sample_41	23	6.502E-03	52.76	52.78	52.73	0.05
57	O	8	16.00	0.00246	13.0	Sample_41	23	1.853E-03	52.72	52.73	52.71	0.02
58	As	33	74.92	0.00863	13.0	Sample_41	23	6.502E-03	52.69	52.71	52.66	0.05
59	O	8	16.00	0.00246	13.0	Sample_41	23	1.853E-03	52.66	52.66	52.65	0.02
60	Al	13	26.98	0.07010	13.0	Backing_41	23	5.281E-02	52.40	52.65	52.15	0.50
61	W	74	183.85	0.512	13.0	Degrader	24	3.857E-01	51.00	52.15	49.85	2.30
62	Al	13	26.98	0.018	13.0	Top Cover	25	1.356E-02	49.78	49.85	49.71	0.13
63	Ti	22	47.90	0.015	13.0	Monitor 6	26	1.130E-02	49.66	49.71	49.62	0.10
64	Al	13	26.98	0.018	13.0	Top Cover	27	1.356E-02	49.55	49.62	49.48	0.13

Appendix

65	Al	13	26.98	0.0024	13.0	Sam_Cover_42	28	1.808E-03	49.47	49.48	49.47	0.02
66	O	8	16.00	0.00178	13.0	Sample_42	28	1.341E-03	49.46	49.47	49.45	0.01
67	As	33	74.92	0.0067	13.0	Sample_42	28	5.048E-03	49.43	49.45	49.41	0.04
68	O	8	16.00	0.00178	13.0	Sample_42	28	1.341E-03	49.40	49.41	49.40	0.01
69	As	33	74.92	0.0067	13.0	Sample_42	28	5.048E-03	49.38	49.40	49.36	0.04
70	O	8	16.00	0.00178	13.0	Sample_42	28	1.341E-03	49.35	49.36	49.34	0.01
71	Al	13	26.98	0.06980	13.0	Backing_42	28	5.259E-02	49.08	49.34	48.82	0.52
72	W	74	183.85	0.512	13.0	Degradar	29	3.857E-01	47.62	48.82	46.41	2.42
73	Al	13	26.98	0.018	13.0	Spacer	30	1.356E-02	46.34	46.41	46.27	0.14
74	Ti	22	47.90	0.015	13.0	Monitor_7	31	1.130E-02	46.22	46.27	46.16	0.10
75	Al	13	26.98	0.018	13.0	Spacer	32	1.356E-02	46.09	46.16	46.02	0.14
76	Al	13	26.98	0.0024	13.0	Sam_Cover_43	33	1.808E-03	46.01	46.02	46.01	0.02
77	O	8	16.00	0.00200	13.0	Sample_43	33	1.507E-03	46.00	46.01	45.99	0.02
78	As	33	74.92	0.00788	13.0	Sample_43	33	5.937E-03	45.96	45.99	45.94	0.05
79	O	8	16.00	0.00200	13.0	Sample_43	33	1.507E-03	45.93	45.94	45.92	0.02
80	As	33	74.92	0.00788	13.0	Sample_43	33	5.937E-03	45.90	45.92	45.87	0.05
81	O	8	16.00	0.00200	13.0	Sample_43	33	1.507E-03	45.86	45.87	45.86	0.02
82	Al	13	26.98	0.06950	13.0	Backing_43	33	5.236E-02	45.58	45.86	45.31	0.55
83	W	74	183.85	0.512	13.0	Degradar	34	3.857E-01	44.03	45.31	42.76	2.55
84	Al	13	26.98	0.018	13.0	Top_Cover	35	1.356E-02	42.68	42.76	42.61	0.15
85	Ti	22	47.90	0.015	13.0	Monitor_8	36	1.130E-02	42.55	42.61	42.50	0.11
86	Al	13	26.98	0.018	13.0	Top_Cover	37	1.356E-02	42.42	42.50	42.35	0.15
87	Al	13	26.98	0.0024	13.0	Sam_Cover_44	38	1.808E-03	42.34	42.35	42.33	0.02
88	O	8	16.00	0.00260	13.0	Sample_44	38	1.959E-03	42.32	42.33	42.30	0.02
89	As	33	74.92	0.01227	13.0	Sample_44	38	9.244E-03	42.26	42.30	42.22	0.08
90	O	8	16.00	0.00260	13.0	Sample_44	38	1.959E-03	42.21	42.22	42.20	0.02
91	As	33	74.92	0.01227	13.0	Sample_44	38	9.244E-03	42.16	42.20	42.12	0.08
92	O	8	16.00	0.00260	13.0	Sample_44	38	1.959E-03	42.11	42.12	42.10	0.02
93	Al	13	26.98	0.06940	13.0	Backing_44	38	5.229E-02	41.80	42.10	41.51	0.58
94	W	74	183.85	0.512	13.0	Degradar	39	3.857E-01	40.15	41.51	38.79	2.72
95	Al	13	26.98	0.018	13.0	Spacer	40	1.356E-02	38.71	38.79	38.63	0.16
96	Ti	22	47.90	0.015	13.0	Monitor_9	41	1.130E-02	38.57	38.63	38.51	0.12
97	Al	13	26.98	0.018	13.0	Spacer	42	1.356E-02	38.43	38.51	38.35	0.16
98	Al	13	26.98	0.0024	13.0	Sam_Cover_51	43	1.808E-03	38.34	38.35	38.33	0.02
99	O	8	16.00	0.00270	13.0	Sample_51	43	2.034E-03	38.31	38.33	38.30	0.03
100	As	33	74.92	0.0118	13.0	Sample_51	43	8.890E-03	38.26	38.30	38.22	0.08
101	O	8	16.00	0.00270	13.0	Sample_51	43	2.034E-03	38.20	38.22	38.19	0.03
102	As	33	74.92	0.0118	13.0	Sample_51	43	8.890E-03	38.15	38.19	38.11	0.08
103	O	8	16.00	0.00270	13.0	Sample_51	43	2.034E-03	38.09	38.11	38.08	0.03
104	Al	13	26.98	0.06980	13.0	Backing_51	43	5.259E-02	37.76	38.08	37.45	0.63
105	W	74	183.85	0.512	13.0	Degradar	44	3.857E-01	35.97	37.45	34.50	2.94
106	Al	13	26.98	0.018	13.0	Top_Cover	45	1.356E-02	34.41	34.50	34.33	0.18
107	Ti	22	47.90	0.015	13.0	Monitor_10	46	1.130E-02	34.26	34.33	34.20	0.13
108	Al	13	26.98	0.018	13.0	Top_Cover	47	1.356E-02	34.11	34.20	34.02	0.18
109	Al	13	26.98	0.0024	13.0	Sam_Cover_53	48	1.808E-03	34.01	34.02	34.00	0.02
110	O	8	16.00	0.00260	13.0	Sample_53	48	1.959E-03	33.98	34.00	33.97	0.03
111	As	33	74.92	0.01423	13.0	Sample_53	48	1.072E-02	33.91	33.97	33.86	0.11
112	O	8	16.00	0.00260	13.0	Sample_53	48	1.959E-03	33.84	33.86	33.83	0.03
113	As	33	74.92	0.01423	13.0	Sample_53	48	1.072E-02	33.77	33.83	33.72	0.11
114	O	8	16.00	0.00260	13.0	Sample_53	48	1.959E-03	33.71	33.72	33.69	0.03
115	Al	13	26.98	0.07030	13.0	Backing_53	48	5.296E-02	33.34	33.69	32.99	0.70
116	W	74	183.85	0.512	13.0	Degradar	49	3.857E-01	31.37	32.99	29.74	3.24
117	Al	13	26.98	0.018	13.0	Spacer	50	1.356E-02	29.64	29.74	29.55	0.20
118	Ti	22	47.90	0.015	13.0	Monitor_11	51	1.130E-02	29.47	29.55	29.40	0.14
119	Al	13	26.98	0.018	13.0	Spacer	52	1.356E-02	29.30	29.40	29.20	0.20
120	Al	13	26.98	0.0024	13.0	Sam_Cover_54	53	1.808E-03	29.19	29.20	29.18	0.03
121	O	8	16.00	0.00210	13.0	Sample_54	53	1.582E-03	29.16	29.18	29.15	0.03
122	As	33	74.92	0.00968	13.0	Sample_54	53	7.293E-03	29.11	29.15	29.07	0.08
123	O	8	16.00	0.00210	13.0	Sample_54	53	1.582E-03	29.05	29.07	29.04	0.03
124	As	33	74.92	0.00968	13.0	Sample_54	53	7.293E-03	29.00	29.04	28.96	0.08
125	O	8	16.00	0.00210	13.0	Sample_54	53	1.582E-03	28.94	28.96	28.93	0.03
126	Al	13	26.98	0.07030	13.0	Backing_54	53	5.296E-02	28.53	28.93	28.14	0.79
127	W	74	183.85	0.512	13.0	Degradar	54	3.857E-01	26.30	28.14	24.46	3.68
128	Al	13	26.98	0.018	13.0	Spacer	55	1.356E-02	24.35	24.46	24.23	0.23
129	Ti	22	47.90	0.015	13.0	Monitor_12	56	1.130E-02	24.15	24.23	24.06	0.17
130	Al	13	26.98	0.018	13.0	Spacer	57	1.356E-02	23.95	24.06	23.83	0.23
131	Al	13	26.98	0.0024	13.0	Sam_Cover_32	58	1.808E-03	23.81	23.83	23.80	0.03
132	O	8	16.00	0.00150	13.0	Sample_32	58	1.130E-03	23.79	23.80	23.78	0.02
133	As	33	74.92	0.00726	13.0	Sample_32	58	5.470E-03	23.74	23.78	23.70	0.07
134	O	8	16.00	0.00150	13.0	Sample_32	58	1.130E-03	23.69	23.70	23.68	0.02
135	As	33	74.92	0.00726	13.0	Sample_32	58	5.470E-03	23.65	23.68	23.61	0.07
136	O	8	16.00	0.00150	13.0	Sample_32	58	1.130E-03	23.60	23.61	23.59	0.02
137	Al	13	26.98	0.08800	13.0	Backing_32	58	6.630E-02	23.00	23.59	22.41	1.17

