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An Experimental Model Exhibiting Anterograde and Retrograde Vascular Occlusion of Facial Fillers to Avoid Vision Loss

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Background: Facial filler injection techniques that help decrease the risk of vascular occlusion are an important growing area of study. This study demonstrates a model of injecting fillers into a simulated bifurcated arterial system, using different sized needle gauges at a constant injection pressure.

Methods: Three facial fillers were injected into a bifurcated intravenous tubing with continuous irrigation at a constant pressure to simulate a vascular system. Videography was used to observe for retrograde flow through the simulated supratrochlear artery to the bifurcation point, where the filler was redirected by anterograde flow into the branch representing the ophthalmic artery.

Results: Filler injection with retrograde flow to the bifurcation occurred with all the 27G needle trials. In comparison, the 30G needle trials were only able to reach the bifurcation point in three of the nine trials. The average time to the bifurcation point with subsequent ophthalmic artery anterograde flow with the 27G and 30G needles were 8.44 (95% confidence interval ±2.06) and 33.33 (95% confidence interval ±16.56) seconds, respectively.

Conclusions: Larger 27G needles consistently reached retrograde flow and the bifurcation point faster than 30G needles. This study suggests thinner needles may be less likely to cause retrograde occlusion. *(Plast Reconstr Surg Glob Open 2023; 11:e5270; doi: 10.1097/GOX.0000000000005270; Published online 13 September 2023.)*

INTRODUCTION

Facial fillers are an important aspect of cosmetic and facial rejuvenation. Dermal filler injections now comprise the second most common nonsurgical aesthetic procedure.[1,2] The number of injectors continues to grow to meet the increasing demand for facial fillers. The total number of procedures that involve soft tissue fillers has increased from 1.6 million to more than 2.4 million per year in the United States.[1,2] Although facial fillers have a low incidence of complications when administered by trained providers, vascular occlusion leading to blindness and stroke continues to be a risk.[3–6] Injection techniques and methods of filler delivery that help decrease the risk of vascular occlusion are an important growing area of study. This study aimed to demonstrate an experimental model of injecting facial fillers into a simulated bifurcated arterial system using different sized needle gauges at a constant injection pressure.

The most common injectable fillers in the United States consist of hyaluronic acid (HA) fillers.[7] HA exists as a natural glycosaminoglycan within the extracellular tissues of the human body. Initially, HA fillers were made from animal origins, such as rooster combs. However, since the invention of bacterial fermentation to produce HA, many different proprietary technologies have been developed to create injectable facial fillers, including NonAnimal Hyaluronic Acid Filler (NASHA), XpresHAn, Hylacross, Vycross, Cohesive Polydensified Matrix, preserved network, and wet milling.[8] Hyaluronic acid is a useful chemical structure for filler because there is an extremely low

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allergy rate, it can be dissolved with hyaluronidase, and can be modified using different methods of cross-linking and particle sizes to alter the final rheology of the filler gel. Other common injectable fillers include calcium hydroxyapatite, poly-L-lactic acid [PLLA (biostimulator)], and fat grafting.

One of the most feared complications of facial fillers is intravascular occlusion of arteries.[3] The areas with the highest risk of blindness include the nose, forehead, glabellar region, and nasolabial folds due to close collateral circulation that anastamose with the ophthalmic artery.[4–6] One anatomic study showed that the range of supratrochlear vessel volumes from the glabella to the orbital apex ranged from 0.04 to 0.12 mL.[9] Another study by Cho et al showed a similar volume.[10] One way to decrease the risk of entering an artery is to direct the needle subdermal, intradermal, or preperiosteal, because arteries tend to travel through fat.[11,12] If injections are placed intraarterially, retrograde flow to an arterial bifurcation point followed by anterograde flow into the other branched artery can cause occlusion of the ophthalmic artery, choroidal circulation, or central retinal artery, leading to permanent blindness if not treated urgently.[13] In the nasal region, improperly placed injections can result in nasal tip necrosis or blindness if they are performed intravascularly.[14]

One area of contention regarding safe techniques for facial fillers revolves around needle size. Some injectors will recommend using a larger diameter needle/cannula because studies have shown they are less likely to enter a blood vessel.[15] Other injectors believe that smaller needles require a greater extrusion force and, thus, you are less likely to inject a high enough volume rapidly enough to cause an occlusion with retrograde flow to the ophthalmic artery. The slow deposition of filler with a small needle would allow a diligent injector ample time for continuous movement of the tip of the needle to a new location outside the vessel. Studies that explore the relationship between needle size and dermal filler vascular occlusion rates are limited. Current literature on this topic mainly revolves around needles versus cannulas but does not specifically focus on needle size.

