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# Ultrasound observational anatomical guideline for retrobulbar hyaluronidase injection

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**Abstract:** The growing use of injectable cosmetic fillers has been accompanied by an increase in reports of acute vision loss, typically caused by inadvertent intravascular injection and subsequent embolization of the ophthalmic artery, resulting in ocular ischemia. Effective management of this complication remains challenging, as clear clinical guidelines for retrobulbar hyaluronidase injection are lacking. This ultrasound-based observational anatomical guideline provides practical recommendations for retrobulbar administration of hyaluronidase. Real-time ultrasonography allows for direct visualisation of orbital anatomy, enabling the injector to identify the optic nerve sheath complex and surrounding vascular structures. The central retinal artery's entry point into the optic canal is a key anatomical landmark for directing treatment. Based on ultrasound observations, the inferolateral quadrant of the orbit is identified as the safest and most accessible entry site, reducing the risk of damage to extraocular muscles, cranial nerves, and major vessels. The use of ultrasonography enhances both precision and safety, supporting timely and effective management of filler-related ocular complications. Ultrasound observation further confirms that the inferolateral orbital approach offers the most reliable and safe access for retrobulbar hyaluronidase injection. The superior orbital rim and close proximity of the globe restrict needle trajectory from above, increasing the risk of ocular injury. In contrast, the inferior approach provides a wider anatomical corridor, reduces the likelihood of direct contact with the eyeball, and allows safer navigation around critical neurovascular structures. Incorporating real-time ultrasound enhances precision, making the inferior approach the preferred route for managing filler-related ocular complications.

**Key words:** Retrobulbar hyaluronidase, Inferolateral orbital approach, Ophthalmic artery occlusion, Ultrasound-guided injection, Optic nerve sheath complex

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## Introduction

Secondary blindness is a rare but devastating complication of dermal filler injection, most often caused by retrograde arterial embolization, a phenomenon where injected filler inadvertently enters a facial artery, is forced proximally, and then propagates distally into the ophthalmic or retinal circulation [1]. This retrograde embolism can occlude vessels supplying the eye, leading to ophthalmic ischemia—a condition characterized by reduced blood flow that results in abrupt, sometimes irreversible vision loss and permanent injury to ocular structures. Because the periocular and midfacial regions contain arterial branches that communicate with the ophthalmic system, this complication poses a significant

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risk in delicate facial areas, underscoring the critical importance of meticulous technique, sound anatomical planning, and robust risk-mitigation protocols to minimize this danger, optimize patient safety, and safeguard outcomes.

High-frequency ultrasound is a valuable, non-invasive imaging modality used to evaluate the anatomical structures surrounding the eyeball within the orbit. By employing specialized techniques, such as the transocular approach (scanning through the globe) and the paraocular approach (scanning with the beam avoiding the globe), clinicians can obtain detailed real-time images of the extraocular muscles, the optic nerve, orbital fat, and lacrimal gland. This allows for the assessment of muscle thickness in conditions like thyroid eye disease, the identification of space-occupying lesions such as tumors or inflammatory pseudotumors, and the measurement of the optic nerve sheath diameter. As a readily available, rapid, and safe tool that does not involve ionizing radiation, orbital ultrasonography serves as an excellent first-line examination for diagnosing and monitoring a wide range of orbital pathologies (Fig. 1).

Furthermore, the diagnostic precision of orbital ultrasound is increasingly being leveraged to enhance the safety and efficacy of aesthetic procedures in the periorbital region. By providing a real-time visualization of the underlying anatomy, ultrasound can guide injectors during treatments such as filler injections (sunken eyelid) and neurotoxin (eyelid toxin) administration [2, 3]. It allows for the precise mapping of blood vessels, nerves, and fat compartments, helping to avoid accidental intravascular injection—a serious complication that can lead to blindness or tissue necrosis—and ensuring neurotoxins are placed accurately for optimal results.

