

Facial Safe Zones for Soft Tissue Filler Injections: A Practical Guide

David L. Freytag,^a Konstantin Frank MD,^a Rami Haidar BDS,^b Christina Rudolph BA,^c Justin Muste,^c Thilo L. Schenck MD PhD,^a Jeremy B. Green MD,^d Nirusha Lachman PhD,^e Christie Bialowas MD FACS,^f Sebastian Cotofana MD PhD^{c,f}

^aDepartment for Hand, Plastic and Aesthetic Surgery, Ludwig – Maximilians University Munich, Germany

^bPrivate Practice, Riyadh, Saudi Arabia

^cDivision of Anatomy, Department of Medical Education, Albany Medical College, Albany, NY

^dSkin Associates of South Florida, Coral Gables, FL

^eMayo Clinic College of Medicine and Science, Mayo Clinic, Rochester, MN

^fDivision of Plastic Surgery, Department of Surgery, Albany Medical Center, Albany, NY

ABSTRACT

Objective: Vascular events are among the most dreaded complications of safe soft tissue filler injections. The aim of the present study is to present a practical guide for regional facial soft tissue filler injections, which is founded in anatomy and considers safety as its first priority.

Material and Methods: The study sample consisted of 20 fresh (non-embalmed) hemi-faces from 10 Caucasian body donors (7 females, 3 males) with a mean age of 83.5±6.8 years and a mean BMI of 25.3±4.3 kg/m². Injections of the upper, middle and lower faces of the body donors were performed using a commercially available hyaluronic acid based soft tissue filler.

Results: The results of the layer by layer dissections revealed that the injected material was separated from crucial neuro-vascular structures by fascial and/or muscular planes, which were not permeated by the product. Utilizing a single cutaneous access point per facial region, safe planes can be reached.

Conclusion: This study provides a practical guide for safe soft tissue filler injections for the upper, middle, and lower face. Using cadaveric dissections and dyed product revealed that the targeted facial planes are separated either by fascial planes or by muscular tissue from arterial vasculature.

J Drugs Dermatol. 2019;18(9):896-902.

INTRODUCTION

The number of soft tissue filler injections performed in the United States continues to increase. According to the annual report of the American Society of Plastic Surgery, 2,676,907 soft tissue filler injections (unspecified) were performed in 2018, which represents a 3-fold increase compared to the year 2000.¹ Recent studies have provided evidence that the number of soft tissue filler associated cases of blindness has concomitantly increased.² Between 2015 and 2018, 48 cases were published,² compared to 98 reported cases between 1906 and 2015.³ Cho et al. simulated the underlying pathophysiologic mechanism of this catastrophic adverse event by using a perfused cadaveric model.⁴ They were able to identify an association between the intraarterial application of the filler material to the supratrochlear artery and the embolization of retinal arteries.⁴

The retinal arteries are linked to a vast network of collateral arteries forming anastomoses with the contralateral side and connecting the external carotid artery circulation with the inter-

nal carotid artery.⁵ A recent anatomic report provided evidence that the facial arteries vary highly between individuals and even between the sides of the face in the same person (2-dimensional variation). However, it was shown that the variation in depth (3-dimensional variation) is less, indicating that facial arteries respect their fascial planes but vary within that plane.⁵ This high variability in the location of the facial arterial vasculature results in the potential for accidental intraarterial injections for even the most expert injectors.⁶

Soft tissue filler injections are performed using either sharp tip needles or blunt tip cannulas. Previous studies have shown that injecting with a needle oriented perpendicular to (in contact with) the bony surface distributes the filler material into all fascial planes, whereas injecting with a cannula parallel to the bone surface positions product solely in the inserted plane.^{7,8} These 2 studies reveal that the injector also contributes to safety in soft tissue filler injections as the product can change planes during needle injections, potentially leading to intraarterial application of the product.

A multitude of factors can influence safe soft tissue filler injections, therefore a practical guide for health care professionals would be useful to help avoid inadvertent intra-arterial product placement. Defining facial danger zones is one useful approach,⁹ however, establishing safe zones and safe layers for filler applications in each of the craniocaudal thirds of the face, might be a better guide for daily clinical use. The aim of the present study is to present a practical guide for the injection of all facial thirds, which is based purely on anatomy with safety as the primary concern.

