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Oncological Aspects of the Eye Enucleation Procedure

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Summary: The removal of the eyeball is one of the earliest surgical procedures recorded in the history of medicine. The decision to perform enucleation is challenging for both the patient and the physician, and it is typically considered a last resort when all conservative treatment options have been exhausted. In recent years, the number of enucleation procedures performed for advanced glaucoma and intraocular tumors has significantly declined. This is largely due to advancements in laser technology, surgical techniques, and local treatments for glaucoma, as well as the widespread use of radiation therapy for intraocular tumors. Although enucleation can negatively impact the patient's quality of life and psychological well-being, it remains the treatment of choice in cases of advanced intraocular tumors, extensive eye injuries that preclude the reconstruction of ocular structures, or painful blind eyes. Fortunately, advancements in orbital implants and modern ocular prostheses now offer patients the possibility of achieving a satisfactory cosmetic outcome.

Key words: enucleation, evisceration, orbital implant, uveal melanoma, post-enucleation socket syndrome (PESS).

Introduction

The removal of the eyeball is one of the earliest surgical procedures in history. According to historical records, it has been practiced in ophthalmology since 2600 BC [1]. The decision to perform enucleation is challenging for both the patient and the physician, and it is typically considered a last resort when all conservative treatment options have been exhausted. The procedure leads to a decline in quality of life and functionality, with an increased risk of depression and anxiety disorders in patients [2]. This article primarily addresses the oncological indications for enucleation of the eye.

Indications for enucleation

Indications for enucleation include:

- ✓ presence of an intraocular tumor, the advancement of which prevents conservative treatment;
- ✓ painful blind eye typically associated with glaucoma, endophthalmitis, sympathetic ophthalmia, uveitis, or ocular atrophy;
- ✓ severe extensive trauma with no possibility of ocular reconstruction;
- ✓ esthetic considerations, when ocular damage caused by another condition (e.g., congenital malformations, atrophy, post-inflammatory changes, etc.) significantly affects the patient's appearance.

According to statistics, the most common cause of enucleation is trauma to the eye. The number of enucleation procedures varies each year, depending on the indication. Recently, the frequency of enucleations performed for advanced glaucoma and intraocular tumors has significantly declined due to advancements in laser technology, surgical techniques, local treatments for glaucoma, and the use of radiation therapy for intraocular tumors [3]. Just a few decades ago, enucleation of the eye was the only effective treatment for retinoblastoma. However, this has changed with the introduction of more effective systemic and local chemotherapy, as well as radiotherapy, laser therapy, and cryotherapy [4]. This progress has significantly improved prognosis and positively impacted the psychological well-being of patients, particularly in cases of bilateral retinoblastoma.

Enucleation in uveal melanoma

With the availability of alternative treatment methods, such as brachytherapy, proton radiotherapy, transpupillary thermotherapy, exoresection and endoresection of tumor (following prior irradiation), and stereotactic radiotherapy, the decision to perform enucleation must be made on a case-by-case basis. Factors to consider include tumor size, location, presence of extraocular invasion (Fig. 1), condition of the other eye, the patient's overall health, and psychological considerations.

Fig. 1. Eye with visible amelanotic extraocular extension.

Even as late as the early 20th century, enucleation was the only treatment for uveal melanoma, and it remained the first-line approach until the 1970s. With the advent and development of radiotherapy techniques such as brachytherapy and proton radiotherapy, the frequency of performing enucleation procedures has decreased significantly. Approximately 40 years ago, the Zimmer-

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man hypothesis was proposed, suggesting that enucleation of the eye increases the risk of distant metastases due to the potential dissemination of tumor cells via the vortex veins into the systemic circulation during the procedure [5]. In 1985, the largest multicenter study in the history of ocular oncology, the Collaborative Ocular Melanoma Study (COMS), was initiated. The study found no statistically significant difference in the 5-year survival rates for large and medium-sized melanomas treated with irradiation compared to those treated with primary enucleation [6]. Enucleation of the eye may be indicated either as a primary treatment or as a second-line option in cases of failed radiation, tumor recurrence, or in the presence of toxic tumor syndrome after other treatment options have been exhausted. If tumors are very large (Fig. 2, 3), with a base diameter greater than 20 mm, which exceeds the size of the brachytherapy plate and does not allow for maintaining a safe margin, or when the tumor thickness exceeds 12 mm (Fig. 4) or significantly affects the disc of the optic nerve (CN II), and in cases with coexisting secondary glaucoma, enucleation still remains the best treatment option (Fig. 2, 3, 4) [7].

