Updates of Ocular Prostheses
A review of biomaterials and design in anophthalmic socket

CLAUDIA FLORIDA COSTEA1,2, CAMELIA MARGARETA BOGDANICI1,2*, ALEXANDRU CARAULEANU1*, GABRIELA DIMITRIU3, ANCA SAVA2, NICOLETA DAMITRESCU4, MIHAELA DANA TURLIUC5, ANDREI CUCU5, MANUELA CIOCIOIU5, RALUCA DRAGOMIR5, CATALIN MIHAI BUDUZDA1
1University of Medicine and Pharmacy Grigore T. Popa, Department of Ophthalmology, 16 Universitatii Str.,700115, Iasi, Romania
2University of Medicine and Pharmacy Grigore T. Popa, Department of Obstetrics and Gynecology, 16 Universitatii Str.,700115, Iasi, Romania
3University of Medicine and Pharmacy Grigore T. Popa, Department of Neurosurgery, 16 Universitatii Str.,700115, Iasi, Romania
4University of Medicine and Pharmacy Grigore T. Popa, Department of Anatomy, 16 Universitatii Str.,700115, Iasi, Romania
52nd Ophthalmology Clinic, Prof. Dr. Niculae Oblu Emergency Clinical Hospital, 2 Ateneului Str.,700309, Iasi, Romania
62nd Neurosurgical Clinic, Prof. Dr. Niculae Oblu Emergency Clinical Hospital, 2 Ateneului Str.,700309, Iasi, Romania
7University of Medicine and Pharmacy Grigore T. Popa, Department of Pathophysiology,16 Universitatii Str.,700115, Iasi, Romania
8University of Medicine and Pharmacy Grigore T. Popa, Department of Oral and Maxillo-Facial Surgery, 16 Universitatii Str., 700115, Iasi, Romania
9University of Medicine and Pharmacy Grigore T. Popa, Department of Endocrinology, 16 Universitatii Str.,700115, Iasi, Romania

Since Ancient Egypt up to present day, there have constantly been attempts at creating a perfect ocular prosthesis, which would complement the outstanding deficit in the orbit as a result of enucleation, evisceration and which should be biocompatible with the orbital tissue. Over time, there have been used numerous clinical materials, which were the basis of these eye prostheses. By revising literature through the search engines PubMed, MEDLINE and other sources, this article aims at emphasizing, in a chronological sequence, the way in which different types of ocular prostheses were created, but also their advantages and disadvantages. The evolution and design of biomaterials improved the eye rehabilitation process and reduced the complications caused by these prostheses in the anophthalmic socket.

Keywords: artificial eye, prosthesis, Graves disease, anophthalmic socket, non-integrated implants, integrated implants

The eye is not only the most sensitive organ, but it also plays an important role in the aesthetic aspect and facial expression. The loss of an eye can be caused by congenital defect or can be acquired secondary to various disorders, like Graves disease where severe exophthalmia can lead to eye loss [1, 2]. The most common causes which lead to the loss of ocular globe are trauma and tumors [3-5]. In this cases, the surgical intervention must be accurate, because wrong therapeutic steps could cause unnecessary mutilation [6], since there are surgical alternatives in such cases, like ocular surface reconstruction with a very useful biological material, namely, amniotic membrane [7, 8]. Besides the loss of vision, these patients become affected both esthetically and psychologically. In these cases, such defects are amendable to surgical correction and a multidisciplinary approach including the ophthalmologist, neurosurgeon, maxillofacial surgeon and the ocularist can prove beneficial [9, 10]. Surgical eye removal was classified by three types: (1) evisceration, during which the contents of the ocular globe are removed with intact sclera, (2) enucleation, during which the entire ocular globe is removed after severing the muscles and optic nerve and (3) exenteration, during which the whole content of the orbit, together with the eyelids, is removed [11, 12].

