Although rare, blindness following facial filler procedures is a devastating outcome. It is invariably permanent and is most common following injections in the glabella or bridge of the nose but may occur from remote sites such as the lip or opposite side of the face. It has been reported with all types of facial filler, with the most common reports following the injection of autologous fat and hyaluronic acid. Blindness is regularly associated with ophthalmoplegia, and skin changes

**Background:** Blindness following facial filler procedures, although rare, is devastating, usually acute, permanent, and attributed to an ophthalmic artery embolus. However, blindness may be delayed for up to 2 weeks, sometimes following injection at remote sites, suggesting alternative pathways and pathogenesis.

**Methods:** Seeking solutions, fresh cadaver radiographic lead oxide injection, dissection, and histologic studies of the orbital and facial pathways of the ophthalmic angiosome, performed by the ophthalmic artery and vein, both isolated and together, and facial artery perfusions, were combined with total body archival arterial and venous investigations.

**Results:** These revealed (1) arteriovenous connections between the ophthalmic artery and vein in the orbit and between vessels in the inner canthus, allowing passage of large globules of lead oxide; (2) the glabella, inner canthi, and nasal dorsum are the most vulnerable injection sites because ophthalmic artery branches are anchored to the orbital rim as they exit, a plexus of large-caliber avalvular veins drain into the orbits, and arteriovenous connections are present; (3) choke anastomoses between posterior and anterior ciliary vessels supplying the choroid and eye muscles may react with spasm to confine territories impacted with ophthalmic artery embolus; (4) true anastomoses exist between ophthalmic and ipsilateral or contralateral facial arteries, without reduction in caliber, permitting unobstructed embolus from remote sites; and (5) ophthalmic and facial veins are avalvular, allowing reverse flow.

**Conclusion:** The authors’ study has shown potential arterial and venous pathways for filler embolus to cause blindness or visual field defects, and is supported clinically by a review of the case literature of blindness following facial filler injection. (Plast. Reconstr. Surg. 146: 745, 2020.)
in the frontal, glabella, and nasal regions occur frequently, reflecting that the entire ophthalmic artery territory can be embolized (Fig. 1).

In recent series, more than 50 percent of patients presented with cerebral signs, including hemiplegia, stroke, and death, indicating filler has gone farther to reach the cerebral circulation. These studies identified 190 cases with outcomes ranging from complete vision loss in more than 95 percent of cases to impairment of visual acuity or visual field defect. The blindness was permanent, and of those patients where follow-up was recorded, ophthalmoplegia usually recovered.

The blindness fell into three clinical patterns:

Type I: Immediate visual disturbance with orbital pain, headache, ophthalmoplegia, and ptosis within minutes.
Type II: Delayed onset of visual disturbance between 1 and 24 hours after injection.
Type III: Late onset of blindness occurring days to weeks after injection.

The current hypothesis for blindness following filler injection is inadvertent cannulation of a cutaneous branch of the ophthalmic artery and retrograde embolization of filler against arterial flow, where injection pressure has exceeded systole. However, blindness still occurs by unintentional arterial injection outside the ophthalmic territory, usually through the facial artery or one of its branches. What is the explanation?

Previous work has revealed that the vascular supply of the skin and deep tissues, including the eye, is provided by a continuous network of anatomical territories (angiosomes) linked together by anastomotic vessels (Figs. 1 and 2). More recent work by our unit has shown experimentally in vivo that these anastomotic vessels are not just conduits, but are functional and control flow between angiosomes. When a toxin is introduced into an artery, it initiates spasm of these anastomotic vessels around the perimeter of the angiosome to contain the toxin within the anatomical territory of that vessel, and to prevent spread, provided that these anastomotic arteries are of reduced caliber (i.e., the choke vessels) (Fig. 2). However, if linked by vessels without reduction in caliber (i.e., the true anastomoses), this protective spasm appears to be lost, so that the toxin will pass freely into the adjacent angiosome territory, effectively joining them together as one, until it impacts in an artery with a choke vessel perimeter. This may occur in the second angiosome or at a remote site linked by a series of true anastomoses.