Studies comparing enucleation as a first-line treatment versus a second-line approach after brachytherapy or proton radiotherapy for uveal melanoma have shown that enucleation as a secondary treatment is technically far more challenging. It prolongs the duration of the procedure and increases the risk of post-enucleation syndrome and eyelid disorders, owing to damage to previously irradiated tissues and the presence of postoperative synechiae from the placement of the radioactive applicator and its removal [8]. A retrospective study conducted among patients at the Department of Ophthalmology and Ocular Oncology at the University Hospital in Krakow (2018–2021) compared treatment methods for uveal melanomas based on patients' gender. The study included a total of 1,336 patients (726 women – 54.34% and 610 men – 45.66%), treated between 1 January 2018 and 31 December 2021. The study found that, at the time of diagnosis, tumor sizes were larger in men, although this difference was not statistically significant (T4 size tumors were diagnosed in 18.03% of men compared to 14.46% of women, $p = 0.068$). Enucleation of the eye was employed as the first-line treatment in 274 patients (20.51%). The decision to enucleate the eye was made significantly more frequently in men than in women (23.44% and 18.04%, respectively; Chi^2 Pearson test $p = 0.015$). Additionally, tumors located anterior to the equator of the eye were more frequently treated with enucleation compared to those located posterior to the equator (38.46% and 14.94%, respectively; Chi^2 Pearson test $p < 0.001$). The study concluded that women were less willing to undergo enucleation, primarily due to a greater fear of cosmetic defects [9].

Enucleation in retinoblastoma

The choice of treatment for retinoblastoma primarily depends on factors including the tumor stage, location, and size; presence of subretinal and intravitreal spread; involvement of the anterior segment of the eye; presence of metastases; infiltration of the optic nerve and orbital tissues; as well as the patient's age, the condition of the other eye, the potential for vision in both eyes, and the presence or absence of the RB1 mutation. Currently, the most common treatment methods include local intra-arterial chemotherapy (increasingly used as a first-line therapy), systemic chemotherapy, intravitreal chemotherapy (melphalan injections into the vitreous chamber), transpupillary thermotherapy, laser photocoagulation, cryotherapy, and brachytherapy. Advancements in modern local and systemic therapies have significantly reduced the frequency of ocular enucleation. At present, it is typically performed in cases where local and systemic treatments fail, retinoblastoma recurs after all other options have been exhausted, or when secondary glaucoma and extraocular tumor invasion coexist [10].

Steps in the eye enucleation procedure

The enucleation procedure involves the removal of the eyeball along with partial resection of the optic nerve (CNII), while preserving the eyelids, palpebral conjunctiva, orbital fat, extraocular muscles, blood vessels, and orbital nerves (Fig. 5). The subsequent stages of the procedure include dissecting the bulbar conjunctiva at the corneal limbus (Fig. 6), securing the rectus muscles with sutures and then severing them (Fig. 7), detaching the oblique muscles, clamping one of the rectus muscles (usually the lateral rectus – Fig. 8, or the medial rectus) to facilitate outward displacement of the eyeball, transecting the optic nerve (CNII – Fig. 9), and finally, removing the eyeball. The operator then performs a macroscopic assessment for signs of extraocular tumor invasion to determine the feasibility of orbital implant placement (Fig. 10). After achieving hemostasis, an orbital implant is placed, and the rectus muscles are sutured to it. If implant placement is not feasible, the rectus muscles are simply sutured. After managing the muscles, the deep tissues, Tenon's capsule, and conjunctiva should be sutured (Fig. 11).

