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Prosthetic eye care – The current state of the art

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ABSTRACT

After eye loss, a fast supply with a visually appealing prosthetic eye is not just a cosmetic solution, it is the key factor for a successful social, occupational, and psychological rehabilitation. For a long time, prosthetic eye care was based on acquired experiences, and there was a significant lack of systematic studies and peer-reviewed literature on this subject. However, in recent decades, research in the field of ocular prosthetics has been driven forward by ophthalmologists, ocularists, optometrists, ophthalmoplastic surgeons, and psychologists. Many essential findings have been made for improving the care of anophthalmic patients. In this extensive review, the current state of the art regarding prosthetic eye care based on the newest scientific findings is summarized. The broad focus includes important historical aspects in ocular prosthetics, in particular the historical development that led to ocularistic care with different prosthetic materials – cryolite glass and polymethyl methacrylate. Furthermore, epidemiology and etiology of eye loss, surgical techniques of eye removal as well as types and production of prosthetic eyes are set out. Important topics with new insights include psychological issues such as living with a prosthetic eye, treatment of children with anophthalmia and microphthalmia, as well as evidence-based prosthetic eye maintenance and handling. In addition, anophthalmic socket complications and associated treatment options with a focus on the common dry anophthalmic socket and post-enucleation socket syndromes were described in detail. Finally, we will speculate how the field of prosthetic eye care will develop in the future.

1. Introduction

The field of ocular prosthetics underwent a major revolution with the introduction of polymethylmethacrylate (PMMA) eyes 75 years ago. By the early 20th century, cryolite glass had become the most widely used material for prosthetic eyes, with Germany serving as the global manufacturing center. However, when German cryolite glass eyes became unavailable at the onset of the Second World War, countries outside the German-speaking region, particularly the USA, adopted polymethyl methacrylate (PMMA) as a substitute. These advancements shifted prosthetic eye care toward a more medical and technical foundation, introducing new production methods and techniques that transformed prosthetic eyes from handcrafted artistic creations into highly precise medical devices. However, the field of ocular prosthetics is only now beginning to focus on evidence-based medicine thus reorganize itself as a research discipline and receive the scientific attention it deserves.

The peer reviewed literature on prosthetic eyes up to the turn of the 21st century is scant, but since then, the number of publications has grown significantly with the first book in 70 years being published in 2015 (Pine et al., 2015b). Of course, there has been no shortage of scientific interest in surgical techniques to remove the eye, including experimentation with orbital implants, or in investigations of contact lens wear. Much of what we currently suspect about the anophthalmic socket surface comes from pure long-term experience as well as from contact lens research and has been mostly adopted without studies on ocular prosthesis wearers. Contact lenses and prosthetic eyes both

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List of abbreviations

DASS – dry anophthalmic socket syndrome
PESS – post-enucleation socket syndrome
PMMA – polymethyl methacrylate

contact the conjunctiva, experience the same eyelid action, accumulate surface deposits and bathe in the same ocular secretions. However, the knowledge about contact lenses cannot substitute for knowledge about prosthetic eyes, as they serve different purposes, are made from different materials, and are fitted in anophthalmic sockets rather than over intact eyes, sharing only a limited part of the ocular environment.

Until relatively recently the making and fitting of prosthetic eyes has been left outside the mainstream of ophthalmology and optometry thought and has carried on, guided by empirical evidence and the experience of individual ocularists. These special individuals have formed societies to disseminate information and the American Society of Ocularists (established in 1957), has consistently published a journal, currently called the Journal of Ophthalmic Prosthetics.

Surgeons once considered the removal of an eye to be a sad final stage of treatment to be left in the hands of ophthalmology residents (Johnson, 2020). However, they now begin to recognize that losing an eye is not the end of ophthalmic care for the patient, but the beginning of a new episode of treatment that requires the services of a much broader team of health professionals including oculoplastic surgeons, ophthalmologists, ocularists, optometrists, opticians, and psychologists, for example. Ocularists are the team members that anophthalmic patients see most often and it is essential that good communication is maintained between the ocularist and the other members of the team.

The field of ocular prosthetics covers prosthetic eyes, scleral shell prostheses, prosthetic contact lens, and orbital prostheses. However, the provision of services is often (depending on country, region, and health care system) divided between ocularists making and fitting prosthetic eyes and scleral shell prostheses, optometrists as well as opticians providing prosthetic contact lenses, and anaplastologists and maxillofacial prosthetists making and fitting orbital prostheses.

This mix of disciplines is due in part from the fall out following the introduction of PMMA prostheses 75 years ago and just as ophthalmologists are revising their views of the importance of ocular prosthetics the industry itself is in a state of transition. Higher educational standards for providers are being introduced, a drift back towards optometry is discernible, and an increasing amount of research into ocular prosthetics is being carried out around the world.

Research into prosthetic eyes by ocular prosthetists, ocularists, ophthalmoplastic surgeons, ophthalmologists, optometrists, and psychologists is now beginning to address the lack of peer-reviewed literature on the subject. This paper on the current state of the art reflects the transition that is taking place with the authors working together to pool ideas and experience from all the various disciplines involved with the evolving state of ocular prosthetics.

2. History of ocular prosthetics

2.1. Ancient Egypt

Prosthetic eyes have a history that stretches back to ancient times. From then, prosthetic eye materials and production techniques have evolved in keeping with the times, with numerous revisions seen before today's modern prosthetic eyes of glass or polymethyl methacrylate (PMMA).

The history of prosthetic eyes emerges hidden in the myths and legends of Ancient Egypt. Horus, the tutelary deity of the time and notably the god of kingship and the sky, was asked by his mother Isis, to protect Egypt from his brother, Seth, who had killed their father Osiris. Horus eventually conquered Seth after many conflicts and formed the United Kingdom of Egypt by unifying Upper and Lower Egypt in about 3000 BC.

Horus was depicted as a falcon-headed man, often wearing the *pschent*, the red and white crown symbolizing kingship over the United Kingdom of Egypt. As the god of the sky, he was believed to hold the sun, his right eye, and the moon, his left eye. During one of their brutal battles, Seth gouged out Horus' left eye tearing it to shreds. Later, Horus' lost eye was restored by Thoth, the god of wisdom, magic and the moon, and obviously the first ocular prosthetist. From then, Horus' left (prosthetic) eye, the moon, was torn from the sky every lunar month and restored by Thoth piece by piece. The segments of moon pieced back together represent fractions of descending order ½, ¼, $^{1}/_{8}$ and so on, and together make approximately one *wedjat*, or whole one. The *wedjat eye*, symbolizing the "Eye of Horus", became a powerful representation of healing and protection. (Pinch, 2004).

2.2. The first prosthetic eyes

The earliest evidence of a prosthetic eye, dating back to around 2900–2800 BC, was found in the orbit of a young woman buried in the "Burnt City" in Shahr-I Sokhte, Iran (Farrokh, 2022). Believed to be made of bitumen paste and covered in a thin layer of gold, the hemispherical form was engraved with a central iris and lines which radiated out like rays from a sun. It was most likely worn like a conventional eye patch as small holes drilled on each side of it allowed the attachment of gold thread, and microscopy showed evidence of gold thread marking the orbit. Further evidence of very early prosthetic eyes comes from the reference to the gold prosthetic eye worn by a woman in a Hebrew text (Yer. Ned. 41c; comp. Yer. Sanh. 13c). However, some artificial eyes from around 2500 BC, displayed in the British Museum in London and the Egyptian Museum in Cairo, show remarkable realism (even from today's perspective) and were mainly made of rock crystal, calcite, and copper. Around 500 BC, Egyptian and Roman priests were similarly making prosthetic eyes to be worn outside of the socket. Made from painted clay, they were held in place by cloth or leather ties. *Ekblepharon* was the Greek term used for this type of external prosthetic eye, and these were made for and worn by living people.

Egyptians, however, made prosthetic eyes for their dead, believing that they would help them see when they entered the afterlife. They would remove the eyes of the dead person, pour wax into the emptied orbits and produce eye inserts of glass and onyx (McKinstry, 1995). The pair of eyes shown in are made from faience, a sintered quartz ceramic showing surface vitrification, and black onyx, and date back to the late Dynastic period (664-332 BC) or later. These prosthetic eyes for the afterlife are also featured on Egyptian sarcophagi. These eyes have bronze eyelids filled with white plaster to hold the onyx iris. Beyond Egypt, the Aztecs, Incas and other ancient cultures also used eyes formed from copper, silver, gold and precious stones to adorn mummies, sarcophagi and statues. Regrettably, records and evidence of prosthetic eyes during the rise of the Roman Empire, the establishment of Christianity, the fall of Alexandria to the Arabs (in 642 AD) and the ensuing dark ages have not been uncovered (Danz, 1990).

2.3. The first prosthetic eyes worn inside the socket

In the 16th century, the French barber surgeon Ambroise Paré, a pioneer in battlefield medicine and surgical techniques, provided descriptions of a prosthetic eye held outside of the socket by a metal rod which extended around the back of the head (Bron et al., 1997). Paré also described some of the first prosthetic eyes worn inside the socket, termed *hypoblepharae*. They were made from silver, gold, or porcelain with colored enamel coatings, and held in place by the eyelids. This may have been around the same time that Georg Bartisch wrote *Ophthalmoduleia*, published in 1583 in Dresden, which provided a detailed

description of enucleation, including illustrations.

By the late 16th century, these in-socket prosthetic eyes were being produced from glass, thus the term *glass eye*. Although still relatively crude and often uncomfortable and fragile, Venetian glass blowers were able to make these solid shell prosthetic eyes more realistic in appearance. An attempt to monopolize glass eye manufacture was made in the Venetian Island of Murano by limiting the number of artisans who could produce prosthetic eyes and guarding trade secrets. The penalty for breaching these restrictions was death as revealed by records in Murano reporting the assassination of two glass makers lured to Germany by Emperor Leopold I (Ott et al., 2002).

Prosthetic eye manufacturers in the United Kingdom were limited, although a prosthetic eye advertisement featured in the 'True Domestick Intelligence' publication (September 1679), proclaimed William Boyse of London as:

'the only person expert in making artificial eyes of enamel, covered after nature … which not only fitted for socket with ease to the wearer, but turned with all the facility of the real organ of vision'.

An advertisement two years later in 'Merlin's Ephemeris' proclaimed him, '*the only English operator in glass and the most expert in making artificial eyes so exact as not to be distinguished from the natural, they are of enamel with colour mixt the same, without either paint or lead, and worn with much ease, and so curious that they have the motion of the natural eye, being exactly made to the colour or bigness of the same which renders them very ornamental and commodious, the like was never made in England*' (Handley, 2006).

Glass eye manufacture techniques were held firmly by the Venetians until the end of the 18th century. Prosthetic eye manufacture then began being seen in Paris, where prostheses were mostly made from enamel, constituting a mix of silicon, potash, lead, and tin, rather than glass. However, the center of prosthetic eye production quickly moved from Paris to Germany, in part as a result of their superior glass blowing techniques. In 1752, Dr Heister of Nuremberg reported that he preferred glass eyes to metal eyes, as metal eyes were resistant to tears and lost their luster. Similarly, Hazard-Mirault the author of one of the first books on prosthetic eyes (*Traité pratique de l'oeil artificial,* 1818) endorsed glass as the best material for prosthetic eyes. His book also outlined the production of prosthetic eyes and provided advice for prosthetic eye wearers.

2.4. Prosthetic eyes in the 19th century: Germany becomes the center of the glass eye industry

Auguste Boissenneau, a French ornithologist, naturalist and ocularist who practiced ocular prosthetics in London and Paris in the 19th century advertised claims for the benefits of the Boissenneau enamel and crystal artificial eye, reminiscent of the claims of William Boyse of London 175 years previously. The designs of his prosthetic eyes were outlined in his patent "Improvements in Artificial Eyes" (Boissenneau, 1854) and he published a book translated as "General observations on artificial eyes, their adaptation, employment and the means of procuring them". His later patent, filed in 1866, put forward a design for a prosthetic eye which could be used for both the right and the left socket (Boissenneau, 1866), although this idea was not widely adopted.

Further accounts of prosthetic eye wear in Europe during that period were given by William McKenzie, who described some of the challenges of prosthesis wear in his book first published in 1830 (McKenzie, 1830), and by a piece published in the Otago Witness from New Zealand (1869) (Otago Witness, 1869), seemingly a reprint of an article from Paris.

Friedrich Phillip Ritterich, a German ophthalmologist who was appointed professor at the University of Leipzig in 1820, was appalled at the cost of prosthetic eyes fromParis and consequently supported the growing glass eye industry in Germany. For 30 years, Ritterich had imported prosthetic eyes from Paris and stocked 400 to 500 samples in his medical practice, charging his patients a meagre amount compared to the price being charged in Paris at the time. Over time, Ritterich encouraged German glassblowers to produce glass eyes and organized lessons in glassblowing technique. He also established a free service to produce custom made glass eyes for patients at the Leipzig Eye Institute. In this way, the production and fitting of prosthetic eyes developed into a service, rather than simply the supply of a commodity purchased from stock (Handley, 2006). By the middle of 19th century, Germany was well established as the center for glass eye production.

Innovation led to improvements in the performance of glass eyes. In 1832, Ludwig Müller-Uri, a glassblower who made dolls' eyes at the renowned Lauscha glass factory in Sonneberg, developed and introduced the more durable cryolite glass for glass eyes, which is still used today.

In 1880, Herman Snellen, a Dutch ophthalmologist, created the so-called Reform glass eye in response to the increased numbers of enucleations being performed after the introduction of anesthesia and asepsis. The Reform eye was hollow with rounded edges and allowed the prosthesis to be thicker than the earlier shell-like glass eyes. This design assisted in the restoration of lost socket volume following enucleation and provided better wearing comfort.

Surgical advancements and the use of orbital implants in the 19th century also led to improved outcomes following eye loss. In 1885, the English ophthalmologist Phillip Henry Mules, who introduced several innovations in ocular surgery, began implanting a glass sphere into the emptied scleral cavity of eviscerated eyes (Laios et al., 2019). The orbital implant facilitated the restoration of lost orbital volume and afforded the overlying prosthetic eye better movement. Mules' achievement was highlighted in his obituary in the British Medical Journal in 1905 J (1905).

By the end of the 19th century, cryolite glass eyes produced in Germany were being exported worldwide. Afar afield as Auckland New Zealand, Peacock Optometrists held stock of these German made glass eyes, assortments of which were displayed in trays. Patients were fitted with the best fitting eye available, meaning that the color or size of the prosthesis would not always be an ideal match. Excerpts from newspapers provide some narrative of the glass eye industry of that time (Post, 1936).

2.5. Prosthetic eyes in the 20th century: the glass eye crisis and plastic prosthetic eyes

In 1930, polymethyl methacrylate (PMMA) was introduced by Imperial Chemical Industries (ICI) a large British chemical company. PMMA was sold under the tradenames Plexiglas, Lucite and Perspex (Chen, 2001; Kollewe and Wearden, 2007), and a medical grade PMMA was rapidly adopted by dentists as a better material for the manufacture of denture bases than vulcanite, which had typically been used for that purpose at the time.

Then when the start of World War II meant that glass eyes became unavailable, investigations by several groups lead to the use of medical grade PMMA as a new material from which to produce prosthetic eyes. Dental technicians of the British Royal Navy pursued this investigation, as did Fritz W. Jardon, a German dental technician who had immigrated to the United States of America in 1932, in his role as the director of the Monoplex Eye Division of the American Optical Company in Massachusetts (Prosthetics, 2022). William Daniel Barker, a British dental technician, who had learned of the application of plastics in dentistry from Dr Oberlander of Germany before the war, had produced possibly the first serviceable PMMA prosthetic eye in 1942 for his son, who had lost his left eye in an accident (Bionity.com, 2007). In 1945, Barker was called on to be the officer in charge of the Ministry of Pensions Plastic Eye Unit, which was established to provide PMMA prosthetic eyes to war veterans who required them (Gazette, 1948). Likewise, Jardon headed the mass production of PMMA prosthetic eyes for American veterans at the American Optical Company (Prosthetics, 2022).

PMMA demonstrated biocompatibility nearly comparable to glass while offering greater durability. However, cryolite glass, though less

durable, may be slightly more biocompatible, as no known allergies to glass have been reported. While PMMA enabled easily the customization of prosthetic eyes through impression molding of the patient's socket, ocularists working with glass rely on their expertise and experience to visually assess and shape the prosthesis without the need for an impression. Early PMMA use was accompanied by experimentation that explored the possibilities of the material. For instance, Jardon worked with Dr William Stone Jr of the Massachusetts Eye and Ear Infirmary to connect an ocular prosthesis to a revised version of Phillip Mules' orbital implant, producing the first pegged implant. The implant was found to be unstable, and the idea was abandoned, until Dr Arthur Perry revisited the concept in 1985 with more success. Dr Perry utilized hydroxyapatite as the material for the orbital implant instead, and this pegged implant gained popularity as it provided excellent motility of the overlying prosthesis. Over time the pegged implant fell from favor as the need for surgical retreatments was more often required, complications developed as a result of the peg, and because satisfactory prosthesis motility could be obtained without pegging (Viswanathan et al., 2007).

During the second half of the 20th century, PMMA prosthetic eyes largely superseded glass eyes, although small pockets of glass eye manufacturers persisted in Europe, most notably in Germany until today. German glassblowing was even recognized by UNESCO as an "Intangible Cultural Heritage of Humanity" in 2023.

Up until the mid of the 20th century, ocular prostheses made from glass had usually been fitted by members of the optometric or ophthalmological profession. However, now with the introduction of PMMA into the field of ocular prosthetics, dental technicians, who were more familiar with PMMA technology, led the field equipped with this new material. Over the subsequent 75 years, at least in the United Kingdom, dental technicians controlled the expansion of the new discipline called maxillofacial prosthetics, which includes ocular prosthetics. By the 1970s, optometrists had, for the most part, relinquished the specialist care and rehabilitation required by disfigured or lost eyes to ocular prosthetists.

Following World War II, the two different origins of PMMA prosthetic eyes appear to have produced two main schools for the profession, namely the American school centered on the American Society of Ocularists, and the English school, centered on dental technology. In the USA, the American Society of Ocularist, established in 1957, began certifying ocularists in 1971. However, since 1980, ocularists are required to become Board Certified Ocularists by passing examinations administered by the National Examining Board for Ocularists. In the USA and other parts of the world, ocular prosthetics is also practiced in the field of anaplastology. Anaplastology is a branch of medicine providing prosthetic rehabilitation to the face or body, which incorporates the creation of orbital, nasal, and aural prostheses, and requires clinicians to pass examinations to achieve Board Certification in Clinical Anaplastology. In the United Kingdom, ocular prosthetists are trained within the Master of Maxillofacial Technology degree available to graduates of the Bachelor of Dental Technology degree. Alternatively, ocular prosthetists are trained by the National Artificial Eye Service in conjunction with the Blackpool Teaching Hospitals NHS Foundation Trust (Handley, 2006).

2.6. *Prosthetic eyes, contact lenses and scleral shell prostheses*

The earliest contact lenses owe their invention to German prosthetic eye makers. In 1887, the innovative glass blowers and specialist prosthetic eye makers Friedrich Müller and Albert Müller were tasked with producing a protective shell for a patient who had had portions of their eyelids removed to treat skin cancer (Gasson, 2017). A clear glass shell was produced and fitted to guard against desiccation and trauma to the ocular surface, as well as permit vision. The patient was able to wear the shell continually for years at a time with no apparent damage to the eye (Phillips and Speedwell, 2007). The Müllers continued the production of these glass shells and were able to modify the optics of the central portion to moderate the refractive outcome (Danz, 1990).

Around this time, the German ophthalmologist Adolf Fick, began designing glass scleral lenses, experimenting first on the eyes of rabbits and then of cadavers. In collaboration with Professor Ernst Abbe of Zeiss Optical who manufactured the lenses for him, Fick was able to fit the lenses to several patients, and also create the first scleral shell prosthesis for a blind, disfigured eye (Kopecky et al., 2018).

In 1946, Norman Bier and Joseph Dallos, who worked independently, both devised a 'ventilated' scleral lens, however it was not until the invention of PMMA that contact lens practice and scleral shell manufacture was revolutionized, in the same way it transformed prosthetic eye practice (Phillips and Speedwell, 2007).

3. Epidemiology and etiology of eye loss

There is very limited data on the general size of the anophthalmic population in different countries, but one 2012 study from New Zealand estimated its population of prosthetic eye wearers to be approximately 3000 people (Pine et al., 2012b). When extrapolated to Germany its number of prosthetic eye wearers would be approximately 56,235 and, in the United States of America (USA), it would amount to approximately 219,452 (Pine et al., 2012b). Extrapolating data from the USA and Germany, it is estimated that there are over 5 million PMMA prosthetic eye wearers worldwide, while the number of glass prosthesis wearers is around 60,000. However, this should be regarded as approximations rather than precise data. The comparison with other first world countries seems to be comprehensible due to similar socioeconomic status and quality of healthcare, but it is difficult to extrapolate these numbers to developing nations (Pine et al., 2012b).

