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Starfill

FILLER INJECTION GUIDEBOOK

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Introduction

Starfill ®(hereinafter, Starfill; is a biomaterial for tissue repair used to temporarily improve facial wrinkles in adults through physical restoration by mid dermis~subcutaneous injection of cross-linked hyaluronic acid that contains lidocaine,) is an innovative and safe hyaluronic acid filler manufactured by JETEMA.

Hyaluronic acid was first produced from animal culture and gained high economic value after the development of bacterial culture. Then, its use became broadened in various fields including tissue repair biomaterials, joint treatment, cosmetics, ophthalmic external preparation, and adhesion inhibitors.

Hyaluronic acid is anionic-non-sulfated glycosaminoglycan, distributed in the connective tissue, epidermis, and nervous tissues in the body. Among the glycosaminoglycans, hyaluronic acid is characterized by the features that it does not undergo sulfation and forms the plasma membrane of Golgi, and is enormous in size seen from its several millions molecular weight.

Likewise, hyaluronic acid is used to improve facial wrinkles in adults by cross-linking hyaluronic acid that is close to human composition. Starfill, a filler researched, developed and manufactured from JETEMA through its independent technology 'The 9 Essential Process', features high safety by minimizing various impurities produced from manufacturing processes and BDDE (1, 4-Butanediol Diglycidyl Ether), a chemical used in the cross-linking process.

There are hundreds of fillers circulating in the cosmetic surgery market. Although the transparent gel properties look similar to each other in naked eyes, the properties including viscoelasticity of the filler products differ due to differences in the manufacturing processes. Therefore, it is necessary to understand the injection method and proper usage guidelines for each filler.

The 'Starfill Filler Injection Guidebook', aims to provide doctors with optimal treatment guideline to help ensure safe and utmost treatment results.

1. Filler manufacturing Process

Recently, the safety of the fillers has been reconsidered due to the increased number of adverse events followed by the increase in range of use, treatment area, and the number of treatments.

Through which processes are fillers produced? Is it rational to understand that the difference in processes by manufacturer is the difference in the safety of the products?

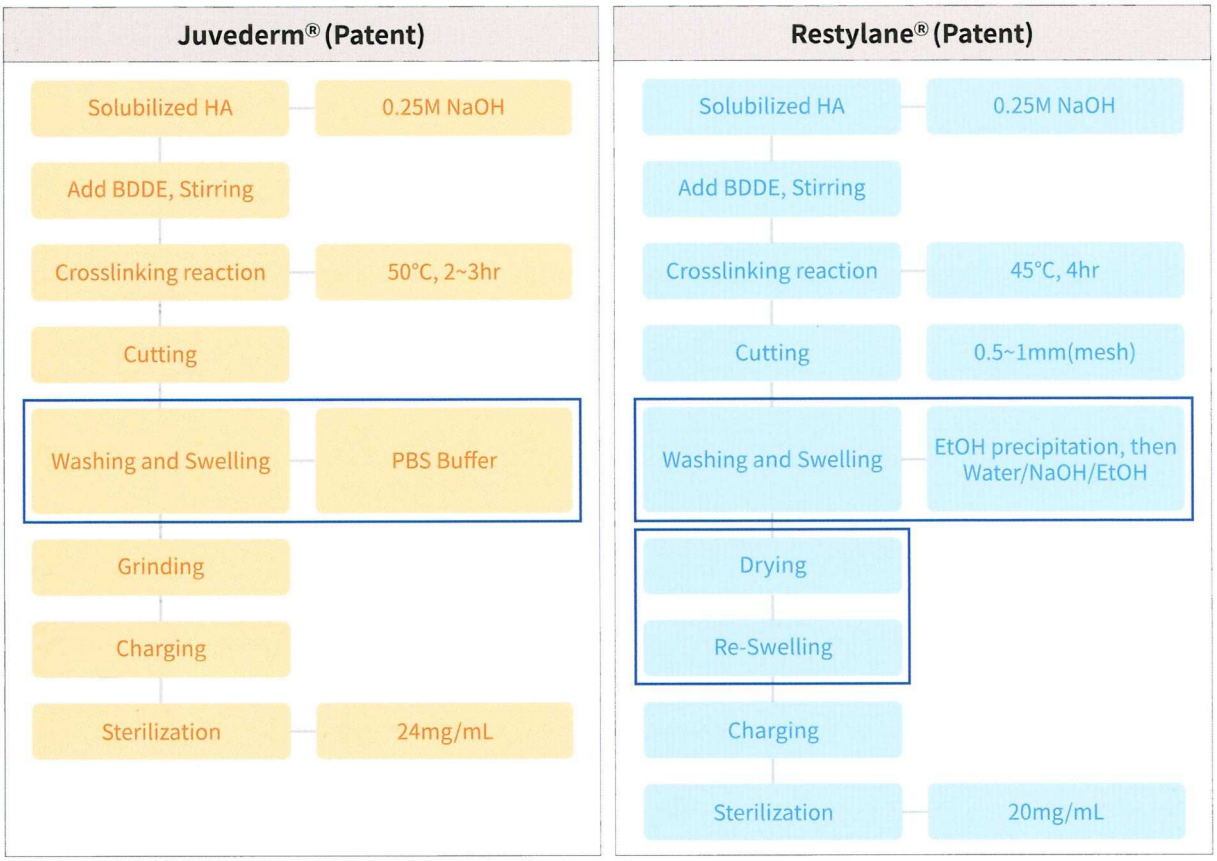


Table 1 _ Understanding the filler manufacturing processes

The manufacturing process of the filler can be summarized as shown in Table 1, simply through the published patents and theses. Most filler go through steps of “weighing-solubilization-reaction-cutting-washing-grinding-charging-sterilization”, similar to the one shown above. The entire process of each manufacturer may seem relatively similar, but there are differences in detailed conditions and methods in a closer look. Although the final gel product can be perceived to be indifferent transparent gel mass, the differences in the detailed process setting determine the difference in the physical property and form of the filler.

The conditions that can be controlled during the filler manufacturing process include concentration, time, and temperature. Since the raw materials and the selected conditions

are different for each manufacturer, the physical properties of the final gel are different. Likewise, the safety of the final gel is also different as the byproduct generated during the manufacturing process and the treatment methods are different. It is easier to understand that the difference in the manufacturing process makes difference in physical properties and safety of the filler.

The most important process in filler manufacturing process is the cross-linking process. The risk of allergy from the chemical catalysts used in the crosslinking process is already well known through many cases of adverse events. Most filler manufacturers say that the product is safe on the basis of the residual chemical catalyst BDDE Test, and release products that pass the approval level of less than 2ppm of residual BDDE. If the product went through a proper washing procedure, there should be no residue detected when the residue outside the gel was measured. The amount of BDDE that is to be injected into the body, the byproduct remaining in the gel, is being neglected.

When considering not only the risk of BDDE as a chemical itself but also the transformed state (there are 4 types of BDDE in the filler manufacturing process: 1. Unprocessed BDDE, 2. BDDE which is hydrolyzed but is not linked yet, 3. Pendant type BDDE that is linked only one side with hyaluronic acid, 4. Fully cross-linked BDDE) during the manufacturing process and the harmful secondary and tertiary materials produced during the metabolism, it is necessary to minimize BDDE during the manufacturing process.

The best way to verify this is to confirm the MoD(%) value, which indicates the sum of fully cross-linked BDDE and pendant type BDDE. MoD(%) identifies the total amount of BDDE contained in the gel, which means that if the MoD(%) value is high, there is a lot of BDDE in the gel and is the higher possibility of BDDE-driven adverse events to arise. Although Starfill filler has the lowest MoD(%) (i.e. the lowest amount of BDDE was added) among our existing fillers, BDDE is fully cross-linked with our technology thereby enhanced safety and highly elastic and cohesive physical properties of the fillers.

However, crosslinking process is not the only factor that determines safety. An environment of pH 10 or higher is essential to increase the cross-linking reaction. Thus, solubilization and reactions proceed in NaOH. In this step, a volatile substance is produced with a stinking odor. If neutralization of NaOH does not proceed in subsequent washing steps, such byproducts may cause safety problems.

Considering the reactions and fusion of various chemicals and the byproducts generated during the metabolism, each factor is important such as the management of entire manufacturing process including washing and total dosage of the involved chemicals. Therefore, it is important to select high-safety filler. This is because the small elements in the manufacturing process accumulate and ultimately determine the difference in physical properties and safety. If so, what criteria can be used to evaluate the physical properties of the filler after different manufacturing processes?

2. Understanding the physical properties of filler

Rheology is the study of the flow and transformation of matter. When using HA fillers, especially when there is no experience with particular product, understanding the rheological evaluation including the viscoelasticity of the filler can be more effective and safe for filler treatments.

Terms	Explanation
Complex modulus G*	$\|G^*\| = \sqrt{(G')^2 + (G'')^2}$ Degree of straining vibratory conditions. Fillers with high complex viscosity are suitable for filling volumes (Although it is important to note the cohesion when filling volume), and fillers with low complex viscosity are easy to deform and soft, thus is suitable for shallow depth injections.
Storage modulus G'	The amount of energy stored and strained when the torsional force is applied. Measures the degree of resistance to external force. 'Lifting capacity = G' x cohesion'. G'is an element directly related to augmentation ability.
Loss modulus G"	The amount of energy dispersed when torsional force is applied. Lost energy = force other than storage modulus. Lost energy is understood to be replaced by viscosity energy thus is understood as viscosity.
Cohesiveness	The degree to which cross-linked HA gels are bound together by the energy acting to maintain the solid form. When the areas injected with filler receive vertical strain, it helps to maintain augmented form. It also prevents filler to move from the injection site.
Phase angle	The angle at which the gel rotates when a torsional force is applied. Larger the angle is measured by larger torsion, it is considered as softer gel.
Tanδ Loss tangent	$\tan\delta = \frac{G''}{G'}$ When the divided value of elasticity from viscosity is 1, it means viscosity = elasticity'. If the value is bigger than 1, it indicates that elasticity is greater and is closer to a solid form than a liquid form. If the value diminishes close to 0, the property is closer to solid.
Endotoxin(EU/mL)	Toxin from dead cells.
BDDE	A type of cross-linking agent for HA cross-linking. Chemical catalyst
MoD(%)	Degree of Modification. The amount of HA transformation by BDDE cross-linking. The total 'fully cross-linked BDDE + pendant type BDDE' included in HA gel.

Table 2 _ Glossary of filler physical properties

1. Understanding the facial artery and vein

Understanding the blood vessels related to filler treatments is very important. Big and small problems may arise in relation to blood vessels including necrosis, blindness, and, mildly, bruises. Therefore, it is important to understand the anatomy of the blood vessels. In addition to the representative guide picture, it is better to have a habit of regurgitating or palpating while performing injection the position and shape of the blood vessels vary by individual.

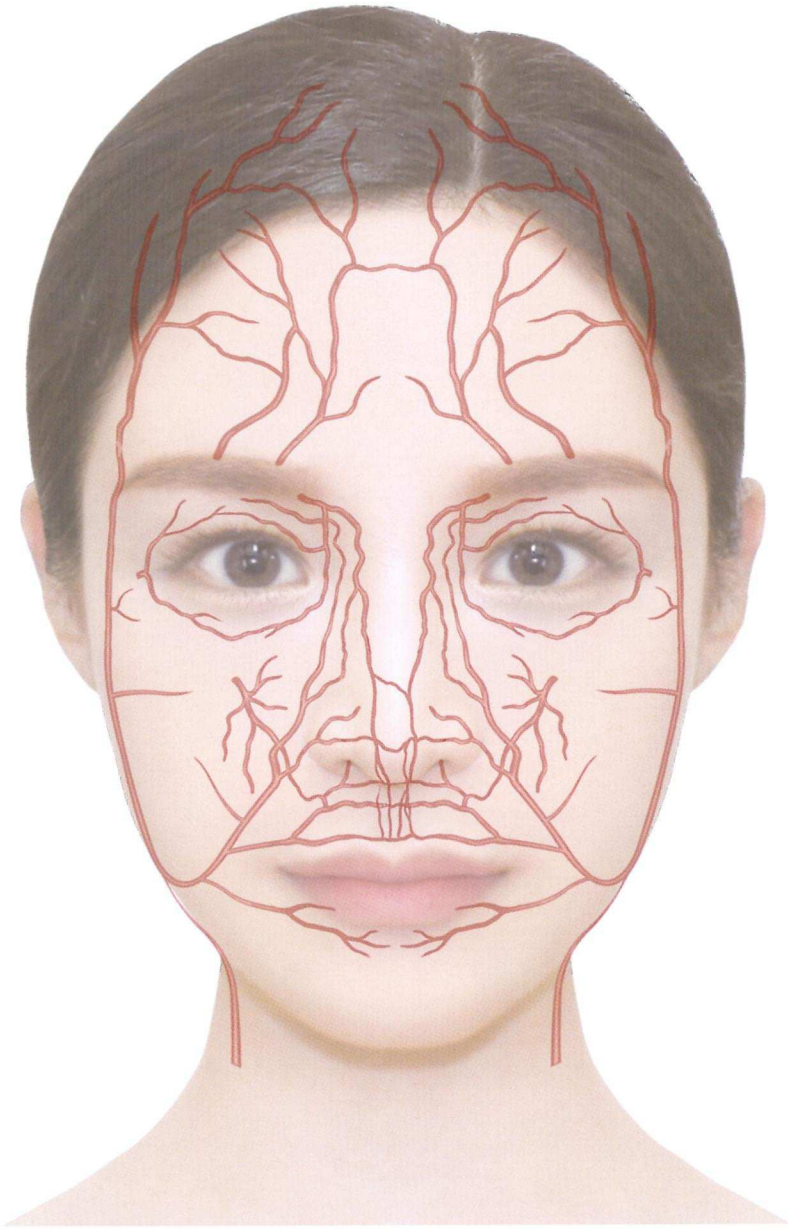


Figure 1 _ Facial blood vessels

2. Understanding the complex lymphatic system

It is necessary to understand the lymphatic system associated with the injection site. The injected filler may interfere with the lymphatic circulation and lead to recurrent and chronic edema.

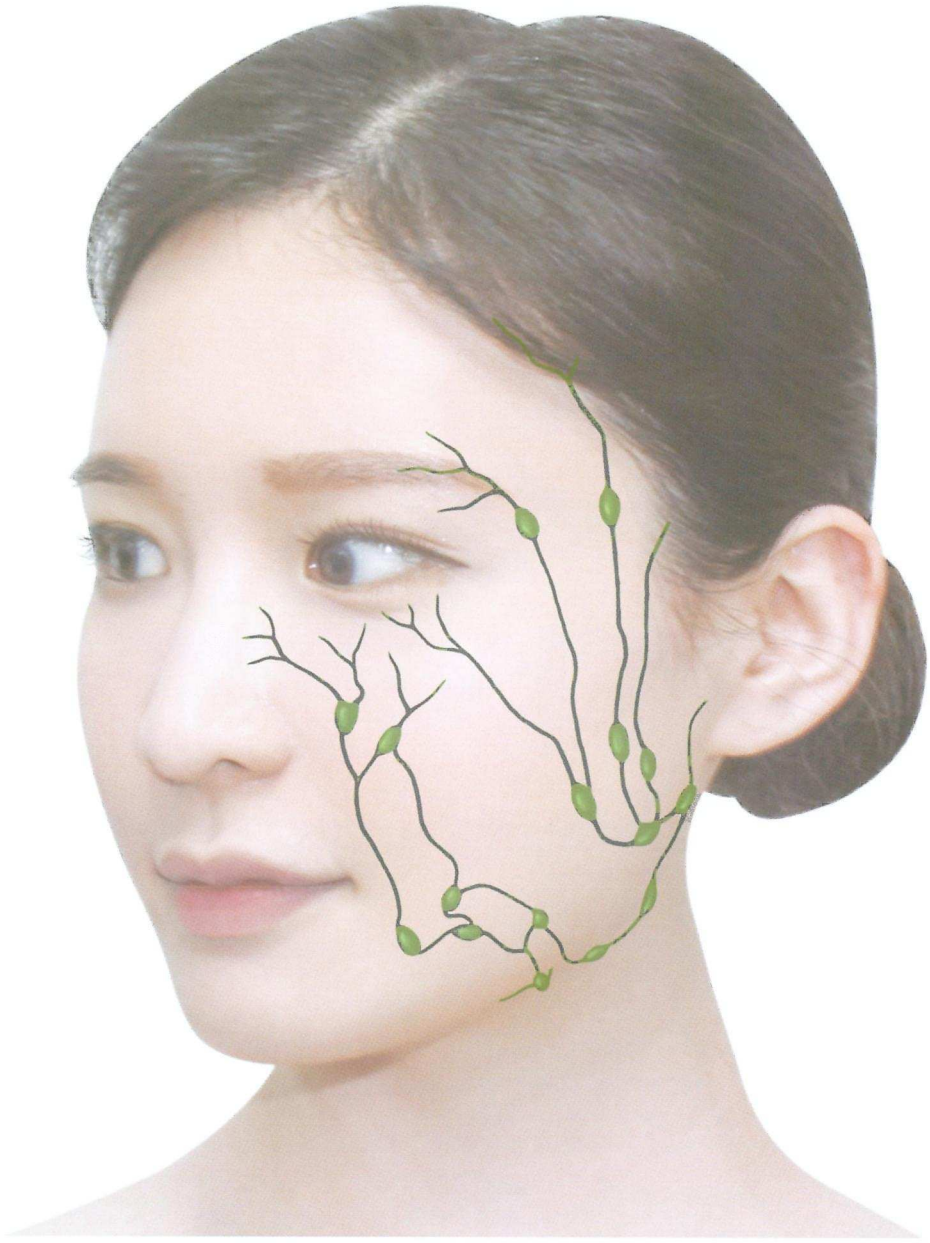


Figure 2 _ Lymphatic system of the face

3. Filler treatment site

Appropriate selections of filler(physical properties) by treatment site and control of injection depth during filler injection are important factors to prevent early edema.

