Ischemic complications of dermal fillers

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How to cite this article: Mehta P, Kaplan JB, Zhang-Nunes S. Ischemic complications of dermal fillers. Plast Aesthet Res 2022;9:57. https://dx.doi.org/10.20517/2347-9264.2022.19

Received: 1 Mar 2022 First Decision: 23 May 2022 Revised: 26 Jul 2022 Accepted: 15 Aug 2022 Published: 8 Oct 2022

Academic Editors: Xiaoming Sun, Rona Silkiss Copy Editor: Peng-Juan Wen Production Editor: Peng-Juan Wen

Abstract

Dermal fillers have become increasingly popular as a cosmetic treatment for facial rejuvenation. Although these injections are generally considered to be safe, as the number of injections has increased, so has the rate of complications. Ischemic complications of fillers include vision loss, ophthalmoplegia, skin necrosis, and cerebral infarction. Knowing the anatomy well is critical to optimally prevent and manage these serious complications. Prevention includes knowledge of the vascular anatomy of the facial area, as well as certain injection techniques such as aspiration, use of a smaller needle, and adoption of a larger cannula. The use of ultrasound has been a recent innovation in preventing and treating filler complications as well. The reversibility of fillers should also be considered when choosing a filler. Some hyaluronic acid (HA) fillers, including the newer ones on the market, are difficult to reverse and non-HA fillers and fat are irreversible. This review aims to discuss facial anatomy, the various ischemic filler complications, the prevention and management of these complications, and the relatively recent use of imaging as an adjunct.

Keywords: Filler complications, soft tissue necrosis, blindness, ophthalmoplegia, cerebral infarction, ischemic complications

INTRODUCTION

Dermal fillers are used to treat changes commonly seen with aging in the face. Since bovine collagen became
FDA approved for cosmetic use in 1981, soft tissue fillers have consistently increased in popularity, with the number of procedures increasing by 50% from 2015 to 2019\cite{1,2}. With this increase in filler injections, there has been a significant increase in the number of products available on the market, with each filler having its own intrinsic properties\cite{3}. While filler injections are generally considered to be a safe procedure, there are still many complications that have been documented and studied in the literature.

The most devastating filler complications are ischemic, which include irreversible vision loss, ophthalmoplegia, and skin necrosis, among other serious complications\cite{4-6}. The incidence of vascular occlusion appears to be up to 3 in 1000 injections\cite{7}, and a total of at least 190 cases of blindness have been reported in literature as reviewed by Chatrath et al. as of 2019\cite{8}. As of January 2022, we have found at least 211 cases, with Table 1 noting some of the more recent cases. Some cases, like a report of bilateral blindness after nasal augmentation with calcium hydroxylapatite\cite{9}, were found to have been missed in previous reviews. Many more cases of blindness have likely gone unreported, so the true incidence is unknown. While the reported cases appear to be a small percentage of the total injections, the rate of this complication appears to be increasing\cite{10,11}. Although the incidence of these complications is low, their severity warrants further studies into how to improve management and prevent these complications from occurring.

This literature review aims to discuss the various ischemic complications seen after injection and their management. Articles until January 2022 were included with a specific focus on recently published literature. This review focuses on the anatomy of the face and ischemic complications seen after filler injections, discusses the management of these complications, reviews prevention techniques, and examines the relatively recent use of imaging as an adjunct.

**ANATOMY**

The anatomy of the face is complex and has a considerable amount of variation. During a glabellar injection, the supratrochlear and supraorbital arteries are at the highest risk\cite{12}. Both of these arteries supply the superomedial aspects of the forehead and provide retrograde flow to the ophthalmic artery [Figure 1]\cite{12,13}. Thus, deep injection is not recommended in this area. However, if the patient understands the risk of injecting in this area and wishes to proceed with this option, an injection with a low G’ filler intradermally with the needle still visible may be considered\cite{12}. For forehead augmentation, an intermediate G’ filler may also be considered, although the forehead is also a more high-risk area for blindness and ischemia\cite{12}.

The facial artery continues midface as the angular artery immediately subjacent to the nasolabial fold [Figure 1]\cite{15}. Afterwards, the artery continues towards the nose, where anastomotic vessels join the internal and external carotid territories\cite{15}. In a study that evaluated the facial and angular artery with doppler ultrasound, the authors emphasize that the anatomic variability of the facial artery and angular artery makes it difficult to truly avoid the vasculature in the nasolabial fold area\cite{16}. Given the popularity of treating the nasolabial area, the facial and angular artery in this area are often affected\cite{15}. Therefore, injecting fillers with sharp, fine needles, especially in the region deep to the orbicularis oris or zygomaticus muscle in the nasolabial fold region, may be considered high risk\cite{15}. A recent study found that the most frequent location with a positive blood aspiration was the subperiosteal plane of the pyriform fossa, closely followed by the deep midfacial fat compartments\cite{17}. Additionally, in the nasolabial fold and nasal dorsum areas, the facial, angular, and lateral nasal arteries anastomose with the dorsal nasal artery, a branch of the ophthalmic artery\cite{13}. These arterial anastomoses are a frequent cause of ophthalmic blindness\cite{13}. For deeper volumization in this area, a higher G’ filler with a cannula is recommended\cite{12}. 


