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Confocal Microscopy–Guided Laser Ablation for Superficial and Early Nodular Basal Cell Carcinoma:

A Promising Surgical Alternative for Superficial Skin Cancers

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Abstract

Importance—Laser ablation is a rapid and minimally invasive approach for the treatment of superficial skin cancers, but efficacy and reliability vary owing to lack of histologic margin control. High-resolution reflectance confocal microscopy (RCM) may offer a means for examining margins directly on the patient.

Observations—We report successful elimination of superficial and early nodular basal cell carcinoma (BCC) in 2 cases-, using RCM imaging to guide Er-:YAG laser ablation. Three-dimensional (3-D) mapping is feasible with RCM-, to delineate the lateral border and thickness of the tumor. Thus, the surgeon may deliver laser fluence and passes with localized control—ie, by varying the ablation parameters in sub-lesional areas with specificity that is governed by the 3-D topography of the BCC. We further demonstrate intra-operative detection of residual BCC after initial laser ablation and complete removal of remaining tumor by additional passes. Both RCM imaging and histologic sections confirm the final clearance of BCC.

Conclusions and Relevance—Confocal microscopy may enhance the efficacy and reliability of laser tumor ablation. This report represents a new translational application for RCM imaging,

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Study concept and design: Chen, Rajadhyaksha.
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which, when combined with an ablative laser, may one day provide an efficient and cost-effective treatment for BCC.

Basal cell carcinoma (BCC) is the most endemic skin cancer in the United States and several parts of the world. It is usually not-fatal, but if left untreated, BCC may become very destructive, and its subsequent treatment can cause significant morbidity or disfigurement. Occasionally, metastasis and fatality may occur. Early detection and treatment is integral in preventing a detrimental outcome.

For the ultimate cure and lower risk of recurrence, surgical approaches are usually the desired treatment for BCC. The location, size, and type of BCC plus individual condition are often determining factors for a specific approach. Treatments using ablative lasers offer potential benefits of speed, less tissue destruction, less bleeding, shorter healing time, and less scarring, making them a promising tool for the treatment of superficial skin cancer.[1] However, laser ablation has not become a mainstream therapeutic option because of inconsistent efficacy owing-, to a lack of histologic guidance for complete treatment. In this report, we show the feasibility of using real-time reflectance confocal microscopy (RCM) to guide laser ablation and successfully eliminate superficial and early nodular BCCs in 2 cases.

Report of Cases

Case 1

A woman in her 30s presented with a newly biopsied BCC on her right upper back. The patient had 20 BCCs, the majority being superficial and early nodular subtypes that were biopsied and treated in the last 4 years. All of her BCCs were on the trunk, and 17 of them were located on her back. Most of these lesions were treated surgically, and thus multiple scars were apparent. She reported significant sun exposure as a child with multiple blistering sunburns. At examination, we found fair skin with mottled telangiectatic and lentiginous background skin on her back and chest, indicative of photodamage. There was a 20 × 14-mm erythematous scaly patch with irregular borders and a slightly depressed cicatricial center, consistent with the recently biopsied BCC (Figure 1A). Mohs surgery was planned.

Case 2

A white woman in her 20s with a history of basal cell nevus syndrome, diagnosed in her childhood, presented with a lesion clinically suggestive of BCC on her left postauricular scalp. The patient had more than 100 BCCs treated in the past 20 years, including several recently treated on her left postauricular region. Multiple treatment techniques, including Mohs surgery, ED&C (shave excision, desiccation, and curettage), cryotherapy, topical 5-fluorouracil, topical imiquimod, and photodynamic therapy (PDT), had been used for each lesion. At examination, we found a 12 × 8-mm erythematous macule with ill-defined borders on her left postauricular scalp-, proximal freshly healed surgical scars. Under dermoscopy, the macule showed arborizing telangiectasia, focal keratosis, and erosion. Two board-certified dermatologists inspected the lesion and concurred with the clinical impression of superficial and/or early nodular BCC (Figure 1B). Mohs surgery was offered.

Procedures in Case 1 and Case 2

Both of our patients agreed to be treated with Mohs surgery and undergo laser ablation as the initial step of tumor debulking. Both also provided written informed consent to undergo RCM imaging, and the study protocol was approved by our institutional review board.

