

Skin cancer

Near-infrared heating of skin to delineate NMSC

■ Heating skin could provide assistance in identifying margins, but questions remain

by JOHN EVANS,
Senior Editor, The Chronicle

A pilot study has shown that heating the skin with near-infrared (NIR) light before delineating the margins of non-melanoma skin cancers (NMSCs) resulted in visible changes to the skin which could make accurate identification of lesion margins easier. According to the study's authors, this finding could reduce the need for further monitoring and treatment by reducing the rate of positive margins.

"From a patient's perspective, they might not mind waiting an additional four hours if the measurement improved the accuracy of the delineation"

—Dr. Kevin Jordan



Dr. Kevin Jordan

Published online ahead of print in *Skin Research & Technology* (July 26, 2020), this research was an attempt to build on earlier investigations that used protoporphyrin IX (PpIX) fluorescence to attempt to clearly delineate NMSC lesions, said study author Kevin Jordan, PhD, in an email interview with THE CHRONICLE OF SKIN & ALLERGY.

"The PPIX fluorescence approach works and is especially useful for poorly defined borders. But, the studies required two to four hours for the reaction to develop in patient's skin," said Dr. Jordan, who is an assistant professor in the department of oncology, Schulich School of Medicine & Dentistry, and the department of medical biophysics at Western University in London, Ont.

"From a patient's perspective, they might not mind waiting an additional four hours if the measurement improved the accuracy of the delineation. For example, if additional measurements reduced the chance of needing re-excision from 15 per cent to five per cent or less they might find it acceptable. However, for most clinics seeing a patient twice on the same day would be a disruption of workflow."

An experience of his own from 2016, where a hot day caused a visible bump to form on his chest at a site that would later be diagnosed as a nodular basal cell carcinoma, as well as his longstanding academic interest in infrared radiation as a diagnostic and therapeutic tool, were factors that inspired this study, he said. Since temperature regulation is a major function of skin, and tu-

mours have abnormal vasculature, the experience made him ask if skin cancers respond differently than adjacent, normal skin to localized heating.

In the pilot study, Dr. Jordan and his colleagues included eleven biopsy-proven NMSC lesions, tracing the lesions' margins onto acetate film both before and after heating with a 175 W NIR heating bulb.

Each of the lesions was then randomly assigned to excision based on pre- or post-heating margins. Composite images were generated by

overlaying the heat and no-heat lesion contours, and all of the specimens were sent for histopathology.



Dr. Daniel Barolet

They found that the range of closest margins in the control group was 2.0 to 3.0 mm, with a median of 2.0 mm. In contrast, the range in the intervention group was 4.0 to 9.0 mm with a median of 5.0 mm. The composite images showed larger heat contours when the initial lesion was larger. And the investigators found a statistically significant difference between the two groups. Overall, heating the lesion area with NIR light caused visible hyperaemia to the skin, and more intense erythema to malignant skin lesions.

"Overall, I am impressed that with such a small number of lesions a thermal effect was demonstrated. It implies the effect is fairly large or we were very lucky in our initial choices. Because it takes a fair amount of energy to raise the skin temperature a few degrees, I would expect these thermal responses are actually robust effects," said Dr. Jordan.

Remaining questions

The idea to use NIR heating to delineate NMSC lesions is innovative, and the simplicity of the equipment used stood out, said Dr. Daniel Barolet, in an email interview with THE CHRONICLE OF SKIN & ALLERGY. Dr. Barolet, a dermatologist based in Montreal and an adjunct professor of dermatology at the McGill University School of Medicine, has focused much of his research career on laser and other light-based applications in dermatol-

Please turn to **Skin heating** page 24 →

Research

H₂O₂ pre-treatment simplifies surgical NMSC removal

by JOHN EVANS,
Senior Editor, The Chronicle

Topical treatment of non-melanoma skin cancers (NMSCs) with a 33% hydrogen peroxide solution appears to effectively reduce the size of lesions prior to surgical excision, simplifying excision and reconstruction. For smaller lesions, this peroxide application may be the only treatment needed.

These findings were published in *Journal of Otolaryngology—Head & Neck Surgery* (June 1, 2020; 49: Article number 33).

Researchers involved in the pilot study had previously studied photodynamic therapy as a treatment modality for NMSC and had an interest in the non-surgical management of these diseases, said the study's lead author Dr. Neil Mundi is a PGY4 resident in the department of otolaryngology—head and neck surgery, Schulich School of Medicine & Dentistry, Western University, London, Ont.

"We had come across [in the literature] the use of hydrogen peroxide in the treatment of seborrheic keratoses and thought that this topical therapy should be investigated in terms of its effect on NMSC," Dr. Mundi said in an interview with THE CHRONICLE OF SKIN & ALLERGY. "Further, we were interested in studying treatment modalities that save healthcare resources and reduce patient wait times."