Table 1. Recent case reports of vision loss following filler injections

| Author | Demographics | Material | Site of injection | Eye | Symptoms | Time to treatment onset | Treatment | Outcome |
|--------|--------------|----------|------------------|-----|----------|------------------------|-----------|---------|
| Davidova et al. (2022)\(^{117}\) | 43-year-old female | Hyaluronic acid | Glabella | Left | Left sided vision loss (NLP), Ptosis, Ophthalmoplegia, Swelling on left forehead and upper lid, Left RAPD | 1 h | Ocular massage, Aspirin, Tinzaparin sodium, Methylprednisolone, Antiseptic compresses, Three hyaluronidase injections in the injection area | Vision remained at NLP at 6 weeks |
| Wu et al. (2021)\(^{55}\) | 49-year-old female | Poly-L-Lactic acid | Temporal region | Right | Right sided central visual defect, Ocular pain, Dizziness, Nausea, Photopsia, Right RAPD | 1 h | Ocular massage, Topical brimonidine, Hyperbaric oxygen therapy twice daily for 5 days, Dual-antiplatelet treatment (from prior) | Vision remained at NLP in the right eye at 1 year |
| Danks et al. (2021)\(^{118}\) | 38-year-old female | Hyaluronic acid | Right side of nose | Right | Right sided visual loss (NLP), Right sided headache, Skin pallor, Right RAPD | 1) Immediately post injection, 2) 4 h after injection | 1) 675 IU hyaluronidase to the filler site, 2) 3 injections of 1500 IU hyaluronidase; one peribulbar and 2 extraorbital, Unknown dose aspirin | Vision improved from NLP to CF at 4 h and 20/20 at 1 month follow up Resolution of right RAPD |
| Nguyen et al. (2021)\(^{119}\) | 27-year-old female | Hyaluronic acid | Nasal dorsum | Right | 1) Right sided vision loss (NLP), Right sided ptosis, Right sided ophthalmoplegia, Frontal and nasal ecchymosis, Headache, Pain, 2) 13 h later, patient developed a headache with ocular pain, Right sided vision loss worsened from CF at 1 meter to NLP | 4 h | 1) 1500 IU hyaluronidase to frontal and nasal areas; 750 IU hyaluronidase retrobulbar; 1500 IU intra-arterial hyaluronidase into the right ophthalmic artery, 2) Alteplase 8 mg, 1500 IU hyaluronidase, Heparin 5000 IU/day, Aspirin, Nitroglycerin patches, Corticosteroid, Antibiotic therapy | 1) Vision improved from NLP to CF at 1 meter, 2) Visual acuity improved from NLP to 20/50 at 3 months, Skin ecchymosis fully recovered at 3 months, Ophthalmoplegia and eyelid ptosis recovered at 3 months |
| Lee et al. (2021)\(^{102}\) | 39-year-old female | Hyaluronic acid | Glabella | Left | Left sided vision loss (NLP), Left sided ocular pain, Drowsy mental status, Motor weakness in right upper and lower limbs, Dysarthria, hypesthesia, right | Unknown | Methylprednisolone 1 g for 5 days | Vision remained at NLP at 6 weeks Ophthalmoplegia and ptosis partially recovered at 6 weeks |
| Authors          | Year | Age | Gender | Location | Symptomology                                                                 | Treatment                                                                 | Outcome |
|-----------------|------|-----|--------|----------|------------------------------------------------------------------------------|---------------------------------------------------------------------------|---------|
| Moore et al.    | 2021 | 59  | Female | Right    | Right sided vision loss (NLP) Left sided ophthalmoplegia and ptosis          | Right sided vision loss (NLP) Unknown volume hyaluronidase at unknown location Ocular massage 250 IU of hyaluronidase in glabella and right forehead Warm compresses Topical Nitroglycerin 2% ointment 650 mg aspirin | Vision remained at NLP at 1 week follow up Right forehead had a 1 × 2 cm eschar at 1 week follow up |
| Eldweik         | 2021 | 32  | Female | Nasal     | Left sided vision loss (NLP) Swelling and tenderness around left eye Bluish discoloration of facial skin Dull, aching pain Limited EOM Ophthalmoplegia Left blepharoptosis | 1) Immediately post injection 2) Less than 1 h 1) 40 IU hyaluronidase at site of injection 2) 300 IU peribulbar injection of hyaluronidase Methylprednisolone 1 g for 5 days Aspirin Antibiotic coverage Antibiotic cream Iopidine 1% 10 min ocular massage 1500 IU hyaluronidase sub-Tenon’s injection Anterior chamber paracentesis | Vision remained at NLP at 8 weeks Skin necrosis resolved with scarring at 8 weeks Left EOM and blepharoptosis improved at 8 weeks |
| Jolly et al.    | 2021 | 29  | Female | Nasal     | Left sided vision loss (LP) only in upper temporal quadrant Left RAPD Left sided ptosis Left sided ophthalmoplegia Reduced EOM Left periorbital ecchymosis Left subconjunctival hemorrhage | 1) Immediately post injection 2) Unknown 1) Unknown dose of hyaluronidase in treated area 2) 300 mL mannitol intravenously High-flow O₂ 3 cycles of ocular massage for 10 s every 4 h 0.15% topical brimonidine 3x daily 250 mg oral acetazolamide 4x daily Aspirin daily 250 mg intravenous methylprednisolone 46h HBOT 2.5 ATA for 90 min daily for 3 weeks | Vision worsened from LP to NLP at 3 months Improvement in EOM and ptosis at 3 months |
| Hung et al.     | 2021 | 31  | Female | Nasal     | Right sided vision loss (NLP) Severe sharp pain in retro-orbital area | 1) Immediately after injection 2) Unknown 1) Unknown dose of hyaluronidase in treated area 2) 300 mL mannitol intravenously High-flow O₂ 3 cycles of ocular massage for 10 s every 4 h 0.15% topical brimonidine 3x daily 250 mg oral acetazolamide 4x daily Aspirin daily 250 mg intravenous methylprednisolone 46h HBOT 2.5 ATA for 90 min daily for 3 weeks | Vision remained at NLP at 5 months Superficial skin necrosis development at 2-week over nasion and rhinion which later resolved at 4-month follow up |
| Zhang et al.    | 2021 | 61  | Female | Radix     | Right sided severe blurred vision Right sided ptosis  | Glucocorticoids Mannitol Right anterior chamber puncture | Vision remained at NLP at 8 months |
| Authors | Case Details | Procedure | Outcomes |
|---------|--------------|-----------|----------|
| Zhang et al. (2021)[123] | 31-year-old female | Hyaluronic acid | Right sided ophthalmoplegia, Swelling in right eye, Pain in right eye, Nausea, Vomiting, Chest tightness | Right sided vision loss, Ophthalmoplegia, Headache, Eye pain, Nausea, Vomiting, Sluggishness |
|  |  | Glabella and Forehead | | 30 min | Unknown hyaluronidase dose at the site of injection, IV infusion of mannitol, Endovascular hyaluronidase application through angiography* |
|  |  | | | Vision improved from NLP to slight light sensation at 8 months |
| Zhang et al. (2021)[123] | 31-year-old female | Hyaluronic acid | Apex nasi | Left sided vision impairment, Palsy, Local nose skin pallor, Nausea, Vomiting, Incontinence |
|  |  | | | 4.5 h | Subcutaneous injection of hyaluronidase, IV infusion of mannitol, Endovascular hyaluronidase application through angiography* |
|  |  | Palpebra superior | Right sided immediate vision loss, Sharp pain at injection site, Palsy | | Vision remained at NLP at 3 months |
| Liu et al. (2020)[124] | 29-year-old female | Autologous fat | Forehead | Left sided vision loss (NLP), Ocular pain, Left RAPD, Decreased IOP, Nausea, Vomiting, Numbness and weakness of right limbs (Grade 2-3) with parietal lobe hyperintense lesion |
|  |  | | | Immediately after injection | IV infusion of dextran glucose with dexamethasone and mannitol |
|  |  | | | Vision remained at NLP at 3 months |
| Liu et al. (2020)[124] | 46-year-old female | Autologous fat | Forehead | Left sided vision loss (NLP), Ocular pain, Nausea, Vomiting, Decreased IOP, Congestion and swelling of injection site, Left exotropia (10 degrees), Limited EOM |
|  |  | | | Immediately after injection | IV infusion of dexamethasone and energy mixture |
|  |  | | | Vision remained at NLP at 3 months |
| Liu et al. (2020)[124] | 38-year-old female | Autologous fat | Forehead | Left sided vision loss (NLP), Ocular pain, Nausea |
|  |  | | | Immediately after injection | IV infusion of dexamethasone and cold compression |
|  |  | | | Vision remained at NLP at 3 months |
| Authors            | Case Details          | Treatment                | Side effects                                                                 | Complications                                                                 |
|--------------------|-----------------------|--------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| Conovaloff et al.  | 59-year-old female    | Hyaluronic acid          | Supraorbital region Right                                                      | Vomiting Left RAPD Decreased IOP                                              |
|                    |                       |                          | Right sided vision loss (NLP) Dizziness Nausea Frontal headache Right RAPD     | 1) Immediately after injection                                                |
|                    |                       |                          | Punctate infarcts in right frontal and occipital lobes                         | 2) 120 min                                                                   |
| Karam et al.       | 61-year-old female    | Platelet-rich plasma     | Glabella Left                                                                  | 1) Left sided vision loss (NLP) Dizziness Vomiting Glabellar bruising         |
|                    |                       |                          | Hypoaesthesia in distribution of first trigeminal branch on left side          | Unknown                                                                      |
|                    |                       |                          | 2) 1 month later, ulceration and skin necrosis in injection area               | Unknown                                                                      |
| Karam et al.       | 63-year-old female    | Platelet-rich plasma     | Forehead Right                                                                 | Right sided vision loss Dizziness Tinnitus                                       |
|                    |                       |                          | Vomiting Iris depigmentation                                                  | Unknown                                                                      |
|                    |                       |                          | Pain Incomplete oculomotor nerve palsy Low intraocular pressure                | Unknown                                                                      |
| Karam et al.       | 52-year-old female    | Platelet-rich plasma     | Nasolabial fold Glabella Right                                                 | Right sided vision loss Transient blue vision preceding loss of vision Headache |
|                    |                       |                          | Nausea Ptosis Urinary urgency                                                  | Unknown                                                                      |
| Karam et al.       | 50-year-old female    | Platelet-rich plasma     | Platelet gel injection Forehead Glabella Right external canthus               | Right sided blurring of vision (LP) Right sided eyelid ptosis                  |
|                    |                       |                          | Periorbital swelling, chemosis, conjunctival congestion                      | 1) Immediately after injection                                                |
|                    |                       |                          | Discoloration and pustules of nose tip, nose bridge, columella, glabella,    | 2) 3 days                                                                     |
|                    |                       |                          | forehead,                                                                   |                                                                               |
| Wibowo et al.      | 40-year-old female    | Hyaluronic acid          | Nasal dorsum Right                                                            | Right sided blurring of vision (LP) Right sided eyelid ptosis                  |
|                    |                       |                          | Periorbital swelling, chemosis, conjunctival congestion                      | 1) Immediately after injection                                                |
|                    |                       |                          | Discoloration and pustules of nose tip, nose bridge, columella, glabella,    | 2) 3 days                                                                     |
|                    |                       |                          | forehead,                                                                   |                                                                               |

