REFERENCES

1. Vinay K, Bishnoi A, Parsad D, Saikia UN, Sendhil Kumaran M. Dermatoscopic evaluation and histopathological correlation of acquired dermal macular hyperpigmentation. *Int J Dermatol*. 2017;56:1395-1399.
2. Ebihara T, Nakayama H. Pigmented contact dermatitis. *Clin Dermatol*. 1997;15:593-599.
3. Debroy Kidambi A, Dobson K, Holmes S, et al. Frontal fibrosing alopecia in men: an association with facial moisturizers and sunscreens. *Br J Dermatol*. 2017;177:260-261.
4. Fernandez-Crehuet P, Rodrigues-Barata AR, Vano-Galvan S, et al. Trichoscopic features of frontal fibrosing alopecia: results in 249 patients. *J Am Acad Dermatol*. 2015;72:357-359.
5. Moreno-Arrones OM, Saceda-Corralo D, Fonda-Pascual P, et al. Frontal fibrosing alopecia: clinical and prognostic classification. *J Eur Acad Dermatol Venereol*. 2017;31:1739-1745.
6. Sharma VK, Gupta V, Pahadiya P, Vedi KK, Arava S, Ramam M. Dermoscopy and patch testing in patients with lichen planus pigmentosus on face: a cross-sectional observational study in fifty Indian patients. *Indian J Dermatol Venereol Leprol*. 2017;83:656-662.
7. Ma SA, Imadojemu S, Beer K, Seykora JT. Inflammatory features of frontal fibrosing alopecia. *J Cutan Pathol*. 2017;44:672-676.
8. Ramot Y, Mastrofrancesco A, Camera E, Desreumaux P, Paus R, Picardo M. The role of PPARγ-mediated signalling in skin biology and pathology: new targets and opportunities for clinical dermatology. *Exp Dermatol*. 2015;24:245-251.
9. Schneider MR, Schmidt-Ullrich R, Paus R. The hair follicle as a dynamic miniorgan. *Curr Biol*. 2009;19:R132-R142.
10. Lin J, Valdebran M, Bergfeld W, Conic RZ, Piliang M, Atanaskova Mesinkovska N. Hypopigmentation in frontal fibrosing alopecia. *J Am Acad Dermatol*. 2017;76:1184-1186.
11. Pirmez R, Duque-Estrada B, Donati A, et al. Clinical and dermoscopic features of lichen planus pigmentosus in 37 patients with frontal fibrosing alopecia. *Br J Dermatol*. 2016;175:1387-1390.
12. Romiti R, Biancardi Gavioli CF, Anzai A, et al. Clinical and Histopathological findings of frontal fibrosing alopecia-associated lichen planus pigmentosus. *Skin Appendage Disord*. 2017;3:59-63.

https://doi.org/10.1016/j.jaad.2018.03.001

Bioimpedance measurement as an assessment of margin positivity in Mohs surgical specimens of nonmelanoma skin cancer: Management implications

To the Editor: Nonmelanoma skin cancer (NMSC) is responsible for significant morbidity, with squamous cell carcinoma also potentially causing mortality.[1] Mohs micrographic surgery (MMS) has become the standard of care for high-risk lesions, but the need for histopathologic margin assessment at each stage significantly adds to the duration of the procedure, particularly in multistage cases.

Bioimpedance spectroscopy is a novel ex vivo technique that relies on differing flow of electric current through diverse tissue types (such as muscle and fat)—a property related to the varying water and electrolyte compositions of cellular components.[2] It has been used to measure total body water, detect lymphedema, and differentiate benign from malignant lesions.[2] This technology has also been applied to intraoperative surgical margin assessment for urologic malignancies.[3] However, it has not yet been applied to margin evaluation in NMSC.

We assessed the sensitivity and specificity of bioimpedance (compared with frozen section histology) for detecting the presence of malignant cells in the margins of MMS specimens of NMSC.