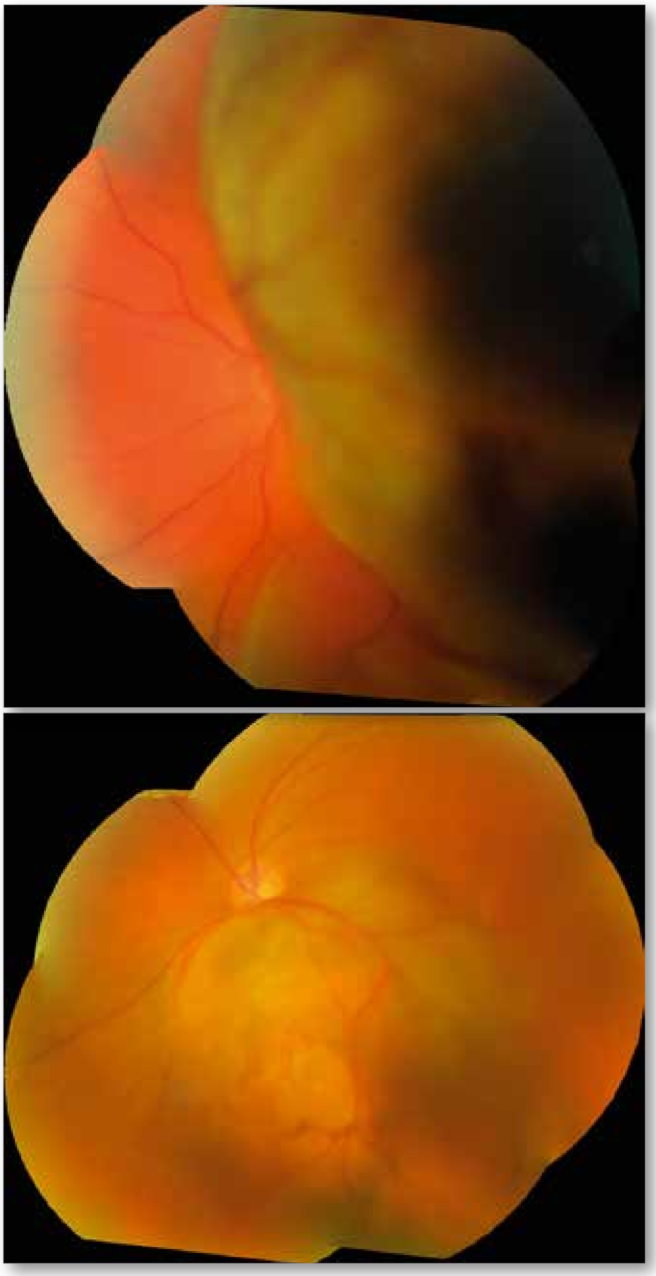

Fig. 2., 3. Fundus photographs showing an advanced intraocular tumor: choroidal melanoma with involvement of the optic disc region.