Figure 3 _ Filler treatment area

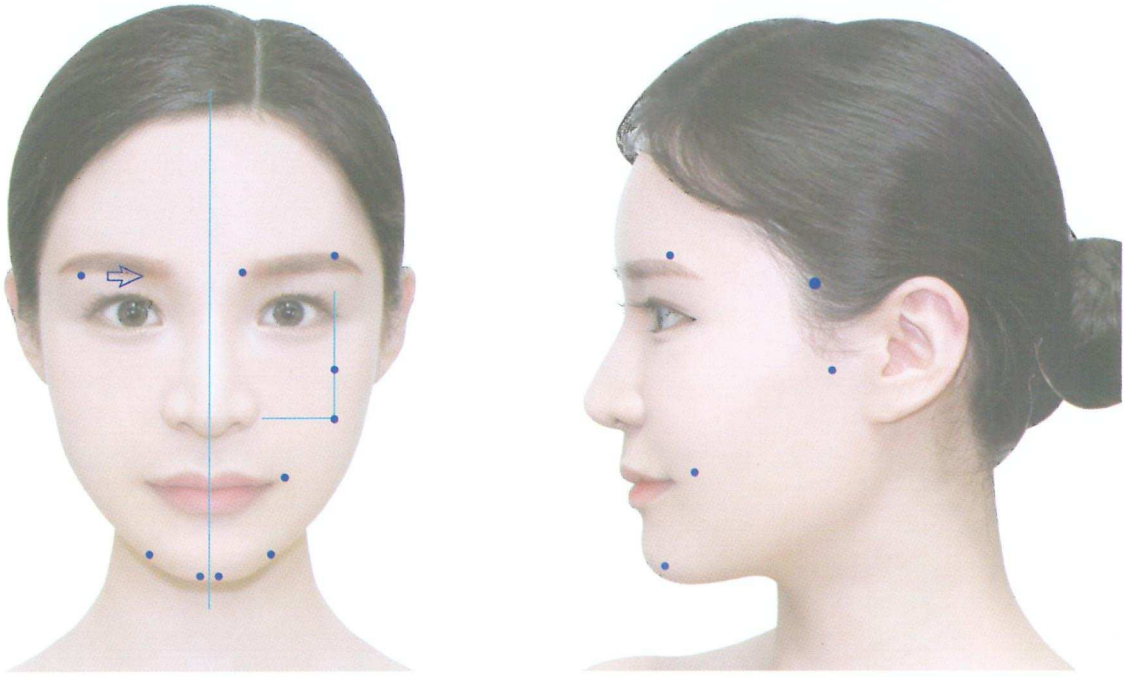


Figure 4 _ Entry points

Layer	Scalp	Forehead	Temple		Cheek (Lateral)	Cheek (Anterior)
1	Skin	Skin	Skin		Skin	Skin
2	Connective tissue	Superficial fat layer	Superficial fat layer (Sub-Q)		Superficial fat layer	Superficial fat layer
3	Aponeurotica	Galeal Frontalis	Superficial temporal fascia(STF) (=Temporoparietal fascia)		SMAS Platysma	Mimetic muscle OOc Zym
4	Loose areolar tissue	Subgaleal space ROOF Galeal fat pad	Loose areolar tissue		Sub-SMAS plane Premasseter space	Deep fat layer SOOF/DMCF Buccal fat Submentalis fat Sub-OOc fat Prezygomatic & Premaxillary space
			Innominate F (in UTC) Upper temporal space	Parotid-temporal fascia(in LTC)		
5	Periosteum	Periosteum	Deep temporal fascia(DTF) (Superficial & Deep layer) Superficial & Deep temporal fat pad		Parotid masseteric F.	
6			Temporalis muscle		Parotid gland Masseter m. Buccal fat	

Table 3 _ Understanding the injection layer and skin layer

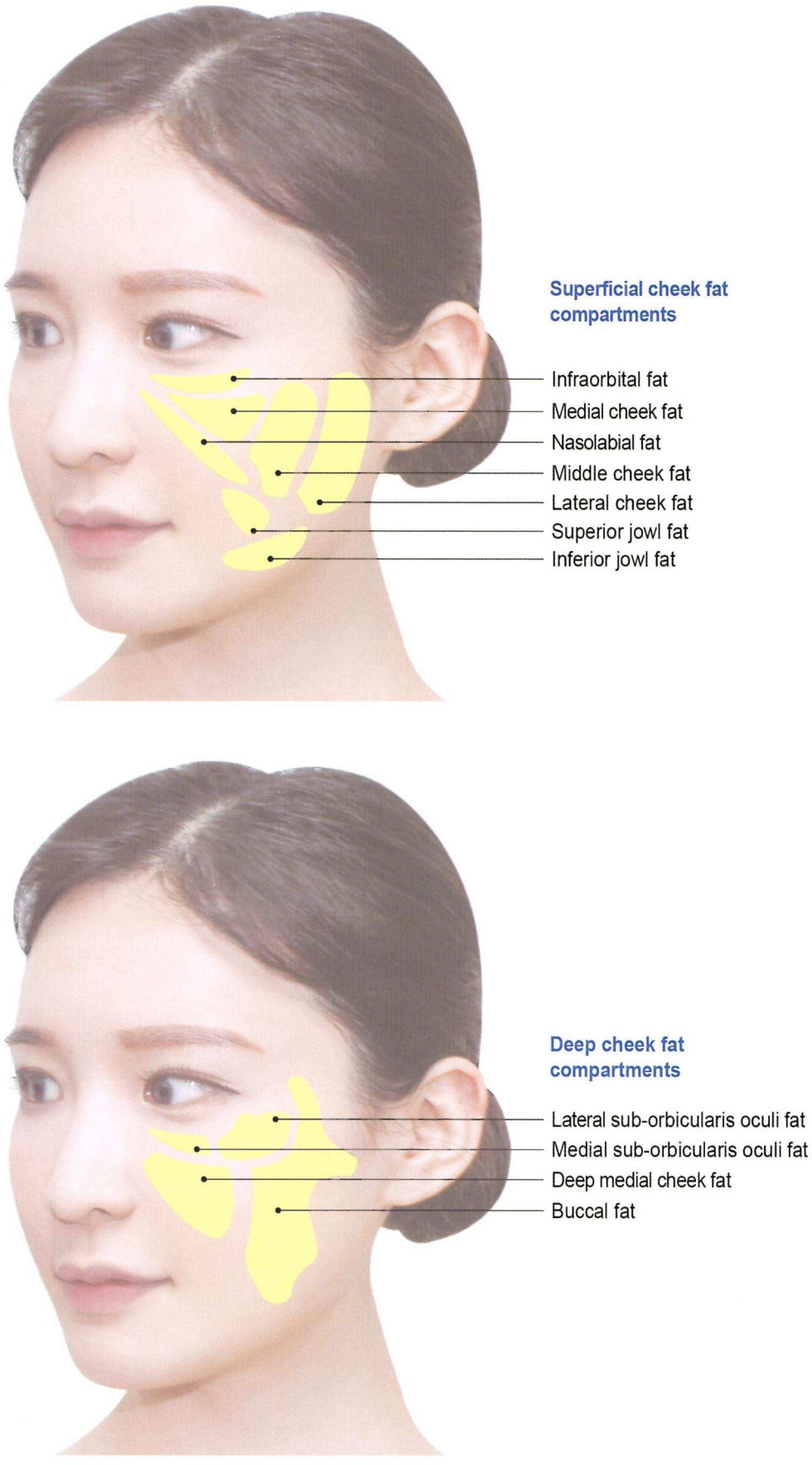


Figure 5 _ Fat layers of the cheek area

4. Nerve distribution of the face and areas of anesthesia

The nerve distribution of the face(right) and corresponding sensory areas(left) are shown below.

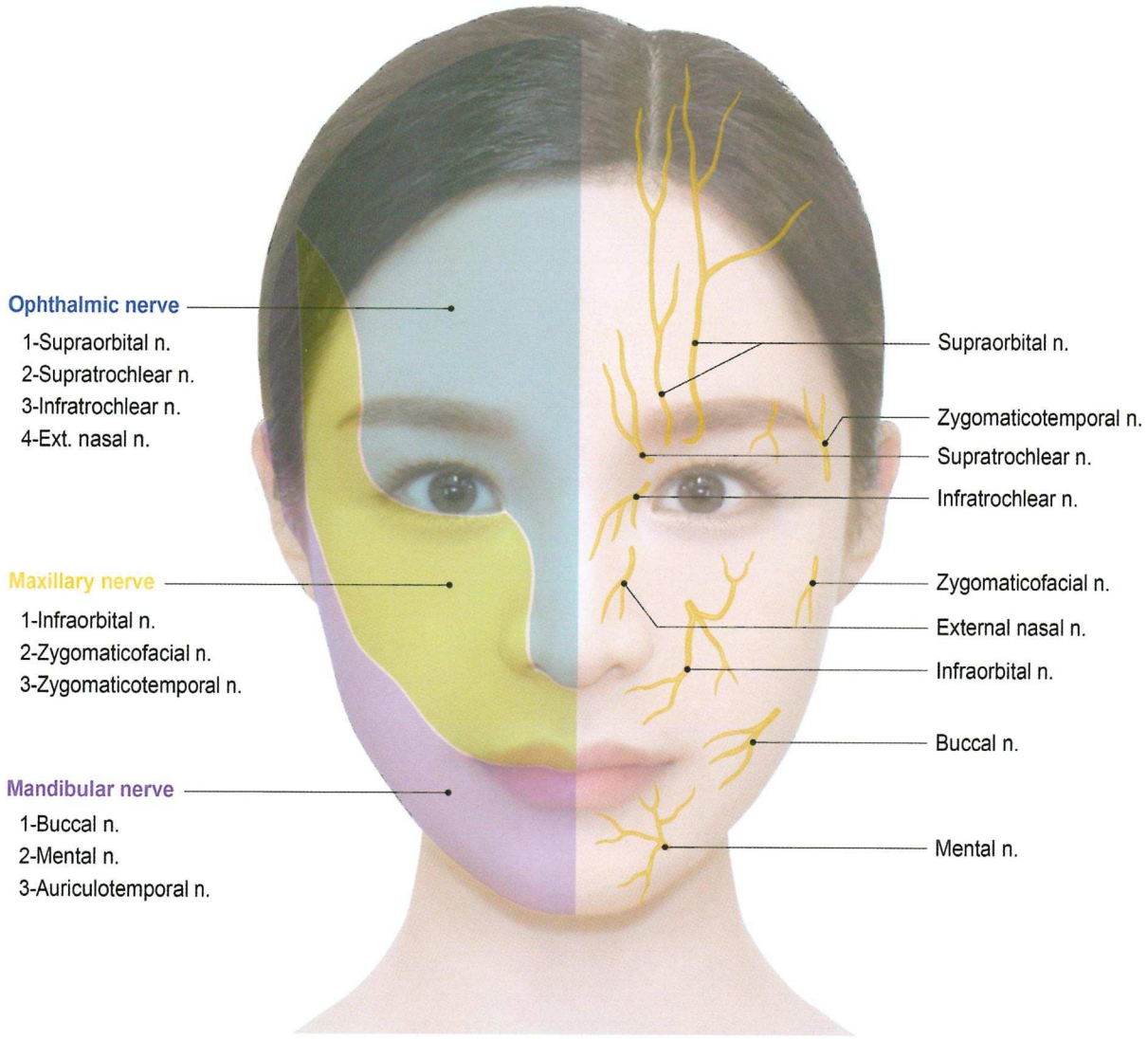


Figure 6 _ Nerve distribution of the face and areas of anesthesia

5. General injection method of the fillers

Select the appropriate filler and needle or cannula for each treatment site. Before injecting the filler, check if the filler ejects properly from the tip of the needle or cannula. Check the position of the needle tip with the fingers of the opposite hand. If you feel resistance while injecting with cannula, proceed and advance by rotating slowly. Never proceed forcefully. Do not push out the contents during the advancement, but inject as you remove the needle or cannula (retrograde injection). Immediately after injection, gently press and spread evenly as you control shapes on the site of injection. Check the shape to see if certain areas are short in contents and perform the procedure. When changing the direction of injection at one entry point, take the cannula completely out and re-inject after reorienting the tip. After the procedure, have a habit of gently pressing around the entry point to remove the remaining filler on the entrance of entry point and wipe it with ethanol cotton to prevent irritation.

6. Principles for safe filler treatments

①Understanding the anatomy of the treatment site.
②Try utmost effort to minimize damage to the injection site.
③Select appropriate filler to the injection site and injection depth.
④To minimize pressure applied to the injection site, slowly inject using a 21G, 23G thick needle or cannula.
⑤Before injection, confirm that it is not located in the blood vessel by regurgitation.
⑥If possible, use linear threading technique rather than single deposit injection.
⑦Avoid over-correction.
⑧After injecting the filler, gently massage and mold to finish the shape.
⑨Prescribe preventive medicine after the procedure.
⑩Be aware of emergency treatment method to confront emergency situations at all times, and prepare emergency kit.

Normally, face of an individual is asymmetrical; left and right sides are different. The goal of the treatments is to check the asymmetry of the face and improve the facial balance as much as possible. In order to make an ideal treatment result, lead various facial expressions to check regions of improvement then design accordingly. Check the position of the blood vessels to avoid intravascular injection of fillers, and be careful not to pressure the blood vessels by excessive injection. It is not recommendable to inject more than 3cc of filler in one area. Avoid treatment on the sites with any history of surgery, and be careful when performing treatment on areas where previously received other types of treatments.

It is preferable to inject either in dual or multiple layers on any regions. After injecting the filler, expansion of the filler should be taken into account, thus do not fill all the insufficient areas at once. About 10 days after the treatment, monitor the progress and take additional treatments(retouch) if necessary. Insufficient filler can be easily corrected by performing additional injection. However, in cases of overcorrection, complications including situations where it requires dissolution with hyaluronidase may occur; avoid overcorrection. It is important that the filler is applied safely to a level that does not give stress to the surrounding tissues and lead to a natural change. Patients who have been treated are recommended to quit smoking for at least one week, for the recovery and prevent inflammation on treated area.

This section will introduce the filler treatments for forehead, temple, pretarsal roll, under the eyes, front zygoma, cheek, nasolabial fold, nose, lips, and chin.