For preoperative tumor mapping, we used 2 RCMs and a large scanner on an articulating arm with mosaic-creation capability (Vivascope 1500; Caliber Imaging and Diagnostics Inc [formerly Lucid Inc]; field of view, 0.5 × 0.5 mm). For intraoperative detection of residual tumor, we used a smaller, handheld scanner with video acquisition capability (Vivascope 3000; field of view, of 1.0 × 1.0 mm). The BCCs in both cases were successfully ablated with Er:YAG laser (Sciton Profile; tunable fluence up to 25 J/cm^2; spot diameter, 4 mm; pulse duration, 250 microseconds) (Figure 1C and D).

In each case, an 8 × 8-mm area within the tumor was designated as the "*imaging and ablation zone*", while the remaining area was control. Three mosaics were acquired, each consisting of 16 × 16 images, to display 8 × 8-mm areas in the epidermis, at the dermal-epidermal junction, and in the papillary dermis. The mosaics allowed delineation of the lateral tumor borders (Figure 2A). Image stacks were also acquired, which facilitated pre-operative delineation of tumor thickness, up to approximately150 μm (maximum possible depth for RCM). With mosaics and stacks available for evaluation, 3-D mapping of the tumor was feasible.

From an initial ex-vivo study of discarded Mohs tissue,[2] we estimated the required laser fluence (25 J/cm^2) and required number of passes of laser energy to be delivered in each quadrant of the 8 × 8-mm areas according to the RCM-delineated 3-D topography of the tumor. After initial ablation, aluminum chloride, 35%, was topically applied for 1 minute, as detailed previously,[3] to enhance the contrast and detectability of residual BCC. The ablated area was imaged again using video mode for screening residual tumor and stacks for depth detection. Additional laser passes were then delivered, as needed, to eliminate the focal residual BCC (Figure 2B). Final RCM imaging confirmed complete tumor clearance in the "test area" (Figure 2C). The number of passes required to achieve tumor-free margins varied from 4 to 12.

The lesion was then excised for histologic margin control by the Mohs method. Once the negative margins were confirmed with Mohs sections, the specimens were re-embedded to create vertical frozen sections in a tip-to-tip bread-loaf fashion for further histologic examination. In both cases, we found no residual tumor in the laser-ablated region, while typical superficial and early nodular BCC was present in the non-ablated area (Figure 2D).

Discussion

Many of the BCC lesions on these 2 cases were superficial and/or early nodular subtypes. Although excisional surgical procedures including Mohs surgery allow for histologic margin examination and provide a superior cure rate, they often result in excess tissue loss, ie, a larger and deeper wound that may lead to significantly increased complexity of wound management and unfavorable scarring. This is particularly bothersome for patients with

frequent episodes of skin cancer. Other options such as laser ablation, ED&C, cryotherapy, radiation therapy, PDT, and topical imiquimod are effective in treating superficial BCCs. But the lack of histologic confirmation often causes some hesitation in decision-making. The choice between the potential risks of surgical complications such as bleeding, pain, infection, and scarring vs risks of incomplete treatment and recurrence can be a difficult one for the clinician and the patient.

Use of RCM imaging has been proven to diagnose BCC in vivo with high sensitivity and specificity.[4,5] The imaging can detect residual BCCs in follow-up after biopsy as well as intraoperatively in Mohs surgical and shave biopsy wounds.[3,6,7] The imaging can also aid in monitoring treatment outcome-, noninvasively and in real time.[8] The capability of RCM to create mosaics allows us to conveniently and readily map the lateral dimensions of the tumor. The depth stacks further allow for 3-D tumor mapping. We can delineate the treatment area and deliver the required laser energy to the targeted tumor with precise local control-, by varying the fluence and/or number of passes with depth. The short-pulsed Er-:YAG laser vaporizes the tissue, resulting in clean ablation and minimum thermal damage (≤20 μm).[9,10] This allows us to image the lesion after initial ablation, identify the residual tumor, and repeat ablation reasonably easily.

A previous study on excised tissue showed that for ablation parameters of 4 passes and fluence of 25 J/cm^2, the thickness of char layer (3-10 μm) and the thermal coagulation zone did not significantly reduce the quality of the RCM images; nuclear morphologic characteristics were clearly seen following ablation and confirmed by traditional histologic analysis.[2] In the present study, there was no cleaning between ablation passes, but after each set of passes, aluminum chloride was topically applied on the ablated tissue to brighten nuclear morphologic characteristics and enhance contrast of residual BCC tumor. We believe that the aluminum chloride application might also have removed the char layer on the ablated skin.