Modern imagistic techniques and studies on animals have changed the way of understanding anatomy and post-enucleation orbit physiology. Since today, we have the proof that by introducing a spherical implant within Tenon’s capsule, we can prevent secondary enucleation modifications of orbital volume loss and fat atrophy [13-16], even when it is placed late after enucleation [17].

Although over time, orbital implants were developed and inserted in the anophthalmic socket in order to restore ocular globe volume [18], unfortunately, the recovery of eye function by implantation is impossible.

Experimental part
Materials and methods
This article aims at emphasizing, in a chronological sequence the way in which different types of ocular prostheses were created and their advantages and disadvantages.

We performed a comprehensive general review synthesizing data from recent relevant studies about the evolution and design of biomaterials, that have been used for ocular prostheses. In this direction we have collected data from the following English medical electronic databases: PubMed and MEDLINE.

Results and discussions
Since Ancient Egypt, Egyptians used to remove the eyes during the process of mumification, in order to fill the orbit with precious stones or wax, to simulate the iris [19]. Even so, the earliest known evidence of an ocular prosthesis was found in Iran, in Shahr - I Sokhta, in the skeleton of a woman, dating back to 2900 -2800 BC [20]. This had a hemispherical form, with the diameter of 2.5 cm and was made of a light material, probably bitum paste. Its surface was covered by a thin layer of gold, engraved with a central circle, representing the iris and gold lines patterned like sun rays [20, 21]. In 1885, Mules P.H. used a
Types of prostheses

In ophthalmology, prostheses can be ocular or orbital. Ocular prosthesis represents the artificial replacement of the eye bulb, while orbital prosthesis involves replacing the entire content of the orbit [26]. At the moment, there are three types of ocular prostheses in use: (1) stock eyes, (2) modified stock eyes and (3) custom-fitted eyes [27].

Ocular impressions and fitting can be: direct (external) impression, impression with stock ocular tray, impression with custom ocular tray, impression with stock ocular prosthesis and wax scleral blank [28].

A prosthesis used for ophthalmoplasty must have the following features: (1) retain the shape of the defective socket, (2) prevent collapse of the eye lid shape and accumulation of the fluid in the cavity, (3) provide proper muscle action of the eye lids, (4) maintain aesthetics: palpebral opening, coloration and gaze similar to the natural eye [29]. The prothetic eye includes: oval whitish palpebral opening, coloration and gaze similar to the natural eye [30]. The prosthetic eye includes: oval whitish palpebral opening, coloration and gaze similar to the natural eye [30]. The prosthetic eye includes: oval whitish palpebral opening, coloration and gaze similar to the natural eye [30]. The prosthetic eye includes: oval whitish palpebral opening, coloration and gaze similar to the natural eye [30]. The prosthetic eye includes: oval whitish palpebral opening, coloration and gaze similar to the natural eye [30].

Non-integrated implants (non-porous)

Non-integrated implants are characterized by the fact that they do not allow the ingrowth of organic tissue into their inorganic substance and do not contain a unique apparatus in order to attach extraocular muscles [30]. The main disadvantage of these types of non-porous ocular implants is represented by migration, which occurs more frequently than in porous implants, especially when there are muscles imbricated over the surface of the sphere [31, 32]. Therefore, researchers have sought to cover these implants with different materials which facilitate the fixation of the extraocular muscles, such as polyester gauze or donor sclera, which also improve implant motility [21]. Non-integrated implants include glass, silicone spheres [33] and PMMA [30].

