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e.p.t.q.

HA filler
& Science

Clinical Studies of e.p.t.q.

Approach to solve
the tragic event of blindness

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Effectiveness of Retrobulbar Hyaluronidase Injection in an Iatrogenic Blindness Rabbit Model Using Hyaluronic Acid Filler Injection

EXPERIMENTAL

Effectiveness of Retrobulbar Hyaluronidase Injection in an Iatrogenic Blindness Rabbit Model Using Hyaluronic Acid Filler Injection

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Background: Blindness caused by soft-tissue filler injection is the most tragic complication, with no standard treatments until recently. Retrobulbar hyaluronidase injection has been proposed as the treatment, but its effectiveness in visual compromise remains to be determined. The authors aimed to determine the effectiveness of retrobulbar hyaluronidase using soft-tissue filler in an iatrogenic blindness animal model.

Methods: New Zealand White rabbits were used to simulate the hyaluronic acid–associated vascular occlusion model. A volume of 0.7 to 1.6 ml of hyaluronic acid filler was injected into the internal carotid artery to create a retinal artery occlusion. The rabbits were administered retrobulbar hyaluronidase (3000 IU) at different postobstruction time points (5 and 10 minutes). No intervention was given to the control group. Fundus photography was performed before and immediately after the filler injection and immediately after the administration of retrobulbar hyaluronidase. Electroretinography was performed after 60 minutes to confirm the retinal reperfusion and electrophysiologic function.

Results: All of the experimental eyes recorded total occlusion after hyaluronic acid injection. Three eyes with a completely occluded retinal artery following retrobulbar hyaluronidase treatment showed improved retinal reperfusion by fundus photography and corresponding electroretinography. Despite admin-

DISCUSSION

Discussion: Effectiveness of Retrobulbar Hyaluronidase Injection in an Iatrogenic Blindness Rabbit Model Using Hyaluronic Acid Filler Injection

Steven Fagien, M.D.
Boca Raton, Fla.

I would like to congratulate the authors on perhaps the first well-designed, physiologic, and encouraging animal model experiment to further our understanding of the potential rescue therapies for a tragic adverse event.[1] The possibility of causing injection-related visual compromise from a cosmetic injectable treatment using hyaluronic acid ranks as one of the greatest fears of cosmetic providers and patients alike.

Another look at the history and progress on this issue is warranted and might explain some of the confusion on this highly debated topic. I first postulated the potential of visual recovery and restoration after injection-related visual compromise by retrobulbar administration of hyaluronidase from seemingly distant sites of injection (i.e., upper lip injections with hyaluronic acid). Furthermore, there was a rivaled concern regarding this theoretic approach and the complexity and risk of delivering a retrobulbar injection by an individual less experienced with this technique, which was quite understandable. Shortly thereafter, Jean Carruthers and I (including a few others from that advisory group) published on this and the debate began.[3] As there was a growing awareness and concern about this adverse event and because there was no proof at that time to support or refute this technique, it seemed prudent to at least convey to our colleagues what seemed to be a relatively reasonable option for an

Lee W, Oh W, Ko HS, Lee SY, Kim KW, Yang EJ. Effectiveness of retrobulbar hyaluronidase injection in an iatrogenic blindness rabbit model using hyaluronic acid filler injection. Plast Reconstr Surg. 2019;144:137–143.

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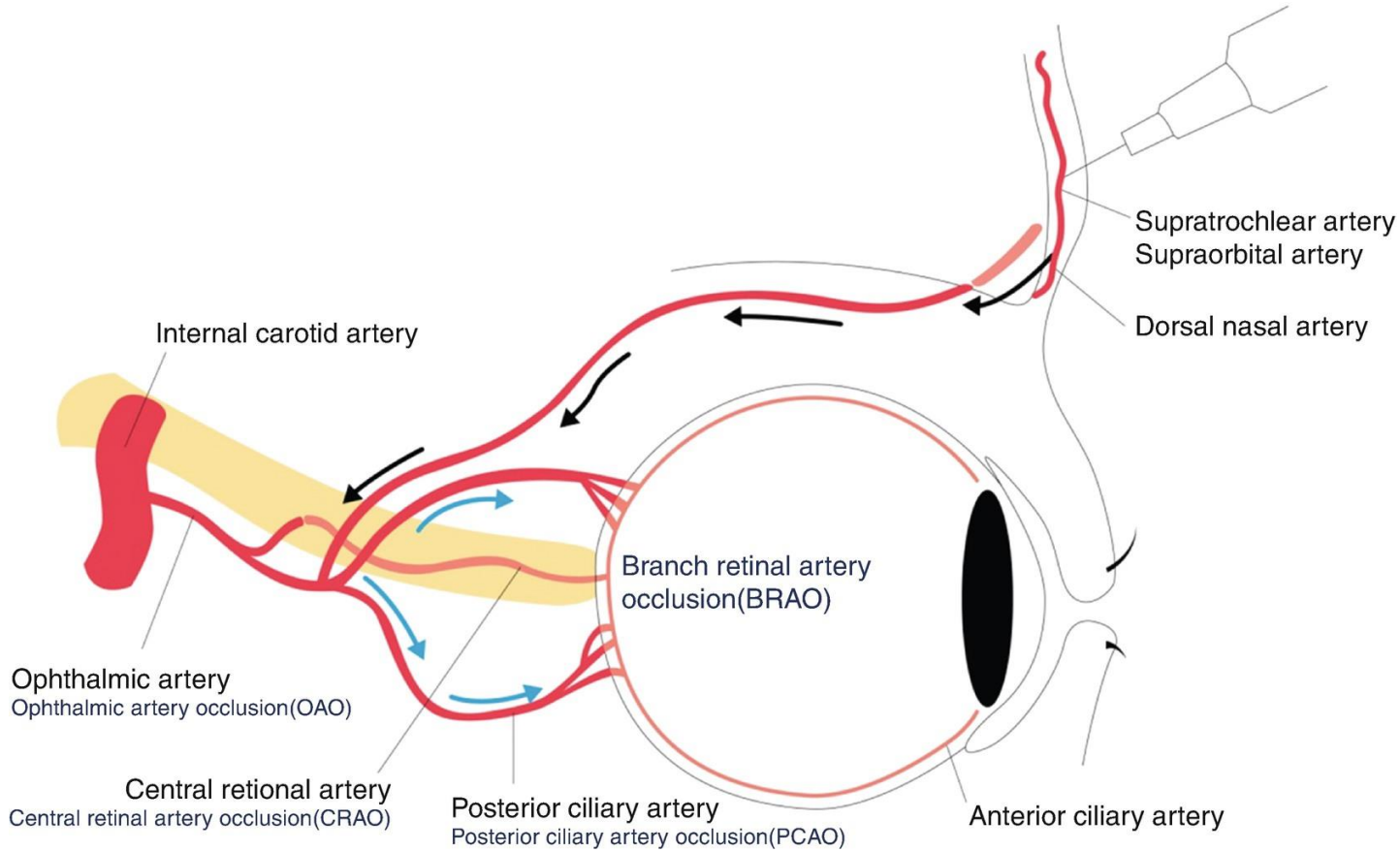

Supratrochlear artery
Supraorbital artery
Dorsal nasal artery
Internal carotid artery
Branch retinal artery occlusion(BRAO)
Ophthalmic artery
Ophthalmic artery occlusion(OAO)
Central retional artery
Central retinal artery occlusion(CRAO)
Posterior ciliary artery
Posterior ciliary artery occlusion(PCAO)
Anterior ciliary artery

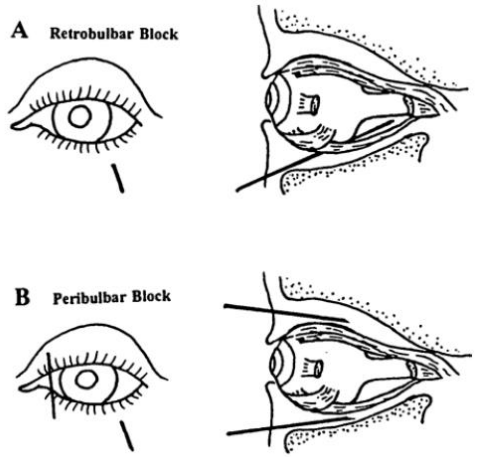
Background & Objective

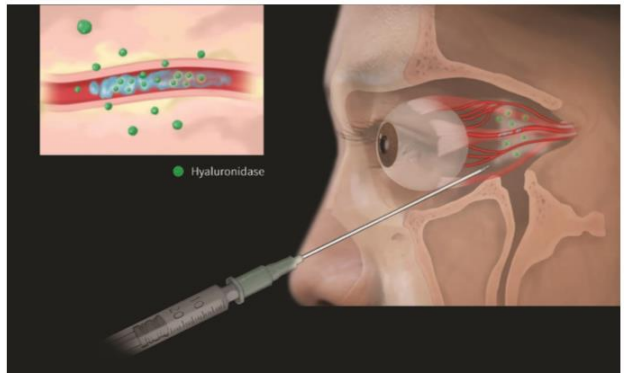
- HA filler complications: visual compromise (**loss of vision**, ophthalmoplegia, and ptosis)

① Subcutaneous hyaluronidase injection[1]

② Peribulbar hyaluronidase injection[2]

③ **Retrobulbar hyaluronidase Injection**





Retrobulbar hyaluronidase injection

- **Can retrobulbar hyaluronidase reach the ophthalmic artery branch ??**
- **Objective: to determine the effects of retrobulbar hyaluronidase on hyaluronic acid –induced retinal occlusion in a rabbit model**

1 Wang M, Li W, Zhang Y, Tian W, Wang H. Comparison of intra-arterial and subcutaneous testicular hyaluronidase injection treatments and the vascular complications of hyaluronic acid filler. Dermatol Surg. 2017;43:246–254.
2 Carruthers J, Fagien S, Dolman P. Retro or peribulbar injection techniques to reverse visual loss after filler injections. Dermatol Surg. 2015;41(Suppl 1):S354–S357.

