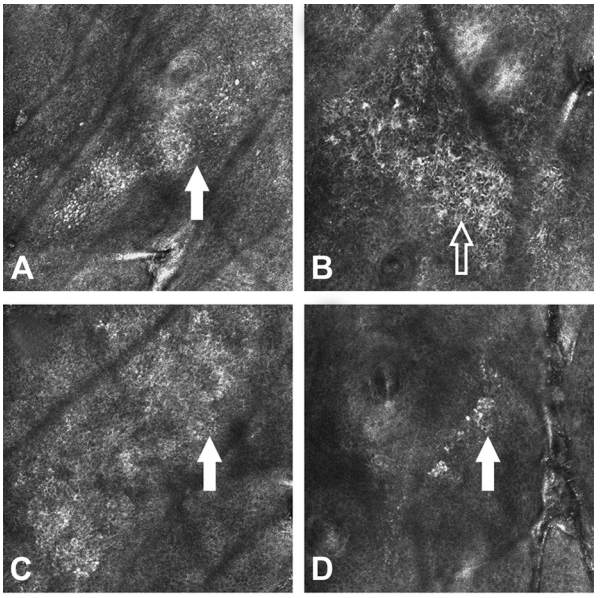

Fig 2. Reflectance confocal microscopy (RCM) images for 1 patient: image from an area of the patient's face randomized to the control (Q-switched alexandrite laser–treated) group before treatment (**A**) and at 2 weeks after treatment with a Q-switched alexandrite laser (**B**) and image from an area of the patient's face randomized to the experimental (picosecond pulsed alexandrite laser–treated) group before treatment (**C**) and at 2 weeks after treatment (**D**). **A** and **C**, Arrows indicate the many high-refractive melanin particles the stratum spinosum. **B**, Arrow indicates the decrease in the number of melanin particles and spines of highly refractive dendritic cells in the stratum spinosum after treatment. **D**, Arrow indicates the decrease in the number of melanin particles in the stratum spinosum after treatment.

The authors speculated that the dendritic cells might be melanocytes and that heat damage led to changes in melanin traits that in turn increased the refractive index, whereas laser stimulation led to the migration of more melanocytes from hair follicles to the normal-appearing epidermis; damaged melanin particles cannot be transported to keratinocytes and thus remain in melanocytes. However, this phenomenon was not observed in the experimental group treated with the PSAL. We speculated that this may due to the relatively lesser photothermal damage by the PSAL (Fig 2).

Our results suggested that the efficacy and safety of using a PSAL for treating freckles in Chinese patients are comparable to those of using a QSAL.

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Funding sources: Supported by the CAMS Innovation Fund for Medical Sciences (CIFMS-2017-I2M-1-017) and Primary Research and Development Plan of Jiangsu Province (BE2017808).

Conflicts of interest: None disclosed.

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REFERENCES

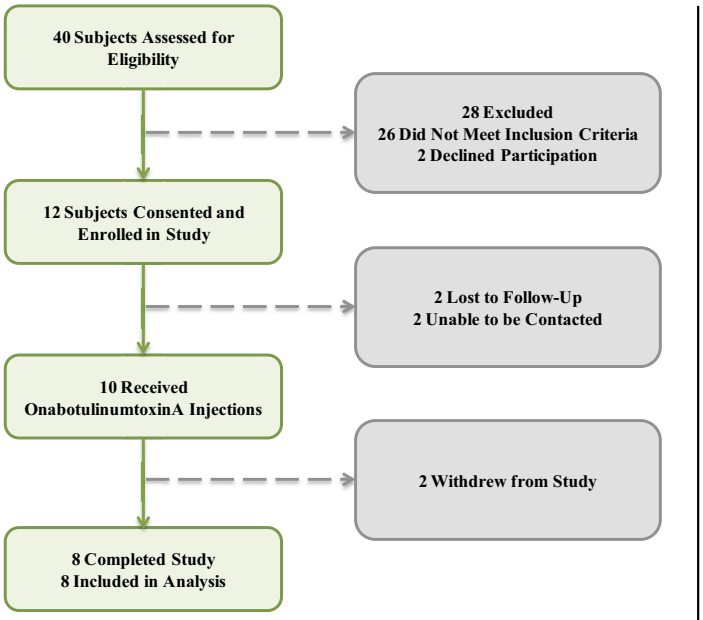
1. Chan JC, Shek SY, Kono T, Yeung CK, Chan HH. A retrospective analysis on the management of pigmented lesions using a picosecond 755-nm alexandrite laser in Asians. *Lasers Surg Med*. 2016;48:23-29.
2. Yamashita T, Negishi K, Hariya T, Yanai M, Iikura T, Wakamatsu S. In vivo microscopic approaches for facial melanocytic lesions after quality-switched ruby laser therapy: time-sequential imaging of melanin and melanocytes of solar lentigo in Asian skin. *Dermatol Surg*. 2010;36:1138-1147.

