Comparative Healing of Human Cutaneous Surgical Incisions Created by the PEAK PlasmaBlade, Conventional Electrosurgery, and a Standard Scalpel

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Background: The authors investigated thermal injury depth, inflammation, and scarring in human abdominal skin by comparing the histology of incisions made with a standard "cold" scalpel blade, conventional electrosurgery, and the PEAK PlasmaBlade, a novel, low-thermal-injury electrosurgical instrument.

Methods: Approximately 6 and 3 weeks before abdominoplasty, full-thickness incisions were created in the abdominal pannus skin of 20 women, using a scalpel (scalpel), the PlasmaBlade, and a conventional electrosurgical instrument. Fresh (0-week) incisions were made immediately before surgery. After abdominoplasty, harvested incisions were analyzed for scar width, thermal injury depth, burst strength, and inflammatory response.

Results: Acute thermal injury depth was reduced 74 percent in PlasmaBlade incisions compared with conventional electrosurgical instrument ($p < 0.001$). Significant differences in inflammatory response were observed at 3 weeks, with mean $CD3^+$ response (T-lymphocytes) 40 percent ($p = 0.01$) and 21 percent ($p \approx 0.12$) higher for the conventional electrosurgical instrument and PlasmaBlade, respectively, compared with the scalpel. $CD68^+$ response (monocytes/macrophages) was 52 percent ($p = 0.05$) and 16 percent ($p \approx 0.35$) greater for a conventional electrosurgical instrument and the PlasmaBlade, respectively. PlasmaBlade incisions demonstrated 65 percent ($p < 0.001$) and 42 percent ($p < 0.001$) stronger burst strength than a conventional electrosurgical instrument, with equivalence to the scalpel at the 3- and 6-week time points, respectively. Scar width was equivalent for the PlasmaBlade and the scalpel at both time points, and 25 percent ($p = 0.01$) and 12 percent ($p = 0.15$) less than for electrosurgery, respectively.

Conclusions: PlasmaBlade incisions demonstrated reduced thermal injury depth, inflammatory response, and scar width in healing skin compared with electrosurgery. These results suggest that the PlasmaBlade may provide clinically meaningful advantages over conventional electrosurgery during human cutaneous wound healing. (*Plast. Reconstr. Surg.* 128: 104, 2011.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, II.

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Received for publication September 8, 2010; accepted January 7, 2011.

Clinical Trial Registry Information: clinicaltrials. gov, a service of the U.S. National Institutes of Health; registration no. NCT00943150 (http://clinicaltrials.gov/ct2/show/NCT00943150).

DOI: 10.1097/PRS.0b013e31821741ed

Disclosure: *This study was funded by PEAK Surgical, Inc. Dominique Y. Atmodjo and Joshua G. Vose are employees of PEAK; Eric J. Huang and Howard L. Rosenberg are consultants to PEAK. Geoffrey C. Gurtner received an unrestricted research grant provided by PEAK. None of the other authors has any relevant disclosures.*

The hemostatic control and dissection capability of conventional electrosurgical devices[1] is fundamental to the practice of surgery. However, their underlying mechanism of action—thermal ablation of tissue by delivery of continuous-waveform radiofrequency energy to the tip of an electrode "blade"[2,3]—is associated with thermal damage to tissues, reduced surgical precision compared with a scalpel, the potential for injury to adjacent structures (e.g., bowel, nerves, blood vessels), and delayed wound healing.[4–12] Incremental improvements in conventional electrosurgical device design have resulted in some reduction in thermal injury,[5–8,12] but these improvements have been modest.

The PEAK PlasmaBlade is a novel electrosurgical device that uses brief (approximately 40 μsec), high-frequency pulses of radiofrequency energy to induce the formation of electrical plasma along the edge of a thin (approximately 12.5 μm), flat, 99.5 percent–insulated electrode.[13,14] With a burst rate less than 1 kHz, a typical duty cycle that does not exceed 5 percent, and a very small exposed electrode surface area, the operating temperature of the PlasmaBlade remains between 40°C and 100°C.[14] This technology has been shown to effectively dissect ophthalmologic tissues as precisely as a scalpel with the hemostatic control of conventional electrosurgery, even when completely submerged in a liquid medium.