- Chromatosis at 3 months in the left forehead skin
- Vision remained at NLP at 2 months
- Pale left optic disc with pigment, pigmentation of peripheral retina and macular fibrosis at 1 month
- Retinal detachment in left eye at 8 months
- Persistent scarring in the injection area at 8 months
- Vision was NLP at 3-week visit
- Vision was NLP at 24 h
- Necrosis of forehead, right peri orbital region, right cheek, and right nasal area at 1 month
- Vision was NLP at 3 weeks along with complete right oculomotor nerve palsy
- Improvement in eyelid ptosis at 3 weeks
- Vision fully recovered from LP at 3 months
- Minimal skin deformity at 3 months
| Authors       | Age          | Treatment               | Symptoms                                                                 | Routes                                                                 | Outcome                                                                 |
|--------------|--------------|-------------------------|--------------------------------------------------------------------------|------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Vu et al. (2018)<sup>25</sup> | 51-year-old female | Calcium Hydroxyapatite Glabella Dorsum of the nose | Right sided vision loss (NLP) and bilateral medial cheeks               | Hyaluronidase retrobulbar (2 doses); 1200 IU retrobulbar injections as 3 serial bolus injections | Vision improved from NLP to LP at 3 month follow up Glabella and forehead had erythematos, depressed scars at 3 months |
| Ramesh et al. (2018)<sup>26</sup> | 23-year-old male | Hyaluronic acid Nasal dorsum | Right sided vision loss (NLP) Cold sensation in his face and brow Drooping of the right upper eyelid Pustular skin lesions across brow, nose, and face Eye pain 2 days after infection 1) Right sided vision loss (NLP) Retrobulbar ache Reduced EOM Edematous and ptotic eyelid Conjunctival injection and subconjunctival hemorrhage Anterior chamber hypopyon Reduced IOP (8 mm Hg) 1 mm proptosis with resistance to retropulsion Fixed dilated pupil Decreased right V1 sensation Crusted lesions on forehead and nose 2) Right sided vision loss (NLP) Ocular massage initiated Oral prednisone 60 mg for 3 days 150 IU/day hyaluronidase for skin ischemia Nitroglycerin paste applied to skin Oral aspirin daily Hyperbaric oxygen therapy for skin necrosis | IV steroids Ocular massage Antibiotics Thrombolytic therapy of urokindase 750 IU hyaluronidase injected into the orbital apex 600 IU injected into the skin lesions | Vision remained at NLP at 21 days Improvement in ptosis and EOM at 21 days |
| Chen et al. (2018)<sup>27</sup> | 31-year-old female | Hyaluronic acid Right front and eyebrow | Right sided vision loss (NLP) Ocular pain Ophthalmoplegia Ptosis Limited EOM Chills Fatigue Nausea Dizziness | Immediate hyaluronidase injection 24 h to thrombolytic therapy 6 days to rest of treatment | Vision remained at NLP at 3 months Complete recovery in ptosis and EOM at 3 months |
| Ansari et al. (2018)<sup>101</sup> | 20-year-old | Hyaluronic acid Glabella | Right sided vision loss (NLP) | Unknown; patient Aspirin 325 mg | Unknown |
female

| Study Authors | Age | Gender | Treatment | Symptoms | Outcome |
|---------------|-----|--------|-----------|----------|---------|
| Kalyam et al. (2017) | 49-year-old female | Platelet-rich Plasma (PRP) | Forehead rhytids | Right | Infarcts of parietal lobes, Violaceous pigmentation on the tip and right ala of her nose | Prednisone taper |
| Kim et al. (2013) | 30-year-old male | Calcium hydroxyapatite | Nose | Bilateral | Vision loss bilaterally (NLP), Blepharoptosis, Total ophthalmoplegia, Reticular pattern affecting nose and frontal area, Conjunctival injection and emboli along conjunctival vessels | Unknown |
| Roberts et al. (2011) | 43-year-old male | Poly-(L)-Lactic acid | Periorbital region | Left | Left sided vision loss (LP), Orbital pain, Ptosis, Fixed and dilated pupil, Decreased IOP, Enophthalmos, Ophthalmoplegia, Conjunctival chemosis, paracentral epithelial defect of the cornea with corneal edema, 2-3+ cellular reaction and pigment | Unknown |

NLP: No light perception; EOM: extraocular motility; RAPD: relative afferent pupillary defect; IU: international units; CF: count fingers; LP: light perception; ATA: atmospheres absolute; IOP: intraocular pressure; IV: intravenous.