https://doi.org/10.1016/j.jaad.2018.07.047

Neuromodulatory treatment of recalcitrant plaque psoriasis with onabotulinumtoxinA

To the Editor: The role of neurocutaneous pathways in the pathogenesis of psoriasis has been suggested in cases of dermatomal improvement in psoriatic plaques following central or peripheral nerve damage[1-3]; however, few studies have assessed the effect of nerve-targeting treatments,[4,5] especially in plaque psoriasis. This study investigated the effect of onabotulinumtoxinA injections on psoriasis severity, epidermal nerve fiber (ENF) density, and expression of the neuropeptides substance P (SP) and calcitonin gene–related peptide (CGRP).

In this single-center pilot study, 8 subjects (Fig 1, *A* and *B*) with plaque psoriasis received a 1-time injection of onabotulinumtoxinA (Botox, Allergan, Inc, Irvine, CA) throughout a single target plaque (average units, 53; range, 25-98) and were followed for 10 weeks after the injection with assessment of their Psoriasis Area and Severity Index (PASI) score and Physician's Global Assessment (PGA) score and clinical photography. Punch biopsy specimens (diameter, 3 mm) obtained from lesional and perilesional skin 2 weeks before and 8 weeks after



A

Demographic	n(%)[a]
Sex	
Men	6 (75.0)
Women	2 (25.0)
Mean Age, yrs (Range)	46 (35-58)
Mean Age at Diagnosis (SD[b])	21.6 (11.1)
Mean Duration of Psoriasis, yrs (SD)	21.5 (13.7)
Race	
Caucasian	6 (75.0)
Asian	2 (25.0)
Target Plaque Location	
Elbow	4 (50.0)
Back	1 (12.5)
Knee	1 (12.5)
Leg	1 (12.5)
Foot	1 (12.5)
Previous Treatments	
Corticosteroids	7 (87.5)
Calcipotriene	3 (37.5)
UVB Phototherapy	3 (37.5)
Coal Tar	2 (25.0)
Methotrexate	2 (25.0)
Retinoids	1 (12.5)

[a]Denominator for (%) is 8, the total subjects enrolled that completed the study.
[b]SD; standard deviation

B

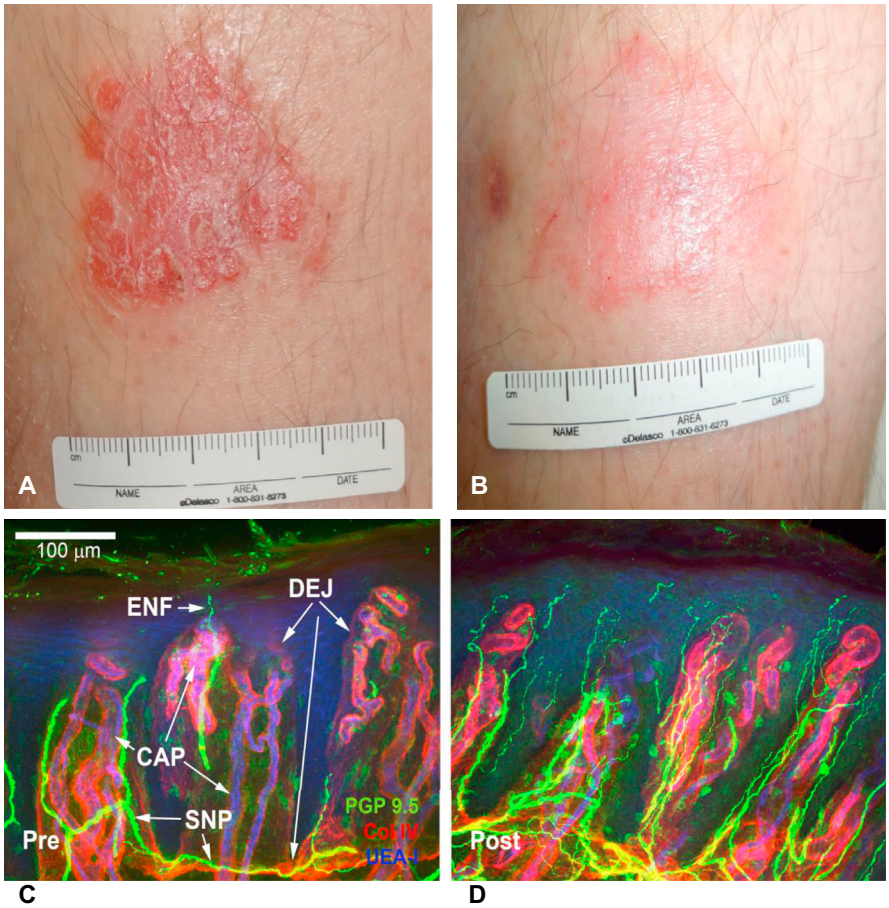
Fig 1. A, Study profile. **B**, Demographics. Eligible subjects had a diagnosis of plaque psoriasis made by a board-certified dermatologist, had failed 2 prior psoriasis treatments, and had a minimum of 2/5 in thickness and erythema according to their Physician's Global Assessment scores. Major exclusion criteria included current treatment with medication for psoriasis (topical immunomodulatory or immunosuppressive medication within 4 weeks, systemic immunomodulatory or immunosuppressive medication within 12 weeks, or topical or systemic retinoid treatment within 12 months), concurrent inflammatory or infectious skin disease, allergy or intolerance of the products of injection, and an underlying disease that could be adversely affected by onabotulinumtoxinA injection (such as myasthenia gravis).