Motion artifact is another concern for imaging quality in vivo. During use of the large RCM scanner (VivaScope 1500), a tissue ring-and-window device is attached to the skin providing physical contact with the objective lens, and-, thus-, the lateral movement is well controlled.[3] With the smaller, handheld RCM scanner (VivaScope 3000), the objective lens-and-window device is not attached but placed in direct contact with the skin. In this case, lateral movement is overcome by the operator gently pressing the lens against the skin. The patient's breathing also introduces a motion along the optical axis (depth) while imaging. This affects the collection of stacks of images, mostly by acquiring overlapping (ie, redundant) images in depth, which can be ignored when reviewing the images. In the present preliminary study, we did not find a significant limitation due to motion during imaging.

The utility of RCM imaging enables laser ablation in a margin-controlled fashion, which potentially enhances the efficacy and reliability of treatment. The speed of RCM-guided laser ablation is at least compatible with a single-stage Mohs surgery. For pre-operative imaging, it requires 10 to 15 minutes to collect 3 mosaics. Image stacks are collected in selected foci. Each stack can be collected in less than 1 minute. It also takes less than 10 minutes for the intra-operative imaging process. The entire procedure, including repeat

imaging and ablation, took 45 to 60 minutes in this preliminary study. Its potential timesaving advantage may become more prominent with the development of smaller RCM scanners with automated and faster collection of mosaics and stacks. Compared with Mohs excision, greater tissue conservation was also evident in our cases, as shown in histologic sections (Figure 2D).

A larger case series is being planned to further validate this novel imaging-guided approach for treatment. One major advantage of combining ablative laser and RCM is that superficial skin cancers may potentially be diagnosed and treated on the same day in a single office visit. This may provide both convenience to the patient and also significantly reduce medical and socio-economic costs.

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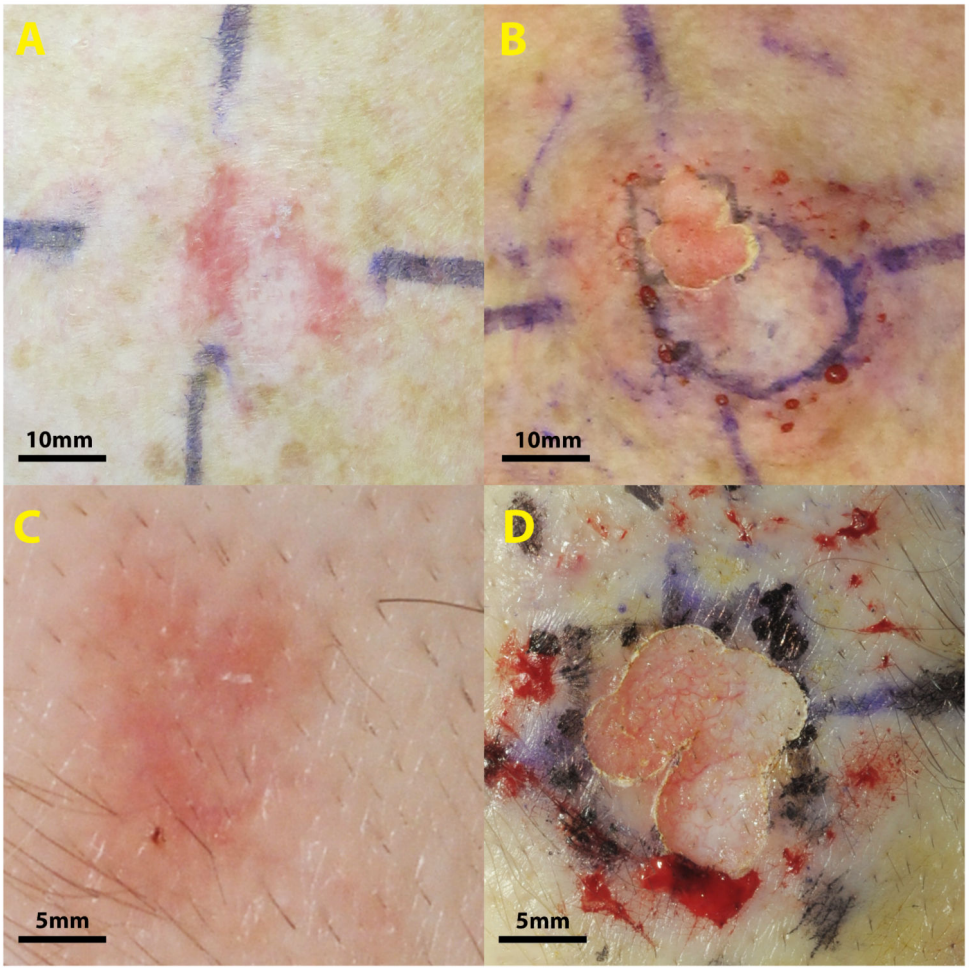

Figure 1.

