

A Predictive Model of Minimally Invasive Bipolar Fractional Radiofrequency Skin Treatment

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Background: A novel bipolar fractional radiofrequency (FRF) system with temperature feedback was recently developed for facial laxity and rhytid treatment. The study objective was to develop a model based on published in vivo human skin data that could be extrapolated to aid physicians in making future dosimetry choices under clinically relevant conditions.

Methods: A standard electrode pair designed for use with the FRF system was modeled using finite element analysis (FEA). The model incorporated temperature feedback from sensors within the electrodes, selectable target dermal temperatures, and an epidermal cooling plate. The model was validated using data obtained during clinical treatments. Thermal injury as a function of target temperatures and electrical conductivity was simulated and then validated using in vivo histology results.

Results: Lesion size predicted by the model matched histology samples. Lesion width and height were 1.65 and 1.24 mm compared to 1.75 and 1.21 mm for the model versus in vivo, respectively. The thermal profile remained confined between the proximal and distal ends of the electrodes. Ninety-six percent of power was deposited in the dermis. Dose–response curves showed a nonlinear volume increase to 1.7 and 4.7 mm³ at target temperatures of 65 and 75°C, respectively, and a low sensitivity to electrical conductivity variation.

Conclusion: FEA of the Bipolar FRF system revealed that isotherms were mainly within the dermis. Lesion volume was found to be less sensitive to changes in electrical conductivity than to target temperature and duration. Simulation results matched well the in vivo lesion dimensions. To our knowledge, this is the first model of bipolar FRF treatment capable of accurately predicting the thermal response of human skin in vivo. The findings of this study allow for the development of accurate dose–response curves to aid physicians in parameter selection and achieving efficacy and safety profiles. *Lasers Surg. Med.* 41:473–478, 2009. © 2009 Wiley-Liss, Inc.

Key words: bipolar radiofrequency; collagen coagulation; deep dermal heating; skin treatment; finite element analysis; fractional radiofrequency; microneedle; minimally invasive; modeling; nonablative; dose.

INTRODUCTION

Devices employing electromagnetic radiation (EMR) have been used clinically to reverse the signs of skin aging

[1–3]. The nonsurgical gold standard for facial rejuvenation and wrinkle reduction remains carbon dioxide laser resurfacing [4,5]. However, this treatment has been associated with prolonged post-operative healing characterized by delayed reepithelialization, persistent erythema, delayed-onset permanent hypopigmentation, and scarring [1,2,5]. This has led to a significant effort by researchers to explore other treatment modalities including radiofrequency (RF) devices. Finite element analysis (FEA) has been an important tool for better understanding EMR-tissue interactions and optimizing treatment algorithms [6–8]. Studies of EMR-tissue interactions have provided novel insights related to both infrared lasers as well as monopolar RF devices and their effects on collagenous skin tissue [3,9,10]. Collagen is the most abundant protein in skin and resides in a water-rich extracellular matrix in the dermis, and is therefore an indirect target of all treatments that focus on water as a chromophore.

We recently introduced a minimally invasive bipolar RF system for the treatment of facial skin laxity and rhytids [11]. Through the use of a direct real-time temperature and impedance feedback system, we showed that fractional radiofrequency (FRF) treatment led to the controlled creation of dermally located thermal coagulation zones, known as radiofrequency thermal zones (RFTZs). Lesions were found to be fractional in pattern and located mainly in the reticular dermis. The epidermis, adipose tissue, vasculature, and adnexal structures were spared by the treatment. In a follow-up study, we found that in vivo FRF treatment of human skin induced a vigorous wound healing response that activated dermal remodeling and complete replacement of RFTZs with new collagen and elastin by 10 weeks post-treatment [12].

Additional Supporting Information may be found in the online version of this article.

Abbreviations: FEA, finite element analysis; FRF, fractional radiofrequency; RF, radiofrequency; RFTZ, radiofrequency thermal zones.

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To date, there remains no published dosimetric study characterizing the FRF system to aid physicians in selecting treatment parameters, or sensitivity study to characterize the system response under various clinically relevant conditions. In the present study, we developed a FEA model capable of accurately predicting the in vivo energy deposition pattern in human skin under various clinically relevant conditions.