Given the limited data available, the relationship between needle size and vascular complications remains to be elucidated. In this study, we aimed to demonstrate how needle size effects the outcome of retrograde flow, using a simulated vascular model.

METHODS

Three facial fillers [Calcium Hydroxyapatite (CaHA), Vycross-20, and NASH-Lyf] commonly used in filler rhinoplasty were selected. These were also chosen because their stock needles are 27G needles that injectors commonly transfer to 30G needles. An Alcon (Fort Worth, Tex.) centurion pump was used to provide irrigation with balanced salt solution through intravenous tubing for a simulated model vascular system. Intravenous tubing with a single bifurcated extension set (4" total length) was selected to allow the flow of saline to model the supratrochlear/dorsal nasal artery and ophthalmic artery.

Takeaways

Question: Does needle size affect the safety of filler injections?

Findings: Larger 27G needles consistently reached retrograde flow and the bifurcation point faster and more frequently than 30G needles when injecting fillers into a bifurcated intravenous tubing with continuous irrigation and constant pressure to simulate a vascular system.

Meaning: Larger needles may decrease the risk of vessel puncture; however, once in a vessel they are more likely to cause retrograde occlusion due to the ease of injecting larger aliquots. The smallest needle that allows for ease of injection should be chosen to limit risk of retrograde flow.

The rubber stopper on the end of the leg marked to demonstrate the ophthalmic artery was punctured with a 16G needle, whereas the rubber stopper on the end of the leg marked to demonstrate the supratrochlear artery was punctured with a 27G needle to reproduce the difference in arterial size and outflow pressure. The bifurcated IV tubing was attached to the peristaltic pump system set at 70 mm Hg, simulating the mean arterial pressure in humans. Dyed filler was injected with a dynamometer at a constant force of 22.5 Newtons into the branch of tubing representing the supratrochlear artery (Figs. 1 and 2) [**See Video (online),** which demonstrates dyed filler being injected at a constant injection pressure of 22.5 Newtons

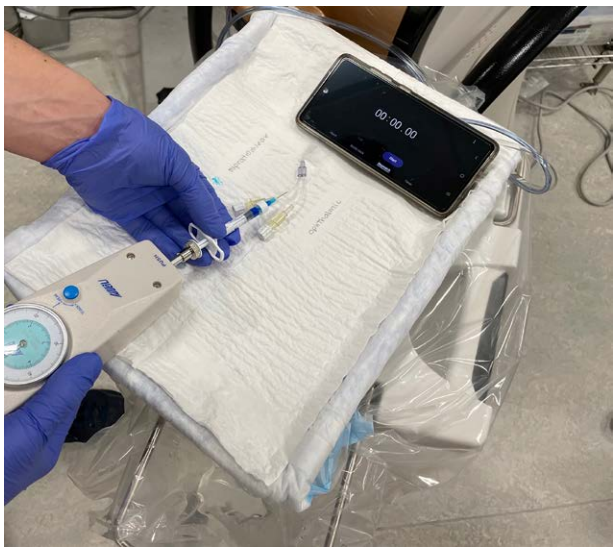

Fig. 1. Experimental setup design. The bifurcation tubing marked supratrochlear was punctured through the rubber stopper on the end of the leg with a 27G needle, whereas the rubber stopper on the leg marked ophthalmic was punctured with a 16G needle to simulate the difference in arterial sizes between the anatomic arteries. A dynamometer was used to keep the injection pressure constant at 22 Newtons. The filler was injected with a 27G and 30G needle through the tubing marked supratrochlear artery, and videography and stopwatch were used to measure the time for filler to cause anterograde flow and retrograde flow, and reach the bifurcation point.

