

Mark S. Nestor MD, PhD<sup>1,2,3</sup>, Angélica C. Marrero-Pérez, MD<sup>1</sup>; Aysham Chaudry, DO<sup>1</sup>; Robert J. Vanaria <sup>1,4</sup> <sup>1</sup>Center for Clinical and Cosmetic Research, Aventura, FL; <sup>2</sup>Department of Dermatology and Cutaneous Surgery; <sup>3</sup>University of Miami, Miller School of Medicine; <sup>4</sup>Hackensack Meridian School of Medicine, Hackensack, NJ

## **Synopsis**

Localized, superficial microwave energy (ME) appears to have promise as a novel, rapid, and tolerated non-invasive approach to induce localized hyperthermic conditions for treating cutaneous non-melanoma skin cancers (NMSCs). Squamous cell carcinoma in situ (SCCis) is a very common NMSC appearing on sun exposed skin including the face<sup>1</sup>. Standard treatments include excision or electrodessication and curettage, but other minimally invasive treatments are desirable, especially for areas with aesthetic importance, like the face, or regions that are slow to heal, such as the lower legs<sup>2,3</sup>. Hyperthermia, a non-invasive treatment that raises tissue temperature above 43 degrees Celsius, has a long history in treating various cancers<sup>4,5</sup>. Traditional hyperthermic treatments require warming large areas of tissue<sup>6</sup>, but new technology now permits focused application of microwave energy (ME) to generate precisely targeted hyperthermic conditions in treated tissues<sup>7</sup>. Literature suggests that localized hyperthermia increases tumor cell immunogenicity by activating stress response pathways in proliferative keratinocytes, promoting lesion clearance through innate and adaptive immune responses as well as apoptosis<sup>8</sup>. Currently, both actinic keratoses (AKs) and human papillomavirus (HPV)-induced warts have been successfully treated with site-specific ME-induced hyperthermia<sup>9,10</sup>. Given the higher incidence of SCCis in individuals with actinic damage and the evidence that ME can clear AK and hypertrophic AK (early stages in the squamous neoplasia continuum<sup>11</sup>), increasing tumor immunogenicity via localized ME-induced hyperthermia may explain the observed clearance of cutaneous SCC (cSCC) lesions in the treated patients presented here. This feasibility work represents the first exploratory step in determining if ME-induced hyperthermia can serve as a novel, non-invasive treatment for NMSCs.

## Objective

To assess the feasibility of treating cSSC lesions with sub-ablative heat generated by ME as a novel non-invasive treatment option.

## **Methods**

- Seven biopsy-confirmed SCCis lesions from 5 patients were treated with ME. • Medical device used to apply highly localized ME was a microwave generator with
- 510(k) clearance by the FDA for surface application of ME to coagulate soft tissue



- during non-invasive procedures.
- temperatures in NMSC lesions.
- to 4-seconds long, were applied to the full area of the lesions.

- 1 month apart (ranging from 21 to 36 days).
- All patients received ME as a monotherapy.
- Follow-up visits and post-treatment excision of lesions were arranged to monitor resolution progression and assess lesion clearance clinically and histologically.

## **Results and Conclusions**

- Four of six excised cSCC lesions showed full histologic clearance after ME treatment.
- Two lesion sites in a single patient contained residual SCCis
- The histology of one patient's lesion is still pending.
- All patients commented that the treatment was a positive experience with few adverse effects.
- ME treatments took only a matter of minutes, did not require any wound management post treatment, and no scarring or hypopigmentation was observed.
- Patients tolerated this non-invasive, fast, and simple treatment modality well with the feasibility showing promise as a novel first approach to superficial NMSC.