Recently, we used this information to explain why the patchy areas of necrosis seen in the face, following inadvertent hyaluronic acid injection into a branch of the facial artery, was confined by choke vessel spasm around the territory of that impacted vessel, yet in other cases, because of a true anastomotic freeway, injection of the nasal tip, for example, could produce necrosis in the forehead, or injection of the right upper lip could produce blindness in the left eye. This mechanism must certainly be involved in the type I clinical picture, with filler injected directly into one of the branches of the ophthalmic artery supplying the face, or one connected distally by a true anastomosis (Fig. 1). However, the clinical picture, especially in the type III cases, suggests another mechanism may be involved as well and could involve the venous system directly or indirectly. This is reinforced by the rabbit ear experiment by Zhuang et al., where a hyaluronic acid embolus introduced into the artery of a skin island flap
initially caused intense inflammation of the vessel wall and thrombosis and was then removed progressively by arteriovenous shunts as it migrated along the vessel. These hyaluronic acid globules, too large to pass through the capillary bed (Fig. 3), entered the associated vein to initiate inflammation and thrombosis once again, producing a combined arteriovenous picture of necrosis in 11 of 13 flaps.8 This mixed picture is often seen clinically with facial filler complications, producing lividity and swelling of the impacted area and may not appear for days.1,9–11

Recent work by Schelke et al.12,13 supports this mechanism. Using duplex ultrasound to identify the site of the hyaluronic acid embolus in an involved facial artery branch, they noted concurrent turbulence and dilatation in the associated vein. After successfully injecting hyaluronidase into and around the artery to dissolve the arterial embolus, not only was normal flow restored to the artery, but the abnormal nonpulsatile flow observed, suggesting a vein, disappeared. This may suggest that some of the hyaluronic acid had been shunted across to the vein from the artery and was dissolved simultaneously by the hyaluronidase. This study aims to reevaluate the arterial and venous anatomy of the ophthalmic angiosome within the orbit and the face; to define the site and character of its extraorbital anastomoses with branches of the other territory often implicated with filler complications, the facial angiosome; and to investigate the possible existence of arteriovenous shunts that may hold the key to our understanding of delayed onset of blindness in this devastating condition.

PATIENTS AND METHODS
To define the arterial and venous pathways to, from, and within the eye, 27 new fresh cadavers were studied. Human ethics approval was obtained (University of Melbourne HEAG 1340286.1)

These head and neck studies consisted of 16 unilateral lead oxide injections of the facial artery: four unilateral lead oxide injections of the internal carotid artery; four unilateral lead oxide injections of the internal jugular vein; three unilateral lead oxide injections of the internal carotid artery and contralateral barium injection of the internal jugular vein; and one lead oxide injection of the midline central forehead vein of the forehead to illustrate connections to both orbits. During injection, pressure was applied on each side of the nose to divert flow and to simulate a clinical scenario.

These were combined with 10 archival total body arterial and 10 total body venous studies over the past 30 years, focusing on the head and neck angiosomes. Arteries had been injected through the femoral artery and veins through the superior and inferior vena cava.
Except for the simultaneous arterial and venous studies, the mixture consisted of lead oxide, gelatin, and warm water described by Rees and Taylor. In the combined studies, lead oxide was replaced with barium in the vein, which was colored blue to distinguish it from the orange lead oxide–perfused artery.

The head and neck was radiographed and dissected the next day to allow the mixture to set. The integument was removed, noting the exit pathways of the vessels from the orbits, and radiographed separately from the skeleton (Fig. 4).

Both orbital contents were removed subperiosteally, dissected, and radiographed stepwise as fat was removed to display the vascular supply to the eyeball and attached muscles (Fig. 5). Finally, a “cap” of sclera was removed from the front or top of the eyeball to display the vascular network of the choroid (Fig. 6).

RESULTS

Notably, in each study, the unilateral injectant reached both orbits. Combining the archival and prospective studies, the following important findings were revealed.

Arterial

Within the Orbit

The ophthalmic artery entered through the superior orbital fissure in juxtaposition to the ophthalmic vein. Together, they crossed above the optic nerve from lateral to medial within the “cone” of rectus muscles. The artery branched into the supratrochlear, supraorbital, and external nasal arteries, before or after emerging from the superomedial border of the orbit, where they were fixed to the periosteum.