MATERIALS AND METHODS

Study Sample

The study sample consisted of 20 fresh (un-embalmed) hemifaces obtained from 10 Caucasian body donors (7 females, 3 males) with a mean age of 83.5 ± 6.8 years (range, 75 – 95) and a mean body mass index (BMI) of 25.3 ± 4.3 kg/m² (range, 17.1 – 31.6). Body donors were screened and not included in this analysis if they had previous facial surgeries, trauma, or diseases that disrupted the integrity of the facial anatomy. Each body donor provided informed consent at the time of bequest for the use of their body for medical, scientific, and educational purposes. All aspects of the study conform to the laws of the country where the study was conducted (USA).

Injection Procedure

Injections of the upper, middle, and lower faces of the investigated body donors were performed using a commercially available hyaluronic acid based soft tissue filler (Perfectha Subskin, Sinclair, London, UK). The filler material was dyed with regular food coloring to enhance the visibility of the (transparent) filler material during anatomical dissections. The technique for the utilized injection algorithm is the 3 point full face fanning (3PF) technique.

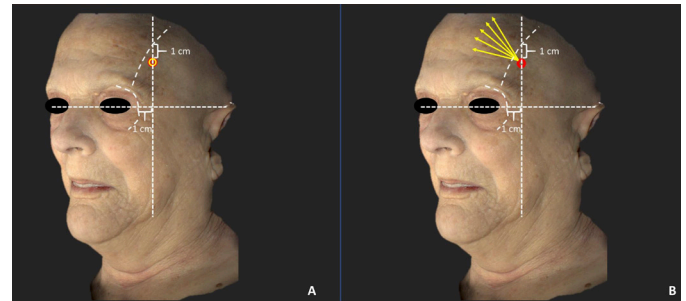
Upper Face (Temple and Forehead)

The injection procedure of the upper face included the application of product deep in the temple in the supraperiosteal (ie, intramuscular) location and deep in the forehead in the supraperiosteal ie, sub-frontalis plane. For both application procedures the same skin penetration point was used: 1 cm inferior to the temporal crest and 1 cm lateral to the lateral orbital rim (Figure 1A).

For the application of product in the temple, a 25G, 38mm needle was inserted perpendicular to the skin surface until bony contact with the temporal fossa was established. The needle was then directed 45° inferiorly and a bolus of 1.0cc of product was injected while in constant contact with the bone.

For the application of product in the forehead, the same skin penetration point was used (as described above). After achieving subdermal access with an 18G 38mm needle, a 21G 70mm

FIGURE 1A, B. 3D photo showing the entry site and the application for the injection of material into the area of the temple (A) and forehead (B). The red circles represent the dermal access puncture, while the yellow markings (circle: bolus; arrow: fanning) represent the path of the cannula/needle during filler application.



cannula was advanced toward the forehead in the supraperiosteal plane while maintaining constant contact with the frontal bone. Utilizing a retrograde fanning technique, 0.5cc of soft tissue filler was equally distributed in the lateral portions of the forehead (Figure 1B).

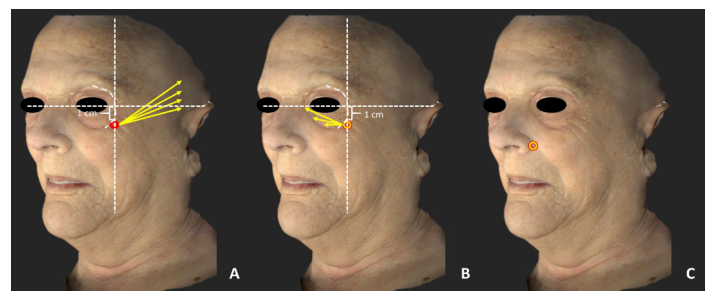
Middle Face (Lateral and Medial Midface, Nasolabial Sulcus)

For the injection procedures of the medial and lateral midface, the same skin penetration point was used: 1 cm inferior to the lateral orbital rim measured from the level of the horizontal mid-pupillary line.

For injections in the lateral midface, a subdermal access puncture point was created with an 18G 38mm needle followed by the insertion of a 21G, 70mm cannula. The cannula was advanced in a superolateral direction in the subdermal plane passing the zygomatic arch. A total of 0.5cc soft tissue filler material was injected using a retrograde fanning technique (Figure 2A).

