

# A novel needle-free microjet drug injector using Er:YAG LASER: A completely new concept of transdermal drug delivery system

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## Abstract

The skin barrier effectively inhibits the penetration of substances; therefore, drug delivery, especially the delivery of drugs that are hydrophilic, through the skin, is challenging. Objectives: Physicians in the esthetic field now use the transdermal drug delivery system to attempt to deliver esthetic materials, such as hyaluronic acid and poly-DL-lactic acid into the skin. Conventionally, esthetic physicians manually injected these materials using needle syringes into the dermis layer. However, the injection is often irregular, imprecise, slow, and painful. Injector devices have been developed to overcome these limitations. A total of five Korean cadavers (that of three men and two women with a mean age of 69.2 years; range, 60–73 years) underwent laser injection. We used a device called Er:YAG LASER to create the pressure needed for microjet delivery to the skin of the cadaver. Discussion: In this study, the first LASER pressure-based, needle-free microjet injector was used to deliver drugs effectively into the dermis of a cadaver. This study showed that a novel needle-free microjet injector using Er:YAG LASER can introduce beneficial, liquid, esthetic drugs into the papillary dermal layer (depth of 300um) with minimal epidermal damage.

## KEYWORDS

Er:YAG LASER, hyaluronic acid, poly-DL lactic acid, transdermal drug delivery system

## 1 | INTRODUCTION

The skin is composed of three layers: epidermis, dermis, and subcutaneous fat. Among them, the epidermal layer is located on the outermost surface. Among the epidermal layers, the outermost layer is called the skin barrier. The skin barrier plays important roles, such as maintaining water balance and preventing the invasion of bacteria and

foreign substances. Because of its lipophilic structure, the skin barrier is especially protective against hydrophilic substances. However, such characteristics are not favorable in terms of esthetic medicine because some drugs are introduced into the dermis for their beneficial effects are ironically blocked by the skin barrier. In other words, the skin barrier decreases the absorption rate of hydrophilic drugs that are effective for the skin.

Physicians in the esthetic field have developed a method called mesotherapy to effectively deliver cosmetic substances into the

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dermis. (El-Domyati et al., 2012; Tedeschi et al., 2015) Mesotherapy utilizes micro-sized needles to pierce the skin barrier and make direct injections into the dermis. This allows drugs to bypass the process of absorption through the skin barrier. Mesotherapy has, therefore, been very popular, but there are disadvantages in that it is irregular, inaccurate, slow, and painful as the injection is manually performed. (Konda & Thappa, 2013).

To overcome such disadvantages, needle injectors, such as the messogun (Choi et al., 2020), have been developed. Compared to the manually performed injections, the needle injector performs more regular and accurate injections. (Srinivas et al., 2017) There remain a few problems; however, as the injection is as slow and painful as when manually performed. Nevertheless, with no suitable alternatives, physicians prefer the use of such injection devices.

An Er:YAG laser is used to generate vapor bubbles, converts laser energy into pressure to deliver drugs to the skin in the form of a jet. A microjet is generated by an expansion of the vapor bubbles induced by the focused laser beam as illustrated in Figure 1. (Jang et al., 2014) It is possible to inject a small amount of drug evenly into the dermal layer. Because the laser does not directly touch the skin, it is the most important feature to deliver a dose

of drug quickly and effectively at regular intervals without thermal heating.

The main objective of this study was to determine the effectiveness of the Er:YAG LASER in creating the pressure needed for microjet delivery. We examined whether the drug was effectively inserted into the dermal layer by observing the tissue samples.

## 2 | MATERIALS AND METHODS

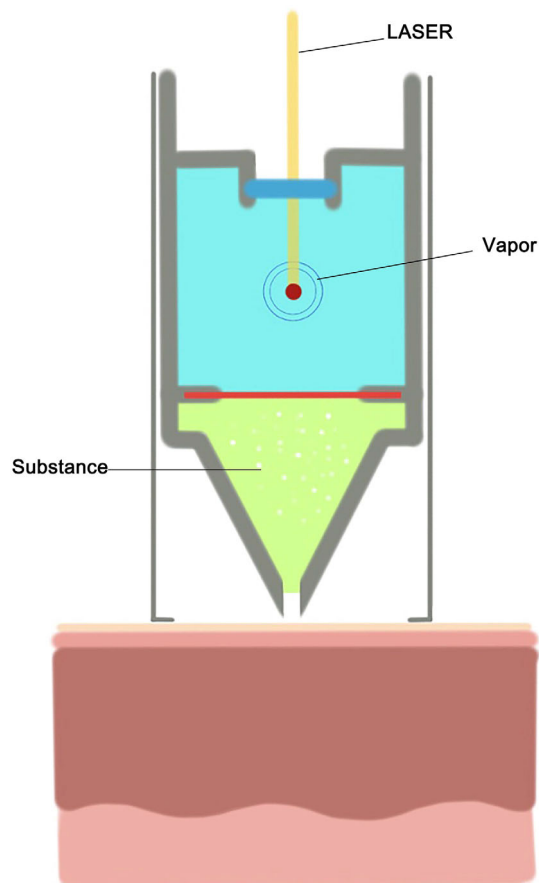
This study was performed in accordance with the principles outlined in the Declaration of Helsinki. Appropriate consent and approval were obtained from the families of cadavers before the experiment was conducted. A total of five Korean cadavers (that of three men and two women with a mean age of 69.2 years; range, 60–73 years) underwent laser injection.