All branches arose early from the main trunk. Short posterior and long anterior ciliary branches supplied the eyeball and ophthalmic muscles. The short ciliary arteries pierced the sclera adjacent to the optic nerve. The long ciliary arteries passed forward to pierce the front of the eyeball at the point of attachment of the rectus and oblique muscles, supplying them en route, in addition to the front of the eyeball (Figs. 5, 7, and 8). These multiple short and long ciliary arteries supplied and formed a rich anastomotic network on the outer surface of the choroid along the inner surface of the sclera. This network consisted of individual territories provided by each ciliary artery, linked together by true or choke anastomoses (Figs. 6 and 8). The retinal artery arose early from the ophthalmic artery near the superior orbital fissure and entered the optic nerve at a variable point (Figs. 5 and 8). Other branches supplied the ethmoid air cells and skin of the outer canthus and connected with the infraorbital branch of the maxillary artery.

In the Face

Whether injected through the ophthalmic or the facial artery, they formed rich interconnections. Characterized by frequent true anastomoses, they revealed how an injectant could reach the orbit from a remote site, especially (1) between the

![Fig. 3. Hematoxylin and eosin staining of (above) the auricular artery in the rabbit ear flap with the lumen partially obstructed by gray-blue hyaluronic acid (arrows) and red blood cells, with a massive inflammatory eosinophilic granulocyte infiltration seen in the muscular wall of the artery and (below) two large veins containing hyaluronic acid globules and inflammation of their vessel walls. Note the size of these globules when compared with that of a red blood cell, which in turn correlates to the lumen of a capillary, suggesting that the hyaluronic acid embolus has bypassed the capillary bed by means of sizable arteriovenous shunts. (Used with permission from Zhuang Y, Yang M, Liu C. An islanded rabbit auricular skin flap model of hyaluronic acid injection-induced embolism. Aesthetic Plast Surg. 2016;40:421–427.)](image)
terminal (angular) branch of the facial artery and external nasal or supratrochlear branches of the ophthalmic artery; (2) between branches of each ophthalmic artery across the bridge of the nose; (3) between opposite facial arteries, especially in the lips and across the nose at its tip and near the nasal spine; or (4) directly via the infraorbital branch of the maxillary artery in the cheek. (Figs. 1 and 4).
Venous

**In the Orbit**

The venous drainage paralleled the arterial supply with a large, superior ophthalmic vein dominating the picture in all prospective studies (Fig. 5, above). A parallel venous network of ciliary veins accompanied the arterial plexus on the outside of the choroid, revealing an avalvular pathway to the ophthalmic vein, both reached by retrograde injection of the internal jugular vein (Fig. 6).

In our single central vein of the forehead injection of just 20 ml of lead oxide, it was diverted to both orbits by pressure on the cheeks and reached the cavernous sinus and a dural vein. [See Figure, Supplemental Digital Content 1, which shows lead oxide that has reached the orbit, cavernous sinus, and the middle meningeal sinus (highlighted orange) through a forehead injection of the midline forehead vein after pressure was applied on either side of the nose to divert flow to the orbit. The eyeball has been removed, http://links.lww.com/PRS/E177.]

*Fig. 5.* Radiographic studies showing (above, left) the large superior and smaller inferior ophthalmic veins draining to the cavernous sinus (arrows); (above, right) the venous drainage of the eyeball and muscles (detached posteriorly) from the long and short ciliary veins to the ophthalmic vein; and (below, left) the arterial supply from the ophthalmic artery to the eyeball and attached muscles. All muscles have been removed for clarity, except the superior rectus (detached posteriorly) and the inferior rectus (detached anteriorly) (arrows). (Below, right) The blood supply to the eyeball, muscles, and optic nerve from the retinal artery (large red arrow), short posterior ciliary arteries piercing the eyeball beside the optic nerve (arrows), the long anterior ciliary arteries supplying the ophthalmic muscles and the eyeball at their attachment anteriorly (black arrow), and the choke anastomosis between these ciliary arteries in the choroid between the small red arrows are shown. (Above, right, and below, left) Artery forceps are attached to the optic nerve, and choke arteries and veins in the muscles are highlighted with red arrows.
In the Face

The majority of the veins of the face were avalvular, revealed by complete retrograde filling regardless of injection site. The most important finding was the presence of a large midline or paramidline central forehead vein in nine of 10 archival and in all prospective studies that traveled down the forehead to form a rich plexus of veins in the glabella region (Fig. 4, below). From this plexus emerged (1) a large connecting vein to each orbit that entered the inner canthus and became continuous with the large superior ophthalmic vein.