When considering the application of hyaluronidase for dissolving hyaluronic acid (HA) fillers, it is crucial to be prepared for vascular complications from filler injections, where the rapid dissolution of the filler can be life-saving. However, there is no established treatment method for cases where the filler enters the ophthalmic artery and damages the optic nerve. Therefore, the best current approach is to inject as much hyaluronidase as possible at short intervals retrobulbarly with ultrasound guided injection, which can be justified with scientific evidence.

Animal experiments to observe the duration of action of hyaluronidase after injection show that researchers injected 0.2 ml of HA filler into a site on a mouse and administered 600 IU of hyaluronidase to dissolve the filler. The area was then re-injected with HA filler at various intervals—30 minutes, 1 hour, 3 hours, 6 hours, 12 hours, 24 hours, 2 days, 4 days, 7 days, and 14 days after the hyaluronidase injection—to check if the previously injected hyaluronidase affected the re-injected filler through tissue examination [4].

This research suggests that the guidelines for using hyaluronidase differ depending on whether it is used to dissolve HA within blood vessels or in other tissues outside of blood vessels. When using hyaluronidase for side effects due to HA filler injections inside blood vessels, the enzyme cannot be directly injected into the filler particles within the vessels, so

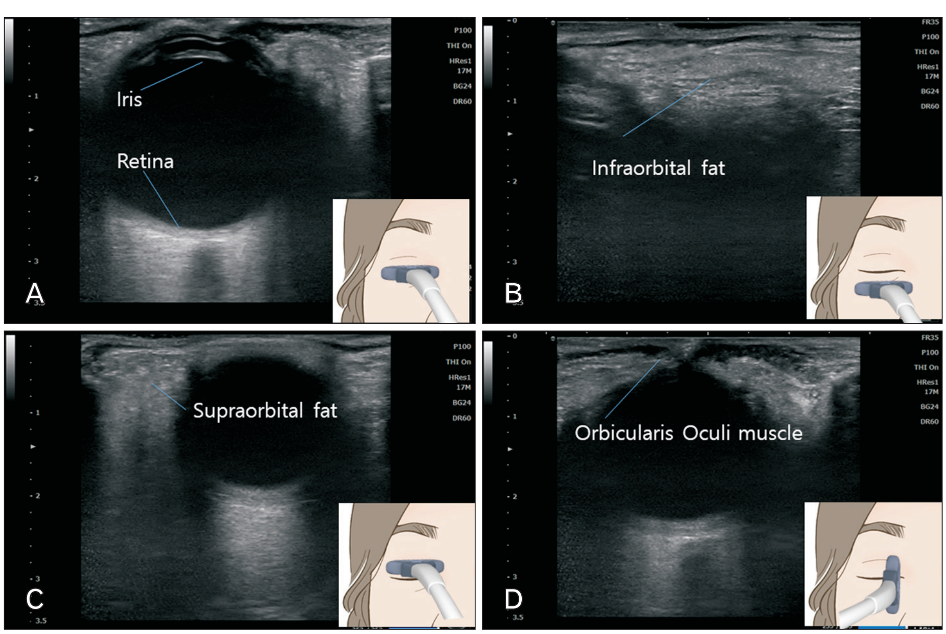


**Fig. 1.** High-resolution ultrasound of the orbital rim in B-mode. (A) Transverse (horizontal) probe placement over the upper eyelid demonstrating the superior orbital rim. (B) Transverse probe placement below the lower eyelid visualizing the infraorbital fat compartment. (C) Transverse probe placement above the upper eyelid outlining preseptal and pretarsal layers. (D) Longitudinal (vertical) probe placement at the medial canthus depicting medial periocular soft-tissue planes.

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it must be injected outside the vessels to allow trans-arterial penetration [5-7]. Since hyaluronidase that has penetrated into the bloodstream disappears quickly, frequent administration at short intervals is necessary to maximize the likelihood of dissolving HA filler particles within the vessels [4].