Prior work comparing the healing dynamics of incisions made in porcine skin using scalpel, PlasmaBlade, and electrosurgery demonstrated that the PlasmaBlade reduced acute thermal injury depth by 7- to 10-fold, decreased T-lymphocyte ($CD3^+$) and macrophage/monocyte ($CD68^+$) inflammatory cell response, produced an approximately 2.6- to 2.78-fold increase in wound burst strength after 6 weeks of healing, and ultimately resulted in superior scar formation compared with conventional electrosurgery.[15] Additional work in rats examining the healing dynamics of midline fascial incisions created by these three instruments demonstrated similar results.[16] Although these results are scientifically interesting, the effect of different forms of electrosurgery on human wound healing has not been investigated.

The present study used all three instruments (scalpel, PlasmaBlade, and conventional electrosurgery) to test the hypothesis that decreased thermal injury would lead to improved cutaneous healing in humans following full-thickness skin incision with primary closure. In addition to objective endpoints such as acute thermal injury depth, healed incision burst strength, and surface scar width, we evaluated wound inflammatory response by quantifying T-lymphocyte ($CD3^+$) and macrophage ($CD68^+$) cell density in excised samples from healing incisions.

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PATIENTS AND METHODS

Subjects and Study Design

The protocol for this clinical study was approved by the Institutional Review Board of El Camino Hospital (Mountain View, Calif.) and conducted in accordance with all accepted standards for human clinical research. All patients gave written informed consent before study enrollment. One-half of the cost of the abdominoplasty procedure was covered for patients participating in the study.

This study was conducted as part of a randomized controlled trial of 20 adult female subjects undergoing abdominoplasty with either the PlasmaBlade or the standard of care (scalpel and conventional electrosurgery).[17] The study population had a mean age of 42.7 ± 10.1 years and a mean body mass index of 24.6 ± 3.4 kg/m^2. Approximately 6 and 3 weeks before abdominoplasty, each subject underwent placement and primary closure of three full-thickness skin incisions, made with the three instruments of interest (scalpel, PlasmaBlade, and a conventional electrosurgical instrument) and located within the area planned for eventual excision (Fig. 1). An additional set was made immediately before abdominoplasty with the patient under general anesthesia. After harvest of the abdominoplasty tissue mass, healing incisions were submitted for burst strength testing and manual and computer-assisted histologic analysis.

Incisional Wound Model Surgical Procedure

Three separate sets of comparison incisions were placed within the subject's planned abdominoplasty area as shown in Figure 1. Incisions were created in advance of abdominoplasty (6-week and 3-week time points) and immediately before abdominoplasty (designated the 0-week, or acute

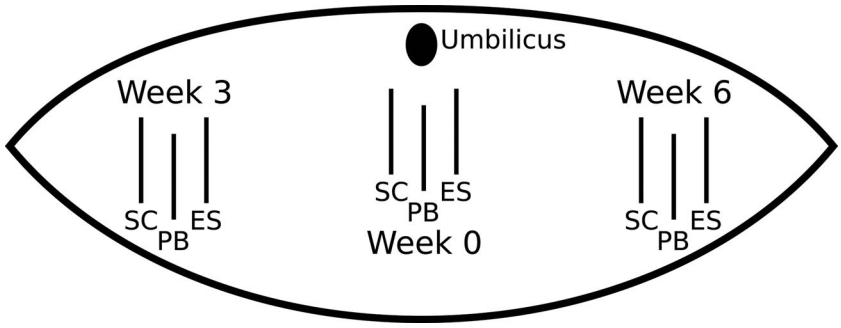

Fig. 1. Arrangement of incisions in the abdominoplasty area, by instrument and time point, just before the harvesting procedure. *SC*, scalpel; *PB*, PlasmaBlade; *ES*, electrosurgery.

time point). Each incision was considered to be an independent data point.