1. Forehead

For filler injections above periosteum, sub-Q, and sub dermis, anesthesia is appropriate.

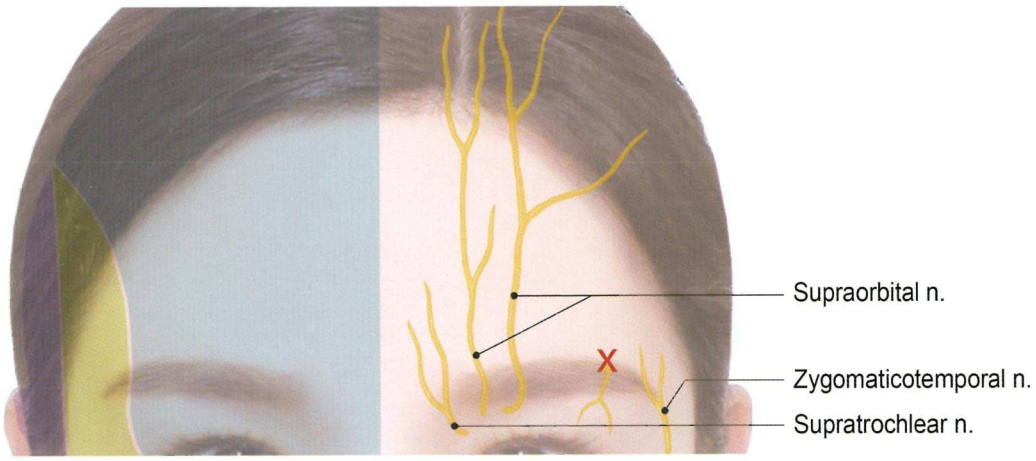


Figure 7 _ Forehead entry point and location of the nerve

Since supraorbital nerve is located near the entry point (= X) around the arch of the eyebrow, anesthetize in small amount.

By touching the lower margin of the eyebrows by hand, it is possible to check the supra-orbital notch and foramen type. Approach to the lower part of the eyebrow and anesthetize the curved part of the margin, that is, the eyebrow area where the supra orbital nerve comes out. Also, anesthetize supratrochlear nerve which is located 1cm medial to the front (i.e. medial side) of the eyebrows. Anesthetize the entire forehead with a small amount of anesthetic injection at the entry point at the arch of the eyebrows.

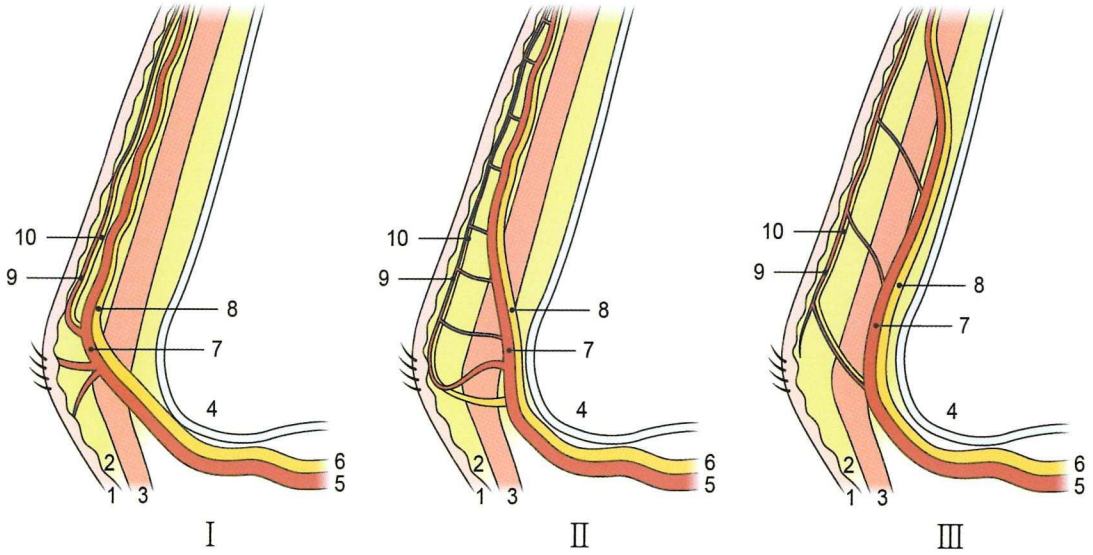


Figure 8 _ Supraorbital neurovascular bundle of forehead

Schematic representation of sagittal view of the neuroarterial structures in the forehead demonstrating penetrate from subcutaneous (I - II) to submuscular(III) the layer in the three patterns: (1)Skin (2)Subcutaneous tissue (3) Frontalis muscle (4)Skull (5)Supraorbital artery (6)Supraorbital nerve (7)Deep branch of the supraorbital artery (8) Lateral branch of the supraorbital nerve (9)Superficial branch of the supraorbital artery (10)Medial branch of the supraorbital nerve

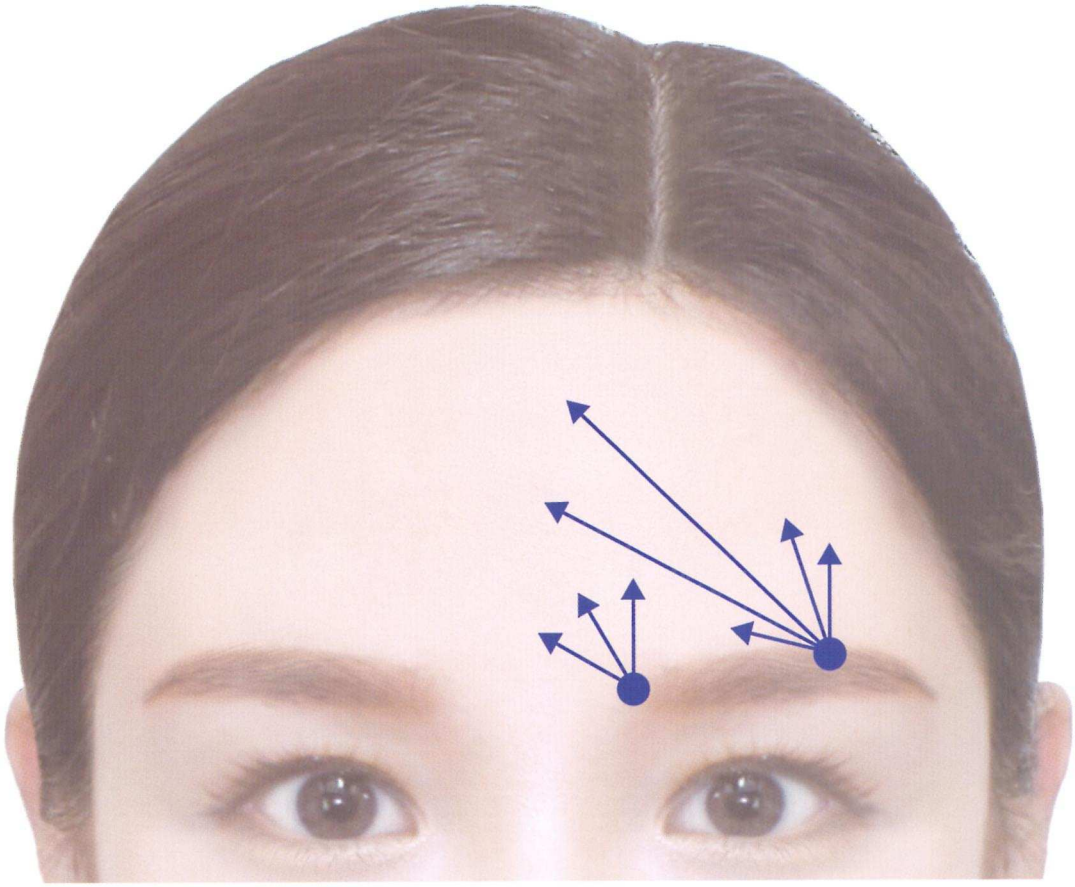


Figure 9 _ Forehead entry point and treatment direction

The forehead filler is injected as if laying the contents on the subgaleal region and periosteum . By using a cannula , enter from the arch of the eyebrows and touch the bone , then approach subgaleal region.

In relation to the forehead filler treatment and considering the physical properties of the filler and anatomical characteristics of the injection site , a comparison study on Restylane ®, Juvederm ®, and all 3 types of Starfill fillers '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) was published . It recommends injecting forehead related fillers on the preperiosteal layer located behind the frontal muscle to reduce vessel-related adverse events. When injecting into the subcutaneous layer at the anterior part of the frontal muscle , it may be easier to make more ideal appearance. However, due to the distribution of blood vessels, more attention should be paid to blood vessel -related adverse events such as external vessel pressure and intravascular injection . When injecting the filler into the preperiosteal layer behind the frontal muscle , there must be enough force to hold the tissue up while maintaining the compressive pressure and shearing force of the filler. Durable filler with suitable elasticity and high cohesive force is suitable . Starfill Deep Plus Lidocaine with high elasticity and cohesiveness is used on the target regions where volume should be given and deep layer.

On the other hand, soft Starfill Plus Lidocaine is used for the regions where wide molding is

required in the thin skin layer. It is recommended to use a cannula of 23G or more to prevent excessive force applied to the forehead during the treatment.

Care should be given as the surface is prone to become bumpy when the injection depth is too shallow. If bi-phasic fillers are used, problem with the shape may sometimes arise from the irregular absorption of the fillers; it is recommended to use mono-phasic filler if possible.

Inject the center of the main target first, and then adjust the overall volume balance. If the patient does not have enough volume on the sides of the forehead, apply an appropriate amount of filler and spread it with thumb or spatula so that the line follows naturally.

2. Temple

When approaching the temporal region, approach from the inside of the hairline to avoid temporal vein and superficial temporal artery. Prepare anesthetic injection on the entry point inside the hairline. If it doesn't bleed on the point of anesthetic injection, it can be understood as a safe position to puncture.

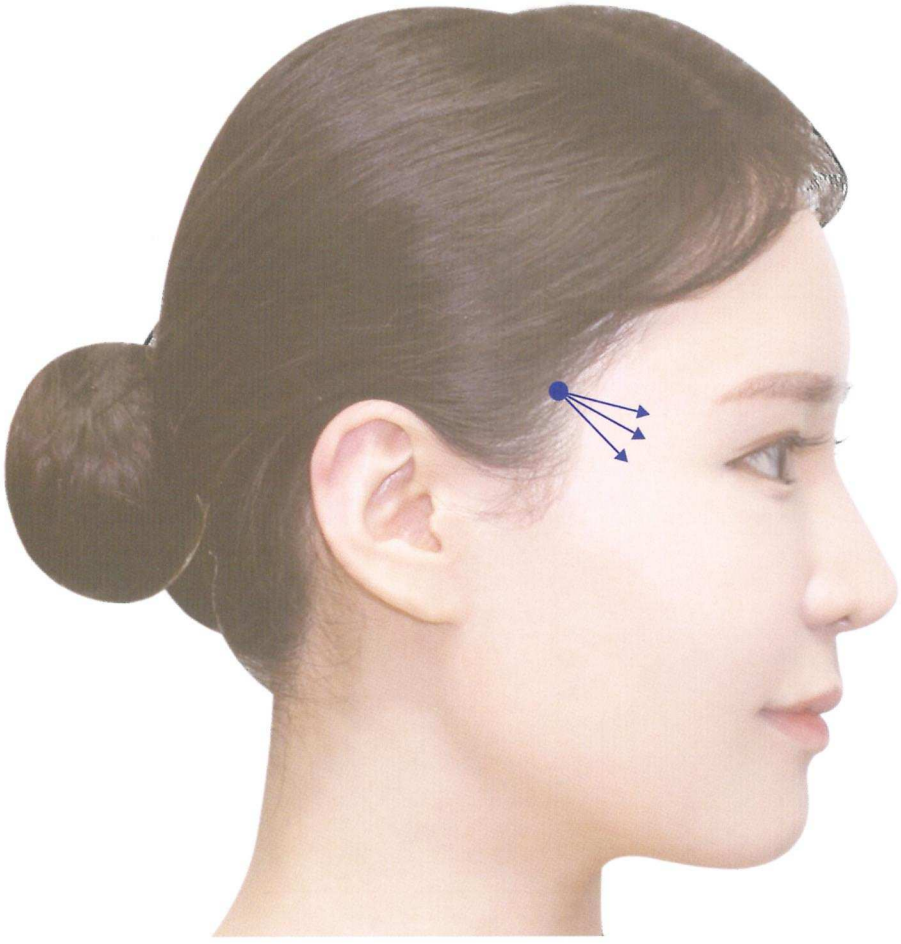


Figure 10 _ Temporal entry point and treatment direction

When injecting in the subcutaneous fat layer, irregular shapes may appear on the surface. In an anatomical approach, since the superficial temporal artery runs through the superficial temporal fascia, it is safe to inject filler between the superficial temporal fascia and deep temporal fascia after penetrating through superficial temporal fascia. Considering that the cannula is a blunt tip, do not apply excessive force but slowly rotate as you advance. Use Starfill Plus Lidocaine as a base to inject, as if spreading out, until the lateral border of the orbital rim, and if the person is in need of a large volume due to deep temples , inject Starfill Deep Plus Lidocaine. After the treatment, gently press to orient natural shape.

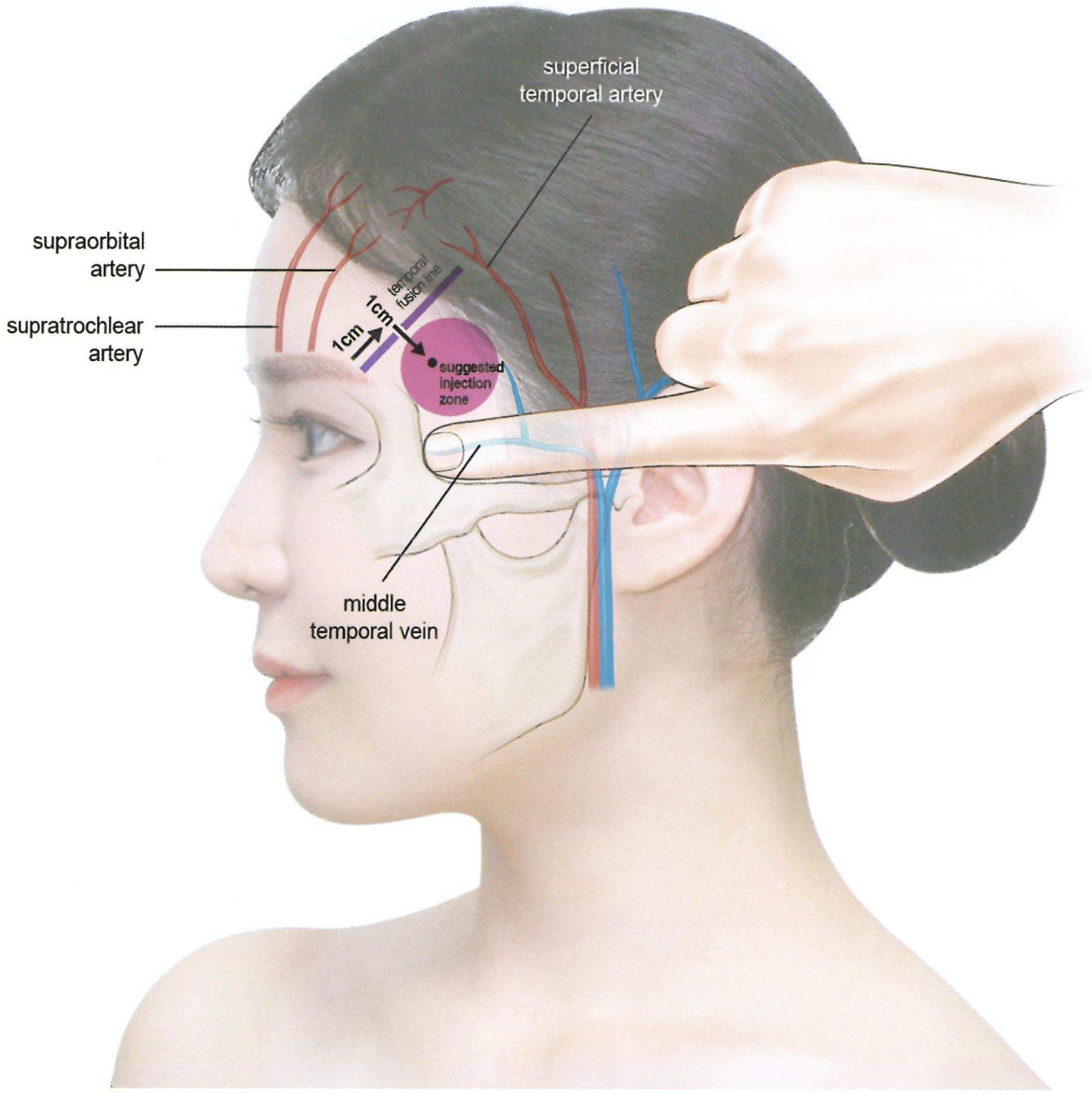


Figure 11 _ Blood vessels to note in the temporal regions

Since the branch of superficial temporal artery runs deep through the superficial temporal fascia, it is safe to inject filler between superficial temporal fascia and deep temporal fascia after penetrating through the superficial temporal fascia. Suggested safe injection zone for the temple lies between the superolateral bony orbital margin, approximately 1cm inferior to the temporal fusion line and over 1 finger breadth above the superior border of the zygoma in order to avoid the middle temporal vein.