Vascular occlusion caused by dermal fillers is a devastating complication that can lead to secondary blindness. Critically, no universally accepted first-line protocol currently exists to rapidly reverse the ischemic damage and restore vision following such an event. This article addresses this urgent need by providing guided instruction on the ultrasound-assisted injection of retrobulbar hyaluronidase, outlining a safe anatomical approach to mitigate vision loss [8-10].

## Review

### *Ultrasonography observation*

This study was conducted in compliance with the Declaration of Helsinki.

The primary proposed mechanism underlying ophthalmic injury following the injection of cosmetic filler involves retrograde embolism through an artery near the injection site, most commonly the supraorbital, supratrochlear, or dorsal nasal arteries. When the filler material is injected into these distal arteries, the higher pressure of the injection compared to arterial pressure causes the filler to travel proximally towards the ophthalmic artery (Fig. 2) [11, 12].

Ischemia occurs due to both the initial obstruction of blood flow by the embolus itself and the subsequent activation of local inflammation, platelet aggregation, and the coagulation cascade. In some instances, larger emboli and clots may fragment into smaller micro-emboli, lodging in distal branches of the ophthalmic artery and resulting in multifocal vessel occlusion [12, 13].

The ischemic outcomes resulting from embolism caused by fillers can vary depending on the specific anatomical site affected. If the filler embolus lodges in the central retinal and posterior ciliary arteries, occlusion leads to non-perfusion of the retina, manifesting as vision loss that may become permanent upon irreversible retinal cell death. Blockage of the posterior ciliary arteries and anterior ciliary arteries can impede blood flow to the iris and ciliary body, leading to ischemia in the anterior segment as well [14].

The nature of the cosmetic filler administered also plays a role in determining the extent of embolism and the consequent ischemic outcomes. Previously reported visual complications have been associated with various fillers, including HA, poly-L-lactic acid, calcium hydroxyapatite, autologous fat, and platelet-rich plasma [15, 16]. Autologous fat, due to its relatively larger particle size, has been shown to be more prone to inducing proximal arterial obstruction. Conversely, it is thought that HA tends to block more distant branches of the ophthalmic artery due to its smaller particle size. Platelet-rich plasma can lead to more severe ischemia, as it is more pro-thrombotic compared to other fillers, given its composition—a highly concentrated combination of a patient's own