A total of 151 specimens from 55 primary malignancies in 50 consecutive patients undergoing MMS for NMSC were assessed to compare ex vivo bioimpedance spectroscopy (MarginScan, NovaScan LLC, Milwaukee, WI) with traditional frozen section histopathologic methods (Fig 1 and Table I). Institutional review board approval was obtained. Bioimpedance measurements were performed and the results were fit to a Cole-Cole function curve to

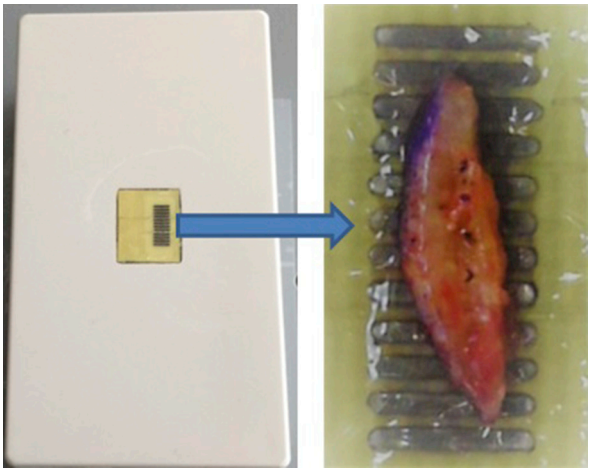

Fig 1. Sample specimen cassette for impedance spectroscopy device.

Table I. Diagnosis and location of studied lesions

Lesion location	No. of BCC cases (n = 43 [78%])	No. of SCC cases (n = 12 [22%])	Total cases
Nose	15	1	16
Cheek	9	2	11
Ear	4	2	6
Scalp	3	2	5
Lip	5	0	5
Forehead/temple	2	2	4
Chin	2	0	2
Finger	0	2	2
Neck	1	0	1
Back	0	1	1
Shin	1	0	1
Shoulder	1	0	1

BCC, Basal cell carcinoma; *SCC*, squamous cell carcinoma.

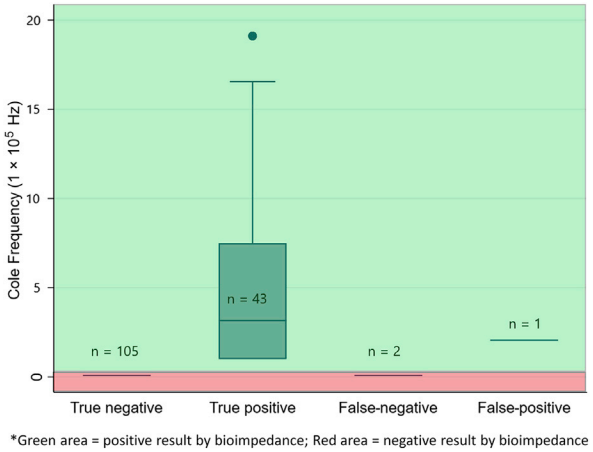

Fig 2. Distribution of Cole frequencies of 151 Mohs specimens of nonmelanoma skin cancer stratified by histopathologic and bioimpedance results.

obtain Cole relaxation frequencies.[4] On the basis of these results, each specimen was labeled as unlikely or likely to contain malignant cells in the margins according to previously described parameters.[4] Sensitivity, specificity, and positive and negative predictive values for bioimpedance were calculated by comparing the results with histopathologic findings.

Of the 151 MMS specimens, 44 (29%) displayed positive margins by histopathologic analysis, whereas 45 (30%) were probable for margin positivity by bioimpedance. Overall, 148 of 151 specimens (98%) displayed concordant results between histopathology and bioimpedance. Three discordant specimens representing 1 false-positive and 2 false-negative bioimpedance measurements were noted (Fig 2). The sensitivity and specificity of bioimpedance were 95.6% and 99.1%, respectively. The respective positive and negative predictive values were 97.7% and 98.1%.

The rate-limiting step of MMS is the preparation and assessment of frozen sections at each procedural stage, which require 20 to 45 minutes for an average procedure but can be much longer for complex cases.[5] In contrast, bioimpedance requires only 7 seconds per measurement (with approximately 20.5 separate measurements required for complete margin assessment per Mohs stage, totaling 2 minutes and 23 seconds on average). Therefore, these findings suggest that bioimpedance may have the potential to reduce case time by eliminating the need to process negative specimens while maintaining high diagnostic accuracy.