Figure A-7: Foil stack for ^{72}Se production using ^{75}As monoisotopic targets. Irradiated at the Injector 2 at PSI.

Appendix A-6: Literature monitor reactions

The monitor reaction plots shown in this appendix provide additional documentation of the beam monitoring procedure applied in the stacked-foil experiments. For each irradiation, selected monitor foils were evaluated, and the resulting cross-sections were compared with recommended excitation functions. This comparison was used to check whether the calculated energy degradation through the stack and the beam-current normalization were consistent with established monitor data.

Since these reactions were not the focus of the present work, the corresponding excitation functions are not discussed in detail in the main text. They are included here to make the underlying quality control of the activation measurements transparent and to support the reported cross-section data for the production routes investigated.

Appendix

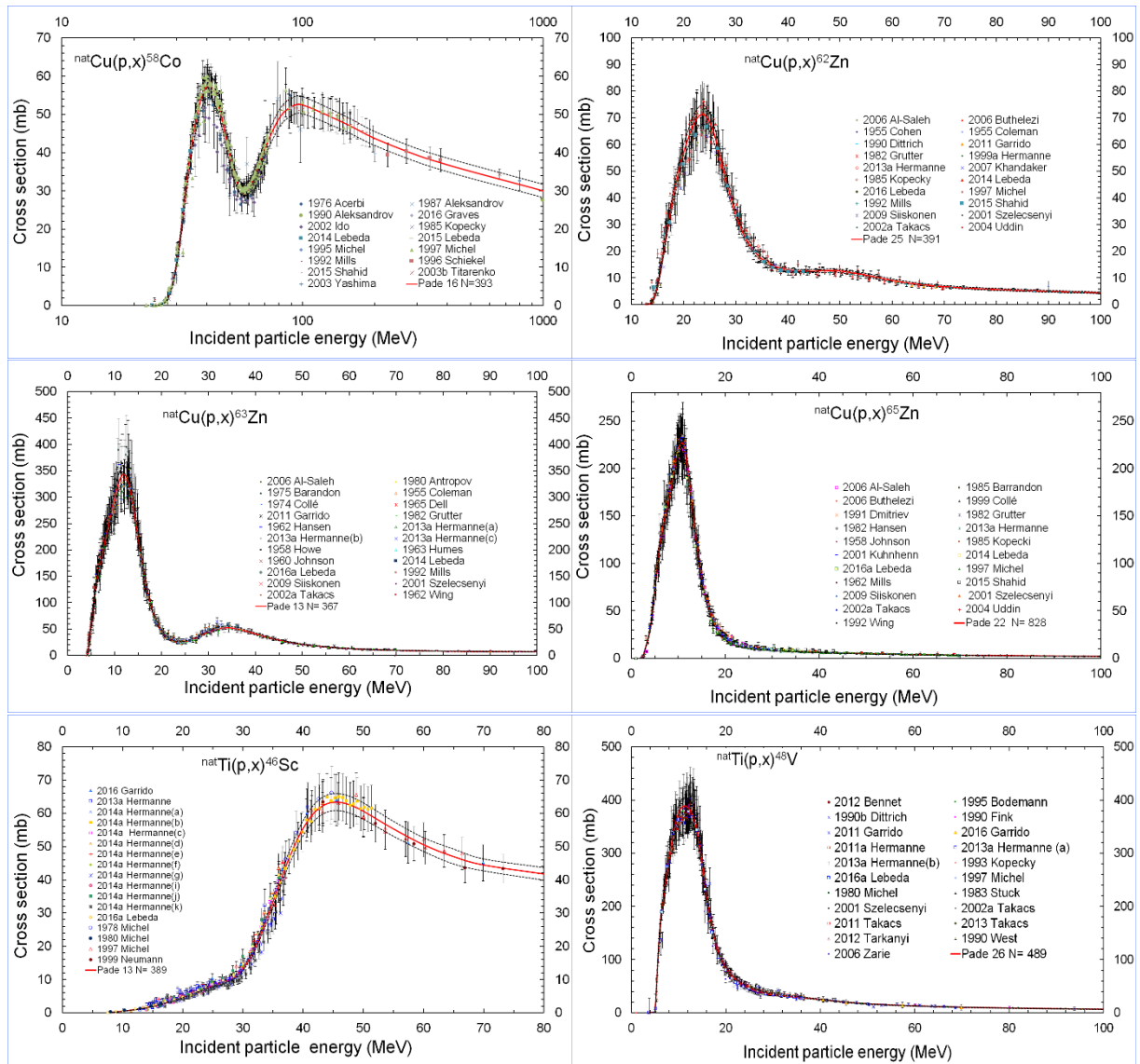


Figure A-8: Monitor reaction fits used for proton-induced irradiation obtained from IAEA [38].

Appendix

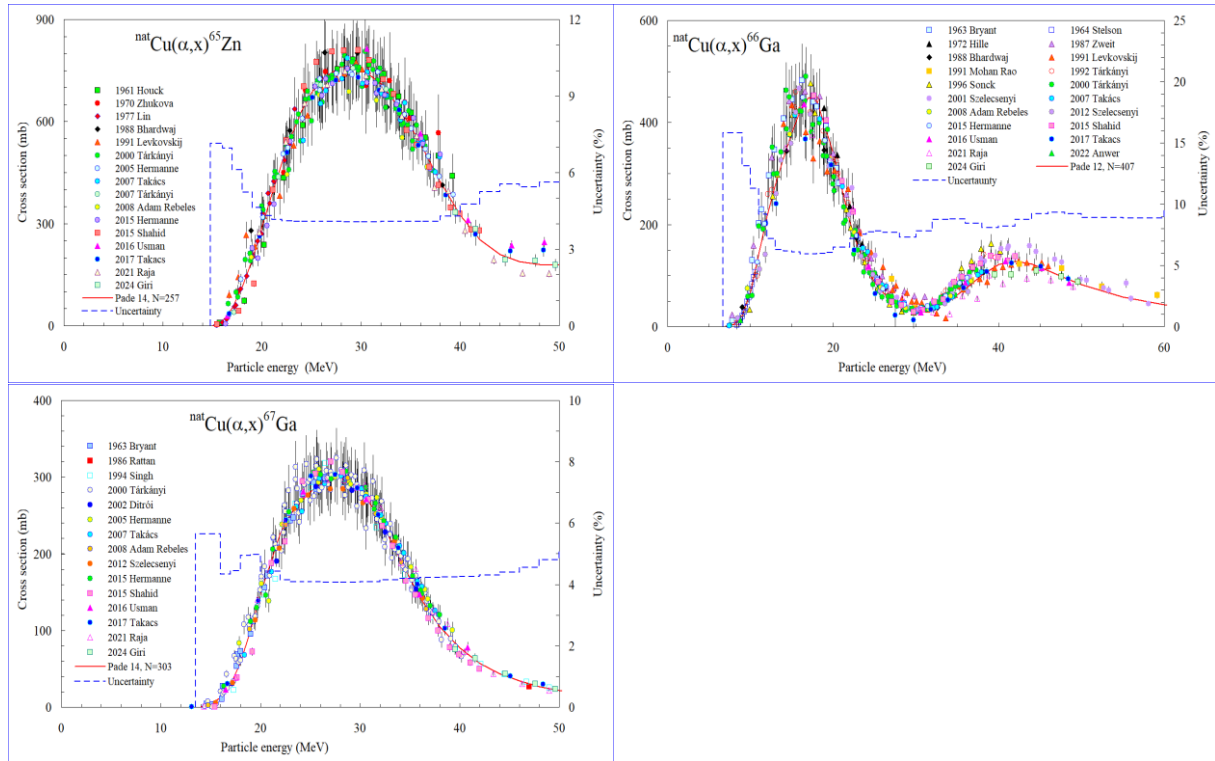


Figure A-9: Monitor reaction fits used for α -particle-induced irradiation obtained from IAEA [38].

Appendix B: Production and processing of ^{211}At

Appendix B-1: Production & Up-scaling

Original pictures

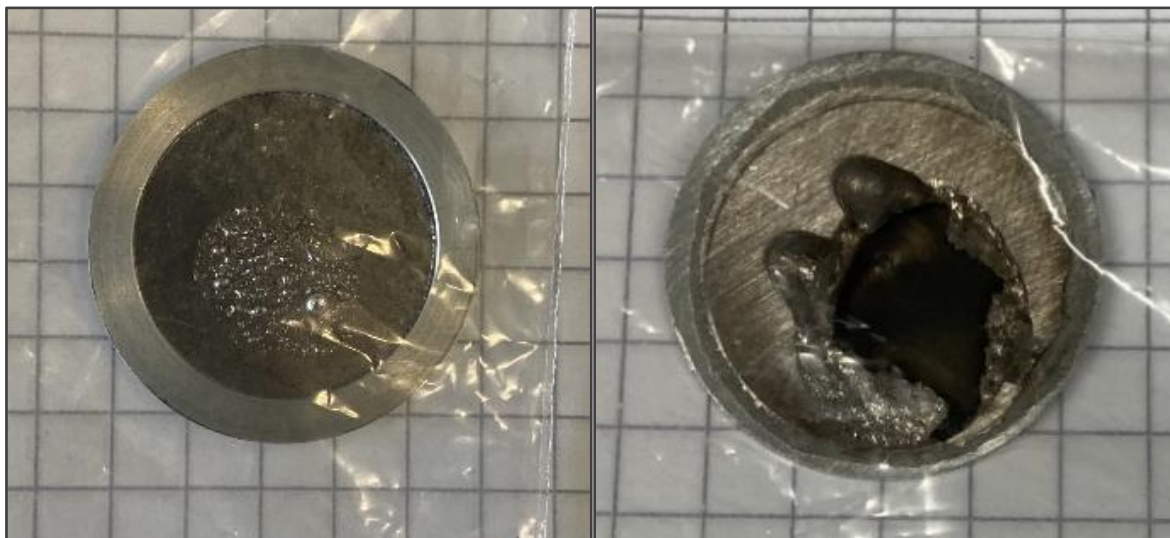


Figure B-1: Original photographs of coin targets prepared by sinter target method irradiated with $\sim 5 \mu\text{A}_e$ α -beam current presented in Section 3.2.1



Figure B-2: Unedited photograph of the target presented in Section 3.2.1, showing a bismuth target prepared by melting technique, irradiated for ~ 4 h with $\sim 50 \mu\text{A}_e$.



