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BRIEF COMMUNICATION
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Anatomical Definition of the Target Structures of a Jet-Based Tissue Penetration

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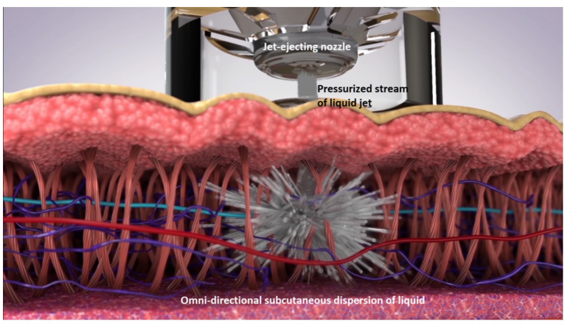
INTRODUCTION

Jet injection provides an intradermal drug delivery through invasive but needle-free route of administration. The modality implements a pressurized stream of liquid that penetrates the skin with a minimal injury to epidermis and dermis. The principal mode of action is based on the synergy between injected drug and the micro-trauma generated in the soft tissues by the dispersion. Once penetrated, the micro-droplets of the injected drug are dispersed in multiple 3-D directions increasing the area and contact between the skin and the drug (Figure 1). Kinetic energy of the jet powers the droplets to travel and originate a micro-trauma impact on the surrounding tissue. Extent of the spread is limited by the friction with surrounding skin and is influenced by heterogeneity and rigidity of the treated region.[1]

FIGURE 1. A schematic representation of liquid jet injection injection: Stream of liquid jet penetrates epidermis and leads to omni-directional subcutaneous dispersion of liquid into layers (fat lobules virtually removed).



The modality steadily gains popularity in aesthetic dermatology for correction of various skin conditions. Clinical use of the jet technology targets different anatomical structures that require absolute precision in the drug delivery: superficial dermis for correction of the age-related dermal atrophy,[2,3,4] dermo-subcutaneous junction for remodeling of atrophic scars,[5,6,7] or deep reticular dermis for skin laxity.[8]

Experiments on the skin-mimicking phantom and porcine skin verified that penetration is a function of the velocity and diameter of jet stream.[9,10] It was clinically revealed that injection pressure is directly related to the jet's depth of penetration[8] and controls the level at which dispersion of the injected drug occurs (Figure 2). The ejection volume of the drug and the skin properties was histologically shown to have a direct effect on the side-wise distribution of the injected material.[1]

As the injection pressure and ejection volume are two parameters that can contribute to the treatment effectiveness, we conducted a series of anatomical experiments in order to investigate further the ability of jet-injection to deliver liquid materials into various dermal and subcutaneous structures.

FIGURE 2. Multi-directional dispersion of the jet-injected hyaluronic acid (Belotero Balance®, Merz Aesthetics, Germany) in skin analog model (polyacrylamide gel). (Courtesy of PerfAction Technologies).

MATERIALS AND METHODS

At the Anatomical Institute of the University of Graz, two heads conserved with Thiel's solution were used to calculate experimental applications.

Substances, prescribed for clinical applications (NaCl, 20 mg/ml cross-linked Restylane hyaluronic acid, 20% glucose) were used as injection substances and mixed with anatomical color markers (Pintasol E-WL5 blue, E-WL41 oxide red, E-WL61 oxide green (Figure 3a). The dyes were added to mark the

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FIGURE 3. Substances, prescribed for clinical applications (NaCl, 20 mg/ml cross-linked Restylane hyaluronic acid, 20% glucose) were used as injection substances and mixed with anatomical color markers (Pintasol E-WL5 blue, E-WL41 oxide red, E-WL61 oxide green (A); Injections of the contrast materials were performed using a commercial jet-injection device, Engerjet 2.0. (B)

(A) (B)

exact application location. We observed and documented the indication and precise penetration depth, using staining evidence surrounding anatomical structures.

In both cases, the process was gradual. Pressure, volume, and depth parameters were empirically assumed and applied to the entire area of half a face. The applications were then visually inspected and meticulously characterized using a precise dissection technique. The settings were recalibrated and consequently applied to the second half of the face. There was a noticeable and accurate penetration into the target area. The second application was initially only carried out using Pintasol blue to observe a specific penetration setting. Afterward, however, all three colors were further applied as on the other face side. The second face side was then visually inspected and meticulously characterized using a precise dissection technique for the previous observation. A hyaluronic acid mixture (marked in red) was used to characterize the structures in the middle subcutaneous area: medial cheek area, perioral, and periocular.