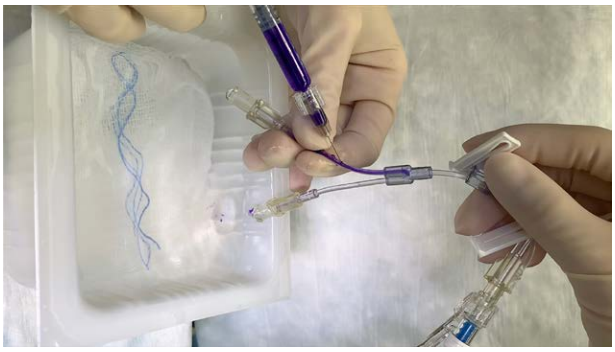

Fig. 2. Photograph showing dyed filler being injected into the simulated supratrochlear branch of the IV tubing. The filler has moved retrograde through the IV tubing toward the bifurcation point and has now come anterograde through the simulated ophthalmic branch of the IV tubing.

into a bifurcated intravenous tubing system with continuous irrigation at a constant pressure to simulate an arterial system. The time to initiate retrograde flow and time to reach the bifurcation point were recorded using videography.] This force was chosen based on the minimum pressure needed for the filler with the highest extrusion force to extrude through the 27G needle. Videography was used to observe retrograde flow through the simulated injected artery to the bifurcation point, where the filler was redirected by anterograde flow into the branch representing the ophthalmic artery. If more than 60 seconds passed, the authors considered this a failure to reach the end point, and the trial was ended. Time to onset of retrograde flow and time to the bifurcation point were measured using three trials for each filler, first using a 30G needle and then using a 27G needle, for a total of 18 injection trials.

RESULTS

Filler injection with retrograde flow to the bifurcation occurred with all the 27G needle trials. In comparison, the 30G needle trials were only able to reach the bifurcation point in three of the nine trials. Vycross-20 and CaHA were the only fillers in the 30G needle trials that were capable of reaching the bifurcation point through retrograde flow. In addition to these findings, there were four trials with the 30G needle where retrograde flow did not occur (Table 1).

For all fillers combined, the average times to onset of retrograde flow with the 27G versus 30G needles were 3.33 [95% confidence interval (CI) ±1.64] and 14 (95% CI ±8.11) seconds, respectively (Fig. 3). The average times to the bifurcation point with subsequent ophthalmic artery anterograde flow with the 27G and 30G needles were 8.44 (95% CI ±2.06) and 33.33 (95% CI ±16.56) seconds, respectively (Fig. 4). These final averages excluded all trials that did not reach the bifurcation point.

DISCUSSION

Our simulated model does not perfectly represent the human arterial system, but the authors believe that this study demonstrates that thinner diameter needles are less likely to encounter retrograde flow when compared with a standardized injection force, tubing length, tubing volume, and fluidic pressure. In this study, the needle size was varied, and time was the dependent variable measurement.

The authors believe this is an important finding because this is one of the only studies the authors are aware of that demonstrates objective data on needle lumen size and outcomes of retrograde flow. Although studies have shown that larger diameter cannulas are more difficult to pierce a vessel,[15] there are case reports in the literature with vascular occlusion occurring with cannulas as large as 20G cannulas.[16]

Table 1. Data from All 18 Trials

Filler (27G Needles)	Time to Onset of Retrograde Flow (s)	Time to Bifurcation Point (s)
Vycross-20	1	4.5
Vycross-20	8	13
Vycross-20	2	9
NASH-Lyf	7	9
NASH-Lyf	2	8
NASH-Lyf	4	13
CaHA	2	7
CaHA	1.5	4
CaHA	2.5	8.5
Filler (30G Needles)	**Time to Onset of Retrograde Flow(s)**	**Time to Bifurcation Point(s)**
Vycross-20	Not possible	Not possible
Vycross-20	7	31
Vycross-20	2	20
NASH-Lyf	23	Not possible
NASH-Lyf	Not possible	Not possible
NASH-Lyf	Not possible	Not possible
CaHA	Not possible	Not possible
CaHA	22	Not possible
CaHA	16	49

The trials for the 27G needles are shown in Blue, and the trials for the 30G needles are shown in yellow.

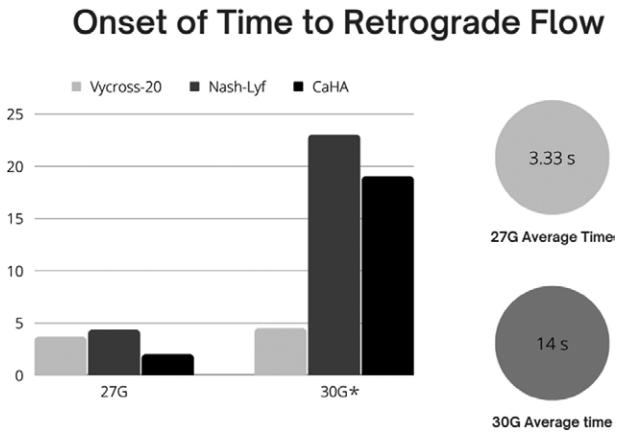

Fig. 3. Each filler is represented with the average time to onset of retrograde flow on the 27G and 30G needles. The * next to the 30G column indicates that for each filler at least one trial was excluded that did not achieve retrograde flow. All 27G trials were able to achieve retrograde flow.

