From the Dermatology Department, Clínica Universidad de Navarra[a]; Pediatric Neurology Department, Hospital Infantil Universitario Niño Jesús[b]; and Dermatology Department, Hospital Infantil Universitario Niño Jesús, Madrid, Spain.[c]

Funding sources: None.

Conflicts of interest: None disclosed.

This study is included in the doctoral thesis entitled "Clinical and ultrasonographic study of the neurofibromatosis type 1 in a pediatric population" (https://www.educacion.gob.es/teseo/irGestionarConsulta.do). This study was also presented at the 75th American Academy of Dermatology Annual Meeting, Orlando, FL, March 3-7, 2017, as an e-poster under the title "Hypopigmented Macules: A Common Finding in Neurofibromatosis Type 1."

IRB approval status: Reviewed and approved by Niño Jesús Hospital Ethics and Clinical Research Committee (R-0055/14 Acta no. 09/14, October 28, 2014).

Reprint requests: Francisco Javier García-Martínez, MD, PhD, C/ Marquesado de Santa Marta 1, 28027, Madrid, Spain

E-mail: fjgarcia@aedv.es

REFERENCES

1. Riccardi VM. Neurofibromatosis and Albright's syndrome. *Dermatol Clin*. 1987;5(1):193-203.
2. Samanta D, Bosanko KB, Zarate YA. An infant with ash-leaf and café au lait spots: a case of double phakomatosis. *Acta Neurol Belg*. 2016;117(1):323-324.
3. Coupe RL. Unilateral systematized achromic naevus. *Dermatology*. 1967;134(1):19-35.
4. Kim SK, Kang HY, Lee ES, Kim YC. Clinical and histopathologic characteristics of nevus depigmentosus. *J Am Acad Dermatol*. 2006;55(3):423-428.
5. Baselga E. Disorders of hypopigmentation. In: Schachner LA, Hansen RC, eds. *Pediatric Dermatology*. 4th ed. Philadelphia, PA: Mosby Elsevier; 2012:719-722.

https://doi.org/10.1016/j.jaad.2020.06.071

A retrospective review of incidental malignancies in veterans seen for face-to-face follow-up after teledermatology consultation

To the Editor: Teledermatology (TD) is a rapidly growing tool within dermatology. However, few studies have evaluated malignancies missed by a referring provider but subsequently found by live in-person dermatologic examination when the initial consult is through teledermatology.[1]

This retrospective chart review was approved for a category 4 exception and waiver status by the University of Wisconsin Health Sciences and the Madison Veterans Affairs institutional review board. Lesion and biographical data were extracted from consult notes and pathology reports. The referrals by nondermatologists represent "index lesions" that were either suspected to be malignant or required further evaluation by a dermatologist. Incidental lesions were any additional found on face-to-face (FTF) skin examination. Statistical analysis was conducted on samples that were obtained when a patient underwent a full-body skin examination (FBSE) within 1 year of the original TD consult. Sample sizes were calculated using positive biopsy results (melanoma and nonmelanoma skin cancer) as the outcome variable.

Of the total 2874 TD consults seen between June 1, 2014, and December 31, 2018, 1,097 (38.1%) required an FTF follow-up with a dermatologist. Of these, 199 patients out of 1097 (18.1%) required biopsy of 1 or more incidental lesions. A total of 295 incidental lesion biopsies were performed on 199 patients, and 171 were found to be malignant (58.0%) (Table I). The most common malignant incidental lesion was basal cell carcinoma (61.4%), squamous cell carcinoma (28.7%), melanoma (5.3%), and dysplastic nevi requiring reexcision (4.8%) (Table II). Malignant lesions were associated with older age and history of nonmelanoma skin cancer compared with benign lesions (Table II).

Without an FBSE provided by a dermatologist, malignancies would have been missed in 15.6% of patients. This is higher than the 3.6% found in a TD referral system and the 6.9% and 15.3% found in non-TD referral systems.[1-3]

Nine of the 31 melanomas detected during the study period were discovered incidentally. The rate of incidental melanoma detection was 9 of 1097 (0.8%), which is consistent with previously reported detection rates from non-TD studies (0.5%-1.5%).[3-5]

Our findings show that the FTF visit after a TD consult resulted in an increased rate of detection of incidental malignancies compared to a standard dermatology referral. There is concern that TD may result in missed skin malignancies, however with appropriate triage via TD, patients with urgent needs are brought in sooner for a FBSE. This increases access for those who are truly at higher risk.

