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Full Length Research

Subdermal Bloodless Space and Prolongation of Collagen in Rats

Li Nguyen[1,5*], Hanh Nguyen[2], Thanh Phung[3] and Joel Sercarz[4,6]

[1]Department of Otolaryngology/Head and Neck Surgery, Automatic Subdermal Injection System, Inc, 15751 Brookhurst Ste 105, Westminster, California 92683, U.S.A.

[2]Department of Radiology,Magnolia Medical Imaging Center 1, 14571 Magnolia Ste 101, Westminster, California 92683, U.S.A.

[3]Department of Radiology, Magnolia Medical Imaging Center 2, 22921 Triton Way Ste 125, Laguna Hills, California 92653, U.S.A.

[4]Department of Radiology,Magnolia Medical Imaging Center 3, 1111 W Town and Country Ste 30, Orange, California 92868, U.S.A.

[5]Department of Anesthesiology,Innovative Drug Injection Technology Inc., 881 Dover Dr. Ste 350, Newport Beach, California 92663, U.S.A.

[6]Department of Otolaryngology/Head and Neck Surgery,University of California, Los Angeles, Medical Plaza, Suite 550, Los Angeles, California 90095, U.S.A.

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Products injected into the subdermal bloodless space imply longer lasting medicinal effects and avoidance of initial toxicity and side effects immediately following injection. This is desirable particularly for cosmetic products such as dermal fillers or BOTOX® since they have no reason to travel to the rest of the body. In this study, we have found dermal filler Zyplast®(bovine collagen) remained for at least twelve weeks post-injection in four out of four rat shoulders when injected into subdermal bloodless space, whereas, Zyplast® randomly injected disappeared betweentwo and twelve weekspost-injection in four out of four rat buttocks. Manual blind injections of Zyplast® could only be successfully injected into the subdermal bloodless space 50% of the time at best; wehad greater success by injecting Zyplast® using the Automated Subdermal Injection System technique.

Keywords: Collagen, electrical stimulation, injectable EMG needle, subdermal bloodless space, subdermal injection, Zyplast.

INTRODUCTION

There are three major parts to our skin: collagen, elastin, and glycosaminoglycans (GAGs; Skin Anatomy). More than 80% (dry weight) ofour skin is made of collagen, which is a main protein found throughout the body. Collagen gives needed strength totissue and organs while elastin enables skin to stretch and recoil (Integumentary System). Over time and through both natural (aging) and

Figure 2. Injectable EMG needle.

unnatural (tanning beds) conditions, collagen degrades, which also causes visible and structural skin damage (Wrinkle Causes). In addition, our skin's ability to develop healthy collagen also diminishes. According to Wrinkles.org, injectable collagen fillers can help improve damaged skin and provide structural support.

ASIS (Automatic Subdermal Injection System) Corporation has developed the only automatic injection system for the delivery of most, if not all, injectable products into the subdermal bloodless space, located just outside of the fascia. The ASIS device is stabilized on the skin surface with negative pressure and emits an electrical current to chase the muscle away, thereby creating that subdermal bloodless space. Bloodless spaces exist subdermally (between the skin and muscle) or inter-fascially (between the deeper muscles) and are contiguous with each other. However, the muscles in question for the majority of injectable products are just beneath the skin, so only the subdermal bloodless space is involved in all practicality. Bloodless space is an empty, potentially dead space until and unless occupied by a product, following which the injectable product takes over control and responsibility.

Every water soluble product must eventually diffuse out of that subdermal bloodless space to reach equilibrium with the rest of the body, and this gradual diffusion process is osmolality dependent and modifiable, rather than being molecular weight-dependent and fixated like we usually assume (Beattie, 1979). Thus, diffusion barely exists for water insoluble products such as injectables/ dermal fillers or BOTOX®, so they may last in the bloodless space indefinitely (BOTOX). This is particularly desirable for injectable cosmetic products since they have no reason to travel to the rest of the body. Injectables within the bloodless space imply longer lasting medicinal effects and avoidance of initial toxicity and side effects immediately following injections.

MATERIALS AND METHODS

Our preliminary studies were conducted in compliance with the Good Laboratory Practice (GLP) and all procedures were approved by the Institutional Review Board. Although rats without hair were intentionally chosen, the ASIS device couldn't work on them due to the lack of surface area to apply suction and lift the skin (shoulder skin crumpled under negative pressure), not to mention their tiny muscles.

Manual blind injections of Zyplast® into that subdermal space could only be correct 50% of the time, at best (Zyplast®). Therefore, we had greater chances to inject into the bloodless space by applying the ASIS concept: manually picking up rats' shoulder skin, then providing an electrical stimulation (1.5 – 2.0 mA) via an injectable electromagnetic (EMG) needle (Figure 2; EMGneedles.com).