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Materials and Methods

Materials

- Subject: New Zealand White rabbits (2.3 to 2.6kg)
  Experimental group1: 2 rabbits / Experimental group2: 2 rabbits:
  Control group: 2 rabbits
- HA filler: e.p.t.q. S100 (JETEMA Co., Ltd.), 30G needle
- Hyaluronidase: Liporase (Daehan New Pharm Co.), 26G needle

Method

- HA was injected into the internal carotid artery to create a retinal artery occlusion
- Experimental group1: administered retrobulbar hyaluronidase (3000IU, 2ml) 5 mins after HA injection
- Experimental group2: administered retrobulbar hyaluronidase (3000IU, 2ml) 10 mins after HA injection
- Control group: No intervention was given
- Fundus photography before/immediately after HA injection/immediately after retrobulbar hyaluronidase injection
- Electroretinography 60 mins after retrobulbar hyaluronidase injection

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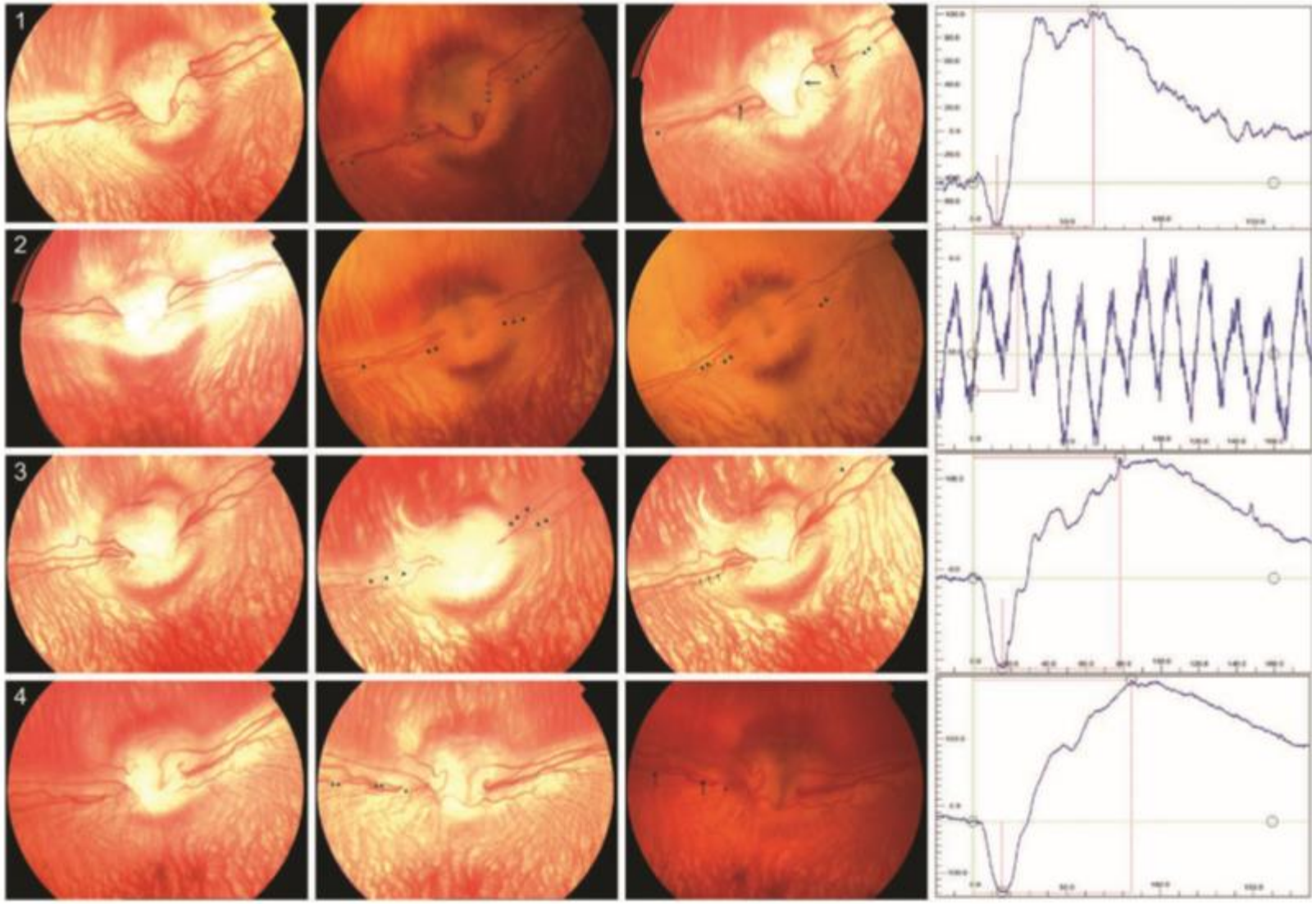
Results for experimental group



Before HA injection | After HA injection | After retrobulbar hyaluronidase injection | Electroretinogram 60 mins after retrobulbar hyaluronidase injection

	Results
1, 3, 4	• Fundi intact before HA injection • Retinal artery occlusion (arrowhead) • Fundus reperfusion (arrow) • Normal electroretinographic findings
2	• Fundi intact before HA injection • Retinal artery occlusion (arrowhead) • No fundus reperfusion (arrowhead) • Abnormal electroretinographic findings

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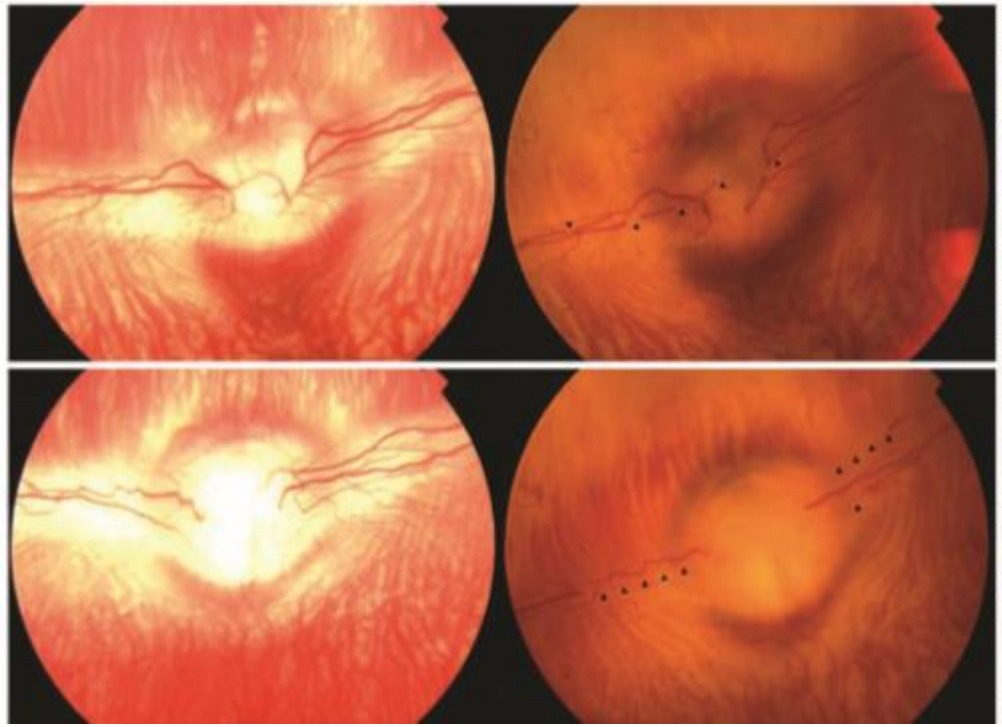
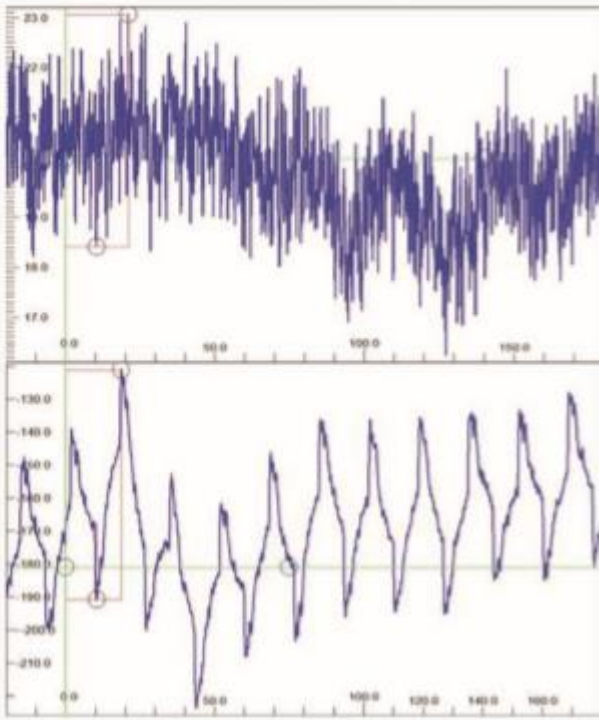
Results for control group