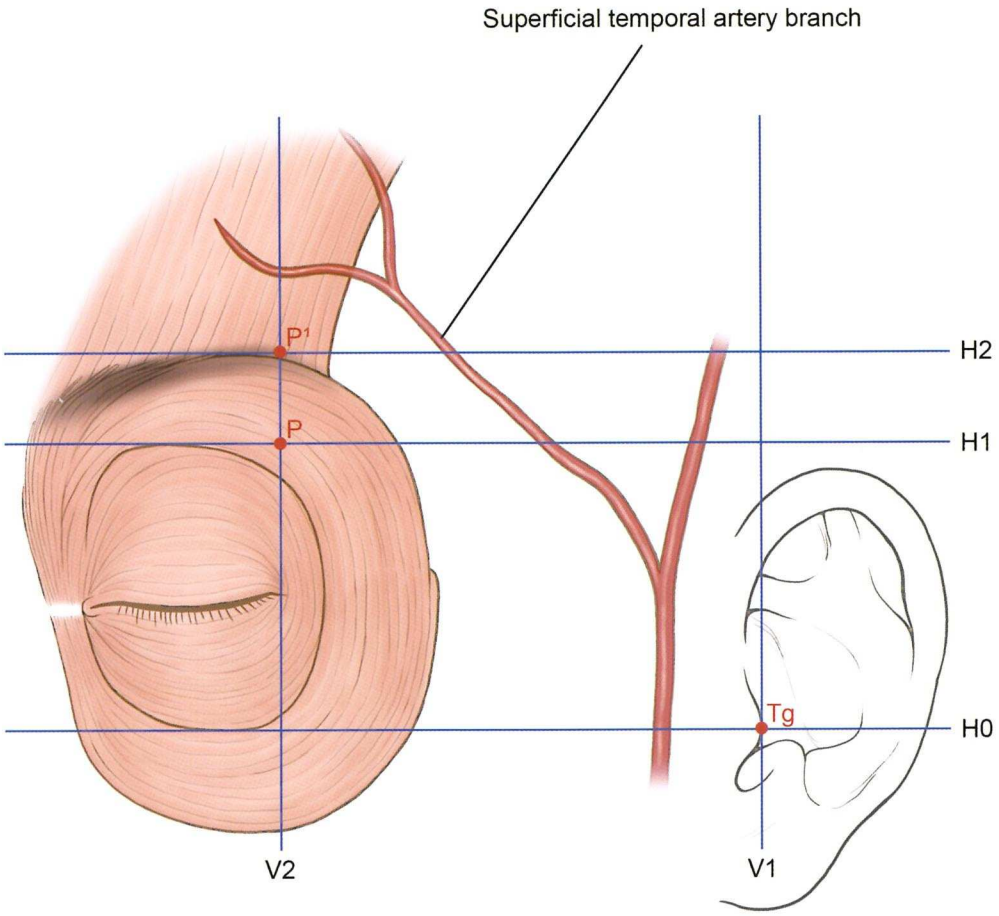


Figure 12 _ Confirmation of frontal branch of superficial temporal artery

Reference points and planes used for measurement of the locations and diameters of frontal branch of superficial temporal artery. (Tg: posterior-most point of tragus, H0: horizontal plane through Tg and the lowermost point of inferior rim of the orbit, H1: horizontal plane parallel to H0 through the uppermost of superior rim of the orbit, H2: horizontal plane parallel to H0 through the uppermost of eyebrow, V1: vertical plane perpendicular to H0 through Tg, V2: vertical plane perpendicular to H0 through lateral epicanthus, P: intersection point of V2 and H1, P^1: intersection point of V2 and H2)

When the filler is applied to the posterior frontal area, the individual differences in the distribution of blood vessels in the frontal branch of superficial temporal artery should be understood. As shown in Fig.12, the locational distribution of the general frontal branch of the superficial temporal artery can be seen by using points and lines. For more information, refer the article Frontal branch of the superficial temporal artery: anatomical study and clinical implications regarding injectable treatments.(Lee et al. Surgical and Radiologic Anatomy, 2015).

The superficial temporal artery and the middle temporal vein are the vessels to be particularly cautious. Referencing from the zygomatic arch, the middle temporal vein runs deep(under the deep temporal fascia) at the level of one fingertip, and just two fingertips above, superficial temporal artery runs under the deep temporal fascia in 45° angle above the eyebrows(2cm above). It is better to inject while feeling pulsation at the time of injection

as there are branches.

Temporal region is relatively thin in the skull as the temporalis muscle is directly attached to the bone without periosteum. It is a region where cerebral hemorrhage can occur if forcefully inject a thick needle. Care should be given at all time to nerve damage during deep region injection, increased edema due to lymph drainage problems, and potential vessel problems due to the injection of large amount of fillers.

3. Pretarsal roll

Molding is rather difficult in this region. When choosing the filler for pretarsal roll region, it is good to select a filler with soft physical property which allows molding and high cohesion that will maintain the shape after the treatment. Since the skin is thin, it is better to choose a filler that does not leave HA gel particles in the form of a wheat after the filler disappears. Use Starfill Plus Lidocaine.

For sophisticated procedures, infra-orbital nerve anesthesia may also be performed to prevent patient from moving. Since the lasting period is longer than other sites, the first procedure is very important. If the shape does not come out as desired, a small amount of hyaluronidase can be injected in irregular areas to reorient shapes.

The depth of injection targets the subcutaneous layer near the eyelashes, preferably between the orbicularis muscle and tarsal plate(tarsus) and deep in the orbitomalar septum. The filler is injected in the direction of the needle pointing toward the eyelashes. Since HA fuses with water, a small amount of wrongly injected filler can lead to severe edema in the soft tissues in the posterior septum. Thus, depending on the patient's condition, inject a small amount of around 0.2~0.3mL per one side. Although it should be aimed to treat 2/3 thickness contrast to the size of the entire eye, it is recommended to inject conservatively, taking the possibility of retouching as tyndall phenomenon may occur. It can be injected at once with cannula or in multiple steps with needle.

If the injection direction faces downward or infusion level is too low, the infraorbital crease may break and the shape may look blunt. In addition, premolar edema may occur when injected anterior to the posterior septum or orbital septum. When injected into the infraorbital area, it can accidentally penetrate anterior to the orbital septum or orbital cortex. This may be the case if the syringe is handled too high, too deep, or too close to the orbital bone, accidentally penetrate the septum, or if the septum originally intact and undivided

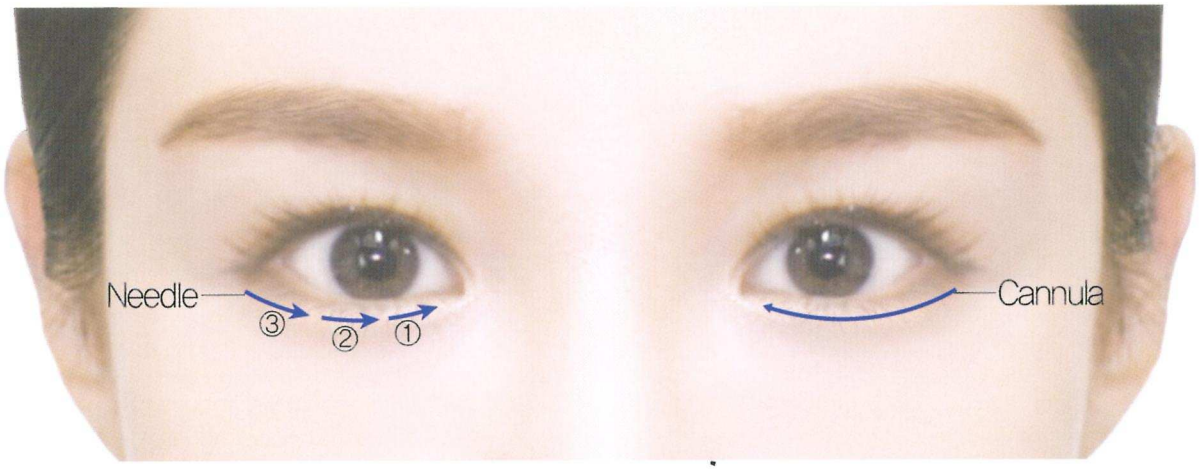


Figure 13 _ Design of pretarsal roll filler injection

was damaged by previous procedures(fat grafting type of blepharoplasty, etc.), or when too much filler is injected. As a result, the pretarsal roll that may occur that did not exist prior to the filler treatment thus it should be treated carefully.

Since the areas around the eyes are prone to swelling after the procedure, treat delicately and carefully to ensure that both eyes are as symmetrical as possible. We do not recommend the use of pretarsal roll filler in cases where the eye fissure is too wide or narrow, thick skin or fat layer, severe dark circles, relaxed skin, or lack of eye roll muscle.

4. Under the eyes

The area under the eyes is treated with Starfill Plus Lidolcaine.

Fill the upper and lower pit holes reference to the nasojugal groove. Inject until the orbital rim margin. Targeting SOOF(Sub-Orbiculariis OculiFat), inject in multiiple layers for areas around eyes and cheeks, such as sub-Q and sub dermal layers. When injecting on the nasojugal groove region, inject from under the muscle by bone touching, and for the upper part, inject as if spreading the filler.

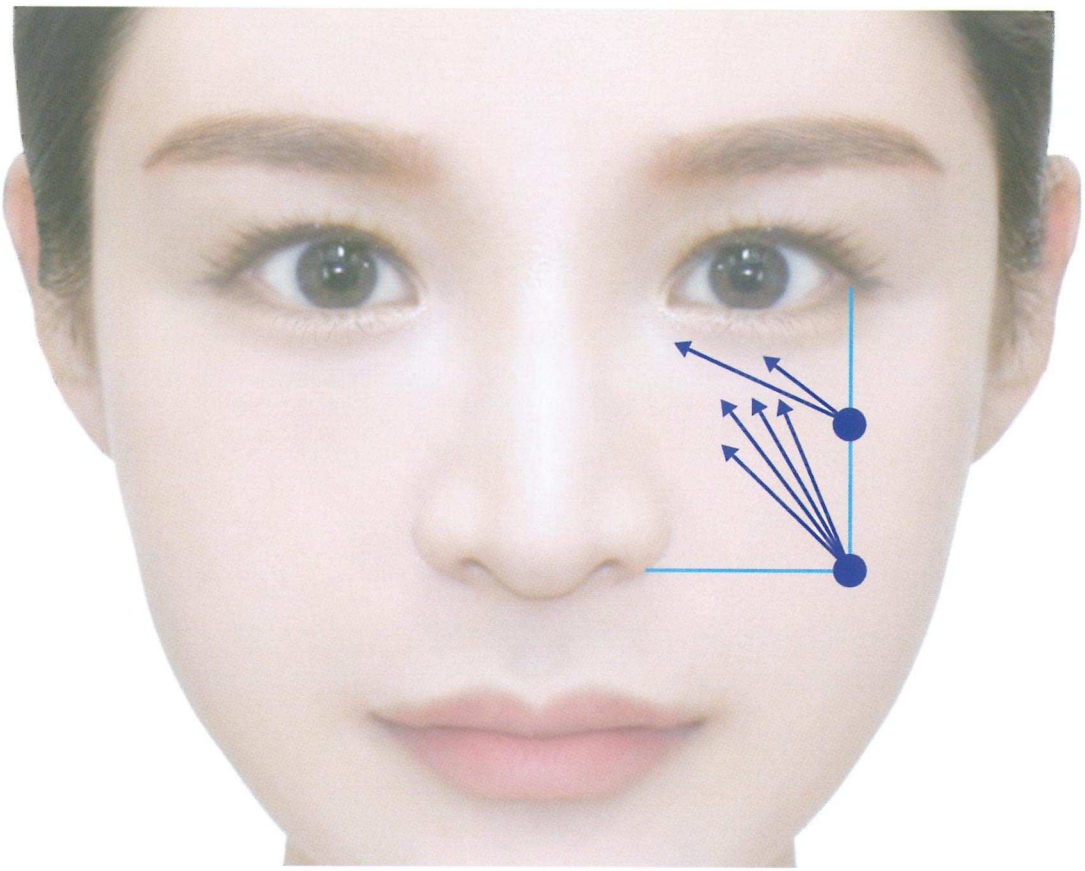


Figure 14 _ Entry point under the eyes and treatment direction

Care should be taken when performing treatment on the subdermal layer along the

Indian band(wrinkles), since if you cannot approach the correct skin layer, the filler may be misaligned below or above the band(wrinkles). Inject as if performing subcision injection technique on where the retaining ligaments are located. Generally, delicate subcutaneous dissection using a cannula can produce the desired result. In severe cases, special injection needles designed for subcutaneous dissection may be used. At this time, it is better to first inject the filler deep enough to allow the supporting ligament to be repositioned in the lower part, and inject a small amount under the dermis immediately below the Indian band. Pay attention to the position of infraorbital artery during the procedure and massage thoroughly after injection to spread the filler evenly.