# **Microwave Energy for Treatment of Superficial and in situ** Squamous Cell Carcinoma

• For this case series, the device was used to generate hyperthermic, sub-ablative tissue

Local anesthesia (1 cc of 1% lidocaine) was given intralesionally before ME was administered. Three repetitive pulses of 4 to 5W of ME, each 3-

• Two treatment sessions were given approximately

## **Case Descriptions & Outcomes**

#### Patient 1

Lesion 1: SCC in situ - Right Inferior Forehead (Temple) Lesion 2: SCC in situ -Right Dist. Dorsal Forearm Lesion 3: SCC in situ -Left Prox. Posterior Upper Arm

2 treatments, one month apart

## Patient 2

Superficial SCC - Right Forehead Device settings: 4 Watts, 4s, 5 repeats Note: increased pulse duration 2 treatments, one month apart

### Patient 3

SCC in situ - Left Prox. Dorsal Forearm Device settings: **4** Watts, **4**s, **5** repeats 2 treatments, one month apart

## Patient 4

SCC in situ - Superior Mid Forehead Device settings: 4 Watts, 4s, 5 repeats 2 treatments, one month apart

## Patient 5

SCC in situ - Left Anterior Shoulder Device settings: **5** Watts, **3**s, **5** repeats Note: increased W, decreased duration 2 treatments, one month apart

## References

- 10.1053/j.seminoncol.2014.09.014.
- doi: 10.1080/02656736.2020.1779357.
- 2017 Oct 1;27(5):511-518. doi: 10.1684/ejd.2017.3086.
- Aug;183(2):222–230. Doi: 10.1111/bjd.18935. 11. Ulrich M, Zalaudek I, Welzel J. Shining into the White: The Spectrum of Clin. 2016 Oct;34(4):459-467. doi: 10.1016/j.det.2016.05.008.



1. Weinstock MA. The epidemic of squamous cell carcinoma. JAMA. 1989 Oct 20;262(15):2138-40. PMID: 2795786. Övermark M, Koskenmies S, Pitkänen S. A Retrospective Study of Treatment of Squamous Cell Carcinoma In situ. Acta Derm Venereol. 2016 Jan; 96(1): 64-7. doi: 10.2340/00015555-2175. Stewart JR, Lang ME, Brewer JD. Efficacy of nonexcisional treatment modalities for superficially invasive and in situ squamous cell carcinoma: A systematic review and meta-analysis. J Am Acad Dermatol. 2022 Jul;87(1):131-137. doi: 10.1016/j.jaad.2021.07.067. Hurwitz M, Stauffer P. Hyperthermia, radiation and chemotherapy: the role of heat in multidisciplinary cancer care. Semin Oncol. 2014 Dec;41(6):714-29. doi:

Datta NR, Ordóñez SG, Gaipl US, Paulides MM, Crezee H, Gellermann J, Marder D, Puric E, Bodis S. Local hyperthermia combined with radiotherapy and-/or chemotherapy: recent advances and promises for the future. Cancer Treat Rev. 2015 Nov;41(9):742-53. doi: 10.1016/j.ctrv.2015.05.009. 6. Kok HP, Cressman ENK, Ceelen W, Brace CL, Ivkov R, Grüll H, Ter Haar G, Wust P, Crezee J. Heating technology for malignant tumors: a review. Int J Hyperthermia. 2020;37(1):711-741.

Gartshore A, Kidd M, Joshi LT. Applications of Microwave Energy in Medicine. Biosensors (Basel). 2021 Mar 26;11(4):96. doi: 10.3390/bios11040096. Skitzki JJ, Repasky EA, Evans SS. Hyperthermia as an immunotherapy strategy for cancer. Curr Opin Investig Drugs. 2009 Jun; 10(6): 550-8. PMID: 19513944; PMCID: PMC2828267. Bristow I, Lim WC, Lee A, Holbrook D, Savelyeva N, Thomson P, Webb C, Polak M, Ardern-Jones MR. Microwave therapy for cutaneous human papilloma virus infection. Eur J Dermatol

10. Jackson DN, Hogarth FJ, Sutherland D, Holmes EM, Donnan PT, Proby CM. A feasibility study of microwave therapy for precancerous actinic keratosis. Brit J Derm. 2020

**Epithelial Tumors from Actinic Keratosis to Squamous Cell Carcinoma. Dermatol** 



Resolving **Biopsy: Pending** cm 1 2 FU

Outcome



Outcome **Biopsy: Clear** 



Outcome **Biopsy: Clear** 



Outcome **Biopsy: Clear** 



Biopsy SCCis Involvement Small Foci Margin

Biopsy SCCis Involvement Small Foci

Outcome **Biopsy: Clear** 



Center for Clinical and Cosmetic Research