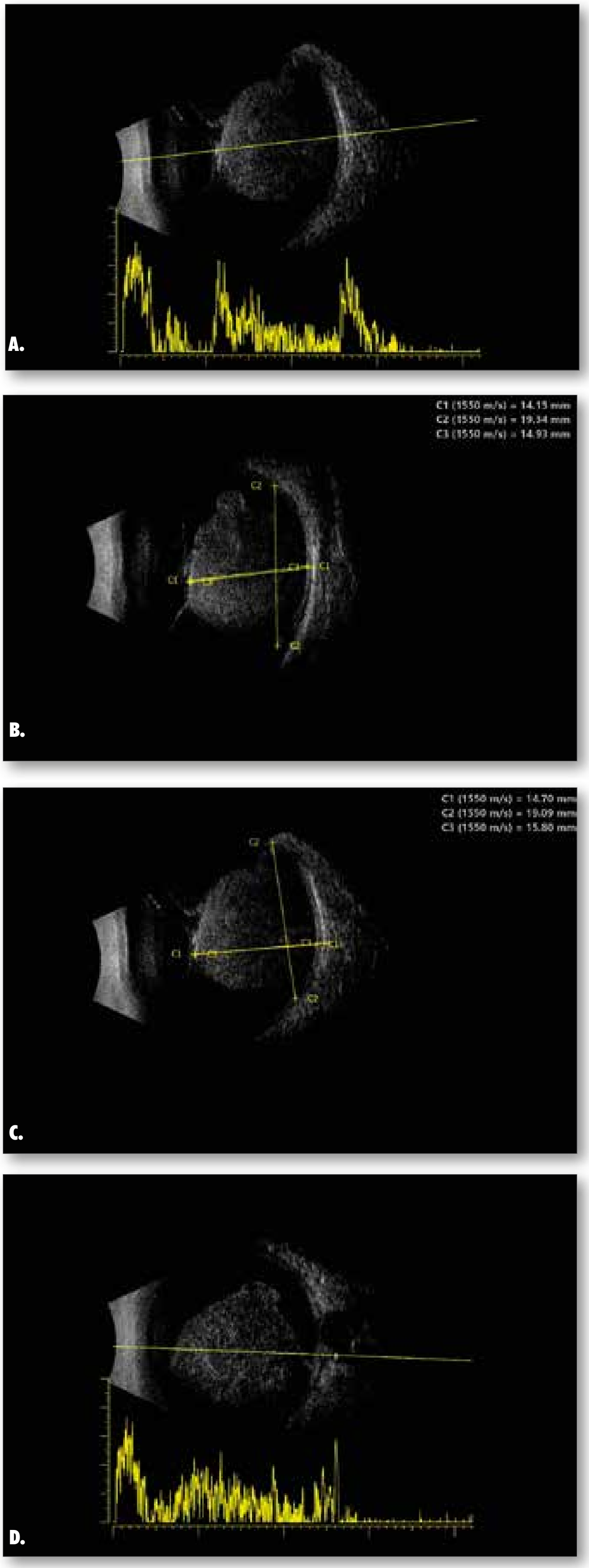

Fig. 4. Ultrasound of the eye showing an advanced intraocular tumor: choroidal melanoma. A – A-scan revealing low echogenicity of the tumor, B – longitudinal B-scan, C – transverse B-scan, D – B-scan of the optic disc region.

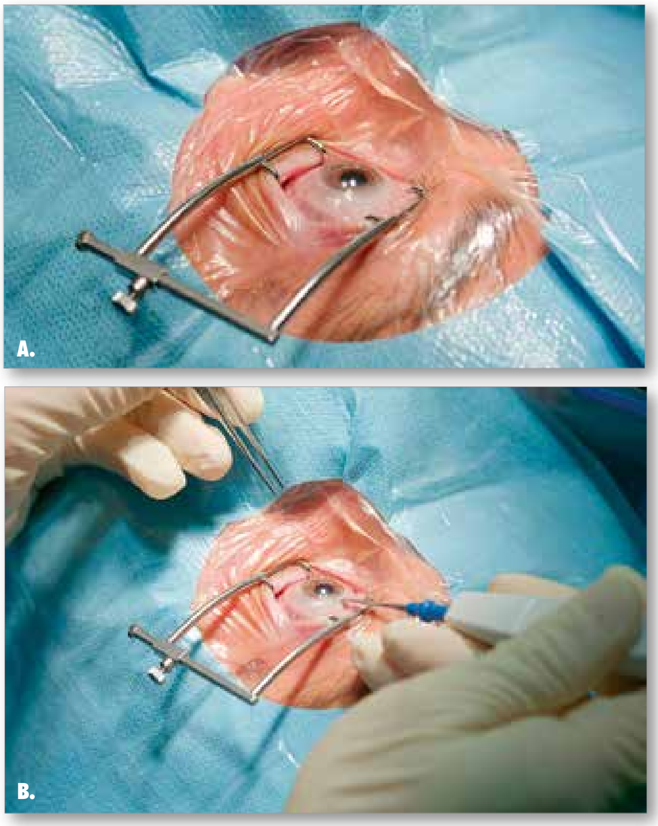

Fig. 5. A – preparation of the operative field before the eye enucleation procedure (surgical drape and eyelid speculum placement), B – diathermic preparation of the bulbar conjunctiva around the corneal limbus.

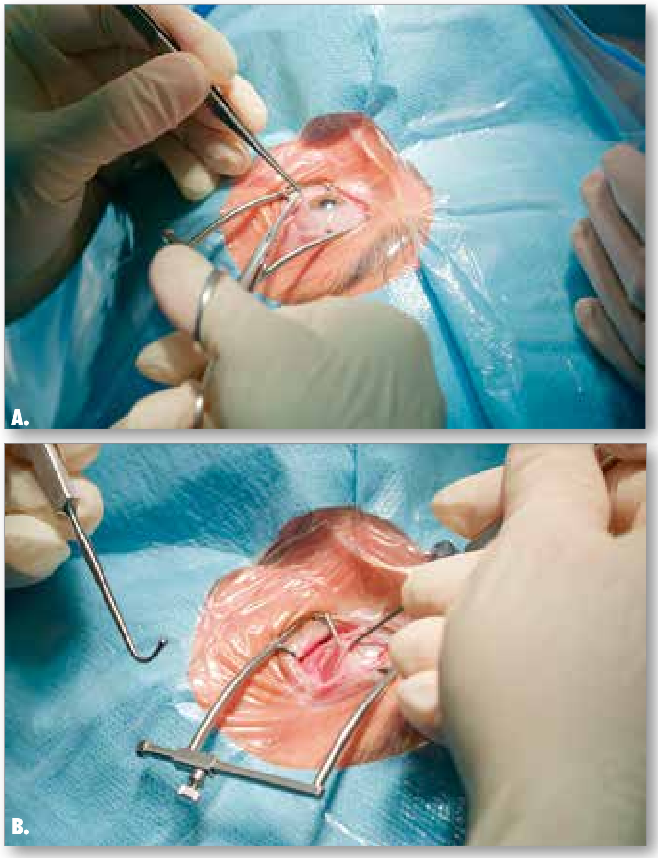

Fig. 6. A – surgical dissection of the bulbar conjunctiva at the corneal limbus, B – identification of the oculomotor muscles.