Before HA injection

After HA injection



Electroretinogram 60 mins
After HA injection

Results

- Fundi intact before HA injection
- Retinal artery occlusion (arrowhead)
- Abnormal electroretinographic findings
- No natural healing occurred

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Summary of the Experiment

	Weight (kg)	HA Filler (ml)	Time (min) to hyaluronidase Injection	Hyaluronidase Concentration (IU)	ERG Waveform response*	a-Wave (V)*	b-Wave (V)*
Control	2.6	0.9	-	Not injected	Abnormal	1.3	2.3
Control	2.62	0.7	-	Not injected	Abnormal	27	68.5
1	2.36	0.8	5	3000	Normal	47.8	168.5
2	2.5	1.4	5	3000	Abnormal	2.8	11.5
3	2.38	0.9	10	3000	Normal	102.8	254.5
4	2.6	1.6	10	3000	Normal	111.5	274

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Key Message

- In case of iatrogenic blindness, e.p.t.q. fillers were degraded by retrobulbar hyaluronidase injection and re-gain vision in rabbit model.
- Retrobulbar hyaluronidase may be an effective evidence-based treatment option for humans
- Key factors: Hyaluronidase concentration & Injection time
- When a patient complains of visual disturbance or ocular pain after filler injection, the doctor should immediately check for direct and indirect pupil reflex and could consider high-dose retrobulbar hyaluronidase.
- e.p.t.q. fillers is a reference filler that can be degraded by retrobulbar injection of 3,000 IU hyaluronidase

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Dermal Integration-Forehead

Clinical application of a new hyaluronic acid filler based on its rheological properties and the anatomical site of injection

Lee *et al. Biomedical Dermatology* (2018) 2:22
https://doi.org/10.1186/s41702-018-0032-9

Biomedical Dermatology

RESEARCH Open Access

Clinical application of a new hyaluronic acid filler based on its rheological properties and the anatomical site of injection

Won Lee[1], Jeung-Hyun Yoon[2], Ik-Soo Koh[3], Wook Oh[4], Ki-Wook Kim[5] and Eun-Jung Yang[6*]

Abstract

Background: Hyaluronic acid (HA) filler is the most commonly used filler for soft tissue augmentation. There are numerous commercially available HA fillers in the cosmetic market, and there are guidelines for each filler as determined by the manufacturing company. The successful use of injectable fillers requires an understanding of each option available so that the most appropriate form of hyaluronic acid may be selected for patients. The purpose of this study was to determine whether newly developed HA fillers are appropriate for forehead augmentation considering their rheological properties and the anatomical site of injection.

Methods: The rheological properties of new HA fillers were assessed e.p.t.q. S100, S300, S500 (Jetema®). Comparing the rheological properties, the authors chose e.p.t.q. S300® for forehead augmentation. The filler

Lee W, Oh W, Ko HS, Lee SY, Kim KW, Yang EJ. Effectiveness of retrobulbar hyaluronidase injection in an iatrogenic blindness rabbit model using hyaluronic acid filler injection. Plast Reconstr Surg. 2019;144:137–143.

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Background & Objective

- Numerous commercially available HA fillers
- Guidelines are determined by the manufacturing company
- Shortage of objective data for all available fillers
- Key to successful use of fillers: Understanding of each option available
- Objective: to determine whether e.p.t.q. S300 is appropriate for forehead augmentation considering its rheological properties and the anatomical site of injection

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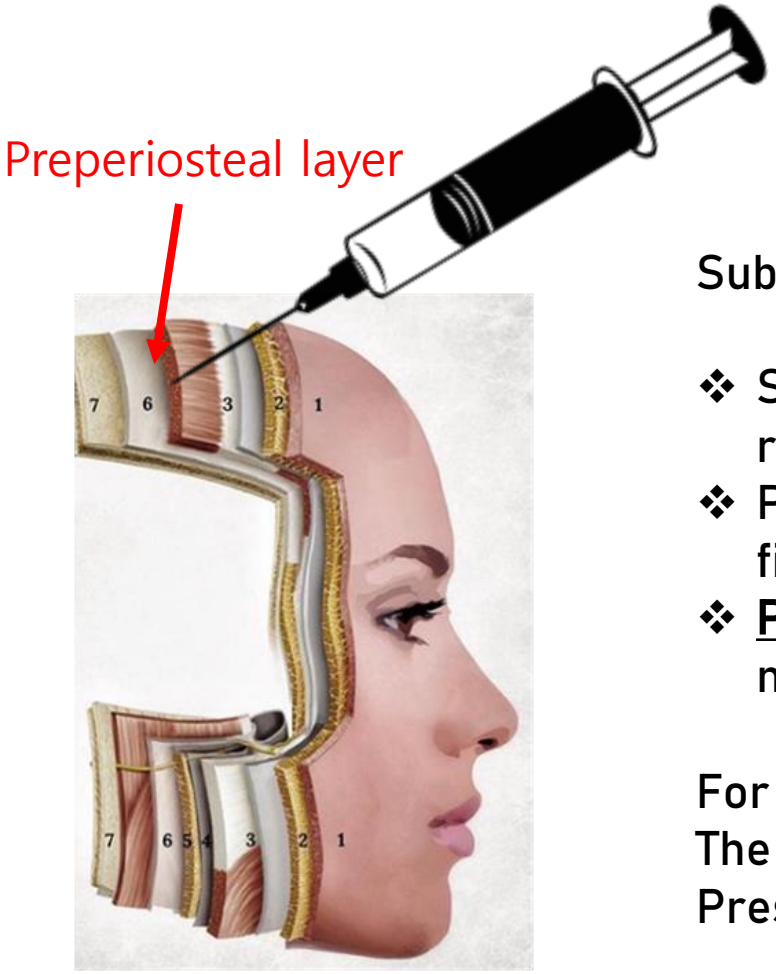
Things to consider in choosing a right filler for forehead augmentation… *anatomy*



Subcutaneous? Postperiosteal? Or **Preperiosteal**?

- Subcutaneous layer → contour irregularities and a relative risk of vascular complications
- Postperiosteal layer → difficult to ensure the space for the filler between the periosteum and skull
- **Preperiosteal layer** → less risk of side effects, clinically the most commonly used layer

For injection in preperiosteal layer,
The filler must have sufficient lift to withstand the compressive Pressure of the frontal muscle.