For injections in the medial midface, the same subcutaneous access point was used as described above for the lateral midface. A 21G, 70mm cannula was introduced until bone contact was

FIGURE 2A, B, C. 3D photo showing the injection site and the application for the injection of material into the area of the lateral midface (A) and (medial) middle face (B, C). The red circles represent the dermal access puncture, while the yellow markings (circle: bolus; arrow: fanning) represent the path of the cannula/needle during filler application.



established in the prezygomatic space and then advanced in a medial direction while maintaining constant contact with bone. When the tear trough was reached, three 0.1cc sequentially applied boluses of soft tissue filler were injected. An additional two 0.1cc boluses were applied at the inferior orbital margin along the palpaebro-malar groove (Figure 2B).

An additional injection point was utilized to treat the nasolabial sulcus accessing the supraperiosteal plane at the lateral aspect of the nasal ala. Here, a 25G, 38mm needle was inserted perpendicular to the skin surface (and to the bone) until bony contact was established. A bolus of 0.5cc was injected while keeping constant contact with the bone (Figure 2C).

Lower Face (Mandibular Angle, Labiomandibular Sulcus, Chin)

The injection point for the lower face was located in the mid portion of the mandible, when measuring the distance between the mandibular symphysis and mandibular angle (Figure 3). A cutaneous access puncture was performed with an 18G, 38mm needle (Figure 3A). Great care was taken to penetrate the skin exclusively and not to advance into structures deep to the platysma. A 21G 70mm cannula was introduced into the subdermal plane and advanced first posteriorly toward the angle of the mandible. There, a bolus of 0.5cc was applied. After changing the direction of the cannula 180 degrees (without fully exiting the subdermal plane) anteriorly the labiomandibular sulcus was targeted. The labiomandibular sulcus was subcised and a total of 0.5cc soft tissue filler was injected using a retrograde fanning technique. Here, the muscular connections attaching the skin to the depressor anguli oris muscle were detached via the performed subcision and the infero-lateral depressions of the perioral region were reached (Figure 3A).

An additional injection point was utilized to address anterior chin projection. Here, a 25G, 38mm needle was inserted perpendicular to the bone (and to the skin surface) until bone contact was established. A bolus of 0.5cc was applied being in constant contact with the bone (Figure 3B).

Anatomical Dissection

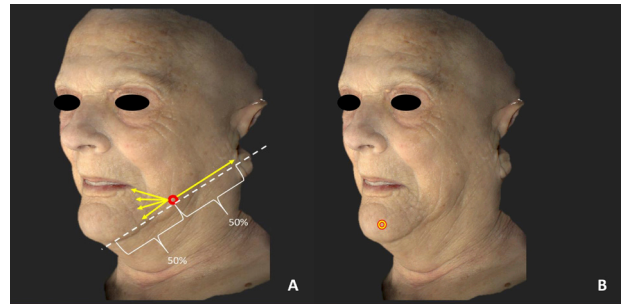
Layer by layer anatomic dissections were carried without magnification to identify the injected product within each of the facial layers. Relationship to adjacent arteries and nerves were evaluated.

RESULTS

Upper Face: Temple

The deep temporal injection was performed with the 25G needle in constant contact with bone. This injection placed the product into the temporalis muscle (layer 9) and can be thus classified as an intramuscular injection. Upon dissection, the majority of the product was identified inside the temporalis muscle. A minor amount of product was identified on the underside of the deep

FIGURE 3A, B. 3D photo showing the injection site and the application for the injection of material into the area of the jawline (A) and chin (B). The red circles represent the dermal access puncture, while the yellow markings (circle: bolus; arrow: fanning) represent the path of the cannula/needle during filler application.



temporal fascia, indicating a retrograde flow along the injection canal of the needle. No product was identified in proximity to the anterior deep temporal artery, which was located intramuscular but posterior to the product distribution.

No product was identified above the fascia, ie, in layer 4 where the motor branches of the facial nerve were identified nor in layer 3 where the anterior branch of the superficial temporal artery was located.

Upper Face: Forehead

The forehead injection positioned the filler material into the supra-periosteal, sub-frontalis plane (layer 4). Upon cadaveric dissection, the material was identified to lie superficial to the periosteum but deep to the fascia covering the underside of the frontalis muscle.

