

PHILADELPHIA, PA

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Disclosure of Relevant Relationships with Industry

<u>Speaker & Honoraria</u> – Allergan, Merz, Lumenis, Revance, Ortho (J&J), Ipsen & Stratpharma

Stockholder - Organogenesis, Revance

<u>Investigator</u> – Abbvie, ChemoCentryx, Revance, Stratpharma

<u>Consultant & Honoraria</u> – Galderma, Ipsen, Johnson & Johnson, Merz, Revance, Stratpharma & Teoxane

Catastrophes in Cosmetic Procedures:

- Embolic obstruction of blood flow (venous or arterial)
 - Ischemia in vascular pathways (0.05%)*
 - Skin Necrosis
 - **Blindness**
 - \rightarrow Cerebral vascular ischemia \rightarrow infarction \rightarrow stroke/hemiplegia
 - Prevention & Treatment

Daines SM. Complications...with...fillers. JAMA Facial Plast Surg. 2013;15(3):226-231.

*Paap MK, et al...retrobulbar hyaluronidase in...filler-induced blindness. Ophthal Plast Reconstr Surg 2020;36:231-38

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Vascular Compromise: Arterial or Venous

- Direct trauma to vessel wall by needle/cannula → Ecchymosis
- Obstruction of blood flow → Necrosis
- Arterial ischemia = immediate blanching + severe pain
 - -Direct intravascular injection of product \rightarrow Embolism \rightarrow Ischemia
 - ► Left untreated → tissue necrosis; blindness +/- CVA
- <u>Venous obstruction</u> = delayed reticulated, violaceous changes; +/- pain
 - -Direct compression of vessel lumen by product
 - -Indirect compression of 2°edema causing external force on vessel
 - ▶ Left untreated → partial/full-thickness necrosis
 → skin slough/scarring

Daines SM. Complications...with...fillers. JAMA Facial Plast Surg. 2013;15(3):226-231.

Urdiales-Galvez F et al. Treatment of . . . Filler Complications: Consensus. . . Aesth Plast Surg (2018) 42:498–510

Progression of vascular compromise after an embolic event





Clinical, Cosmetic and Investigational Dermatology 20

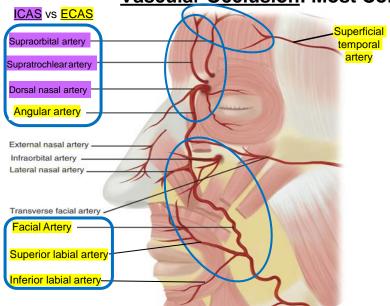
Vascular Compromise: Arterial or Venous Trauma

- Caused by fanning/threading technique in <u>subdermal plane</u>
- Injecting too much, too hard, too fast
- Narrow gauge needles or cannulas
- ? Blunt cannulas (No guarantee)
- Depot technique in supra-periosteum
- Large gauge needles
- Slow, gentle injections (<0.1 ml/min) Cohen JL. Drugs in Dermatol 2012:11s40-41



Funt, D; et al. Clinical, Cosmetic and Investigational Dermatology. 2013;6:295-316 Gladstone HB et al. Semin Cutan Med Surg. 2007;26(1):34-39.

Vascular Occlusion: Most Common Sites



Anatomic Danger Zones

- **≻**Forehead
- **≻Glabella**
- **≻Nose**
- ➤ Nasal Labial Fold
- **≻Lips**
- **≻**Temple

Signs and Symptoms of Vascular Occlusion

- **≻Acute Pain**
- **≻Blanching**
- > Reticulated Hyperemia
- **≻Necrosis**
- **≻Blindness**

Shancheng S, et al. A new injury severity scale for ocular complications. . . Front. Biosci (Landmark Ed) 2022; 27(2): 059 Kleydman, K; et al. Dermatol Surg 2012; 38:1-9; Kleintjes WG. Forehead anatomy. J Plast Reconstr Aesthet Surg 2007;60:593–606

Tissue Necrosis after Vascular Compromise: "No area of the face that is risk free"*



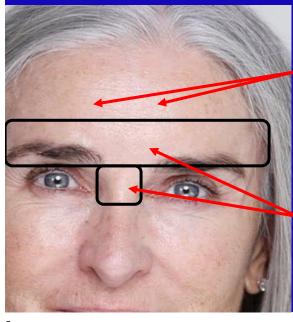




Funt, D; et al. Clinical, Cosmetic and investigational Dermatology 2013;6:299-316 *Li X, et al... visual loss secondary...filler injection. Ann Plast Surg 2015;75:258–260.