As for the different indications, trauma accounts for the most enucleations globally (Davanger, 1970; de Gottrau et al., 1994; Erie et al., 1992; Margo, 1989; Moshfeghi et al., 2000; Olurin, 1973; Shapira et al., 2021b; Spraul and Grossniklaus, 1997), but its percentage among other causes of enucleation varies in different parts of the world. A ten-year clinicopathological study of enucleated eyes in Germany suggested that trauma was the cause of 37% of enucleations (de Gottrau et al., 1994) and two long-term studies from the USA suggested 35% (Erie et al., 1992) and 41% (Spraul and Grossniklaus, 1997), respectively. In developing countries, however, the proportions are different with trauma accounting for 51% in Uganda (Davanger, 1970) and 50% in Nigeria (Olurin, 1973). The second leading cause of enucleation in industrialized countries was glaucoma at 35% (de Gottrau et al., 1994) in Germany and 33% in an American study (Erie et al., 1992), followed by intraocular tumors at 20% (de Gottrau et al., 1994) in Germany and 17% (Erie et al., 1992) or 24% (Spraul and Grossniklaus, 1997) in the USA. These indications only play a minor role in developing countries as the second leading cause in Uganda and Nigeria was corneal disease, accounting for 18% (Davanger, 1970) and 31% (Olurin, 1973), respectively. There are several different factors that might cause this disparity between the Global North and the Global South with lower life expectancy, poor medical infrastructure, and a socio-economic divide certainly playing a role, but it is also apparent that choroidal melanoma is less common among sub-Saharan African populations as Caucasian ethnicity, fair skin, and light iris color have been established as major risk factors (Chattopadhyay et al., 2016; Yonekawa and Kim, 2012).

The loss of an eye is a truly life-changing event for the patient, not only altering their physical appearance but also having major functional, mental, and social consequences (Koch et al., 2016; Moshfeghi et al., 2000; Rokohl et al., 2018a, 2018c, 2019b). Therefore, these issues must be addressed together with the medical reasons in the decision to remove an eye (Koch et al., 2016; Moshfeghi et al., 2000; Rokohl et al., 2018a, 2018c, 2019b). The decision to perform the removal of an eye often lies at the end of a failed medical treatment and/or diagnosis indicating an unsalvageable eye (de Gottrau et al., 1994; Moshfeghi et al., 2000; Rokohl et al., 2019b). There are different techniques of eye removal surgery, such as enucleation, evisceration, and exenteration,

but those are to be addressed at a later point (Moshfeghi et al., 2000). As already described, indications for enucleation can be divided into three major groups.

The worldwide leading cause of eye loss is trauma with youth, male gender, poor visual acuity, and blunt nature of the trauma being major risk factors for posttraumatic enucleation (Davanger, 1970; de Gottrau et al., 1994; Erie et al., 1992; Koch et al., 2016; Margo, 1989; Moshfeghi et al., 2000; Olurin, 1973; Rokohl et al., 2018a, 2018c; Spraul and Grossniklaus, 1997). Primary enucleation after trauma should be performed if the eye is unsalvageable, its functions are highly impaired, and the patient or guardian is able to give their informed consent (Moshfeghi et al., 2000). Normally though, the surgeon will try to spare the affected eye with primary closure of the globe, enabling the patient to assess the functionality of their eye at a later point, and then potentially planning for secondary enucleation (Moshfeghi et al., 2000). Many surgeons also opt for the more sparing technique of evisceration for the affected eye, however although it is very rare, sympathetic ophthalmia must always be considered, as there are several case reports of this following evisceration (Green et al., 1972; Griepentrog et al., 2005; Ikui and Ueno, 1965; Migliori, 2002; Ruedemann, 1963). This severe complication of ocular trauma can be circumvented by primary enucleation, but some authors suggest evisceration is also acceptable when patients are reliable for follow-up (Moshfeghi et al., 2000; Walter, 1985; Zheng and Wu, 2013).

The second major indication is a blind and/or shrunken painful eye (phthisis bulbi) (de Gottrau et al., 1994; Erie et al., 1992; Koch et al., 2016; Moshfeghi et al., 2000; Rokohl et al., 2018a, 2018c; Spraul and Grossniklaus, 1997). Aside from tumor and trauma, common underlying causes of a blind painful eye are neovascular glaucoma, chronic retinal detachment, as well as inflammatory and infectious eye diseases such as uveitis and endophthalmitis (Moshfeghi et al., 2000). However, in these cases, if some degree of vision remains and the eye is not completely blind, maintaining vision may become even more important. Maintaining functional vision, even if limited, can significantly enhance the patient's quality of life, especially if the visual function of the other eye is also reduced. In such cases, a thorough discussion with the patient is essential to carefully weigh the benefits and risks, considering both the affected and the healthy eye, before making a treatment decision.

Intraocular malignancies are the third major indication for eye removal (de Gottrau et al., 1994; Koch et al., 2016; Moshfeghi et al., 2000; Rokohl et al., 2018a, 2018c, 2019b; Walter, 1985). Although nowadays there are more modern treatment alternatives, enucleations are still considered in certain tumor stages, also taking into consideration patient's preference (Moshfeghi et al., 2000). The most common primary intraocular tumor in adults is choroidal melanoma and despite the surge of newer therapeutic approaches including mainly radiation plaque therapies but also Cyberknife (photon therapies) or proton therapies, it is still an indication for enucleation, especially in cases of large tumors (de Gottrau et al., 1994; Erie et al., 1992; Margo, 1989; Moshfeghi et al., 2000; Spraul and Grossniklaus, 1997). This is not fully without controversy, as it has been postulated that manipulation of the globe during enucleation might cause metastasis and therefore cautious surgical technique during removal is imperative (Moshfeghi et al., 2000). In addition, some theories suggest that clinically undetectable micro metastases develop early in uveal melanoma patients, making life expectancy largely independent of enucleation. However, these theories are not fully proved. Nevertheless, enucleation is mostly not the primary treatment option in many uveal melanoma cases, with radiotherapy today being the preferred first-line therapy whenever feasible. The primary goal in uveal melanoma today is to preserve the globe, marking a significant distinction from retinoblastoma, where patient survival largely depends on the success of enucleation.

The most common primary intraocular tumor requiring enucleation in children, however, is retinoblastoma (Davanger, 1970; de Gottrau et al., 1994; Erie et al., 1992; Moshfeghi et al., 2000; Olurin, 1973; Spraul and Grossniklaus, 1997). Patients mostly present with strabismus and leukocoria and after careful consideration of different tumor properties as well as other treatment options including intravenous or intraarterial chemotherapies, a lot of affected eyes have to be enucleated (Moshfeghi et al., 2000). In general, enucleation should be considered for any other intraocular malignancy with a potential to metastasize, failure to respond to conventional treatment, or creation of a blind, painful eye (Moshfeghi et al., 2000).

4. Surgical techniques and orbital implants

4.1. Enucleation

There are several different surgical techniques for eye removal with enucleation being the oldest (Moshfeghi et al., 2000). Enucleation consists of removing the globe from the orbit along with all intraocular contents as well as a part of the optic nerve (Ababneh et al., 2015; Kowanz et al., 2023; Leister et al., 2024; Moshfeghi et al., 2000; Reed et al., 2020). Standard technique starts with eyelid retraction and 360° peritomy around the corneoscleral limbus, opening conjunctiva and Tenon's fascia (Cleres and Meyer-Rusenberg, 2014; Kowanz et al., 2023; Moshfeghi et al., 2000). Subsequently extraocular muscles are isolated and transected at their insertion, leaving a muscle stump to enable better mobilization of the globe during transection of the optic nerve (Moshfeghi et al., 2000; Walter, 1985). After the optic nerve and all remaining attachments are dissected, the globe is removed from the socket, the orbital implant is put in place, extraocular muscles are attached (here to each other, but it is also possible to attach them to the implant or the cover material, always depending on the surgeons preference, technique, and the used orbital implant), and Tenon's fascia and conjunctiva are closed in front of it (Fig. 1) (Cleres and Meyer-Rusenberg, 2014; Leister et al., 2024; Moshfeghi et al., 2000; Walter, 1985). Subsequent histopathologic analysis is mandatory in order to exclude malignancy or other disorders in need of further treatment.

4.2. Evisceration

Another anophthalmic surgical technique is evisceration during which the contents within the scleral shell of the eye are removed while extraocular muscles are preserved (Ababneh et al., 2015; Dortzbach and Woog, 1985; Kowanz et al., 2023; Migliori, 2002; Moshfeghi et al., 2000;

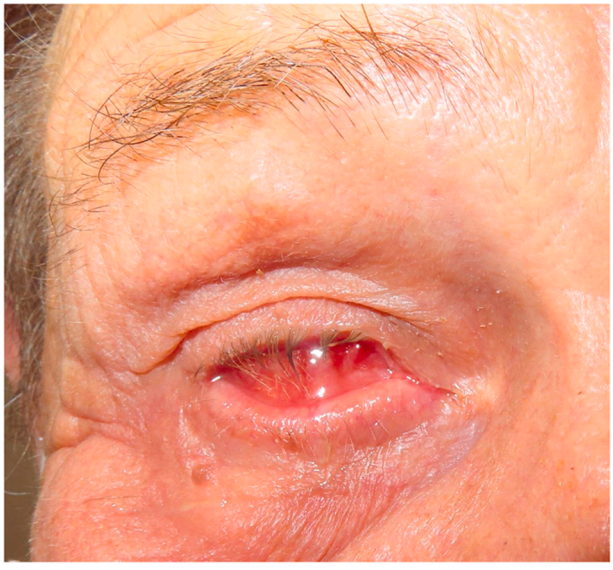

Fig. 1. Anophthalmic socket after enucleation years ago without wearing a prosthesis.

Reed et al., 2020; Walter, 1985). Similar to enucleation, the surgeon will begin with peritomy around the corneoscleral limbus, but this is followed by a limbal corneoscleral incision (Walter, 1985). The intraocular contents are then completely removed, and the implant can be placed into the scleral shell (Walter, 1985). However, nowadays, the preferred technique of many surgeons involves opening the posterior sclera to accommodate a larger orbital implant, thereby also reducing the risk of extrusion (Phan et al., 2025).

Rinsing the sclera (with hydrogen peroxide or alcohol, for example) before inserting the orbital implant remains a controversial practice without conclusive evidence supporting its necessity. While it may help remove organic and uveal residues and reduce microbial load, potentially lowering the risk of infection or sympathetic ophthalmia, some surgeons avoid it due to concerns about cytotoxicity, which could compromise scleral integrity and delay healing.

Evisceration is a simpler and quicker technique with less complications, less postoperative pain, and in most cases, it will lead to better outcomes regarding cosmesis and motility, therefore it may be preferable to many patients subjectively (Ababneh et al., 2015; Dortzbach and Woog, 1985; Migliori, 2002; Moshfeghi et al., 2000; Reed et al., 2020; Walter, 1985). Subsequently, the removed intraocular content should be evaluated histopathologically.

Choosing between the two procedures can be controversial, but when an intraocular malignancy is present, enucleation should be performed to allow for thorough histological examination of the globe and prevent spreading of tumor cells (Ababneh et al., 2015; Dortzbach and Woog, 1985; Migliori, 2002; Moshfeghi et al., 2000; Walter, 1985). Indications for evisceration include especially secondary blind painful eyes or other benign disorders, such as endophthalmitis (Ababneh et al., 2015; Dortzbach and Woog, 1985; Migliori, 2002; Moshfeghi et al., 2000; Walter, 1985). Ocular trauma can be treated with either evisceration or enucleation, depending on the severity. Although the risk of sympathetic ophthalmia is very low, it should not be disregarded and must be thoroughly discussed with the patient (Ababneh et al., 2015; Dortzbach and Woog, 1985; Migliori, 2002; Moshfeghi et al., 2000; Reed et al., 2020; Walter, 1985).

4.3. Exenteration

Another form of anophthalmic surgery is exenteration. This is mostly performed when an orbital tumor or tumors with orbital invasion are present or in the rare cases of orbital necrotizing fasciitis or mucormucosis (Kasaee et al., 2019; Kowanz et al., 2023; Martel et al., 2020; Moshfeghi et al., 2000). It involves the radical removal of the globe and surrounding orbital and periorbital soft tissue, either including or sparing the eyelids and therefore leaves the patient anatomically disfigured and in need of an epithesis (Justusova et al., 2016). In addition, there will often be a loss of sensation throughout the first division of the trigeminal nerve following this procedure. Due to the emerging molecular therapies for different malignancies, it is not performed frequently anymore (Kasaee et al., 2019; Martel et al., 2020; Moshfeghi et al., 2000).

4.4. Orbital implants

To achieve the best possible result, little postoperative complications and ensure successful rehabilitation of patients undergoing eye removal surgery, it is vital to choose a well fitted and appropriate orbital implant (Cleres and Meyer-Rusenberg, 2014; Moshfeghi et al., 2000; Norda and Meyer-Rusenberg, 2000, 2003; Rokohl et al., 2018b, 2019b; Thiesmann et al., 2018; Wladis et al., 2018). Categories that define good postoperative results are cosmesis as well as motility of the prosthetic eye. There are several things to consider in choosing the proper implant, namely adequate volume replacement of the extirpated eye, transfer of motility to the prosthetic eye, biocompatibility, difficulty of surgical technique, and price of the implant (Cleres and Meyer-Rusenberg, 2014; Moshfeghi et al., 2000; Norda and Meyer-Rusenberg, 2000, 2003; Rokohl et al., 2018b, 2019b; Thiesmann et al., 2018; Wladis et al., 2018).

Two major groups of orbital implants can be discriminated by their properties, porous and integrated versus nonporous and nonintegrated implants. Historically nonporous implants consisted of glass, rubber, and metals such as steel, gold, or silver, but nowadays frequently used materials are silicone, acrylic, and polymethyl methacrylate (PMMA) (Moshfeghi et al., 2000; Rokohl et al., 2019b; Wladis et al., 2018).

One of the commonly used porous orbital implant is the coralline hydroxyapatite implant (Fig. 2) (Reed et al., 2020; Rokohl et al., 2019b; Walter, 1985). It is made from calcium carbonate from a certain species of coral reefs and has a spongious microstructure similar to cancellous bone, consisting of numerous pores that are all connected by tubular structures (Cleres and Meyer-Rusenberg, 2014; Norda and Meyer-Rusenberg, 2003). Contrary to nonporous implants, it is the complete interconnectivity in coralline implants in addition to good biocompatibility that allows effective fibrovascular growth into the implant, constituting its integration after roughly four weeks (Cleres and Meyer-Rusenberg, 2014; Norda and Meyer-Rusenberg, 2003). The size of the pores as well as their interconnectivity differ in the various porous implants and are determining factors in their integration (Cleres and Meyer-Rusenberg, 2014; Norda and Meyer-Rusenberg, 2003). In addition, porous mammalian bone-derived hydroxyapatite orbital implants are also available, but normally used rather rarely (Han et al., 2021; Heindl and Rokohl, 2021). Furthermore, newer studies showed that these mammalian bone-derived hydroxyapatite orbital implants might shrink by osteoclastic activity which is a significant disadvantage (Han et al., 2021; Heindl and Rokohl, 2021).

Most porous implants are to be wrapped in a different material. Suitable tissues for wrapping are either autologous or allogenous biological materials, such as fascia or sclera, or synthetic materials, such as vicryl or mersilene (Cleres and Meyer-Rusenberg, 2014; Norda and Meyer-Rusenberg, 2003; Rokohl et al., 2019b). Choice of wrapping material depends on diagnosis, availability, and surgeon's preference (Cleres and Meyer-Rusenberg, 2014; Heindl and Rokohl, 2021; Norda and Meyer-Rusenberg, 2003; Rokohl et al., 2019b). While there is some controversy about this, generally the purpose of wrapping is to facilitate easier insertion of the implant, improve extraocular muscle attachment, motility, and lower extrusion rates (Cleres and Meyer-Rusenberg, 2014; Li et al., 2001; Norda and Meyer-Rusenberg, 2000, 2003; Rokohl et al., 2019b). Alloplastic materials may be preferable due to lower cost and infection risk as well as better availability (Cleres and Meyer-Rusenberg, 2014).

There is also an porous alternative which is similar but made purely from synthetic hydroxyapatite (Cleres and Meyer-Rusenberg, 2014; Norda and Meyer-Rusenberg, 2003; Rokohl et al., 2019b). Nowadays, its

Fig. 2. Orbital hydroxyapatite implant.

structural quality is comparable to the coralline counterpart while being 10–12% lighter in weight (Norda and Meyer-Rusenberg, 2003). A synthetic hydroxyapatite implant also ought to be wrapped (Norda and Meyer-Rusenberg, 2003).

Ceramic hydroxyapatite such as aluminum oxide or hydroxyapatite silicone may also be used. The former is structurally similar to hydroxyapatite, has good interconnectivity, and shall be wrapped (Cleres and Meyer-Rusenberg, 2014; Norda and Meyer-Rusenberg, 2003). The latter is also known as "Guthoff-Plombe", it has four grooves in the anterior segment to improve extraocular muscle attachment, and need not be wrapped (Cleres and Meyer-Rusenberg, 2014; Norda and Meyer-Rusenberg, 2003).

Porous polyethylene (Medpor) is now the most used porous orbital implant in many countries but especially in the United States of America (Cleres and Meyer-Rusenberg, 2014). Good fibrovascular ingrowth can be observed and its smooth surface allows for simple insertion of the implant (Rokohl et al., 2019b). Furthermore, extraocular muscles can be attached directly to the material, so there is no need for wrapping (Cleres and Meyer-Rusenberg, 2014; Norda and Meyer-Rusenberg, 2003; Rokohl et al., 2019b).

Although not without controversy, it is possible to integrate a pegging system into the implant to further improve motility by connecting implant and prosthetic eye directly (Cleres and Meyer-Rusenberg, 2014; Li et al., 2001; Norda and Meyer-Rusenberg, 2003). This should occur at least six months after eye removal surgery and is applicable to all the porous orbital implants mentioned above, except the "Guthoff-Plombe" (Cleres and Meyer-Rusenberg, 2014; Li et al., 2001; Norda and Meyer-Rusenberg, 2003).

Overall, many studies investigating long term results of porous orbital implants have shown good biocompatibility, stability, low extrusion rates due to fibrovascular ingrowth and good motility due to muscle attachment (Ababneh et al., 2015; Busin et al., 1994; Chattopadhyay et al., 2016; Cleres and Meyer-Rusenberg, 2014; Dortzbach and Woog, 1985; Kasaee et al., 2019; Martel et al., 2020; Migliori, 2002; Norda and Meyer-Rusenberg, 2000, 2003; Olurin, 1973; Reed et al., 2020; Rokohl et al., 2018b; Thiesmann et al., 2018; Walter, 1985; Wladis et al., 2018; Yonekawa and Kim, 2012). So theoretically, porous implants should be better and are often preferred, however comparing porous and nonporous implants is difficult because, overall, there are far more data on the former than the latter (Jordan, 2018; Rokohl et al., 2019b). In the studies that do compare both, nonporous implants have similarly good compatibility and low complication rates (Jordan, 2018; Rokohl et al., 2019b; Wladis et al., 2018). In summary, there is no clear evidence that porous orbital implants offer significant advantages over non-porous ones. However, non-porous implants are significantly cheaper. Therefore, they can be considered clinically equivalent, allowing the surgeon to choose the implant based on clinical circumstances, cost, personal preference, and experience (Cleres and Meyer-Rusenberg, 2014; Jordan, 2018; Norda and Meyer-Rusenberg, 2000; Rokohl et al., 2019b; Wladis et al., 2018).

5. Living with a prosthetic eye – psychosocial and vision related issues associated with eye loss

5.1. Anxiety, depression, and stress

The face is a particularly important part of the human body communicating awareness, perceptions, emotional intensity, and ideas, and is predominantly how people are recognized. Eyes have a significant role in self-expression and non-verbal communication and express understanding and insight. For these reasons, when an eye is lost or disfigured, the significant psychological, social, and practical impacts are not surprising. There are a wide range of accident, medical and congenital etiologies for the loss or disfigurement on an eye and consequent use of an ocular prosthesis. Those who lose an eye due to an accident experience greater initial negative feelings and maintain greater feelings of anger over time compared to a medical event (Pine et al., 2017b).

Prosthetic eye wearers do not necessarily experience anxiety, depression or stress more or less than the general population; however, studies have found that a disproportionally high number do report elevated or extremely high levels of anxiety, depression or stress (Heindl et al., 2021; Keys et al., 2021; McBain et al., 2014; Pine and Pine, 2020; Sadiq et al., 2020; Wang et al., 2020; Ye et al., 2015). Anxiety and depression rates may be under diagnosed in prosthetic eye wearers (Heindl et al., 2021). During the first three months after receiving a prosthesis, patients experience moderate to strong negative feelings as they process the event, grieve, and come to terms with the appearance and functional changes associated with eye loss. At the same time, there is evidence of positive feelings of happiness, relief and acceptance likely in the context of having a prosthetic eye fitted and returning to some sense of normality (Pine et al., 2017b). Prosthetic eye wearers can experience difficulties in their employment, leisure and social functioning (Keys et al., 2021; Pine et al., 2017a), which can negatively impact their mental well-being and put them at greater risk of being depressed, anxious, and stressed, as well as of feeling less accepted by society and suffering appearance anxiety (Pine et al., 2017a).

5.2. Health and function of the remaining eye

A significant cause of concern for anophthalmic patients is the health of their remaining eye (Korani et al., 2021; Pine et al., 2011; Rokohl et al., 2018c). Anxious preoccupation with loss of sight and fear of injury is an ongoing issue for prosthetic eye wearers (Keys et al., 2021) and can lead to depression, social anxiety, and withdrawal in visually impaired individuals (Binder et al., 2020; Rokohl et al., 2023a; Soleimani et al., 2017; Visagie et al., 2017). Previous research has also established that prosthetic eye wearers are particularly concerned about changes in visual perception due to acquired monocular vision (Pine et al., 2011; Rokohl et al., 2018c; Shapira et al., 2022).