MATERIALS AND METHODS

Radiofrequency Device

The bipolar FRF device (Miratone™, Primaeva Medical, Inc., Pleasanton, CA) modeled in this study consists of a 5-pair 30 gauge microneedle array in combination with thermoelectric cooling maintained at 10°C to protect the epidermis during RF application [11]. The proximal end of each microneedle is insulated with a biocompatible Teflon layer, leaving the distal 3 mm exposed to form the electrode in tissue. A thermocouple embedded in the tip of each electrode pair measures tissue temperature during treatment to provide real-time feedback to the generator via a proportional integration derivative (PID) control algorithm. The treating physician can select the desired target temperature and pulse duration as clinical endpoints.

Model

A single electrode pair of the FRF system as well as a portion of the epidermal cooler were modeled in 3D with Comsol Multiphysics software (Comsol, Burlington, MA). As shown in Figure 1, the pair consisted of two 6 mm long needles obliquely positioned at 20° within skin. The skin model consisted of three sections representing the epidermal, dermal, and subcutaneous layers. Electrical, thermal, and blood perfusion properties were assigned to each layer, as described in Table 1. The effect of a cooling plate maintained at 10°C to protect the epidermal layer was also modeled. A PID controller with selectable target temperature was incorporated in the model to control power delivery based on temperature feedback. An iterative numerical method was used to generate the results. First, the initial voltage applied between the bipolar needles by the PID controller was calculated using the PID algorithm.

Then, RF energy deposition, temperature profile, and thermal dose were calculated for the entire 3D model. This process was repeated to calculate the electromagnetic and thermal solutions for the subsequent time increments, until the simulation of a 5-second pulse duration was completed. Thermal modeling continued for an additional 5 seconds after RF power delivery ended to monitor cooling of the skin layers. For further details on the physics and mathematical formulation of the model, see the supplemental Materials and Methods Section.

Lesion Dimensions and Volume Calculations

Lesion volumes were calculated using a thermal dose model which considers the combined effects of temperature and exposure time on collagen denaturation [10]. The thermal dose (Ω), formulated as an Arrhenius integral, was implemented in the model and calculated at all time increments. A thermal dose of $\Omega = 1$ corresponds to the optimal value for collagen denaturation [10], and indicates that 63% of the collagen fibers have been denatured. According to Ref. [10], a thermal dose of $\Omega = 1$ for collagen is reached after 7, 0.38, and 0.002 seconds at constant temperature of 65, 70, and 75°C, respectively (see Fig. 2). Using isotherm to calculate lesion volumes would lead to inaccuracies [13] since the target temperatures used in this study are in this range. The volume bounded by the surface where $\Omega = 1$ was used to calculate the lesion dimensions and volumes [10,13,14].

Model Validation

Real-time temperature, impedance, and delivered power data from previously published in vivo treatments were used to validate the model output [11]. In this study, 15 female patients (mean age 52.0 ± 8.8 years, Fitzpatrick skin type II–IV) received FRF treatment of abdominal or preauricular facial skin prior to planned abdominoplasty or facelift procedures allowing for tissue collection for histological evaluation. PID coefficients for use in the model were selected to replicate temperature elevation observed in Ref. [11]. We compared the following four aspects of the temperature data: tissue temperature after 1 second of RF application, time to reach target temperature, time at target temperature, and tissue temperature 1 second post-FRF application. We also compared the delivered power at 2 and 5 seconds of RF application.