The study limitations include small sample size, a single surgeon, and the fact that all lesions were already biopsy-proved NMSCs. However, because MMS is typically performed only on malignancy-confirmed lesions, this sample is representative of real-world practice. Additionally, squamous cell carcinomas and basal cell carcinomas were analyzed together owing to the small sample size. In the future, studies separately analyzing bioimpedance for detection of squamous cell carcinoma and basal cell carcinoma in MMS specimens could be beneficial.

Larger multicenter studies are suggested to increase the generalizability of these results. However, these preliminary data suggest that bioimpedance may provide an expedient, novel approach for evaluating the presence of malignant cells in MMS NMSC specimens, thereby making the process more efficient without loss of efficacy.

Ryan M. Svoboda, MD, MS,[a] Manish J. Gharia, MD,[b,c] John Shell, PhD,[d] and William D. Gregory, PhD[d,e,f]

From the National Society for Cutaneous Medicine, New York, New York[a]; Madison Medical Mohs Surgery, Milwaukee, Wisconsin[b]; Medical College of Wisconsin, Milwaukee, Wisconsin[c]; NovaScan Inc, Milwaukee, Wisconsin[d]; and College of Engineering and Applied Science[e] and College of Health Sciences, University of Wisconsin, Milwaukee, Wisconsin[f]

Funding sources: Supported in part by the National Science Foundation under grant award numbers 0944454 and 1058413.

Disclosure: Dr Svoboda served on an advisory board for NovaScan Inc. Dr Gharia is on the advisory board for NovaScan Inc and has received an honorarium. Dr Gregory and Dr Shell are employed by and have a financial interest in NovaScan Inc.

Data on this subject were presented as a poster presentation at the 2017 American College of Mohs Surgeons Annual Meeting, San Francisco, CA; April 27-30, 2017. A poster consisting of the data from this study was presented at the 2018 American Academy of Dermatology Annual Meeting, San Diego, CA; February 16-20, 2018.

Correspondence to: Ryan M. Svoboda, MD, MS, National Society for Cutaneous Medicine, 35 E 35th St, Rm 208, New York, NY 10016

E-mail: rmsvoboda@gmail.com

REFERENCES

1. Stratigos A, Garbe C, Lebbe C, et al. Diagnosis and treatment of invasive squamous cell carcinoma of the skin: European consensus-based interdisciplinary guideline. *Eur J Cancer.* 2015;51(14):1989-2007.

2. Braun RP, Mangana J, Goldinger S, French L, Dummer R, Marghoob AA. Electrical impedance spectroscopy in skin cancer diagnosis. *Dermatol Clin*. 2017;35(4):489-493.
3. Khan S, Mahara A, Hyams ES, Schned AR, Halter RJ. Prostate cancer detection using composite impedance metric. *IEEE Trans Med Imaging*. 2016;35(12):2513-2523.
4. Shell J, Gregory WD. A cancer detection device utilizing multi-tiered neural networks for improved classification. Paper presented at: Healthcare Innovation Point-Of-Care Technologies Conference (HI-POCT). November 9-11, 2016; Cancun, Mexico.
5. Longo C, Gardini S, Piana S, et al. Ex vivo fluorescence microscopy: clinical applications in dermatology and surgical pathology. In: Hamblin MR, Avci P, Gupta GK, eds. *Imaging in Dermatology*. San Diego, CA: Academic Press; 2016:95-102.

https://doi.org/10.1016/j.jaad.2018.02.075

Effect of psoriatic arthritis on ixekizumab clinical outcomes in moderate-to-severe psoriasis patients: A post hoc analysis

To the Editor: Patients with plaque psoriasis might experience a number of inflammatory musculoskeletal problems, which is consistent with a diagnosis of psoriatic arthritis (PsA).[1] A recent study reported that 30% of patients with plaque psoriasis who were evaluated also had a diagnosis of PsA on the basis of rheumatologists' assessments; in addition, 41% of those patients had not been previously given the diagnosis.[2] Plaque psoriasis with PsA is debilitating[3] and significantly affects overall quality of life.[4] It is unclear whether patients with psoriasis and comorbidities, such as PsA, respond to therapy differently than patients with psoriasis and no comorbidities. Effective therapies that can adequately treat patients with and without PsA are needed. Ixekizumab has a high response rate among patients with moderate-to-severe psoriasis[5] and is a suitable treatment for patients with psoriasis and PsA.