In cases of temporal hollowing, the frontal branch of the superficial temporal artery and the middle temporal vein should be avoided [Figure 1] (12). The vein lies within the temporal fat pad, while the artery lies within the temporoparietal fascia and travels superficially to above the lateral eyebrow (12,18). The superficial temporal artery also anastomoses with the supraorbital, supratrochlear and zygomaticotemporal arteries, providing a pathway into the central retinal artery (13). The author prefers injecting using high G’ fillers deep on top of the bone in this high-risk area; however, the exit of the zygomaticotemporal artery traverses into the orbit just above the zygomatic arch, usually more anteriorly, and may also be a source of orbital ischemia. Poly-L-lactic acid is another alternative due
Figure 1. Representative figure of the arteries of the face, ocular, and nasal area. Shaded areas represent communication between the external carotid system and the end branches of the ophthalmic artery (OA) that are implicated in filler induced blindness. This includes the angular branch (AngA) of the facial artery (FA), the transverse facial artery (TFA) that arises from the superficial temporal artery (STempA) and the deep temporal branch (DTA) of the maxillary artery (MA) in the shaded zones. The frontal branches of the superficial temporal artery (FBSTA) anastomoses with the supraorbital (SOA) and supratrochlear arteries (STA), but the FBSTA has not been directly implicated in blindness after filler injections. Other vessels mentioned are the internal carotid artery (IC), external carotid artery (EC), inferior labial artery (ILA), superior labial artery (SLA), inferior alar artery (AIA), dorsal nasal artery (DNA), zygomaticofacial artery (ZF), zygomaticotemporal artery (ZT), and lacrimal artery (LA). Figure and caption reproduced with permission from Goodman et al. 2020 by permission of Oxford University Press on behalf of The Aesthetic Society.

to the volume available when diluted 8:1 or 9:1 with sterile water and lidocaine. The less viscous preparation is easier to see reflux, if in an artery.

When injecting the cheek, one should be aware of the infraorbital bundle, which lies approximately 1 centimeter below the orbital rim at the medial limbus, the transverse facial artery along the zygoma, and the zygomaticofacial artery higher up on the zygomatic arch laterally. Two main danger zones exist in the infraorbital and cheek area. Periosteal injections for tear-trough deformities or infraorbital hollow correction can be dangerous due to anastomoses of the nasal branch of the infraorbital artery with the supratrochlear artery, dorsal nasal artery, or angular artery. Secondly, for cheekbone enhancement fillers, superficial injections may cause problems with the cutaneous perforations of the zygomaticomalar branch of the infraorbital artery. In these areas, a high G’ product is recommended. Additionally, for tear trough deformities, retromuscular, pre-orbital microfat injections may be considered, while for cheekbone enhancement, injections should be performed in supraperiosteal layers. However, fat injections are not reversible, and there is a wide variation in how HA fillers can be reversed. For example,
Restylane-Lyft for the cheek takes very little hyaluronidase to dissolve, while Voluma and RHA4 are very difficult to reverse\cite{21-23}. Calcium hydroxylapatite is also not reversible, although some have seen improvement with simple saline diffusion\cite{24}, hyaluronidase\cite{25}, sodium thiosulfate\cite{26}, steroids\cite{27}, and 5-fluorouracil injections\cite{28}.

Given the vascularity of the nose, filler injections in the nasal area are commonly associated with complications\cite{12,26,30}. Although the major nasal arteries at risk for complications are the lateral nasal artery and dorsal nasal artery, the presence of several anastomoses in the nose also predisposes to blood flow that can be reversed with filler injection\cite{11}. The vasculature typically lies in the subdermal plane above the superficial musculoaponeurotic system [Figure 1]\cite{11,12}. The tip and ala of the nose are most commonly prone to necrosis secondary to compression or vascular injury\cite{12}. If one were willing to risk injecting this area, one author recommends reassessing the patient 15 min after injection to check for vascular compromise\cite{12}.

The superior labial artery (SLA) and inferior labial artery (ILA) also have variability in their course and depth\cite{31}. While the SLA is not very likely to be found subcutaneously at the vermillion border, the vasculature is superficial in the midline and Cupid’s area, which can carry a high risk\cite{31}. Additionally, the lips become thinner with aging, which may predispose the arteries to intravascular injection\cite{31}. Therefore, for lip injections, injections should be limited to approximately 3 mm depth in order to avoid the SLA and ILA that course deeper within the lip\cite{12}.

In cases of jawline contouring, one study found an anatomic variation in which the transverse facial artery travels from the masseter muscle to the angular artery and dorsal nasal artery\cite{32}. This could be one pathway for how lateral face injections, including masseter and jawline contouring, could lead to blindness\cite{32}. Toure et al. recommend a safe zone for injection below a line from the lobule of the auricle to the labial commissure\cite{32}. The facial artery branches into the submental artery and ascending submental artery, which, if cannulated, can lead to skin necrosis of the lower face\cite{33}.

**COMPLICATIONS**

**Vision loss**

As cited in the introduction and the Table, there are at least 211 cases of blindness reported in the English literature as of January 2022, and the actual number is likely many folds higher, since most cases are not published in literature. The presentation of a patient with vascular occlusion of the ophthalmic artery involves blindness and periorcular symptoms, usually very soon after filler injection, and can present with concurrent ptosis and ophthalmoplegia\cite{29,34}. In a recent review paper, 35 out of 39 cases had immediate vision loss symptoms and 2 cases developed symptoms within 10 min\cite{29}. However, in several cases, the symptoms developed a day after injection\cite{29}. The etiology of this vision loss is usually due to retrograde arterial embolism into branches of the ophthalmic artery, including the retinal branches\cite{35-37}. The glabella, temple, and nasolabial folds have vasculature that commonly anastomoses to the ophthalmic artery\cite{38}. Thus, the most common locations that cause vision changes are the nasal region, followed by the glabella, forehead, and nasolabial folds\cite{5,29}. The most common occluded vessels are the ophthalmic artery, central retinal artery, branch retinal artery, and naso ciliary artery\cite{29,30}. Occlusion of the ophthalmic artery is usually secondary to injections in the nose, while occlusion of the retinal artery is secondary to glabellar injections\cite{30}. Given the various anastomoses in the different facial arteries, there are several injection locations that can cause ocular complications.