Post-enucleation complications

In the early period after the enucleation procedure, patients often experience symptoms such as tissue edema and conjunctival and palpebral hyperemia. Hematoma, inflammation, and pain in the periorbital region may also develop. In the later postoperative period, possible complications include tissue inflammation with purulent discharge, dehiscence of the surgical wound requiring re-suturing, granulomas in the orbit causing discomfort when using a prosthesis, and post-enucleation socket syndrome. The most common complications associated with the use of epiprosthesis include giant cell conjunctivitis and allergic reactions to epiprosthesis components. Orbital implant placement also carries potential risks, such as implant exposure, extrusion, or tissue infection associated with the presence of the implant. Independent risk factors for implant exposure include cigarette smoking and treatment with immunomodulatory drugs [12].

Post-enucleation socket syndrome

The first descriptions of anatomical changes in the orbits following eye removal were published in the 1960s [13] and later documented in orbital radiographs. They included inferior and anterior redistribution of the orbital fat tissue, with its subsequent subsidence due to gravity. Additionally, there was inferior displacement of the superior rectus and levator palpebrae superioris muscles, leading to ptosis and deepening of the superior sulcus. The disorders listed above result in eyelid retraction, lower eyelid malpositioning, shallowing of fornices, lagophthalmos, and, consequently, pronounced facial asymmetry [14]. These changes were termed post-enucleation socket syndrome (PESS) by Tyer and Collin in 1982 [15].

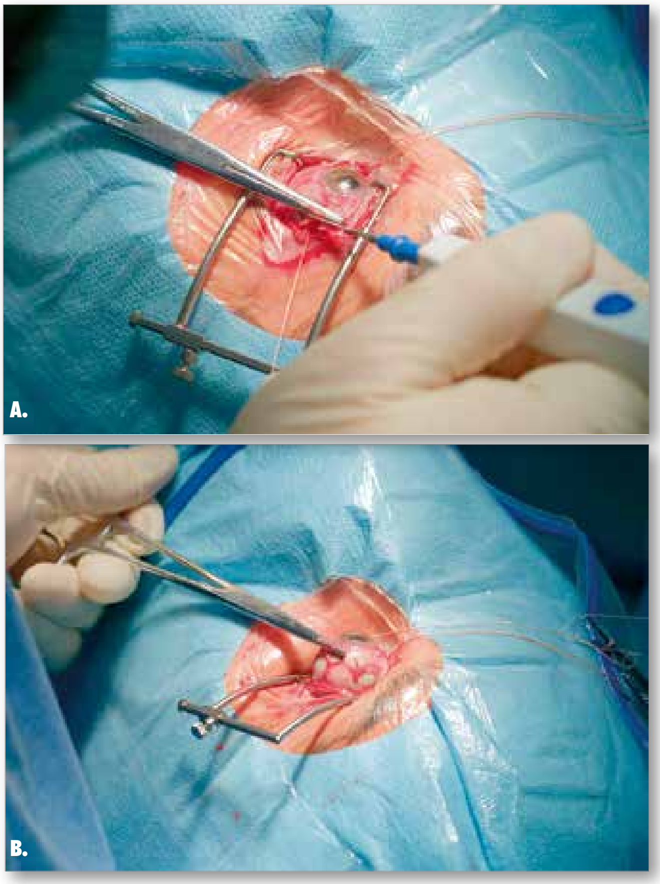

Fig. 8. A – clamping the lateral rectus muscle, B – severing the lateral rectus muscle.