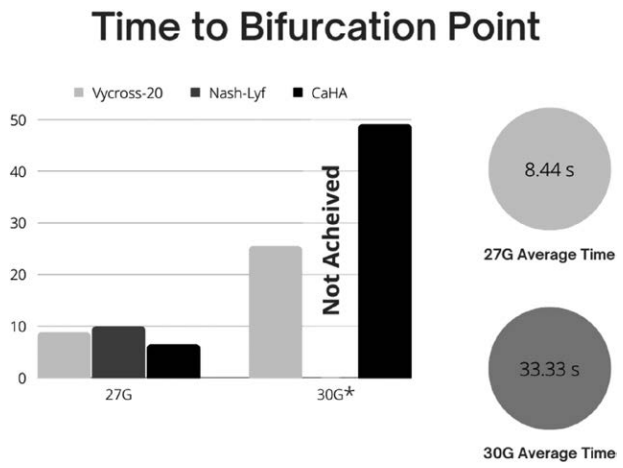

Fig. 4. Each filler is represented with the average time to reach the bifurcation point of our simulated vascular system (simulating the bifurcation from the supratrochlear artery to the ophthalmic artery), on the 27G and 30G needles. The * over the 30G columns indicates that at least one trial where the bifurcation point was not reached were excluded. All 27G trials were able to reach the bifurcation point.

Plastic surgeons should be aware that although a larger gauge needle may be more likely to lacerate a vessel instead of cannulating the vessel, offering a degree of safety over smaller gauge needles, the ease of pushing enough filler through a vessel to cause a retrograde occlusion is much more easily achieved with larger gauge needles, as shown in this study. This study theorizes that a 30G or smaller needle would give the injector ample time to move the needle to a new location before enough filler could be injected into a vessel to cause retrograde flow (33 seconds versus 8 seconds). This study did not address cannulas; so this could be an area for future research.

There is controversy over whether vascular complications such as blindness occur from retrograde flow versus anterograde flow through collateral circulation that feeds into the orbit. However, a study by Cho et al repeatedly demonstrated that retrograde filler embolus to the ophthalmic artery can be reproduced by cannulation of the supratrochlear artery.[10] Their study also suggested that due to the superficial location of the supratrochlear artery that retrograde emboli may occur even with superficial injections.

To obtain retrograde flow in our model, the authors noted that a central plug had to be formed within the tubing lumen first. This central plug was almost always immediately formed with the 27G needle trials, and retrograde flow would quickly follow. When testing with the 30G needles, this central plug would not always form, and in the absence of this plug, no retrograde flow would occur. In this scenario, the filler would flow anterograde along with the balanced salt solution, which would theoretically cause an embolus with skin necrosis, rather than retrograde flow, that could cause vision loss. The difficulty in achieving this central plug with the 30G needle trials was most likely due to the opposing force of the outward pressure in the IV tubing not allowing the decreased extrusion of filler to reach an amount of adequate volume as opposed to the 27G needles. One previous rheologic filler study demonstrated that extrusion force increases as the internal lumen of a needle decreases. Because our experiment kept the injection force constant, the flow rate was decreased for the 30G needle trials when compared with the 27G needle trials. This decrease in flow rate increased the difficulty in achieving retrograde flow. In addition, when the central plug was formed and retrograde flow was initiated, the 30G needle trials were significantly slower in reaching the bifurcation point.

One strength of our model was that the IV bifurcation tubing internal volume measured on average 0.04 mL for each leg (simulated supratrochlear and simulated ophthalmic) to the bifurcation point. The length of the IV tubing was 4" in total, with each leg measuring 2" from the bifurcation. These are measurements similar to those of previous cadaver anatomy studies of the supratrochlear artery in humans [0.04–0.12 range of measured volume; 51.75 mm (2.04 inches) average length].[9]

The authors chose Vycross-20, CaHA, and NASH-Lyf in this study because these are commonly used in filler rhinoplasty procedures. These were also chosen because 27G needles are provided as stock needles, but these are often transferred to smaller needles to decrease flow rate. As the nose and glabellar region are among the highest risks for blindness,[4–6] the authors focused on liquid rhinoplasty versus less-reported areas of blindness such as the tear trough and malar areas.