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Injection Depth for Fillers



A. Glabella & Lower Forehead

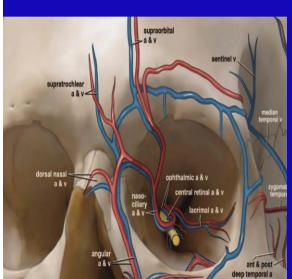
<u> ~ 2.5 cm At or Below Orbital Rim</u>
Inject Superficially → Intradermally

Beleznay K, Carruthers JDA et al. Avoiding...blindness. Dermatol Surg 2015;41:1097-17

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Injection Depth for Fillers

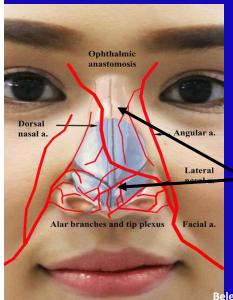




- 2.5 cm Above Orbital Rim
 Inject Deeply above periosteum b/c
 (ICA) supratrochlear & supraorbital
 a/v travel subcutaneously up the
 forehead
- <u> ~ 2.5 cm At or Below Orbital Rim</u> <u>Inject Superficially</u> → Intradermally

Beleznay K, Carruthers JDA et al. Avoiding...blindness. Dermatol Surg 2015;41:1097-17

Injection Depth for Fillers



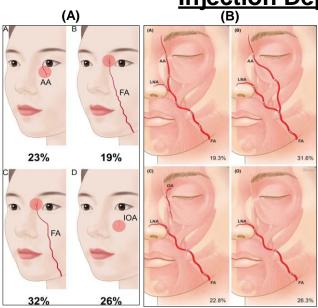
B. Nose Dorsum

- Lateral Nasal Artery (LNA) → (ECAS)
 ✓ blood to tip
- Dorsal Nasal Artery (DNA) → (ICAS)✓ blood to upper nose
- Inject in avascular deep supra-periosteal & supra-perichondral plane below the nasal SMAS

Beleznay K, Carruthers JDA et al. Avoiding...blindness. Dermatol Surg 2015;41:1097-17

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Injection Depth for Fillers



C. <u>Nasolabial Fold; Medial Cheek;</u> Periorbital Region

Aberrant course in subcutaneous plane:

(A) Facial artery:

- ▶23% Ophthalmic aa
- >26% Infraorbital aa or absent

(B)Angular artery:

- >22.8% Ophthalmic aa
- **▶26.3% Absent**
- <Supra-periosteal plane is safer>

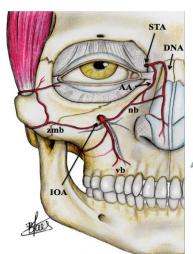
A) Lee H-J, et al. The Facial Artery: A comprehensive anatomical review. Clinical Anatomy 2018; 31:99-108.

B) Kim YS, et al. The anatomical . . .course of the Angular Artery. . . Dermatol Surg 2014;40:1070-6.

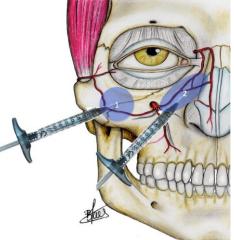
When Injecting *Nasolabial Fold*; *Medial Cheek*; *Periorbital Region* → Aspirate Before Injecting!!!



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IOA: infraorbital artery; zmb: zygomatico-malar branch; vb: vestibular branch; nb:nasal branch; AA: angular artery.; STA: supratrochlear artery.; DNA:dorsal nasal artery.



Injection patterns in infraorbital area: (1) supraperiosteal injection for malar enhancement and (2) retroorbicularis oculi injection for tear trough deformity correction. Note proximity to IOA and its branches.



Danger zones in infraorbital area: area #1 shows zygomaticomalar branch with risk of skin necrosis through skin perforators; area #2 shows risk of arterial embolization into internal carotid system through retrograde flow into the DNA and the STA, before reaching the ophthalmic, retinal artery, or even cerebral arteries.

Hufschmidt K. The infraorbital artery: . . . J. of Plastic, Reconstructive & Aesthetic Surgery (2019) 72, 131–136.