No major neuro-vascular structures could be identified in proximity to the injected material. The motor branches of the facial nerve were located superficial to this plane and inside the frontalis muscle (layer 3). The sensory frontal branches of the supraorbital and supratrochlear nerves were likewise located superficial and separated from the injected product by the frontalis muscle (layer 2). The anastomosis between the anterior branch of the superficial temporal and supraorbital artery was located in layer 2, as in the forehead the anterior branch of the superficial temporal artery changed planes (from layer 3 to layer 2) after passing superomedially over the temporal crest. The supraorbital and supratrochlear arteries were located in layer 2, as they changed planes (from layer 4 to layer 2) at the level of the middle frontal septum.

Middle Face: Lateral Midface

Injections into the lateral part of the midface with a 21G cannula through an access point in the infraorbital region positioned the material into the subdermal plane of the temple. The injected material was identified in the subdermal plane (layer 2) cranial to the zygomatic arch.

FIGURE 4. Layered cadaveric dissection of the right temple showing the injected blue material (encircled in blue) deep to temporalis muscle in contact with the bone. The skin and the deep temporal fascial (DTF) are indicated. The superficial temporal artery runs inside the superficial temporal fascia, whereas the frontal branch of the facial nerve runs in the intra-fascial plane between the superficial and the deep temporal fascia.

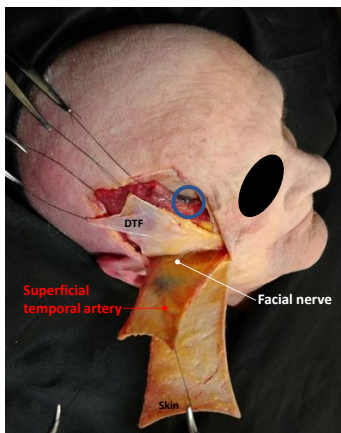


FIGURE 6. Layered cadaveric dissection of the right temple showing the injected blue material (encircled in blue) subdermally. The product is located superficial to the superficial temporal artery and the frontal branch of the facial nerve inside the subdermal plane.

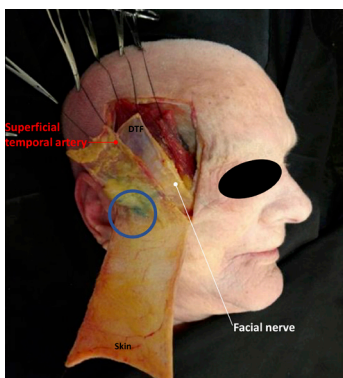
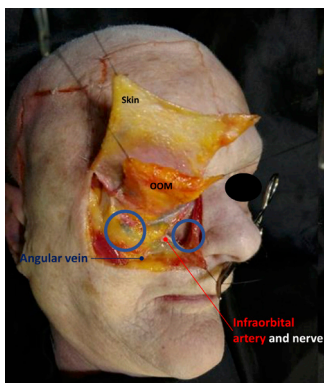


FIGURE 7. Layered cadaveric dissection of the midface showing the injected blue material (encircled in blue) deep to orbicularis oculi muscle (OOM) and deep inside the deep pyriform space. The angular vein and the infraorbital neurovascular bundle are located lateral to the deep pyriform space.



The zygomatico-facial nerve and artery were located deep to the subdermal access point (layer 6). The frontal/temporal branches of the facial nerve were located in layer 4 superior to the anterior half of the zygomatic arch and inferior to the posterior half of the zygomatic arch. The product was identified to be located strictly in the subdermal plane (layer 2) and thus superficial to the superficial temporal artery (located in layer 3).

Middle Face: Medial Midface

Injections with a 21G cannula into the medial part of the midface with access established in the infraorbital region positioned the material into the tear trough and the palpaebro-malar groove. The material was located in the supra-periosteal plane (layer 3 (tear trough) and layer 6 (palpaebro-malar groove).

FIGURE 5A, B. Layered cadaveric dissection of the right forehead showing the injected blue material (encircled in blue) deep to frontalis muscle. The supraorbital artery is shown in the upper forehead to be located superficial to frontalis muscle (A), whereas in the lower forehead the supraorbital and supratrochlear artery (accompanied by the respective nerves) are located deep to frontalis muscle.