For lesion size validation, histology samples from a previous study [11] were analyzed to identify cross-sections of a lesion with visible collagen coagulation in at least four consecutive tissue samples. Lesion dimensions were measured using calibrated digital photography. All slides were read by two board-certified dermatologists (BMH and RK, see Acknowledgement Section) in blinded fashion. Hematoxylin and eosin is commonly used to delineate changes in the histological appearance of collagen before and after thermal exposure. Zones of coagulated collagen appear homogenized with enhanced eosinophilic staining relative to uncoagulated collagen. The means and standard deviations for the main axis dimensions were measured for the four planes (Fig. 3). We simulated parameters for target

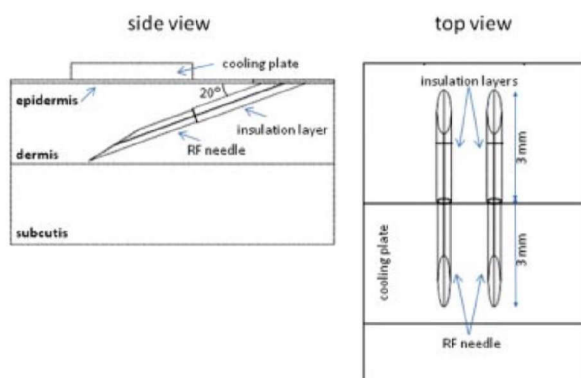


Fig. 1. Model geometry.

TABLE 1. Tissue Properties

	Electrical		Thermal		Physical		
	Conductivity (S/m)	Dielectric constant	Conductivity (W/m °C)	Heat capacity (J/kg °C)	Thickness (mm)	Density (kg/m ³)	Perfusion rate (1/second)
Epidermis	0.026 [18]	858 [20]	0.24 [19]	3,590 [19]	0.08 [10]	1,200 [10]	0
Dermis	0.195 [20]	5,289 [20]	0.45 [19]	3,300 [19]	2.00 [10]	1,200 [10]	1.25×10^{-3} [21]
Subcutis	0.026 [20]	34.3 [20]	0.19 [19]	2,500 [19]	5	1,000 [10]	1.25×10^{-3} [21]
Blood	N/A	N/A	N/A	3,770 [21]	N/A	1,060 [21]	N/A

temperature (70°C) and pulse duration (3 seconds) based on the settings used to produce the lesion [11]. Lesion width and height were obtained in a plane perpendicular to the needle located 1.5 mm proximal to the needle tips. These measurements were then compared to histology results obtained 13 days post-treatment.

Model Prediction—Dose–Response Curves and Sensitivity

Target temperatures between 65 and 75°C, within the range used in Ref. [11], were modeled to predict the temperature profiles, lesion dimensions, and dynamics of injury creation. The percentage of RF power deposited in skin layers was calculated under conditions where the electrode surface is completely surrounded by dermal tissue and when half of the needle surface is embedded in the subcutis. Lesion volumes were modeled under a variety of electrical impedance values typical of those observed during clinical procedures (range 300–2,000 Ω [11]).

RESULTS

Model Validation

The numerical model was well-behaved and converged for all iterations tested. Results simulating a 70°C target temperature treatment with a pulse duration of 5 seconds are shown in Figure 4. Tissue temperature 1 second into RF application was 67°C, and 2 seconds later, reached the target temperature of 70°C without overshoot. Tissue had cooled to 55°C 1 second following energy delivery,

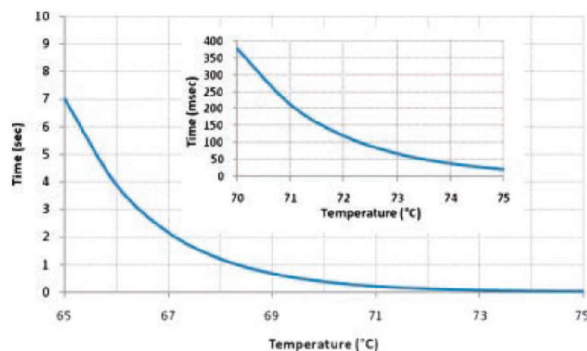


Fig. 2. Time needed to reach a thermal dose of $\Omega=1$ for collagen denaturation at constant temperature. The inner figure shows the time needed for temperatures between 70 and 75°C.

consistent with our previously published study [11]. The corresponding predicted electrical impedance was 1,142 Ω , also well within the range of 1,000–1,750 Ω reported previously. A voltage of ~ 100 V was initially applied by the PID controller. This resulted in the steep initial thermal response shown in Figure 4. The applied voltage was decreased to 35 and 30 V after 2 and 5 seconds, respectively, to reach the target temperature without overshoot. This corresponds to an applied power of 1.1 and 0.8 W after 2 and 5 seconds, respectively, values in line with previous studies [11]. Lesion width and height predicted by the model were 1.65 and 1.24 mm compared to 1.75 ± 0.16 and 1.21 ± 0.14 mm, respectively, for in vivo histology samples.