We used a device called Er:YAG LASER to create the pressure needed for microjet delivery to the skin of the cadaver. The laser pulse mode was set to 40us, the operating frequency to 10 Hz or 40 Hz, and the output energy to 600 mJ. Hyaluronic acid (HA) mixed with dye and poly-DL-lactic acid (PDLA, itemized name Juberuc) was injected into both sides of the forehead, the periocular, the cheek, and the perioral areas. After confirming through observation with the naked eye that the dye-mixed substances had been injected sufficiently into the cadaver, the tissue samples from the injected areas were incised and collected. The collected tissue samples were stained with hematoxylin and eosin and observed using an optical microscope under 50× and 100× magnification, respectively.

This study was conducted in compliance with the principles of the Declaration of Helsinki. Consent was received from the patients and families of the deceased cadaver prior the procedure and dissections. The exclusion criteria for this study included pregnancy, history of drug allergy, other serious medical conditions, or surgical or non-surgical treatment of the facial area (including HA filler) within the previous 6 months. All subjects received a sufficient explanation of the study purpose and protocols, and they were free to withdraw from the treatment and research at any time. After the anatomical experiment one clinical cases have been presented with the exact same procedures. In addition, the patient satisfaction was assessed according to the “very satisfied,” “satisfied,” “disappointed,” and “very disappointed” scales with a self-report questionnaire at the last visit.

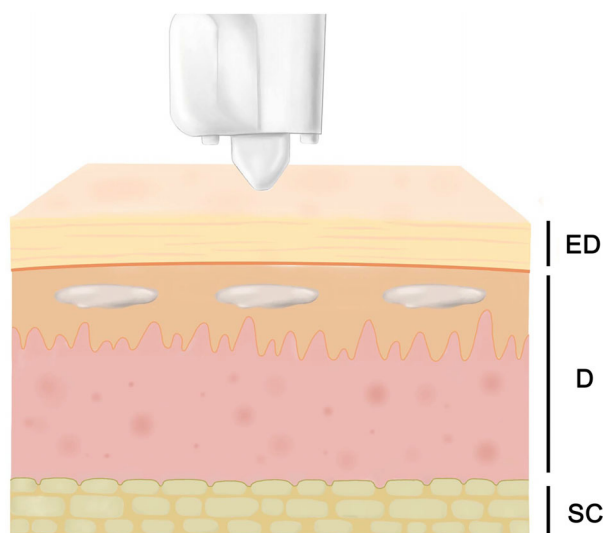
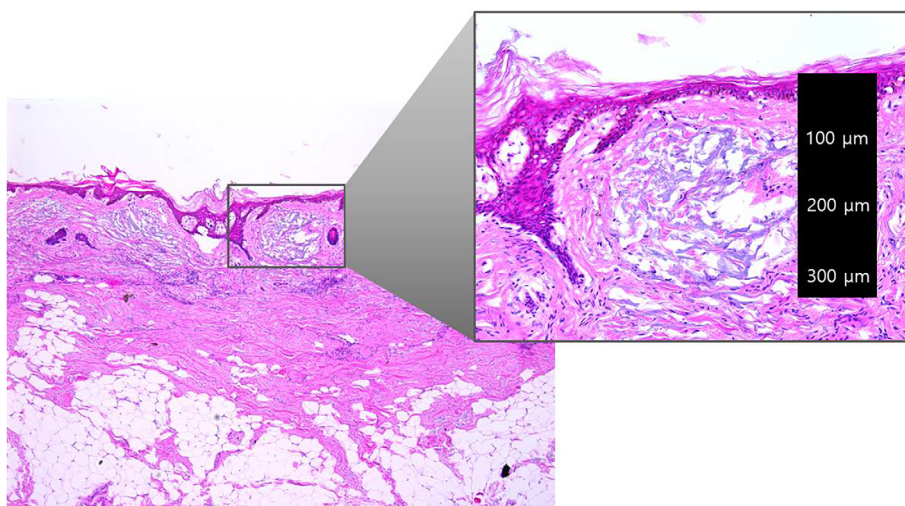
## 3 | RESULTS