The limitations to this study include its retrospective nature and a predominantly elderly, white, male demographic. Furthermore, there is no direct comparison with a similar matched

Table I. Incidental lesion characteristics

Years	Consults, n	FTF follow-up, n	Incidental biopsies, n	Patients underwent biopsy, n	Incidental cancer, n	BCC, n	SCC, n	Dysplastic nevi, n*	Melanoma, n
2014	153	61	14	11	9	6	2	1	0
2015	544	201	45	32	23	12	6	3	2
2016	744	259	54	36	39	21	14	0	4
2017	672	269	51	39	28	15	12	0	1
2018	761	307	131	81	72	51	15	4	2
Total	2874	1097	295	199	171	105	49	8	9

BCC, Basal cell carcinoma; *FTF*, face-to-face; *SCC*, squamous cell carcinoma.
*Dysplastic nevi in this column required further excision.

Table II. Patient characteristics relating to incidental lesion malignancy

Characteristics	Incidental biopsy, n (%) (n = 201)	No incidental biopsy, n (%) (n = 900)	*P* value,* RR, and 95% CI	Malignant, n (%) (n = 128)	Only benign, n (%) (n = 73)	*P* value,* RR, and 95% CI
Age, y						
Mean (SD)	72.8	68.0 (11.9)	$P < .001$	74.7 (9.9)	69.5 (9.8)	$P < .001$
Range	26-96	23-98		42-96	26-90	
Sex						
Male	198 (98.5)	862 (95.8)	RR: 1.14	127 (99.2)	71 (97.3)	RR: 1.86
Female	3 (1.5)	38 (4.2%)	95% CI: 1.04-1.25	1 (0.8)	2 (2.7)	95% CI: 0.82-4.23
			$P = .065$			$P = .271$
History of NMSC						
Yes	63 (31.3)	163 (18.1)	RR: 1.17	51 (39.8)	12 (16.4)	RR: 2.32
No	138 (68.7)	737 (81.9)	95% CI: 1.07-1.27	77 (60.2)	61 (83.6)	95% CI: 1.35-3.99
			$P < .001$			$P = .001$
History of melanoma						
Yes	11 (5.5)	24 (2.7)	RR: 1.20	7 (5.5)	4 (5.5)	RR: 1.00
			95% CI: 0.96-1.50			95% CI: 0.45-2.23
No	190 (94.5)	876 (97.3)	$P = .04$	121 (94.5)	69 (94.5)	$P = .997$

CI, Confidence interval; *NMSC*, nonmelanoma skin cancer; *RR*, relative risk; *SD*, standard deviation.
**P* values are from *t* tests or chi-square tests.

patient population. Despite these limitations, to our knowledge, this is the largest study evaluating incidental malignancies found on follow-up after initial consult via TD. TD provides a way to triage patients who need to be seen more urgently. Given the number of incidental malignancies found, there should continue to be a low threshold for recommending an FTF visit for FBSE by a dermatologist.

Sarah Mortimer, MD,[a] *and Anne Rosin, MD*[a,b]

From the Department of Dermatology, University of Wisconsin Hospital and Clinics[a]*; and William S. Middleton Memorial Veterans Affairs, Madison, Wisconsin.*[b]

Funding sources: None.

Conflicts of interest: None disclosed.

IRB approval status: Given category 4 exemption by the University of Wisconsin Health Sciences IRB and waiver status by the Veterans Affairs research safety officer.

Reprint requests: Sarah Mortimer, MD, One South Park St, Madison, WI 53705

E-mail: smortimer@uwhealth.org

REFERENCES

1. Keleshian V, Ortega-Loayza AG, Tarkington P. Incidental skin malignancies in teledermatology and in-person cohorts in the Veterans Affairs Health System. *J Am Acad Dermatol*. 2017;77(5):965-966.
2. Kingsley-Loso JL, Grey KR, Hanson JL, et al. Incidental lesions found in veterans referred to dermatology: the value of a dermatologic examination. *J Am Acad Dermatol*. 2015;72:651-655.
3. Viola KV, Tolpinrud WL, Gross CP, et al. Outcomes of referral to dermatology for suspicious lesions: implications for teledermatology. *Arch Dermatol*. 2011;147:556-560.