5.3. Monocular vision

Acquired monocular vision occurs after the loss of an eye and primarily reduces one's visual range and impairs depth perception (Ihrig and Schaefer, 2007). These visual changes can cause psychosocial challenges (Keys et al., 2021), significant levels of anxiety (Pine and Pine, 2020) as well as feelings of anger in anophthalmic patients (Pine et al., 2017b). Due to these monocular limitations, prosthetic eye wearers can have difficulties in employment and recreational functioning, particularly in tasks with high visual demand (e.g., ball sports, horse jumping, skiing, trade work – electrician, builder) (Pine et al., 2017a). Due to these significant impacts on functioning and the consequent distress, it is important to inform patients that there are compensatory strategies and behaviors to help cope with acquired monocular vision. Once learnt and put into practice, these can reduce the functional impacts and allow for return to previous work and leisure activities (Heindl et al., 2021; Pine et al., 2017c). Examples of such compensatory strategies include positioning mirrors on work desks or in cars on one's blindside, scanning and turning one's head more to the side of eye loss, and when walking or sitting ensuring others are on their sighted side (Pine et al., 2015b). Although acquired monocular vision significantly impacts patients' lives, this effect appears to be most pronounced immediately after eye loss (Shapira et al., 2022). The duration of artificial eye wear plays a crucial role in various quality-of-life aspects, including visual functioning (Shapira et al., 2022). Patients who have worn a prosthetic eye for a longer period (since their initial fitting) tend to show better performance in near and distance vision activities (Shapira et al., 2022). Conversely, a prolonged adjustment period to monocular vision is linked to poorer outcomes in visual function, social interactions, mental health, and role-related challenges (Shapira et al., 2022). This highlights the importance of early rehabilitation training

focused on adapting to monocular vision.

5.4. Mucoid discharge

A high percentage of prosthetic eye wearers experience mucoid discharge (Pine et al., 2011, 2017c), which is a source of significant levels of anxiety for these patients (Pine and Pine, 2020), as well as feelings of insecurity, preoccupation with hiding one's eye, and reduced feelings of acceptance (Pine et al., 2017b). Initially, discharge concern is due to the wearer's negative interpretation of what it might mean (e.g., poor hygiene, sign of infection, that it is abnormal) and later in the recovery process, is due to the discomfort from wiping the discharge and how it appears to others (Pine et al., 2017c). Due to the distress that socket discharge can cause, it is recommended that patients be informed early on in the process of the likelihood of discharge and its lack of harm, and be provided with best management protocols (see Daily Care and Handling) (Pine et al., 2017c).

5.5. Appearance concerns

Prosthetic eye wearers with appearance concerns have greater negative emotions (Pine et al., 2017b), significant levels of stress (Pine and Pine, 2020), and recreational, social and occupational difficulties (Pine et al., 2017a; Rokohl et al., 2019b; Shapira et al., 2022). It is the disguisability of their eye that is particularly important (e.g., their prosthesis moving in line with or matching their companion eye, upper eyelid ptosis, rotating in the socket) (Korani et al., 2021; Pine et al., 2017b). Prosthetic eye wearers are concerned with how they appear to others (Pine et al., 2017c) and those who believe their prosthesis is unnoticeable to others have greater satisfaction with it (Song et al., 2006). The visibility of a disfigurement can lead to issues with quality of life, body image, self-esteem, and social interactions and have a significant psychological impact (Rumsey and Harcourt, 2004).

Anophthalmic patients who are adolescents (12–18 years) when they first receive their prosthesis are more likely to experience a greater intensity of negative feelings compared to other age groups (Pine et al., 2017b). This is understandable given that identity and acceptance by peer group are particularly important during the adolescent developmental stage (Erikson, 1963). Older prosthetic eye wearers are less concerned about their appearance and have significantly less depression, anxiety, stress, and appearance anxiety than younger wearers (Pine and Pine, 2020). This is consistent with the idea that older people are less concerned with their outward appearance and have a more established sense of identity and self-esteem (Franzoi and Koehler, 1998; Reboussin et al., 2000). This suggests that it is particularly important to offer psychological support to adolescents who lose their eye. Patients in the young adulthood group (19–40 years) should also be considered as they experience higher levels of intensity of negative emotions, including feelings of inferiority, insecurity, and shyness (Pine et al., 2017b).

Satisfaction among prosthetic eye wearers is closely tied to the prosthesis's ability to disguise disfigurement, with better self-rated appearance (Rokohl et al., 2018b; Shapira et al., 2022). Previous studies identified perceived prosthetic motility as a very strong predictor of appearance satisfaction and seem to influence the quality of life (Rokohl et al., 2018b; Shapira et al., 2021a). Additionally, better general appearance ratings, longer prosthesis experience, older age, and shorter adjustment time were key factors in motility satisfaction (Shapira et al., 2021a). Over time, satisfaction with motility improved as expectations adjusted (Pine et al., 2011; Shapira et al., 2021a, 2022). Younger patients seem to be more concerned about the motility of the prosthetic eye, while older individuals seem to prioritize functionality over aesthetics (Shapira et al., 2021a). Research suggests that both appearance and motility concerns decrease with age due to greater self-acceptance and coping strategies (Pine et al., 2011; Shapira et al., 2021a, 2022).

Since the motility of the prosthetic eye plays an important role in the perception of appearance and social confidence, reconstruction teams should focus on both cosmetic adaptation and optimization of motility (Pine et al., 2011; Rokohl et al., 2018b; Shapira et al., 2021a, 2022). While extreme gaze duction may not be essential, natural eye motions remain crucial for social integration and interactions (Rokohl et al., 2018b; Shapira et al., 2021a).

5.6. Social interactions

Social interactions are deeply influenced by appearance, affecting stigma, eye contact, relationships, and self-confidence (Shapira et al., 2021a, 2022). Individuals with facial disfigurement most commonly have difficulties concerning social interaction (Clarke, 1999; Shapira et al., 2022). Eyes play a significant role in communication, and it is therefore reasonable to expect a negative impact on ones' social interactions when an eye is lost (Rokohl et al., 2018b; Shapira et al., 2021a, 2022). It has been established that those with eye loss have high levels of social anxiety and avoidance (Clarke, 1999; McBain et al., 2014) and experience role difficulty and impairments in social functioning (Ahn et al., 2010; Coday et al., 2002; Hirneiss et al., 2009; McLean, 2011; Pine et al., 2017a). Better movement seems to reduce social avoidance, emphasizing the role of synchronized eye motion in disguising disfigurement (Shapira et al., 2021a, 2022). However, prosthetic eye wearers with social difficulties have concerns with not only their appearance, but also with mucoid discharge and visual perception changes (Pine et al., 2017a).

In social interactions, it is important to consider the role of one's thoughts and behavior (Frech et al., 2022). The behavior and cognitive processing of anophthalmic patients can be negatively impacted by eye loss and prosthetic eye wear (Pine et al., 2017a). This in turn, can have negative impacts on areas of functioning, thus increasing the prospect of greater negative psychological impacts (Rathus, 2013). For prosthetic eye wearers, other peoples' reactions are a common source of stress (Pine et al., 2017a), and in facial disfigurement populations, it is commonly noted that individuals are sensitive to their disfigurement and have a propensity to attribute all negative social experiences to their appearance (Partridge, 1994). The occurrence of information processing biases are likely where individuals are selective in their interpretation of social reactions, focusing on evidence which supports their internalized self-views and ignoring information that opposes it (Kenny and DePaulo, 1993). These cognitive biases can maintain one's belief system and contribute towards mood difficulties. Behavior such as avoidance due to discomfort or distress can also maintain negative beliefs as disconfirming information is never obtained (Beck and Beck, 2011).

5.7. Psychological and social support

It is important to take note of unhelpful beliefs and behaviors observed in anophthalmic patients when considering the need for psychological support. One's adjustment process and level of disfigurement-associated distress is influenced by their interpretation of their disfigurement, themselves and their interactions with others (Thompson and Kent, 2001). Having good social skills is also associated with successful adjustment (Kapp-Simon et al., 1992; Robinson et al., 1996) and social skills training could be valuable for anophthalmic patients (e.g., staying calm, assertive confrontation of negative reactions, educating others (Partridge, 1994)). It has been noted in previous research that a combination of social skills training and cognitive behavioral therapy (CBT), which addresses one's thoughts and behaviors (based on a model of psychosocial distress in people with disfigurements (Kent, 2000)) may be beneficial for anophthalmic patients (Keys et al., 2021; McBain et al., 2014). There is increasing evidence for the efficacy of this combined approach for supporting individuals with disfigurement (Norman and Moss, 2015; Williamson et al., 2015). A supportive family and social environment also has an important role in coping with disfigurement (Goiato et al., 2013) and it has been well established that social support

is important for the psychological well-being of prosthetic eye wearers (Clarke et al., 2003; James et al., 2011; McBain et al., 2014; Pine and Pine, 2020; Ye et al., 2015). In addition, Frech et al. found that patients treated for congenital anophthalmos or blind microphthalmos over a decade ago reported emotional stability and successful social integration, with minimal limitations (Frech et al., 2022). These findings validate the long-term effectiveness of surgical and prosthetic interventions in enhancing self-perception, social acceptance, and overall well-being (Frech et al., 2022).

There are lingering negative feelings for some experienced prosthetic eye wearers (mainly pre-occupation with hiding the eye and shyness) possibly due to poor behavior from others, negative social, occupational, or recreational experiences, and/or unhelpful coping strategies (Pine et al., 2017b). However, it is reassuring for new prosthetic eye wearers to hear that concerns around appearance, mucoid discharge and visual perception can significantly decrease over time (Pine et al., 2017c), and not only does emotional stress and negative feelings associated with eye loss also decrease (Goiato et al., 2013; Keys et al., 2021; Korani et al., 2021; Pine et al., 2017b), but positive feelings such as happiness and acceptance increase (Pine et al., 2017b). This suggests adjustment over time, the impact of getting older (Nelson et al., 2008), and the development of coping strategies (Knudson-Cooper, 1981; Malt, 1980).

Losing an eye, going through the process of receiving an ocular prosthesis and subsequently adjusting to the practical, social, and emotional impacts of this can be an incredibly difficult and confusing time for patients. It is crucial that support, reassurance, and good advice be provided. Due to the well-established psychological impact of eye loss and disfigurement, psychometric screening should be included in standard care practices and psychologists included in the multidisciplinary teams (Heindl et al., 2021). It is important that concerns regarding appearance, mucoid discharge, and acquired monocular vision be addressed and that anophthalmic patients are prepared for the possible functional impacts of their eye loss on employment, social and leisure activities. Tailored education, coping strategies, social skills training, and emotional/psychological support (e.g., CBT) is expected to be particularly beneficial for this population and their overall physical and mental health.

6. Material and types of PMMA prosthetic eyes

6.1. Background and types of PMMA prosthetic eyes

As mentioned in the introduction, the production of PMMA prostheses began evolving during World War II and was increasingly researched and developed for use as ocular prostheses.(Pine et al., 2015a). The PMMA (or acrylic) artificial eye appeared stronger, longer lasting and easier to adapt for custom use (compared to the glass eyes). In different parts of the world, ocular prosthetists started to further develop the technique, and currently the use of PMMA ocular prosthesis is predominant in most countries throughout the world.

With ocular prostheses made of PMMA, a distinction can be made between stock prostheses and customized prosthesis types. Stock acrylic (or PMMA) prostheses are available in fixed shapes and colors, and the deeply concave posterior enables a fit over all types of implants. They are cheap, easily available and can be inserted in a socket by anyone without specialization. Stock prostheses are however likely to have a misaligned iris position, imperfect eyelid contour or uncomfortable fit. Stock eyes may be an outcome in poor countries or areas with decreased resources, they may be used as a temporary postoperative conformer (Patil et al., 2008) or they may be modified to a partial customized ocular prosthesis (Taicher et al., 1985).

A full custom fit prosthesis can be adjusted to any desired shape, size, color, and comfort and is therefore considered as the best option in developed countries. Analogous to the customized glass prostheses, there are different types of customized PMMA protheses. After enucleation or evisceration patients receive a PMMA prosthetic eye for replacing the orbital volume deficit. Compared to the hollow, double-walled reform eye made from cryolite glass, PMMA prostheses are usually made of solid material and not hollow (Rokohl et al., 2019b; Worrell, 2016). However, hollow PMMA ocular prostheses can also be produced, but these are not standard practice and are only used in selected cases (Worrell, 2016). These prostheses are about a third lighter than full prostheses, which significantly improves rehabilitation (Worrell, 2016). By reducing strain on the lower eyelid, discomfort, irritation, discharge and redness, they offer a more comfortable, aesthetically pleasing and inconspicuous alternative that significantly improves patient outcomes (Worrell, 2016). Alternatively, a shell prosthesis can be used after enucleation or evisceration if there is less volume to be filled. Data from a study in the UK suggest that approximately 25% of the patients are using a scleral shell (cosmetic shell), while 75% are wearing a prosthetic eye (Shapira et al., 2021b). These shell prostheses are thin single-walled PMMA prosthetic eyes that take up less space and are lighter in weight additionally. Around 25% The shell prosthesis can also be placed in front of a non-functional and unsightly globe including phthisis bulbi or microphthalmia (Rokohl et al., 2019b).

Despite using the same core technique, the production process of PMMA prosthetic eyes has evolved with various adaptations. Many ocularists develop their own methods, relying on experience, making the final product's quality dependent on their skill. While literature attempts to standardize techniques, it cannot fully capture the nuances of daily practice. The fundamental principles of PMMA prosthesis manufacturing are detailed in Chapter 8.

6.2. Polymethylmethacrylate (PMMA)

Polymethylmethacrylate (PMMA) prostheses are a polymerized product of a dough mixture of acrylic powder (mainly PMMA) and liquid monomer (mainly methylacrylate (MMA)) (Pine et al., 2021) and has good biocompatible properties, provided it is polymerized in the right way (da Silva et al., 2021). For use in ocular prostheses, polymerization must be carried out long enough to prevent residual monomer which is toxic and can cause reactions in the socket. However, polymerizing for too long can lead to color change. Manufacturers of the raw material have optimized the material over the years, so that correct processing gives good appearance and biocompatibility.

Due to its biocompatibility, excellent optical clarity, processability, and durability, PMMA is the standard material for plastic ophthalmic prostheses. The major advantage in the manufacturing process is that a PMMA prosthesis can be adjusted at any time in the process, both in terms of color and shape. In case of an incorrect estimate, the shape can still be adjusted afterward. This property makes acrylic eye production easily accessible for fine-tuning. Even, if minor shape adjustments are required over time, an additional amount of material can be pressed, or the model can be planed off locally to adapt to the new socket situation. In addition, any obtained rough or scratched surface can easily be removed by polishing. These aspects make the PMMA prosthesis a very durable prosthesis.

Despite its frequent and numerous advantages, a potential drawback of PMMA is that it is hydrophobic, meaning that water tends to cohere in droplets rather than form a smooth tear sheath that equally moistens the surface as in the naturally hydrophilic eye (Ko et al., 2017; Litwin et al., 2018; Pine et al., 2021). Irritation, crusting, and increased mucus production are known problems of the prosthetic eye wearer (Jones and Collin, 1983; Mourits et al., 2017; Pine et al., 2011), and it is expected that increased wettability (hydrophilicity) will improve the tear film with reduced dry eye symptoms as is also seen in hydrophilic contact lenses (Ko et al., 2017; Pine et al., 2021). Studies are being done to increase the wettability (hydrophilicity) of the artificial eye. Promising options are to adjust the proportion of ethylene glycol dimethacrylate (EGDMA) already available in the liquid monomer of the PMMA mixture (Pine et al., 2021). The addition of poly ethylene glycol makes the surface more hydrophilic and reduces bacterial adhesion (Ko et al., 2017).

Further studies are needed to test the effect of both methods in prosthetic wearers. Litwin et al. found that a high-performance polishing technique resulting in a smoother surface reduced early deposit formation and improved subjective symptoms for up to one year in a prospective comparative study (Litwin et al., 2018).

6.3. Other applications of PMMA

Except for use as the definite prosthesis, PMMA (or acrylic prostheses) can be used as (custom) peri-operative conformers. Any preferred model can be created and, if desired, holes can be drilled or extensions can be added for suture fixation (Groot et al., 2021a).

PMMA is also used for expansive conformer therapy in congenital microphthalmic and anophthalmic children (Changal and Khandekar, 2021; Christiansen et al., 2008; Dootz, 1992; El Essawy and Abdelbaky, 2016; Kuijten et al., 2017; Price et al., 1986; Taha Najim et al., 2020; Tucker et al., 1995). The firm PMMA material makes it possible to use the conformer as a socket and eyelid expander without the risk of breaking. For more information on the treatment of anophthalmia and microphthalmia, see chapter 11.

Three-dimensional printing for medical purposes has become popular in recent years, and developments are also emerging for 2D and 3D printing of an artificial eye. The application of digital techniques will probably not replace the work of the ocularists fully within the next years, but it can reduce fabrication time as well as costs and may also reduce patient discomfort during the fitting process, which is especially helpful in children. Printing can be divided in single-color conformer printing, and multicolor prosthetic printing, the latter being produced either in a hybrid form, combining conventional methods with digital printing, or in the full print of a complete prosthesis.

7. Material and types of cryolite glass prosthetic eyes

7.1. Background and types of cryolite glass prosthetic eyes

Cryolite glass is a type of glass which gets its whitish color from a sodium-aluminum fluoride (Martin and Clodius, 1979). Cryolite glass is exclusively produced in the glassworks of Lauscha, Thuringia in Germany (Rokohl et al., 2019b). The advantage of the cryolite glass compared to the previously world-wide used lead crystal glass is the improved color, the easier workability, and a better compatibility (Koch et al., 2016). The German glassblower Ludwig Uri-Müller developed the first cryolite glass eye in 1832 and in 1880 Dutch eye surgeon Hermann Snellen enhanced it by designing a hollow prosthetic eye from the same material, which was then called the Snellen “reform eye” (Martin and Clodius, 1979; Rokohl et al., 2018a). Even today, the vast majority of ocularists (>90%) in Germany, Austria, and Switzerland use cryolite glass from Thuringia (Koch et al., 2016; Rokohl et al., 2018a, 2018c, 2019b).

There are different types of cryolite glass eye prostheses. After enucleation or evisceration specifically, there are two kinds of most commonly used cryolite glass eye prostheses for German anophthalmic patients (Koch et al., 2016; Rokohl et al., 2019b). The reform eye (Fig. 3) is placed in front of the orbital implant following enucleation or evisceration (Koch et al., 2016; Rokohl et al., 2018a, 2018c, 2019b). As briefly mentioned before, the reform eye is double walled, hollow, and therefore lighter than PMMA, while providing large volume for replacing the orbital volume deficit post eye removal (Koch et al., 2016; Rokohl et al., 2018a, 2018c, 2019b). Alternatively, a glass shell prosthesis (Fig. 4) can be used after enucleation or evisceration if there is less volume to be filled (Rokohl et al., 2019b). These are thin single-walled glass prosthetic eyes that take up less space and are lighter in weight additionally (Rokohl et al., 2019b).

The globe shell (Fig. 5) is also a single-walled cryolite glass prosthesis, but it can be placed in front of a non-functional and unsightly globe, as it is even thinner and formed more sharply (Cote and Haddad,

Fig. 3. Hollow, lightweight, and double-walled cryolite glass prosthetic eye (“reform eye”). This type of glass prosthesis is used following enucleation or evisceration for replacing orbital volume deficit. The back wall is a little bit translucent since it is very thin.

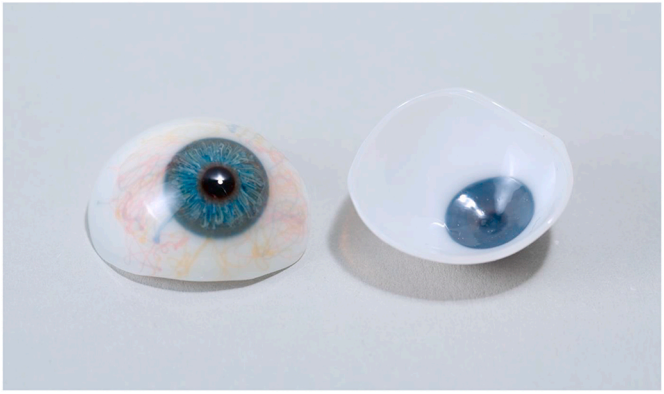

Fig. 4. Single-walled cryolite glass shell prosthetic eye for patients following enucleation or evisceration if less orbital volume replacement is necessary.

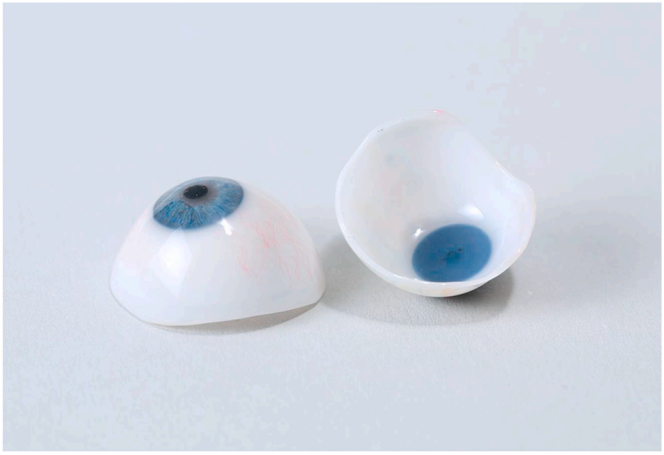

Fig. 5. Single-walled cryolite glass globe shell prosthesis for patients with phthisis or microphthalmos. The globe shell prosthesis is thinner, slightly more pointed, and more sharply tapered.