Fig. 6. Dissections showing superior aspect of the choroidal blood supply with cap of sclera removed (left). (Right) In another study, the venous drainage of blue barium-filled avalvular ciliary veins that parallel the arteries and have filled retrogradely from the internal jugular and ophthalmic veins revealing their avalvular pathway is shown. Note (left) the territorial pattern of the short ciliary arteries in this study (numbered), entering the choroid near the optic disk; the long ciliary branches entering at the muscle attachments (large arrow); and their anastomotic interconnections (white arrows). The pupil and optic nerve are located (arrows).

Fig. 7. Dissection showing arteriovenous shunts in our first combined arterial and venous study where orange lead oxide in the artery has entered the blue barium-filled veins. (Left) Eyeball, optic nerve (large black arrow) with some of the ophthalmic muscles detached posteriorly, and the shunt (1) highlighted between the ophthalmic artery and vein. Labeled also are the (2) short ciliary, (3) long ciliary, and (4) supratrochlear arteries. (Right) Close-up view of this study showing the ophthalmic artery and vein crossing the optic nerve (large arrow) in juxtaposition. The vein contains lead oxide globules, some escaping through a branch, that have reached there through arteriovenous shunts (small arrows).
lower border of the mandible to pierce the deep fascia together (Fig. 4, below, right). [See Figure, Supplemental Digital Content 2, which shows (left) current and (right) archival studies showing overflow of arterial injections through arteriovenous shunts into veins of the glabella and face. (Left) Radiograph of our first combined arteriovenous study where the barium in the veins was too weak to register, but allowed the shunted lead oxide (black arrows) to be seen in the veins (blue arrows) in what is essentially an arterial study. (Right) Lead oxide has reached the veins colored blue through an archival total body artery-only injection. Note the interconnecting venous network in the glabella region and the separate pathways of the facial artery and vein in the nasolabial fold, http://links.lww.com/PRS/E178.]

Notably, venous drainage of the nose was directed upward from the nasal tip toward the root of the nose joining the rich plexus of veins in the glabellar region. In our archival studies,15 this was one of the few sites where valves were found directing flow toward this destination (Fig. 4, below, right).

Potential Arteriovenous Shunting

This pathway was demonstrated in archival and all prospective combined arterial and venous studies7,15 (Figs. 7 and 9). In our first combined study, amazingly, we found large globules of lead oxide from the artery (1) in the blue-stained superior ophthalmic vein beside the ophthalmic artery on both sides, close to the superior orbital fissure (Fig. 7); and (2) in the facial veins commencing near the inner canthus and traveling down the face. In the radiographic study of this

(Fig. 5, above); and (2) a large facial vein on each side, initially related to the facial artery at the inner canthus, which traveled separately near the nasolabial fold and then rejoined the artery at the

![Figure 8](https://example.com/figure8.png)

*Fig. 8. Schematic diagram showing the right ophthalmic artery viewed from above, with its branches to the face, the eyeball, some of the muscles, the anastomosis in the choroid between the long anterior and short posterior ciliary arteries, and the possible site of an arteriovenous (A-V) shunt. Potential sites, depending on the embolus size, that could produce (A and B) acute blindness, (C) delayed blindness, or (D and E) a visual field defect are indicated. Dotted line suggests choke vessel spasm and the ciliary territory that could be involved from the embolus D.*

![Figure 9](https://example.com/figure9.png)