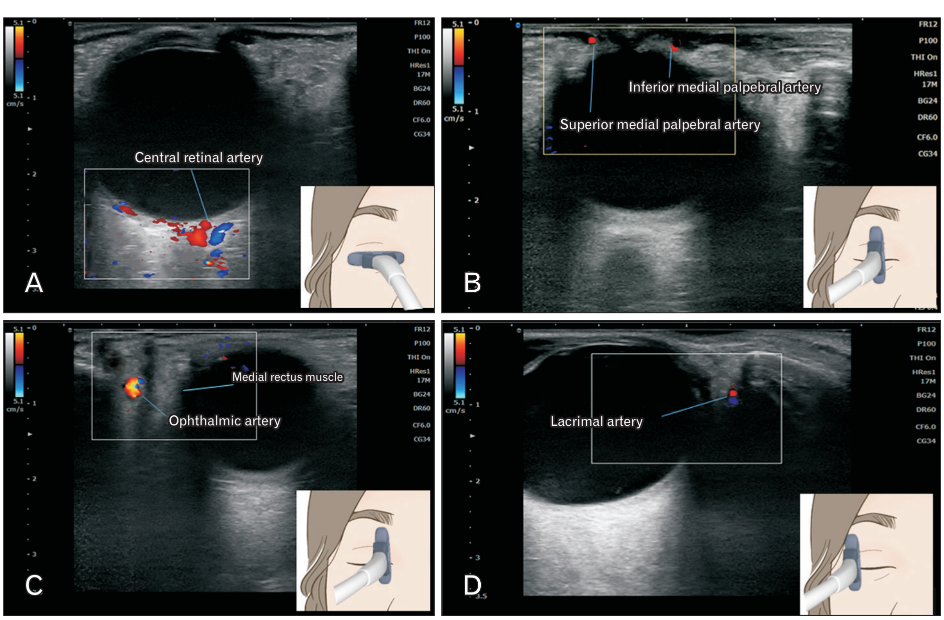


Fig. 2. Periocular vascular mapping with Doppler ultrasonography. (A) Transverse probe placement over the upper eyelid demonstrating flow consistent with the central retinal artery. (B) Longitudinal probe placement along the mid-pupillary line demonstrating the superior and inferior medial palpebral arteries. (C) Longitudinal probe placement at the medial canthus showing the ophthalmic artery prior to division into the supratrochlear, supraorbital, and dorsal nasal branches. (D) Longitudinal probe placement at the lateral canthus demonstrating the lacrimal artery.

platelets and associated growth factors, ranging from 2.5 to 8 times higher than normal serum concentration [17].

From an anatomical perspective, an inferior approach to the orbital region is considered ideal because the eyeball itself is situated directly above the infraorbital fat pad. This inferior pad is notably thicker than the supraorbital fat pad located above the eye, providing a more substantial and protective buffer zone for instrumentation. Furthermore, the superior part of the orbital rim offers insufficient space for a safe approach, as the anatomical confines are tighter and riskier for navigation. Therefore, accessing the area from below leverages the more forgiving anatomy to enhance safety and efficacy (Fig. 1).

The management of ophthalmic filler embolism is centered on the urgent objective of reestablishing blood flow and oxygen supply to ischemic tissues, utilizing strategies such as embolus displacement, hyperbaric oxygen therapy, and thrombolytic agents to dissolve obstructive material. It is critical to acknowledge that the evidence for these interventions is not derived from randomized trials, which is understandable given the rarity of these events, but their application is justified by the critical need for rapid reperfusion, a principle well-established in retinal and stroke medicine. Notably, HA is the only filler with a specific reversal agent, hyaluronidase, which enzymatically breaks down the substance. Studies have explored its delivery via subcutaneous, retrobulbar, or intra-arterial routes, with subcutaneous administration allowing for tissue permeation and diffusion across the arterial wall; however, a systematic review of cases shows that outcomes for vision recovery, even with prompt treatment, remain inconsistent [18, 19].

### *Guideline for retrobulbar hyaluronidase*

During a retrobulbar hyaluronidase injection, the objective is to target the area where the central retinal artery enters the optic canal (Fig. 2). Dividing the orbital rim into quadrants results in inferior lateral, inferior medial, superior lateral, and superior medial divisions. Typically, approaching from the superior quadrant is not recommended, as the central retinal artery usually enters below the optic canal. Methods for approaching from the inferior medial and inferior lateral directions have been confirmed through anatomical examination.

Upon anatomical examination, it was observed that by scraping the orbital floor after advancing under the orbital rim below the medial canthus, a method of entry was established. The distance to the central retinal artery was found to be short. However, entering in this way involves the needle scraping the floor, and afterwards, it needs to be lifted slightly to target the optic nerve. During this process, there is a higher probability of puncturing the eyeball, potentially causing damage to the inferior rectus muscle. It may also be challenging to control the angle of the syringe, which could risk hitting the medial rectus (Fig. 2).

The inferior periocular compartment (infraorbital region) contains a more capacious fat volume than the superior (supraorbital) compartment and, relative to the upper orbit, typically presents fewer superficial vascular structures. In contrast, the superior medial orbit is traversed by branches of the ophthalmic artery, while the superolateral region contains the lacrimal gland and its vascular supply. These differences influence access routes for retrobulbar procedures by affecting working space and the likelihood of encountering vessels.