Thermal Profiles

Thermal profiles in a cross-sectional view containing the skin layers and in the plane of the needles are shown in Figure 5. The thermal profile was confined within the dermal layer and between the needles from the proximal to the distal extremities of the exposed metallic portions. Data also showed that the epidermal layer temperature underneath the cooling plate was at or below initial temperature (37°C) at all times during and after the RF application. A maximal epidermal temperature of 24°C was observed at

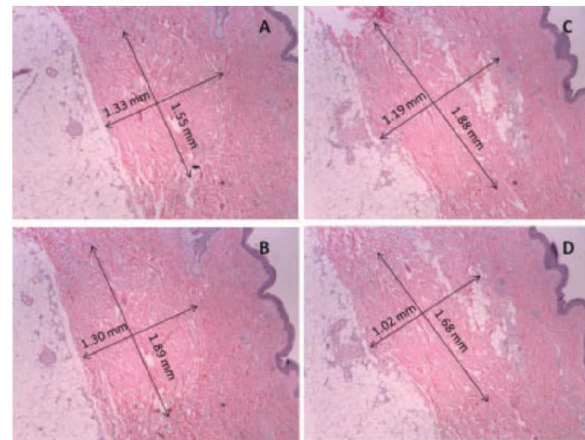


Fig. 3. Lesion size assessed histologically 13 days post-treatment. The distance between panels A and C was 0.5 mm. The distance between panels A and B, as well as panels C and D was 10 μ m. The target temperature and energy application duration used during treatment were 70°C and 3 seconds, respectively. The original magnification was 4 $\times$.

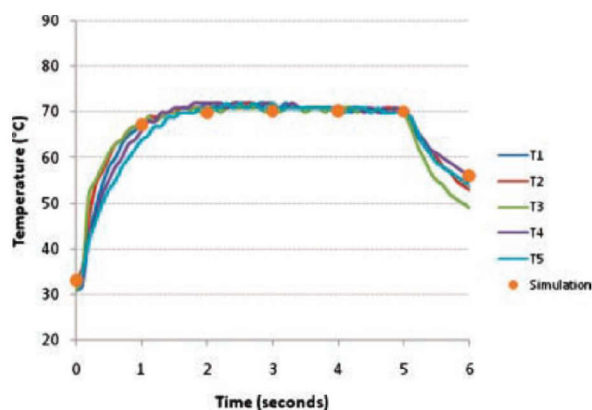


Fig. 4. Simulated versus measured temperatures (PID input). RF energy was applied for the first 5 seconds, and then turned off for the remaining 5 seconds.

the interface between the epidermis and dermis after 5 seconds of RF application.

Dose–Response Curve

Dose–response curves for a 5-second pulse duration at varying target temperatures are shown in Figure 6, and indicate that the volume growth rate peaks by 2 seconds and declines thereafter. Since target temperatures were reached within 2 seconds in all simulated cases, the rate of volume increase may be in part due to the effects of thermal conduction. At a target temperature of 65°C, lesion volumes increased from 1.1 to 1.7 mm³ between 3 and 5 seconds, respectively, and from 3.1 to 4.7 mm³ at 75°C. The volumes

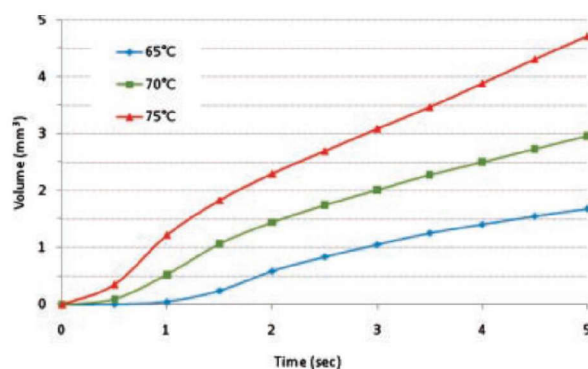


Fig. 6. Lesion volume ($\Omega = 1$) versus target temperature.

at 3 and 5 seconds were linearly proportional to the target temperature. The volumes at 3 and 5 seconds increased by 0.2 and 0.3 mm³/°C, respectively.