*Fig. 9. (Left) Deep surface of the second combined arteriovenous study revealing the bilateral sites of arteriovenous shunts (arrows) with the right side of the figure enlarged, (right) which demonstrates large globules of orange lead oxide that have filled through a 0.5-mm arteriovenous shunt (black arrow) into the blue barium-filled facial vein and its metal clipped branch to the orbit (yellow arrows). Compare with Figure 4, below, right.*
subject, our barium concentrate was too weak to register and therefore did not mask this result. In the second study, not only did we find arteriovenous connections in the orbit and face, we found at least one connecting vessel 0.5 mm in diameter on each side in the inner canthus and nasolabial groove (Fig. 9) and another 0.3-mm-diameter shunt in the right orbit between the ophthalmic vessels. [See Figure, Supplemental Digital Content 3, which shows (left) a 0.3-mm arteriovenous shunt (arrow) that has diverted orange lead oxide from the artery and partially filled the blue ophthalmic vein (arrow) in our second combined arteriovenous study, and (right) the orange clumps of lead oxide (arrows) along the entire length of the ophthalmic vein that has extended to the glabella plexus, shunted from the adjacent ophthalmic artery in our third combined arteriovenous study (arrows). The optic nerve and pupil are highlighted (arrows), http://links.lww.com/PRS/E179.]

A third study was undertaken with a similar result involving the glabella plexus and ophthalmic vessels of the right orbit. It is noteworthy that arteriovenous connections are appearing in our studies where major arteries and veins are in juxtaposition (1) near the apex of the orbit, (2) in the glabella and inner canthal region of the face, and (3) elsewhere in the body.7

**DISCUSSION**

There are many questions. Why is the glabella region most commonly implicated and why can injection in virtually any area of the face produce blindness? Why does it occur literally at the end of the needle yet be delayed for hours, days, or weeks? Why are most totally blind yet some have only a visual field defect?

Our studies reveal the glabella and inner canthal region to be a vascular “bag of worms” offering easy targets for inadvertent filler injection, because the ophthalmic artery branches are concentrated and fixed to the orbital margins, making them vulnerable; there is a plexus of large-caliber, easily injected avalvular veins connected to both orbits that permit flow in any direction; there are arteriovenous connections joining these systems; and this is a common site for true anastomoses between the ophthalmic artery and angular branch of the facial artery. This last anastomotic connection, combined with the frequent true anastomotic freeways identified between ipsilateral and contralateral ophthalmic and facial artery angiosomes, explains the arterial pathway for embolic impaction from a remote site (Figs. 4 and 10).

The following scenarios provide plausible explanations, based on our anatomical findings, to explain the variable clinical presentations of visual involvement. The acute blindness in type I, associated with severe eyeball pain, must be attributable to impaction of the embolus and inflammation of the wall of the main trunk of the ophthalmic artery with associated spasm of the choke vessels around the perimeter of its anatomical territory within the orbit and in the face.5,6 This must be so because, if it were just a mechanical blockage of the main artery, there would be inflow of blood through these anastomotic vessels to rescue the impacted territory as shown in Figure 2.

In the face, vascular spasm of the ophthalmic branches produces pain, blanching, and late necrotic skin changes in the forehead, glabella, and nose6,11 (Figs. 1, above, left, and 4, above, right). In the orbit, the embolus impacts on the retinal...
artery and the choke vessels connecting the short and long ciliary arteries that supply the choroid, the eyeball ciliary muscles, and their nerve supply (Figs. 5, 6, and 8). This produces immediate blindness and ophthalmoplegia. If the bolus is large, especially fat, it is propelled farther against systolic pressure into the cerebral circulation through the circle of Willis to produce similar consequences ranging from headache to hemiplegia.\(^6\)

This arterial spasm then initiates the protective mechanism of arteriovenous shunting that we have demonstrated in the orbit and face, similar to that seen in the rabbit ear experiment by Zhuang et al.\(^8\) The embolus is then removed by means of shunts between the ophthalmic artery and vein, or between their branches, to escape into the cavernous sinus and beyond. However, this takes time. Because of the ischemic time of the retina of minutes, versus hours for muscle and nerve, it is too slow to prevent blindness, whereas in most cases, the ophthalmoplegia recovers as the embolus is dispersed and the spasm abates.\(^17\)

Alternatively, if the embolic bolus or particle size is smaller or breaks down to produce multiple emboli, especially hyaluronic acid, having reached the main trunk of the ophthalmic artery retrograde near the apex of the orbit, the hyaluronic acid is then flushed antegrade into one or more of its branches as the injection pressure is relaxed. This produces variable patterns of embolic obstruction, spasm, and visual impairment, depending on whether or not the retinal artery is compromised and whether some or all of the segmented areas of the choroidal circulation, interconnected by either choke or true anastomoses, are involved (Figs. 6 and 8).