1990; Koch et al., 2016). Indications for the use of this specific prosthesis are phthisis bulbi or microphthalmia (Rokohl et al., 2019b). The prosthesis is placed in the conjunctival sac and due to its very low weight, there is little mechanical strain on the eyelids, lowering the risk of certain complications including the post-enucleation socket syndrome (Cote and Haddad, 1990; Koch et al., 2016; Thiesmann et al., 2018).

7.2. Differences and similarities between cryolite glass and PMMA

One important difference between PMMA and glass is the frequency of renewal (Table 1). While PMMA-wearing patients receive a new prosthesis mostly every 2 years (or up to every 5–6 years in some countries), glass prostheses are renewed at least every year (Koch et al., 2016; Rokohl et al., 2018a, 2019b). This is largely due to the hydrophilic properties of cryolite glass that on the one hand eliminate the necessity of eye drops (Harting et al., 1984; Koch et al., 2016). On the other hand, however, the slightly alkaline lacrimal fluid constantly reacts with silicate structures in the cryolite glass, causing remodeling and in effect roughening of the surface (Clodius et al., 1981; Harting et al., 1984; Koch et al., 2016). The outer surface of the glass eye is otherwise comparatively smooth, durable, and therefore less likely to collect deposit, but over the course of a year these hydrolytic changes as well as some mechanical scratching will lead to its deterioration (Clodius et al., 1981; Harting et al., 1984). If not addressed, this eventually results in poor wetting, decreased comfort, and conjunctival irritation (Clodius et al., 1981; Harting et al., 1984; Koch et al., 2016; Rokohl et al., 2018a, 2019b). It seems, that this practice of renewing glass prostheses in shorter intervals can sometimes lead to significantly better outcomes regarding fit and appearance of the prosthesis as the ocularist can adjust to the patient's individual experience on a yearly basis (Rokohl et al., 2018a).

Compared to PMMA, cryolite glass prostheses are lower priced on average (Koch et al., 2016; Rokohl et al., 2019b). In some rare cases, especially when a high orbital volume has to be replaced by the prosthesis, the hollow cryolite glass prostheses can have the advantage of being lighter compared to PMMA prostheses, normally made of full material (Koch et al., 2016; Rokohl et al., 2019b).

Cryolite glass prostheses also seem to have better biocompatibility for there are virtually no recorded cases of acute allergic conjunctivitis in reaction to them, as opposed to PMMA where this is a rare but known complication that ought to be addressed at a later point in this review (Koch et al., 2016; Rokohl et al., 2019b).

Although it is rather rare, higher rates of breakage are often viewed as a disadvantage of glass prostheses (Rokohl et al., 2019b, 2019d, 2021a). While there are reports of breakage in the ophthalmic socket due to abrasion, chemical manipulation, or extreme temperature differences (Goldfarb, 1966; Harting et al., 1984), there is one single-center study that aims to extrapolate the most common causes of breakage (Rokohl et al., 2019d). In this study, the mean rate of breakage was one per 26.63 years of wearing while 94% of defects occurred due to dropping of the prosthesis during removal or cleaning (Rokohl et al., 2019d). 97% of participants had a replacement in case of defect (Rokohl et al., 2019d). In a 2017 survey comparing the concerns of glass- and PMMA-wearing anophthalmic patients respectively, 7% of patients in the cryolite glass group reported they were concerned about breakage of their prosthesis while PMMA wearers reported none (Rokohl et al., 2018c, 2019d). While the difference in level of concern between the two groups is significant, the risk of breakage is low and not a major hindrance in the everyday life of most cryolite glass prosthetic eye wearers (Rokohl et al., 2018c, 2019d). Exceptions are made for patients with whom there is an increased risk of breakage, such as children and adolescents up to 16 years of age or patients unable to properly grasp objects (Koch et al., 2016).

Overall, it can be noted that cryolite glass prosthetic eye wearers are very content as their level of concern in many other regards seems to be lower than in PMMA wearing patients (Pine et al., 2011; Rokohl et al., 2018a, 2018c). Cosmetic issues were also less of a concern in the cryolite group tested. However, the cause of these differences and the role of the prosthetic material itself needs to be established in further comparative multicenter studies (Pine et al., 2011; Rokohl et al., 2018a, 2018c).

Table 1
Comparison: Features of PMMA vs. Cryolite Glass Prosthetic Eyes.

Feature	PMMA (**Polymethyl Methacrylate**)	Cryolite Glass
Renewal interval	2–6 years (yearly polishing recommended)	6–12 months (no polishing possible)
Price	~2500 Euros (Germany)	~600 Euros (Germany)
Weight	Usually solid material, usually heavier, especially when replacing larger volumes	Hollow structures (reform eyes), mostly lighter
Surface	Rougher	Smoother (fire polished)
Fragility	Almost unbreakable	Fragile, but with very low breakage rates
Biocompatibility	Good, but may cause allergic conjunctivitis	Excellent, no reported allergies

8. Making and fitting of PMMA prosthetic eyes

8.1. Parts of making and fitting of PMMA prosthetic eyes

The production of a PMMA prosthesis can be divided into several parts: 1. Input: shape (geometry) and color determination; 2. Manufacturing (iris, core, full prosthesis); 3. Output: end product fitting and fine-tuning (Fig. 6). Different variations are possible for each step with admixture of digital processes currently emerging.

An overview of the various techniques can be found in the morphologic map (Table 2). Depending on which techniques are chosen, 3 types of prostheses can be distinguished: conventional, hybrid (partly digital), and fully digital. The three main steps are discussed in the following paragraphs.

8.2. Part 1: Prosthetic shape (geometry) and color

The first step in the production of a prosthesis is shape determination (or geometry). In the ocularist profession that makes acrylic eyes, there are basically two schools, one uses an impression to define the model and the other defines the geometry by empirical fit. Both methods have their reasoned advantages and disadvantages, but there are no comparative studies. Ultimately, the same criteria must be taken into account for each method (Table 3).

8.2.1. The impression technique

An impression of the socket is often used to define the geometry of the prosthetic model (Pine et al., 2015c). The posterior lining, including curves and irregularities of the socket is captured and a prosthesis can be made that exactly follows the curves and irregularities of the individuals' socket.

Usually, an impression tray with hollow tube is inserted in the patient's socket. The impression material is then injected via the hollow tube and in the socket where it captures the socket lining after hardening. In general, ready-made trays are used that are available in different sizes, but all kinds of variants are possible (customized tray, stock prosthetic tray or customized prosthetic tray) (Goiato et al., 2014; Mathews et al., 2000). Impression materials are available from alginate to polyvinylsiloxane with their own specific properties. Because the socket is flexible, the type of tray, and the stiffness of the impression material will influence the final outcome, and the necessary adaptations will therefore also be dependent on the technique and materials used. Usually, the impression model is copied to a wax model, and the wax model is adjusted mainly on the anterior side, leaving the posterior side in the original state. The ocularist will have to make quite a few

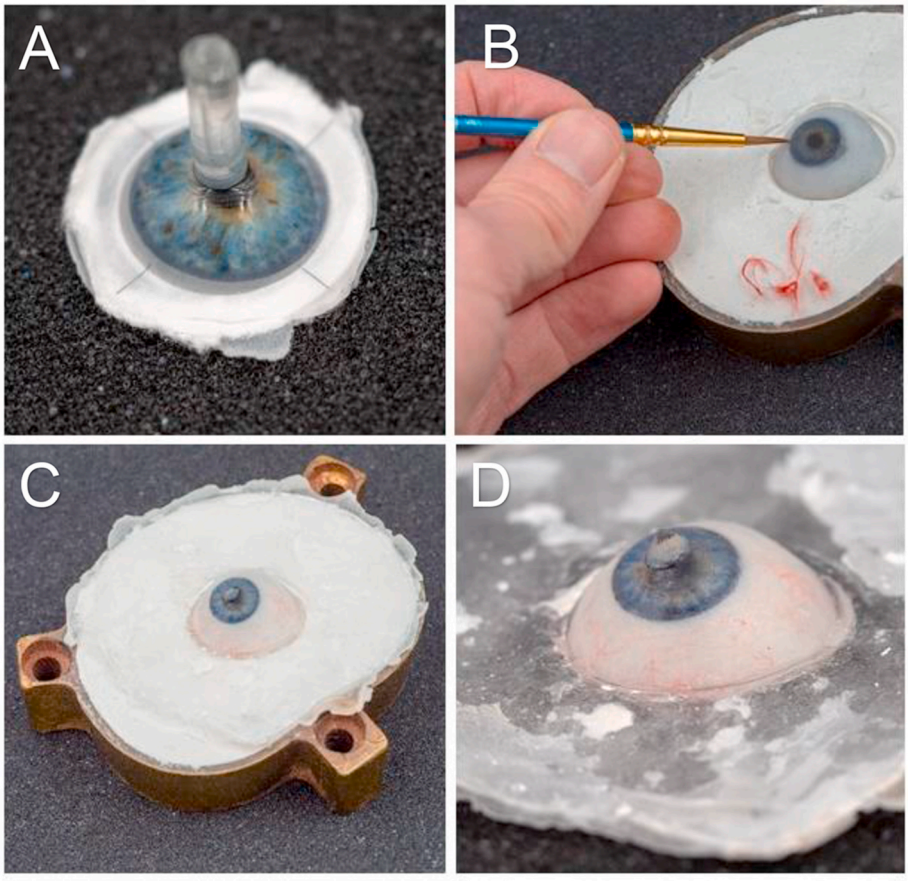

Fig. 6. Conventional PMMA prosthetic eye production: iris/cornea button (A) as well as sclera and additional iris painting (B). Red silk fibers are used to simulate the conjunctival blood vessels. Processed transparent PMMA in the plaster cast (C). Polymerized PMMA ready for final trimming, burnish, and polish (D). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

modifications on the wax model to avoid bulging, unstable or immobile fit of the prosthesis (Allen and Webster, 1969). The final wax model is fitted in the patient and the position of the iris is marked on this model. The wax model is then used to produce the PMMA prosthesis.

Suggested advantages using the impression technique include a better motility due to direct translation of implant motion and less death space behind the prosthesis, resulting in less accumulation of mucus (Bartlett and Moore, 1973; Mathews et al., 2000). In cases where the own atrophic eye is still in situ, the impression technique will also allow a tailor-made match between prosthesis and the atrophic eye, resulting in more comfort. A socket with complex anatomy will also benefit from an impression technique. Disadvantages are the use of the impression which can be uncomfortable for the patient and irritate the socket. A socket impression also needs patient cooperation which can be difficult in children.

8.2.2. *Empirical fit technique*

By inspecting the socket, a trained ocularist can select a primary model (out of a whole set of different models) including iris to fit in the socket. If necessary, more models can be tested and assessed for features important for artificial eye fitting. The selected model is then modified with the addition of wax or by local grinding. Adjustments are made step by step until the ideal shape is obtained. The final shape is used to produce the definitive PMMA prosthesis using the procedure described below.

The fitting of the prosthesis may become suboptimal after a while (around two years in adults or earlier in the first postoperative year or in children). At this stage, it is an option to make changes to the original prosthesis, or to produce a completely new prosthesis for which the old prosthesis can often serve as the primary fitting model. Experienced advantages are that the process is less time consuming, and that the procedure allows more fine-tuning on the final prosthesis. The empirical fit eyes are lighter in weight because they do not necessarily fill the complete socket. This is likely to reduce the chance for sagging of the lower eyelid, but it may at the same time increase the pooling of mucus in the resulting dead space.

Both above mentioned methods for geometry determination are dependent on the subjective fitting skills of the ocularist and will therefore not be fully reproducible. It is currently being investigated whether it is possible to create a reproducible workflow for accurate fit in the living patient that excludes the need of inconvenient impression, and/or a time-consuming fitting process. Ruiters et al. described a potential method using cone beam scanning to merge a posterior part (socket lining) to an anterior part (scanned mirror image of the healthy fellow cornea) in ex-vivo models (Ruiters et al., 2021), and Sagoo et al. suggest the use of optical tomography scans to capture the socket lining (Sagoo et al., 2020).

8.2.3. *Color*

Iris and sclera color are defined by pure visual inspection, use of (stock) samples, or pre-rendered images in a color database. A digital alternative is that the iris (and conjunctiva) is captured with high quality photographs, printed and added to the prosthesis (Buzayan et al., 2015; Jauregui Ulloa et al., 2021; Walshaw et al., 2018). The workflow requires standardized photography and computer processing. The permanence of the ink and the color changes after polymerization when incorporated in the prosthesis should however be further explored (Zoltie et al., 2021).

Table 2
Morphological chart for manufacturing acrylic ocular prosthesis.

1 - INPUT	**determine geometry**	**CONVENTIONAL impression**	**impression materials**	**empirical fitting**	**model modification**		**DIGITAL/3D 3D scan socket**	**digitalize impression**	**3D scan periorbital tissue**
		- with impression tray	- alginate	- stock acrylic prosthesis	- by removing material		- oct	- CT	- CT
		- stock tray	- polyvinyl siloxane	- waxmodel	(grinding and polishing)			- MRI	- MRI
		- patiënt specific	- dental impression waxes	- patiënts own previous prosthesis	- by adding material			- surface scan	- surface scan
		- with (stock) ocular prosthesis	- irreversible hylocolloids	- primary made try-in model	(rebasing technique)			- CBCT	- CBCT
		- without impression tray							
		- secondary impression with primary impression inserted							
	determine colour	**samples (stock)**	**by visual inspection**	**iris/pupil diameter**	**iris position**		**HD photograph**	**colour database**	
		- sclera	- painting in clinical session	- caliper/vernier gauge	- by photograph		- iris	- pre-rendered iris images	
		- iris		- pre fabricated diameter samples	- mark on try- in model		- sclera		
		- prefab colored iris buttons		- photo measurement	- additional facial 3d scan		- both		
					- mark on waxmodel				
2 - MANUFACTURING	**geometry**	**curing**	**heatcuring PMMA**	**conventional methods**			**3D printing**		
		- hot water	- white	- processing			- Polyjet		
		- microwave	- transparent	- trial-processing with polyethylene sheet			- DLP (digital light processing)		
				- mold adaptation			- SLA (stereolithography)		
							- FDM (fused deposition modeling)		
							- PBF (powdered fusion)		
	colour	**corneal unit**	**conv.colouring iris**	**conv. colouring sclera**	**painting additional layer(s)**	**veining**	**2D printing**	**3D printing**	
		- disk black	- acrylic based paint	- waterpaint	- iris, sclera, limbus, stroma and pupil	- silk	- iris on paper	- Polyjet	
		- disk transparent	- waterbased paint	- color pensils	- waterbased paint	- cotton	- iris and sclera on paper		
		- prefab button with pupil	- oil based paint		- acrylic based paint	- pencil	- sublimation		
		- prefab button			- oil based paint		- directly on corneal unit		
		- flat posterior surface					- directly on prosthesis		

(*continued on next page*)

Table 2 (*continued*)

		- convex posterior surface - prefab colored iris buttons - transparent iris button with 2d printed iris								
	additional proceedings	**surface finishing**	**making/ modification mold**	**colour-geometry fusion**			**photo rendering**		**3D model rendering**	**3D iris structure**
		- trim	- two- piece gypsum/dental stone	- wrapping			- remove artefacts		- remove artefacts	- add 3D iris structure
		- burnish	- putty	- sublimation			- rendering colors		- design based on impression	- apply displacement mapping
		- polish	- silicone (one piece)	- adjust iris diameter and add			- rendering circular shape		- smoothing	- non-patiëntspecific structure
		- optical standard polish	- remove gypsum in order to make space for transparent layer - smooth	corneal unit to white PMMA dough						
3- OUTPUT	**try-in model**	**conventional** - monocolour transparent PMMA - waxmodel					**3d/digital** - monocolor Biocompatible type II printing resin			
					conventional		**3D/digital**			
					-wrapped iris and sclera - sublimation transfer - photo iris - etc	- digital impression - CT socket scanning		- fullcolor 3D printed		

Table 3
General criteria evaluating ocular prostheses.
When assessing the criteria, it must be taken into account that the orbicularis muscle needs 15–20 min to relax from the moment the prosthesis is placed in the socket. Initially, the muscle contracts slightly, causing an enophthalmic translation of the prosthesis. When the orbicularis muscle is relaxed and the prosthesis has settled, the criteria can be evaluated. The goal and challenge of the ocularist is to achieve a balanced situation. Due to the fact that de orbital and peri- orbital anatomy is distorted, perfect symmetry is not always possible and should not necessarily be the highest achievable goal. The ocularist should strive for a situation in which the affected side attracts as little attention as possible and gives the illusion of correctness. To evaluate the prosthetic situation, above mentioned criteria must be taken into account. Too much attention to one of these criteria can cause a disbalanced, unsatisfactory situation.
Many of the above criteria are not fully compatible. Every alteration/improvement of one of the criteria affects another element, sometimes in a negative way. For example:
1) A larger peripheral shape is more stable in certain situations but will cause less motility.
2) In a ptosis situation, a more convex anterior surface and/or thicker prosthesis can lift the upper eyelid slightly, but also causes a sagging lower eyelid or lagophthalmos.
3) With smaller horizontal/vertical palpebral fissure length, a deliberately smaller iris (compared to the contralateral side) gives a better cosmetic result due to the better balance between visible iris and sclera.
4) An adequately connected posterior surface prevents moisture build-up due to less death space, but a concave posterior surface can induce more stability.
5) Due to the altered anatomy, a perfect horizontal alignment of the pupils can result in the limbus not connecting to the lower lid, while this is the case in the unaffected eye. This attracts more attention than the misaligned pupils, so the prosthesis must be adjusted slightly downwards.
It should be noted here that patients (and companions) own opinion must be included in this consideration, because the concept "well balanced situation" is subjective. The ocularist should explain the compromises and trade-offs.

appearance		**comfort**
peri-ocular	**ocular**	
curvature (upper and lower eyelid)	gaze alignment	free lacrimal puncta
upper eyelid fold	pupil diameter	connection to posterior socket
pretarsal show	iris:	pressure points
superior sulcus volume	diameter	irritation
upper lid position (ptosis, retraction, entropion)	colour	quantities of tears and mucus
lower lid position (entropion, sagging)	details	sharp edges
presence of lower lid folds	limbus	
horizontal appearance	arcus senilis	
vertical appearance:	stroma	
lagophthalmos (gently closed)	position	
lagophthalmos (firmly closed)	sclera:	
prominence:	nasal surface area	
exophthalmos	temporal surface area	
enophthalmos	colour	
	number of veins	
	balance iris/scleral show	
motilty		**stability**
gaps and edge exposure		during blinking
ticking noise		during rubbing
nasal movement (adduction)		when looking upwards and
temporal movement (abduction)		holding down the lower eyelid
elevation		
depression		

8.3. Part 2: manufacturing

The iris button is usually created as a first step in the manufacturing process. An iris disk of about 0.5 mm smaller than the patient's cornea should be chosen to allow for the magnification effect of the later added clear cornea. The iris color is painted on the disk using high quality paint and fine brushes to simulate the small iris strands. A clear corneal cap, often prefabricated with pupil of different available sizes, is merged on top of the painted iris disk, finishing the iris/cornea button (Goiato et al., 2014; Pine et al., 2015c).

Now that the geometry and the position of the iris are defined, and the iris button is created, the ocular prosthesis can be produced. The previously obtained model (wax model after impression, or empirical fitted model) will be embedded in plaster, resulting in the negative in the plaster after removal of the model. The plaster cast is used to press the PMMA prosthesis.

To make the PMMA, acrylic powder is mixed with liquid monomer, creating a dough that is pressed into the cast together with the iris/cornea button. The entire unit is then polarized in a warm water bath. Of note is that polymerization can also be done in a microwave or through autopolymerization, but these methods may lead to more toxicity (Alanazi et al., 2021). The result after polymerization is a white core prosthesis with colored iris. The anterior parts are trimmed including the area around the limbus to obtain a soft transition between limbus and sclera, and the scleral surface is roughened. Now painting of iris and sclera can be completed and vascularization (red silk or cotton fibers) is added. The next step is to seal the model with a transparent layer. This process involves a proof press with transparent plastic dough mixture and a plastic foil protecting the painted parts, and finally a final press. The set is then again polymerized in a warm water bath, and after gradual cooling, the prosthesis can be released and finally trimmed, burnished, and polished.

To reduce manufacturing time, the prosthesis can also be produced with a three-dimensional printer. Custom three-dimensional printed monocular conformers proved to be successful as long-term (2–3 months) postoperative conformers in contracted sockets and as expansive conformers in the early treatment of congenital anophthalmia and microphthalmia (Kuijten et al., 2017; Mourits et al., 2018). For a complete ocular prosthesis, a hybrid model can be created where the geography of the model is defined using a conventional wax-fitting process, after which the wax model is scanned and 3D-printed before final conventional color additions are made (Alam et al., 2017), or with later addition of color to the printed prosthesis using a method called sublimation transfer (Ko et al., 2019). A complete printed prosthesis using a design with textured and three-dimensional shape and color of the iris and sclera, and realistic anatomy with hollow pupil and anterior chamber can be printed in a single print job using a stratasys-printer (Fig. 7) (Groot et al., 2021c).