4. Hanson JL, Kingsley-Loso JL, Grey KR, et al. Incidental melanomas detected in veterans referred to dermatology. *J Am Acad Dermatol*. 2016;74:462-469.
5. Aldridge RB, Naysmith L, Ooi ET, et al. The importance of a full clinical examination: assessment of index lesions referred to a skin cancer clinic without a total body skin examination would miss one in three melanomas. *Acta Derm Venereol*. 2013;93:689-692.

https://doi.org/10.1016/j.jaad.2020.06.079

Clinically meaningful change in itch intensity scores: An evaluation in patients with chronic kidney disease–associated pruritus

To the Editor: Clinical trials to assess the antipruritic effect of a treatment commonly use a numerical rating scale (NRS) ranging from 0 (no itching) to 10 (worst imaginable itching) to evaluate the worst itch intensity. However, for the drug effect to be clinically relevant, the magnitude of the reduction in the NRS scores must represent a meaningful improvement to the patients. Clinically meaningful changes with respect to NRS scores have been characterized in dermatologic conditions,[1-4] but to our knowledge, the threshold for such changes among patients with systemic chronic kidney disease–associated pruritus (CKD-aP) has not been established.

To address this knowledge gap, we conducted a secondary analysis of data pooled across treatment groups from a phase 2, multicenter, double-blind, randomized, placebo-controlled study (NCT02858726) to determine the magnitude of change required for a meaningful reduction in itch intensity on the Worst Itching Intensity-NRS

Table I. Thresholds for clinically meaningful change for Worst Itching Intensity Numerical Rating Scale (*WI-NRS*) using primary and secondary anchor-based methods*

Criteria	WI-NRS change score (week 8 − baseline), mean	Change from baseline, mean, %	Effect size (Cohen *d*)
Primary anchor			
PGI-C minimally improved	−2.26	−33.56	1.29
PGI-C minimally and much improved	−3.02	−42.99	1.65
PGI-C much improved	−3.41	−47.81	1.83
Secondary anchors			
PGI-S improved 1 point	−2.49	−37.10	1.40
PGI-S improved at least 1 point	−3.45	−49.61	1.75
5-D Itch Direction (Itch)			
A little better	−1.94	−26.37	1.19
A little better or much better	−3.32	−49.61	1.80
5-D Itch Degree (Itch Intensity)			
Improved 1 point	−3.02	−45.23	1.82
Skindex-10 (item 1) Itch	−2.65	−39.05	1.47
Bothersome improved 2 points			
Mean (secondary anchors)	−2.81	−41.16	

PGI-C, Patient Global Impression of Change; *PGI-S*, Patient Global Impression of Severity.
*Anchor-based methods were linked to patients' reports of perception of change in WI-NRS at week 8 and were selected a priori to most closely relate to the concept measured by the WI-NRS. The PGI-C was the primary anchor variable because it is commonly used to evaluate meaningful change, including within populations with pruritus, and is recommended by the United States Food and Drug Administration. "Minimally improved," "minimally and much improved," and "much improved" anchor categories were used to represent minimal to larger improvements. The use of these anchors was justified by the absence of approved therapies for moderate to severe chronic kidney disease–associated pruritus (CKD-aP). Secondary anchors included (1) a 1-point and at least 1-point categorical severity change on the PGI-S, which corresponded to a shift in itch severity category (eg, from severe to moderate). The clinical significance of single-category shifts for CKD-aP is reinforced by data indicating that greater itch severity is linked to higher mortality; (2) the 5-D direction and degree questions asking patients whether itching got better or worse on a scale of 1 (completely resolved) to 5 (getting worse) within the past 2 to 4 weeks and to rate the intensity of their itching on a scale of 1 (not present) to 5 (unbearable), respectively; and (3) the Skindex-10 item 1 asking how often patients were bothered by itching on a scale of 0 (never bothered) to 6 (always bothered) within the past week.