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Things to consider in choosing a right filler for forehead augmentation… *its rheological properties*

Cohesiveness: a resistance to compression/stretching forces in a vertical plane once the product is implanted
G' (storage, elastic modulus): elasticity of the gel, its capacity to recover its initial shape to resist deformation

If the filler is too soft, a filler can spread relatively, difficult to shape the target area
If the filler is too rigid, it becomes difficult to attain the desired shape
You need a filler <u>not too soft, not too rigid, volume well maintained</u>

Table 1 Rheological property of hyaluronic acid fillers

Product	G′ (Pa)	G″ (Pa)	Complex viscosity (cP)	Cohesiveness (*N*)	Tan δ	Complex modulus	Elasticity (%)
Restylane	349	145	3,011,188	0.3509	0.4180	378	71
Juviderm Volbella	99	21	814,593	0.3046	0.2189	101	83
e.p.t.q. S100	37	15	323,859	0.4184	0.4269	40	71
e.p.t.q. S300	128	27	1,048,864	0.6102	0.2137	131	83
e.p.t.q. S500	224	57	1,847,607	0.8776	0.2551	231	80

→ **e.p.t.q. S300 exhibited sufficient <u>cohesiveness</u> and <u>elastic moduli</u>**

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Method and Result

Method

- 40 patients (40Female, mean age 31.3 yrs)
- Preperiosteal injection for forehead augmentation
- e.p.t.q. S300 2~5cc
- Follow-up visit average 3 months
- Questionnaire to patients to rate the degree of satisfaction based on a 4-point scale
  at end of treatment & 15 days later in terms of result and treatment convenience
  (0, worse; 1, little satisfied; 2, satisfied; 3, very satisfied)

Result

- Result of Questionnaire:
  at end of treatment: 90% very satisfied; 10% satisfied
  15 days later: 95% very satisfied; 5% satisfied
- None of the patients experienced bleeding, hematomas, bruising, or vascular compromise, delayed filler migration, granulomas, or swelling.

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Key Message

- e.p.t.q.S300 has sufficient cohesiveness and elastic modulus for forehead augmentation in preperiosteal layer.

- Sufficient cohesiveness makes molding easier and migration less likely.

- When injected for forehead augmentation, 95% of patients were very satisfied with the result and treatment convenience.

  → e.p.t.q.S300 is a good option for forehead augmentation

- None of the patient had complications

  → e.p.t.q.S300 is a safe filler for forehead augmentation

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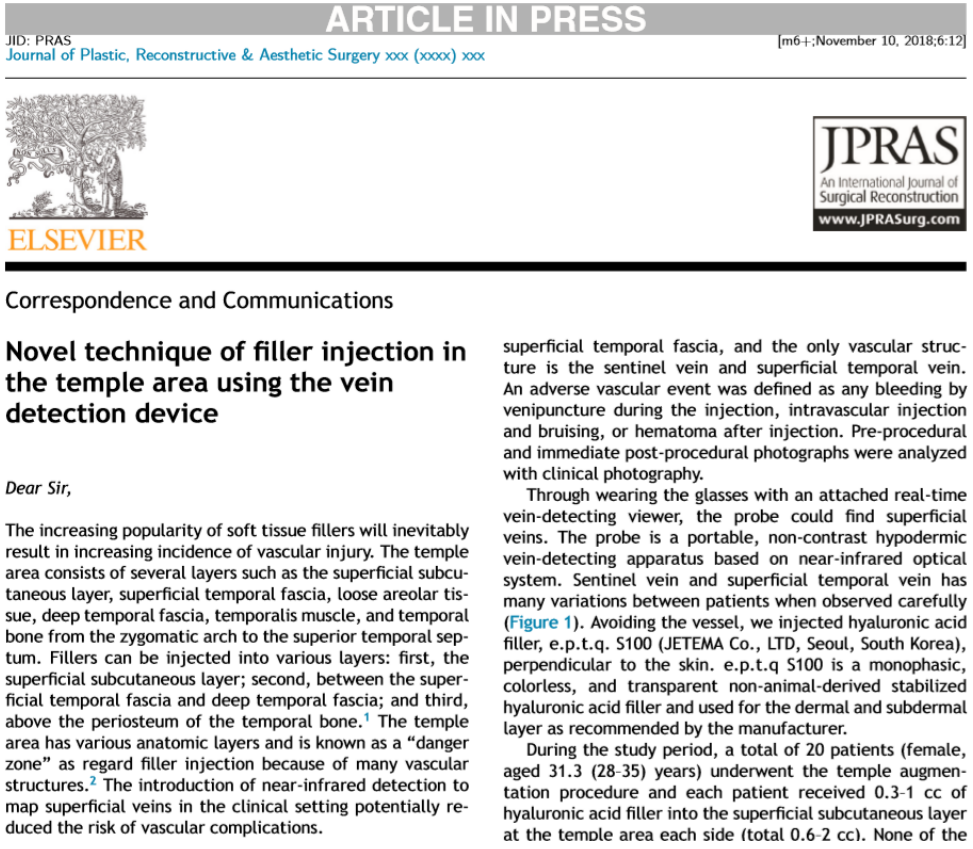
Dermal Integration-Temple

Novel technique of filler injection in the temple area using the vein detection device



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Journal of Plastic, Reconstructive & Aesthetic Surgery xxx (xxxx) xxx
[m6+;November 10, 2018;6:12]

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Correspondence and Communications

Novel technique of filler injection in the temple area using the vein detection device

Dear Sir,

The increasing popularity of soft tissue fillers will inevitably result in increasing incidence of vascular injury. The temple area consists of several layers such as the superficial subcutaneous layer, superficial temporal fascia, loose areolar tissue, deep temporal fascia, temporalis muscle, and temporal bone from the zygomatic arch to the superior temporal septum. Fillers can be injected into various layers: first, the superficial subcutaneous layer; second, between the superficial temporal fascia and deep temporal fascia; and third, above the periosteum of the temporal bone.[1] The temple area has various anatomic layers and is known as a "danger zone" as regard filler injection because of many vascular structures.[2] The introduction of near-infrared detection to map superficial veins in the clinical setting potentially reduced the risk of vascular complications.

superficial temporal fascia, and the only vascular structure is the sentinel vein and superficial temporal vein. An adverse vascular event was defined as any bleeding by venipuncture during the injection, intravascular injection and bruising, or hematoma after injection. Pre-procedural and immediate post-procedural photographs were analyzed with clinical photography.

Through wearing the glasses with an attached real-time vein-detecting viewer, the probe could find superficial veins. The probe is a portable, non-contrast hypodermic vein-detecting apparatus based on near-infrared optical system. Sentinel vein and superficial temporal vein has many variations between patients when observed carefully (Figure 1). Avoiding the vessel, we injected hyaluronic acid filler, e.p.t.q. S100 (JETEMA Co., LTD, Seoul, South Korea), perpendicular to the skin. e.p.t.q S100 is a monophasic, colorless, and transparent non-animal-derived stabilized hyaluronic acid filler and used for the dermal and subdermal layer as recommended by the manufacturer.

During the study period, a total of 20 patients (female, aged 31.3 (28-35) years) underwent the temple augmentation procedure and each patient received 0.3-1 cc of hyaluronic acid filler into the superficial subcutaneous layer at the temple area each side (total 0.6-2 cc). None of the

Lee W, Oh W, Ko HS, Lee SY, Kim KW, Yang EJ. Effectiveness of retrobulbar hyaluronidase injection in an iatrogenic blindness rabbit model using hyaluronic acid filler injection. Plast Reconstr Surg. 2019;144:137–143.

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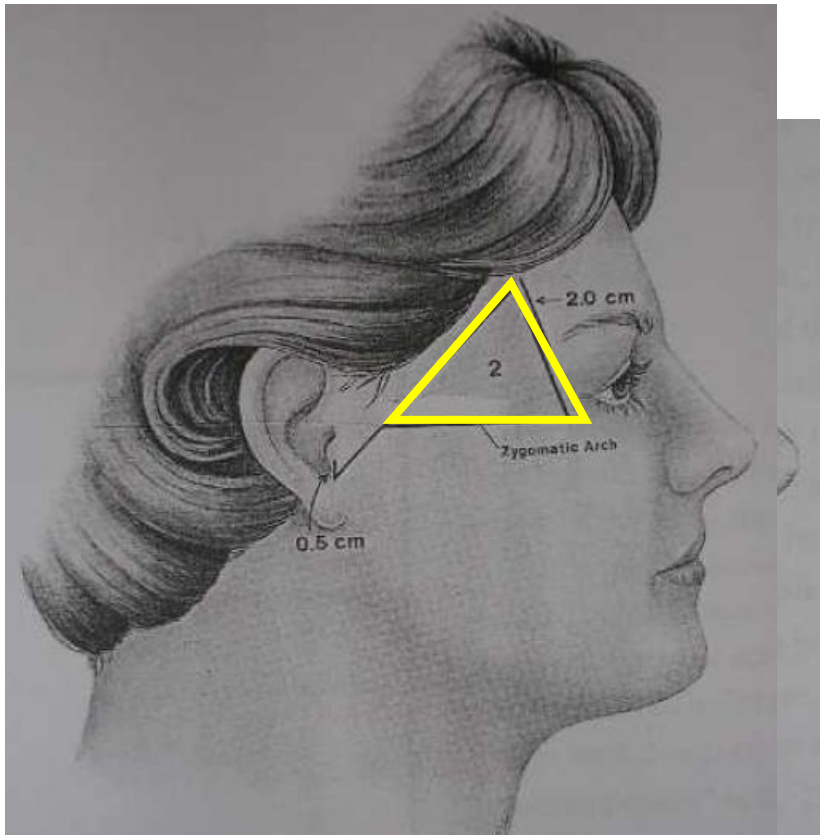
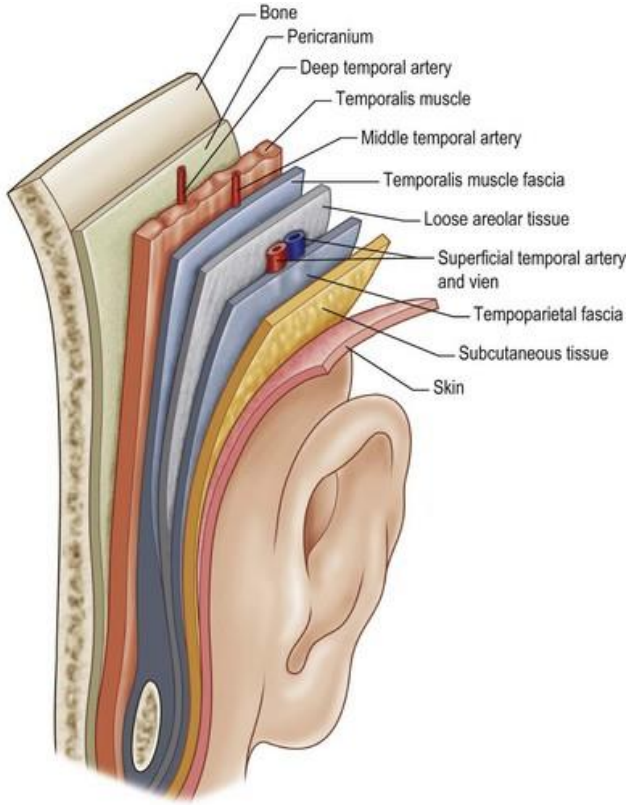
Background & Objective