Figure B-3: Original photograph of a bismuth target processed in a vertical oven DD assembly as presented in Section 3.2.2

Appendix

Target decontamination

Table B-1: Target decontamination study Target 1 (17.12.2025): measured astatine activities, relative activity decrease, and corresponding equivalent α -beam energy.

	^{210}At (EOB) [Bq]	^{211}At (EOB) [Bq]	Ratio [ppm]	Rel. Target Activity (^{211}At)	Prod. Yield [MBq $\mu\text{Ae}^{-1}\text{h}^{-1}$]	Respective α -energy [MeV]
Untreated target	5.19E+03	2.15E+08	24.13	100%	32.1	29.00
Target after wipe 1	3.59E+03	2.10E+08	17.12	97%	31.3	28.85
Target after wipe 2	2.72E+03	2.04E+08	13.34	95%	30.4	28.75
Target after wipe 3	2.14E+03	1.95E+08	10.96	91%	29.2	28.60
Wipe cloth 1	2.10E+03	9.16E+06	229.23			
Wipe cloth 2	9.41E+02	7.27E+06	129.50			
Wipe cloth 3	9.98E+02	1.13E+07	87.91			

Table B-2: Target decontamination study Target 2 (11.01.2026): measured astatine activities, relative activity decrease, and corresponding equivalent α -beam energy.

	^{210}At (EOB) [Bq]	^{211}At (EOB) [Bq]	Ratio [ppm]	Rel. Target Activity (^{211}At)	Prod. Yield [MBq $\mu\text{Ae}^{-1}\text{h}^{-1}$]	Respective α -energy [MeV]
Untreated target	4.52E+03	1.34E+08	33.79	100%	32.1	29.00
Target after wipe 1	3.67E+03	1.31E+08	27.93	98%	31.5	28.90
Target after wipe 2	3.00E+03	1.29E+08	23.26	96%	30.9	28.80
Target after wipe 3	2.63E+03	1.29E+08	20.33	97%	31.0	28.80
Wipe cloth 1	1.01E+02	4.06E+05	248.41			
Wipe cloth 2	3.81E+01	1.86E+05	205.60			
Wipe cloth 3	3.17E+01	1.73E+05	183.22			

Appendix B-2: Dry distillation setup

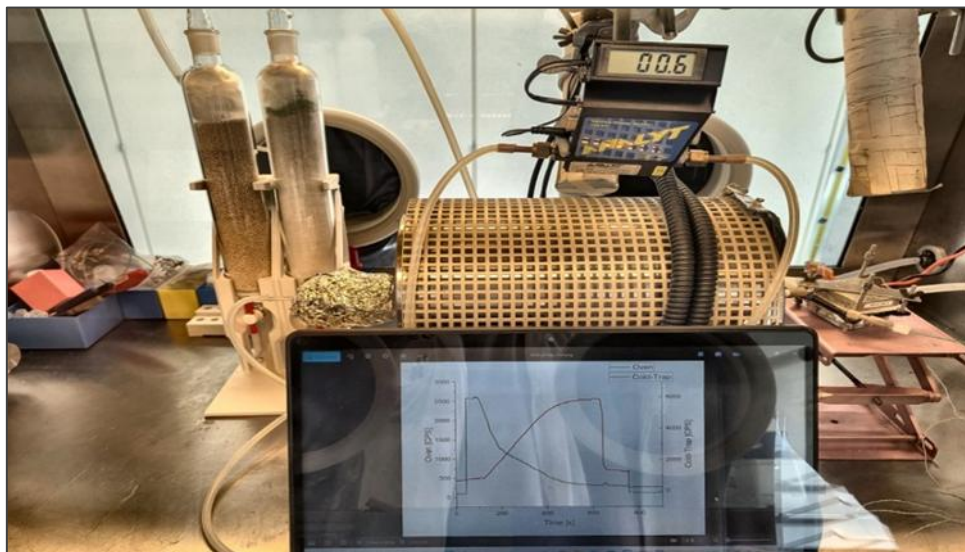


Figure B-4: Photograph of the dry distillation assembly in a glove box environment.

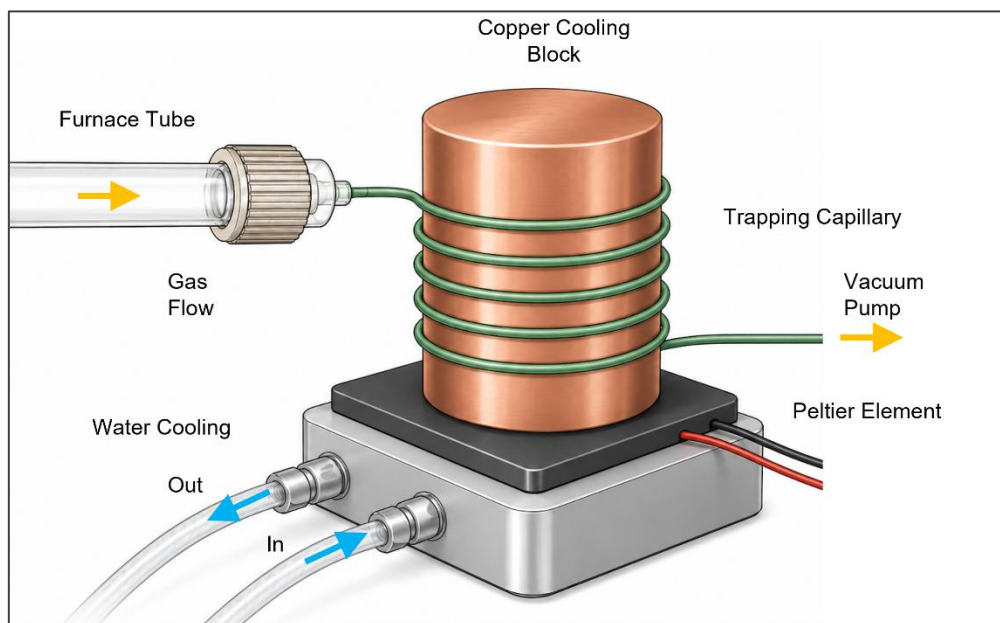


Figure B-5: Schematic illustration of the cold trap design applied for dry distillation experiments. This illustration was modified using AI supported tools.