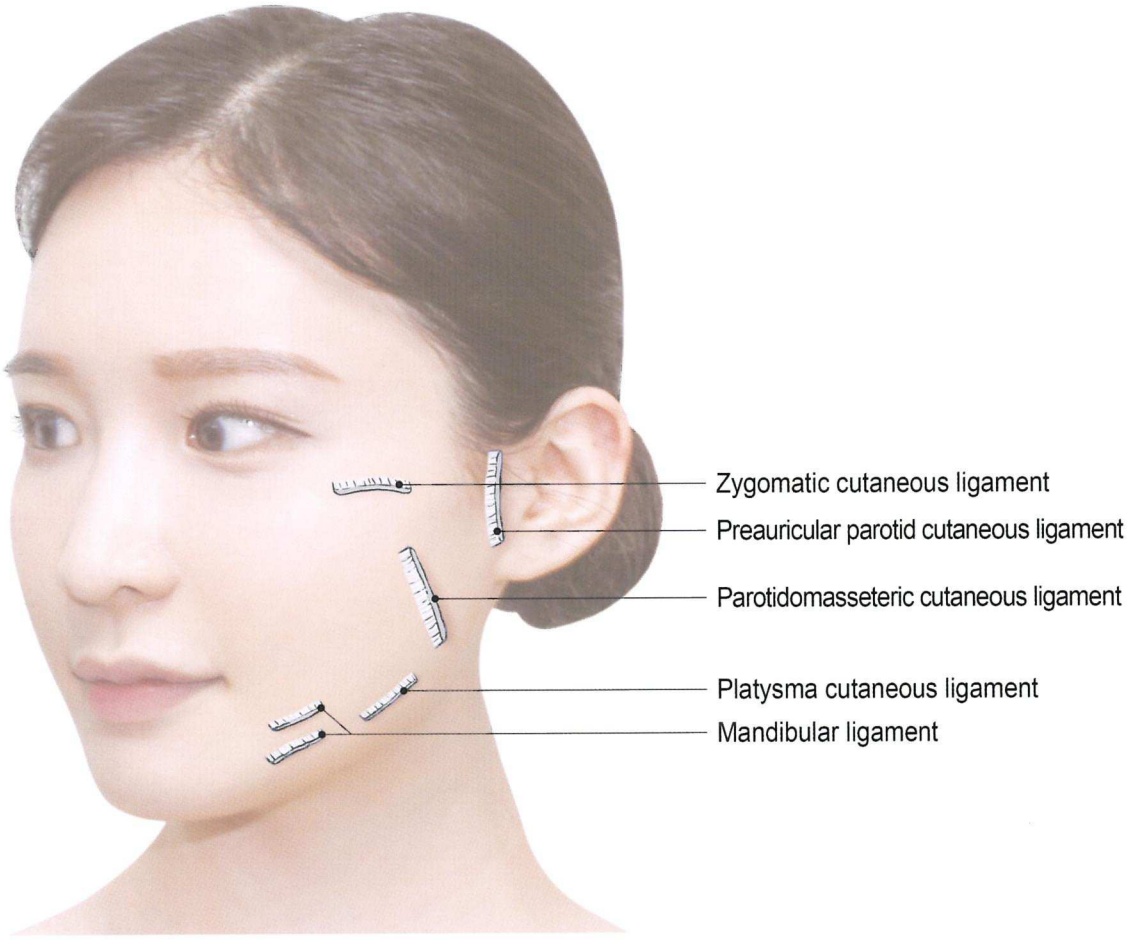


Figure 15 _ Location of the face retaining ligaments

5. Front zygoma . Cheek

Anesthetize the infraorbital nerve for the mid-face region treatment including the front zygoma, nasolabial fold, and cheek. The infraorbital nerve can be approached in 2 ways: from outside the skin as shown in Fig. 16, and through the pallet as shown in Fig. 17. Anesthesia inside the mouth using a dental syringe is recommended, as there is no worry of nerve damage. When approaching the pallet using a dental syringe, inject by approach between first and second premolar.

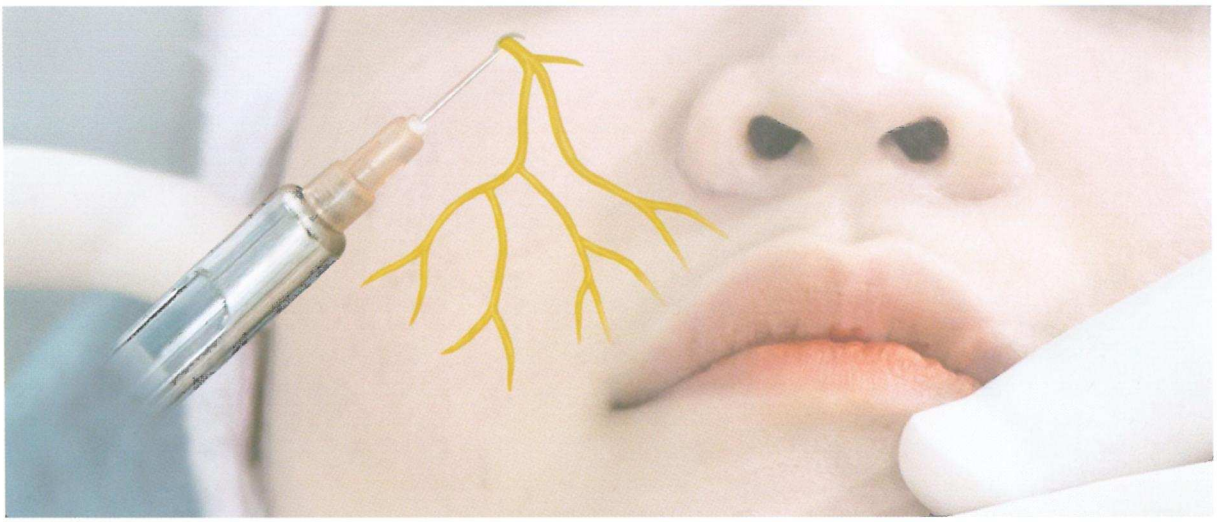


Figure 16 _ Infraorbital nerve approaching for outer skin

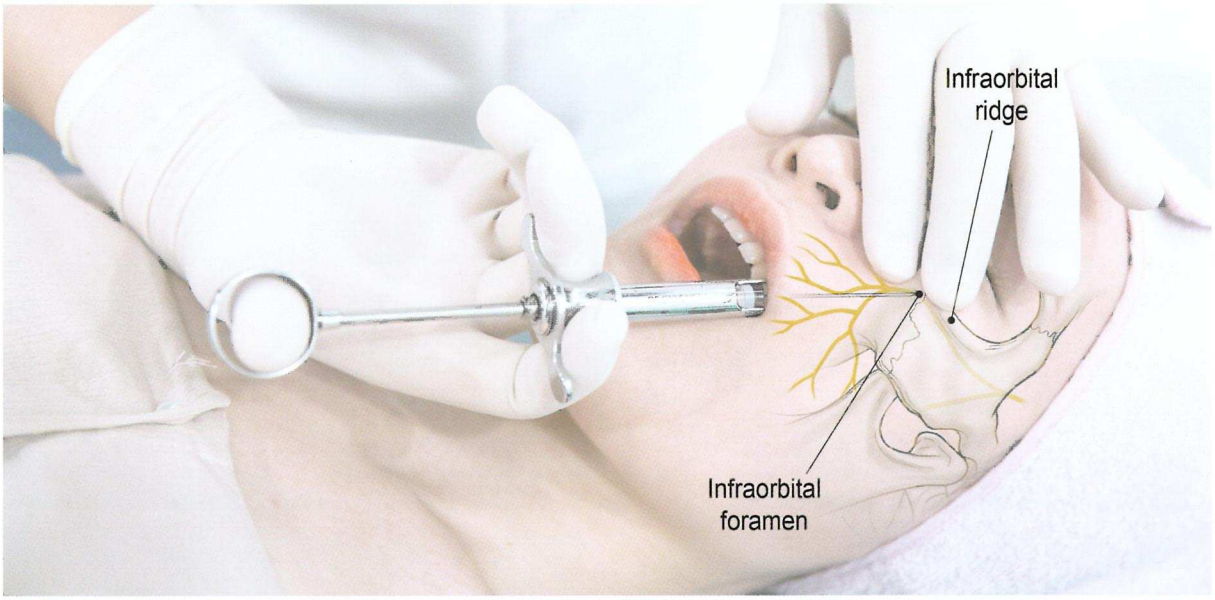


Figure 17 _ Infraorbital nerve approaching through the oral cavity

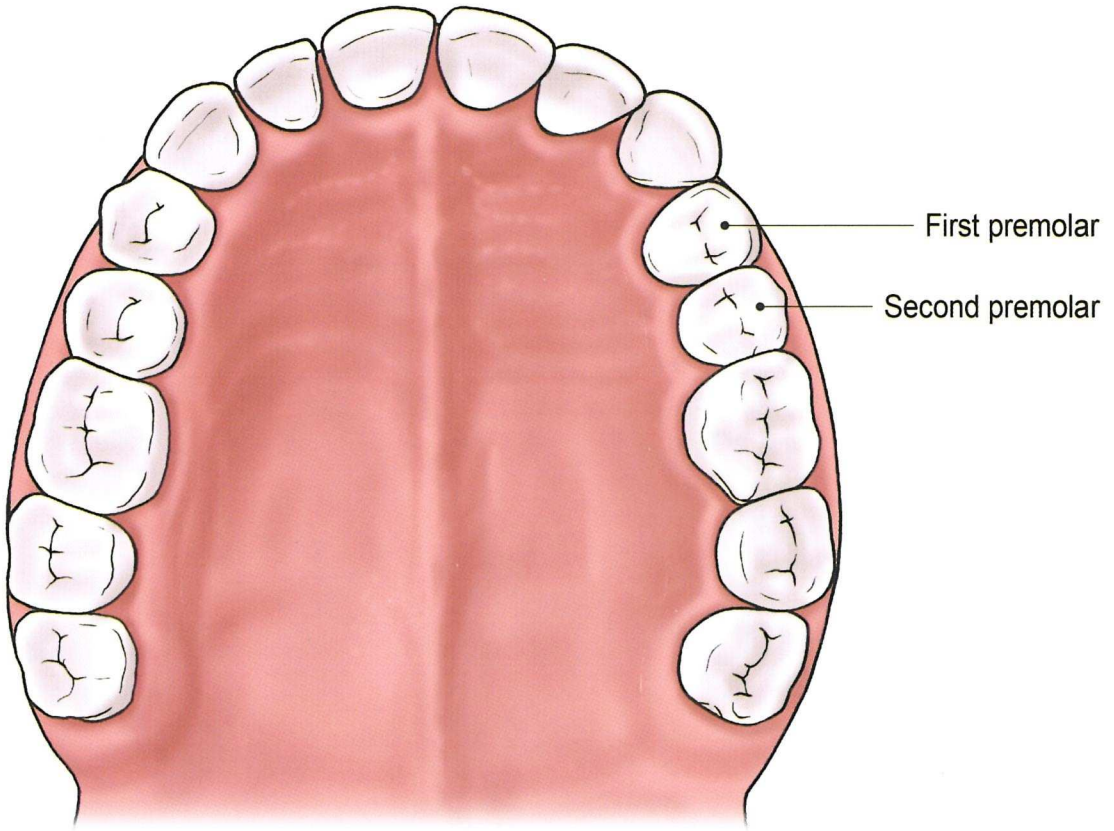


Figure 18 _ The location of the first premolar and second premolar

For front zygomatic region, inject in the deep malar fat pad for augmentation. To make the shape more natural, it is better to inject filler in the subcutaneous layer as well. To provide a firm sense of volume in the malar area, use Starfill Implant Plus Lidocaine with high elasticity and cohesion.

There are two approaches to the malar: l) direct injection by needle and 2) cannula injection. For safer and larger amount injection targeting SOOF layer, cannula injection is recommended. Reference to the pupil, SOOF layer exists on the outside of the pupil, but barely any inside; this should be considered when performing procedure. Protect the orbital rim margin by pressing it with opposite hand of injection, and advance until tear trough then inject as you feel the content ejection.

To give volume to the cheek area, use Starfill Deep Plus Lidocaine with moderate elasticity and cohesion.

When advancing with the cannula, resistance to the retaining ligament(refer Figure 15) can be felt at the lateral cheek. Do not force it in and advance by rotating slowly and gently. Retrograde injection should be used for the filler injection.

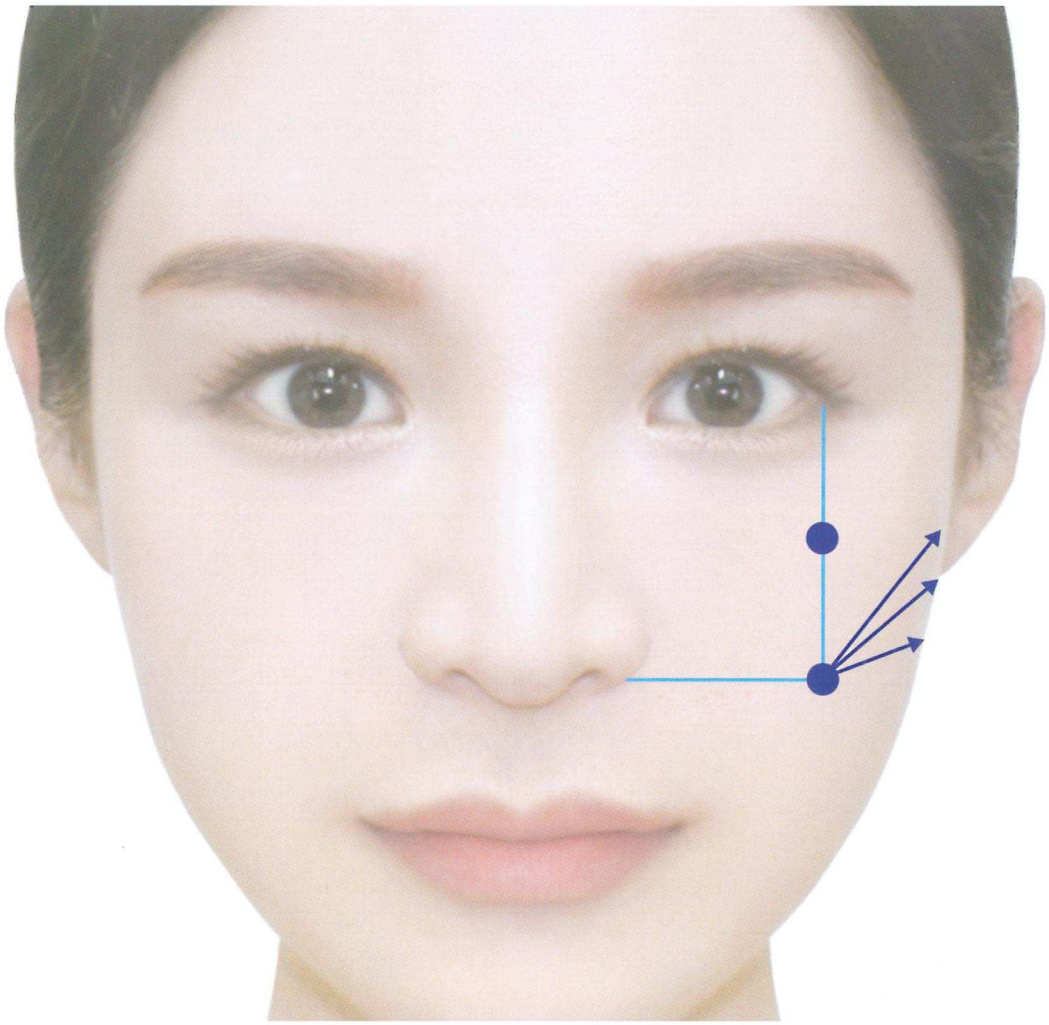


Figure 19 _ Entry point for front zygoma and cheek treatment and treatment direction

6. Nasolabial fold

Approach as you target the triangular part of the malar base. The multiple deposition of 2 or 3 layers injection method should be utilized for areas around nasolabial fold. It is better to inject more rigid filler in the deeper region and use a filler of a soft physical property as you move up. For the deep region, use Starfill Deep Plus Lidocaine with moderate elasticity and cohesion, and for the higher region, use Starfill Plus Lidocaine with softer property.

When injecting in a tilted angle, first select a target area where the cannula tip will finally positioned, and choose an entry point considering the length of the cannula. Use the cannula to approach near the bone deeply and inject the filler into the subdermal space. Use a needle for intradermal depth injection.

In the case of using an injection needle for nasolabial injection, advance the needle perpendicularly at the Ristow's space and position the needle tip near the bone. Apply negative pressure to confirm vessel infiltration then apply adequate amount and adjust the depth to sub-Q layer and inject once more. Thereafter, inject one more time in the dermal layer to correct nasolabial crease.

A method to confirm if the needle is positioned correctly in the intradermal depth is to see if the needle is caught in the skin and is not easily movable.

If lump forms from shallow injection, use the cotton swab to spread it immediately. The pressure of blood vessels in the area stressed by the filler is also reduced, and the adverse events due to the pressure of the blood vessels can be minimized.

Figure 20 _ Blood vessels around the nasolabial fold

To be cautious of the angular artery that runs from the side of the lips to the side of the nose, it is necessary to check whether the needle is placed in the blood vessel. Before injection , pull the push stick of the syringe and apply negative pressure of about 0.05mL to check if blood is withdrawn.

It is necessary to take caution when performing the procedure because the vascular accidents after filler treatment for nasolabial fold occur as much as in nose filler treatment. In fact, it is more common to cause circulation problems by pressing the peripheral blood vessels rather than directly from the fillers pressing the blood vessels. After injection, it is recommended to mold with a cotton swab or fingers to make shape, and prevent circulatory problems of the surrounding tissues.