A recent study found that filler particles disintegrate into smaller particles immediately after injection, supporting the hypothesis that emboli, rather than a column of filler, cause an obstruction\cite{39}. Another study
further supported this idea by showing that the force required to push a column of filler retrograde was higher than the normal injection force\(^{[41]}\). However, one study also found that only 0.085 mL was required to fill the supratrochlear artery from the glabella to the ophthalmic and central retinal artery bifurcation, highlighting that even a small volume of filler could cause this complication\(^{[42]}\). Per the 48 published case reports by Beleznay et al. of filler-induced vision changes, 81% of cases were treated with hyaluronic acid filler followed by calcium hydroxylapatite (10.4%), and one case each was from autologous fat and poly-L-lactic acid (PLLA)\(^{[5]}\). This is likely secondary to the fact that hyaluronic acid is the most common type of filler injected, followed by autologous fat and calcium hydroxylapatite\(^{[39]}\). However, visual loss has even been noted to occur secondary to platelet-rich plasma (PRP) injections and PLLA injections\(^{[43,44]}\). In the 4 reported cases, one woman developed painful vision loss with no light perception in the left eye after PRP injection into the left glabellar region\(^{[43]}\). Her fundus exam was suggestive of an embolus within the central retinal artery\(^{[43]}\). At her 1-month visit, she was noted to have a pale optic disc with pigment in the superior temporal region and developed a retinal detachment 8 months after her initial injection\(^{[43]}\). In one reported case of blindness secondary to PLLA, a patient received an injection in the left periorbital region and reported immediate pain in the left eye as well as blurring of vision\(^{[44]}\). On exam, the patient was found to have a decrease in vision to light perception with projection, a fixed and dilated left pupil, as well as ophthalmoplegia and ptosis\(^{[44]}\). While the ophthalmoplegia and ptosis improved over time, the patient’s vision still declined\(^{[44]}\).

Although irreversible damage to the retina has been previously studied to occur within 90 min, a recent study found that retinal infarction can happen as early as 12-15 min after complete occlusion\(^{[45,46]}\). Given the low incidence of cases, no high-level studies currently exist that allow for a clear management recommendation for this devastating complication\(^{[47]}\). Ocular physical maneuvers, including compression and paracentesis, are a rapid intervention\(^{[47,48]}\). An ocular massage can be performed with manual firm compression to the globe in 10-20 second intervals followed by a sudden release. This compression can be performed with a Goldman lens or trans palpebral with 2 fingers\(^{[47]}\). The goal of these maneuvers is to lower the intraocular pressure, dilate the occluded artery and allow for the migration of the emboli to a peripheral vessel, preserving central vision\(^{[47]}\). Rebreathing in a brown paper bag for 10 min every 30 min can also increase CO\(_2\) and cause vasodilatation\(^{[49]}\). Methylprednisolone and other intravenous steroids can be used to decrease the retinal edema caused by damage to the cells\(^{[11,47]}\). Intraocular pressure reduction can be achieved with timolol, mannitol, and acetazolamide to restore retinal vascular flow and avoid visual loss\(^{[47]}\). Lastly, hyperbaric oxygen (HBOT) can be used when available, as it provides a subjective relief and can also work to improve plasma oxygen concentration and dilate the retinal arteries\(^{[47,50]}\). While nitroglycerin paste has been considered, questions remain on whether it is able to penetrate the deep orbital vessels\(^{[47]}\). One study with a rabbit eye model found that there was no improvement in perfusion with nitroglycerin paste, and the veins were also found to have a more congested appearance\(^{[51]}\). Additionally, dilation of the arterioles could push the product further into the smaller arterioles and capillaries\(^{[51]}\). The use of hyaluronidase can also be considered, especially when the filler is HA-based, within 60-90 min after visual loss\(^{[47]}\). While hyaluronidase has been noted to also be administered outside the 90-min window, the newest cases have not been able to show significant improvement in visual acuity.

There has been some interest in the use of HBOT in the treatment of ophthalmic artery occlusion. HBOT is defined as an intervention in which an individual "breathes near 100% oxygen intermittently while inside a treatment chamber at a pressure higher than at sea level pressure (> 1 atm)\(^{[52]}\)." The main goal is to increase the amount of oxygen dissolved in the plasma. Increased dissolved oxygen works to improve the diffusion distance, supporting oxygen-dependent processes that do not get enough arterial blood supply\(^{[53]}\). One report discussed the case of a 31-year-old woman who received HA filler at the nasal dorsum and developed
immediate vision loss in the right eye. After being diagnosed with central retinal artery occlusion, she received a multitude of treatments including high-flow O₂, ocular massage, steroids, and blood thinners. She also received daily 90-min therapy of HBOT at 2.5 atmospheres absolute (ATA) or 253 kilopascals (kPa) for 3 weeks. However, the patient had no improvement in the vision in the right eye, with her visual acuity remaining at no light perception. In another case, a 49-year-old woman was also found to develop a central visual defect in her right eye after the injection of poly-L-lactic acid (PLLA). Her visual acuity was found to be 20/200 in the right eye. She received ocular massage, brimonidine, and HBOT (unknown pressure) twice daily for 5 days, but did not have any improvement in her vision. A 41-year-old woman who had vision loss in her right eye after a forehead filler injection received retrobulbar hyaluronidase and 2 h of daily hyperbaric oxygen therapy, among other treatments. This patient had recovery of vision from no light perception to hand motion. It appears that an optimal HBOT protocol is daily use for several days or weeks after the onset of blindness. The typical HBOT protocol for compromised grafts and flaps is 2.0 to 2.5 ATA for 90 to 120 min twice a day, and it appears that preliminary case reports are following that protocol. While the use of HBOT has been shown to have some effect on skin vascular occlusion, discussed later in this review, there is still the question of whether HBOT has the same effect on visual loss from occlusion. It is worth noting that data from studies solely looking at artery occlusions outside of emboli from facial filler have documented some improvement with HBOT. The disease processes in these studies looked at idiopathic CRAO and Factor V Leiden mutations. However, at this stage, the data for HBOT for ophthalmic artery occlusions and central retinal artery occlusions secondary to facial filler emboli remain preliminary and inconclusive.

The use of hyaluronidase through a retrobulbar injection is currently being debated and further studied. A 2018 case report discussed a retrobulbar injection of 450 IU of hyaluronidase, which completely restored a patient’s vision after receiving HA filler injections near the infraorbital neurovascular bundle. However, this report did not document an objective visual acuity before and after hyaluronidase treatment. Another case study also showed improvement from light perception to hand motion. This patient had vision loss in her right eye after receiving HA filler injections near the infraorbital neurovascular bundle. The authors found that a dose of 3000 IU could lead to a compartment syndrome with readily available preparations (since the powdered form is not widely used in the US) and injecting within 5-10 min of occlusion would prove to be very difficult in the clinical setting. Another in-vitro study showed that hyaluronidase could not cross the dural sheath of the optic nerve, which can prevent access to the central retinal artery. Ugradar et al. also found that hyaluronidase was not able to reduce the particle size in a substantial manner, creating particles that were still greater than the size of the vessel. These in-vitro studies highlight that physiologically, it is difficult to replicate how retrobulbar hyaluronidase can effectively relieve filler occlusion.
obstructions. This translates to what has been seen clinically as well, in that some patients have a full recovery of vision with retrobulbar hyaluronidase while other cases do not[29]. An additional literature review concluded that the efficacy of retrobulbar hyaluronidase was not clear and that there was not enough evidence to support retrobulbar hyaluronidase given the inherent risks[48]. This treatment has a level of evidence V, which confers a grade D recommendation from the American Society of Plastic Surgeons[46,71].