We have summarized the 12-week efficacy and safety data of 80 mg ixekizumab given every 2 weeks (with a 160-mg initial dose) on skin involvement (Psoriasis Area Severity Index [PASI] response), joint pain (Visual Analog Scale, only in patients with self-reported PsA), and quality of life (Dermatology Life Quality Index [DLQI]). The data was taken from an integrated database of patients with moderate-to-severe psoriasis, both with and without self-reported PsA, derived from 3 phase 3 trials: NCT01474512 (UNCOVER-1), NCT01597245 (UNCOVER-2), and NCT01646177 (UNCOVER-3). Psoriasis and self-reported PsA involvement were initially evaluated on the basis of patient responses to the following 4 questions: 1) Is there palmoplantar involvement?; 2) Is there scalp involvement?; 3) Is there fingernail involvement?; and 4) Has the patient been diagnosed with PsA? Only patients randomized to ixekizumab every 2 weeks (the approved induction dosing regimen for moderate-to-severe psoriasis and PsA) were included in this post hoc integrated analysis.

Of the 1169 patients who were randomized to ixekizumab every 2 weeks, ~24% (283/1169) self-reported PsA at baseline. The mean baseline PASI scores for ixekizumab patients with and without PsA involvement were 21.6 and 19.6, respectively ($P < .001$). Similarly, the mean baseline body surface area values were 29.1 and 26.6 in ixekizumab

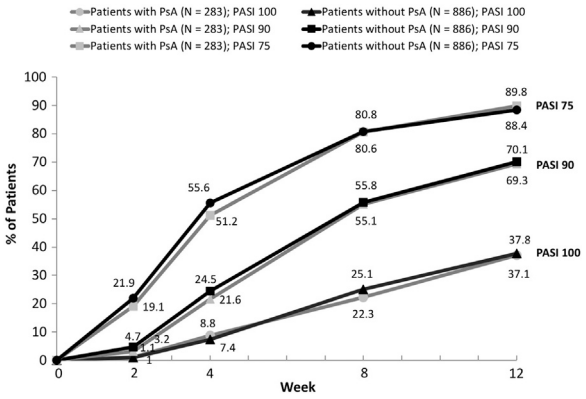

Fig 1. PASI 75, PASI 90, and PASI 100 responses over 12 weeks (NRI) in IXE Q2W patients with plaque psoriasis, by PsA involvement. Comparisons between groups were based on the Cochrane-Mantel-Haenszel test stratified by study. *IXE Q2W*, Ixekizumab 80 mg every 2 weeks; *NRI*, nonresponder imputation; *PASI*, Psoriasis Area Severity Index; *PsA*, psoriatic arthritis.

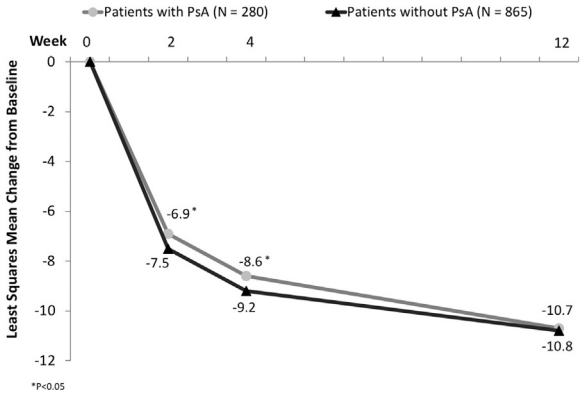

Fig 2. Change from baseline in total DLQI score over 12 weeks in IXE Q2W patients with plaque psoriasis, by PsA involvement. Comparisons between groups were based on the Cochrane-Mantel-Haenszel test stratified by study. *$P < .05$, IXE Q2W patients with PsA versus without PsA. *DLQI*, Dermatology Life Quality Index; *IXE Q2W*, ixekizumab 80 mg every 2 weeks; *PsA*, psoriatic arthritis.