8.4. Part 3: final fitting

During the final fit in the patient (Fig. 8), the prosthesis should be rechecked for iris position, ocular alignment, and eyelid contour, as described in Table 3. Small deviations in iris position can be manipulated by adjusting the contour or thickness of the prosthesis. However, adjustments may also alter the exact fit of the posterior lining if the fitting is obtained using the impression technique.

The application of a full digital designed and printed prosthesis in a patient has recently been announced in the media, and a clinical trial comparing these printed prostheses with conventional prosthesis is underway (Nct, 2021).

9. Making and fitting of a cryolite glass prosthetic eye

9.1. Part 1: producing a "half-done" cryolite glass eye

Manufacturing of cryolite glass eye prostheses can be divided into two major steps, the first of which is producing a spherical precursor of the later used prosthesis, a "half-done" cryolite glass eye (Koch et al., 2016; Rokohl et al., 2019c) (Fig. 9). The components of cryolite glass are

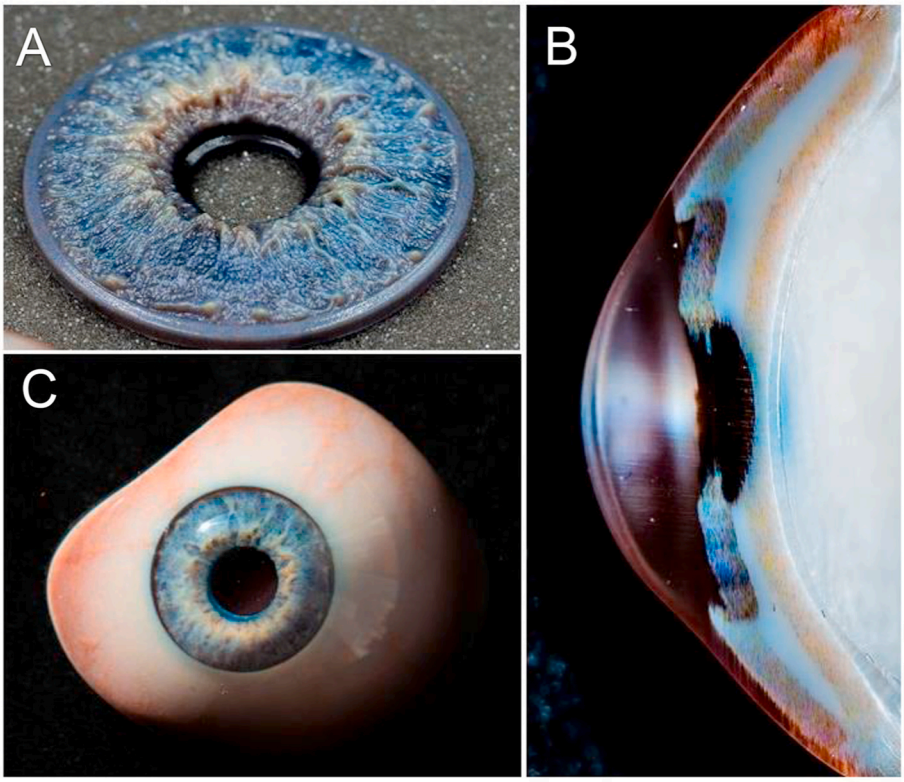

Fig. 7. 3D design allows fabrication of a layered, colored, and structured iris (A) resembling natural anatomy (B), which can be merged with a geometry model for 3D printing of an artificial eye (C).

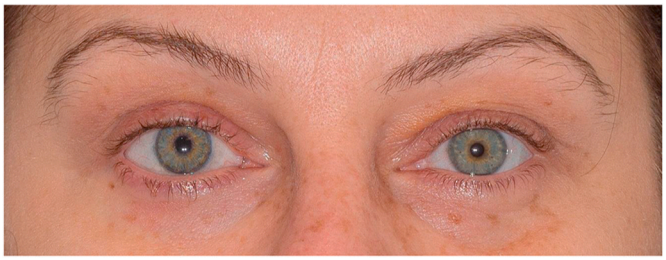

Fig. 8. Example of a well well-fitting conventional made PMMA prosthesis with a very good symmetry between right and left.

melted in the glassworks at temperatures above 1200 °C and drawn into long tubes with a final diameter of 2–3 cm, which are then used by the ocularists for further manufacturing (Koch et al., 2016; Rokohl et al., 2019c). At first, after heating with a Bunsen burner, the ocularist uses these tubes to blow white hollow glass spheres and then differently colored glass sticks are melted onto it, mimicking iris and pupil (Koch et al., 2016; Rokohl et al., 2019c). At this stage these "half-done" prosthetic eyes are stored for later usage (Koch et al., 2016; Rokohl et al., 2019c). A stock with a selection of about 3000 different "half-done" cryolite glass eyes having various iris colors is available for patient care on average per ocularist (Koch et al., 2016; Rokohl et al., 2019c).

9.2. *Part 2: producing and fitting of the final cryolite glass eye*

After choosing the best match for the iris color of the patient's healthy fellow eye from a large assortment of "half-done" prostheses (Fig. 10), the second major step is customizing and fitting the glass individually for the respective patient (Fig. 11) (Koch et al., 2016; Rokohl et al., 2019c). For this purpose, first of all the current prosthetic eye should not be removed and the patient should be examined thoroughly wearing his current prosthesis and looking straight ahead, paying special attention to general fitting, retention, direction of gaze, eye lid contour, size, and volume (Table 3) (Rokohl et al., 2019c). After removing the prosthetic eye, the anophthalmic socket is also thoroughly examined, paying attention to the condition of the conjunctiva, potential orbital implant extrusion, and the depth of the fornices and sulci (Rokohl et al., 2019c). If there are any significant concerns, the patient should be referred to an ophthalmologist or an ophthalmoplastic surgeon before manufacturing a new glass prosthesis. The selected "half-done" cryolite glass eye and a hollow skewer are then heated up using a Bunsen burner, merging the skewer to the posterior side of the half-done" cryolite glass eye to be used later as a mouthpiece for the ocularist (Rokohl et al., 2019c). While being constantly rotated and heated to roughly 600 °C, the ocularist now makes small adjustments like drawing conjunctival vessels and clouding onto the front side of the glass eye using heated glass steams in different colors (Rokohl et al., 2019c). The fellow eye of the patient is used as model (Rokohl et al., 2019c). Using the old prosthesis as a template and keeping in mind the previous examinations, the shape and volume of the prosthesis can now be further adjusted by blowing or suction through the mouthpiece (Rokohl et al., 2019c). The prosthesis is then held by a glass stem melted to the front and the posterior side of the prosthesis is now reduced to the desired shape by means of suction (Rokohl et al., 2019c). After that, the skewer and the stem are melted away and the prosthesis is again heated all over to fully smoothen the surface (Rokohl et al., 2019c). Finally, the prosthesis is slowly cooled down after which it can be inserted, the fit can be checked, and the prosthesis can be readjusted within the next hours, if the fit is not appropriately (Koch et al., 2016; Rokohl et al., 2019c).

As mentioned before, the approach to fitting and readjusting the glass prosthesis postoperatively is mostly different (Rokohl et al., 2018a, 2019b). After enucleation, cryolite glass receiving patients wear a transparent conformer in their conjunctival sac to prevent scarring of the

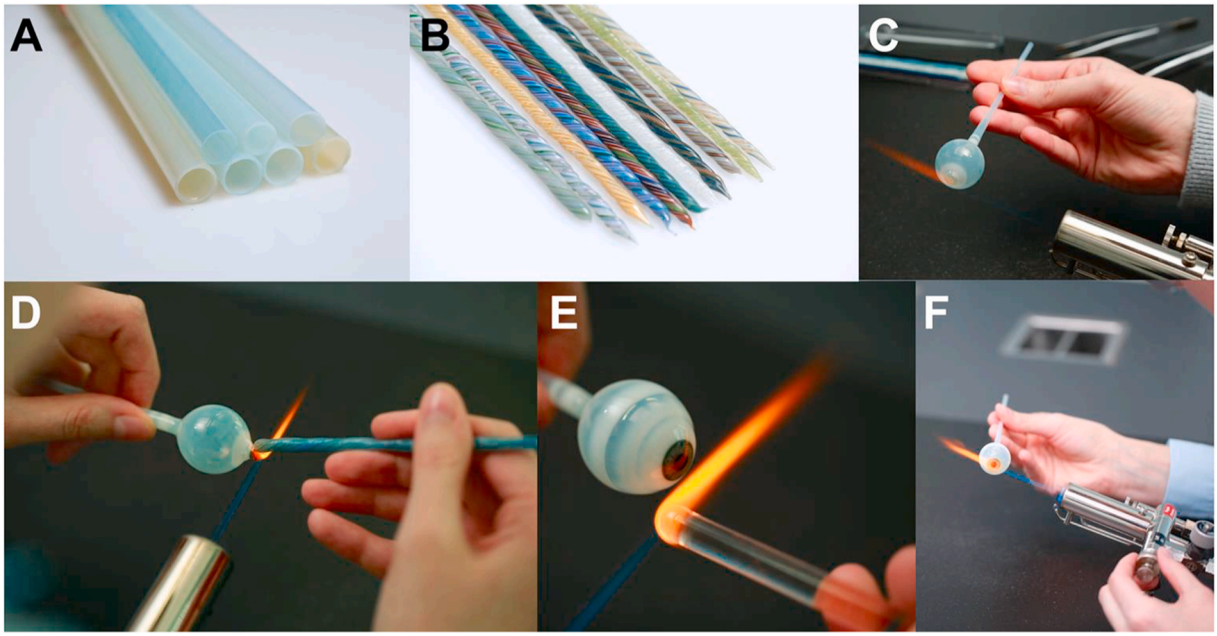

Fig. 9. Manufacturing of a "half-done" cryolite glass eye. The components of cryolite glass are melted in the glassworks drawn into long tubes (A). In addition, the ocularist uses differently colored glass sticks for "drawing" the iris and pupil (B). At first, after heating with a Bunsen burner, the ocularist uses the long tubes to blow white hollow glass spheres (C) and then colored glass sticks are melted onto it, mimicking iris and pupil (D). Afterward, another layer of translucent glass is melted onto it to achieve a three-dimensional effect, similar to an anterior chamber of a "normal" eye (E). Finally, the whole sphere is heated, smoothed, and fire-polished (F).

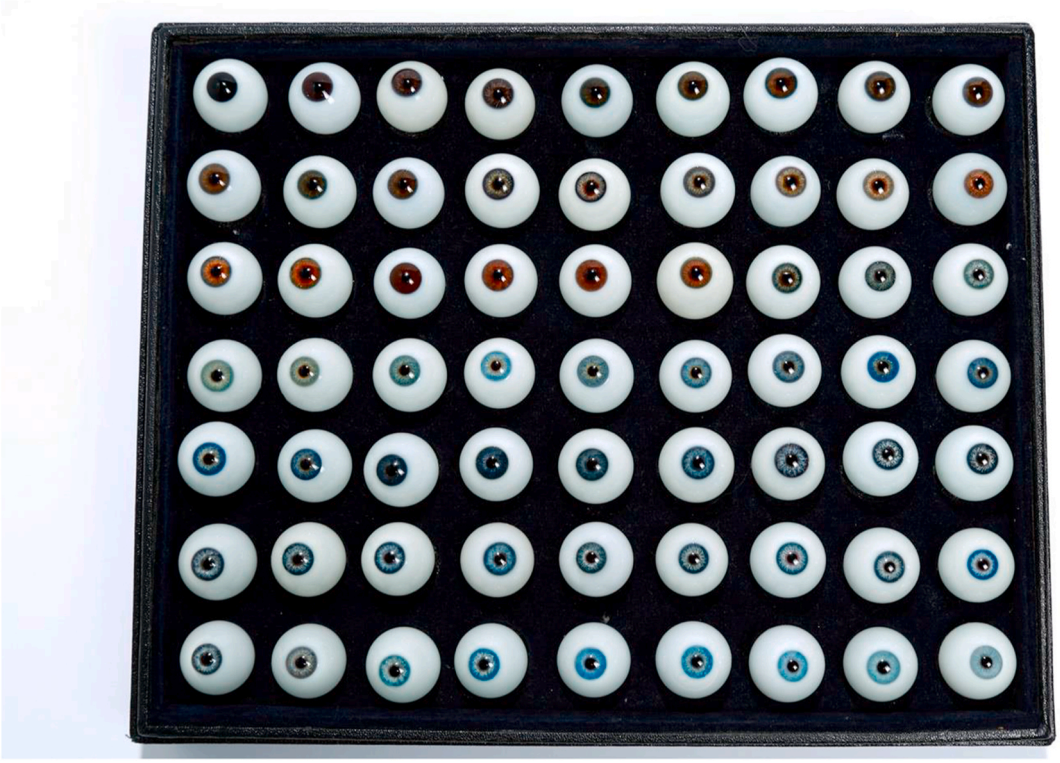

Fig. 10. Choosing the best match for iris color of the patient's healthy fellow eye can be done from a large assortment of "half-done" prostheses. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

conjunctival fornices which would prevent the patient from later being able to wear a prosthesis (Koch et al., 2016; Rokohl et al., 2018a, 2019b). Patients then receive a preliminary prosthesis as early as 7–14 days after surgery which helps lower the psychological impact of enucleation and does not hinder postoperative healing in most cases (Chin et al., 2006; Koch et al., 2016; Rokohl et al., 2019b). However, if the surgery site is severely irritated or the patient has a past medical history of systemic or eye-related disease that would disrupt wound

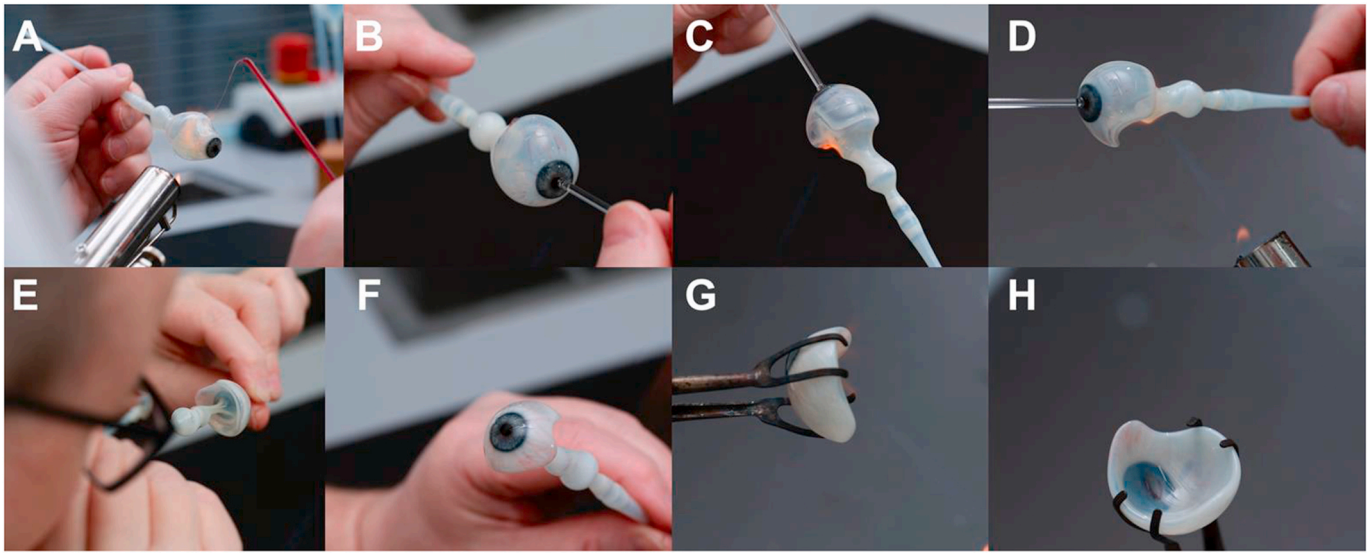

Fig. 11. After merging a hollow skewer to the posterior side of the half-done" cryolite glass eye, while being constantly rotated and heated 600 °C, the ocularist now makes small adjustments like drawing conjunctival vessels (A). The prosthesis is then held by a glass stem melted to the front (B) and the posterior side of the prosthesis is now reduced to the desired shape by melting (C, D). Further adjustments of the shape can be made by blowing or suction (E) through the mouthpiece using the old prosthesis as a template and keeping in mind the previous examinations. The stem (F) and the skewer (G) are melted away and the prosthesis is again heated all over to fully smoothen the surface, especially the thin backwall (H).

healing, the conformer should be left in place as long as necessary (Koch et al., 2016). After postoperative swelling has fully subsided at around 5–8 weeks, the patient receives two customized prostheses and a third one around 6 months after eye removal depending on the changes of their socket over time (Rokohl et al., 2018a, 2019b). After that cryolite glass wearing patients get a new prosthesis at least every year due to hydrolytic reactions of the glass to lacrimal fluid in order to circumvent complications (Koch et al., 2016; Rokohl et al., 2018a, 2019b).

There are different scenarios that require even more frequent adjustment of ocular prostheses, a major one of which being children and adolescents experiencing eye loss (Dos Santos et al., 2017; Koch et al., 2016; Rokohl et al., 2018a, 2019b; Shaikh et al., 2014). Due to orbital growth and the accompanying risk of asymmetry, children should be examined at least six monthly, and the prosthesis should be adjusted or replaced, if necessary, regardless of material (Dos Santos et al., 2017; Koch et al., 2016; Rokohl et al., 2018a, 2019b; Shaikh et al., 2014). For infants, toddlers, and young children's examinations and potential adjustments should occur even more frequently, about every 3 months (Koch et al., 2016; Shaikh et al., 2014).

10. Prosthetic eye maintenance and handling: an evidence-based protocol

10.1. Tear protein deposits

An optimal protocol for prosthetic eye maintenance is required to minimize conjunctival inflammation, socket tissue micro-trauma, and non-specific mucoid discharge; and thus, promote socket health and the psychological well-being of the patient. The maintenance protocol recommended here is underpinned by research into the response of the anophthalmic socket to polymethyl methacrylate (PMMA) prosthetic eye wear and a three-phase model of prosthetic eye wear (Pine et al., 2013c).

When a prosthetic eye is worn continuously, there are two distinct areas on the surface of the prosthetic eye where surface deposits accumulate. There is the interpalpebral zone, which is the part of the prosthesis exposed when the eyelids are open; and the retro-palpebral and posterior zones, which stay in constant contact with the conjunctival lining of the socket (Pine et al., 2012c).

Deposits in the interpalpebral zone are exposed to the air and the wiping action of the eyelid margin on blink. When deposits in this zone build up and dry out, they become a source of irritation as the eyelids slide over them. In contrast, the retro-palpebral and posterior deposits, do not dry out as they are not exposed to the air; and are in fact beneficial to prosthesis wear. Deposits in this zone increase the wettability of the prosthesis surface and thereby reduce friction between the prosthesis and conjunctiva. Retro-palpebral and posterior deposits are associated with less conjunctival inflammation and less socket discharge (Pine et al., 2012c; Rokohl et al., 2019a).

10.2. Three-phase model of the response of the anophthalmic socket to prosthetic eye wear (Fig. 12)

10.2.1. Phase 1: establishing homeostasis

When a new, or newly cleaned, prosthetic eye is first inserted into an anophthalmic socket, several changes are seen as physiological homeostasis is established, or re-established within the socket. Within the first hour the socket tissues recover from the mechanical forces of insertion, the eyelids relax, the prosthesis warms to body temperature, and the tear meniscus forms along the lower eyelid margin. Prosthesis insertion is also associated with disruption of the mucus substrate of the conjunctival lining of the socket. Mild mucoid discharge and conjunctival inflammation commonly occurs as results of these stressors.

Full physiological homeostasis is later achieved when any foreign debris introduced with prosthesis insertion is encased with mucus and eliminated, when the balance between tear production and tear loss is re-established, and when a mucus substrate is re-distributed evenly around the prosthesis. A "biofilm" of tear protein deposits covering the retro-palpebral and posterior surfaces of the prosthesis also forms. The key characteristics of physiological homeostasis in the socket are the renewed mucus substrate, well-established retro-palpebral and posterior surface deposits that facilitate lubrication of the prosthesis, and the absence of inter-palpebral surface deposits (Pine et al., 2013c).

10.2.2. Phase 2: stable homeostasis

Although anophthalmic patients have different socket anatomies and physiologies, different general health conditions, and live in different environments, it generally takes a month before the microclimate within

the socket reaches the phase of stable homeostasis (Pine et al., 2013c). During this equilibrium phase, conjunctival inflammation and socket discharge is at its lowest. Although more gram-negative bacteria are typically found in anophthalmic sockets compared to their companion eyes, they do not appear to have any adverse effects on the socket during this period of equilibrium (Christensen and Fahmy, 1974).

10.2.3. Phase 3: breakdown of homeostasis

Although the beneficial state of equilibrium may last many months with continuous prosthetic eye wear, eventually a breakdown phase is reached. During breakdown, inter-palpebral deposits build and encroach on the interpalpebral zone of the prosthesis. During stable homeostasis, low levels of inter-palpebral deposits can be kept at bay by the window-wiper action of the eyelids, however once these deposits accumulate in more significant amounts, they dry and harden on the anterior surface of the prosthesis. This increases friction between the eyelid and the prosthesis and inflicts micro-trauma on the socket lining and lid margins. As a consequence, the socket becomes prone to irritation, inflammation (Pine et al., 2012c), giant papillary conjunctivitis (Srinivasan et al., 1979), lid wiper epitheliopathy (Korb et al., 2002), and meibomian gland dysfunction (Jang et al., 2013). Giant papillary conjunctivitis is an allergic disease of the eye associated with increased numbers of conjunctival eosinophils, mast cells, and (Bozkurt et al., 2007) and is thought to be a combination of an immune response to antigenic protein deposits and physical trauma to the conjunctiva (Meisler et al., 1981; Srinivasan et al., 1979). Similarly, friction is a key factor in the pathophysiology of lid wiper epitheliopathy (Efron et al., 2016), and the persistent rubbing of the eyelids margins against the prosthesis is postulated to produce hyperkeratinization and inflammation of the tarsal epithelium and contribute to meibomian gland dysfunction related dry eye disease (Jang et al., 2013).