- Increasing popularity of soft tissue fillers → increasing incidence of vascular injury
- Temple area has various anatomic layers & vascular structures→ danger zone





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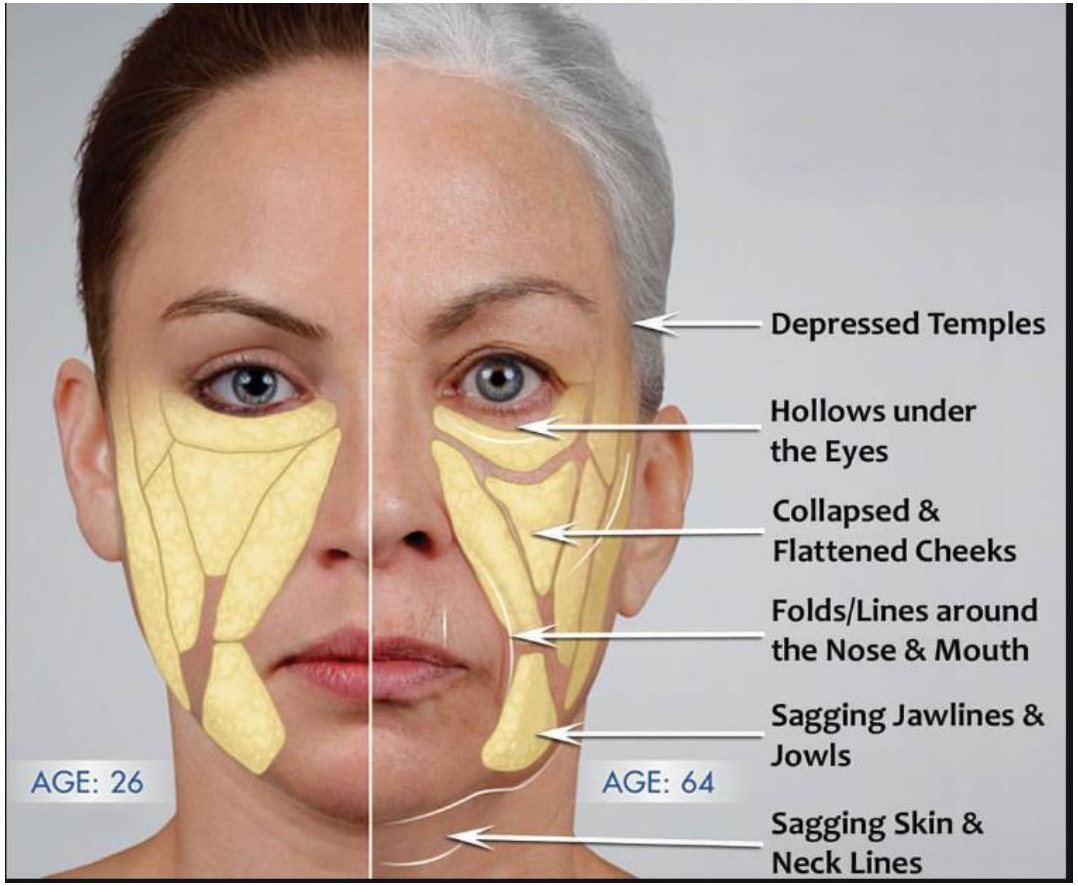
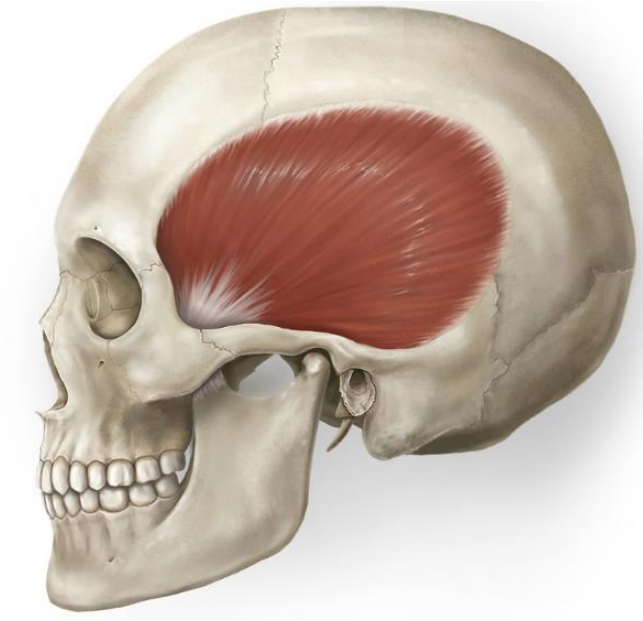
Background & Objective





temporal muscle (temporalis)

https://amoderm.tumblr.com/post/169633176678/fat-compartments-of-the-face-aging

Materials and Methods

Materials	▪ Subject: 20 female patients (aged 31.3 (28 – 35 years) ▪ HA filler: e.p.t.q. S100 (JETEMA Co., Ltd.) ▪ Single practitioner, private clinic ▪ Glasses with an attached real-time vein detecting viewer
Method & Result	▪ HA was injected to superficial temporal subcutaneous layer (less veins) ▪ Wearing glasses with an attached real-time vein detecting viewer (using near-infrared optical system), the probe could find superficial veins. ▪ Avoiding the vessel, hyaluronic acid, e.p.t.q.S100 was injected perpendicular to the skin. ▪ Each patient received 0.3-1 cc of hyaluronic acid filler into the superficial subcutaneous layer at the temple area each side (total 0.6-2cc) ▪ None of the patients showed adverse vascular event (any bleeding by venipuncture during the injection, intravascular injection and bruising, or hematoma after injection