### *Rationale for the inferolateral approach*

Targeting the midpoint of the inferolateral orbital quadrant allows entry that generally minimizes contact with extraocular muscles, neurovascular bundles, and major arterial trunks. The ophthalmic artery—a branch of the internal carotid artery—enters the orbit through the optic canal alongside the optic nerve, courses medial to the nerve for much of its path, and gives off branches that predominantly traverse the medial and superior orbit. With the exception of laterally directed short posterior ciliary arteries, the inferolateral quadrant contains no additional muscle bellies between the lateral and inferior rectus and is comparatively sparse in critical vascular structures, making it a preferable and safer corridor for retrobulbar needle placement than other quadrants. A demonstration of the ultrasound-guided inferolateral retrobulbar injection is provided in Fig. 3.

## Discussion

Furthermore, the challenges of enzymatic penetration and vascular access underscore the critical importance of precise anatomical delivery. The inability of hyaluronidase to reliably reach the embolized vessel lumen may be compounded by suboptimal injection placement. This highlights the potential value of the ultrasound-guided inferolateral approach outlined in this protocol. By enabling real-time visualization to position the needle tip in close proximity to the optic

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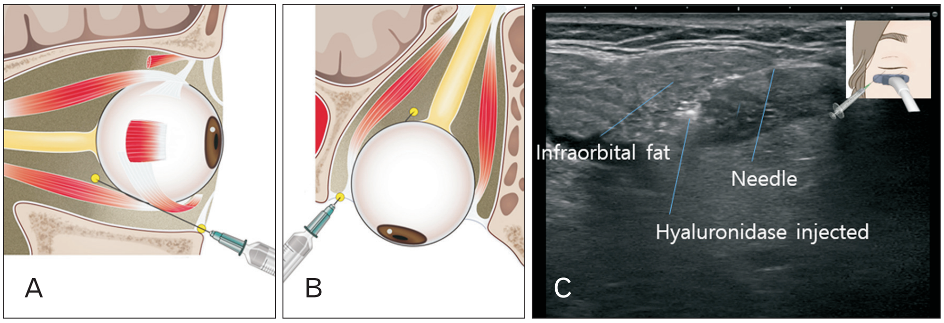


**Fig. 3.** Ultrasound-guided access to the retrobulbar space at the lateral orbital rim. (A) Sagittal view of the lateral orbital rim. (B) Transverse view of the same region. (C) Ultrasound-guided needle approach from the inferolateral quadrant; a 35-mm needle is depicted as suitable to reach the retrobulbar space. Injection of hyaluronidase is shown with reflux/backflow visible along the needle tract.

nerve sheath and the origin of the central retinal artery, this method aims to maximize the local concentration of hyaluronidase at the most critical site of occlusion. While it may not overcome all biological barriers, such precise anatomical targeting could enhance the probability of enzyme diffusion into the affected arterial branches, thereby addressing a key factor in recanalization failure.

Retrobulbar injections ranging from 1,500 to 3,000 IU of hyaluronidase, administered once or twice, may not meet the criteria for a prompt and effective rescue treatment, especially in achieving retinal artery recanalization within a four-hour timeframe [20-23]. The absence of recanalization failure does not seem attributable to an inadequate hyaluronidase dose, given that the enzyme's half-life in the retrobulbar space is estimated to be sufficient for the intended duration [19, 24].

Even with an ample amount of active hyaluronidase present in the retrobulbar region, recanalization failure can still happen due to inadequate penetration of hyaluronidase into the ocular branches of the ophthalmic artery, which may have lower permeability compared to the facial artery in cadavers. Moreover, blood stagnation in blocked ophthalmic artery branches and the existence of hyaluronidase inhibitors in human blood may hinder the enzyme's ability to reach distal HA emboli after it breaches the arterial wall and enters the ophthalmic circulation.