As the socket approaches breakdown, retro-palpebral and posterior deposits incorporate increasing amounts of bacteria environmental debris, and metabolic waste accumulates. Spaces, especially behind deeply vaulted prostheses, can trap socket secretions which stagnate and provide growth mediums for bacteria (Jones and Collin, 1983), and allow foreign materials to accumulate, further accelerating homeostatic breakdown. All of these factors contribute to increased inflammation of the socket lining, mucoid discharge and symptoms of discomfort.

10.3. Response of the anophthalmic socket to prosthetic eye wear: Implications for wear and care

The three-phase model for prosthetic eye wear described above can be used to formulate recommendations for prosthetic eye wear, so that the socket and the prosthesis stay in equilibrium, where comfort and socket health outcomes are best. Research evidence for the protocol has been obtained from wearers of PMMA prosthetic eye wearers (Pine et al., 2013b) and cryolite glass eye wearers (Rokohl et al., 2019a).

10.3.1. Prosthetic eyes should usually not be removed and cleaned more frequently than monthly

The ideal care protocol for ocular prostheses remains controversial. Studies suggest that a more frequent prosthesis removal and cleaning was associated with more severe discharge and discomfort, but the direction of cause and effect has not been established (Pine et al., 2012a). As a general guideline, prostheses should not be removed and cleaned more than once a month unless individual circumstances require otherwise. For specific risk factors and personal needs, a tailored approach dependent on the material of the ocular prosthesis and other external factors, developed in collaboration with ocularists and ophthalmologists, may be more effective (Heindl and Rokohl, 2023).

The act of removing and re-inserting a prosthetic eye is sufficient in and of itself to irritate the conjunctiva and stimulate mucoid discharge. Physically removing the prosthesis disturbs the mucus substrate of the socket and exposes the conjunctiva to a sudden temperature drop, while re-insertion introduces foreign matter and bacteria into the socket. Thus, hand washing prior to handling a prosthesis is important. Patients who frequently handle their prosthesis have a significantly more gram-negative bacteria in their sockets than in their companion eye (Vasquez and Linberg, 1989), and display greater conjunctival inflammation (Rokohl et al., 2019a), and mucoid discharge (Pine et al., 2012a, 2012c).

When cleaning a prosthetic eye, beneficial retro-palpebral and posterior surface deposits are eliminated in the process. Their absence results in a more hydrophobic prosthesis surface, which restricts tear distribution and consequently promotes frictional irritation of the conjunctiva. In line with this, it has been shown that the presence of tear protein deposits is associated with less inflammation of the socket, and that deposits do not inflame the conjunctiva of patients who do not clean their prosthesis frequently (Pine et al., 2012c).

Conjunctival inflammation is also positively correlated with mucoid discharge so to avoid excessive mucoid discharge it is best to leave tear protein deposits in place for as long as possible by limiting the frequency of cleaning (Pine et al., 2013b). Patients who clean their prosthetic eyes monthly experience less mucoid discharge than those who clean daily or weekly (Pine et al., 2012a), suggesting that prosthetic eyes should usually not be cleaned more frequently than monthly. In short, the deleterious effects of removing, cleaning, and re-inserting a prosthetic eye are best avoided by leaving the prosthesis in place for as long as possible.

10.3.2. Prosthetic eyes should be removed and cleaned only when they feel uncomfortable

Beyond monthly, the length of time prosthetic eyes should be cleaned varies between individuals (Ullrich et al., 2022). For example, those with allergies may need to clean more frequently as evidenced by contact lens wearers with papillary conjunctivitis that occurs more frequently in allergy sufferers (Donshik, 2003). The time between cleanings may also depend on the patient's environment and the surface finish of the prosthetic eye which affects deposition rates (Pine et al., 2013c). There is no evidence for how often prosthetic eyes should be cleaned except that they should not be cleaned more frequently than monthly. Wide variation in protein deposition between patients in the contact lens literature has been reported (Keith et al., 2003). Pine et al. suggested six monthly as an arbitrary time (Pine et al., 2012c), as deposits accumulate continuously and after six months may be thick enough to start encroaching on the inter-palpebral zone (Pine et al., 2013c). The ideal cleaning regime for most individuals will be influenced by allergic conjunctivitis, the presence of giant papillary conjunctivitis, dry eye, tear film quality, lid function, blink efficiency and lagophthalmos, general medical conditions and medications, as well as the standard of surface finish of the prosthesis and the wearing environment. A practical rule might be that the prosthesis should be cleaned only when it becomes uncomfortable due to surface deposits encroaching on the inter-palpebral zone and drying out.

10.3.3. Prosthetic eyes should be cleaned by firmly wiping all surfaces with a disposable paper towel wetted with cold water

The object of cleaning a prosthetic eye is to remove coatings and films that have accumulated over time and dulled the surface. These coatings and films contain lipids and mucin as well as tear proteins and are beneficial in the short to medium term but dry out and become rough over time. They also thicken and become contaminated with environmental debris, micro-organisms, and metabolic waste. These coatings and films behave in a similar way to other biofilms found in nature, such as slime on a rock. Dry slime is difficult to clean off but once wet, the slime comes away easily. It is the same for the coatings and films that build up on prosthetic eyes – if dry, they are nearly impossible to remove, but once wet, they are very easy to clean off (Pine et al., 2015b).

The goal of cleaning a prosthetic eye is solely to remove these deposits, and the cleaning method used should accomplish this effectively

and efficiently. One way is to wipe the prosthesis firmly with a disposable paper towel wetted with cold water. Firstly, the anterior surface should be wiped, then the back taking particular care with hollows and grooves, and then the edges. Since the biofilm that is being cleaned off cannot be seen, so it is important to carefully wipe the entire surface. A wet cloth is as effective as wiping with a wet paper towel, but a cloth is less hygienic to use as it is not disposable like a paper towel. Wetted tissue paper breaks up too easily under wiping pressure. Cleaning the prosthesis with a dry paper towel should be avoided as it is mildly abrasive in its dry state as it contains coarse wood fibers and glue in its composition. However, it is safe to use a wet paper towel. Polishing a prosthetic eye with a dry tissue appears to remove the biofilm but in fact it is the biofilm that is polished and not the underlying PMMA.

A prosthetic eye should never be cleaned or soaked in household cleaners, as they can dissolve PMMA and damage the surface. Toothpaste should not be used to clean a prosthetic eye, as its gritty particles can scratch the surface. Additionally, the prosthesis should never be placed in water hotter than lukewarm, as high temperatures can create internal pressure within its multi-layered structure, leading to delamination. Drying can also cause delamination, as PMMA retains a small amount of water. If left dry for several days, changes in water content can generate internal pressure similar to that caused by heat. If a prosthetic eye needs to be stored for any period, it should be wrapped in wet gauze or tissue paper and kept in a dark container (Pine et al., 2015b).

10.3.4. Prosthetic eyes should be blemish free with smooth rounded edges and polished (to optical quality contact lens standard)

Le Grand was one of the first ocularists to recognize the importance of a perfectly smooth, blemish free prosthetic eye to avoid mechanical irritation of the conjunctiva and consequent mucus discharge (LeGrand, 1999). Mechanical irritation from prosthetic eyes with scratches or chips is one of the causes of chronic discharge with recurrent symptoms not responding to topical antibiotics listed in a classification of the causes of discharging sockets (Jones and Collin, 1983).

The authors recommend that PMMA prosthetic eyes should be finished to an optical quality standard of surface polish using aluminium oxide paste applied with a polyurethane foam rubber rotating cone or wheel (Litwin et al., 2018; Pine et al., 2015b). This standard of surface polish not only produces a smoother surface but the surface is also more wettable than a normal standard of finish (Pine et al., 2013c), and more comfortable to wear (Litwin et al., 2018). An optical quality contact lens standard of polish may be especially important when applied to the inter-palpebral surface of a prosthetic eye to assist the window wiper action of tears. In addition, achieving an optical-quality contact lens standard of polish may be particularly important for the inter-palpebral surface of a prosthetic eye, aiding the window wiper action of tears. Litwin et al. demonstrated that enhancing the polish of PMMA prosthetic eyes to optical quality significantly reduced deposit buildup after one month, though this effect was not sustained at 12 months (Litwin et al., 2018). However, patients with enhanced polish experienced significantly fewer symptoms and a lower frequency of discharge (Litwin et al., 2018). The authors concluded that this modification improved patient tolerance over 12 months. Nevertheless, due to limited data, this remains a topic of debate, and further studies are needed to substantiate these findings and clearly establish the benefits of improved polishing to optical quality contact lens standard.

10.3.5. Prosthetic eyes should be professionally re-polished (to optical grade contact lens standard) annually

An annual review of anophthalmic patients is important, not only to check the prosthetic eye but also to reassure patients that they are part of a system that supports them and is willing to listen to their concerns. During the review, the prosthetic eye is checked for damage and the socket is carefully inspected for anomalies and complications that may affect ongoing socket health and comfort. The fit of the prosthesis is also checked along with wider aspects of facial symmetry including signs of post-enucleation-socket-syndrome and eyelid malposition (Johnson, 2020). The prosthetic eye is cleaned to remove all vestiges of tear protein deposits and re-polished to optical grade contact lens standard which removes micro scratches and restores the wettability of the inter-palpebral zone of the prosthesis (Pine et al., 2015b).

11. Treatment of children with anophthalmia and microphthalmia

11.1. Epidemiology and clinical manifestations of anophthalmia and microphthalmia

Congenital anophthalmia or microphthalmia are rare eye development disorders occurring in 1–3 per 10.000 live births and are caused by either genetic alterations or environmental factors. The complete absence, or underdevelopment of one or both eyes may present as an isolated finding, or it co-exists with other developmental disorders.

Congenital clinical anophthalmia refers to the extremely rare true congenital anophthalmia, characterized by the absence of histologically detectable ocular structures (Table 4) (Schittkowski et al., 2003). Clinically, this condition presents with collapsed eyelid structures, a severely shortened palpebral fissure, and a small, contracted conjunctival sac that is not initially suitable for prosthetic fitting (Schittkowski et al., 2003). However, in almost all cases of apparent anophthalmia, rudimentary ocular structures can be identified using advanced imaging techniques (Schittkowski et al., 2003). From a strict embryological perspective, such cases should be classified as microphthalmia (Schittkowski et al., 2003). Clinically, however, this distinction is not always practical (Schittkowski et al., 2003). Therefore, the term “clinical anophthalmia” is generally used when no ocular structures are macroscopically visible within the palpebral fissure (Schittkowski et al., 2003).

The opposite end of the spectrum is nonfunctional microphthalmia, where a small, non-seeing globe is visible within the palpebral fissure (Schittkowski et al., 2003). This condition is typically associated with near-normal eyelid and conjunctival structures, particularly deep fornices, which allow for early prosthetic fitting (Schittkowski et al., 2003).

The differentiation between clinical anophthalmia and nonfunctional (blind) microphthalmia represents the two extremes of the clinical spectrum (Table 4) (Schittkowski et al., 2003). This pragmatic, action-oriented classification is useful in clinical decision-making (Schittkowski et al., 2003). However, many patients present with transitional forms that do not fit neatly into either category (Schittkowski et al., 2003).

Since most eyes turn out to be blind, the attention then turns to the facial appearance. The eye itself (if present) may look deformed, and the lack of normal eye volume is often accompanied by a sunken eye

Table 4
Clinical presentation of congenital clinical anophthalmia and nonfunctional microphthalmia.

Feature	Congenital Clinical Anophthalmia	Nonfunctional Microphthalmia
Visual Function	None	None (Flash-VEP not elicitable)
Ocular Structures	Absent (rare) or only detectable with imaging	Visible in the palpebral fissure
Eyelids	Appears collapsed, sometimes ptosis, epicanthus	Almost normal
Horizontal Palpebral Fissure	Severely shortened	Slightly shortened
Conjunctival Sac	Extremely small, contracted	Variably reduced to normal
Conjunctival Fornices	Absent	Usually present
Prosthetic Feasibility	Not possible initially	Usually possible initially

appearance with small eyelids and small orbits with the risk of facial asymmetry (Ragge et al., 2007). Treatment options and treatment urgency depend on the severity, and, if started, always involves prosthetic treatment, with or without additional expansive therapies.

11.2. Treatment of anophthalmia and microphthalmia

By far, the most difficult sockets to treat are the severe cases, also referred to as (clinical) anophthalmia, where no eye structure is recognized and where the volume loss of soft tissue and orbital bone is most pronounced. The aim of treatment is to stretch and reform the eye cavity so that it can retain an artificial eye, and to enlarge the eyelids and if possible orbital bones for better facial symmetry. Literature on the treatment effects for an-microphthalmia is rather sparse, probably due to the rarity of the disease. Results are often presented as subjective judgement, or as in increase in the horizontal eyelid fissure or orbital bone volume.

Conventional therapy with gradual increasing solid conformers (Fig. 13) in the conjunctival sac increases the volume of the sac, and improves the horizontal palpebral fissure (Changal and Khandekar, 2021; Christiansen et al., 2008; Dootz, 1992; El Essawy and Abdelbaky, 2016; Kuijten et al., 2017; Price et al., 1986; Taha Najim et al., 2020; Tucker et al., 1995). Conjunctival sac expansion may however not have a full effect on the orbital growth (Tucker et al., 1995) and the expansive effect is slow. A faster expansive effect on the socket is achieved with custom-made silicone injectable socket expanders (Berry, 1991) or self-inflating socket expanders (Gundlach et al., 2005; Wiese et al., 1999). Bony orbital expansion is also obtained by direct insertion of an inflatable silicone implant in the orbit, either introduced via de conjunctiva or temporal sparing the conjunctival sac (Gossman et al., 1999; Morrow et al., 2016; Tse et al., 2011). The effect on orbital growth is generally good, but a contrary effect has also been described in an older child of 4 years old. Repeated inflation and anesthesia are required, and complications include deflation migration or extrusion. However, due to the disadvantages of the bony orbital expanders and the availability of better treatment alternatives, this technique has been abandoned. More recent is the introduction of self-inflatable spheres for anophthalmia or self-inflating injectable pellets for microphthalmia (Gundlach et al., 2005; Hou et al., 2012, 2016) with positive, but sometimes modest effect on the orbital dimensions. Complications also include migration and extrusion as well as problems with prosthetic fitting and one group described an inability to fit a prosthesis in 7 out of 11 cases (Alanazi et al., 2021; Schittkowski, 2010; Tao et al., 2010). In 2018, the company that manufactured self-inflating expanders (osmed GmbH, Ilmenau) ceased production due to bankruptcy. A well-tolerated strategy with increase in horizontal eyelid fissure (at least until the surgery) is the combination of early external prosthetic treatment in combination with a surgical dermis-fat-graft. The dermis-fat-graft will allow for an improved socket anatomy with deeper fornices to fit a regular conformer (Modugno et al., 2018).

Solely prosthetic (or conformer) treatment in microphthalmia and anophthalmia will be described here. For clinical practical and study purposes the severity can be expressed as mild, moderate or severe (Groot et al., 2020) based on (relative) axial lengths measured with b-scan ultrasonography usually available in ophthalmology practice.

11.2.1. Mild microphthamia

Slight perceived volume differences compared to the normal side are seen in patients with relatively large eyes with axial length more than 75% of the age-adjusted (Groot et al., 2021b) or normal fellow eye (corresponding to more than 14 mm in a term newborn) (Groot et al., 2020). Depending on the exact development disorder (i.e. coloboma, persistent fetal vasculature, anterior segment disorder), the aspect of the eye will vary from relative normal to a deviated appearance. Most of these eyes will show further growth, and therefore no extreme orbital volume deficiencies are expected in the future. This group does not need expansive treatment, but unappealing blind eyes can be improved using ocular prostheses (Groot et al., 2020). The eye should not be enucleated since ongoing growth of the deformed eye can still stimulate the orbital growth. However, a few eyes will arrest in their growth and may become

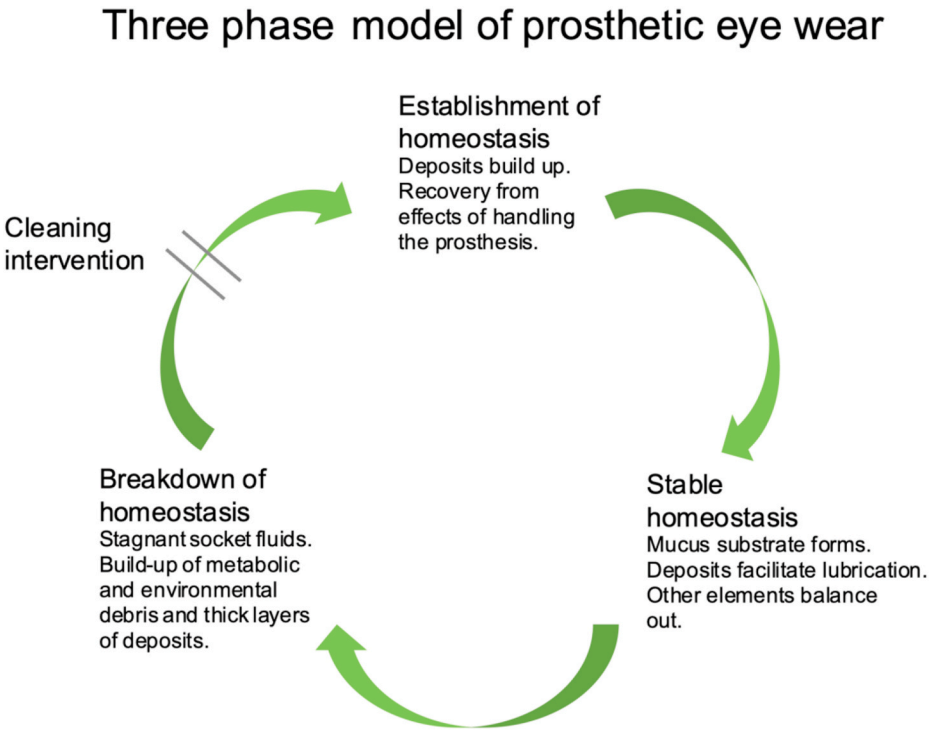

Fig. 12. Three-phase model describes the response of an anophthalmia socket to prosthetic eyewear. The three-phase includes an initial period of wearing a new prosthesis when homeostasis is being established within the anophthalmic socket. In the second period beneficial surface deposits have built up on the prosthesis and wear is safe and comfortable in this equilibrium phase. In the breakdown phase (third period) there is an increasing likelihood of harm from continued wear.

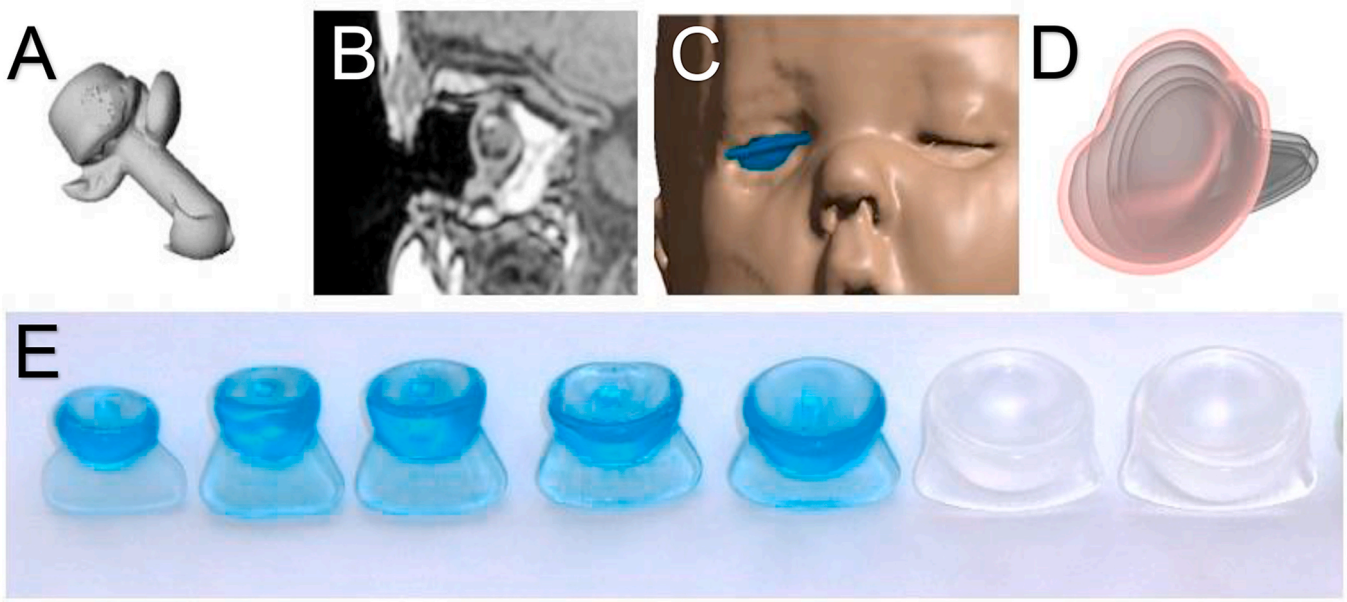

Fig. 13. Female patient (51-years old) with PESS on the left side wearing a cryolite glass prosthesis. The clinical findings include significant volume displacement resulting in a deep upper eyelid sulcus, enophthalmos of the artificial eye, backward tilt, and upwards and left gaze of the prosthesis.

subject for orbital expansion during follow-up.