The incision area was shaved, prepared with ChloraPrep (2% chlorhexidine gluconate/70% isopropyl alcohol solution; CareFusion, Inc., San Diego, Calif.), and draped in the usual sterile fashion. The location for each incision was measured and labeled, and local anesthesia was induced by means of subcutaneous injection of approximately 5 ml of 1% lidocaine without epinephrine (VWR, West Chester, Pa.). Each incision was 5 cm in length and made through the full thickness of the skin in a single stroke, with repetitive strokes made only to ensure a full-thickness wound. Incisions were made in parallel orientation and separated from each other and the abdominoplasty border by a minimum of 2.5 cm in all directions. Incisions were made with a no. 10 scalpel blade (Bard-Parker, Franklin Lakes, N.J.), the PlasmaBlade 4.0 using the PULSAR Generator (PEAK Surgical, Inc., Palo Alto, Calif.) on Cut setting 3 (6 W), and the Valleylab Electrosurgical Pencil (model E2516) with a standard stainless-steel blade electrode (model E1551X) using a Force 2 Generator (Valleylab, Boulder, Colo.) on Cut mode (30 W). Settings for the PlasmaBlade and conventional electrosurgical instruments were chosen based on widely accepted settings for routine use. The approximate cost of the PlasmaBlade device was $300, the cost of the Valleylab pencil was $43, and the cost of the scalpel blade was $0.28.

Each incision was closed with 5-0 nylon suture (Johnson & Johnson/Ethicon, Inc., Somerville, N.J.) in running fashion, and covered with bacitracin-neomycin-polymyxin ointment (Johnson & Johnson) and sterile gauze. Sutures were removed after approximately 7 days and incisions monitored for healing.

Histologic Preparation and Thermal Injury Examination

After harvest of the abdominoplasty sample, the excess underlying adipose tissue was dissected away and 8 × 2-cm samples containing the healing incision for each instrument (scalpel, PlasmaBlade, and electrosurgery) and time point (0, 3, and 6 weeks) were labeled and excised (Fig. 2). Each healing incision sample was subsequently sharply divided in half. One-half was immediately placed in sterile 0.9% sodium chloride solution (VWR) and submitted for burst-strength testing in a fresh state (described below). The remaining half was immersed in 10% neutral buffered formalin (VWR) for a minimum of 24 hours and then embedded in paraffin for histologic analysis. Representative 4-μm sections were stained with hematoxylin and eosin, Masson's trichrome stain, and human immunohistochemistry stain for T-lymphocytes (CD3 M7254; Dako, Carpinteria, Calif.) and macrophages (CD68 NCL-L-CD68; Novacostra, Newcastle, United Kingdom). All slides were coded and the 0-week time point slides were evaluated by light microscopy (BX 40 microscope, with a DP70 charge-coupled device camera; Olympus, Center Valley, Pa.) for acute thermal injury depth by a single pathologist (E.J.H.) blinded to the wounding modality. The zone of coagulation necrosis resulting from thermal injury was determined in microns by direct microscopic measurement using the hematoxylin and eosin–stained sections. Slides from all time points were then scanned for digital immunohistochemical analysis (described below).

Digital Immunohistochemical Analysis

Computational analysis of $CD3^+$ T-lymphocyte and $CD68^+$ macrophage/monocyte density was performed using a previously described image-analysis software package[18] adapted by the authors