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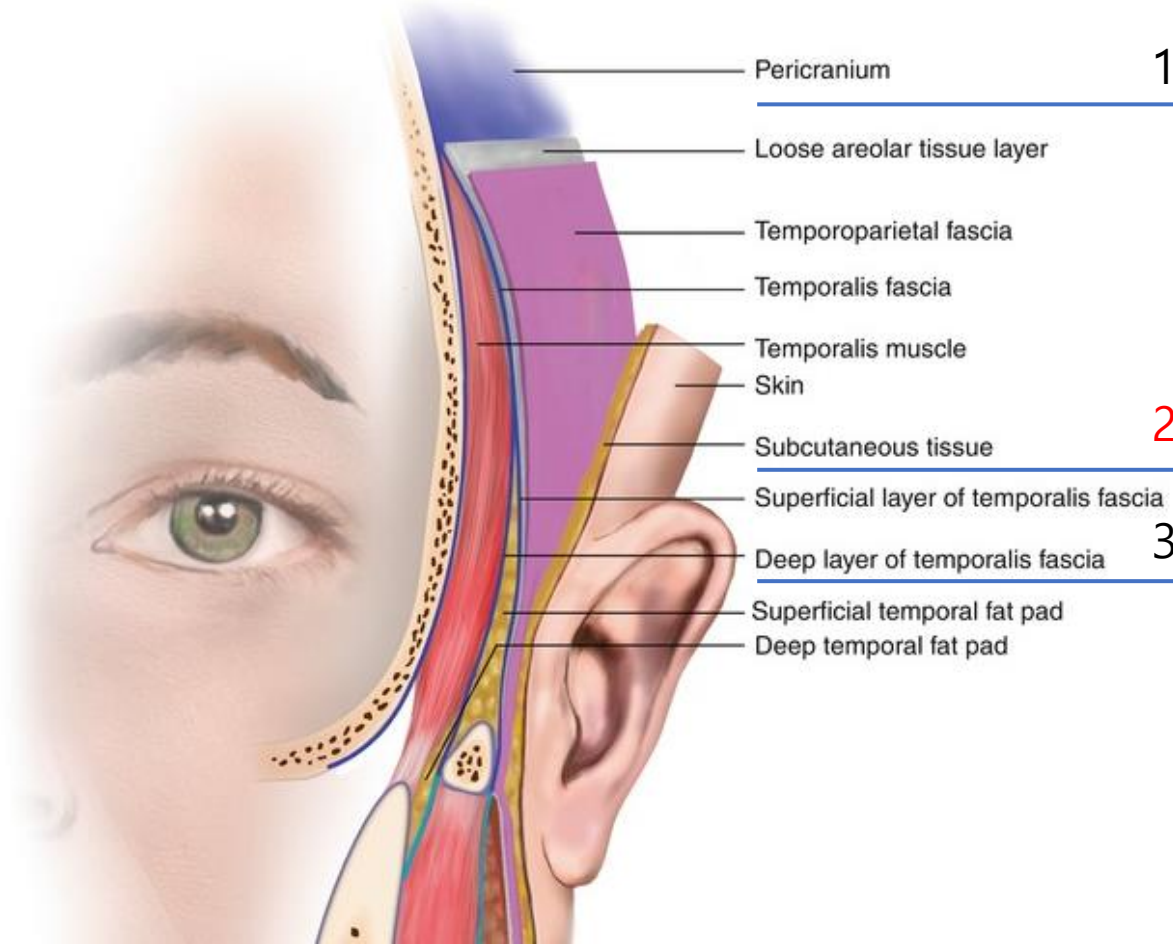
Fillers can be injected into…



1. Above the periosteum of the temporal bone
2. Superficial subcutaneous layer
3. Between the superficial temporal fascia and deep temporal fascia

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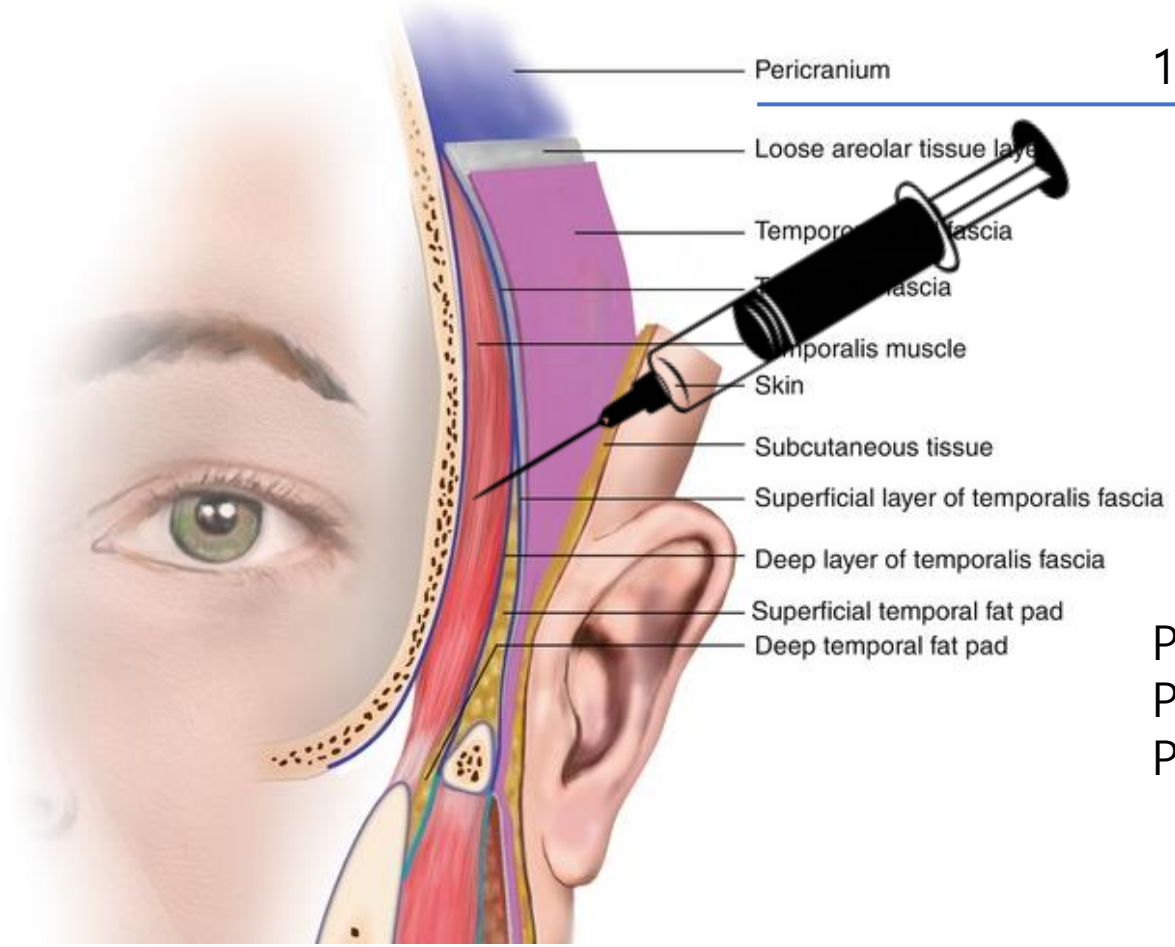
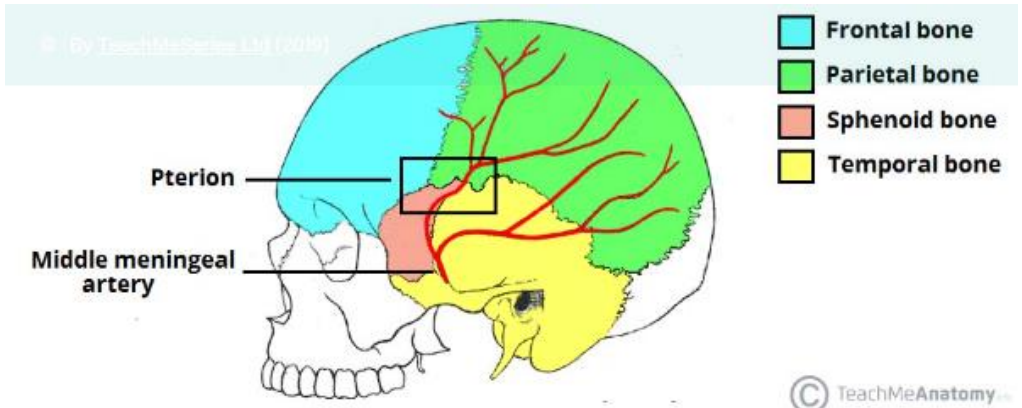
Fillers can be injected into…



1. Above the periosteum of the temporal bone



Pterion: a "H-shaped' junction between temporal, Parietal, frontal, and sphenoid bones. The thinnest Part of the skull. → intracranial penetration??