A green-colored NaCl mixture was introduced to observe submandibular and submental fat body penetration. The procedure mimicked different energy settings of volume and pressure created to be used as chemical lipolysis.

Injections of the contrast materials were performed using a commercial jet-injection device (Enerjet 2.0, PerfAction Technologies, Rehovot, Israel). The device operates on compressed air and ejects a powerful stream of liquid (liquid jet) under control of the device software. The injection pressure can be set between 2 to 4 bars; the injection volume is ranged from between 50 to 150µl. The maximum jet velocity is 150 m/sec and allows for easy and fast skin penetration at the entry point of ø200 micron. The dispersion zone has an average diameter of 10 mm, according to the device manufacturer.

TABLE 1.

Specifically Applied Parameter	
A	**B**
left side of head 1	right side of head 1
low pressure (50%)	high pressure (100%)
small volume (50µl)	high volume (100µl)
C	**D**
right side of head 2	left side of head 2
low pressure (65–75%)	high pressure (90–100%)
small volume (70–90µl)	high volume (70–90µl)

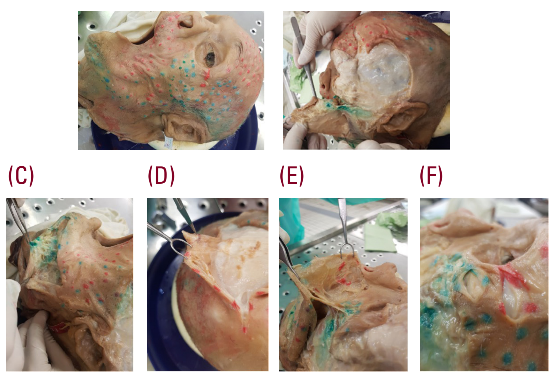
RESULTS

Fascial and periosteal structures were targeted to test the distribution effectiveness of solutions, which would ultimately initiate lifting. A mixture of 20% glucose, NaCl, lidocaine, and blue color marking was used as a tightening and lifting solution. The following served as target structures: superficial temporal fascia, the mandible zygomatic arch, the mandible, the SMAS in the lateral cheek area, and the retinacula cutis (zygomatic, buccal, mandibular).

Moderate energy was used (35–50%). There is a clear external marking of the Enerjet application (A). However, the glucose-NaCl mixture did not penetrate down to the temporal fascia, the SMAS or the zygomatic arch (B). In contrast, the same mixture did show a high penetrance into the fat bodies located in the submandibular and submental region (C). Both mixtures (glucose-hyaluron) applied low energy applications showing dermal and subdermal penetration, deep facial structures remain unaffected. At high energy levels (pressure 100%, volume 100µl), deep regions were perforated with the blue colored glucose-NaCl mixture. There was explicit penetration to the temporal fascia, to the periosteal structures, and the cheek fat structurally bonding retinacula. A more intensive

FIGURE 4. (Head 1, Left). Moderate energy was used (35-50%). There is a clear external marking of the Enerjet application (A). However, the glucose-NaCl mixture did not penetrate down to the temporal fascia, the SMAS or the zygomatic arch (B). In contrast, the same mixture did show a high penetrance into the fat bodies located in the submandibular and submental region (C). Dermal low-energy application of a red-colored hyaluron-NaCL mixture (D). (E) Deeper penetration in the loose perioral tissue (Philtrum) using the same energy as in d). (F) Both mixtures (glucose-hyaluron) applied low energy applications showing dermal and subdermal penetration, deep facial structures remain unaffected.

(A) (B) (C) (D) (E) (F)



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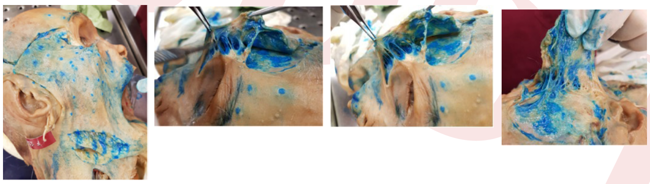
high-pressure application was used (D), indicating sharper penetration markings of the superficial temporal fascia (E), which is also visible after lifting of the temporal fat body (F).