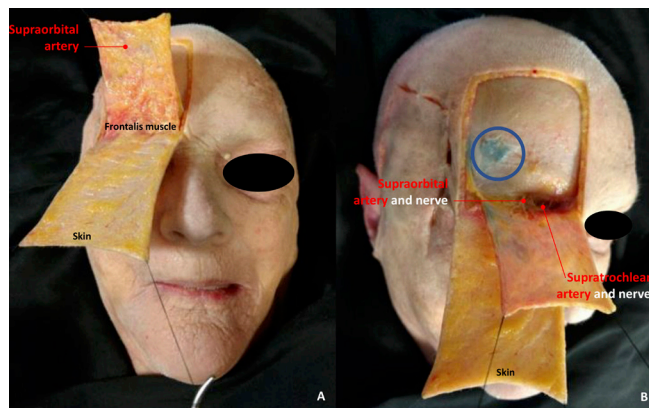
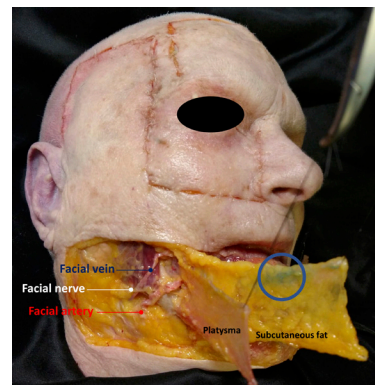


FIGURE 8. Layered cadaveric dissection of the right lower face showing the injected blue material (encircled in blue) inside the subcutaneous fat. The material is located superficial to the platysma, which covers the facial artery and vein and the marginal mandibular branch of the facial nerve.



The zygomatico-facial nerve was located deep in layer 6 below the subdermal access point. The product was positioned in the tear trough, deep to the orbicularis oculi muscle, cranial to the angular vein and inferior to the tear trough ligament. Due to the advancement of the cannula into the supraperiosteal plane, a distinct detachment of the orbicularis oculi muscle from the bone was observed. In the palpaebro-malar groove, the product was positioned into the pre-zygomatic space and thus deep to the sub-orbicularis oculi fat (SOOF) compartment.

Middle Face: Nasolabial Sulcus

The additional injection point in the medial midface was located at the cutaneous junction between the nasal ala and the cranial portion of the nasolabial sulcus. A supraperiosteal bolus injection was performed utilizing a 25G needle. The product was placed into the deep pyriform space (layer 6).

The product was identified deep to the angular artery and medial to the infraorbital neurovascular bundle, which ran in the lateral wall of the deep pyriform space.

Lower Face: Mandibular Angle

The subcutaneous access point was located in the middle of the mandible (when measured from symphysis to the angle). The subdermal plane of the mandibular angle was targeted using a 21G cannula.

The injected product was identified in the subdermal plane (layer 2) superficial to the platysma. The platysma (layer 3) separated the injected product from the marginal mandibular branch of the facial nerve (layer 4), the facial artery (layer 4), the facial vein (layer 4) and from the masseter muscle (layer 7). The parotid duct was located cranial to the injected area.

Lower Face: Labiomandibular Sulcus

The subcutaneous access point was located in the middle of the mandible (when measured from symphysis to the angle). The subdermal plane of the perioral area was targeted using a 21G cannula.

The injected product was identified in the subdermal plane (layer 2) superficial to the orbicularis oris, the depressor anguli oris and to the depressor labii inferioris muscles (all layer 3). A distinct separation of the depressor labii inferioris (layer 3) and the skin (layer 1) was observed deep to the labiomandibular sulcus (fusion of layer 1 and 3) due to the fanning technique. The mental nerve and its branches were covered by the peri-oral musculature (layer 3) and the deep labiomandibular fat (layer 4). The perioral arterial vasculature, consisting of the inferior labial, mental, and the horizontal labiomental arteries were located deep to the muscular plane (layer 3). The motor branches of the facial nerve were identified to run inside the muscular plane.

Lower Face: Chin

Injections into the anterior aspect of the chin were performed using a 25G needle, positioning the product in the midline into the supraperiosteal plane.

The product was located inside the mental fat pad deep to the muscle fibers of the mentalis muscle (here: layer 3). The ascending mental artery (layer 2) was not encountered in any of the performed dissections as the artery would be expected to run in the para-median plane. No other neuro-vascular structures were observed.