The study of Chesnut [25] presented a case of retrobulbar hyaluronidase injection from secondary blindness recovery. A 39-year-old woman experienced complete visual loss in her right eye after receiving a HA filler injection in the midface. Immediate discontinuation of the injection and implementation of a protocol for intravascular filler complications were followed by multiple hyaluronidase injections, including retrobulbar injections, which led to significant visual improvement. The patient was subsequently transferred to the emergency department for further evaluation, which confirmed normal results with full restoration of vision [22, 24-26].

A study by Lee et al. [26] evaluated the effectiveness of retrobulbar hyaluronidase injection in treating iatrogenic blindness caused by HA filler injection in rabbits. Rabbits were used to simulate the vascular occlusion model, and retrobulbar hyaluronidase was administered at different time points after occlusion. The results showed improved retinal reperfusion in three out of four eyes treated with retrobulbar hyaluronidase, as confirmed by fundus photography and electroretinography. The study suggested that retrobulbar hyaluronidase may be an effective treatment option for HA-induced retinal occlusion. It also indicated the importance of hyaluronidase concentration and injection time for faster recovery, but further studies are needed. The findings provide evidence for considering retrobulbar hyaluronidase as a potential treatment for iatrogenic blindness but highlight the need for additional research.

Despite its advocacy in the literature, the efficacy of retrobulbar hyaluronidase for HA filler-induced vision loss remains inconclusive. Concerns regarding ocular perforation risk with repeated injections have prompted the exploration of alternative methods, such as direct intra-arterial infusion via selective angiography. Furthermore, while a combination of hyaluronidase and fibrinolytic drugs may be theoretically beneficial to address secondary thrombosis, clinical evidence for this approach is inconsistent. Any alteration in the dose or frequency of retrobulbar hyaluronidase injections carries unforeseeable risks to delicate orbital structures. Consequently, optimal delivery methods, dosing, and potential adjuvant therapies require urgent further investigation through rigorous clinical studies [20, 23].

The protocol outlined in this paper provides a structured, ultrasound-guided framework for performing retrobulbar hyaluronidase injection, a critical intervention in emergencies where immediate ophthalmological care is unavailable.

By detailing each step—from anesthesia to precise needle navigation—this guideline aims to standardize the procedure, mitigate risks, and empower clinicians to act promptly. However, it is crucial to acknowledge that this technically challenging intervention carries inherent risks, and its execution should be approached with caution. The urgent need for such a protocol is underscored by the rising incidence of vision loss from filler embolization and the current absence of established clinical guidelines for managing this devastating complication.

## Conclusion

This paper establishes a critical, ultrasound-guided anatomical framework for the emergency management of filler-induced central retinal artery occlusion—a devastating complication for which no standardized treatment protocol currently exists. The findings robustly demonstrate that real-time ultrasonography is indispensable for this procedure, enabling precise visualization of the optic nerve sheath complex and surrounding vasculature to ensure accurate and safe needle placement. The systematic anatomical evaluation confirms the inferolateral orbital quadrant as the optimal and safest access route, providing a wider anatomical corridor that minimizes the risk of injury to the globe, extraocular muscles, and major neurovascular structures compared to other approaches.

While the efficacy of retrobulbar hyaluronidase remains an area for further clinical investigation, this guideline provides a vital, evidence-based strategy to maximize the potential for restoring perfusion and vision during a sight-threatening emergency. By integrating ultrasound observation into a structured procedural protocol, clinicians can enhance the precision and safety of intervention. This work underscores the urgent need for standardized guidelines in aesthetic medicine and positions ultrasound-guided retrobulbar injection as a foundational step toward improving patient outcomes in the face of this rare but catastrophic complication.

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Conceptualization: KHY. Data acquisition: KHY. Data analysis or interpretation: KHY. Visualization: SBK. Drafting of the manuscript: KHY, SBK. Critical revision of the manuscript: HJK, JW, HH, JT. Supervision: HJK. Approval of the final version of the manuscript: all authors.

## Conflicts of Interest

Hee-Jin Kim has been a member of the journal's editorial board, but had no role in the decision to publish this article. No potential conflict of interest relevant to this article was reported.

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