One day after intravascular occlusion of the angular artery¹



38 yo 3 days after NLF injection with hyaluronic acid gel²

1) Cox, S; et al. Complications of Injectables. Dermatologic Therapy. 2011;24,524-536

2) Grunebaum, L; et al. The Risk of Alar Necrosis. Dermatol Surg. 2009; 35: 1635-1640

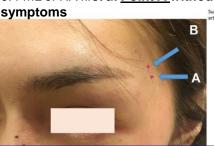
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Injection Depth for Fillers

D. Temple

- <u>Superficial temporal artery</u> → (ECAS)
 - ✓ blood to lateral face; scalp; forehead
- ◆Anastomoses w/supraorbital + supratrochlear aa → (ICAS)

A 31 yo ♀ patient was injected with 0.4 mL of HA first at **Point A** without





Point B: deep HA bolus 0.1 mL needle touched bone,
Left blurred vision + ptosis
Right picture: Point B likely into frontal br superficial temporal artery → anastomoses w/brs of supraorbital artery, causing HA embolus to ophthalmic or central retinal artery

Thanasarnaksorn W, Cotofana S C, et al. Severe vision loss. . . J Cosmet Dermatol 2018;17:712–718.

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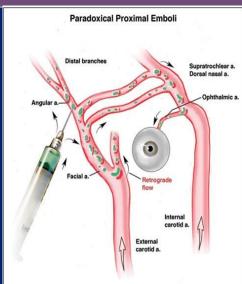
Thanasarnaksorn W, Cotofana S C, et al. Severe vision loss. . . J Cosmet Dermatol 2018;17:712–718.

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Vascular Compromise

► <u>Collaterals</u>: alternative pathways <u>Protective</u> – disperse product

<u>Anastomoses</u>: between internal/external carotid systems can be catastrophic: forceful injections into Right NLF → blindness in Left eye!

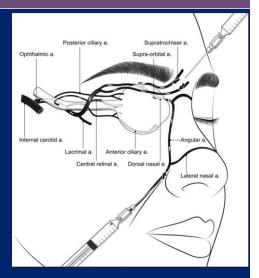


DeLorenzi C. Part 2: vascular complications. Aesthet Surg J. 2014; 34(4): 584-600.

Carruthers JD, Fagien S, Rohrich R et al. Blindness caused by cosmetic filler injection. . . Plast Reconst Surg 2014;134:1197–201

Retrograde embolization:

- √ High volume (>0.1mL)
- √ High force of injection
- ▲ Small syringe w/narrow g needle/cannula
 - Blocked needles/cannulas
 - Remove from patient to unblock

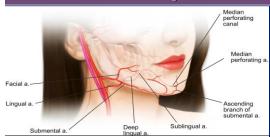


DeLorenzi C. Part 2: vascular complications. Aesthet Surg J. 2014; 34(4): 584-600.

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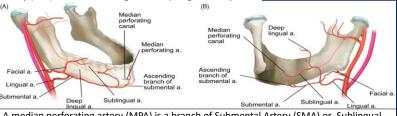
Vascular Compromise



Lingual artery is divided into two branches, a sublingual artery [SLA] near root of tongue & deep lingual artery

(1) Vascular variations in chin send filler emboli through anastomoses of SMA, SLA & DLA, necrosing the tongue

(2) SMA runs anteriorly thru mentum via Median Perforating Canal (MPC). Filler forced in chin can embolize into SMA, travel retrograde occluding DLA or SLA, necrosing the tongue.



A median perforating artery (MPA) is a branch of Submental Artery (SMA) or Sublingual (SLA) passing through the median perforating canal (MPC).

Arteries' through the 'Median Lingual Foramen' occluding the DLA or SLA, necrosing the tongue

the 'Median Perforating

(3) Filler emboli can flow into

Thanasarnaksorn W et al. Tongue necrosis...after chin... HA. J Cosmet Dermatol. 2023;00:1-8



48 hrs after HA chin injection: hyperemia & atrophic papillae

1-year later slight atrophy of tongue papillae

31 yo ♀: 1ml HA w/27g needle on periosteum into center of mentum, after 5 mins sharp pain in right <u>ear</u>; after 4 hrs pain on right side of tongue & slurred speech. Right side of tongue turned purple and papillae atrophied. Approx'ly 48 hrs later 9000U HAase injected around floor of mouth and right side of tongue → relief of pain w/in 30 mins.