Sensitivity—Energy Deposition in Skin Layers

The percentage of RF power deposited in each skin layer was derived by calculating the volumetric integral of the SAR pattern for the nominal configuration using a dermal thickness of 2 mm. We found that 95.7% of the power was deposited in the dermal layer, 2.3% in the subcutaneous, and 2.0% in the epidermal layer. A total energy of 2.78 J was applied during the 5 seconds RF application. We next simulated a dermal thickness of 1.25 mm with the needles partially inserted in the subcutaneous layer. This resulted in 87.3% of the power deposited in the dermal layer, 15.0% in the subcutaneous layer, and 2.3% in the epidermal layer. In this configuration, the electrical impedance was 1,952 Ω . Despite half of the needle length being located in the subcutaneous layer, the thermal profile remained preferentially located in the dermal layer.

Sensitivity—Skin Impedance

Electrical conductivity was arbitrarily modified to values lower and higher than the nominal values reported in Table 1 to investigate the sensitivity of the system to a range of skin impedances (300–2,000 Ω) typically observed during clinical applications. The lesion volume was calculated and compared to the nominal results (Fig. 7). For all simulated conditions, the target temperature was reached and maintained. Lesion volumes showed low sensitivity to electrical conductivity after the first 3 seconds of RF application. Higher conductivities were associated with faster initial lesion growth. Volumes were within 5% of the nominal value after 5 seconds.

DISCUSSION

Results from the model showed good correlation with data collected during clinical evaluation of the FRF system. The temporal response of tissue temperature and power deposition mirrored the profiles observed during in vivo treatments. Lesion dimensions also matched the histology results, lending a high level of confidence in the model.

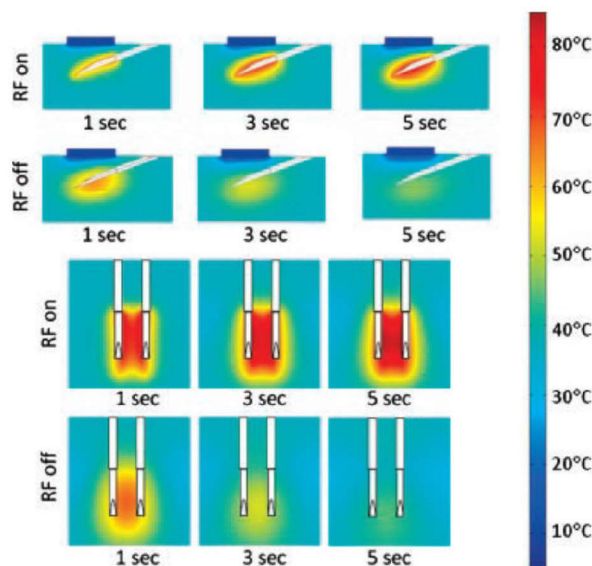


Fig. 5. Thermal profiles at 1, 3, and 5 seconds during and after RF application for a target temperature of 70°C (top, cross-section along one needle; bottom, plane containing both needles).

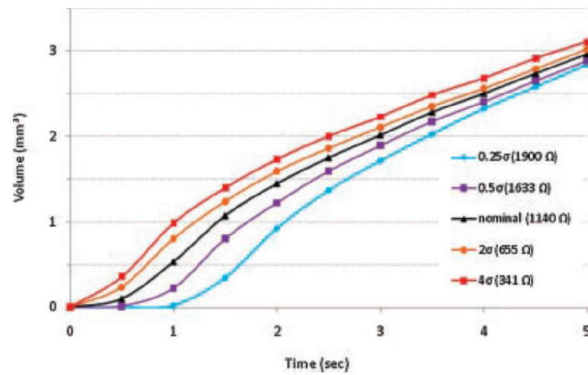


Fig. 7. Lesion volume ($\Omega=1$) at nominal and modified electrical conductivity (target temperature was set at 70°C).