The study's senior author, Dr. Corey C. Moore, evaluated the lesions of 11 consecutive patients who presented at a cutaneous malignancy clinic, and measurements of the length and width of the lesions were taken.

Dr. Moore is an associate professor and chief of the division of otolaryngology-head and neck surgery at the Schulich School of Medicine & Dentistry.

Each included lesion had a 33% hydrogen peroxide solution applied to it until blanching was observed. The lesions were then re-measured at a follow-up before excisional biopsy and histopathological diagnosis.

Unexpected results seen

For the 17 biopsy-proven NMSC lesions included, statistically significant reductions in the length ($p < 0.001$) and width ($p < 0.001$) were

Please turn to **NMSC** page 24 →

Skin heating: May help to delineate excise margins



Image from Damian Greika stock.adobe.com

Continued from page 22

ogy. However, he said this pilot study left him with a number of questions.

"Several critical pieces of information on the NIR light source are missing, including fluence, spectroscopic analysis, beam profile, and others," Dr. Barolet said. He noted that the angle of the light beam during exposure could affect the results since angle determines beam uniformity, potentially leading to hot or cold spots.

Dr. Jordan also noted a number of questions were raised by the pilot study. As with Dr. Barolet, he mentioned the questions of uniformity of heating and light spectrum and how they might influence the results.

Other questions he said would need to be answered in follow-up research include: "Does the time spent at elevated temperature affect the results?" Dr. Jordan said. "Do underlying blood vessels distort the temperatures near the surface? We might need to image the larger vessels and correct for their effects. What is the most practical method to image these vessels?"

"Some lesions rise with heating. What does an increase in lesion height with heating imply? Some skin lesions are heterogeneous. Does heating detect heterogeneity? For example, do BCC's [basal cell carcinomas] and nodular or diffuse BCC's respond differently? If larger areas were heated, would more lesions reveal themselves?"

Notable limitations

"Many of these questions can be partially answered by studying what has been published," he said. "The effects of temperature in medicine is a broad field. Answers to some of the above questions should result in a more valuable delineation protocol and more definitive results."

A lack of objective measurements limit the strength of this study, noted Dr. Barolet.

"The erythema induced post-NIR exposure was delineated manually and no erythema index was objectively measured by a dermaspectrometer. But foremost, no NIR-exposed control sites on normal skin were performed. It would have been important to see if erythema is also triggered on adjacent skin without a tumour," Dr. Barolet said.

"Additionally, they should have explained light-tissue interactions triggering inside-out heating generated by NIR photons in the dermis. The great variability in tumoural vasculature is also a factor to consider and worth mentioning in the discussion."

In the context of Mohs surgery

Dr. Barolet noted that the paper does not mention Mohs micrographic surgery, which currently remains the best method to remove BCCs with controlled surgical margins. "This simplistic method using a NIR lamp appears like a too-good-to-be-true study."

It need not be a question of either-or, suggested Dr. Jordan. "In the case of Mohs surgery [NIR heating] may provide information about lesion thicknesses. This would be helpful for planning the [Mohs] procedure. I expect all delineation modalities will benefit from testing the impact of local heating, especially the faster technologies where dynamic thermal response images could be easily generated. In oncology, I suspect localized heating and ultrasound imaging of blood flow may become an effective diagnostic procedure."

Overall, Dr. Barolet said that thermal imaging is likely not precise enough for tumour delineation. "Other more precise technologies such as OCT [optical coherence tomography] or confocal microscopy will eventually provide live biopsies."

NMSC: Patients interested in topical treatments

Continued from page 22

observed with H₂O₂ treatment. Some of the lesions did not need further treatment after H₂O₂, as post-treatment biopsy demonstrated no evidence of malignancy.

The patients reported minimal discomfort during treatment and no long-term side effects were observed, with no recurrences seen at a six-month follow-up.

"Our initial thoughts [on these findings] were those of excitement and frankly surprise," said Dr. Mundi. "Keep in mind, the aim of our study was to determine whether hydrogen peroxide could be used as a neoadjuvant therapy to reduce the size of NMSC prior to definitive excision. Yet we found that in multiple cases, it was the only treatment needed."

This study was only a proof of concept, though, he emphasized, noting that these findings regarding hydrogen peroxide as a treatment approach for NMSC, while promising, require further study.

Unexpected result

Dr. Mundi and his colleagues intend to build on these findings by conducting a randomized controlled trial comparing hydrogen peroxide to other topical therapies in the treatment of NMSC. The participants in this pilot study will also be followed over time so that recurrence rates over a longer period can be assessed, he said.

"In addition, we aim to conduct wet lab experiments in the future to discover the way in which hydrogen peroxide combats NMSC."

The participating patients seemed comfortable and satisfied with the procedure, Dr. Mundi said.

"Patients were genuinely interested in having the topical treatment performed and we witnessed very little hesitation on the part of our patients in participating in the investigation. For those individuals whose lesions were completely cured, the procedure brought a great sense of relief as it meant they could avoid the risks of surgical excision," he said.