The fillers used in this study have large particle sizes and medium/high G prime rheology (G prime: 1407, 549, and 307 for CaHA, NASH-Lyf, and Vycross-20, respectively). These properties make it more difficult to inject through smaller needles, but we were able to extrude the filler in all experiments through the 30G needle. There are case reports in the literature supporting the use of 30G needles for liquid rhinoplasty procedures, with fillers at concentrations of 25 mg/mL, which are similar to those found in our study.[17]

Additionally, Rivkin's recent review of 2488 nonsurgical rhinoplasty procedures discusses that he avoids cannulas and instead uses 31G needles to allow precise aliquots of filler to prevent vascular occlusion.[18] The study notes serious adverse events such as ischemia and necrosis occurred at a rate of 0.2%.[18] Rivkin suggests that adverse events in the nasal tip were likely caused by the compartment syndrome rather than by an embolic event due to the small size of the vessels in that area. On the other hand, adverse events in the sidewall may have been embolic in nature due to the larger size of the angular artery and its branches, as well as the ease of puncture while injecting the nasal sidewall.[18]

Vycross-20, which had the lowest G' in our study overall, had more trials achieve retrograde flow than the higher G' prime fillers with a 30G needle. However, on the 27G needle trials, there was no statistical difference in time to retrograde occlusion. These findings suggest that higher G' fillers are more difficult to push through a 30G

needle, making it more difficult to achieve the necessary volume to push against the mean arterial pressure during its retrograde path and cause occlusion. On the larger needle gauges, G' does not correlate directly with ease of retrograde occlusion. A recent study showed that higher G' fillers had a higher subjectively perceived injectability difficulty and that this was associated with statistically significant increase in adverse events.[19]

Our study also focused only on 27G needles and 30G needles, but did not aim to conclude that one specific needle size is dangerous and should not be used. The goal of the study was to evaluate whether needle size increases the probability of filler going retrograde. Larger needles and cannulas may decrease the risk of direct vessel puncture; however, that is no guarantee, and once in a vessel, they are more likely to cause retrograde occlusion due to the ease of injecting larger boluses in shorter amounts of time. Thus, in the authors' opinion, the smallest needle that allows for ease of injection should be chosen to limit the probability of retrograde flow.

Limitations of this experiment revolve around the difficulty in replicating the human arterial system. The endothelial lining of the arterial system, along with the contents of blood (including platelets and coagulation factors), could not be reproduced in this model. How these variables alter the results of this study cannot be known. The intravenous tubing is also made of plastic and has thicker, noncompliant walls compared with the lumen of a blood vessel. The way the filler gels interact with the plastic composition of the internal lumen is likely different than how it interacts with live tissue. However, the authors feel that this study demonstrates clear significance in the ease of achieving retrograde flow with larger needles and that these findings are relatable to decreasing the risk of vision loss after retrograde flow of filler with injection techniques.

In summary, our simulated vascular model demonstrates the differences in time of onset of retrograde flow and time to reach the bifurcation point, with three commonly used facial fillers at a constant injection force with different needle sizes. Larger 27G needles consistently reached retrograde flow and the bifurcation point faster than 30G needles. All fillers with 27G needles were able to reach the bifurcation point followed by anterograde flow. The 30G was unable to reach the bifurcation point in six of the nine trials and took significantly longer to do so when achieved. We believe our study suggests that thinner needles may be less likely to lead to retrograde occlusion, especially when injection force is constant.

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DISCLOSURES

This study did not receive funding and was not sponsored by any participating institution. There are no conflicts of interest present in this study. Gabriel Scott MD, Meghana Khonda MD, and S. Tammy Hsu MD do not have any disclosures. Alexander Rivkin MD has the following disclosures as a consultant with Allergan, Merz, Galderma, and Suneva. Julie Woodward MD has the following disclosures as a consultant with Allergan, Galderma, Merz, Prollenium, Revance, SkinCeuticals, and Tarsus. Konstanin Frank MD has the following disclosures as a consultant with Allergan, Galderma, Croma, and Hugel. John Fezza MD has the following disclosures as a consultant with Allergan, Revance, Merz, Arya Medical, and Visant Medical.

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