Glass

The first glass orbital implant was used by Mules P.H. after enucleation was made in 1885 [22]. It consists of a hollow blown glass sphere and was used largely until the Second World War [34]. The main complication was represented by the extrusion of the glass sphere, which had a rather high rate of 50 – 90%, as reflected by the study of Mules P.H. [22, 34]. Due to the improvement of surgical techniques, this rate was to decrease over time to 21% and later, to 10% [35, 36]. The main disadvantage of this implant is the risk of break, caused by trauma or the risk of implosion, caused by temperature changes [34]. Moreover, the implant was hazardous, brittle and heavy [37]. Today, glass was abandoned, because better materials for the fabrication of ocular implants were invented. Nevertheless, Baino F. recently published a study in 2018 which proved that new glass-ceramic porous material are used for orbital implants, made of foam-like CaSiO3 – containing glass-ceramics. It presents architectural characteristics, proper to be used as orbital implant material, a promising alternative to existing ceramic or polymeric bioinert orbital implants [38].

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Fig.2. The ocularist paints the iris on the artificial eye (Oculist's personal collection, Trofin C).

Fig.3. The surgeon makes an incision around the cornea and iris and then removes the intraocular contents, preserving the remaining scleral shell and extraocular muscles. An spherical implant made of acrylic, PMMA, silicone or HA is placed into the evisceration cavity to maintain appropriate orbital volume. The ocularist is fitting the prosthesis after 6-8 weeks following the surgery (Oculist's personal collection, Trofin C).

Fig.1. Surgeon at work, modified after an image from Ophthalmodouleia by Georg Bartisch (1583), History of Science Collections, University of Oklahoma Libraries (public domain and U.S. public domain).
Silicone
For more than 50 years, silicone was largely used not only for different types of surgical applications, but also for orbital implants, due to its beneficial properties: chemical inertia, flexibility, easy handling [34].

At the end of the 1960s, Soll D.S. proposed an inflatable silicone implant, filled with silicone gel [39, 40], which was abandoned because of its pressure-related problems, which occurred both in intra-operative and post-operative [34]. A few years later, at the end of the 1980s, silicone orbital implants, with non-porous spheres, either bare or wrapped and extraocular muscle covered, attached to the four rectus muscles, were introduced [34]. Today, silicone orbital implant is recommended in case of severe orbital trauma, when the extraocular muscles are unidentifiable and cannot be attached to the implant.

Polymethylmethacrylate
PMMA is an important material in ophthalmology, due to its excellent biocompatibility with ocular tissues and to its transparency [34]. Thanks to these qualities, PMMA is used not only in making intraocular lenses [41] or contact lenses [42], but also for orbital implants, as well as in fixing extensive orbito-facial defects caused by trauma [43] and useful in neurosurgery and maxillofacial surgery.

PMMA ocular implants appeared in the 1980s, when Frueh and Felker described for the first time, baseball implant, a PMMA sphere in an envelope of sclera [44]. Among the subsequent complications, there were: post-operative edema [45], unacceptable pain, implant exposure or migration [46] or necrosis of the conjunctiva [47].

Integrated implants (porous)
The porous surface of the integrated implants was proved to allow the fibrovascular ingrowth in depth all over the implant, and also the insertion of posts and pegs [33].

In the absence of a vascular base, this fibrovascular base ingrowth should: (1) lead to the increase of the surgical success rate, (2) decrease the risk of infection, so that this vascular supply allows the defense and immune surveillance and (3) reduce the rate of extrusion or migration of the implant [19, 32, 48].

This porous surface of the implant helps in anchoring the implant and immune surveillance consecutively [19, 34], in providing blood supply within the implant and in reducing the risk of infection [49].

Moreover, some studies revealed the superiority of the porous implants compared to the one of the non-porous implants. Hence, donor sclera-covered HA implants have higher late exposure rates than sclera-covered silicone implants [48, 50]. Also, excellent outcomes by suturing the rectus muscles, reinforced with autogenous fascia or sclera in patients with silicone implant, with no cases of implant migration were obtained [51].