Thermal profiles were confined within the dermal layer (Fig. 5). Results showed that target temperatures were reached within 2 seconds and maintained within the plane containing the electrodes. The thermal profiles extended from the plane containing the electrodes during the pulse. The limited lateral spread of the thermal profile allows fractional lesions to be produced with multiple electrode pairs, in line with the observed clinical treatments as assessed histologically [11]. Minimal temperature elevations in the subcutaneous layer were also observed. The cooling plate was effective at keeping the epidermal surface temperature well below 37°C at all times. Furthermore, the thermal pattern disappeared within 5 seconds after the RF power was turned off.

Target temperature and duration of application are the main predictors characterizing the dose–response curves (Figs. 6 and 7). In all simulated conditions, the temperature feedback provided by the PID controller insured tissue reached and maintained a predefined target temperature irrespective of needle position or skin conductivity.

We found that 96% of the applied power was absorbed in the dermal layer when the exposed lengths of the electrodes are located in the reticular dermis, 1–2 mm below the epidermal surface. When half of the exposed lengths of the electrodes were intentionally inserted in subcutaneous tissue, 87% of the applied power remained absorbed in the dermal layer. These data confirm that bipolar RF current, when delivered from within tissue, preferentially follows the path of highest conductivity—which in this case leads to energy deposition almost entirely in the dermis. This phenomenon improves the safety of the device and potentially avoids fat necrosis, a previously reported adverse event following monopolar RF treatment [15].

Treatment discomfort is a concern during many thermal aesthetic EMR procedures. Collagen coagulation occurs at temperatures that induce a significant pain response. While treatment at lower temperatures may improve patient comfort, clinical efficacy, and predictability of outcomes are compromised. Topical anesthetics can partially reduce discomfort, but are insufficient for many patients during deep dermal heating. Infiltration with

local anesthesia to eliminate treatment discomfort during aesthetic EMR procedures has been a source of controversy, since it may alter clinical outcome through affecting the energy deposition and heating patterns [16]. Indeed, tissue impedance measured during FRF was previously reported to be lower in tissue infiltrated with local anesthetic than in adjacent noninfiltrated sites [11]. Manufacturers of laser and monopolar RF devices without active dermal response monitoring and feedback systems have recommended against the use of local anesthesia [17]. In contrast, it was previously suggested that the presence of infiltrated local anesthetic did not influence the size of the RFTZ for FRF treatments with closed-loop feedback of dermal temperature response [11]. Simulation results revealed that lesion volume sensitivity to skin impedance was low. Lesion volumes were within $\pm 5\%$ of nominal values after 5 seconds of RF application when electrical conductivities were increased or decreased by up to fourfold to match impedance values observed clinically. These findings confirm previously published observations and suggest that real-time feedback enables creation of predictable lesion volumes within the skin impedance conditions tested in this study.

FEA modeling has shown that minimally invasive bipolar RF treatment is a method capable of depositing predictable fractional thermal coagulation patterns within the reticular dermis that are insensitive to dermal impedance over the range of impedances observed during clinical use. The ability to obtain a known and robust dosimetric response within the dermal layer removes many of the uncertainties associated with existing technologies which currently lack real-time tissue response feedback systems.

CONCLUSION

The bipolar FRF system was characterized and validated using FEA analysis. The model showed that the novel system is capable of creating a well-demarcated thermal pattern confined within the dermal layer without spreading to collateral skin layers. Using this model, a full-range dose–response curve was generated. The thermal pattern obtained with the system showed low sensitivity to conditions affecting electrical impedance. Target temperatures were met without overshoot for all simulated conditions. The modeled thermal profile and lesion size mirrored the data obtained in vivo. The dose–response curves and sensitivity analysis provided in this study will aid physicians in treatment parameter selection to optimize safety and efficacy profiles.

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