7. Nose

Nose filler treatment is a region where vascular accidents most frequently occur, thus is important to understand the blood vessel distribution in the nose. Care should be taken not only on the intravascular injection but also the risks such as external vessel pressure. Before injecting the contents, have a habit of regurgitating around 0.05mL to see if blood is withdrawn.

The filler with high cohesive force is able to maintain its shape for a long time because the margin of the molding does not deteriorate after injection. If bolus injection of low elasticity and cohesive filler is applied, the shape may look better right after the procedure, but it can spread over time.

For nose augmentation, use Starfill Implant Plus Lidocaine with high cohesion and elasticity.

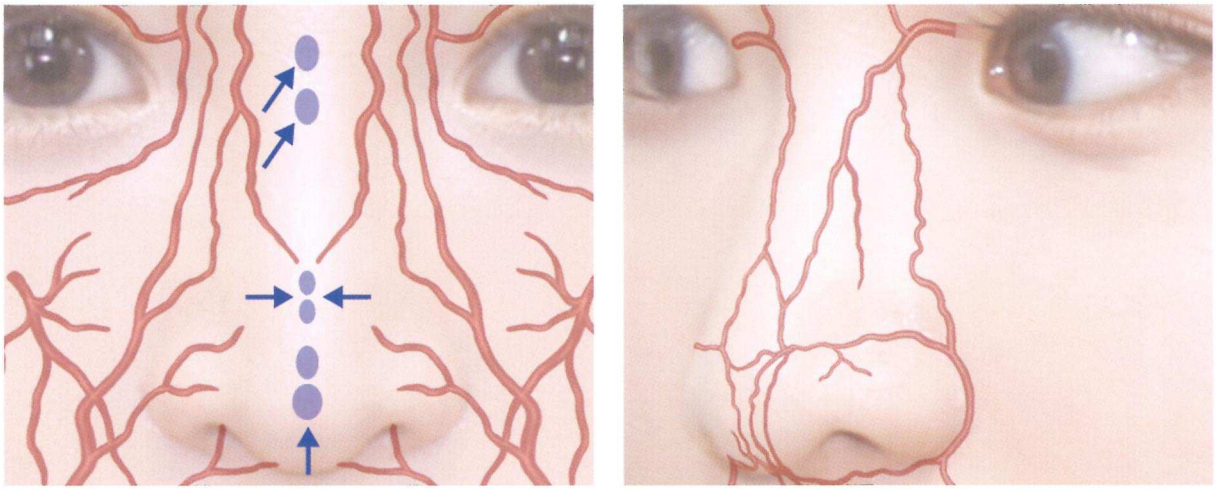


Figure 21 _ Understanding the vessels running in the nose region

Generally, the soft tissue layer of the nose is composed of skin, shallow fat layer, fibrous muscle layer, deep fat layer, periosteum, and perichondrium. The blood supply to the tip of the nose is mostly based on the lateral nasal artery, and the dorsal nose is distributed by the branches of the dorsal nasal artery and the branches of angular artery. In case of the dorsal nose, there is angular vein on both sides and intercanthal vein that connects them. Depending on the individual, the position and mode of run are slight different and has to take caution during injection.

For nose bridge treatment, bone touch technique is not recommended. The periosteal injection is the method used to inject permanent fillers. Using 26G and 27G needles, inject the needle at the subdermal depth with the bevel of the needle facing up. Since arterial branches are located above the deep fat layer just below the fibrous muscle layer, vascular accidents can occur when injected into deep fat layers.

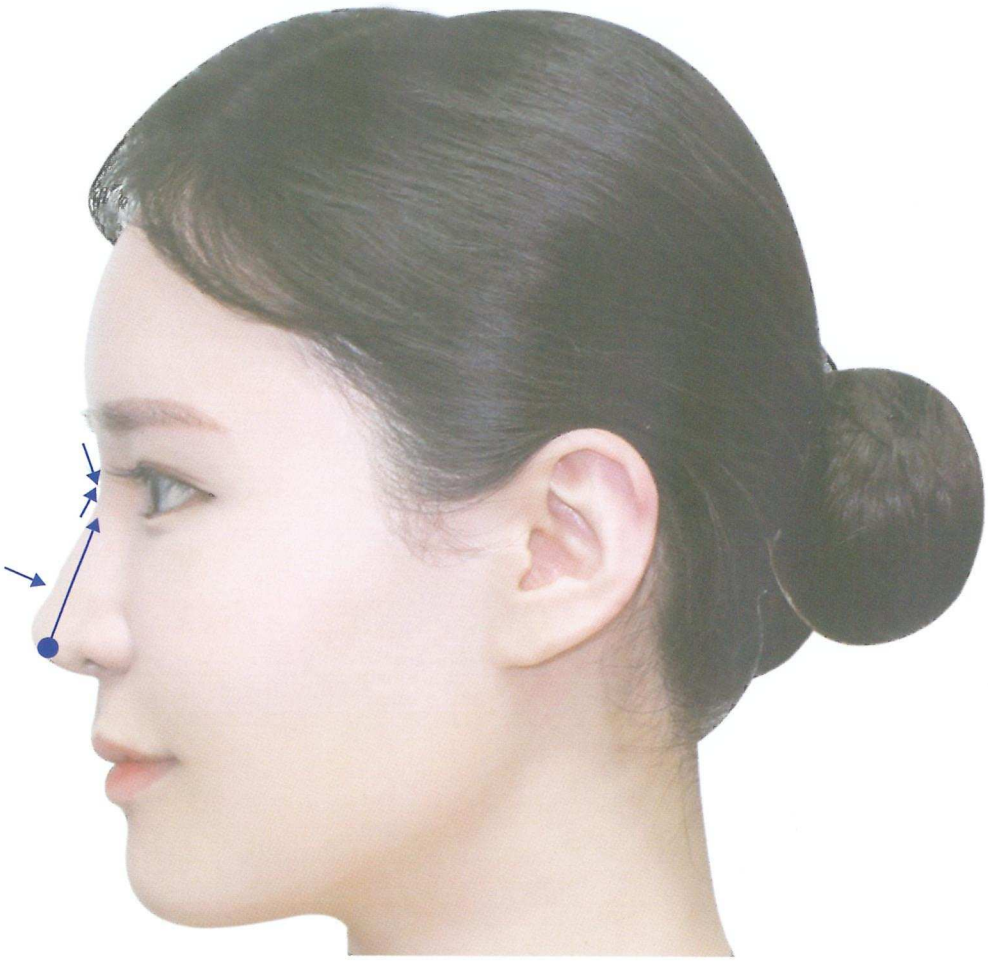


Figure 22 _ Nose treatment entry point and treatment direction

Be careful not to let the filler deviate from the centerline of the nose. It is safe to inject the tip of the needle to not cross the center line of the nose, and it can be reasoned from an anatomical vessel run shown in Fig. 21.

The supratip part can be supplemented from the side. The nose tip area is injected by holding the nose with thumb and the index finger of the left hand with pressure and inject by beveling up the needle. This area is made up of areolar fat, so a small amount of filler injection will give out good results.

The columella can also be injected with filler in the centerline from the front. Because the columella artery runs outwards, the procedure is safe to perform.

Patients who have enlarged nose from previous filler treatment, it is recommended to dissolve the old filler and then perform the procedure. As the time passes after the filler treatment, the treatment margin may collapse and spread out laterally. If the re-treatment is performed in such area, the nose portion may spread even wider. It is better to dissolve with hyaluronidase and perform procedure after one week. However, if there is not enough time to dissolve in advance, and if it is necessary to dissolve on the same day and to perform the filler treatment, inject the filler only in the center line, and dilute the hyaluronidase 1/5-1/10 and treated in the widened area by slightly injecting into the enlarged lateral area.

8. Outer lips

Anesthesia for lips filler treatment requires an infraorbital nerve block for upper lips anesthesia and a mental nerve block for lower lip anesthesia.

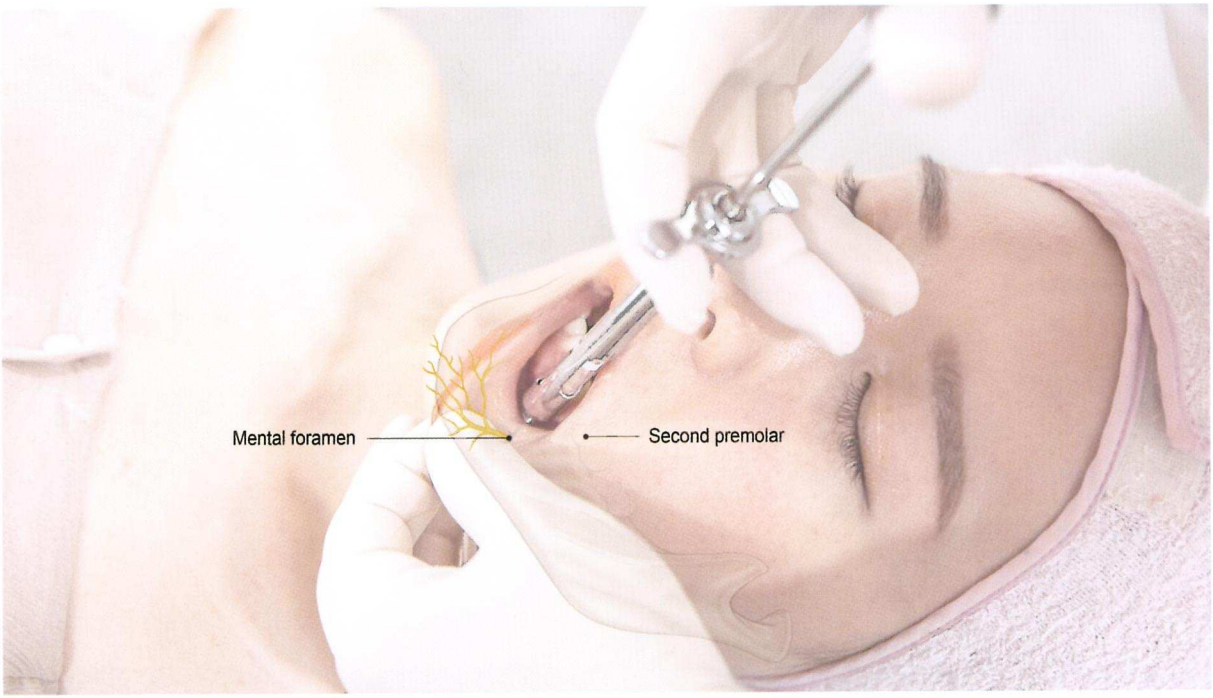


Figure 23 _ Approach from the oral cavity for mental nerve block

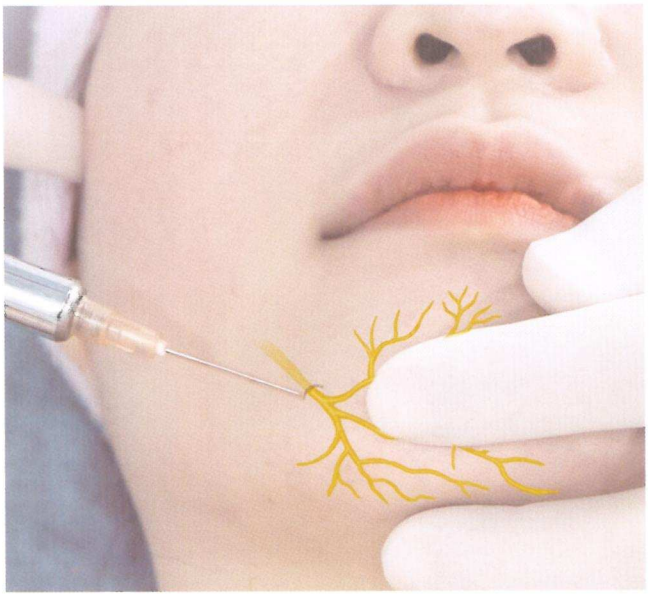


Figure 24 _ Approach from outer skin for mental nerve block

Both infraorbital nerve block and mental nerve block are accessible through the outer skin and within the mouth. You can choose according to your preference, but it is recommended to approach it through the mouth without the risk of nerve damage.

Since the skin of the lips are thin, the HA gel and its particles can occasionally be felt by the tip of the tongue inside the mouth when the bi-phasic product is used. The use of small and smooth mono-phasic type filler in the gel particle is effective for higher patient satisfaction.

We recommend using Starfill Plus Lidocaine for the volume of the lips, and Starfill Deep Plus Lidocaine for forming lip lines.

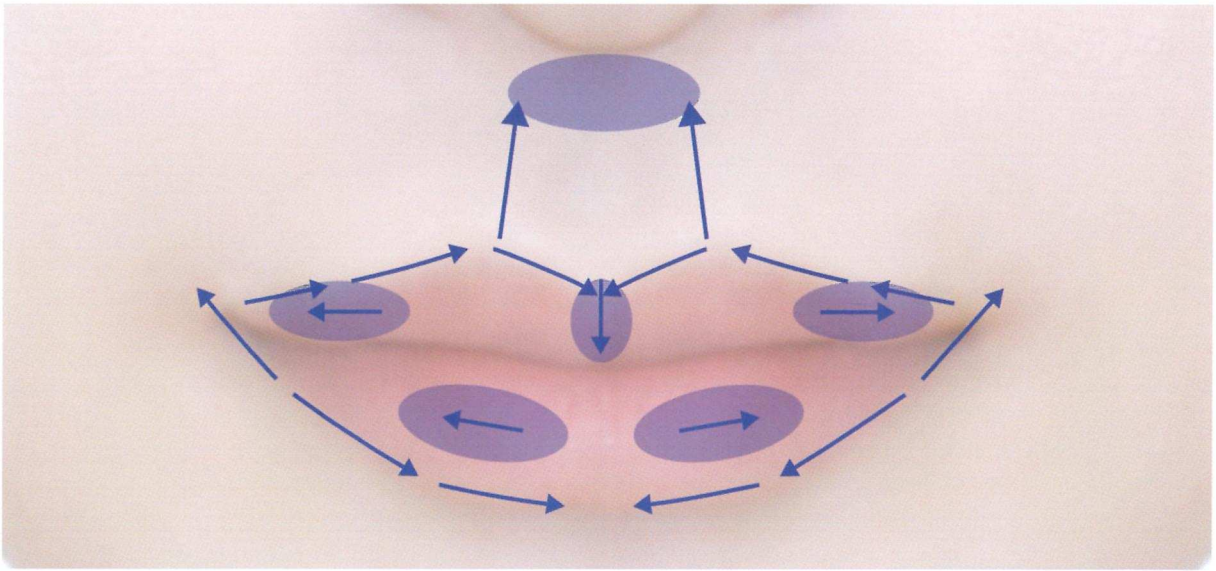


Figure 25 _ Lips filler treatment site and treatment direction

Depending on the patient, overall improvement is possible including volume of the lips, lip line, oral angle, philtrum line, and the volume of the philtrum.

Depending on the patient, selectively make volume in the medial part of the lip line of the upper lip. The lower lip is injected with filler in the dry portion of both sides except the middle to form two chambers. Lip mucous membranes can become rugged if it goes beyond the wet portion. It is also injected deep into the lips to prevent lumps. It is possible to expect a better shape when injected as if spraying the filler, rather than a method of making a lump.

As a method to improve the oral angle, an extension of lcm(45 degrees) from the vermilion border to the nasolabial fold pass the oral angle can improve the oral angle line and curled lips, and lifting effect can be expected. Using a 23G injection needle, extend to the same depth along the vermilion border and perform injection. To increase the volume on the inner portion of the oral angle, gently open the mouth, and inject the filler into the wet portion to improve the lip curl.