Advancements in medical and prosthetic care, coupled with evolving patient preferences, seem to drive a growing trend toward cosmetic scleral shells for blind or deformed eyes. However, corneal sensitivity poses risks of erosion and infection, potentially limiting their use due to concerns about discomfort. Custom prosthetic fittings can be attempted, but in cases of severe corneal sensitivity, a surgical conjunctival flap (Gunderson flap) or mucous membrane graft may facilitate successful prosthesis placement (Ding et al., 2013; Ma'luf and Awwad, 2005).

This shift toward cosmetic scleral shells is particularly relevant as more individuals—including those beyond congenital cases—opt to retain blind or disfigured eyes rather than undergo enucleation or evisceration. This approach is also beneficial for elderly patients with comorbidities, for whom general anesthesia poses significant risks. Notably, up to 25% of individuals needing ocular prosthetics already choose scleral shells (Shapira et al., 2021b; Ullrich et al., 2022).

Given these trends, traditional ocular prosthetic approaches should be reconsidered, recognizing the growing clinical and psychological benefits of cosmetic shells (Shapira et al., 2021b; Ullrich et al., 2022). Studies indicate they offer superior appearance and motility compared to prosthetic eyes (Shapira et al., 2021b; Ullrich et al., 2022). Additionally, their lightweight design may minimize anophthalmic socket complications while preserving ocular structures without requiring enucleation or evisceration.

Concerns regarding tolerability remain, but emerging evidence suggests that proper counseling, advanced surgical techniques, and structured fitting, cleaning, and care protocols significantly enhance patient acceptance (Shapira et al., 2021b; Ullrich et al., 2022). Gradual adaptation and individualized fitting strategies may further improve tolerability. Given these factors, the authors anticipate a growing trend in the adoption of cosmetic shells in the coming years (Shapira et al., 2021b; Ullrich et al., 2022).

11.2.2. Moderate microphthalmia

In cases with axial length between 45 and 75% of an age-adjusted or fellow normal eye (between 8 and 14 mm in a term newborn) a malformed but obvious eye structure is recognized, but often with apparent deficiency of periocular volume and smaller eyelids. For this moderate group it is generally advised to start expansive treatment within several months after birth. Even though many of these eyes also show some growth, they are not likely to have the same expansive effect as the fast-growing normal eye. The socket of a moderate microphthalmic eyes is comparable to a situation after evisceration or enucleation with adequate fornices to fit a prosthesis. The cornea is usually small and insensitive, but custom-made fit with help of an impression is preferred for both comfort and a maximal filling of the remaining socket. Clear conformers can be used instead of opaque prostheses in case of potential light perception (Fahnehjelm et al., 2022; Schittkowski et al., 2022). Expansive effect is obtained by regularly exchanging the ocular prosthesis for a slightly bigger size. Authors prefer to make one impression during general workup MRI under anesthesia at around 3 months of age. The subsequent models will be based on the primary one and all fittings can be done without anesthesia in an outpatient clinic.

11.2.3. Severe microphthalmia

Severe microphthalmia, also referred to as clinical anophthalmia, involves early perturbation of eye development with no visible eye structure. Ultrasonography may reveal an ocular remnant or no eye structure at all. Although all variations are possible, these children usually present with extremely small eyelids that are difficult to separate. Since a lot of growth needs to be caught up and the child will grow fast in the first weeks of life, it is advised to start conformer therapy as soon as possible, preferably within the first month of life. The anophthalmic socket cavity does not resemble a regular socket but is rather cone-shaped without fornices to fit a regular shaped conformer. The initial goal is to enlarge the palpebral aperture which can be achieved by introduction of round to oval conformers. Authors prefer a wing-shaped attachment that facilitates insertion and retrieval of the conformer and at the same time, gives some horizontal stretch to the eyelids. In case of an ocular remnant the posterior part may be shaved off in a concave shape to respect the remaining eye structure. Using a gliding gel, the conformer can be inserted without anesthesia in an outpatient setting. At start the conformer is exchanged on a one- or two-weekly basis, allowing for a reasonable eyelid opening after several weeks. At that time the shape of the conformer can gradually be changed to a model that stimulates the growth of the fornices, while still increasing the total volume. The cavity is thus gradually expanded to a point where the socket is able to retain a prosthesis. The process can be done with conventional conformers or prostheses, but it can also be facilitated with 3D planning and printing (Fig. 13).

12. Socket complications and associated treatment options

12.1. Conjunctivitis

For patients wearing prosthetic eyes, there are many different pathomechanisms that lead to discomfort, discharge, pain, or other complications reaching as far as the inability to wear a prosthesis (Bailey and Buckley, 1991; Bilkhu et al., 2013; Bischoff, 2014; Bohman et al., 2014; Bozkurt et al., 2007; Christensen and Fahmy, 1974; Ibrahiem and Abdelaziz, 2016; Kenny et al., 2020; Koch et al., 2016; Meisler et al., 1981; Patel et al., 2009; Pine et al., 2012a, 2012c, 2013c; Quaranta-Leoni, 2008; Rokohl et al., 2020b; Srinivasan et al., 1979; Swann, 2001; Vasquez and Linberg, 1989). It has been shown that subjectively the main problems regarding the prosthetic eye specifically are visible mucoid discharge and crusting which occur in more than 2/3 of patients (Koch et al., 2016; Pine et al., 2011, 2012a, 2012c, 2013c; Rokohl et al., 2018a, 2018c). There is no significant difference in the prevalence of these symptoms between cryolite glass and PMMA prosthetic eye wearers (Ibrahiem and Abdelaziz, 2016; Pine et al., 2011, 2012a, 2012c; Rokohl et al., 2018a, 2018c). Conjunctivitis of differing pathogenesis are among others a major cause of these symptoms (Bailey and Buckley, 1991; Bilkhu et al., 2013; Bischoff, 2014; Bohman et al., 2014; Bozkurt et al., 2007; Christensen and Fahmy, 1974; Ibrahiem and Abdelaziz, 2016; Kenny et al., 2020; Koch et al., 2016; Meisler et al., 1981; Patel et al., 2009; Pine et al., 2013c; Quaranta-Leoni, 2008; Srinivasan et al., 1979; Swann, 2001; Vasquez and Linberg, 1989). Ophthalmologists are likely to encounter the clinical manifestations of these and they shall be discussed in the following (Rokohl et al., 2019b).

12.1.1. Acute allergic conjunctivitis

As mentioned in a previous paragraph, one cause of prosthesis-associated conjunctivitis is an acute allergic response to the acrylic ocular prosthesis that occurs within 48 h after insertion of the prosthesis (Bohman et al., 2014; Koch et al., 2016; Patel et al., 2009). It is a rather rare condition wherein unpolymerized methylacrylate monomers are thought to be the antigen (Bohman et al., 2014; Koch et al., 2016; Patel et al., 2009). Clinically, these patients present with upper eyelid edema and itchiness as well as conjunctival papillary reaction and edema (Patel et al., 2009). These symptoms are treated by topical application of steroids, mast cell stabilizers, and non-steroidal anti-inflammatory drugs, but long-term solutions to this are either extended curing of the prosthesis in order to minimize the amount of residual monomer by converting it into polymer but impairing the aesthetic of the prosthesis, or replacement with a glass prosthetic eye (Bilkhu et al., 2013; Bohman et al., 2014; Koch et al., 2016; Patel et al., 2009).

12.1.2. Giant papillary conjunctivitis (GPC)

The more common giant papillary conjunctivitis (GPC) is an inflammatory condition of the conjunctiva in which a delayed allergic response of immune cells most likely to debris and bacterial antigens on a foreign body such as contact lenses or ocular prostheses takes place (Bailey and Buckley, 1991; Bischoff, 2014; Bozkurt et al., 2007; Kenny et al., 2020; Koch et al., 2016; Meisler et al., 1981; Srinivasan et al., 1979; Swann, 2001). This, especially in combination with possible mechanical irritation of conjunctival cells due to roughening of the prosthetic surface, leads to the characteristic clinical presentation of "giant" papillae preferably on the superior tarsal conjunctiva (Bailey and Buckley, 1991; Bischoff, 2014; Bozkurt et al., 2007; Kenny et al., 2020; Koch et al., 2016; Meisler et al., 1981; Srinivasan et al., 1979; Swann, 2001). Risk factors include poor hygiene and long wearing time of the prosthesis (Koch et al., 2016). Patients suffering from GPC experience pruritus, burning sensation, pain, and markedly increased mucoid discharge (Koch et al., 2016; Srinivasan et al., 1979; Swann, 2001). Given that deterioration of the prosthesis plays a key role in the pathophysiology of GPC, PMMA ocular prostheses should be polished and their cryolite glass counterpart should be replaced respectively (Koch et al., 2016). Analogous to an acute allergic reaction, topical medications such as steroids, mast cell stabilizers like cromoglicic acid, and non-steroidal anti-inflammatory drugs can be used additionally (Bailey and Buckley, 1991; Bilkhu et al., 2013; Bischoff, 2014; Bozkurt et al., 2007; Kenny et al., 2020; Koch et al., 2016; Meisler et al., 1981; Srinivasan et al., 1979; Swann, 2001).

12.1.3. Infectious conjunctivitis

Infectious conjunctivitis can also occur in the anophthalmic socket just like in the normal eye (Bailey and Buckley, 1991; Bohman et al., 2014; Christensen and Fahmy, 1974; Koch et al., 2016; Lauber et al., 2023; Pine et al., 2013c; Vasquez and Linberg, 1989). This might have viral or bacterial origins, and the bacterial organisms causing this are also mostly the same as in normal eyes, namely gram positive organisms like *Staphylococcus aureus*, Hemophilus spp., and streptococci (Bailey and Buckley, 1991; Bohman et al., 2014; Christensen and Fahmy, 1974; Koch et al., 2016; Vasquez and Linberg, 1989). Symptoms and therapy are also analogous to those of conjunctivitis in the normal eye and the prosthesis should be removed for the administration of any drugs (Bailey and Buckley, 1991; Bohman et al., 2014; Koch et al., 2016). However, when swabbed gram negative organisms such as *E. coli* are found significantly more frequently in the conjunctiva of anophthalmic socket of patients who frequently manipulate their prosthesis, suggesting that atypical pathogens are introduced to the microenvironment of the anophthalmic socket with handling (Christensen and Fahmy, 1974; Koch et al., 2016; Pine et al., 2013c; Vasquez and Linberg, 1989). Presumably, this is caused by frequent removal of the prosthesis in combination with poor hand hygiene (Koch et al., 2016). This is also why a swab should be performed in severe cases for pathogen diagnosis and resistance testing (Koch et al., 2016). Sterile handling of the prosthetic eye and sterilization would be a good measure in attempt to prevent this, however commonly used substances or instruments are potentially harmful to its structure and integrity (Vasquez and Linberg, 1989).

12.1.4. Conjunctivitis associated with mechanical irritation and the cleaning protocol

Most cases of irritation or chronic discharge, however, are not allergic reactions and unless there are further signs of infection, typically there is no significant difference in bacterial flora between symptomatic and asymptomatic patients suggesting that the symptoms are not caused by alteration of the bacterial flora in most cases (Pine et al., 2013c; Vasquez and Linberg, 1989). These specific causes of mucoid discharge are well understood but the more common non-specific discharge that affects so many patients is likely due to mechanical irritation as well as minor changes in the microenvironment of the anophthalmic socket over time (Pine et al., 2013c; Vasquez and Linberg, 1989). The focus should be shifted toward fit, shape, surface quality, and proper lubrication of the prosthesis in these cases (Pine et al., 2013c; Vasquez and Linberg, 1989). Provided that it is fitted correctly, it is also imperative that the patient follows a proper cleaning protocol that includes professional prosthetic eye care and individually adapted cleaning intervals (chapter 10) (Pine et al., 2012a, 2012c, 2013b, 2013c). Cleaning removes deposits from tear proteins that initially play a beneficial role in wettability and therefore one should not remove their prosthetic eye more than monthly, but beyond this period the necessity of removal and cleaning varies depending on individual and environmental factors as too much build-up of deposit again leads to irritation (Pine et al., 2012a, 2012c, 2013b, 2013c). This establishes once again why polishing of PMMA and replacement of cryolite glass prostheses should take place in appropriate time intervals for the respective material (Pine et al., 2012a, 2012c, 2013b, 2013c).

As alluded to before, proper fit, good care, hygiene, and adequate therapy of these specific complications play a vital role in the prevention of long-term inflammatory and infectious changes in the anophthalmic socket (Koch et al., 2016; Quaranta-Leoni, 2008). This in turn will prevent irreversible scarring of the same (Ibrahiem and Abdelaziz, 2016;

Koch et al., 2016; Quaranta-Leoni, 2008). This scarring can otherwise lead to shallowing of the conjunctival fornices, making it impossible to insert the ocular prosthesis (Ibrahiem and Abdelaziz, 2016; Koch et al., 2016; Quaranta-Leoni, 2008). Should this be the case, surgical intervention is indicated and consists of enlargement of the fornices by way of mucous membrane, amniotic membrane, or dermis fat transplant (Ibrahiem and Abdelaziz, 2016; Koch et al., 2016).

12.1.5. Dry anophthalmic socket syndrome (DASS)

Another very important and prevalent complication is the dry anophthalmic socket (Allen et al., 1980; Bohman et al., 2014; Colorado et al., 2016; Jang et al., 2013; Kim et al., 2008, 2019; Koch et al., 2016; Lauber et al., 2023; Messmer, 2015; Pine et al., 2013b; Rokohl et al., 2019b, 2020a, 2021b, 2023b, 2023c; Zhao et al., 2016). Similar symptoms as in dry eye disease can be experienced in the anophthalmic socket and this is a multifaceted pathology of the tears and ocular surface that results in impaired tear film homeostasis (Allen et al., 1980; Bohman et al., 2014; Colorado et al., 2016; Jang et al., 2013; Kim et al., 2008, 2019; Koch et al., 2016; Messmer, 2015; Pine et al., 2013b; Rokohl et al., 2019b, 2020a, 2021b, 2023b, 2023c; Zhao et al., 2016). More than half of all prosthetic eye wearers suffer from severe tear deficiency with volume deficiency and hyperevaporation of tear fluid being the two major components that cause this (Allen et al., 1980; Koch et al., 2016; Pine et al., 2013b).

One of the main causes of a dry socket is meibomian gland dysfunction (MGD) and it is widely recognized that prosthetic eye wearers have significantly higher rates of dysfunction and loss of the same (Bohman et al., 2014; Jang et al., 2013; Koch et al., 2016; Zhao et al., 2016). The friction that results from rubbing of the conjunctiva on the ocular prosthesis and the debris on its surface leads to irritation and microtrauma (Bohman et al., 2014; Koch et al., 2016; Rokohl et al., 2019b). This in combination with reduced blinking frequency causes conjunctival inflammation and hyperkeratinization of the lid margins which in turn leads to obstruction and morphologic changes of the meibomian glands among other cytologic alterations of the conjunctiva (Bohman et al., 2014; Jang et al., 2013; Kim et al., 2008; Koch et al., 2016; Rokohl et al., 2019b; Zhao et al., 2016). Subsequently, the secretion of tear film lipids that make up its outer layer is impaired and decreased, resulting in an unstable lipid layer and favoring evaporation of lacrimal fluid (Jang et al., 2013; Zhao et al., 2016).

Another important factor in the pathogenesis of a dry socket is the inflammation-induced reduction of conjunctival goblet cells (Colorado et al., 2016; Kim et al., 2008). This leads to decreased secretion of mucins that otherwise favor wettability, further impairing tear film stability and causing more friction between prosthetic eye and conjunctiva (Colorado et al., 2016; Kim et al., 2008, 2019).

Reduced blinking frequency in anophthalmic patients also favors evaporation and the lack of corneal reflex leads to decreased tear production (Bohman et al., 2014; Koch et al., 2016). Other factors that might aggravate dryness and discomfort in the anophthalmic socket are severe debris contributing to the altered distribution of tear fluid (Pine et al., 2012c, 2013b), poor eye lid congruency due to poor fitting or malposition of the prosthesis (Bohman et al., 2014), lacrimal gland insufficiency (Zhao et al., 2016), and various environmental factors (Zhao et al., 2016).

Common symptoms of a dry socket are redness, stinging, pruritus, burning sensation, sandy or gritty sensation, and discomfort with prosthetic eye wear (Messmer, 2015; Rokohl et al., 2019b, 2023b, 2023c).

Depending on the quality of the prosthesis and its surface, a cryolite glass prosthesis should be replaced and PMMA prosthetic eyes should be repolished in case of a dry socket as this improves wettability and enables proper tear film distribution by preventing excessive deposit buildup (Koch et al., 2016; Pine et al., 2013a). Aside from preventing mucoid discharge, as mentioned before, it is also imperative in the prevention of a dry socket that the patient follows a cleaning protocol with appropriate intervals, because cleaning on the one hand removes beneficial deposits that improve wettability and create a physiologic microenvironment but on the other hand too much buildup of deposit again leads to irritation (Pine et al., 2012a, 2012c, 2013a, 2013b). Additionally, the patient can incorporate daily care of their lid margins to prevent crusting and keratinization of meibomian gland opacities, thereby promoting their preservation and secretion (Ko et al., 2018; Koch et al., 2016). The patient can apply an eyelid scrub along with warm compresses (Ko et al., 2018). This in combination with artificial tears (Bohman et al., 2014) and topical application of anti-inflammatory drugs like corticosteroids such as loteprednol etabonate (Ko et al., 2018) or calcineurin-inhibitors like cyclosporin (McLaughlin et al., 2014) have been shown to be effective in treating meibomian gland dysfunction (Bailey and Buckley, 1991; Bozkurt et al., 2007). If all of the aforementioned conservative treatment options fail, punctum plugs or surgical treatment via labial salivary gland transplantation shall be considered (Bohman et al., 2014; Franca et al., 2011).

It is apparent that most unilaterally anophthalmic patients subjectively complain of more dryness on the anophthalmic side and as it can be seen in the previous paragraphs, the different possible causes for this have been investigated separately (Rokohl et al., 2020a). However, recently there has been a systematic and integrative approach to the symptoms and signs of a dry socket, introducing the Dry Anophthalmic Socket Syndrome (DASS) which aims to establish standardized diagnostic criteria for anophthalmic patients complaining of dryness (Rokohl et al., 2020a, 2021b). DASS is defined as “a disease of the socket surface characterized by a loss of tear film homeostasis accompanied by socket discomfort, in which tear film instability, conjunctival inflammation and damage, as well as eyelid and neurosensory abnormalities play etiological roles“ (Rokohl et al., 2020a, 2021b).

It is essentially a synthesis of different mutually related socket complications resulting in dryness and there are two components to its diagnostic criteria (Rokohl et al., 2020a, 2021b). One component is the presence of subjective dryness symptoms that are assessed with standardized questionnaires, namely OSDI $\geq$13, SANDE $\geq$13, or DEQ-5 $\geq$ 6 (Rokohl et al., 2020a, 2021b). Additionally, one of the following objective clinical abnormalities is present: “blepharitis anterior, blepharitis posterior, abnormalities of meibomian glands in the in vivo laser scanning confocal microscopy (LSCM), reduced tear meniscus height, or conjunctival inflammation resulting in conjunctival staining” (Rokohl et al., 2020a, 2021b).

A critical finding in the studies regarding DASS was that patients complained of more subjective dryness and signs of meibomian gland dysfunction in LSCM were increased even in the absence of absolute tear volume deficiency or clinical blepharitis (Rokohl et al., 2021b). This suggests that it might not be the intensity of current socket inflammation that correlates with these findings but rather the duration, as chronic inflammation has been shown lead to loss of meibomian gland acinar units (Rokohl et al., 2021b). This is also why eyecare practitioners should consider the above-mentioned diagnostic criteria for DASS in anophthalmic patient encounters and consider early treatment (Rokohl et al., 2020a, 2021b). However, the exact roles and interactions of etiological causes of DASS are not completely understood and more research into DASS must be done with the aim of establishing a standardized examination protocol and an evidence-based treatment algorithm (Rokohl et al., 2020a, 2021b; Shapira et al., 2021a).

12.2. Post-enucleation socket syndrome (PESS)

Another important complication that typically occurs after enucleation is the post-enucleation socket syndrome (PESS), firstly described by Tyers and Collin in 1982 (Tyers and Collin, 1982). The PESS is sometimes also named anophthalmic socket syndrome since this syndrome can also occur after evisceration (Keseru et al., 2015; Koch et al., 2016; Lauber et al., 2023; Pine et al., 2011, 2017c; Quaranta-Leoni et al., 2021; Rokohl et al., 2018a, 2018c, 2019b, 2022; Ruiters and Mombaerts, 2021; Shah et al., 2014; Thiesmann et al., 2018). Patients with

several years of experience wearing a prosthetic eye are typically satisfied with their general appearance, however they are more concerned with their eyelid contour compared to the healthy fellow eye specifically than patients who have recently experienced eye loss (Koch et al., 2016; Pine et al., 2011, 2017c; Rokohl et al., 2018a, 2018c; Thiesmann et al., 2018). This can be attributed to PESS which includes several clinical signs and symptoms regarding the eye lid, including ptosis of the upper eyelid and laxity or ectropion of the lower eyelid but also enophthalmos, sulcus deformity, shallow lower fornix, and backward tilt of the prosthesis (Fig. 14) (Keseru et al., 2015; Koch et al., 2016; Rokohl et al., 2018c, 2022; Thiesmann et al., 2018; Vistnes, 1976). PESS occurs both in glass as well as PMMA prosthetic eye wearers and symptoms vary in severity, can occur separately or in combination, and therefore treatment revolves around pertinent findings in the individual patients (Rokohl et al., 2018c).