A more novel way to treat blindness from filler complications may be to consider it a stroke, because the optic nerve is part of the central nervous system. Activating a stroke protocol may be prudent. Baley-Spindel et al. noted the occlusion is likely composed of both HA gel and red thrombi; therefore, a combination of hyaluronidase and alteplase yielded the best results in clearing HA gel thrombi in their rat model[72].

Ophthalmoplegia/Double vision

While vision-threatening complications are better known, facial fillers have also been seen to cause ophthalmoplegia, as noted in Table 1. A recent study showed that 50% of patients with occlusion of the ophthalmic artery presentation is not always as clear, as some patients also presented with ophthalmoplegia[73]. Another study found that 15 (71%) of 21 patients over a 9-year period with artery occlusion also developed ophthalmoplegia at initial presentation, with an average of 2.8 rectus muscles involved[74]. The mechanism behind this is theorized to be from ischemia to the cranial nerves or extraocular muscles[74,75]. However, a recent report of 2 isolated ophthalmoplegia cases illustrated that this side effect could also be secondary to an inflammatory response[76].

Management of ophthalmoplegia, if a hyaluronic acid (HA) filler is used, can be performed with 1500 IU of hyaluronidase subcutaneously around the site of injection, and in the case reported by Bae et al., hospitalization was required[77]. Even though the ophthalmoplegia is resolved in some cases, sometimes the ocular misalignment persists, requiring strabismus surgery[76]. In 2 case reports where an ischemic etiology was not suspected, one patient improved after Medrol Dosepak and aspirin 81 mg, and the other did not improve as she presented 3-4 months after the complication[76].

Soft tissue necrosis

The presentation of a patient with vascular occlusion is often characterized by pain disproportionate to the injection, along with blanching[78]. This is followed by livedo reticularis secondary to venule swelling[79,80]. However, in a clinical setting, the presentation is not always as clear, with pain often not accompanying these events[81]. For example, a net-like reddish/blue appearance may be hard to distinguish from bruising or simple erythema, but a delayed capillary refill would support ischemia. A recent study also showed that in a survey of 52 injectors, 62% had reported one or more intravascular injections, highlighting the frequency of these events[81].

The etiology of vascular complications involves arterial compromise causing tissue anoxia and progression to necrosis[15]. As the filler is being injected, it may flow in either direction in the vessel, and lead to an obstruction of the blood supply[83]. Given that fillers have inherently different properties in viscoelasticity and cohesivity, the outcomes have different severity[3,15]. Case reports with polymethylmethacrylate (PMMA) have had complications showing more dramatic skin necrosis compared to other fillers[82-84].

The glabella, nose, and nasolabial folds are at higher risk because they depend on a single arterial branch[13]. Out of all the cases of vascular necrosis, nasolabial fold injection was associated with the highest number of cases, followed by injections into the nose[85]. Nasal necrosis is likely secondary to the dorsal nasal artery having variable anatomy, occurring only 34% of the time as a pair of arteries, with other variations including
a single large dorsal nasal artery or in random distribution\cite{86}. Given the potential for embolization of facial fillers, vascular complications also have been seen to occur far from the injection area in the mid and lower face. The vascular supply of the internal nose arises from branches of the superior labial artery, the sphenopalatine artery, the posterior ethmoidal artery and the anterior ethmoidal artery\cite{87}. After an injection of HA above the anterior nasal spine and nasal bones, a 42-year-old female developed gingival necrosis of the right upper incisor, partial lip mucosa necrosis, and an exophytic palatal lesion\cite{87}. The gingival necrosis was likely related to embolization of the septal branches of the superior labial artery and compression of the distal arteries from the septal branch of the posterior ethmoidal artery\cite{87}. In one author’s personal experience, she received an injection of hydroxylapatite in her left cheek, in which she noted that the needle was directed somewhat tangentially. After injection, she immediately developed blanching and mottling, which later took on a reticulated appearance due to the involvement of the infraorbital artery. She did not receive hyaluronidase at that time. The following morning, the mottling of her skin extended towards her lower eyelids and the left nasal bridge [Figure 2]. On day three, she developed pustules, necrosis of the skin, and eventually left permanent scarring [Figure 3]. Her erythema of the gums was suggestive of infraorbital artery involvement [Figure 4]. Injections into the infraorbital artery may be performed from the cheek augmentation, with the subsequent embolization extending to the facial artery below.

Skin necrosis has also been seen to occur from filler injected into the lower face. One patient, after receiving dermal fillers in the lip to correct an atrophic scar, presented with pain and blanching of the upper lip with a blue tinge 2 hours after her initial injection\cite{88}. The authors did note that the necrosis may have been secondary to an alteration of the blood vessel course from scarring already present in the area\cite{88}. Injections in the lower lip may need to be cautious of the inferior labial artery, which has been studied to have variation in its dominant arterial sources [Figure 5]\cite{89}.

Skin necrosis with chin injections has also been reported\cite{90,91}. In one case, the patient developed numbness on the right side of her tongue during an injection of her chin and was found to have an obstruction of her deep lingual artery\cite{90}. In another case, after chin augmentation injection, a patient developed pain with swelling as well as livedo reticularis and mottling from the mental crease to the upper cervical area 10 min after injection\cite{91}. Pain with swallowing can be explained by ischemia in the submental branches supplying the digastric, mylohyoid, and platysma muscles\cite{90}. It is worth noting that the main blood supply of the chin comes from the ascending mental artery, branching off the submental artery\cite{33}. If that ascending mental artery is cannulated, the filler can travel retrograde to the submental artery and facial artery, causing infarction to the lips, nasolabial fold, nose, and paranasal skin\cite{33}. Additionally, if filler travels through the submental artery and crosses anastomosis to the sublingual artery, it can also cause necrosis of the root of the tongue and floor of the mouth through the involvement of the dorsal lingual and sublingual arteries\cite{33}.

If vascular occlusion is suspected with pallor and blanching, the injection must be stopped immediately\cite{13,78,92}. Aspiration of the product should be attempted before withdrawing the needle\cite{13,78}. With the goal of improving blood flow, warm compresses and a massage of the area should be done\cite{13,76,90}. Regardless of filler type, hyaluronidase should be injected as it has been shown to reduce edema\cite{60,94}. Aspirin should also be started to limit clot propagation and platelet activation and be given with an antacid\cite{13,92}. In one case report, low level light therapy (LLLT) was used with the intention of reducing pain and inflammation, and improving tissue repair and regeneration\cite{77}. The goal of LLLT is to use photons at a non-thermal value to change biological activity\cite{95}. Through the enhancement of specific enzyme activity, LLLT has been shown to activate intracellular signaling pathways and transcription factors involved with cell proliferation, survival, and tissue repair\cite{96}. Nishioka et al. have also shown that LLLT therapy increases skin flap viability in rats, with the percentage of necrosis area of the flap decreasing in the LLLT group\cite{96}. 
Figure 2. Mottling of the skin the morning after cheek injection, extending from the lower eyelid to the upper lip and part of the nose due to involvement of the infraorbital artery.