injection were immunostained to visualize ENFs, SP and CGRP. Informed consent was obtained. The University of Minnesota Institutional Review Board approved this study (institutional review board approval No. 0808M45282).

For nerve quantification, 60-μm-thick vertical sections of the biopsy specimen were immunostained with antibodies to the pan-neuronal marker protein gene product 9.5, type IV collagen (a basement membrane marker), and the neuropeptides SP and CGRP. Immunoreactive ENFs were imaged with spinning disk confocal microscopy and quantified with Neurolucida tracing software (MBF Bioscience, Williston, VT). Protein gene product 9.5–labeled ENFs crossing the dermoepidermal junction were expressed as ENFs/mm of basement membrane. SP- and CGRP-immunoreactive nerve fibers, expressed as SP or CGRP per section, were visualized and counted by using epifluorescent microscopy.

The analyses for PASI score, PGA score, ENF density, and SP- and CGRP-immunoreactive nerves were performed with use of mixed linear models with the restricted maximum likelihood method and JMP software (version 12 Pro; SAS Institute, Inc, Cary, NC).

The results are summarized in Figure 2. Lesional samples had lower ENF density (lesional mean density, 4.6; perilesional density, 12.0 [$P < .01$]) and higher SP-immunoreactive (lesional mean density, 9.2; perilesional density, 4.5 [$P < .01$]) and CGRP-immunoreactive (lesional mean density, 22.0; perilesional density, 10.6 [$P = .057$]) nerve densities than the perilesional samples did. After injection, SP ($P = .061$) and CGRP ($P = .053$) immunoreactivity decreased in the lesional and perilesional samples whereas ENF density ($P = .10$) increased. OnabotulinumtoxinA injections were associated with significantly decreased PASI and PGA scores ($P < .01$ for both).



Clinical Effect	Pre-Injection Mean Severity[a]	Post-Injection Mean Severity[b]	*P*-Value
PASI	6.3	4.1	< 0.01*
PGA	2.6	2.1	< 0.01*

Nerve Fiber and Neuropeptide Quantification	Mean Density[c]	Mean Density[c]	*P*-Value
ENFs/mm[d]	6.3	8.7	0.10
SP/section[e]	7.6	6.1	0.061
CGRP/section	18.5	14.4	0.053

*Signifies a statistically significant value ($P < 0.05$).
[a]Average baseline (pre-injection) psoriasis severity was determined for 2 weeks prior to injection; average of visits 1, 2 and 3.
[b]Average post-injection psoriasis severity was determined at 8 weeks post-injection (visit 6).
[c]Includes lesional and perilesional densities.
[d]For two patients, less than 30 µm of section depth was available. Densities were corrected accordingly.
[e]SP quantification calculated from 5 patients with adequate immunostaining.