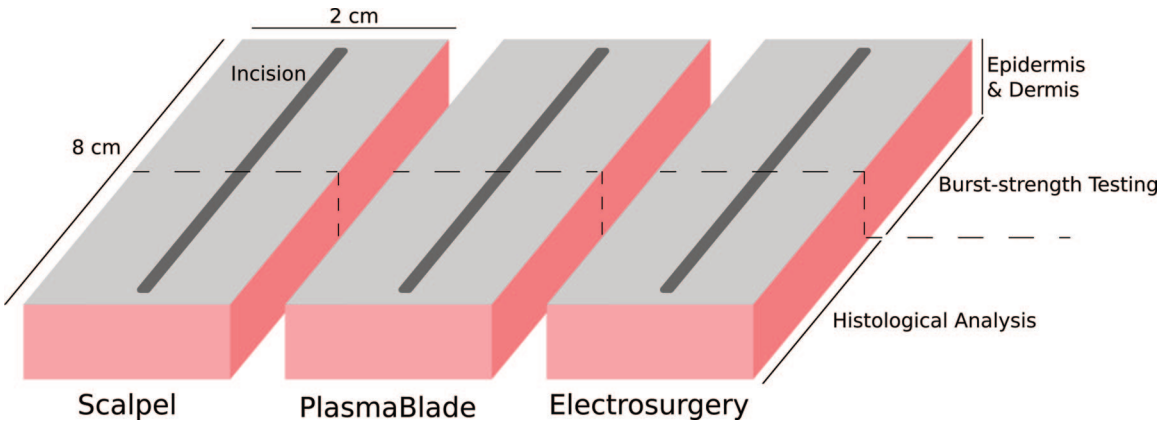

Fig. 2. Tissue dissection and preparation for burst-strength testing and histologic analysis. Each healing incision sample was sharply divided in half. One-half was immediately placed in sterile 0.9% sodium chloride solution and submitted for burst-strength testing in a fresh state. The remaining half was immersed in 10% neutral buffered formalin for a minimum of 24 hours and embedded in paraffin for histologic analysis.

to the current study. (**See Document, Supplemental Digital Content 1,** which shows a complete description of this method, ***http://links.lww.com/PRS/A331***; and **Figure, Supplemental Digital Content 2,** which shows the tissue collection methodology and analysis hierarchy described in **Supplemental Digital Content 1,** ***http://links.lww.com/PRS/A332***.) Briefly, 632 slides of stained tissue sections from all study subjects were scanned (Fig. 3) on a ScanScope XT slide scanner (Aperio Technologies, Inc., Vista, Calif.) at 20× magnification and processed in 2 × 2-mm increments. After segmentation and colorimetric thresholding, noise correction, filtering, and manual verification, a total of 605 slides were included in the subsequent statistical analysis.

Wound Burst Strength

The burst strength of freshly excised healing wound samples immersed in normal saline was measured in pounds-force per inch according to previously reported methods,[15] using a Chatillon TCD200 digital force tester (Ametek TCI Division, Largo, Fla.). Briefly, each incision sample was divided into three equally sized test units, each with

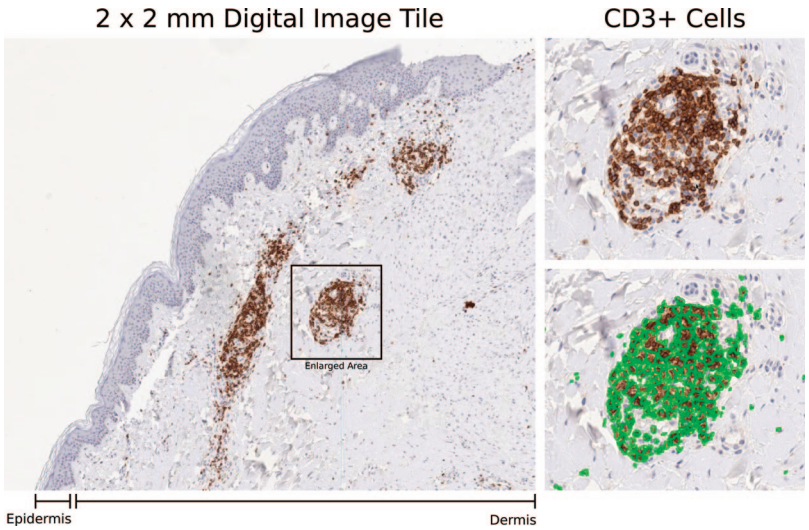

Fig. 3. (*Left*) Typical 2 × 2-mm processing tile from a 3-week scalpel incision, stained for CD3. (*Inset*) $CD3^+$ cluster is enlarged on the right. (*Above*, *right*) $CD3^+$ cluster seen at 20× magnification. (*Below*, *right*) Automated segmentation outlines of positively stained tissue.

the healing incision centered in the sample. The maximum width of each test unit at the location of the healing incision was then measured three times using digital calipers (Absolute 500 Digimatic Calipers; Mitutoyo America Corporation, Aurora, Ill.) and averaged. Each test unit was then secured in the jaws of the clamp, with the healing incision centered between 1 cm of tissue above and below the clamp jaws. Bursting strength of each incision was then determined by slow, progressive stressing of the segment to disruption at a speed of 2 inches/minute. The peak force was then recorded and converted to pounds-force per inch.