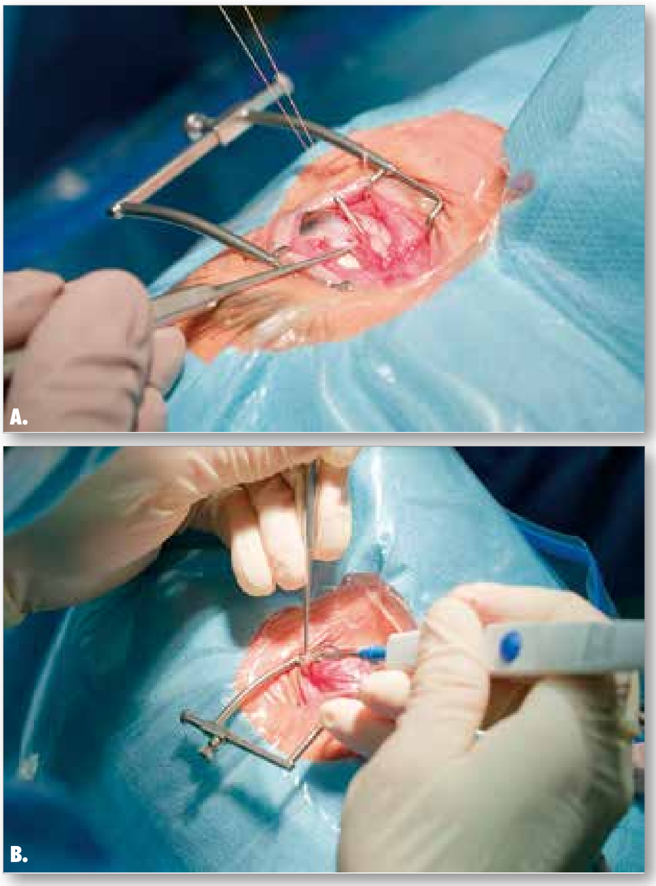

Fig. 7. A – securing the rectus muscles with sutures, B – severing the rectus and oblique muscles.

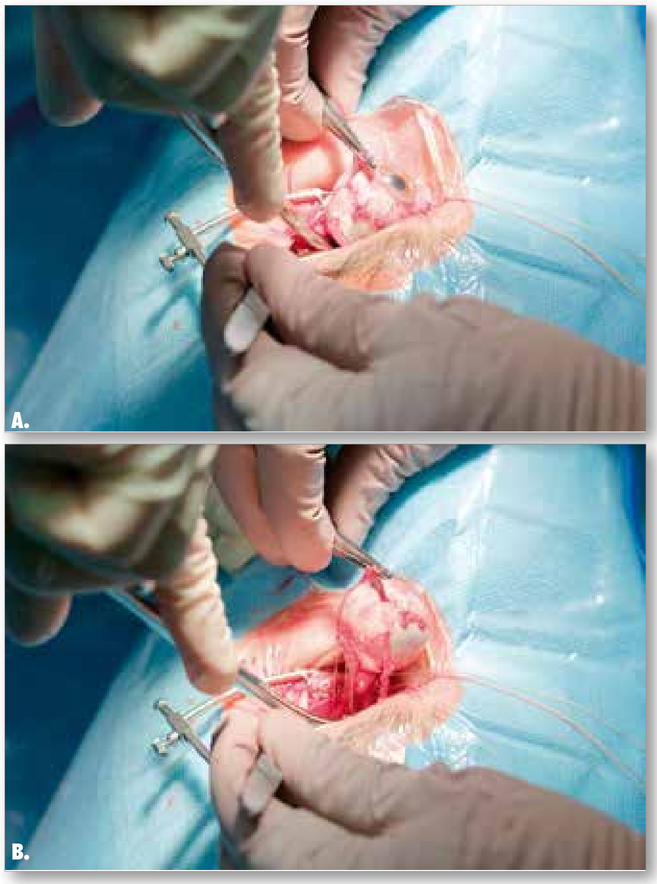

Fig. 9. A – outward displacement of the eyeball and transecting the optic nerve (CNII), B – eyeball removal.