Appendix

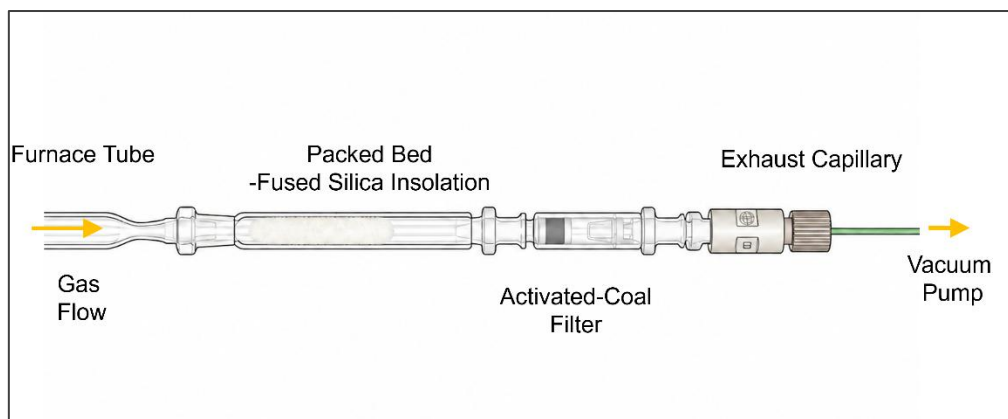


Figure B-6: Schematic illustration of the non-cooled packed-bed trap design applied for dry distillation experiments. This illustration was modified using AI supported tools.

Detector application

An auxiliary low-cost PIN-diode detector was used in selected parts of this work for supplementary qualitative observations and exploratory count-rate measurements. The detector concept was based on the setup reported by Keller et al. [123] for mobile and educational radiation-sensing applications. The system was not developed as part of this thesis, and the Python-based data-acquisition script used for recording the detector response was provided by a colleague.

The setup was used only as an auxiliary detector system and not as a primary measurement device for absolute activity determination. All quantitative activity measurements discussed in the main chapters of this thesis were obtained using calibrated laboratory instrumentation. Accordingly, the PIN-diode detector is documented here only to clarify the experimental setup and the scope of its use.

A photograph of the assembled detector setup is shown in Figure B-7.



Figure B-7: Auxiliary low-cost PIN-diode detector setup used for supplementary qualitative count-rate observations. The detector concept was based on Keller et al. [123], while the Python-based data-acquisition script was provided by a colleague. The setup was not used for traceable absolute activity quantification in this thesis.

Appendix

Appendix B-3: Wet chemical separation

Table B-3: Solvents and their respective supplier and purity used during wet chemical separation and distribution studies. ^aSolid sample dissolved in 1-octanole. ^bSolid sample dissolved in toluene.

Solvent	Solvent Class	Supplier	Purity [%]
1-Octanole	Alcohol	Sigma-Aldrich	> 99
3-Octanone	Ketone	thermo scientific	98
Methyl-Isobutyl-Ketone	Ketone	Sigma-Aldrich	> 99
Cinnamaldehyde	Aldehyde	Sigma-Aldrich	97
Cyclohexanone	Ketone	thermo scientific	99.8
2-Hexanone	Ketone	Sigma-Aldrich	98
Tributyl phosphate	Phosphate	Sigma-Aldrich	> 99
Octanal	Aldehyde	thermo scientific	99
2,4-Nonadione	Ketone	thermo scientific	> 98
1-Dodecanol ^a	Alcohol	Sigma-Aldrich	98
Di(2-ethylhexyl) phosphoric acid	Acid	Roth	> 95
Iso-propyl ether	Ether	Sigma-Aldrich	> 98.5
Tri octylamine	Amine	Fluka Analytical	> 99
Toluol	Cyclic-Alcohol	Sigma-Aldrich	99.8
DB21C7 (0.1 M) ^b	Crown-Ether	Sigma-Aldrich	97
CMPO	Phosphate	BLDpharm	95
Oleic Acid	Acid	Sigma-Aldrich	90
Dodecane thiol	Thiol	Sigma-Aldrich	> 98
Dodecanal	Aldehyde	Sigma-Aldrich	> 95
Diocetyl sulfide	Sulfide	Sigma-Aldrich	96

Distribution

Table B-4: Comparison of K_D values obtained by direct phase measurement and by back-calculation from total activity and upper-phase aliquots.

Organic Phase	Aqueous Phase	Direct Phase Measurement			Back-Calculation		
		K_D	SD	RSD	K_D	SD	RSD
3-Octanone	6 M HNO ₃	33.55	3.38	10%	21.88	18.71	86%
3-Octanone	2 M HNO ₃	20.64	2.41	12%	9.73	2.11	22%
3-Octanone	0.1 M HNO ₃	12.64	0.59	5%	7.42	0.4	5%

Appendix

Table B-5: Distribution coefficient of investigated solvents against 0.1 M, 2 M and 6 M HNO₃. ²¹¹At was obtained by dissolving the target material in conc. HNO₃ and diluted. ^aSolid sample dissolved in 1-octanole, ^bSolid sample dissolved in toluene, ^cNo clear phase separation was observed.

Org. Solvent	Aq Phase	KD(avrg)	SD	RSD
1-Octanole	6 M HNO ₃	9.73	2.04	21%
1-Octanole	2 M HNO ₃	2.75	1.41	51%
1-Octanole	0.1 M HNO ₃	5.93	0.98	17%
3-Octanone	6 M HNO ₃	33.55	3.38	10%
3-Octanone	2 M HNO ₃	20.64	2.41	12%
3-Octanone	0.1 M HNO ₃	12.64	0.59	5%
Cinnamaldehyde	6 M HNO ₃	74.22	4.31	6%
Cinnamaldehyde	2 M HNO ₃	43.50	1.54	4%
Cinnamaldehyde	0.1 M HNO ₃	33.23	6.30	19%
di-isopropyl ether	6 M HNO ₃	5.48	0.68	12%
di-isopropyl ether	2 M HNO ₃	4.82	0.54	11%
di-isopropyl ether	0.1 M HNO ₃	6.25	2.89	46%
Tri octylamine	6 M HNO ₃	187.89	14.47	8%
Tri octylamine	2 M HNO ₃	234.31	50.27	21%
Tri octylamine	0.1 M HNO ₃	37.94	1.18	3%
Tributyl phosphate	6 M HNO ₃	59.42	0.83	1%
Tributyl phosphate	2 M HNO ₃	40.57	8.93	22%
Tributyl phosphate	0.1 M HNO ₃	5.49	0.43	8%
Toluol	6 M HNO ₃	0.35	0.02	7%
Toluol	2 M HNO ₃	0.94	0.31	33%
Toluol	0.1 M HNO ₃	0.32	0.05	15%
DB21C7 (0.1 M) ^a	6 M HNO ₃	0.79	0.01	1%
DB21C7 (0.1 M) ^a	2 M HNO ₃	3.25	0.06	2%
DB21C7 (0.1 M) ^a	0.1 M HNO ₃	1.16	0.78	67%
CMPO	6 M HNO ₃	2.84	0.19	7%
CMPO	2 M HNO ₃	0.13	0.04	35%
CMPO	0.1 M HNO ₃	0.09	0.01	12%
Octanal	6 M HNO ₃	301.99	8.68	3%
Octanal	2 M HNO ₃	271.46	14.46	5%
Octanal	0.1 M HNO ₃	114.63	26.53	23%
2,4-Nonadione	6 M HNO ₃	182.06	16.30	9%
2,4-Nonadione	2 M HNO ₃	130.17	9.31	7%
2,4-Nonadione	0.1 M HNO ₃	92.99	2.48	3%
Methyl-Isobutyl-Ketone	6 M HNO ₃	87.11	2.71	3%
Methyl-Isobutyl-Ketone	2 M HNO ₃	129.59	26.21	20%
Methyl-Isobutyl-Ketone	0.1 M HNO ₃	118.95	11.89	10%
3-Octanone	6 M HNO ₃	32.25	0.04	0%
3-Octanone	2 M HNO ₃	24.14	1.34	6%