Clinical Images of the 2 BCC Lesions From Case 1 (A-, and B) and Case 2 (C-, and D)

A and C, Preoperative photographs showing pearly and/or scaly erythematous appearance typical for basal cell carcinoma (BCC). Case 1 presented with a pale scar in the center of the lesion, which was previously biopsied. B and D are taken immediately after laser ablation showing bloodless superficial wound beds.

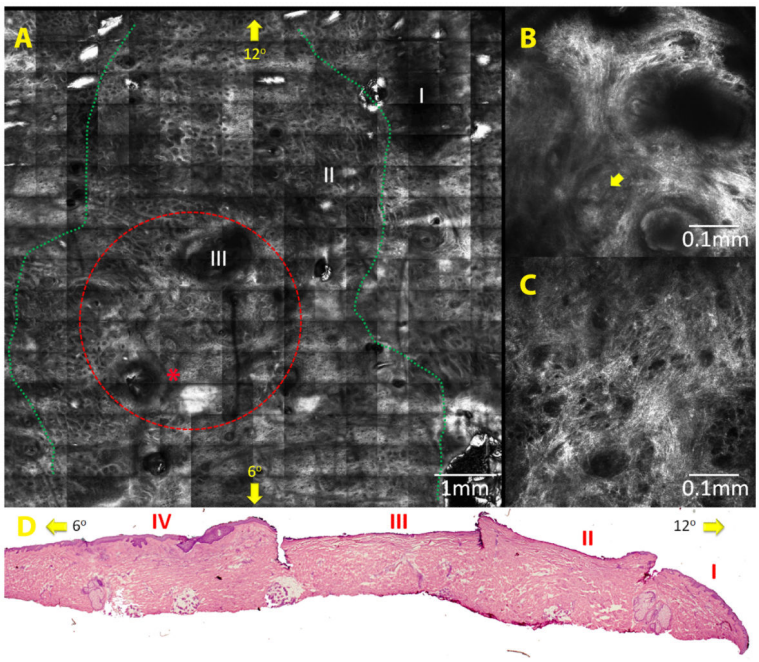

Figure 2.

Reflectance Confocal Microscopic (RCM) and Histologic Images

A, Pre-operative RCM mosaic image of case 1 was acquired at the dermal-epidermal junction. It is composed of 16 × 16 individual images that display an 8 × 8-mm area, representing the entire view of the "test area" in a horizontal plane. The lateral borders of the Zone tumor are delineated in dotted green lines. Tumor was not detected in zone I, which is the area outside of the green boundary. Within the green boundary is zone II, where the depth of the tumor was estimated to be approximately 120 μm. In zone III, which is inside of the dotted red circle, the depth of tumor was estimated to be at least (and possibly deeper than) 150 μm. Images taken from the area marked with a red asterisk inside zone III in the later stages of the procedure are illustrated in panels B and C. The arrows and 12°, and 6° notations are markers in clockwise orientation that correspond to the direction of histologic section shown in panel D. B, Intra-operative RCM image demonstrates the detection of a residual BCC nest (arrow). This is a single 1 × 1-mm image within z-stacks that were captured inside of zone III (marked with a red asterisk in panel A) after the initial laser ablation (5 passes, 25 J/cm^2). C, same field as in panel B after repeat ablation (total of 8 passes, 25 J/cm^2) showing complete elimination of tumor. D, Panoramic view of the representative post-operative histologic section from case 1 (hematoxylin-eosin stain, original magnification ×20). For histologic confirmation of the efficacy of laser ablation, the specimen was re-processed for serial vertical frozen sections after routine Mohs histologic examination. The arrows and 12° and 6° notations on each end of the section indicate the orientation of the section that corresponds to the markings in panel A. Several shallow slits were made during histologic preparation to distinguish different zones. Zone I, zone II, and zone III each corresponds to the same zoning in panel A). Zone IV is outside of the "imaging and ablation" area and therefore is not included in panel A). No tumor was detected preoperatively- or post-operatively in zone I. Zone II was ablated with 4 passes of

Er:-YAG laser at a fluence of 25 J/cm^2. Zone III received 8 passes. Zones II and III both demonstrate total elimination of the tumor. Zone IV is a non-ablated area and served as control, with BCC clearly preserved.