Surface Scar Width

The width of the surface scars for the 6-week time point incisions were recorded at 3 and 6 weeks after placement; the 3-week incisions were recorded on the day of abdominoplasty. Measurements were obtained, in millimeters, by one author (H.L.R.) using a calibrated ruler (Standard Ruler F04609; Office Depot, Inc., Delray Beach, Fla.) from one edge of the scar to the other at three distinct points: scar center, 2 cm above the center point, and 2 cm below the center point. Measurements for each incision were averaged and recorded by age (in days) since incision for comparison.

Statistical Analysis

Statistical analysis was performed using the R statistical environment software program, version 2.11.0.[19] All endpoints are reported as mean (SD), except where indicated. A general linear model was constructed with main effects of instrument and time point to evaluate differences between study endpoints; summaries of the least squared means differences between overall healing scores were evaluated with this model. Linear regression was also performed to evaluate each endpoint over the 6-week assessment period. Statistical significance was defined as $p < 0.05$.

RESULTS

Mean (SD) operative time was 1 hour 38 minutes 40 seconds (13 minutes 9 seconds) for patients in the PlasmaBlade abdominoplasty group and 1 hour 35 minutes 48 seconds (9 minutes 9 seconds) for patients in the standard-of-care abdominoplasty group ($p = 0.47$). The clinical course of healing and time to drain removal was comparable between the two groups.

Skin scar width, acute thermal injury depth, and wound burst strength are summarized in Table 1. When compared with conventional electrosurgery, incisions made with the PlasmaBlade reduced thermal injury depth by 74 percent ($p < 0.001$). At the 3- and 6-week time points, PlasmaBlade incisions demonstrated equivalent burst strength compared with scalpel and an improvement of 65 percent ($p < 0.001$) and 42 percent ($p < 0.001$), respectively, over conventional electrosurgery incisions. PlasmaBlade skin incision scar width was equivalent to scalpel at the 3- and 6-week time points, with a 25 percent ($p = 0.01$) and 12 percent ($p = 0.15$) reduction in scar width, respectively, compared with conventional electrosurgery.

$CD3^+$ and $CD68^+$ responses by time point and instrument are shown in Figures 4 and 5, and mean responses are summarized in Table 2. The week-0 samples served as an internal control; because there were no significant differences between the measured densities of $CD3^+$ and $CD68^+$ cells in week-0 samples from the three instruments, the data were judged to be reliable. After 3 weeks of healing, $CD3^+$ and $CD68^+$ inflammatory response in PlasmaBlade incisions was 21 percent ($p \approx 0.12$) and 16 percent ($p \approx 0.35$) greater compared with scalpel incisions, respectively; however, these differences were not statistically significant. Conventional electrosurgery incisions dem-

Table 1. Comparison of Scar Width, Thermal Injury Zone, and Burst Strength Measurements in Human Skin Incisions Made with the PlasmaBlade, Electrosurgery, and Scalpel

	PlasmaBlade Mean (SD)	Electrosurgery			Scalpel		
		Mean (SD)	%*	*p*	Mean (SD)	%*	*p*
Acute thermal injury depth, μm	195 (127)	763 (208)	74†	<0.001	—	—	—
Overall scar width, mm							
3 wk	2.0 (0.6)	2.5 (0.8)	25	0.01	1.8 (0.7)	10	0.23
6 wk	2.5 (0.7)	2.8 (0.5)	12	0.15	2.5 (0.9)	0	0.85
Wound burst strength, lb-f/in							
3 wk	43.44 (26.65)	26.28 (14.42)	65†	<0.001	43.14 (24.39)	1	0.95
6 wk	59.32 (37.53)	41.78 (21.71)	42†	<0.001	51.99 (30.38)	12	0.25

*Percentage differences and corresponding *p* values are calculated relative to the PlasmaBlade unless otherwise noted.
†Percentage difference calculated relative to electrosurgery.