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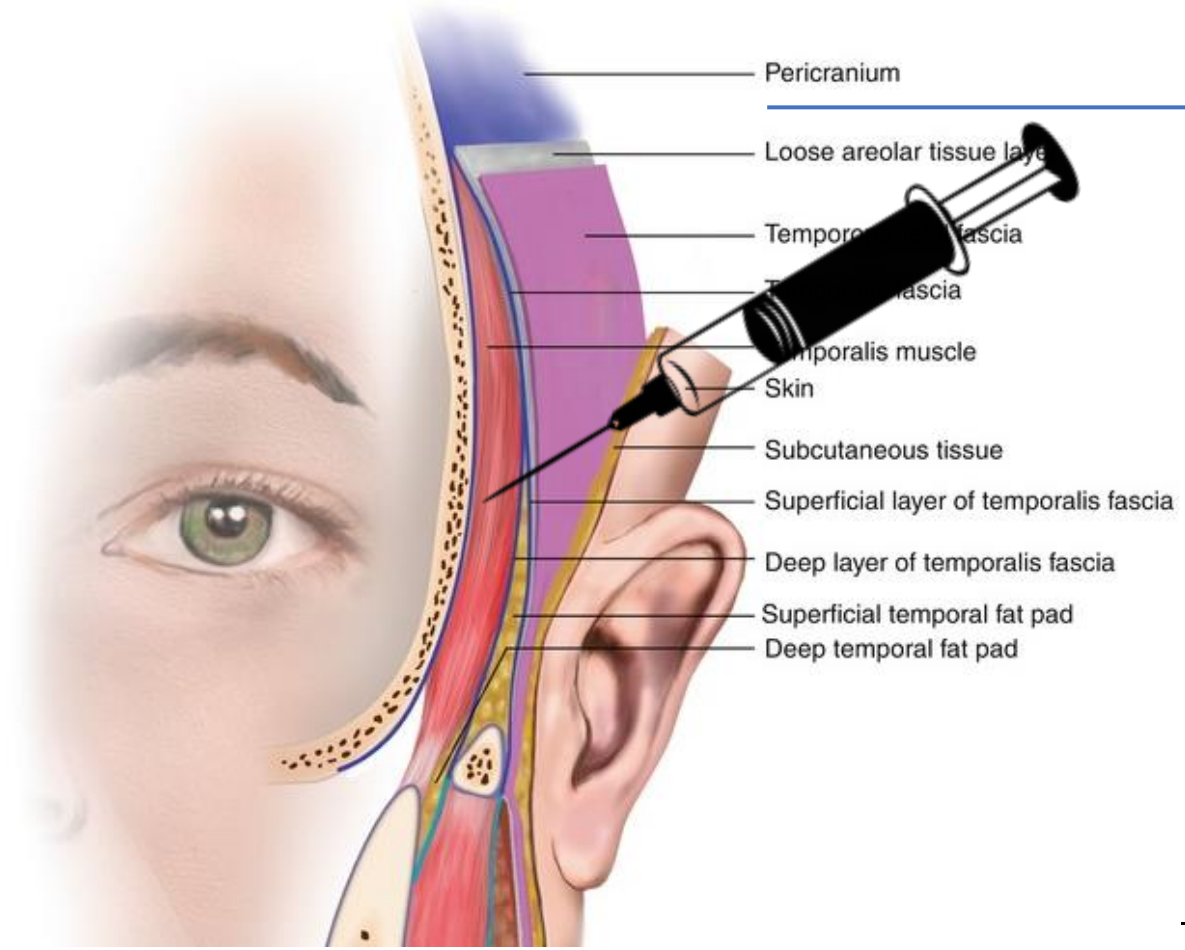
Fillers can be injected into…



1. Above the periosteum of the temporal bone

Intracranial Penetration During Temporal Soft Tissue Filler Injection—Is It Possible?

Wolfgang G. Philipp-Dormston, MD,* Lara Bieler, MSc,†‡ Mathias Hessenberger,§ Thilo L. Schenck, MD, PhD,‖ Konstantin Frank,‖ Johann Fierlbeck,¶ and Sebastian Cotofana, MD, PhD#

BACKGROUND Treating temporal volume loss for aesthetic and reconstructive purposes can be achieved by superficial or deep injections of soft tissue fillers into the temples. The latter is performed with bone contact that can lead to intracranial penetration when the bone is accidentally penetrated.

OBJECTIVE Based on a clinical case, the potential risk of accidental intracranial penetration was investigated.

MATERIALS AND METHODS Twenty fresh-frozen hemi-faces (all Caucasian ethnicity, 10 women, 10 men, mean age 72.8 ± 11.2 years) were investigated. Shape of pterion and bone-stability parameters of the temporal fossa were investigated. Bone stability was tested using uniaxial mechanical indentation (18-G, 1.25-mm diameter, 15-mm length blunt-tip device) until intracranial perforation occurred.

RESULTS Variations in the shape of the pterion, bone thickness, and density correlates were detected, however, without statistical significant differences in side symmetry. Minimum force necessary to penetrate intracranially was 40.4 N. Maximum force generated by an 18-g, 70-mm length blunt-tip cannula was 32.1 ± 4.2 N in 70 mm length and 75.3 ± 10.2 N in 15 mm length.

CONCLUSION Based on the results of this investigation, it can be concluded that there is a risk for intracranial penetration performing the deep temple injection technique with direct pressure on the bone.

Conclusion:
"There is a risk for intracranial penetration performing the deep temple injection technique with direct pressure on the bone. "

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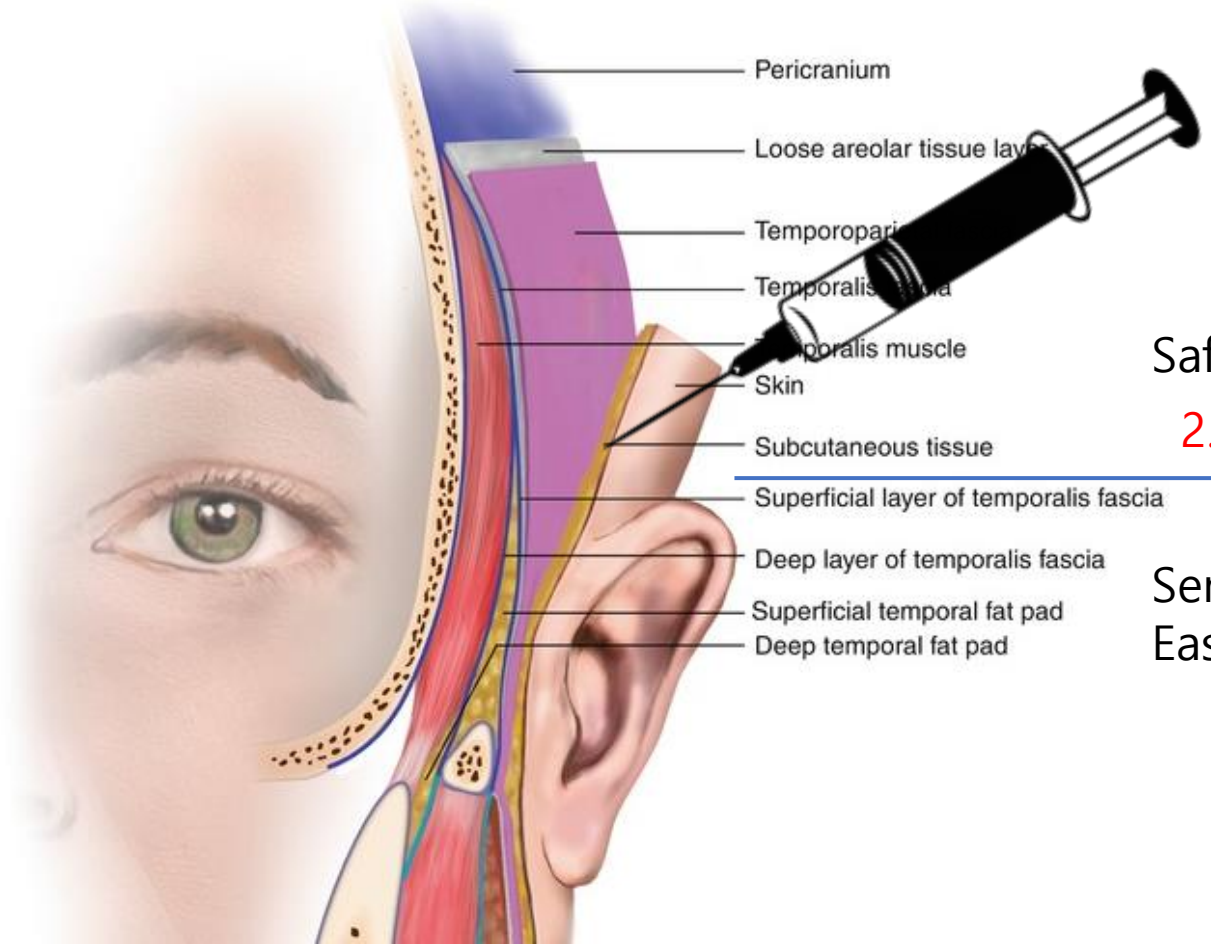
Philipp-Dormston, Wolfgang G., et al. "Intracranial Penetration During Temporal Soft Tissue Filler Injection—Is It Possible?." *Dermatologic Surgery* 44.1 (2018): 84-91.

Fillers can be injected into…



Safest layer is…

2. Superficial subcutaneous layer

Sentinel vein and superficial temporal vein,
Easily noticeable using near infrared vein detector

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Key Message

- Temple area has various anatomic layers → “Danger Zone”
- Superficial subcutaneous layer is a safe layer for temple augmentation using vein detector.
- E.p.t.q.S100 is a safe and effective filler for temple augmentation.