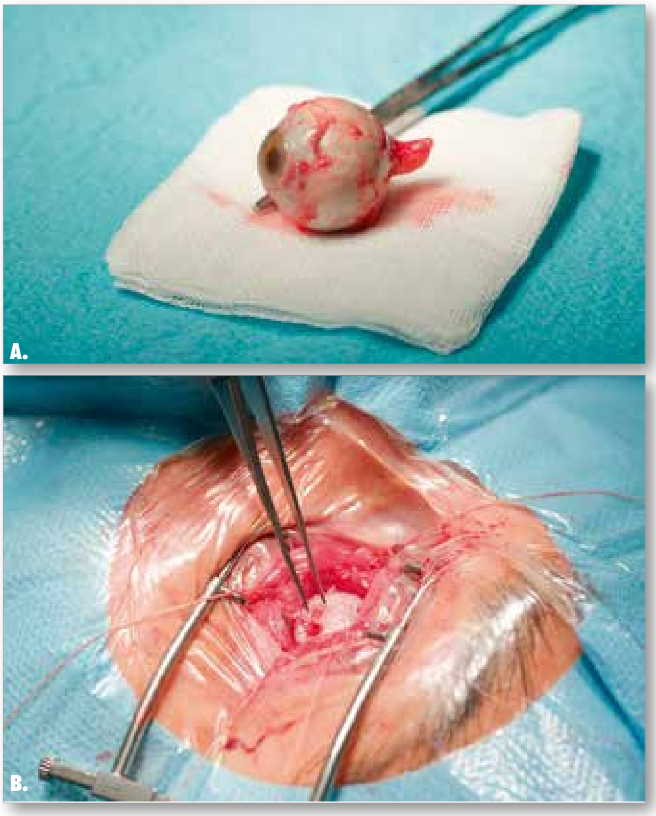

Fig. 10. A – inspection of the eye for macroscopic features of extraocular invasion, B – orbital implant placement.

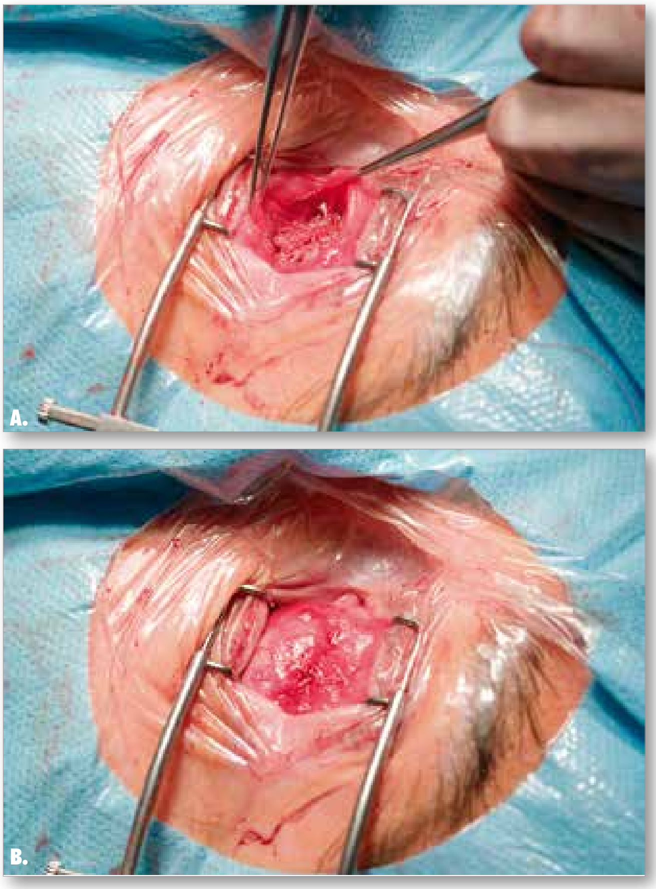

Fig. 11. A – suturing the oculomotor muscles to the orbital implant surface, B – suturing deep tissues, Tenon's capsule, and conjunctiva.

Implants

To maintain optimal cosmetic appearance and ensure improved eyelid mobility and prosthesis placement after enucleation, an orbital implant can be inserted, provided anatomical conditions permit (Fig. 12.) A contraindication to implant placement is the suspicion of extraocular tumor invasion. Therefore, each time, the operator must macroscopically evaluate the removed eye for signs of invasion.

The implant fills the socket, preventing orbital fat redistribution and providing support to the rectus and oblique muscles as well as the upper eyelid, thereby preventing drooping. Additionally, suturing the extraocular muscles to the implant surface markedly improves the mobility of the prosthesis, considerably improving the cosmetic outcome. Orbital implant placement is especially important in children, as it supports the normal, symmetrical development of the craniofacial bones. Implants are available in various sizes (standard 16 mm, 18 mm, 20 mm, and 22 mm), allowing for individual adjustment to each patient. The first orbital implant, a glass ball with gold and silver components, was implanted by Mules in 1885 [16]. Over time, glass and metal implants were replaced with alternative materials due to poor tolerance by orbital tissues. Glass and metal were prone to temperature fluctuations, heating up and cooling down with ambient temperature, and were heavy and rigid [17]. Currently, two types of implants are used. There are implants made of hydroxyapatite or polyethylene, with a porous structure, allowing tissues to grow into their interior and integrate seamlessly with the orbital tissues (Fig. 12A). Implants of the other type are made of silicone and do not integrate with the orbital tissues. There are also hybrid implants, such as the Guthoff implant (Fig. 12B), which consists of an anterior portion made of hydroxyapatite and a posterior portion made of silicone [18]. These implants are lightweight, minimize the risk of extrusion, and are made of materials that help reduce the likelihood of infection in the orbit.