Thanasarnaksorn W et al. Tongue necrosis...after chin... HA. J Cosmet Dermatol. 2023;00:1-8

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Vascular Compromise

Sign of 'impending necrosis'

- Reticulated ecchymosis after injection into the NLF/oral commissure with any filler
- Ischemia extends to limits of blocked vascular perfusion

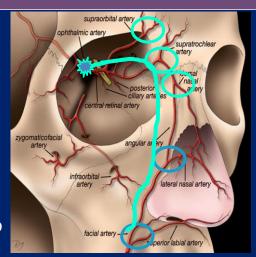


Kleydman, K et al. Nitroglycerin: A Review of Its Use . . . *Dermatol Surg* 2012; 38: 1889-97 Park SW, et al. Am J Ophthal 2012; 154(4): 653-662

Sign of 'impending necrosis'

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Lip or Nose injections can also cause blindness when filler emboli are forced to cross-over into internal carotid system



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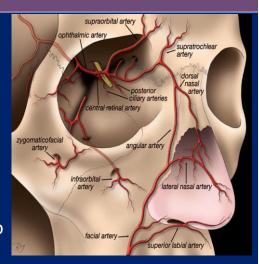
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Vascular Compromise

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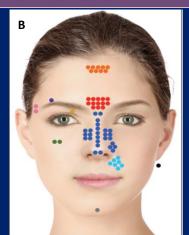
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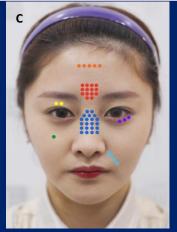


Kleydman, K et al. Nitroglycerin: A Review of Its Use... Dermatol Surg 2012; 38: 1889-97 Park SW, et al. Am J Ophthal 2012; 154(4): 653-662

Virtually Every Anatomic Location Where Filler is Injected on the Face is at Risk for Blindness*







Location of filler injection for each case of blindness

A.*Beleznay K, Carruthers JDA et al. Avoiding...blindness. *Dermatol Surg* 2015;41:1097-17.

B. Beleznay K, Carruthers JDA et al. Update on avoiding...blindness... *Aesthet Surg J* 2019; 39:662–674.

C. Lee W et al. Ocular complications: A review of literature *J Cosmet Dermatol*. 2020;19:772–781.

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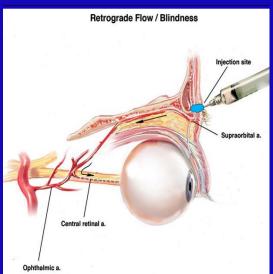
"There are no proven preventive measures or treatments for blindness secondary to soft tissue filler injections"*

Complete unilateral vision loss - initial symptom or sign:

- Ocular pain or headache → blurry vision
- Dizziness, nausea and vomiting
- Ophthalmoplegia
- Ptosis
- Violaceous reticulated changes → Skin necrosis
- Exotropia (eyes deviated outward)
- CNS infarction, hemiplegia
- 1 death 4 days after 5 mL of autologous fat into glabella (in 1 min)

Beleznay K, Carruthers JDA et al. Avoiding . . .blindness. *Dermatol Surg* **2015**;41:1097-17 Beleznay K, Carruthers JDA et al. Update... avoiding... blindness. *Aesthet Surg J* **2019**;39:662–74 *Lee W et al. Ocular complications of filler. . .A review of literature *J Cosmet Dermatol*. **2020**;19:772–78:

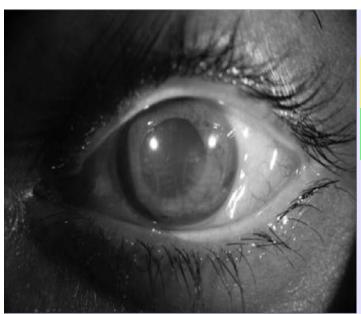
Arterial Occlusion: Central Retinal Artery



- A forceful injection can push a filler into an artery, exceeding its intraarterial pressure, driving the filler proximal to the origin of central retinal artery
- When injection stops and pressure is released, the filler moves distally occluding the retinal artery
- Abrupt pain in eye
- Immediate blurring or loss of vision

Park SW, et al. Am J Ophthal 2012; 154: 653-662; Kim YJ, et al. Ophthal Plast Reconstr Surg. 2011;27:e152–e155 DeLorenzi C. Part 2: vascular complications. Aesthet Surg J. 2014; 34: 584-600

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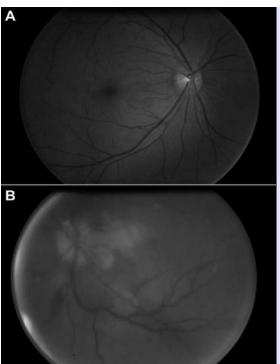


3 days after **PLLA** injected into periorbital area of the left eye:

Corneal epithelial defect and Descemet's membrane folds after injury. The left upper eyelid is manually retracted, masking the ptosis. Note the temporal conjunctival chemosis.