The delayed blindness is harder to explain and could involve progressive migration of the embolus.\(^8\) Functionally, the retina has two separate circulations. The outer layer of photoreceptors in the retina is supplied by the high-volume, partially regulated choroidal circulation of ciliary arteries, and the inner layer of nerve cells is supplied by the lower volume, tightly regulated retinal circulation.\(^18\) Obstruction of either produces field defects or total blindness. Unfortunately, few reports include fundal and angiographic studies of the retina. Some do, and the largest is the Korean series of 44 cases.\(^2\) Except for 14 with visual field defects, there was either immediate blindness caused by retinal artery occlusion, or severe visual disturbance caused by ciliary artery involvement that progressed over hours or days to no light perception. In these delayed cases, there was early edema of the retina with severe choroidal ischemia on funduscopy and progressive thickening of the retina and choroid with leakage of fluorescein\(^19\) on angiography. This suggests a combined arterial and venous pattern of ischemia similar to that observed in the skin with hyaluronic acid filler complications,\(^6,10–12,19\) and in the rabbit ear experiment.\(^8\)

The other pathway involving the venous return could result from injecting the supratrochlear or glabella plexus of large thin-walled veins, easier to penetrate than an artery. Especially with raised orbital venous pressure and distended aural facial veins, the embolus could have been diverted into the ophthalmic artery through the extraorbital or intraorbital arteriovenous connections that we have demonstrated. This raises pressure could have resulted from the patient holding their breath, from laying the patient flat, or from steadying the head with fingers either side of the nose (e.g., while injecting a large bolus to augment the nasal bridge), thereby diverting the flow as demonstrated in our injection of the central forehead vein (see Figure, Supplemental Digital Content 1, http://links.lww.com/PRS/E177).

It is noteworthy that these arteriovenous connections were seen only in our combined arteriovenous cadaver studies when both the artery and vein were distended with the injectant. This suggests that if indeed these arteriovenous connections become active clinical shunts, factors leading to raised venous pressure should be avoided when injecting facial fillers or, alternatively, used to access the ophthalmic artery with hyaluronidase to dissolve the embolus.

Finally, on a purely speculative note, if intraorbital spasm of the ophthalmic artery does indeed occur in response to intraarterial emboli and produces total blindness, perhaps an antispasmodic could be administered immediately to allow the embolus to migrate farther into a side branch, possibly to produce a smaller field defect rather than total blindness, not unlike sublingual trinitrin used to relieve the arterial spasm of angina pectoris, or verapamil used by our radiology department to relieve catheter-induced arterial spasm complicating endovascular angiography.

Obviously, this would require preliminary studies, perhaps in the rabbit model used already.\(^20,21\) Because in every case of acute total blindness that occurred within minutes of impaction of the filler embolus, no case ever recovered spontaneously,\(^1,3\) it would seem that there would be nothing to lose, and perhaps something to gain with such a study.
CONCLUSIONS

We have demonstrated anatomically the vulnerable sites from where a filler injection could arise and then impact and cause ischaemia that may lead to spasm of the choke anastomoses that define the ophthalmic artery territories to produce field defects or total blindness, either (1) directly through its cutaneous branches, (2) indirectly through true anastomoses from a remote site, or (3) potentially through arteriovenous connections revealed in the glabellar region and orbit. We have shown also an avalvular venous pathway to the retina that may be implicated, especially with delayed presentation of visual involvement.

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REFERENCES


13. Schelke LW. Personal demonstration, July 24, 2019, 7th Floor Department of Anatomy and Neuroscience, Medical Building, University of Melbourne, Parkville, Melbourne, Victoria, Australia.