DISCUSSION

This cadaveric study investigated the relationship between injected soft tissue fillers and facial neuro-vascular structures following a standardized full-face injection protocol. A total of 20 hemifaces originating from 10 human body donors were injected with dyed soft tissue fillers and consecutively dissected. The results of the layer by layer dissections revealed that the injected material was separated from crucial neuro-vascular structures by fascial and/or muscular planes that were not permeated by the product. This indicates that the applied injection protocol was suitable to deliver safe filler application while avoiding crucial facial neurovascular structures. Using a blunt tip cannula (except in the temple, chin and upper nasolabial sulcus where a needle was utilized), it was confirmed that the product did not migrate out of its intended plane.

In the temple, the product was separated from the facial nerve and from the superficial temporal artery by the deep temporal fascia and from the anterior deep temporal artery by muscle fibres of the temporalis muscle. In the upper forehead, the product was separated by the frontalis muscle and its underlying fascia from the supraorbital and supratrochlear arteries and nerves. The lateral midface injection positioned the product in the subdermal plane. The product was thus superficial to the facial nerve and superficial to the superficial temporal artery. The medial midface injection targeting the tear trough positioned the product deep to orbicularis oculi muscle and in contact with bone, which was free of major neurovascular structures. The injection into the cranial portion of the nasolabial sulcus placed the product into the deep pyriform space. The angular artery was located superficial to this deep facial fat compartment whereas the infraorbital neurovascular structures were located in its lateral walls. Injections into the lower face positioned the product into the subdermal ie, supra-platysmal plane both at the mandibular angle and at the labiomandibular sulcus. The facial artery and vein and the facial nerve were located deep to the platysma. The anterior chin injection placed the product into the mental fat pad, which was deep to the mentalis muscle and medial to the mental neuro-vasculature.

One strength of the present study is that the injected material was colored with blue dye. This enabled us to identify the position and the extent of the product during the subsequent layer by layer dissections. Commercially available hyaluronic acid-based soft tissue fillers are achromatic, and their visibility in facial soft tissue tissues is thus limited. Another strength of the present study is that a commercially available hyaluronic acid-based soft tissue filler was utilized (Perfectha Subskin, Sinclair, London, UK). This filler is used in (living) patients, and the applied pressure on the plunger, the distribution of the product inside the facial soft tissues, and the tissue feedback in the cadaveric model are comparable to the living model.

A limitation of the study however is that only 10 body donors of Caucasian ethnicity were investigated. Increasing the sample size and choosing body donors of different ethnic backgrounds might have enhanced the generalizability of the results by reducing the inter-subject variability. Another limitation, which inherent in any cadaveric study, is that the investigated subjects are not alive. Thus, they lack blood pressure, basic muscle tone, regular tissue turgor pressure and have a different body temperature when compared to living individuals. The aim of the present study was to identify the spatial relationship of the product injected into commonly treated aesthetic facial units to nearby neuro-vascular structures. The layers of the face and the course of the facial neuro-vascular structures are not expected to change with aging or post-mortem. Thus, the layered position of the nerves and vessels of one individual should be identical when compared to the same individual at a younger age or while alive. This could provide additional validity for the selected cadaveric model.

The results of this cadaveric study can be used as a practical guide for soft tissue filler injections for daily clinical applications. The subdermal access points were chosen to reach multiple areas of one facial region through the same injection site, ie, forehead and temple, medial and lateral midface, perioral and mandibular angle. This minimally invasive full-face approach results in fewer cutaneous access points (3x) thereby potentially reducing patient discomfort during soft tissue filler injections and procedural morbidity like bruising. Since these subdermal access points are based on standardized facial landmarks that can be easily identified by palpation (temporal crest, lateral orbital rim, mandibular symphysis, mandibular angle) the results are highly reproducible.

Another advantage of the chosen cutaneous access points is that a safe plane can be accessed to position the filler material into the respective facial region. Deep supraperiosteal injections in the temple result in product placement in the intramuscular plane of the anterior and superior aspect of the temporalis muscle. This location positions the product deep to the anterior

branch of the superficial temporal artery, which is continuous with the supraorbital artery and ultimately with the ophthalmic artery circulation.⁵ It additionally positions the product anterior to the anterior deep temporal artery, a direct branch of the internal maxillary artery, which has been shown to have connections to the ophthalmic artery circulation.⁵

In the midface the cutaneous access point is located 1cm inferior to the lateral orbital rim. From there, the subdermal plane of the temple and the supraperiosteal plane of the infraorbital region can be targeted. The subdermal plane of the temple is located superficial to the superficial temporal artery. In the supraperiosteal plane of the infraorbital region, the tear trough and the SOOF can be found, which are free of major arteries. The injection in the superior aspect of the nasolabial sulcus (performed with a needle) positions the product deep to the angular artery in the supraperiosteal plane.