Severe Visual Loss and Orbital Infarction Following Periorbital Aesthetic Poly-(L)-Lactic Acid (PLLA) Injection.

Roberts, Steve; Arthurs, Bryan *Ophthalmic Plastic & Reconstr-uctive Surgery.* 28(3):e68-e70, May/June 2012. DOI: 10.1097/IOP.0b013e3182288e4d

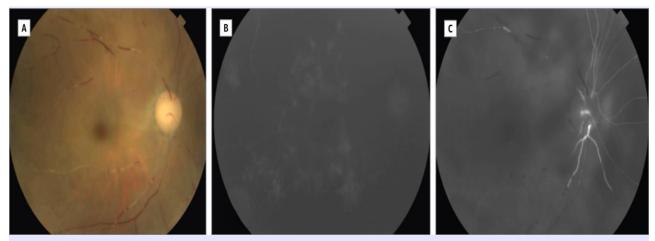


A: Normal, posterior pole fundus, photograph of unaffected (R) eye.

B: 3 days after **PLLA** injected into periorbital area of the left eye: Macular pallor, venous dilatation, mild arteriolar narrowing, & large inner retinal hemorrhage. Corneal edema limits clarity of fundus photograph.

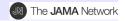
Severe Visual Loss and Orbital Infarction Following Periorbital Aesthetic Poly-(L)-Lactic Acid (PLLA) Injection. Roberts, Steve; Arthurs, Bryan *Ophthalmic Plastic & Reconstructive Surgery.* 28(3):e68-e70, May/June 2012. DOI:0.1097/IOP.0b013e3182288e4d

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Same Day: Autologous Fat injected into Forehead. A., Color photograph of fundus of the right eye reveals diffuse retinal whitening and lipid filled arterioles. B, Fluorescein angiography of the right eye in an early frame demonstrates delayed patchy choroidal filling. C, Later frame of the fluorescein angiogram demonstrates incomplete filling of retinal arteries and patchy choroidal filling.

JAMA Ophthalmol. 2014;132(5):637-639.



Urgent Treatment of Retinal Embolus

60 - 90 minutes to salvage eye!



Abrupt pain in eye!? Stop injecting - stay calm

- > Attempt aspiration
- ➤ Watch for local skin changes of vascular compromise
- ► Get Hyaluronidase out of refrigerator
- Check visual acuity: patient reads text
 - ✓ Swinging flashlight fixed pupil; no accommodation
 - ✓Ocular motility ophthalmoplegia; exotropia
 - ✓ Eyelid position ptosis
 - ✓ Fundus evaluation ?
- Headache; nausea & vomiting; focal hemiplegia

1) Beer K et al. J Clin Aesthet Dermatol. 2012;5(5):44-47; 2) Carruthers JDA, et al. Plast Reconstr Surg 2014; 134(6): 1197-1201 3) DeLorenzi C, Dermatol Surg 2014;40:832-841; 4) Weinberg MJ, Solish N. Facial Plast Surg. 2009;25(5):324-328

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Urgent Treatment of Retinal Embolus





Pain continues in eye + focal signs!? - stay calm

- Call for an ambulance to ER!
- Induce vasodilation: beware of patient's medical conditions/allergies
 - Nitroglycerin 2% paste/patch; or sublingual 0.6 mg pill
 - Procardia (nifedipine) 10mg gel cap, chewed [Ca-channel blocker]
 - Viagra (sildenafil) 100mg, chewed
 - Breathe in paper bag (increase CO₂)
 - Warm compresses → supine
 - Vigorous ocular massage, repetitive (look downward w/eyes closed)

1) Beer K et al. J Clin Aesthet Dermatol. 2012;5(5):44-47; 2) Carruthers JDA, et al. Plast Reconstr Surg 2014; 134(6): 1197-1201 3) DeLorenzi C, Dermatol Surg 2014;40:832-841; 4) Weinberg MJ, Solish N. Facial Plast Surg. 2009;25(5):324-328