Appendix

3-Octanone	0.1 M HNO ₃	23.79	0.54	2%
Oleic Acid	6 M HNO ₃	24.76	2.34	9%
Oleic Acid	2 M HNO ₃	9.55	2.01	21%
Oleic Acid	0.1 M HNO ₃	16.14	1.41	9%
Dodecane thiol	6 M HNO ₃	27.43	0.73	3%
Dodecane thiol	2 M HNO ₃	26.74	0.58	2%
Dodecane thiol	0.1 M HNO ₃	15.79	1.70	11%
2-Hexanone	6 M HNO ₃	34.31	1.32	4%
2-Hexanone	2 M HNO ₃	34.13	0.60	2%
2-Hexanone	0.1 M HNO ₃	36.99	0.53	1%
Cyclohexanone	6 M HNO ₃	-	-	-
Cyclohexanone	2 M HNO ₃	45.37	7.29	16%
Cyclohexanone	0.1 M HNO ₃	106.24	6.26	6%
Dodecanal	6 M HNO ₃	105.22	2.48	2%
Dodecanal	2 M HNO ₃	81.66	5.81	7%
Dodecanal	0.1 M HNO ₃	17.62	8.50	48%
Di(2-ethylhexyl) phosphoric acid	6 M HNO ₃	56.13	15.50	28%
Di(2-ethylhexyl) phosphoric acid	2 M HNO ₃	65.29	5.71	9%
Di(2-ethylhexyl) phosphoric acid	0.1 M HNO ₃	72.27	9.50	13%
Dioctyl sulfide	6 M HNO ₃	72.58	2.27	3%
Dioctyl sulfide	2 M HNO ₃	33.93	1.48	4%
Dioctyl sulfide	0.1 M HNO ₃	14.82	1.10	7%
1-Dodecanol (0.1 M) ^b	6 M HNO ₃	6.22	3.17	51%
1-Dodecanol (0.1 M) ^b	2 M HNO ₃	2.07	0.39	19%
1-Dodecanol (0.1 M) ^b	0.1 M HNO ₃	6.34	4.37	69%

Appendix

Table B-6: Distribution coefficient of investigated solvents against 0.1, 2 and 6 M HNO₃. ²¹¹At was obtained by DD processing before translation into acid medium.

Org. Solvent	Aq Phase	KD_Avrg.	Avrg_SD	RSD
1-Octanole	6 M HNO ₃	4.16	1.73	42%
1-Octanole	2 M HNO ₃	1.70	0.04	2%
1-Octanole	0.1 M HNO ₃	2.10	1.37	65%
3-Octanone	6 M HNO ₃	128.31	18.07	14%
3-Octanone	2 M HNO ₃	107.16	16.43	15%
3-Octanone	0.1 M HNO ₃	58.69	3.17	5%
Methyl-Isobutyl-Ketone	6 M HNO ₃	69.21	1.66	2%
Methyl-Isobutyl-Ketone	2 M HNO ₃	102.70	2.18	2%
Methyl-Isobutyl-Ketone	0.1 M HNO ₃	132.64	2.80	2%
Cinnamaldehyde	6 M HNO ₃	164.04	18.11	11%
Cinnamaldehyde	2 M HNO ₃	203.42	5.60	3%
Cinnamaldehyde	0.1 M HNO ₃	329.60	13.22	4%
Cyclohexanone	6 M HNO ₃	-	-	-
Cyclohexanone	2 M HNO ₃	28.50	0.99	3%
Cyclohexanone	0.1 M HNO ₃	73.38	0.18	0%
2-Hexanone	6 M HNO ₃	110.45	1.34	1%
2-Hexanone	2 M HNO ₃	153.32	4.43	3%
2-Hexanone	0.1 M HNO ₃	32.73	2.06	6%
Tributyl phosphate	6 M HNO ₃	58.87	4.69	8%
Tributyl phosphate	2 M HNO ₃	98.09	2.36	2%
Tributyl phosphate	0.1 M HNO ₃	64.48	10.43	16%
Octanal	6 M HNO ₃	45.36	2.72	6%
Octanal	2 M HNO ₃	115.85	4.24	4%
Octanal	0.1 M HNO ₃	47.09	1.21	3%
2,4-Nonadione	6 M HNO ₃	77.26	30.99	40%
2,4-Nonadione	2 M HNO ₃	69.06	1.13	2%
2,4-Nonadione	0.1 M HNO ₃	37.29	1.49	4%
Di(2-ethylhexyl) phosphoric acid	6 M HNO ₃	40.06	0.44	1%
Di(2-ethylhexyl) phosphoric acid	2 M HNO ₃	26.92	2.88	11%
Di(2-ethylhexyl) phosphoric acid	0.1 M HNO ₃	32.66	1.85	6%

Appendix B-4: Radioluminescence of ^{211}At

In the following, estimation calculations are presented to approximate whether Cherenkov radiation generated by the decay series of ^{211}At is possible. First and foremost, since the same blue radiation was visible in liquid as well as gas atmosphere, it is to be assumed that the occurring effect, be it Cherenkov radiation or excitation effects, originates from the glass vial instead of the added medium, since this was the constant medium factor present in all experiments. As presented in Table 25, the energy threshold for electrons in borosilicate glass is roughly 185 keV which we use as our benchmark value for further calculations.