As observed with the naked eye, punctures from the laser injections were not visible on the surface of the skin. When the tissue samples were observed under the microscope, it was observed that the HA and PDLA substances had penetrated through the epidermal layer and were localized in the upper dermis at a depth of 300um (Figure 2). This result was the same for all 10 sides (from five cadavers) of the forehead, the periocular, the cheek, and the perioral areas of the tissue samples. The injection cycle at 10 Hz or 40 Hz confirmed that the



**FIGURE 1** A microjet is generated by an expansion of the vapor bubbles induced by the focused laser beam as illustrated. The substance is injected into the skin with the pressure produced by vapor bubbles

**FIGURE 2** The histological section of skin after the esthetic substance is inserted by needle-free microjet drug injector using laser

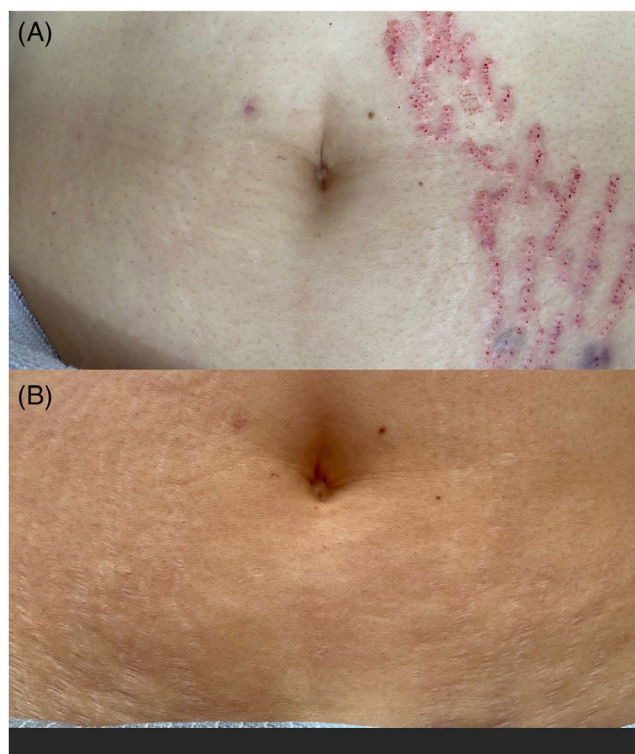


**FIGURE 3** The shape of the HA or PDLA inserted is oval shape. The shape was similar when using the either of the different solutions. HA, hyaluronic acid; PDLA, poly-DL-lactic acid

absorption uniformly reached at the same level of the papillary dermis. The shape of the localized HA or PDLA inserted was oval in shape in the papillary dermal layer (Figure 3). As observed with the naked eye, no visible damage was observed on the epidermal layers.

#### 4 | DISCUSSION

In this study, the performance of the Er:YAG laser injector is demonstrated. This device utilizes a laser to vaporize cosmetic substances and create pressure from this process to disseminate cosmetic substances into the skin in the form of microjets. Compared to clear holes made by mesotherapy or messogun (Srinivas et al., 2017), the damage to the epidermis is hardly visible to the naked eye in the tissue



**FIGURE 4** The injection of PDLA with microjet right after (A) and 2 months later (B). PDLA, poly-DL-lactic acid

specimens. This suggests that the laser device minimizes damage to the epidermis.

The papillary dermis is considered to be the best target for injection of cosmetic materials because it is a layer where esthetic effects, such as collagen stimulation, can be maximized (Srinivas et al., 2017; Zhou et al., 2020). The laser device penetration was at a depth of 300 μm, which is the upper part of the dermis. In addition, regardless of whether the operating frequency was 10 Hz or 40 Hz, it was confirmed that the absorption uniformly reached at the same level as

the papillary dermis, indicating that faster treatment can be conducted.

A limitation of this study is that the outcome from a pre-fixed cadaver may be different from that obtained in living human tissues. The tissue of the cadaver loses its elasticity and consistency over time after death. In future studies, to overcome this limitation, a method such as injecting a substance like HA into a living person and observing the effect using high-resolution ultrasound.

#### 4.1 | Case 1

A 44-year-old man presented with a severe abdominal striae distensae. A preliminary clinical photograph showed prominent striae distensae in the abdominal region. The Er:YAG LASER microjet injector was used to inject PDLA. On day 2 months after the injection, the bruise and swelling were well removed. The scar tissue was lightened (Figure 4). This volunteer responded as “satisfied” in the patient satisfaction questionnaire.

## 5 | CONCLUSION

This study showed that a novel needle-free microjet injector using Er:YAG LASER can introduce beneficial, liquid, esthetic drugs into the papillary dermal layer (depth of 300  $\mu$ m) with minimal epidermal damage, bypassing the skin barrier, which is a huge blockage of skin penetration of drugs. This makes this device an ideal transdermal drug delivery system.

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