Zyplast® is manufactured by Allergan and is composed of highly purified bovine dermal collagen that is lightly cross linked with glutaraldehyde and dispersed in a phosphate-buffered physiological saline containing 0.3% lidocaine. Using the ASIS device technique, .5cc of collagen was injected into the bloodless space within shoulders in four rats (Figure 3), while .5cc of collagen was injected into the buttocks of four rats using standard injection techniques. .5cc was an adequate dosage for a visible and palpable observation. Study protocol called for twelve weeks of observation, with images taken every week.

RESULTS

Pathology at the end of twelve weeks confirmed that the foreign body (Zyplast®) remained in the

*Corresponding Author Email/contacts: dr.li.nguyen@asis-inc.com, Phone: 714-453-7857, Fax: 714-775-6256

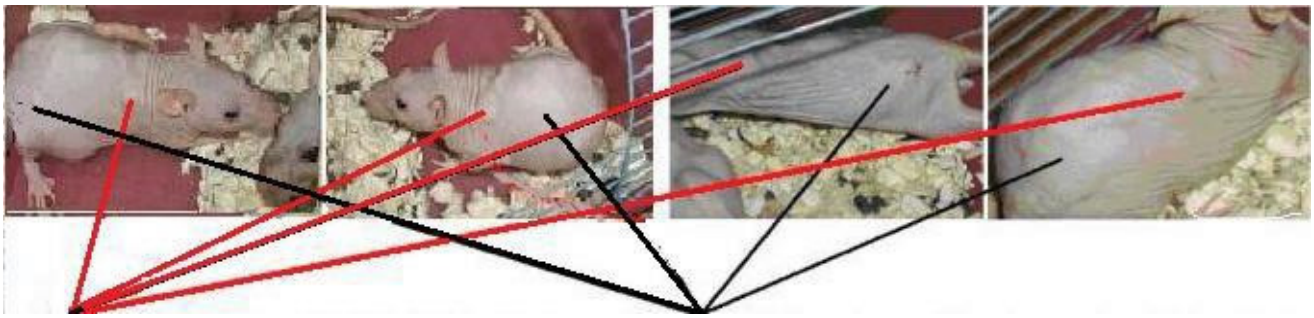

Figure 3. Red arrows indicate subdermal injection sites using the ASIS technique and black arrows indicate injection sites using standard injection techniques.

Figure 4. Pathology of rat shoulder confirmed foreign body in subdermal space.

Figure 5. Pathology of Rat buttock confirmed no foreign body.

subdermal space in four out of four rat shoulders (Figure 4) versus the absence of the foreign body in four out of four rat buttocks (Figure 5). Over the testing period, there was an absence of any visible side-effects from either the injection or foreign body.

DISCUSSION

The fibrous connective tissue that constitutes the fascia varies from loose areolar tissue to dense fibrous bands (What Causes Wrinkles). This fascia

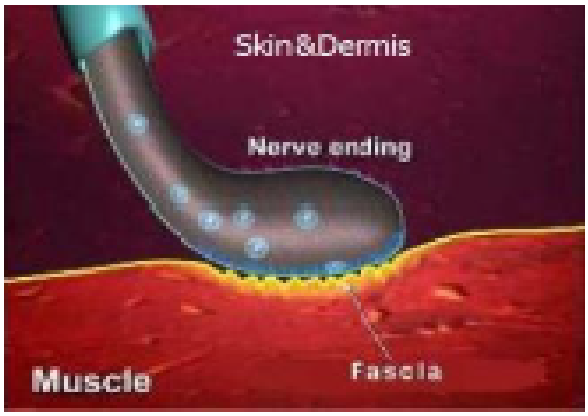

Figure 1. Fascia Anatomy.

(Figure 1) serves to envelope the muscles, nerves, and vessels, thereby forming planes and potential spaces that divide them into functional units. Nerve endings exist only on the fascia, and not inside the muscle, otherwise the nerves would suffocate with each muscular contraction. The subdermal bloodless space is the optimal spot for injectables, especially for implants or fillers, since these products act on nerve endings and therefore should be injected on the fascia nerve where nerve endings exist, instead of inside the muscle, as they have been all along. Using the ASIS technique, collagen injected subdermally in the bloodless space (shoulder) remained there longer than collagen injected in intra-muscularly (buttocks). The subdermal bloodless space is the optimal injection site for collagen fillers due to an increased period of time in which water insoluble injectates remain.

The ASIS technique and device itself offers benefits for non-cosmetic injectables or fillers. Since the bloodless space has the natural ability to expand rapidly and contain abscesses or hematoma, this will allow rapid, effortless, and painless infusion of injectable products that come in high volume such as GAMMAGARD (20-30 mL) and antibiotics (50 mL; Gidley and Stiernberg, 1997; Miller et. al.,1999; Panoessa and Goldstein, 1976; Scott et. al., 1998).

CONCLUSION

The ASIS technique and device itself offers benefits for non-cosmetic injectables or fillers. Because the bloodless space has the natural ability to expand rapidly and contain abscesses or hematoma, this will allow rapid, effortless, and painless infusion of injectable products that come in high volume such as GAMMAGARD (20-30 mL) and antibiotics (50 mL).Further studies are necessary using the ASIS device itself on different skin types.

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