An estimation of how much alpha energy (E_α) is required to kick out electrons from their shell can be done by the Bethe-Bloch-kinematic elaborating the maximum kinetic energy (T_{max}) an electron can carry on from a direct hit with an alpha particle according to equation B1 [143]:

$$T_{max} = \frac{2m_e c^2 \beta^2 \gamma^2}{1 + 2\gamma \frac{m_e}{m_\alpha} + \left(\frac{m_e}{m_\alpha}\right)^2} \quad (\text{B1})$$

In the case of heavy alpha particle hitting light electrons (so be $m_\alpha \gg m_e$) equation B1 can be simplified:

$$T_{max} = 2m_e c^2 \beta^2 \gamma^2 \quad (\text{B2})$$

For non-relativistic alpha particles ($E_\alpha(\text{decay})$ generally < 10 MeV) the relativistic term $\gamma \approx 1$ and thus equation B2 can be transformed using equation B3 yielding equation B4:

$$E_\alpha = \frac{1}{2} m_\alpha v^2 = \frac{1}{2} m_\alpha (\beta c)^2 \rightarrow \beta^2 = \frac{2E_\alpha}{m_\alpha c^2} \quad (\text{B3})$$

$$T_{max} = 4 \frac{m_e}{m_\alpha} E_\alpha \quad (\text{B4})$$

With $m_e c^2 = 0.511 \text{ MeV}$ & $m_\alpha c^2 \cong 3727 \text{ MeV}$ a maximum energy of $T_{max} \approx 5.5 \cdot 10^{-4} E_\alpha$ can be calculated. Yielding a minimum E_α required to generate electrons potent to produce Cherenkov radiation of:

$$E_\alpha \approx \frac{0.18}{5.5 \cdot 10^{-4}} \text{ MeV} \approx 327 \text{ MeV} \quad (\text{B5})$$

Which are orders of magnitude higher than 5.9 MeV (^{211}At) or 7.5 MeV (^{211}Po) occurring during the decay of ^{211}At . Therefore, this method of production is not expected to yield Cherenkov radiation.

Another route to produce electrons with enough energy to generate Cherenkov radiation might be by Compton scattering, where photons interact with electrons transferring by inelastic scattering where parts of their energy into the electron liberating it from the electron shell.

To energy introduced to the electrons can be estimated using the Compton edge equation:

$$E'_\gamma = \frac{E_\gamma}{1 + \frac{E_\gamma}{m_e c^2} (1 - \cos\theta)} \quad (\text{B6})$$

Where the kinetic energy of an electron T_e equals the difference between the impinging photon energy E_γ and the energy of the scattered photon E'_γ , where the energy of the scattered photon is a function of E_γ and the scattering angle θ with minimum energy at 180° corresponding to a maximum electron energy T_e .

There is an ideal case of creating a photo electron, where all the photon energy is introduced into the electron. In this case $T_e = E_\gamma - E_b$ where E_b is the binding energy of the electron. However, in the 0.5–0.9 MeV range, the dominant source of fast secondary electrons especially in low Z media like borosilicate is Compton scattering [143, 183]; hence we refer to these as *Compton electrons*, with an endpoint energy given by the Compton edge:

$$T_{e,max} = E_\gamma \left(1 - \frac{1}{1 + \frac{2E_\gamma}{m_e c^2}} \right) = \frac{2E_\gamma^2}{2E_\gamma + m_e c^2} \quad (\text{B7})$$

Applying this equation on the three most dominant photon energies occurring during the ^{211}At decay series (569.7 keV (0.31%), 687.0 keV (0.26%) and 897.8 (0.32%)) yielding maximum electron energies $T_{e,max}$ of ~393 keV, ~501 keV and ~699 keV respectively. From the energy point of view would this be enough to generate fast electrons in borosilicate glass. However, this only encompasses the maximum Compton energy and does not account for interaction probability of the photon with an electron.

In the following section, the probability for the formation of Cherenkov photons is estimated by approximation of emitted photons creating electrons for the three major photon energies of the ^{211}At decay series.

In Table B-7, the energy dependent photon emission rates $\dot{N}_\gamma(E)$ of 1 GBq ^{211}At and their respective mass attenuation coefficient (μ/ρ) [184] are presented and linear attenuation coefficient (μ) and the interaction probability (P_{int}) are calculated for an average glass wall thickness of $d = 3 \text{ mm}$ and a density of $(\rho \cong 2.23 \text{ g cm}^{-3})$ for borosilicate glass using Eq. (B8):

$$P_{int}(d) = 1 - e^{-\mu d}, \quad \mu = \left(\frac{\mu}{\rho}\right) \rho \quad (\text{B8})$$

Using the Klein–Nishina formula, [185] the fraction of Compton recoil electrons exceeding the Cherenkov threshold energy T_t (here $T_t = 185 \text{ keV}$) can be calculated from Eq. (B9) together with the rearranged Compton-kinematics relation (Eq. B6):

$$\frac{d\sigma}{d\Omega} = \frac{r_e^2}{2} \left(\frac{E'_\gamma}{E_\gamma}\right)^2 \left[\frac{E'_\gamma}{E_\gamma} + \frac{E_\gamma}{E'_\gamma} - \sin^2 \theta \right], \quad \frac{E'_\gamma}{E_\gamma} = \frac{1}{1 + \frac{E_\gamma}{m_e c^2} (1 - \cos \theta)} \quad (\text{B9})$$

Here, σ denotes the (Compton) scattering cross-section, Ω the solid angle, and $r_e \approx 2.82 \times 10^{-15} \text{ m}$ the classical electron radius.

To estimate the above-threshold fraction in borosilicate glass, we first determine the minimum scattering angle $\theta_{\min}$ from Compton kinematics by imposing $T_e(\theta_{\min}) = T_t$. Using Eq. (B7), this yields the compact threshold-angle relation from Eq. (B10)

$$1 - \cos \theta_{\min} = \frac{T_t}{\frac{E_\gamma}{m_e c^2} (E_\gamma - T_t)} \quad (\text{B10})$$

The fraction of Compton events producing electrons above T_t is then obtained by integrating the Klein–Nishina angular distribution over $\theta \geq \theta_{\min}$ and normalizing to the total Compton cross-section:

$$f(T_e > T_t) = \frac{\int_{\theta_{\min}}^{\pi} \left(\frac{d\sigma}{d\Omega}\right) d\Omega}{\int_0^{\pi} \left(\frac{d\sigma}{d\Omega}\right) d\Omega}, \text{ with } d\Omega = 2\pi \cdot \sin \theta d\theta \quad (\text{B11})$$

The interaction probability $P_{int}(d) = 1 - e^{-\mu d}$ and the above-threshold fraction f are then used to estimate the production rate of electrons above the Cherenkov threshold:

Appendix

$$\dot{N}_{e>T_t} \approx \sum_i \dot{N}_{\gamma,i} P_{int}(d) f_i(T_e > T_t) \quad (\text{B12})$$

Table B-7: Interpolated NIST mass attenuation coefficients for borosilicate glass (0.5–1 MeV) and derived interaction probabilities for $d = 0.3$ cm.

E_γ [keV]	$\dot{N}_\gamma(E)$ [s ⁻¹]	μ/ρ [cm ² g ⁻¹]	μ [cm ⁻¹]	$P_{int}(0.3 \text{ cm})$	$f(T_e > T_t)$	$\dot{N}_{e>T_t}$ [s ⁻¹]
569.7	$3.1 \cdot 10^6$	0.0824	0.184	0.054	0.54	$9.0 \cdot 10^4$
687.0	$2.6 \cdot 10^6$	0.0761	0.170	0.050	0.64	$7.8 \cdot 10^4$
897.8	$3.2 \cdot 10^6$	0.0670	0.149	0.044	0.75	$9.7 \cdot 10^4$

Using the interpolated NIST (National Institute of Standards and Technology) attenuation data (0.5–1 MeV) for a glass thickness of $d = 0.3$ cm the calculation yields a total of $2.65 \cdot 10^5$ electrons per second produced by γ -induced Compton scattering for a 1 GBq ²¹¹At source.