Bone-derived orbital implants
The first orbital implant of this type was introduced in 1899, by Schmidt H. and it was made from mineral matrix of bovine cancellous bone [52]. The process of creating this implant implied heating spheres of cancellous bone to destroy all organic matter, leaving only calcium phosphate mineral framework behind, which was subsequently proved to contain ultramicroscopic crystals of HA with small quantities of calcium carbonate and calcium citrate [34, 53-55]. These were used until 1950s, when biologically inert non-integrated polymeric spheres (PMMA and silicone) appeared and took their place [34].

Proplast-Teflon
Proplast was introduced by Lyall M.G. at the end of the 1970s [56] and it was an inert felt-like composite material, composed of carbon fibers and polytetrafluoroethylene (Teflon), out of which hemispherical orbital implants were made, and had the advantage of being invaded by fibrous tissue. Hence, the problem of rejection or extrusion was exceeded [34]. Nevertheless, the use of this type of implant has decreased, mainly due to post-operative complications, such as long-term infections [57].

Hydroxyapatite
Due to the chemical similarity to the biological apatite of hard tissues, HA was largely used in the field of oculoplasty.

Introduced by Perry A.C. in 1991 [58], coralline porous HA - Ca$_x$(PO$_4$)$_y$(OH)$_z$. was to become the most frequently used material in ocular implant after primary enucleation [59]. Made from a specific genus of reef-building coral, porous HA has a similar architecture to human cancellous bone, with interconnecting channels. Per se, HA represents primary inorganic portion of human bones and the process by which implants of HA are made from sea coral, imply intense heat, which denatures proteins in order to reduce the immune response [19]. When it is implanted in soft tissues, porous HA allows the ingrowth of fibrovascular tissues in pores [58], and some studies showed that unwrapped HA does not become encapsulated, like PMMA spheres or silicone [58, 60, 61].

Like other ocular porous implants, HA implants allow the fibrovascular ingrowth, reducing the risk of infection, extrusion and migration [62]. Another advantage is the fact that these implants allow the safe attachment of extraocular muscles, improving implant motility [58, 60]. Studies have also shown that the rate of vascularization depends on the pore dimensions, thus vascular ingrowth was faster in HA implants with 200 mm pores than in HA implants with 500 mm pores [63]. HA stimulates the occurrence of a foreign-body giant cell reaction [64], and in animal models, this reaction can last up to one year from the orbital implant [65, 66].

For a better efficiency, wrapping material for HA implants were looked for, such as temporalis fascia or fascia lata, rectus abdominis sheath, human donor pericardium, expanded polytetrafluoroethylene, bovine pericardium, acellular human cadaveric dermis, polyglactin mesh or polymer-coated HA implants [67-75]. However, the use of HA implants has decreased in the last time [76].

Nevertheless, porous HA implant presents the disadvantage of having very high costs and causes damage to sea-life ecosystems, as a result of natural corals harvesting [34]. In this respect, an attempt at creating synthetic HA implants was made [77], but the scanning electron microscopy showed that although it has an identical composition to coralline porous HA, there are some architecture-related differences, such as lower porosity and interconnectivity, the existence of closed pores and blind pouches [78]. Despite this, by using a rabbit model study, Jordan et al. proved that the fibrovascularization occurs both in the natural and artificial implant [79].

Cheaper versions of this implant were developed in many countries, with different results. Thus, Brazilian HA implant was proved to have a lower porosity and pore interconnectivity and a higher weight than coralline porous HA sphere, with a limited fibrovascularization and increased risk of implant migration [79, 80]. The Chinese HA implant was proved to contain CaO impurities, and after hydration...
in host tissues, it can result in Ca(OH)₂, which is caustic [81, 82].

Other disadvantages and main complications of HA implants are: difficult suture of extraocular muscles directly to the implant, chronic infection, pyogenic granuloma, socket discharge, conjunctival thinning and discomfort or persistent pain [34, 83-87].

**Conclusions**

According to the current state of art and orbital implants existing on the market, there is no ideal implant. For all the patients, follow-ups must be done regularly, in order to detect the first signs of potential complications, regardless of the used implant.

**References**


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