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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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. However, laser ablation has not become a mainstream therapeutic option because of inconsistent efficacy owing to a lack of histologic margin control. High-resolution reflectance confocal microscopy (RCM) may offer a means for examining margins directly on the patient.

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 (3D) 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 sublesional areas with specificity that is governed by the 3D topography of the BCC. We further demonstrate intraoperative 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.

Confocal microscopy may enhance the efficacy and reliability of laser tumor ablation. This report represents a new translational application for RCM imaging, which, when combined with an ablative laser, may one day provide an efficient and cost-effective treatment for BCC.

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 le-
sion 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, shave excision, ED&C (electric desiccation and curettage), cryotherapy, topical 5-fluorouracil, topical imiquimod, and photodynamic therapy (PDT), whichever was deemed appropriate, had been used for her BCC lesions. 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.

Two RCMs were used in this study. For preoperative tumor mapping, we used 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/cm²; spot diameter, 4 mm; pulse duration, 250 microseconds) (Figure 1B 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 preoperative delineation of tumor thickness, up to approximately 150 μm (maximum possible depth for RCM). With mosaics and stacks available for evaluation, 3D mapping of the tumor was feasible.

From an initial ex vivo study of discarded Mohs tissue, we estimated the required laser fluence (25 J/cm²) and required number of passes of laser energy to be delivered in each quadrant of the 8 × 8-mm areas according to the RCM-
After initial ablation, aluminum chloride, 35%, was topically applied for 1 minute, as detailed previously, 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 reembedded to process 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 nonablated 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 bother-
some 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. The imaging can detect residual BCCs in follow-up after biopsy as well as intraoperatively in Mohs surgical and shave biopsy wounds. The imaging can also aid in monitoring treatment outcome non-invasively and in real time. 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 3D 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). 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/cm², 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. 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. 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.

Conclusions
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 preoperative 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 intraoperative 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 socioeconomic costs.

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Conflict of Interest Disclosures: Dr Rajadhyaksha is a former employee of and owns equity in Caliber Imaging and Diagnostics Inc (formerly, Lucid Inc), the company that makes and sells the VivaScope confocal scanning laser microscope. The VivaScope is the commercial version of an original laboratory prototype that was developed by Dr Rajadhyaksha when he was in the Department of Dermatology at Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts.

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REFERENCES
The Ethnic Health and Beauty Section in the US Army and Air Force Post Exchange System

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The US Department of Defense establishes retail stores (known individually as a post or base exchange [PX or BX]) on military bases to let military personnel buy consumer goods at low cost. Even in combat zones, rudimentary exchanges are often set up within days—or even hours—of the military’s arrival. The shelves of frontline exchanges are well stocked with comfort and convenience items, such as candy, tobacco products, magazines, and personal hygiene items.

Both of us have participated in military deployments to remote, austere, and risky locations overseas. While working together in our university’s dermatology clinic, we compared observations about the surprising array of items in the “Skin, Hair, and Health Care” sections of the field-based exchanges. Even in the most austere environments, the exchange system has a formally designated “Ethnic Health & Beauty Section,” which, for practical purposes, is used mainly by black women, who comprise less than 5% of military personnel.

The Army & Air Force Exchange Service (AAFES) has lists of core items that must be in stock, even in the most rudimentary facilities. Through the Freedom of Information Act, we obtained parts of the 2012 list of items that “a new Exchange must have on its shelves prior to opening its doors for service.” AAFES stores require a minimum of 57 items designed for hair care of black women. To establish a PX (irrespective of the location—even in the field environment, deployed setting, or combat zone), the list requires specific items for all Ethnic Health & Beauty sections: 15 pomades, 12 oil sheens, 12 shower caps, 7 relaxers, 6 texturizers, 3 coloring kits, and 2 bristle brushes.

Although black women constitute a small segment of the military, the AAFES evidently realized it must carry a wide array of health and hygiene items to maintain morale among this sector of the military population. Black women, soldiers and civilians alike, generally spend a higher proportion of disposable income on hair care (procedures, devices, and topical products). America’s black community emphasizes women’s hair styles despite the challenges—and expenses—associated with fashionable coiffure (eg, to maintain moisture, straighten hair, obtain weaves or extensions). As a result, black women are likely to spend 2 to 3 times as much money on their hair as white women.

It is unlikely that military regulations on personal grooming standards compel women of color to use more products to obtain acceptable hair styles. Nevertheless, even in combat zones, where one might think that hair styles were relegated unimportant and inconsequential, a diverse array of hair care products for black women continues to fill a large amount of shelf space in the military exchanges.

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