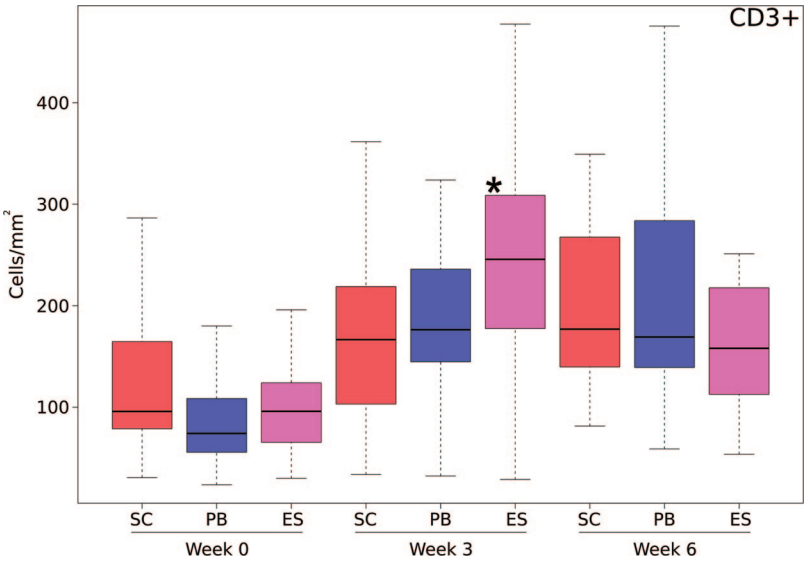

Fig. 4. Box plot of $CD3^+$ cell density by instrument and time point. The *black bars* denote median response, whereas *boxes* indicate interquartile range. The $CD3^+$ responses at week 0 are similar as expected, whereas at week 3, median $CD3^+$ response was 40 percent higher in the electrosurgery incisions than in PlasmaBlade or scalpel incisions ($p = 0.02$).

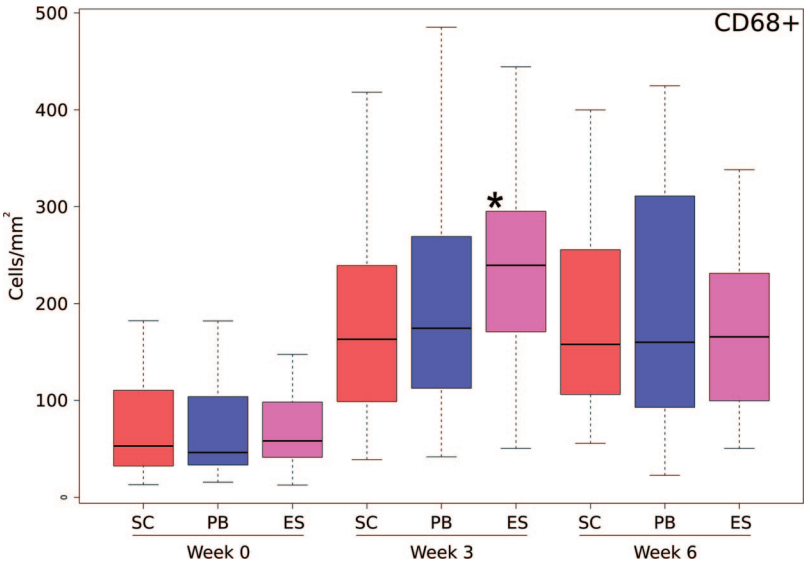

Fig. 5. Box plot of $CD68^+$ cell density by instrument and time point. The largest differences were observed during week 3, with electrosurgery incisions exhibiting a 52 percent increase in $CD68^+$ cell density response compared with PlasmaBlade and scalpel incisions ($p = 0.01$).

onstrated a 40 percent ($p = 0.01$) and 52 percent ($p = 0.05$) increase, respectively. There were no significant differences between values at the 6-week time point (Figs. 4 and 5).