Figure 3. Formation of pustules on the nose and a full thickness defect near the nasolabial fold 3 days after injection due to involvement of the facial artery.
Figure 4. Erythema of the gums indicating involvement of the infraorbital artery.

Figure 5. Representative figure of the main arteries of the lower face and chin, with depiction of the variation of arterial sources of the inferior labial arteries. Figure reproduced from Tansatit et al. [89].

Sildenafil, tadalafil, and vardenafil can also be used to relax smooth muscles, dilate blood vessels, and increase blood flow [97]. The use of nitroglycerin has not been fully defined. Although nitroglycerin paste has innately vasodilatory properties, an animal study showed no improvement in perfusion and raised the question of whether arterioles dilation could cause further propagation of filler and worsen the ischemia [51]. Given its inherent risks of headaches and hypotension, van Loghem et al. did not make a clear recommendation on whether to incorporate nitroglycerin paste [13].

Hyperbaric oxygen has also been reported to be an effective adjunct treatment for vascular occlusion. A 32-year-old female who developed vascular occlusion after HA filler on her nose received 1 month of biweekly 90 min HBOT sessions at 2.4 ATA, after which her nose showed improvement in vascularization [98]. Another report also remarked on a 37-year-old female who developed ischemic changes to her face after an
injection on her proximal temple\textsuperscript{[99]}. After receiving 6 treatments twice daily (2 treatments at 3.0 ATA followed by 4 treatments at 2.4 ATA), the patient showed improvement in ischemic discoloration\textsuperscript{[99]}. Two cases, one involving a 46-year-old man who received poly-methylmethacrylate and calcium hydroxylapatite and a 40-year-old white woman who was treated with hyaluronic acid, showed improvement in their skin necrosis after HBOT\textsuperscript{[94]}. One treatment lasted 14 days, while the other lasted 2 days\textsuperscript{[94]}. Thus, while HBOT remains an inconclusive treatment for vascular occlusion of the ophthalmic and retinal artery, it has been shown to potentially have more benefit in skin necrosis treatment.

Recently, a new protocol has been released in which high dose pulsed hyaluronidase is used for vascular adverse events. For low volume events (0.1 mL or less of HA filler), 450 IU of hyaluronidase is used in a single area, for an area half of an upper lip\textsuperscript{[100]}. If the nose has involvement, 900 IU of hyaluronidase should be used\textsuperscript{[100]}. The dosing should also be hourly rather than the traditional daily dosing to maintain high concentrations in the ischemic zone\textsuperscript{[100]}. The injections should be given at injection sites, and if there are distal sites that appear ischemic, one should consider injecting distal sites of ischemia\textsuperscript{[15]}. Delorenzi et al. have remarked that hyaluronidase is able to diffuse through an arterial wall, so the most important area of injection would be areas that show ischemia\textsuperscript{[15]}. However, the article did comment on a case in which the patient did not initially improve with hyaluronidase injection into the ischemic tissue, but showed improvement after hyaluronidase was injected into the affected artery\textsuperscript{[15]}. Thus, further studies may be needed to elucidate the most effective area for hyaluronidase injection immediately after vascular occlusion.

Cerebral infarction
Filler injections can lead to very severe complications. Cerebral infarction secondary to vascular occlusion has been noted as a complication of filler injections. A review article of 44 cases showed that 8 patients (18.2\%) had CNS involvement, including upper limb weakness, acute infarction, or hemorrhage\textsuperscript{[29]}. A 20-year-old female who presented with non-improving vision loss in her right eye was found to have multifocal infarcts in her parietal lobes\textsuperscript{[101]}. This patient received injections in the glabella, an area known to cause combined ophthalmic and cerebral complications\textsuperscript{[102]}. Anatomically, the supratrochlear and supraorbital arteries were injected with enough force that the filler traveled retrogradely to enter the cerebral circulation via the Circle of Willis\textsuperscript{[101]}. Another study involved a 39-year-old female who presented with vision loss in the left eye after filler injection into the glabella\textsuperscript{[102]}. This vision loss was concurrent with ptosis and total ophthalmoplegia\textsuperscript{[102]}. The next day, an MRI found several cerebral infarctions that were embolic in nature\textsuperscript{[102]}. After one week, the infarction transformed into a parenchymal hematoma, after which the patient received methylprednisolone\textsuperscript{[102]}. While her limb weakness improved, she continued to have a right arm monoparesis\textsuperscript{[102]}. Another case involved a 40-year-old female who developed a cerebral infarction after nasal augmentation\textsuperscript{[103]}. With a GCS of 4 and on mechanical ventilation, the patient developed gastric ulceration, pulmonary infection, respiratory failure, and cerebral herniation, dying 6 days after the filler injection\textsuperscript{[103]}. For this patient, the theory was that there were several small HA particles in the capillaries from this filler injection\textsuperscript{[103]}. The authors recommended immediate thrombolysis within the 12-h window of functional impairment (90 min for concomitant ophthalmic arterial occlusion) and consideration of decompressive craniectomy\textsuperscript{[103]}.

**PREVENTION**
Given the severity of these intravascular complications, prevention is key in delivering high-quality patient care. Knowledge of various injection techniques and the relatively new utilization of imaging have been studied in the prevention of these outcomes.
Injection techniques

There are several injection techniques that have been studied to help prevent vascular occlusions. Aspiration before injection (with an unprimed needle, especially if the filler is thick or sticky) and using lower volumes of the product (0.1 mL) can help indicate that the needle has not entered a blood vessel and reduce the severity of complications if a blood vessel is entered\cite{7,17}. Sometimes aspiration can give you a false sense of security, as the filler may be too thick to detect reflux of blood when in a vessel. If injecting in the areas of the supratrochlear artery, supraorbital artery, and dorsal nasal artery, compression of the vessel pathway can help prevent retrograde flow\cite{104}. The use of a reversible HA filler will allow for treatment with hyaluronidase if a reversal of vascular occlusion is needed\cite{7}. Given that the pressure of the filler injection can cause retrograde flow, injecting at a slow pace can help in preventing complications\cite{7,105}.

Needle size has also been seen to have an impact on vascular obstruction. While a smaller needle may improve the precision of the injection, it may increase the likelihood of penetrating the vessel wall rather than a larger bore needle which would roll on the side of the artery\cite{15,104}. Additionally, more pressure is required to inject through a smaller bore needle which could lead to more pressure into a vessel, should vasculature be entered. A recent study also found that the use of microcannulas had 77% lower odds of occlusion compared to needle injections, due to the fact that blunt tips could avoid piercing vessel walls\cite{106}. However, small bore microcannulas still have the potential to penetrate the facial artery with a small amount of force (0.23 kg for a 27G cannula)\cite{107}. Epinephrine may also help with vasoconstriction, but may make it more difficult to distinguish an early manifestation of necrosis\cite{104}. Thus, administering local anesthesia without epinephrine may be considered\cite{104,108}.