The primarily postulated pathomechanism of the PESS was the atrophy of orbital tissues, especially of fat (Tyers and Collin, 1982). However, the major aspect in the pathogenesis of PESS is volume redistribution in the orbit which causes a downward and anterior shift of orbital tissue including the orbital implant (Fig. 15) (Keseru et al., 2015; Koch et al., 2016; Rokohl et al., 2018c, 2022). In contrast, orbital tissue volume loss was not observed (Detorakis et al., 2003; Rokohl et al., 2022; Smit et al., 1990). The volume redistribution also leads to sagging and retraction of the superior rectus, straining of the levator palpebrae muscle, therefore deepening of the superior fornix, and causing ptosis along with the other signs of PESS, as mentioned above (Keseru et al., 2015; Koch et al., 2016; Rokohl et al., 2018c, 2022). This along with the mechanical strain that the weight of the ocular prosthesis puts on the lower eyelids leads to their laxity and the backwards tilt and caudal anterior shift of the prosthesis, resulting in an upwards gaze of the prosthesis with cosmetic disfigurement of the patient's affected side (Fig. 16) (Keseru et al., 2015; Koch et al., 2016; Rokohl et al., 2018c, 2022).

While previous studies did not find orbital tissue volume loss in the development of the PESS (Detorakis et al., 2003; Rokohl et al., 2022; Smit et al., 1990), Han et al. detected in 2021 a reason for potential orbital volume loss contributing to the PESS (Han et al., 2021; Heindl and Rokohl, 2021; Rokohl et al., 2022). Han et al. observed shrinking of mammalian bone-derived hydroxyapatite orbital implants by osteoclastic activity (Han et al., 2021; Heindl and Rokohl, 2021; Rokohl et al., 2022). However, since mammalian bone-derived hydroxyapatite orbital implants are used rather rarely, this will play only a role in a few patients (Han et al., 2021; Heindl and Rokohl, 2021; Rokohl et al., 2022).

An orbital implant too small, an ocular prosthesis too large, and frequent manipulation and rubbing of the lower lid are risk factors, again highlighting why choice of orbital implant with proper size for optimal replacement is vital in avoiding such socket complications (Koch et al., 2016; Rokohl et al., 2022; Thiesmann et al., 2018). The objective is that orbital implant and ocular prosthesis together completely replace the volume lost due to enucleation or evisceration (Koch et al., 2016; Thiesmann et al., 2018; Wladis et al., 2018). On the one hand, selection of a larger orbital implant means that the ocular prosthesis can be created light and thin, lowering the risk of PESS (Koch et al., 2016). On the other hand, large implant size increases the risk of extrusion which can be counteracted by fixation of extraocular muscles however (Koch et al., 2016). One thing to consider is that even if there is good volume replacement and postoperative outcome, redistribution of orbital tissues might still cause enophthalmos in some patients (Keseru et al., 2015).

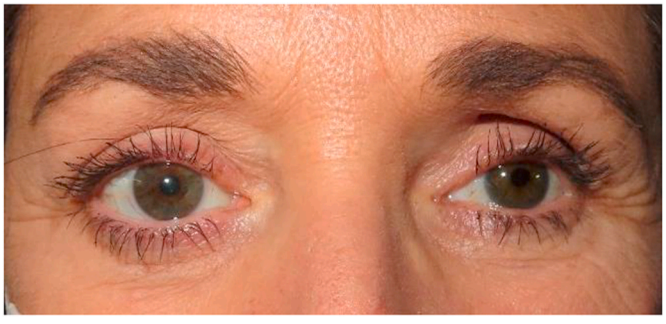

Fig. 14. Orbital volume redistribution includes a downward and anterior shift of orbital tissues as well as a sinking of the orbital implant in the course of the post-enucleation socket syndrome (PESS). In addition, there is a potential shrinking of the (mammalian bone-derived) hydroxyapatite orbital implants by osteoclastic activity.

It has been shown that enophthalmos is of less concern to patients subjectively compared to ptosis or ectropion (Rokohl et al., 2018a, 2018c). Nevertheless, if treatment is required, the orbital volume can be enhanced by replacement or secondary insertion of an orbital implant (if there was no primary implant or the primary implant was too small), or orbital floor augmentation to compensate for sinking of the implant (Keseru et al., 2015). Another possibility is the implant of a dermis fat graft (Aryasit and Preechawai, 2015; Keseru et al., 2015; Kim et al., 2010). However, the most common disadvantage of this procedure is an unpredictable rate of subsequent fat atrophy (Inchingolo et al., 2012). A less invasive solution, but also unfortunately mostly a less lasting procedure compared to a dermis fat graft, is an injection of autologous fat, previously aspirated from the abdomen, thigh or hip (Keseru et al., 2015; Kim et al., 2010). The use of injectable hyaluronic acid, calcium hydroxyapatite, or expanding hydrogel pellets has also been described (Crochelet et al., 2012; Keseru et al., 2015; Kim et al., 2010; Schittkowski and Guthoff, 2006; Vagefi, 2013; Vagefi et al., 2011). Using a larger prosthetic eye in attempt to treat enophthalmos is often inadvisable as this would only increase the risk of lower lid laxity and ectropion (Hatt, 1992; Koch et al., 2016; Thiesmann et al., 2018).

As previously mentioned, PESS is often a long-term complication of prosthetic eye wear and but its signs can already occur within the first year after enucleation (Rokohl et al., 2018c, 2022; Thiesmann et al., 2018). However, in a group of patients with at least 10 years of experience all of them had ptosis and ectropion was found in 50% of them (Thiesmann et al., 2018). Severe cases of ectropion can be treated surgically using the tarsal strip procedure (Hatt, 1992). Ptosis is treated surgically using levator aponeurosis advancement or levator resection (Kwitko and Patel, 2022).

12.3. *Contracted anophthalmic socket*

Contraction of the socket is another complication that needs attention. Patients experience irritation, or cosmetic changes or have difficulties to retain their prosthesis because of a reduced fornix. Socket contraction has been divided in several stages in the literature, where the stage 1 is not actual contraction, but considers fornix loss due to lower eyelid laxity, and is associated with absent orbital implant and large, thick prostheses (Krishna, 1980; Tawfik et al., 2009). For these cases the eyelid laxity is restored with standard ectropion correction (Anderson, 1981). This may also reform the fornix, but if still needed, the fornix can be restored with sutures that pull the fornix in the direction of the orbital rim. The other stages refer to progressive shortening of the fornices that occur in the course of an acute or chronic inflammatory response, probably due to overaction of the myofibroblasts (Tawfik et al., 2016). Triggers can be acute conjunctivitis, chemical burns, radiation, initial trauma, previous surgeries, chronic irritation from implant exposure, or is related to the ocular prosthesis itself due to a wrong fit with or irregular prosthetic surface. Stage 2 refers to mild contraction with actual shortening of the fornices so that the prosthesis no longer fits properly (Tawfik et al., 2009). The upper and/or lower lid may retract, or the eyelids tend to roll inwards (entropion). If possible, the causing trigger is treated and the prosthesis should be polished, renewed or adapted. When mild entropion is present, it can be corrected with standard surgical entropion procedures

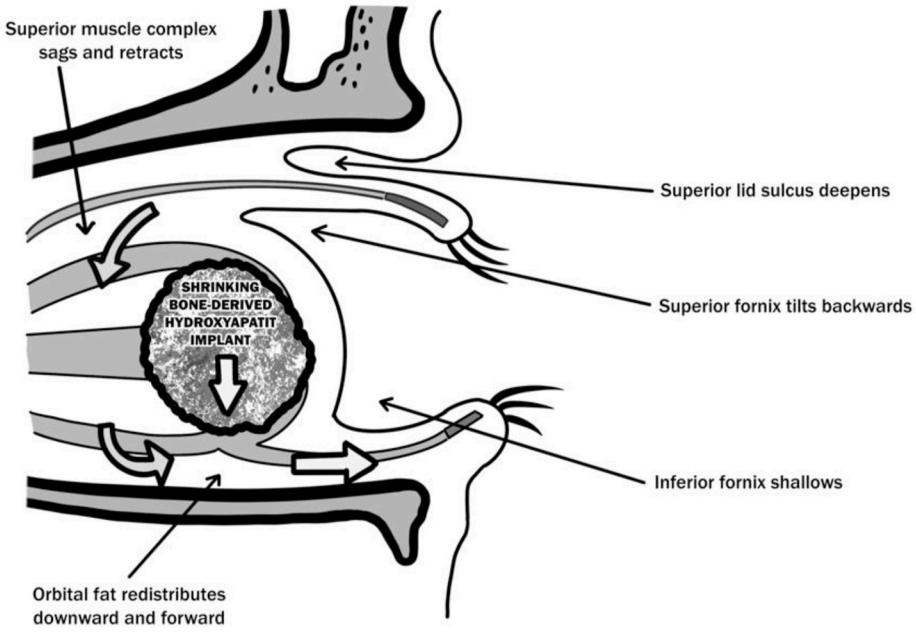

Fig. 15. Clinical elements of the post-enucleation socket syndrome (PESS) resulting in a backward tilt of the prosthesis, upwards gaze, and forward pressure on the lower eyelid with shallowing of the lower fornix.

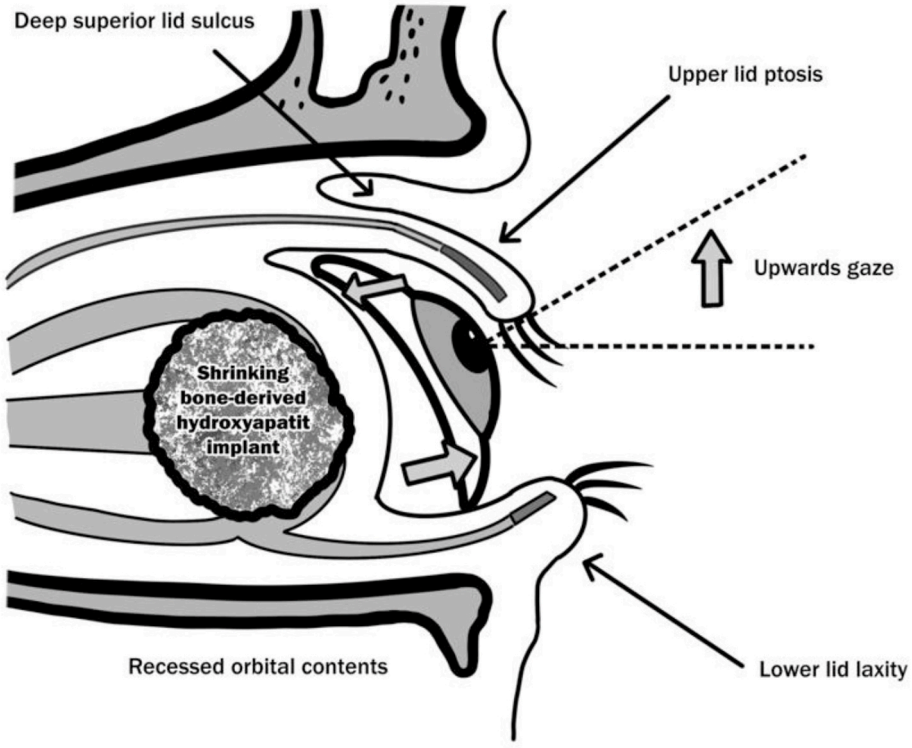

Fig. 16. Digitalized socket impression (A) and MRI scan (B) of a severe microphthalmia patient are used to design a series of conformers. Computer simulation of the face with the conformer (C) and the conformer alone (D). A series of growing larger conformers (D) for expansive treatment. The conformers are 3D printed in a biocompatible class IIa resin with a SLA printer.

(Quaranta-Leoni et al., 2021). More severe contractions (grade 2 and 3) have a lack of conjunctiva, that will have to be supplemented, which is generally done with harvested buccal mucus membrane (Kim et al., 2014). The application of mitomycin (intraoperative or postoperative) seems to result in slightly deeper fornices (Mandour et al., 2016; Mattout et al., 2021). Other options are amniontic membrane (Kumar et al., 2006) and dermis-fat-graft, both promoting epithelial cell growth over its surface, (split) skin grafts (Aggarwal et al., 2015; AlHassan et al., 2018) or stiffer grafts like hard palate for more support (Ding et al., 2018; Lee et al., 2002). The worst socket contractions are grade 4 with severe phimosis in all directions and include recurrent cases and cases after radiation and chemical burns (Tawfik et al., 2009). A large mucosal

transplant in combination with long-term (2–3 months) conformer fixation is often effective to retain a prostheses (Groot et al., 2021a; Yang et al., 2020). However, when insufficient vascular supply is expected, vascularized flaps are used, such as local temporalis muscle flaps or free microvascular flaps (Groot et al., 2021a; Quaranta-Leoni et al., 2021).

In all cases, mild or severe, the use of an adequately sized post-operative conformers is mandatory to prevent early post-operative recurrent contraction. The conformer can also help to form the correct socket cavity for future prosthetic wear. Commercially available conformers can be used, but custom conformers can be designed in the desired format and equipped with various extensions or drill holes to fix the eyelids (tarsorrhaphy) and fornices in the postoperative phase, hereby increasing the chance of success in case of recurrent contraction (Groot et al., 2021a). It is therefore important that the surgeon collaborates with the ocularist who will be able to provide custom adapted conformers (Fig. 17).

When surgery is not an option or needs to be postponed, or when the contraction is only mild, modest improvement of fornix depth can be obtained with non-surgical compressive conformer therapy using conformers (or the patient's own artificial eye) in combination with pressure bandage or a personalized pressure mask (Quaranta-Leoni et al., 2021). In addition, in mild cases, the eyelids can be closed over a conformer using non-toxic cyanoacrylate glue for a few days as an alternative to a pressure bandage or mask.

13. Future directions

For a long time, prosthetic eye care was based on acquired experiences and there was a significant lack of systematic studies and peer-reviewed literature on this subject. However, in recent decades, research in the field of ocular prosthetics has been driven forward by ophthalmologists, ocularists, optometrists, ophthalmoplastic surgeons, and psychologists. Many essential findings have been made for improving the care of anophthalmic patients and have now to be established in the daily clinical routine.

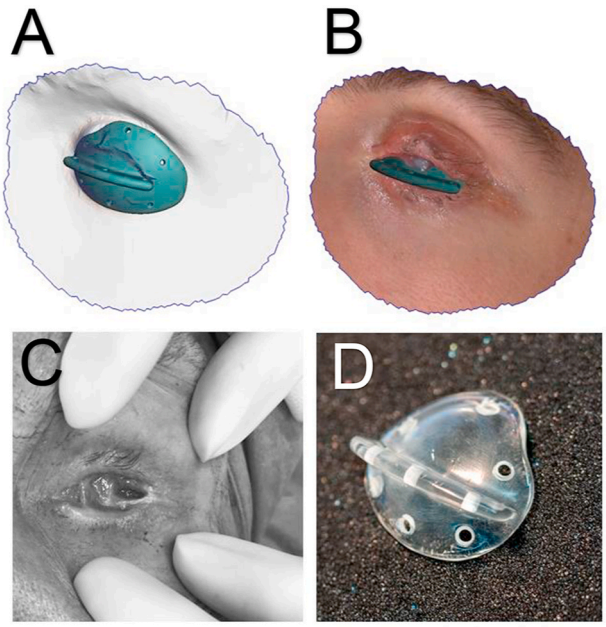

Fig. 17. Conformers can be adapted to any desired model. The top images show a design for the conformer (future prosthetic model) based on facial scanning (A, B). The left lower image shows a severely contracted socket with insufficient conjunctival lining and a complete lack of superior and inferior fornices to insert a prosthesis (C). The conjunctival lining can be enlarged surgically by inserting an oral mucosal graft. To adequately reshape the fornices, a patient-specific conformer (D) is inserted at the end of the surgery. To prevent subsequent contraction and extrusion of the conformer, fornix-fixating sutures can be introduced through the conformer openings to extend at the skin side, and the tarsal plates can be fixed to the central extension keeping the conformer in the correct position for several weeks to be released only after the healing process.

Several important issues have emerged in anophthalmic patient care in recent years. First, various and multifactorial psychosocial problems have become more central (Heindl et al., 2021; Pine et al., 2017a, 2017b, 2017c). In particular, anxiety and depression disorders seem to be underdiagnosed which is why a psychometric screening should be implemented in the routine of clinical care (Heindl et al., 2021). Since the general physical condition seems to have a significant influence on psychological issues, prosthetic eye wearers need also good and professional general healthcare (Heindl et al., 2021).

Secondly, the health of the remaining eye seems to be one of the major concerns of unilateral prosthetic eye wearers (Pine et al., 2011; Rokohl et al., 2018a, 2018c). Therefore, regular preventive ophthalmological checkups should be established in the health care system, independently of age (Pine et al., 2011; Rokohl et al., 2018a, 2018c). This might reassure the patients (Pine et al., 2011; Rokohl et al., 2018a, 2018c).

Thirdly, another important major topic for anophthalmic patients is the dry anophthalmic socket syndrome (DASS) (Rokohl et al., 2020a, 2021b; Shapira et al., 2021a). The DASS is one of the key factors for socket discomfort in prosthetic eye wearers (Rokohl et al., 2020a, 2021b; Shapira et al., 2021a). Unfortunately, the exact pathophysiological mechanism is not fully understood and there is a lack of an evidence-based treatment protocol (Rokohl et al., 2020a, 2021b; Shapira et al., 2021a). Further studies should be undertaken to investigate the role and the interactions of etiological causes for the DASS in detail, especially concerning anophthalmic socket inflammation (Rokohl et al., 2020a, 2021b; Shapira et al., 2021a). Based on these insights, the development of a treatment algorithm is crucial in the future for improving the quality of life in many prosthetic eye wearers (Rokohl et al., 2020a, 2021b; Shapira et al., 2021a).

Fourthly, another potential future development will be most likely the establishment of the latest technologies for producing personalized conformers and prosthetic eyes (Groot et al., 2021a, 2021c; Kuijten et al., 2017, 2018; Mourits et al., 2018). The key technique will be presumably three-dimensional (3D) printing of prosthetic eyes (Groot et al., 2021a, 2021c; Kuijten et al., 2017, 2018; Mourits et al., 2018). Since 3D printed conformers are already in use in the daily routine care in some tertiary eye clinics, 3D printed prosthetic eyes are not until today (Groot et al., 2021a, 2021c; Kuijten et al., 2017, 2018; Mourits et al., 2018). However, there are already very promising approaches to producing a full-color ocular prosthesis with textured iris and sclera in one single print job using three-dimensional computer-aided design (Groot et al., 2021c). The authors are sure, that this technique will be established in the next decades for routine care and revolutionize prosthetic eye care.

Fifthly, improving the tolerance of an ocular prosthesis could be a future topic (Litwin et al., 2018). Socket discomfort and especially the DASS as well as increased mucoid discharge are key problems for anophthalmic patients (Pine et al., 2012a, 2012c, 2013b, 2013c, 2017c; Rokohl et al., 2019a, 2020a, 2021b; Shapira et al., 2021a). A potential solution for addressing these issues could be to improve the surface finish of ocular prostheses by enhanced polishing or novel innovative coatings (Litwin et al., 2018).

Sixthly, the last point – probably one of the most important findings – is that the very individual and multifactorial issues of prosthetic eye wearers are concerning many different medical specialties (Heindl et al., 2021). These insights suggest the need for integrated care beyond individual medical specialties for a successful long-term cosmetic, social, occupational, and psychological rehabilitation of anophthalmic patients (Heindl et al., 2021). Integrated care of anophthalmic patients by a multidisciplinary team should at least include ophthalmic-plastic

surgeons, ophthalmologists, ocularists, optometrists, general practitioners, psychologists, and also advisory as well as information services (Heindl et al., 2021).

CRediT authorship contribution statement

Alexander C. Rokohl: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Funding acquisition, Conceptualization. **Keith R. Pine:** Writing – review & editing, Writing – original draft. **Nicola S. Pine:** Writing – review & editing, Writing – original draft. **Erik Gordon:** Writing – review & editing, Writing – original draft. **Janice Yeoman:** Writing – review & editing, Writing – original draft. **Jelmer S. Remmers:** Writing – review & editing, Writing – original draft. **Dyonne T. Hartong:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization. **Ludwig M. Heindl:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization.

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Declaration of competing interest

Alexander C. Rokohl, Keith R. Pine, Nicola S. Pine, Erik Gordon, Janice Yeoman, Dyonne T. Hartong, and Ludwig M. Heindl have no financial or proprietary interest in any materials or methods mentioned in the manuscript. Alexander C. Rokohl, Keith R. Pine, Nicola S. Pine, Erik Gordon, Janice Yeoman, Jelmer S. Remmers, Dyonne Hartong, and Ludwig M. Heindl declare that they have no conflict of interest. Jelmer S. Remmers is owner and operator of a private practice as ocularist.

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Data availability

No data was used for the research described in the article.

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