DISCUSSION

The healing dynamics of surgical incisions made with various electrosurgical instruments have been explored in many animal models. However, a comparison of the healing dynamics of human cutaneous incisions made with conventional electrosurgical instruments versus lower thermal injury instruments, such as the PlasmaBlade, have not yet been described in the literature. To investigate this issue, a novel, in vivo,

Table 2. Density of CD3+ and CD68+ Cells in Sectioned, Immunostained, Human Skin Incisions Made with the PlasmaBlade, Electrosurgery, and Scalpel*

	CD3+					CD68+				
Time	SC	PB	ES	*p*†	LSM	SC	PB	ES	*p*†	LSM
0 weeks	138	93	120	0.33	9265	87	71	75	0.67	1355.9
3 weeks	171	207	239	0.02	42,928	173	201	263	0.01	77,827
6 weeks	196	216	223	0.71	7702.3	202	232	185	0.48	21,385

SC, scalpel; PB, PlasmaBlade; ES, electrosurgery; LSM, least-squared mean (the best unbiased linear estimate of the mean value at this time point).
*Mean cell density is expressed in cells per square millimeter.
†One-way analysis of variance *p* values calculated across different blades by time point.

human cutaneous wound-healing model that takes advantage of the planned removal and disposal of a large area of human skin during abdominoplasty was developed. By recruiting patients who have elected to undergo this procedure, the healing of incisions over a time frame that closely matches the clinical course of healing following a surgical procedure could be monitored and quantified, ensuring that patients were not subject to long-term residual scarring left by the experimental procedure.

In agreement with previous work in porcine skin[15] and rat fascia[16] models, it was found that use of a conventional electrosurgical instrument produced a wider scar, a deeper zone of thermal injury, and weaker healed incision strength when compared with scalpel and the PlasmaBlade (Table 1). The correlation between thermal injury depth, scarring, and the inflammatory process associated with healing was also investigated. Although inflammation marks a well-documented phase of wound healing,[20] recent studies have suggested that postinjury inflammation is not necessarily an essential component of tissue repair, and that it may delay wound healing and worsen scarring.[21] It has been suggested that faster resolution of the inflammatory phase might lead to more rapid healing and less scarring. To further investigate the correlation among healing wound strength, scarring, and healing-associated inflammation, an in-depth quantification of $CD3^+$ T cells and $CD68^+$ macrophages was performed with our histologic samples. These two cell types are central to the inflammatory phase of healing and, in this study, serve as a surrogate measure of inflammation.[22–26]

For the quantification of cell density, a previously developed[18] color-based (YUV thresholding) computational method was adapted for this application. This method was used because YUV transformation provides a computationally simple method for separating color information (chrominance) from image intensity (luminance). This focus on color allows for increased specificity and improved identification of cells with positive staining.

Cell densities were similar for the 0-week time point, as was expected with incisions that had been freshly harvested and analyzed, with no time for cell recruitment or initiation of the inflammatory phase. This time point served as a convenient internal control with which to validate the slide analysis method. The largest and most significant differences in instrument-dependent response were observed at 3 weeks, with inflammatory cell counts much higher in the conventional electrosurgery samples than in those created with the PlasmaBlade or scalpel (Figs. 4 and 5 and Table 1). Given the deeper thermal injury zone observed in the conventional electrosurgery incisions, the increased inflammatory response is likely attributable to phagocytotic removal of debris and necrotic tissue.

In contrast, by 6 weeks, when wounds would be expected to have progressed to the remodeling/proliferative phase, inflammatory cell density had equalized among the three instrument types. Considered together with the other data presented here, it is likely that the lower degree of inflammation at 3 weeks in the scalpel and PlasmaBlade groups is directly related to the observed improvement in scarring and wound burst strength at the end of the study.

CONCLUSIONS

These findings are consistent with the PlasmaBlade's favorable effects on human skin (i.e., improvement in healed scar width and strength, and reduction in thermal injury depth) and are similar to those seen in animal models and human ocular applications. Furthermore, this study begins to clarify the correlation between these observations and the reduced inflammatory response induced by the PlasmaBlade during incision. The results

suggest that the PlasmaBlade provides useful advantages over conventional electrosurgery during human wound healing.

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ACKNOWLEDGMENTS

The authors thank Jeanne McAdara-Berkowitz, Ph.D., and James R. Johnson, Ph.D., for assistance in the preparation of this article; and Robbin Newlin, Ph.D., and Guillermina Garcia for assistance with the digital imaging of histologic samples.

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