E

Fig 2. Psoriasis vulgaris. Effect of onabotulinumtoxinA on target plaque and the peripheral nervous system. **A**, Target plaque on the anterior aspect of the right leg 2 weeks before the onabotulinumtoxinA injection. **B**, The same plaque 8 weeks after the injection. **C**, Few epidermal nerve fibers (ENFs) in lesional skin 2 weeks before the injection, **D**, Dense ENFs in lesional skin 8 weeks after the injection. **E**, Calculated mean values for all subjects. *CAP*, Capillaries; *ColIV*, type IV collagen; *DEJ*, dermopidermal junction; *PGP 9.5*, protein gene product 9.5; SNP, subepidermal nerve plexus; *UEA-1*, ulex europaeus agglutinin 1.

No serious adverse events or adverse effects directly related to the study drug were reported during this study. None of the subjects discontinued participation secondary to side effects.

There are several limitations to this study, including the small population size, predominance of males, lack of a placebo control, cost of onabotulinumtoxinA, and variance in body site of target plaque and average ENF and neuropeptide densities by body site.

In conclusion, the findings from this study support the idea that neurocutaneous pathways are altered in psoriasis and that onabotulinumtoxinA could be a potential treatment for recalcitrant, localized, psoriatic plaques. Its clinical effect of decreasing plaque severity may be mediated by decreasing SP- and CGRP-immunoreactive nerve expression and increasing ENF density. These injections were well tolerated by subjects. Future investigations evaluating the effect of onabotulinumtoxinA in a larger number of patients with recalcitrant plaque psoriasis are needed to confirm clinical efficacy and safety.

We are indebted to James Hodges, PhD, of the University of Minnesota School of Public Health—Biostatistics Division, for his expertise in statistical analysis applied to this project, and to Dr James Andrews, DO, of Physical Medicine and Rehabilitation in Alexandria, Minnesota, for his initial observations that contributed to the development of this study.

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Funding sources: Supported in part by an investigator-initiated grant from Allergan to Dr Hordinsky and a grant from the University of Minnesota Undergraduate Research Opportunities Program.

Disclosure: At the time of submission, Dr Hordinsky was an investigator for an Allergan, Inc, clinical trial focused on the therapy of male androgenetic alopecia. Dr Aschenbeck, Dr Kennedy, Dr Wendelschafer-Crabb, Dr Ericson, Dr Kavand, Dr Bertin, Dr Dykstra, and Dr Panoutsopoulou have no conflicts of interest to disclose.

Presented in poster and oral presentation at the 75th Annual Meeting of the Society for Investigative Dermatology in Scottsdale, AZ, on May 11-14, 2016.

Reprints not available from the authors.

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REFERENCES

1. Joseph T, Kurian J, Warwick DJ, Friedmann PS. Unilateral remission of psoriasis following traumatic nerve palsy. *Br J Dermatol*. 2005;152(1):185-186.
2. Raychaudhuri SP, Farber EM. Are sensory nerves essential for the development of psoriatic lesions? *J Am Acad Dermatol*. 1993;28(3):488-489.
3. Dewing SB. Remission of psoriasis associated with cutaneous nerve section. *Arch Dermatol*. 1971;104(2):220-221.
4. Saber M, Brassard D, Benohanian A. Inverse psoriasis and hyperhidrosis of the axillae responding to botulinum toxin type A. *Arch Dermatol*. 2011;147(5):629-630.
5. Zanchi M, Favot F, Bizzarini M, Piai M, Donini M, Sedona P. Botulinum toxin type-A for the treatment of inverse psoriasis. *J Eur Acad Dermatol Venereol*. 2008;22(4):431-436.

https://doi.org/10.1016/j.jaad.2018.07.058

Increasing frequency and share of dermatologic procedures billed by nonphysician clinicians from 2012 to 2016

To the Editor: As a response to the increasing demand for dermatologic care and the geographic maldistribution of dermatologists, nonphysician clinicians (NPCs) (nurse practitioners and physician assistants) have become a significant component of the US dermatology workforce.[1,2] Recent studies have raised concerns that NPCs may at times deliver care at a higher cost.[3,4] These concerns have intensified as private equity firms have entered the dermatology field and preferentially employed NPCs to increase profits.[5] The purpose of this study is to characterize recent trends in independent billing for dermatologic procedures by NPCs. Prior literature on NPCs in dermatology has been limited to studies of practice scope at single points in time.[1-3]

We hypothesized that growth in common dermatologic services provided by NPCs would exceed that