In Vivo Histological Evaluation of a Novel YSGG Ablative Fractional Device for Cutaneous Remodeling

Walfre Franco, PhD\textsuperscript{a}, Brian D. Zelickson, MD\textsuperscript{b}, Victor E. Ross, MD\textsuperscript{c}

\textsuperscript{a}Cutera Inc., Brisbane, CA

\textsuperscript{b}Abbott Northwestern Hospital, Minneapolis, MN

\textsuperscript{c}Naval Medical Center San Diego, San Diego, CA

Abstract

Background and Objectives: Fractional photothermolysis induces an array of microscopic zones of ablative and thermal injury in the skin, leaving intervening areas of normal skin unaffected, which rapidly repopulate the ablative zones of tissue. The objective of the present study is to evaluate a novel YSGG ablative fractional laser device for cutaneous remodeling on \textit{in vivo} human skin. Study Design/Materials and Methods: An investigational 2790 nm YSGG laser device (Pearl Fractional, Cutera, Brisbane CA) was used to induce arrays of microscopic treatment zones in human face skin. Pulse energies of 160 and 240 mJ and 600 ms exposures were used to induce microscopic zones of skin injury. The wound healing process in these zones was monitored micro and macroscopically using day-0 (immediately after laser exposure), day-4 and day-14 tissue histology—hematoxylin and eosin standard staining—and photography, respectively. Results: As expected, the investigational YSGG laser device induced a controlled microscopic array of ablative and thermal skin injury. Day-0 histology shows tapering ablative zones lined by a thin eschar layer surrounded by columns of thermal coagulation within the epidermis and part of the dermis. Day-4 histology shows invagination of epidermis into the ablative zone, complete re-epithelialization and a sustained coagulation zone, which is still present in day-14. Day-0 and day-4 digital pictures show minimal erythema and edema. Day-14 digital pictures show a fully recovered skin. Conclusions: A controlled array of microscopic treatment zones of ablation and thermal coagulation

\textsuperscript{1}Address correspondence to Walfre Franco, Cutera Inc., 3240 Bayshore Blvd., Brisbane, CA 94005; email: wfranco@cutera.com
were induced within the epidermis and part of the dermis by means of a novel YSGG ablative fractional resurfacing device. Macroscopically, the skin recovered in 7–14 days. Microscopically, tissue histology from the same time point suggests an ongoing collagen remodeling response.

1 Introduction

Carbon dioxide (CO₂) and erbium-doped yttrium aluminum garnet (Er:YAG) ablative lasers remain the gold standards for laser resurfacing; i.e., nonsurgical skin rejuvenation. However, their use is associated with significant risks of side effects, such as scarring, and a prolonged, unpleasant postoperative recovery period: delayed re-epithelialization, persistent erythema, delayed and permanent hypopigmentation [1]. Newer non-ablative rejuvenating laser systems have been introduced in an effort to stimulate collagen production and remodeling while preserving the epidermis and, consequently, reducing or eliminating healing time and patient discomfort [2]. An intermediate, more recent, approach to laser skin rejuvenation is ablative fractional resurfacing, which stems from the concept of fractional photothermolysis; a method of skin treatment that generates an array of microscopic zones of thermal injury in the epidermis and dermis [3]. In order to overcome the aforementioned risks, side effects and postoperative recovery concerns associated with current ablative laser modalities, a novel yttrium scandium gallium garnet (YSGG) ablative fractional resurfacing device was developed by our group. This device thermally ablates microscopic columns of epidermal and dermal tissue in regularly spaced arrays over a fraction of the skin surface.

2 Objectives

The objective of the present study is to evaluate a novel YSGG ablative fractional laser device for cutaneous remodeling on *in vivo* human skin; specifically, the wound healing response to a
controlled array of microscopic treatment zones of ablation and thermal coagulation.

3 Materials and Methods

The study protocol was approved by an institutional review board and all subjects were consented prior to participation in the study. An investigational YSGG laser device was used to treat subjects with 600 ms laser pulses of 160 and 240 mJ. The laser beam was delivered through multiple deflective and refractive elements and focused to a spot size of approximately 300 μm in diameter at the skin surface in order to deposit a microscopic array of laser beams across the surface. Each treatment site covered approximately 1.3 cm × 0.9 cm with a spot density of 40 microscopic treatment zones per cm² and 1000 μm in-between micro-lesions.

Four subjects of Fitzpatrick skin type I and III were treated on the left and right preauricular area, and a third subject of Fitzpatrick skin type II was treated on the entire face. Topical anesthesia was administered locally 30–45 min prior to the laser treatment and wiped off before laser exposure. Biopsies excisions were made immediately (day-0), 4 days (day-4) and 14 days (day-14) after treatment. Each biopsy sample was fixed in 10% v/v neutral buffered formalin overnight and then embedded in paraffin. Samples were sectioned into 5–10 μm thick slices and stained with hematoxylin and eosin (HE). Lesions depth and width were estimated from the stained sections.

4 Results

The microscopic effect of fractional resurfacing on human face skin at different pulse energies immediately after treatment is shown in Figs. 1(a)–(b) and 3(a)–(b). The wound healing response, from day-4 to day-14, to microscopic lesions induced by different pulse energies is shown in Figs. 1 and 3. The macroscopic effects of fractional resurfacing from day-0 to day-14 are shown in Figs.
2, 4, 5 and 6. Histology in Figs. 1 and 3 correspond to anatomical locations in Figs. 2 and 4, respectively.