In the lower face, the plane of choice is subdermal. In this plane, no major arteries are located as the platysma acts like a protective covering, securing the facial artery and vein (and their branches). In the chin, the ascending mental artery is found in the paramedian plane in superficial layers.¹⁰ The product of the chin injection (performed with a needle) can therefore be positioned inside the deep mental fat pad with a midline dermal access point.¹¹

All arteries of the face are connected with each other and have multiple anastomoses with the contralateral side and have collateral branches to the ophthalmic artery circulation.⁵ The presented practical guide for the full-face approach utilized a 21G blunt tip cannula, which allows one to position the product into safe planes and limit the risk of vascular events. A previous study found that the larger the diameter of the cannula, the more force was needed to penetrate a facial vessel, providing evidence for the increased safety of larger diameter blunt tip cannulas.⁸ Needles however were used when supraperiosteal access was needed in order to position a bolus of product in the deep plane.

CONCLUSION

This study provides a practical guide for safe soft tissue filler injections for the upper, middle, and lower face. Utilizing a single cutaneous access point per facial third, proper depth in safe planes can be reached both in the medial and in the lateral aspects of the face. Using cadaveric dissections and dyed product this investigation found that the targeted facial planes are separated from critical arterial vasculature by either fascial planes or muscular tissue. By targeting the presented safe planes for soft tissue filler injection, the clinician can mitigate the risk for potentially catastrophic vascular compromise.

DISCLOSURE

None of the authors listed have any commercial associations or financial disclosures that might pose or create a conflict of interest with the methods applied or the results presented in this article.

Funding: This study received funding by Sinclair Pharmaceuticals Limited, London, UK (Grant no. 12112018).

REFERENCES

1. American Society of Plastic Surgeons. 2018 National Plastic Surgery Statistics. Web. Available at: <https://www.plasticsurgery.org/documents/News/Statistics/2018/plastic-surgery-statistics-report-2018.pdf>. Published 2019. Accessed April 14, 2019.
2. Beleznay K, Carruthers JDA, Humphrey S, et al. Update on avoiding and treating blindness from fillers: a recent review of the world literature. *Aesthetic Surg J*. February 2019.
3. Beleznay K, Carruthers JDA, Humphrey S, et al. Avoiding and treating blindness from fillers. *Dermatologic Surg*. 2015;41(10):1097-1117.
4. Cho K-H, Dalla Pozza E, Toth G, et al. Pathophysiology study of filler-induced blindness. *Aesthetic Surg J*. 2019;39(1):96-106.
5. Cotofana S, Lachman N. Arteries of the face and their relevance for minimally invasive facial procedures: an anatomical review. *Plast Reconstr Surg*. 2019;143(2):416-426.
6. Goodman GJ, Roberts S, Callan P. Experience and management of intravascular injection with facial fillers: results of a multinational survey of experienced injectors. *Aesthetic Plast Surg*. 2016;40(4):549-555.
7. van Loghem JAJ, Humzah D, Kerscher M. Cannula Versus sharp needle for placement of soft tissue fillers: an observational cadaver study. *Aesthetic Surg J*. 2016;38(1):sjw220.
8. Pavicic T, Webb KL, Frank K, et al. Arterial Wall Penetration Forces in Needles versus Cannulas. *Plast Reconstr Surg*. 2019;143(3):504e-512e.
9. Scheuer JF, Sieber DA, Pezeshk RA, et al. Facial danger zones: techniques to maximize safety during soft-tissue filler injections. *Plast Reconstr Surg*. 2017;139(5):1103-1108.
10. Tansatit T, Phumyoo T, Jitaree B, et al. Investigation of the presence and variation of the ascending mental artery: Conventional dissections and ultrasonographic study. *J Cosmet Dermatol*. March 2019;jocd.12928.
11. Cotofana S, Lachman N. Anatomy of the facial fat compartments and their relevance in aesthetic surgery. *J der Dtsch Dermatologischen Gesellschaft*. 2019;17(4):399-413.

AUTHOR CORRESPONDENCE**Sebastian Cotofana MD PhD**

E-mail:..... cotofas@amc.edu