FIGURE 5. (Head 1, Right). Cutaneous application topography in the cheek area with deep penetration in the submandibular fat body (A). (B and C) Visibly recognizable topography of the fascia temporalis and the upper parts of the zygomatic ligaments (Mcgregor Patch). (D) Fascia temporalis and zygomatic ligaments from a lateral perspective. (E–H) Fascia temporalis, buccomaxillary and masseteric ligaments. (I) Additional penetration in the superficial malar and melolabial fat bodies.

(A) (B) (C) (D)



(E) (F) (G) (H) (I)

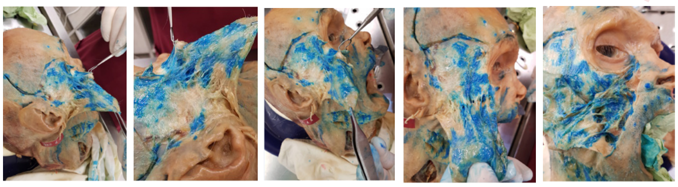
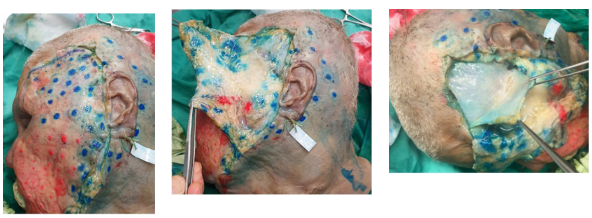


FIGURE 6. (Head 2, Left). (A–C) A more intensive high-pressure application was used (A), indicates sharper penetration markings of the superficial temporal fascia (B), which is also visible after lifting of the temporal fat body (C).

(A) (B) (C)



DISCUSSION

The jet-injecting device of our experiment delivers therapeutic material intra- and sub-dermally and acts as a micro-trauma generating device for achieving therapeutic changes in the skin. The micro-trauma caused by the forceful spread of the drug micro-droplets stimulates activity of the skin fibrocytes toward neo-collagenases.[2]

As an effective treatment modality, transcutaneous jet injections are applicable for dermal tightening, improvement of the age-related skin atrophy,[4,11] and adapted for remodeling of various scars (acne scars, hypertrophic scars, keloids).[5,7]

Cadaveric study of Seok et al[12] confirmed dependency of the skin penetration on the amount of pressure applied with jet injection. Although the study was limited by inconsistency and lowered elasticity of the cadaveric tissue, the authors were able to demonstrate that viscosity of the injected materials additionally contributes to the penetration depth. Viscosity of the substances injected in our experiment was orginaly low (normal saline, 20% glucose) or was lowered (dermal filler, Restylane) through dilution in order to achieve an optimal skin penetration at any tested pressure level.

Due to the complexity of facial anatomy, precise studies of accessibility and penetration of various structures are necessary and must be documented.[13] Facial skin tightening can be effectively acquired either by manipulation of the deep fascia or retinacula cutis or dermis layer.[14] Fat bodies are primarily submandibular and can be aesthetically disturbing.[15,16] These fat bodies, however, can also be easily reached using lipolytic substances. Scar therapy requires both superficial and deep applications (depending on the scar thickness). An exact characterization of the affected structures will optimize the quality of the application and treatment result.

The specific application format of Enerjet 2.0 enables several combined aesthetic treatment effects. Volumizations of the active aging process in layers of the dermal and subcutaneous fat with fat or various hyaluronic preparations can minimize or correct the deflation or thinning process.[17,18] Also, facial skin smoothing can be supplemented with fractional laser or radio-frequency methods.[13]

Radial shock wave or tightening radio-frequency techniques can also be paired to enhance regenerative treatments.[17,19,20] Deactivating facial expressions (botox) can additively complement tissue remodeling. The Enerjet procedure is a pearl in the mosaic of non-surgical facial rejuvenation, once facial anatomy is mastered.

We did not completely cover all possible structures in our study. However, the ongoing three-dimensional introduction of denser substances to patients with the Enerjet delivers comparable therapeutic results.

CONCLUSIONS

In a study with anatomical specimens, various cutaneous and subcutaneous facial structures were treated with the Enerjet system. Color-marked substances were introduced with different volume and pressure parameters. The location of the possible effect was finally sought by dissection, respectively, the so-called hit rate was verified. Fascia and retinacular should be evaluated for firming effects, subdermal and intradermal structures for volumization, tightening, and scar therapy, and subcutaneous fat structures for lipolytic effects should be shown. Further

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indications regarding drug delivery can be assigned to both curative and aesthetic indications.

DISCLOSURES

AQ: Please list any conflicts/financial relationships, or state if none.

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