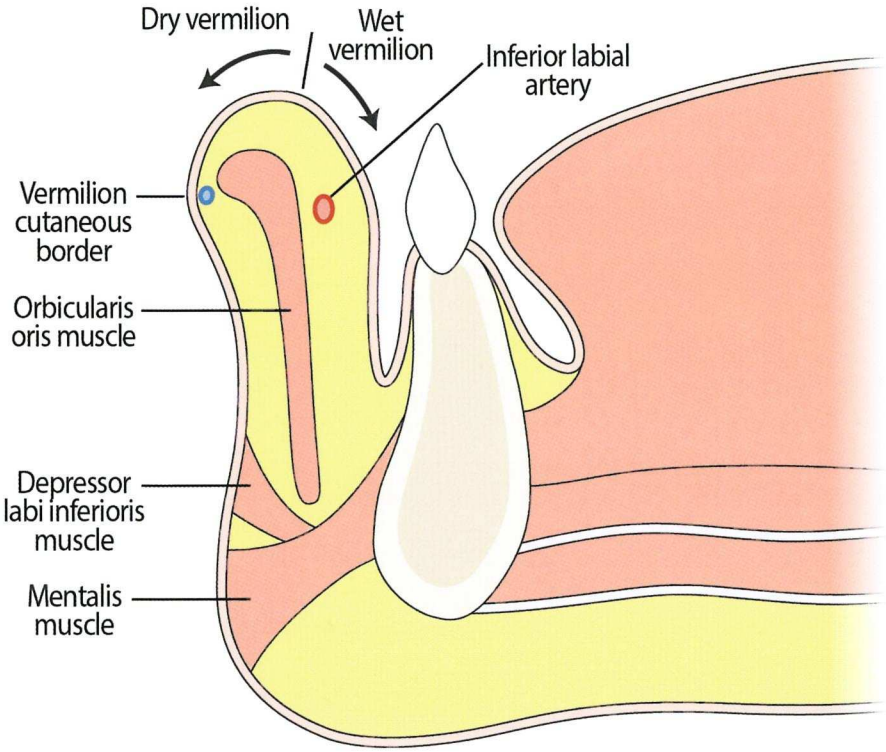


Figure 26 _ Anatomical structure of the lower lip

The blood vessels to note during the lips filler treatment are the inferior labial artery and the submental artery; these two blood vessels connect to each other to provide blood to the entire lips. A careful approach is needed to prevent bruising and edema after the procedure.

The lips and the front cheeks are the most swollen parts of the face, and also prone to bruise. Before the procedure, explain to the patient about the initial swelling and bruise that may occur temporarily(about one week) after the procedure.

If too much filler is injected, it may cause tyndall effect. Do not overdose and consider to perform a retouch after 2~3 weeks.

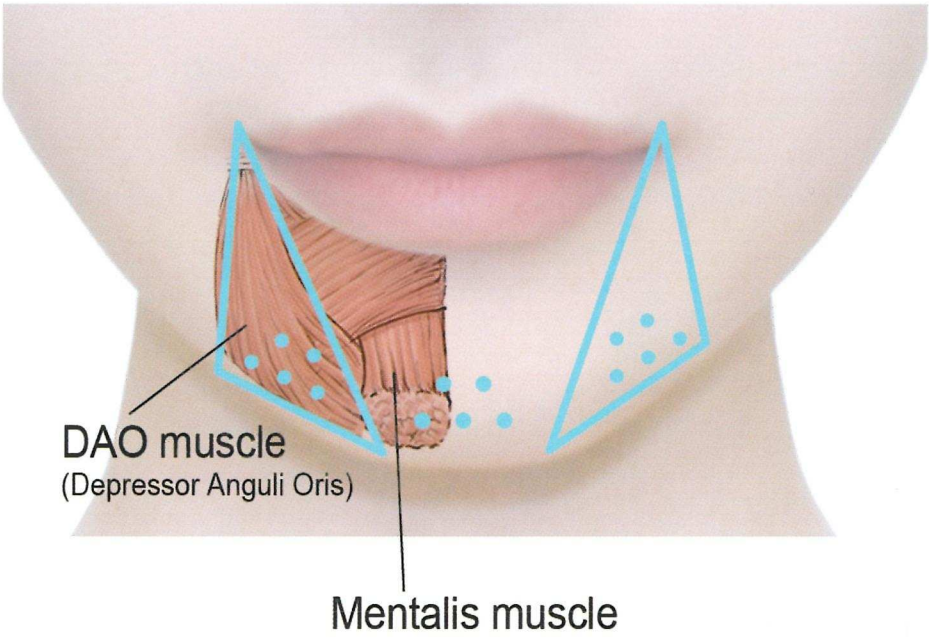


Figure 27 _ Botulinum toxin injection site for oral angle lifting

Botulinum toxin can also be used to raise the oral angle. Because the subdermis and muscle are attached to each other, it can be improved by injection with dermo-toxin technique instead of muscle injection. Inject Botulinum toxin into Mentalis muscle and DAO(Depressor Anguli Oris) muscle. Since muscle asymmetry can occur depending on the depth and speed of the injection, care should be taken with respect to both symmetries. Draw a hypothetical line on from the oral angle to the jaw line and inject it so that it does not cross the lower half. In some cases, injection is performed in the intersection point of Depressor Labii Inferioris (DLI) and DAO.

9. Chin

The total face ratio should be considered when designing the chin filler treatment. If the length of the chin or the entire chin is short, appropriate, or long, the volume is given only to the front of the chin. If the length of the chin is short, treat the bottom of the chin as well to increase the chin length, to achieve harmony.

After mental nerve(see Figure 23, Figure 24) anesthesia, inject the filler in the subdermal, sub-Q and over periosteum. When entering into the muscle, it is difficult to use a cannula, so inject it using a needle.

If the development of the chin muscles results in a cobblestone chin, botulinum toxin can be used in parallel(see Figure 27) to maintain the shape of the filler.

Harder filler is suitable, and for Starfill, use Starfill Implant Plus Lidocaine.

Because the submental artery runs to the center of the jaw approximately 10-15% of the time, avoid the injection from the center line to avoid it, or approach it carefully from the side.

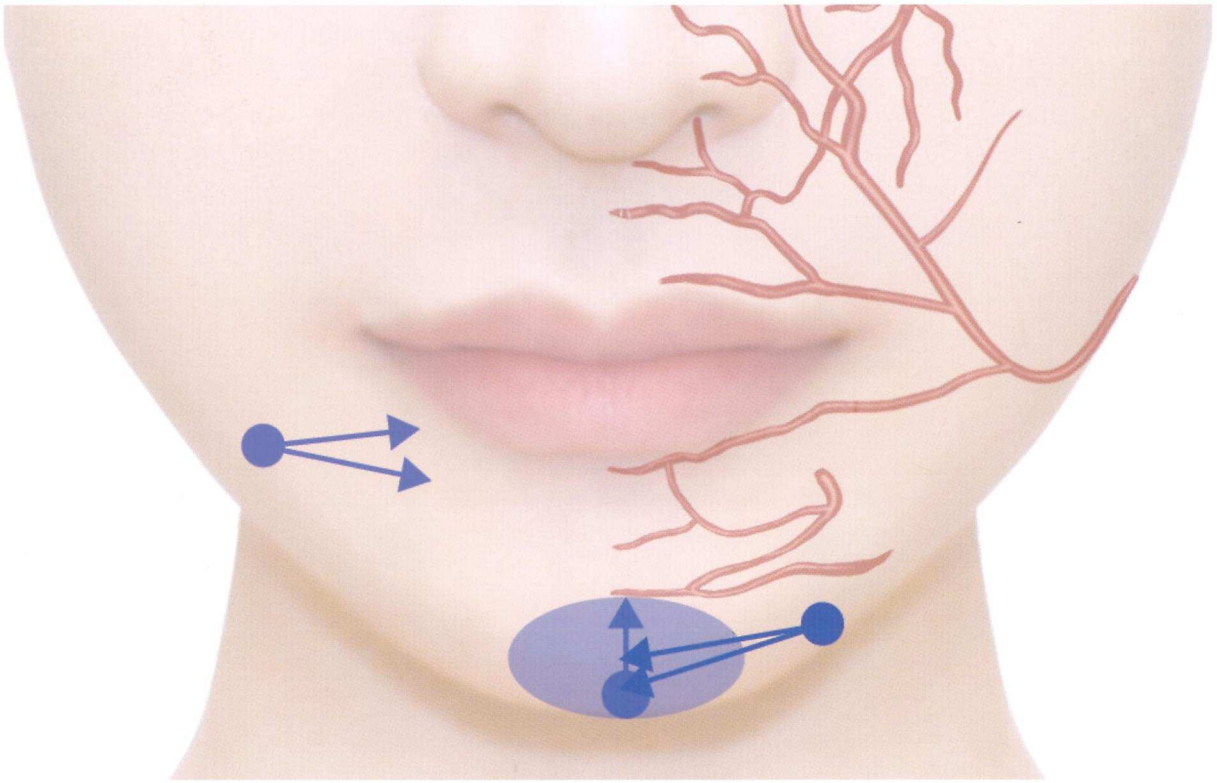


Figure 28 _ Entry point for chin treatment and treatment direction

For patients with jowl, injecting the filler under the DAO muscle may produce better results.

1. Types of adverse events by the time of occurrence

Because the filler is a foreign substance, some patients may be hypersensitive to the injection product due to immunoglobulin E(IgE) mediated immune response and may cause edema by the water swelling of the HA filler. The adverse events that may occur early in the use of fillers are temporary initial edema and inflammation or hypersensitivity. This is mostly controlled by antibiotics or steroids. A mild inflammatory reaction with initial swelling can be solved by medication alone, but if it is accompanied by hypersensitivity, it is right to treat with hyaluronidase or squeeze the injected filler. The types of filler adverse events according to the time of occurrence are shown in the table below.

Early (days to weeks)	**Delayed** (weeks to years)
Injection site reaction Swelling Redness Bruising/ecchymosis Pain Itching Infections	Granulomatous inflammation/foreign body reaction Nodules, erythematous or not
Allergic reaction/hypersensitivity Inflammation Solid nodules	Migration of the implanted filler
Lumps caused by misdistribution	Scarring
Tissue necrosis	Asymmetry
Embolism with blindness	

Table 4 _ Types of adverse events by the time of occurrence

2. Countermeasures for adverse events of the filler

By choosing a safe product and following only a few principles for safe filler treatment, you can prevent adverse events from the filler.

Nonetheless, the initial response is very important for filler adverse events. Even the skin color change at the injection site immediately after injection can be checked to minimize serious adverse events.

When a problem occurs, the initial response method is as follows.

I) Squeeze out the filler

After puncturing using an 18G needle, gently squeeze out the filler. Avoid skin tissue damage from applying excessive force.

Figure 29 _ Removal of the filler from the complication area

As shown in the picture on the left, there are cases where inflammatory cells appear to be mixed with pus, and blood is mixed together as shown in the right picture.

When the filler removed from the complication area was dissolved in hyaluronidase, no reaction was confirmed. This phenomenon can be understood as an encapsulated isolated form or transformed to a granuloma form.

Figure 30 _ Confirmation of the non-reactivity of the squeezed filler in hyaluronidase

2) Hyaluronidase injection

There are various hyaluronidase products used for dissolving hyaluronic acid filler. It is advisable to select products that do not cause hypersensitivity reactions. Most of the products sold in Korea are 1500 IU and in the case of HA filler, Hl is injected according to the filler capacity originally injected. It is also known to be better to use 2~3 times the injected filler capacity thus, a sufficient amount of injected filler may be used if necessary.

The newest journal, New High Dose Pulsed Hyaluronidase Protocol for Hyaluronic Acid Filler Vascular Adverse Events(Claudio DeLorenzi, Aesthetic Surgery Journal, 2017) introduced contents indicating 'it is effective to treat vascular accidents by injecting hyaluronidase every hour', that leads to a point "Hyaluronidase alone, without any other treatment, has the same effect". However, many oppose to this view and argue that there are few clinical cases and injections on the affected area from time to time cannot be good for wound recovery. Hyaluronidase may be injected at intervals of 4 hours, which may be thought to lead in better results if the treatment is compromised.

	New	Traditional
Avoidance	Yes	Yes
Treatment timing	Immediate	Immediate
Hyaluronidase dosing strategy	Variable, based on volume of tissue affected	Fixed dose
Dose interval	Hourly	Daily
Ancillary treatment	None	Multipronged, vasodilators, NTP(nitropaste), hyperbaric O_2, etc.
Outcomes	Excellent – complete resolution	Occasional partial treatment failures, scabbing, crusting, mild scarring, mild textural changes in the skin

Table 5 _ Comparison of the new and traditional therapies of hyaluronidase

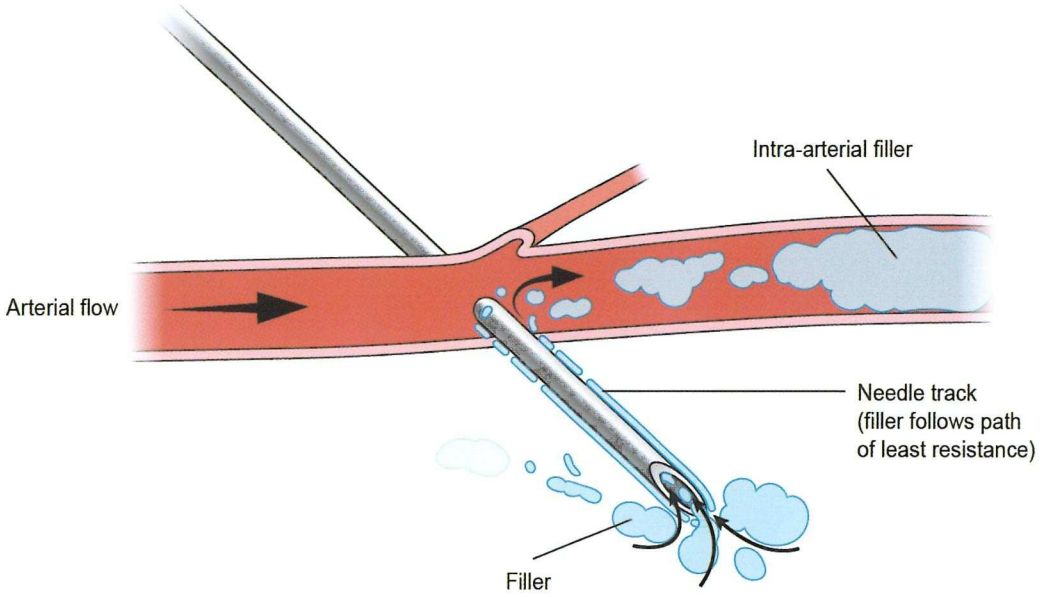


Figure 31 _ Routes and potential of intravascular filler injection

The risk of filler leakage into the blood vessel is not only limited to the direct entry through the tip of the needle or cannula placed in the lumen of the vessel, but is also possible through piercing of the blood vessel and the infiltration process. This can lead to intravascular embolism. The filler can flow into the bloodstream along the sides of the pierced needle or cannula. The risk of the filler flowing into the paths with lower resistance escalates especially when the needle or cannula pierces the blood vessels in the scar tissues which are relatively harder.

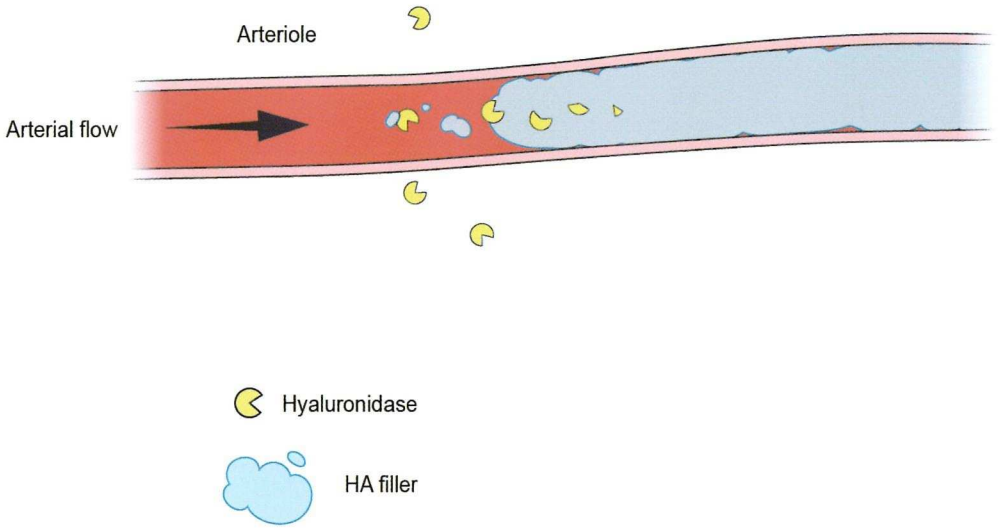


Figure 32 _ Relationship between hyaluronidase concentration and diffusion rate

Hyaluronidase diffusion rate is concentration dependent. It seems probable that high concentrations of hyaluronidase can result higher intra-arterial concentrations, and therefore more efficient hyaluronic acid hydrolysis.