Imaging

Mapping vasculature to prevent intravascular filler injection

Various studies have now started incorporating ultrasound as a method to map vasculature and reduce the incidence of vascular complications seen with filler injections. Doppler ultrasound has been seen to detect anatomy, such as the facial artery lateral to the nasolabial fold, along with its different anatomical variations\cite{109}. One other study commented that although ultrasound may be difficult to manage in conjunction with injection, a new technique combining 3D time of flight magnetic resonance angiography (3D-TOF MOTSA MRA) and infrared (IR) facial heating could visualize the following arteries: facial, angular, superior labial, inferior labial, lateral nasal, dorsal nasal, supratrochlear, supraorbital, and superficial temporal\cite{110}. These images could be acquired on a 1.5 or 3 Tesla (T) system with a head coil, with an additional surface coil on top, to improve signal reception\cite{110}. The authors showed that these MRA images could be projected on the patient’s face before injection, albeit without the same 3D depth aspect\cite{110}. The main benefit of this method was visualization of the facial arteries in a non-invasive and contrast-free manner\cite{110}. However, the cost of MRI in these individual countries may need to be considered before the widespread adoption of this technology. Our team has also looked at the utilization of 7T MRI and shown its ability to depict small orbital and eyelid structures, as well as the orbital branch of the infraorbital artery (article in press).

The use of ultrasound has been adopted at various points in the filler injection procedure. Firstly, ultrasound has successfully determined that the needle or cannula is positioned in the correct plane and not within or near a vessel\cite{111}. Schelke et al. discussed how the use of doppler ultrasound can help distinguish vessels as well as the direction of blood flow [Figure 6]\cite{112}. Rocha et al. recommended that once the needle or cannula is determined to be in the correct location, the filler can be injected without aspiration\cite{111}. After the injection of filler, doppler ultrasound can again be used to confirm the vascularization of the area\cite{111}. As seen in Figure 7, the placement of filler deposits, such as hyaluronic acid, can be distinctly visualized on ultrasound to confirm correct depth and placement.
Diagnosing areas of ischemia from filler complications

Imaging can also be used in the early diagnosis and treatment of filler complications. Another study evaluating laser doppler imaging (LDI) found that LDI was able to accurately delineate a hypo-perfused area to help target hyaluronidase treatment\textsuperscript{[113]}. Color Doppler flow imaging (CDFI) was able to successfully detect retinal artery occlusions and ophthalmic artery caused by filler injections by showing decreased retrobulbar blood flow\textsuperscript{[114]}. Doppler ultrasound may be able to be used to detect the lack of perfusion, and in rare cases, an ischemic vessel may be able to be injected with hyaluronidase under ultrasound guidance. Schelke et al. reported on a case of how, upon crusting under the lip after upper lip augmentation, 150 U of hyaluronidase was injected with ultrasound guidance\textsuperscript{[112]}. A case in which ultrasound was used to inject hyaluronidase into a visualized filler deposit is seen in Figure 8. In another case, after a patient presented with mottling of her chin following filler injection, ultrasound was used as guidance for hyaluronidase injection [Figure 9]. Ultrasound imaging appears to be valuable in helping the injector decide where to place the hyaluronidase. However, this may be very difficult to do, and it is unclear how much an ultrasound may help or distract from the process of trying to cannulate a vessel.

Magnetic resonance imaging (MRI) has also been studied as the primary mechanism to evaluate for infarctions after ischemic complications. Many of the case reports that were reviewed showed that an MRI
or magnetic resonance angiography (MRA) was used to evaluate intracranial infarctions and embolisms\cite{101,102,115}. Additionally, the use of MRI is finding an increasing role in the detection of other non-ischemic complications associated with fillers such as inflammation, foreign body granulomas, and filler migrations, which we will expand upon in another review paper\cite{116}. While the use of imaging in this field is still relatively recent, it represents an area for further development and utilization.

**REVERSIBILITY**

Understanding the reversibility of fillers is important, should an ischemic or non-ischemic complication occur. Fat and calcium hydroxylapatite are not reversible, although some reports have seen improvement in calcium hydroxylapatite injections with simple saline diffusion\cite{24}, hyaluronidase\cite{25}, sodium thiosulfate\cite{26}, steroids\cite{27}, and 5-fluorouracil\cite{28} injections. Additionally, many of the new hyaluronic acid gel fillers require high doses of hyaluronidase and multiple injections to reverse. For example, Restylane-L and Restylane-Lyft are easy to dissolve, whereas the Vycross products, RHA3-4, and the newer Restylanes are much more difficult to reverse. Refer to previous publications\cite{21-23} and upcoming papers to remain updated on all the different filler products.

**CONCLUSION**

As filler injections become more widespread, it is important to be aware of and know how to manage the devastating ischemic complications that can occur. Most of these ischemic complications occur with pain disproportionate to the injection and with a sudden change in vision or blanching or dusking of the skin. Ischemic complications may also present in a more delayed fashion in the first day or two after injection with mottled reticular-appearing skin. Treatment of ischemic complications begins with early identification of the ischemia, including being aware of cerebrovascular events, and early treatment of ophthalmic artery occlusions within 90 min. Aspirin and other anticoagulation can be used, but the main tool is early delivery of hyaluronidase of 450–3000 units in areas that can accommodate that volume, spread over multiple boluses, depending on the area and severity of ischemia. Cannulating an artery, perhaps with image and doppler guidance, for hyaluronidase injection would be ideal, but this is very challenging. For blindness, activating a stroke protocol at a nearby hospital may even be considered to treat the red thrombi component of arterial occlusions. Warm compresses and ocular massage (for ocular ischemia), hyperbaric oxygen
therapy or low-level light therapy (for soft tissue ischemia) can also be considered. Nitroglycerin paste is controversial. Hyperbaric oxygen can be considered to help salvage marginal tissue that may otherwise become necrotic. No panacea exists except for prevention. Due to simple mathematics, occlusion may not be entirely avoidable if one is injected enough, despite one’s best efforts. However, minimizing the incidence of these complications requires knowledge of the local anatomy, filler properties (reversible non-permanent filler is safer), and utilizing the safest injection techniques. New advances in the field include utilizing imaging to help avoid and diagnose intravascular injection. Higher concentrations of hyaluronidase may
also be required to reverse the thicker and newer hyaluronic acid gel fillers.

**DECLARATIONS**

**Authors’ contributions**

Made substantial contributions to conception and design of the study and performed data analysis and interpretation: Mehta P, Kaplan JB, Zhang-Nunes S

**Availability of data and materials**

Not applicable.

**Financial support and sponsorship**

This work was supported by an unrestricted Grant to the Department of Ophthalmology from Research to Prevent Blindness, New York, NY and the Keck School of Medicine Dean’s Research Scholar Award.

**Conflicts of interest**

All authors declared that there are no related conflicts of interest.

**Ethical approval and consent to participate**

Not applicable.

**Consent for publication**

Not applicable.

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