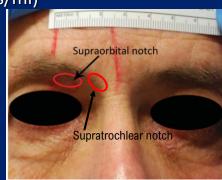
Urgent Treatment of Retinal Embolus

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Pain continues in eye + focal signs!? - stay calm

- ➤ Inject Hyaluronidase (HYAL) stat:
 - ♦ > 2 5⁺ mL (>300-1500 U) HYAL (150 to 200 units/ml)
- ➤ Supratrochlear & Supraorbital notch
 - Beneath upper orbital rim
 - 2 depressions (medial/mid pupillary line)
 - Insert needle/blunt cannula into foramina from above



Goodman GJ, Clague MD. Dermatol Surg. 2016;42(4):547-549

Thanasarnaksorn W, Cotofana S, et al. Severe vision loss. . . J Cosmet Dermatol 2018;17:712-718

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Urgent Treatment of Retinal Embolus

60 - 90 minutes to salvage eye!





- ➤ Supratrochlear & Supraorbital notch
- ✓ HYAL → immediate relief of visual Sx's
 - ➤ Blue circle = injected HYAL
 - ➤ Blue arrows = retrograde flow of HYAL
 - ➤ Supratrochlear aa → Ophthalmic aa →
 - Green arrows = Central Retinal aa Dissolves HA embolus





Goodman GJ, Clague MD. *Dermatol Surg*. 2016;42(4):547-549 Thanasarnaksorn W, Cotofana S, et al. Severe vision loss. . . *J Cosmet Dermatol* 2018;17:712–71



Urgent Treatment of Retinal Embolus

60 - 90 minutes to salvage eye!



Consult ophthalmologist & neurologist stat

- Decrease intraocular pressure:
 - Diamox 500 mg, po (acetazolamide) [carbonic anhydrase inhibitor] [sulpha]
 - lopidine gtt (apraclonidine) [selective α-adrenergic agonist]
 - Timoptic XE gtt (timolol) [non-selective $\beta_{1&2}$ adrenergic receptor blocker]
 - Lumigan gtt (bimatoprost) [prostamide → antiglaucoma]

Send patient for emergency ophthalmic/neurologic care

- Corticosteroids, oral (reduce inflammation)
- > ASA 325mg, sublingual (anti-coagulation/thrombolysis)
- Vigorous ocular massage, constant/prolonged

Urdiales-Galvez F. et al Treatment of. . . Filler Complications: Consensus Recommendations. Aesth Plast Surg (2018) 42:498-510. Weinberg MJ, Solish N. Facial Plast Surg. 2009;25(5):324-328; Carruthers JDA, et al. Plast Reconstr Surg 2014; 134(6): 1197-1201

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Urgent Treatment of Retinal Embolus

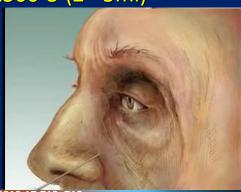




- Wait for transport to Emergency Room
- ➤ Retro-bulbar injections of HYAL >300-1500 U (2 5ml)
- > 25g needle or blunt cannula (1 ½ inch)
- ► Inferotemporal quadrant ~1 inch into orbit
- $\triangleright O_2$
- ▶ Legs up → patient horizontal
- Vigorous ocular massage, constantly

Goodman GJ, Clague MD. Dermatol Surg. 2016;42(4):547-549 Thanasarnaksorn W, Cotofana S, et al. Severe vision loss. . . J Cosmet Dermatol 2018;17:712-718





How to Avoid Filler Vascular Complications

- Know anatomy; caution in areas of large vessels
- >Inject slowly, gently & deliberately
 - » Slow, low pressure & volumes: 0.1 0.2 ml per minute
 - » Large bore needles/cannulas at proper depth
 - » Aspirate before injecting
 - » Epinephrine + lidocaine for vasoconstriction
 - » Move needle tip while injecting → retrograde
- Beware of patients with post-op scars

Cohen JL. Dermatol Surg. 2008;34:S92-99. Bailey SH et al. Aesthet Surg J. 2011;31(1):110-121. Carruthers JDA, et al. Plast Reconstr Surg 2014; 134(6): 1197-1201. Glogau RG, Kane MA. Dermatol Surg. 2008;34(suppl1):S105-S109. Thanasarnaksorn W, J Cosmet Dermatol 2018;17:712-718 Beleznay K, Carruthers JDA et al. Avoiding...blindness. Dermatol Surg 2015;41:1097-17