4.1 Microscopic Effects of YSGG Ablative Fractional Laser Treatment

Fractional resurfacing laser exposure resulted in immediate ablation of the epidermis and dermis, Figs. 1(a)–(b) and 3(a)–(b). The width and depth of ablative zones approximately ranged from 250–400 $\mu$m and 300–800 $\mu$m, respectively, for pulse energies 160–240 mJ. Stained images show ablative zones lined by an eschar thin layer which in turn is surrounded by columns of thermal coagulation (clearly shown in Fig. 3(b)), suggesting that adequate homeostasis was achieved after fractional resurfacing laser treatment.

Four days after treatment, the ablative zone was completely replaced by invaginating epidermal cells, Figs. 1(c)–(d) and 3(c)–(d). The microscopic treatment zone surrounded the invaginated epidermal tissue; however, the basement membrane remained partially disrupted as evidenced by basal layer vacuolar change, Fig. 3(c). Exudative necrotic debris, commonly observed in treatments using fractional resurfacing, was observed at the stratum corneum level [4].

Fourteen days after treatment, the exudative necrotic debris was not longer evident, it was replaced by normal stratum corneum, Figs. 1(e) and 3(e)–(f). In addition, the epidermal invagination had regressed. Presumably, the epidermal invagination eventually regressed completely, and the space vacated was replaced by newly synthesized collagen [5]. Columns of thermal coagulation are not as evident as in day-4 but still present in day-14, most likely indicating ongoing dermal remodeling. The circled area in Fig. 1(e) appears to be fibroplasia.

4.2 Macroscopic Effects of YSGG Ablative Fractional Laser Treatment

For both 160 and 240 mJ pulse energies, fractional resurfacing laser exposure resulted in mild skin edema and erythema, Figs. 4(a)–(b), which persisted on day-4, Figs. 4(c)–(d), and vanished by
day-14, Figs. 4(e)–(f). These images, acquired prior to biopsy excisions, correspond to treatments in Figs. 3(a)–(f). Progression in skin appearance after an entire face treatment with 160 mJ is shown in Figs. 5(a)–(c): immediately after, mild skin edema and erythema everywhere but the nose; day-4, persistent edema and erythema on the cheeks; day-14, improved skin appearance with no evidence of treatment. Figs. 6(a)–(d) show the progression in skin appearance for the same treatment on a different subject: immediately after, mild skin edema and erythema everywhere but the nose; 90 min after, persistent edema and erythema and little bleeding; day-1, reduced edema and erythema; day-7, improved skin appearance with no evidence of treatment.

5 Conclusions

A controlled array of microscopic treatment zones of ablation and thermal coagulation were induced within the epidermis and part of the dermis by means of a novel YSGG ablative fractional resurfacing device. Histology results suggest that adequate homeostasis is achieved when utilizing this device. Macroscopically, the skin recovered in 7–14 days. Microscopically, tissue histology from the same time point suggests an ongoing collagen remodeling response.

References


[3] Dieter Manstein, G Scott Herron, R Kehl Sink, Heather Tanner, and R Rox Anderson. Frac-


Figure 1: Wound healing of ablative fractional microscopic lesions: biopsies taken (a) immediately and (c) 4 days after 160 mJ Pearl Fractional laser exposure; and, (b) immediately, (d) 4 days and (e) 14 days after 240 mJ Pearl Fractional laser exposure. The circled area in (e) may be fibroplasia. Microscopic lesions may not be sectioned across the right plane indicating nominal lesions depths. (HE stained images provided by Dr. Victor E Ross.)
Figure 2: Wound healing of ablative fractional microscopic lesions: images taken (a) immediately, (c) 4 days and (e) 14 days after 160 mJ Pearl Fractional laser exposure; and, (b) immediately, (d) 4 days and (f) 14 days after 240 mJ Pearl Fractional laser exposure.
Figure 3: Wound healing of ablative fractional microscopic lesions: biopsies taken (a) immediately, (c) 4 days and (e) 14 days after 160 mJ Pearl Fractional laser exposure; and, (b) immediately, (d) 4 days and (f) 14 days after 240 mJ Pearl Fractional laser exposure. Black arrows indicate thermal coagulation zones. Microscopic lesions may not be sectioned across the right plane indicating nominal lesions depths. (HE stained images provided by Dr. Brian D Zelickson.)
Figure 4: Wound healing of ablative fractional microscopic lesions: images taken (a) immediately, (c) 4 days and (e) 14 days after 160 mJ Pearl Fractional laser exposure; and, (b) immediately, (d) 4 days and (f) 14 days after 240 mJ Pearl Fractional laser exposure.
Figure 5: Progression in skin appearance after an entire face treatment with 160 mJ laser pulses: (a) immediately after, mild skin edema and erythema everywhere but the nose; (b) day-4, persistent edema and erythema on the cheeks; (c) day-14, improved skin appearance with no evidence of treatment.
Figure 6: Progression in skin appearance after an entire face treatment with 160 mJ laser pulses: (a) immediately after, mild skin edema and erythema everywhere but the nose; (b) 90 min, persistent edema and erythema and little bleeding; (c) day-1, reduced edema and erythema; (d) day-7, improved skin appearance with no evidence of treatment. Left frame on each image corresponds to the anatomical baseline; i.e., before laser exposure.