Last, the Cherenkov photon yield from Compton recoil electrons can be estimated using the Frank-Tamm formula [186],

$$\frac{d^2 N_{Ch}}{dx d\lambda} = \frac{2\pi\alpha}{\lambda^2} \left(1 - \frac{1}{\beta^2 n^2(\lambda)}\right), \quad \left(\beta > \frac{1}{n}\right) \quad (\text{B13})$$

Where N_{Ch} denotes the number of emitted Cherenkov photons, therefore with x as electron path length (m) and the wavelength λ (nm), $\frac{d^2 N_{Ch}}{dx d\lambda}$ is the spectral photon yield (Cherenkov photons per pathlength per wavelength). And α is the fine structure constant ($\alpha \approx 1/137$).

Integrating over 400–700 nm and the mean Compton electron energies (Table B-8) the number of Cherenkov photons emitted in visible spectrum per electron path length can be calculated

$$\left(\frac{dN_{Ch}}{dx}\right)_{vis} = 2\pi\alpha \left(1 - \frac{1}{\beta^2 n^2}\right) \left(\frac{1}{\lambda_1} - \frac{1}{\lambda_2}\right) \approx 131 \text{ ph cm}^{-1} \quad (\text{B14})$$

Combined with the range of electrons in borosilicate glass, the above-threshold track lengths are of order 0.25–0.7 mm for 0.3–0.5 MeV electrons (mean electron energy after Compton scattering) [187], results in only a few visible Cherenkov photons per recoil electron (1.8 – 8.8 ph e^{-1}). The major photons emitted by ²¹¹At decay and their respective Compton energies, path length through borosilicate glass and photon emission per electron are presented in Table B-8

Using the previously derived rate of $\sim 2.65 \cdot 10^5$ by the combined Compton electron emission rates above-threshold (Table B-7), this corresponds to $\sim 1.3 \cdot 10^6$ Cherenkov photons per second generated in the glass (400–700 nm) per 1 GBq ^{211}At , before accounting for optical losses and collection efficiency.

Table B-8: Mean Compton electron energies and the corresponding Cherenkov photons per electron for the three main γ -lines during the decay of ^{211}At decay.

E_γ [keV]	$T_{e,max}$ [keV]	$T_{\bar{e}, > 185 \text{ keV}}$ [keV]	$\Delta l_{> T_t}$ [mm]	$f(ph\ e^{-1})$
569.7	393	304	0.239	1.8
687.0	501	365	0.389	3.8
897.8	699	478	0.667	8.8

Classical threshold-vision experiments showed that dark-adapted human vision can respond to only 54–148 quanta at the cornea, corresponding to an estimated 5–14 photons absorbed by retinal rods under optimized conditions [188]. Consequently, a source emitting 1.3×10^6 visible photons s^{-1} lies near the regime where naked-eye visibility may be marginal and strongly geometry-dependent, while long-exposure camera imaging should be considerably more feasible.

This analysis shows that Cherenkov light generated by Compton or photoelectrons originating from a ^{211}At decay may be mathematically possible, yet it is unlikely to account for the intense blue glow shown in Figure 52. This is particularly evident because even small spots at the rim of the glass exhibited visible blue emission, although the activity present in these regions was likely far below the 1 GBq assumed in the calculations. Moreover, if the observed light were primarily caused by electrons generated by photons traversing the glass, a more homogeneous light distribution throughout the vial wall would be expected, rather than the strongly localized emission observed at the rim. These observations are in agreement with Ackerman et al. [142], who stated that direct generation of Cherenkov radiation by α particles is essentially impossible, whereas indirect production via Compton electrons is expected to be very weak.

A more plausible explanation for the localized blue emission is therefore radioluminescence of the borosilicate glass induced by the deposition of α particle energy at the glass surface. In the decay of ^{211}At , each parent decay ultimately leads

to one α decay, either directly or via the short-lived daughter ^{211}Po . If the astatine is present as a dry deposit adhering directly to the inner glass wall, a substantial fraction of these α particles will be emitted into the glass rather than into the gas phase (2π geometry). In this case, the deposited energy is not distributed throughout the vial volume but concentrated within a very thin near-surface region of the borosilicate wall.

Even though the total deposited power is small in absolute terms, it is highly localized. For an order-of-magnitude estimate, an activity of 1 GBq was assumed. If the activity is distributed as a thin dry layer at the glass interface and the emission is treated as isotropic, approximately half of all emitted α particles will enter the glass (2π geometry). Using the dominant α energies of about 5.87 MeV direct ^{211}At decay and 7.45 MeV the subsequent ^{211}Po decay, the mean energy deposited in the glass is of the order of a few MeV per parent decay, corresponding to a deposited power of approximately $P_{\text{dep}} \approx 5 \times 10^{-4}$ W. Although this value is small in absolute terms, it is deposited within only the first few tens of micrometers of the glass surface and therefore gives rise to a high local excitation density. Such intense local excitation is expected to generate large numbers of electron-hole pairs in the silicate network, which may recombine radiatively or become trapped at pre-existing or radiation-induced defect sites, thereby giving rise to defect-related excited states and luminescence [144].

Consequently, the observed blue glow is more consistently explained as defect-mediated radioluminescence of the borosilicate glass than as Cherenkov light. This assumption fits those of Yamamoto et al. 2018 coming to the same conclusion that even when Cherenkov light in glass is possible, it is strongly rivaled by scintillation effects [145] This interpretation is also more compatible with the strongly localized emission pattern at the rim of the vial.

Additionally, the reduced blue glow observed after dissolving the astatine in chloroform may be explained by the loss of a highly localized surface deposit, as the activity becomes diluted and more uniformly distributed throughout the liquid phase, resulting in the smoother emission pattern shown in Figure 54. This interpretation is consistent with the literature, which documents radiolysis of chloroform under ionizing radiation, including in the context of ^{211}At chemistry, but does not appear to specifically describe prompt visible radioluminescence of pure chloroform under α -irradiation [146]. Moreover, chloroform is widely known as a chemical quencher in scintillation systems

[189]. Taken together, these considerations support the interpretation that the glass surface is the dominant origin of the observed radioluminescence.

Appendix B-5: Waste handling

Table B-9: Cost estimation of ^{211}At related waste handling

Waste fraction	Quantity	Unit cost	Estimated cost [€]
High-activity solid waste, combustible	20.1 kg	142 € kg ⁻¹	2854.2
High-activity solid waste, non-combustible	30 L	1698 € per 200 L barrel	254.7
High-activity liquid waste	60 L (0.060 m ³)	4900 € m ⁻³	294.0
Total			3402.9