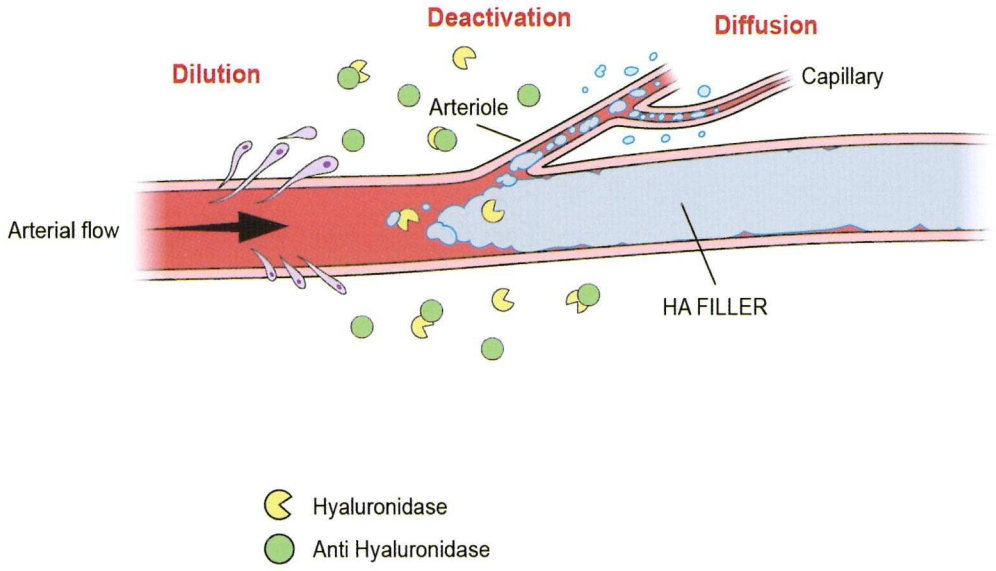


Figure 33 _ Causes of reduced concentration of injected hyaluronidase

As soon as hyaluronidase is injected into the tissues, its concentration is decreasing through several concurrent processes. Serum is leaking out into the ischemic tissues, diluting the hyaluronidase, as tissue anti-hyaluronidase agents start breaking down the enzyme. Simultaneously, diffusion occurs, reducing the local concentration.

3) Heparin 5000 IU

There are opinions stating that intravascular injection for about a week prevents thrombosis and helps to improve it, but nevertheless this may cause secondary problems. Thus, needle puncture at the site of the filler accident followed by gauze soaked with heparin, helps the tissue to regenerate increasing collateral circulation.

4) Vasodilator(PGEl(Eglandin))

To improve blood circulation, dilute the Eglandin inj. with 2cc of lOOmL of physiological saline, and inject into the blood vessel for about one week.

5) Medication

① Antibiotics: 4th generation quinolone antibiotics, Ciprobay 250mg 3T#3 * 3 days
② Steroid (Prednisolon) 40mg/daily, 4mg 3T#3 * 3 days
③ Vasodilator-Opalmon 6T#3 * 3 days
④ Aspirin lOOOmg/day, 375mg#3 * 7 days

6) Ointment treatment

① Steroid ointment
② EGF gel
③ Diluted nitroglycerin ointment, 3 times a day
④ Geschenk product (& wet dressing)

7) PRP, Stem celt, PDRN

There are a variety of methods, but PDRN is easy to obtain and is effective. It accompanies pain but is good for wound healing. It is injected at the periphery of the necrosis area and under the clot at intervals of 2~3 days.

8) Botulinum toxin injection for scar treatment

9) LD, LED lamp

10) Others, oxygen treatment

It is also a good idea to supply oxygen with an oxygen tank or an oxygen mask. An oxygen mask can also boost blood oxygen levels up to 100%, like oxygen tanks, so you can expect a similar effect.

Figure 34 _ Example of first aid kit

In cases of encountering emergency, medical equipment and medicines can be prepared as a kit as shown above.

3. First aid protocol in case of acute ocular adverse events followed by filler injection

Regretfully, Korea is ranked first in the blindness caused by medical malpractice of facial fat transplantation or filler procedures. There are more than 40 clinical cases reported in Korea. The greatest number of filler procedures in the world is one of the reasons behind this.

An anatomical understanding of vascular distribution is important to prepare for emergencies. It is important to check if the needle positioned inside the blood vessel before injecting the filler, slowly injecting the filler, not injecting too much filler at once, and so on.

When the filler is injected into the blood vessel, it tends to absorb water to maintain its volume and this causes local occlusion. Peripheral blood vessels around the eyes are small in diameter but enough in size for fillers or fat oils to enter directly or indirectly. Care should be taken as the risk increases when the treatment is performed with thin cannula or needles.

If there is a disturbance in the blood supply to the periphery of the retina, it will have a partial visual field disorder or blindness. The most common sites for filler associated blindness are nose, glabella, and nasolabial fold, and fillers injected into the blood vessels in these areas travel to the back of the eye through blood, causing vascular occlusion around retina. Vascular retinal occlusion should be reopened immediately within 30 minutes of the occurrence. If the arteries of the retina are blocked, some ophthalmologists say that golden time is 5 minutes, just like in brain death.

If signs of retinal damage appear, a filler-degrading enzyme hyaluronidase must be injected not only on the filler injected sites but also to the retrobulbar space before sending to a large hospital for better results. Injecting hyaluronidase into the retrobulbar space can improve the embolization by hyaluronic acid.

In case of acute blindness due to filler injection, and if the ophthalmologist cannot respond immediately, we would like to introduce a step of emergency treatment with direct retrobulbar hyaluronidase injection.

1) Retrobulbar injection

① Documentation of the loss of visual acuity including demonstration of relative afferent pupil defect.

② Informed consent.

③ Topical anesthesia using tetracaine 0.5% or other topical anesthetic drops for transconjunctival injections.

④ Injection of a bleb of 0.1~02mL of lidocaine 1% in the lower eyelid skin midway between the central and lateral lower eyelid if the retrobulbar injection is to be performed from the skin surface.

⑤ Use of a 25gauge 1.5inch long needle with syringe loaded with hyaluronidase, at least 500units.

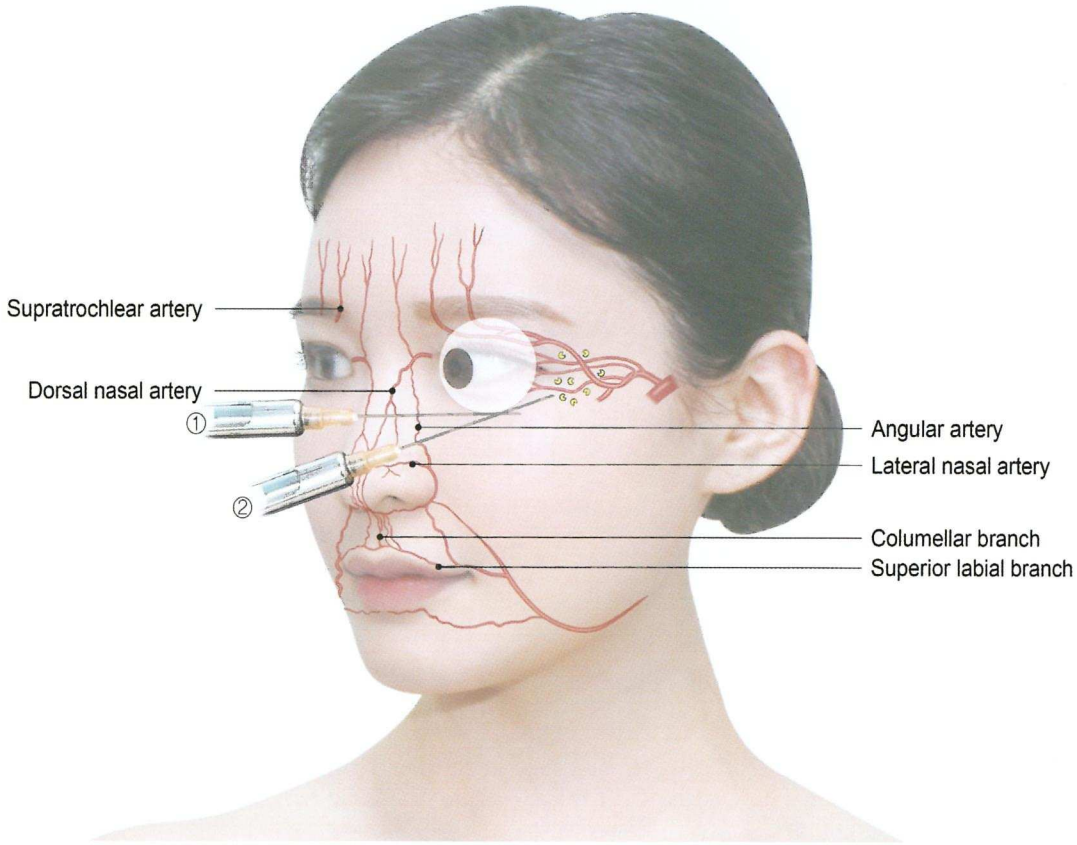


Figure 35 _ Injection angle of retrobulbar injection

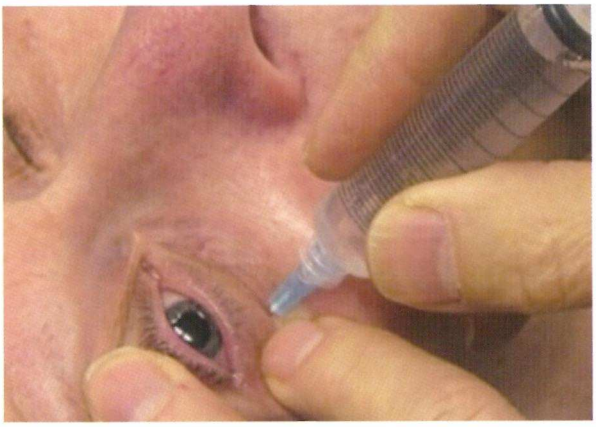
Retrobulbar space is located about 25mm behind the orbit and just behind the eyeball. The inferotemporal (IT quadrant of the orbit) of the orbit is a safer route to retrobulbar injection because the blood vessels are relatively smaller than other regions. There is no problem if you take an orbital bone while injecting laterally.

⑥ Gentle advancement of the needle in the inferotemporal quadrant of the orbit, aiming the needle parallel to the orbital floor for the first half inch and then aiming it to the space immediately posterior to the globe. The needle can be gently wiggled in the horizontal plane while the patient looks slightly upward to endure that the globe or optic nerve are not being engaged by the moving needle.

⑦ Gentle depression of the plunger to deliver the hyaluronidase into the retrobulbar space. The white orbit is deeper than the Asian orbit, and the female orbit is shallower than the male. Between 3mLs and 8mLs of enzyme is injected.

⑧ Documentation of change in visual acuity. Possible reinjection if required.

⑨ Urgent referral to an experienced ophthalmologist or oculoplastic surgeon for participation in ongoing management.



This outlines the steps in a retrobulbar injection in the event of an acute vision loss because of filler Injection, where an ophthalmologist is not immediately available (see digital Content, http://links.lww.com/DSS/A25).

Figure 36 _ Performing retrobulbar injection

Although the efficacy of retrobulbar hyaluronidase injection is controversial, we would like to introduce a paper that recently proved its efficacy in animal experiments.

In the published journal "Effectiveness of retrobulbar hyaluronidase injection in an iatrogenic blindness rabbit model using hyaluronic acid filler injection"(Lee et al. Plastic and Reconstructive Surgery , 2018), the research team used Starfill Plus to artificially induce blindness by retinal vascular occlusion in the eyes of 6 rabbits , and performed retrobulbar hyaluronidase injection after 5minutes . 20minutes after retrobulbar hyaluronidase injection , it showed improvement in blindness, demonstrating that this injection can be a first aid treatment for filler-associated blindness.

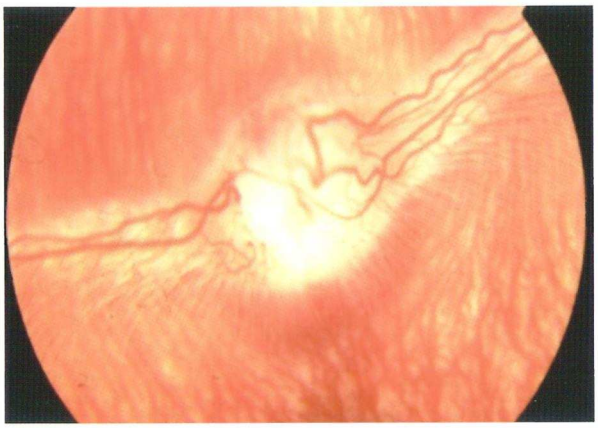


Figure 37 _ The retinal vessels of the rabbit before the experiment

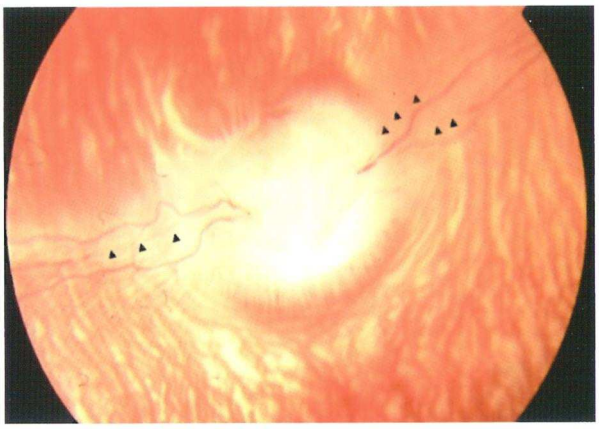


Figure 38 _ Occluded retinal vessels of the rabbit after filler injection

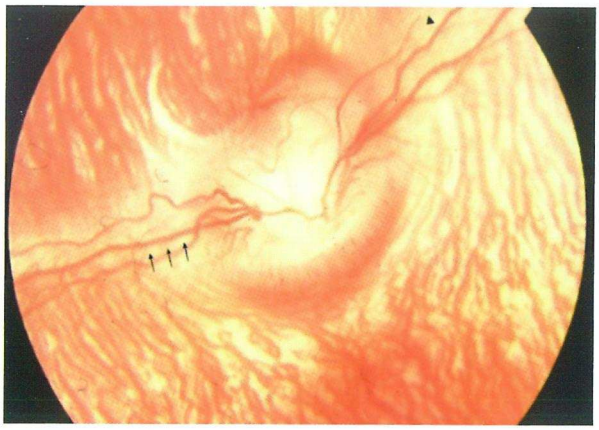


Figure 39 _ Recovered retinal vessels after the retrobulbar hyaluronidase injection

Figure 37 shows the initial retinal vascular status before the experiment. Figure 38 is a state in whcih HA filler Starfill Plus 0.3mL was injected artificially , and the retinal vessel occlusion can be seen from the decreased blood flow at the arrow points. After 5minutes, 3000 IU of hyaluronidase was diluted in 2mL of physiological saline and retrobulbar injection was performed . As shown in the arrow in Fig. 39, it can be seen that the occluded retinal blood flow is recovered.

In other words, retrobulbar hyaluronidase injection is like cardiopulmonary resuscitation(CPR) of the filler induced blindness. As mentioned above, emergency situations such as blindness can be dealt with quick diagnosis and countermeasures. Further research suggests that retrobulbar hyaluronidase injection is the gold standard to prevent blindness, the most dangerous among filler adverse events, and filler surgery is expected to lead the cosmetic surgery market as a safer procedure in the future.

When performing filler procedure, it is necessary not only to implement an ideal shape, but also to constantly strive for safe procedure results. Have a safe filler treatment environment in preparation for emergencies such as emergency kits and retrobulbar hyaluronidase injection method.

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