Fig. 12. A – Oculfit orbital implant, B – Guthoff orbital implant.

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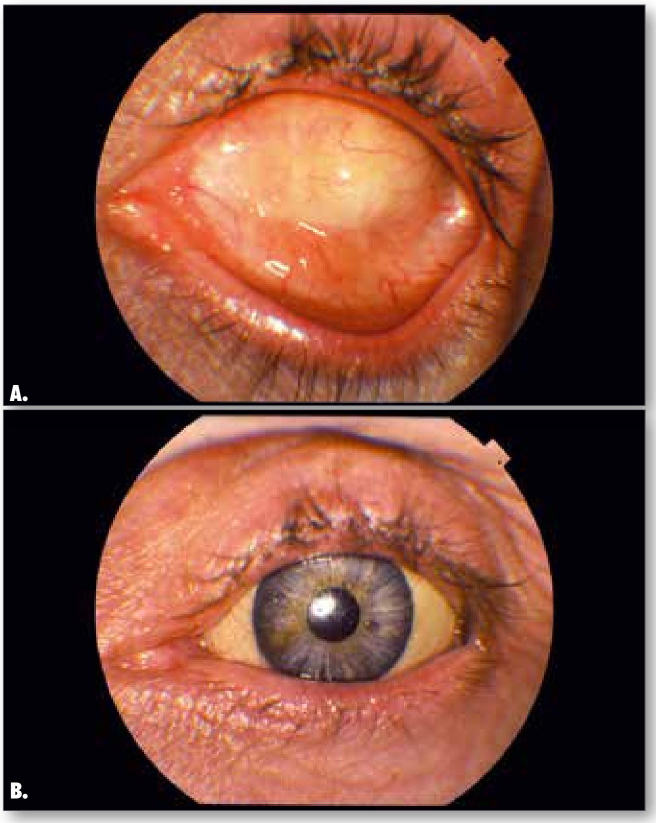

Fig. 13. A – photograph of the orbit after eye enucleation before ocular prosthesis placement, B – photograph after ocular prosthesis placement.

Ocular prostheses

Following the surgical procedure, regardless of whether or not an implant has been placed, the patient should report to a prosthetic clinic to have an ocular prosthesis made. Immediately following the procedure, a temporary conformer is typically placed in the orbit to prevent tissue fusion and separate the fornices, and thereby ensure healthy healing of the conjunctiva. Next, a temporary prosthesis is fitted to help shape the orbit during the healing process. After several months, the final prosthesis is crafted, tailored in both appearance and size to match the other eye (Fig. 13.). Glass, acrylic and 3D-printed prostheses are available. Modern prostheses, made using 3D printing technology, allow for precise reproduction of the iris, pupil, and even the eye's natural reflection, based on a photograph of the healthy eye [19].

Evisceration and exenteration

Alternative methods of eye removal include ocular evisceration and orbital exenteration. Evisceration is the surgical removal of the cornea and the internal contents of the eye including the iris, ciliary body, lens, vitreous humor, choroid, and retina, but with the sclera left behind. An absolute contraindication to evisceration is the suspicion of a malignant intraocular tumor. Therefore, when assessing eligibility for the procedure, the presence of a tumor must be ruled out [20, 21]. Exenteration involves the removal of the entire contents of the eye socket. The procedure is performed in patients with malignant ocular tumors with large extraocular invasion or orbital tumors penetrating into the orbit from adjacent tissues [11]. It is a far more extensive procedure compared to enucleation of the eye.

Conclusions

Although enucleation of the eye contributes to a decrease in the patient's quality of life and negatively affects their mental well-being, it remains the method of choice, particularly in cases of advanced intraocular tumors, after conservative treatment options have been exhausted, or in cases of extensive eyeball injury and painful blind eye. Continuous technological advancements in orbital implants and modern ocular prostheses improve patients' chances of achieving satisfactory cosmetic outcomes.

Disclosure
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