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Soft Tissue Filler Properties Can be Altered by a Small-Diameter Needle

Soft Tissue Filler Properties Can Be Altered by a Small-Diameter Needle

Won Lee, MD, PhD,* Wook Oh, MD,† Hyoung-Jin Moon, MD,‡ Ik-Soo Koh, MD, PhD,§ and Eun-Jung Yang, MD, PhD‖

BACKGROUND Small-bore needles reduce the complications associated with soft tissue filler injection. Gel particles must be sized appropriately to pass through fine-bore needles with an acceptable extrusion force. However, most soft tissue filler particles are larger than the inner diameter of the needle. The authors hypothesized that the physical properties of these particles change as the gel passes through the needle.

OBJECTIVE The authors aimed to investigate whether the predesigned physical and rheological properties of the filler change after passage through the small-bore needle.

METHODS AND MATERIALS Particle sizes of 4 hyaluronic acid (HA) fillers were analyzed using a particle size analyzer. Five soft tissue fillers with different particle sizes were subjected to rheological characterization. All tests were performed using fillers with and without a 30-G needle.

RESULTS Monophasic HA fillers with smaller particle sizes exhibited small changes between particle sizes but no differences in rheological properties. Biphasic HA fillers with larger particle sizes exhibited remarkable changes in particle size and rheological properties. Calcium fillers exhibited changes in rheological properties.

CONCLUSION Injection through small-bore needles can alter the physical properties and rheological equilibrium of soft tissue fillers. The authors suggest avoiding small-bore needles as they may affect the rheological equilibrium and clinical performance of fillers.

Lee, W., Oh, W., Moon, H. J., Koh, I. S., & Yang, E. J. (2019). Soft Tissue Filler Properties Can Be Altered by a Small-Diameter Needle. *Dermatologic surgery: official publication for American Society for Dermatologic Surgery [et al.]*.

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Background and Materials

Background

- Small bore needles reduce the complications of soft-tissue filler injection

Most soft tissue filler particles are larger than the inner diameter of the needle

→ physical and rheological properties of HA particles change as the gel passes through the needle.

Materials

- Subject: 2 monophasic fillers (e.p.t.q.S500, Chaeum Style No.3), 2 biphasic fillers (Cutegel Max, Neobelle Edge)
- Particle sizes were evaluated using laser scattering particle size distribution analyzer.
- Rheological characterization was performed using an automated controlled stress rheometer
- 30G needle was used

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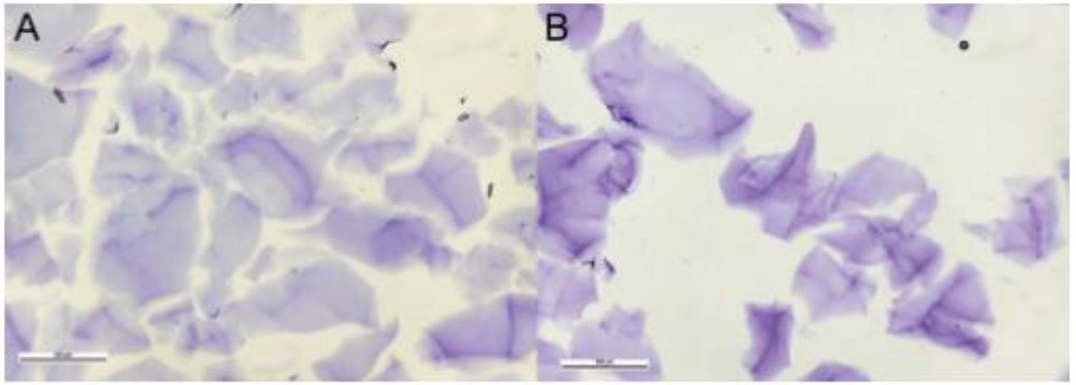
Result (Particle Size and Microscopic findings)

Particle size

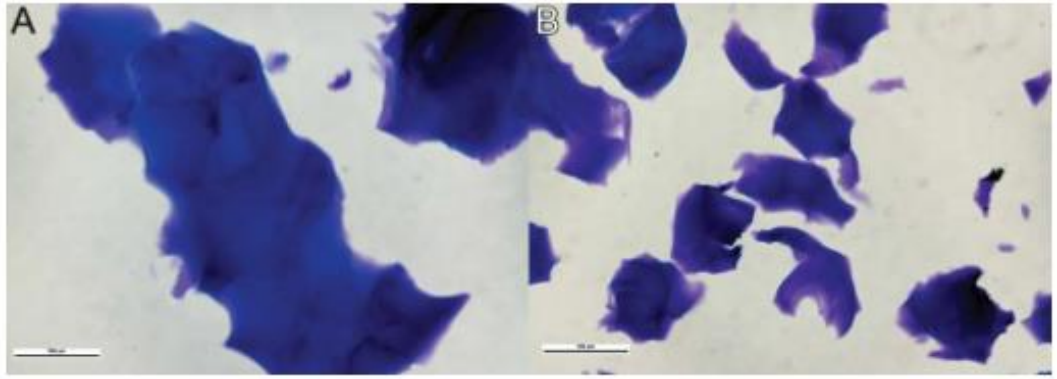
- **e.p.t.q. S500 exhibited a change of less than 9.8% after passage through the 30G needle.**
- **Chaeum Style No.3 decreased 24.5%, Cutegel Max 58.8%, Neobelle Edge 49.4%.**

→ Effect of passing through a needle on particle sizes was stronger in biphasic fillers.

Microscopic findings



<Monophasic Filler>
Slight difference before and after passing through 30G needle
A: original product B: After passing 30G needle



<Biphasic Filler> large difference before and after passing through 30G needl
A: original product B: After passing 30G needle

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Result (rheological test)

Rheological test result						
	Rheology before passing through a 30G needle			Rheology after passing through a 30G needle		
Filler	G' (Pa)	G" (Pa)	Complex viscosity (Pa·s)	G' (Pa)	G" (Pa)	Complex viscosity (Pa·s)
e.p.t.q.S500	282.02	48.03	455.33	291.18	46.47	467.29
Chaeum Style No.3	250.99	29.98	402.31	262.38	34.47	421.18
Cutegel Max	739.86	241.16	1,240.99	623.65	274.92	1,084.74
Neobelle Edge	753.63	169.03	1,229.24	492.17	181.36	834.81

Monophasic filler showed no remarkable differences in rheological properties.

Biphasic filler: viscoelastic properties changed more markedly, indicating intensity of filler rheological changes during passage through a 30G needle might be dependent on particle size.

→ Changes in physical parameters (rheological and physical parameters) can cause deviation in clinical performance. But e.p.t.q. S500 showed very small change in both particle size and rheology allowing safe small-bore needle injection.

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	Article Title	Authors	Summary	Journal Title/ Year
1	Effectiveness of retrobulbar hyaluronidase injection in an iatrogenic blindness rabbit model using hyaluronic acid filler injection	Won, Lee Wook, Oh Hyung Seok, Ko Sang Young, Lee Ki Wook, Kim Eun Jung, Yang	In case of iatrogenic blindness, e.p.t.q. S100 was degraded by retrobulbar hyaluronidase injection and re-gain vision in rabbit model.	Plastic and Reconstructive Surgery /2019
2	Clinical application of a new hyaluronic acid filler based on its rheological properties and the anatomical site of injection	Won, Lee Jeung Hyun, Yoon Ik Soo, Koh Wook, Oh Ki Wook, Kim Eun Jung, Yang	e.p.t.q. S300 has sufficient cohesiveness and elastic modulus for forehead augmentation when applied to the preperiosteal layer.	Biomedical Dermatology / 2018
3	Novel technique of filler injection in the temple area using the vein detection device	Won, Lee Wook, Oh Gi Woong, Hong Ji Soo, Kim Eun Jung, Yang	e.p.t.q. S100 is a safe and effective choice for temple augmentation when injected to superficial subcutaneous layer using the vein detection device.	Journal of Plastic Reconstructive and Aesthetic Surgery /2018
4	Practical guidelines for hyaluronic acid soft-tissue filler use in facial rejuvenation	Won, Lee Seung Gook, Hwang Wook, Oh Chang Yeol, Kim Jin Liang, Lee Eun Jung, Yang	Rheological properties of 41 fillers (including e.p.t.q. S100, 300, 500) directly linked to product performance were measured. Understanding the fillers' properties can help physicians select the appropriate fillers for more predictable and sustainable results.	Dermatologic Surgery / 2019
5	Soft tissue filler properties can be altered by a small-diameter needle	Won, Lee Wook, oh Hyoung Jin, Moon Ik Soo, Koh Eun Jung, Yang	Large sized gel particles containing fillers should not be used with small-bore needles, given the potential effects on particle size and rheological equilibrium. e.p.t.q.S500 showed no noticeable differences in rheological properties and size after passage through a 30-G needle.	Dermatologic Surgery / 2019