Table III. Effect of strong predictors of actinic keratosis count on mean number of baseline actinic keratoses on the face and ears

	Mean no. of baseline AKs	
Strong predictor variables	**VATTC**	**VAKCC**
Latitude		
Highest*	7.2	6.4
Lowest†	14.0	15.2
Age, y		
<50	3.4	6.0
≥80	8.8	11.8
Sex		
Female	3.0	6.8
Male	7.4	11.0
Sun sensitivity		
≤25th percentile	5.0	10.2
≥75th percentile	9.8	13.7
History of 5-FU use		
No	6.1	9.9
Yes	12.3	15.4
No. of prior invasive SCCs		
Lowest quintile	5.3	11.3
Highest quintile	13.6	16.0
No. of prior in situ SCCs		
Lowest quintile	6.5	10.5
Highest quintile	12.4	12.8
Photodamage		
Absent/mild	6.5	n/a
Severe	11.4	n/a
Focal dermatitis		
None	5.6	n/a
Moderate/severe	14.3	n/a
Rosacea with rhinophyma		
None	6.3	n/a
Moderate/severe	12.0	n/a

AK, Actinic keratosis; *FU*, fluorouracil; *SCC*, squamous cell carcinoma; *VAKCC*, Department of Veterans Affairs Keratinocyte Carcinoma Chemoprevention Trial; *VATTC*, Department of Veterans Affairs Topical Tretinoin Chemoprevention Trial.
*Hines, IL (VATTC) and Minneapolis, MN (VAKCC).
†Department of Veterans Affairs Medical Center where the participant was followed up. Lowest latitude was Miami Department of Veterans Affairs Medical Center (VATTC and VAKCC).

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REFERENCES

1. Siegel JA, Korgavkar K, Weinstock MA. Current perspective on actinic keratosis: a review. *Br J Dermatol*. http://dx.doi.org/10.1111/bjd.14852. Published online August 8, 2016.
2. Pomerantz H, Hogan D, Eilers D, et al. Long-term efficacy of topical fluorouracil cream, 5%, for treating actinic keratosis: a randomized clinical trial. *JAMA Dermatol*. 2015;151(9):952-960.
3. Weinstock MA, Bingham SF, Digiovanna JJ, et al. Tretinoin and the prevention of keratinocyte carcinoma (basal and squamous cell carcinoma of the skin): a Veterans Affairs randomized chemoprevention trial. *J Invest Dermatol*. 2012;132(6):1583-1590.
4. Flohil SC, van der Leest RJT, Dowlatshahi EA, Hofman A, de Vries E, Nijsten T. Prevalence of actinic keratosis and its risk factors in the general population: the Rotterdam study. *J Invest Dermatol*. 2013;133(8):1971-1978.
5. Chen GJ, Feldman SR, Williford PM, et al. Clinical diagnosis of actinic keratosis identifies an elderly population at high risk of developing skin cancer. *Dermatol Surg*. 2005;31(1):43-47.

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Successful treatment of actinic keratoses using nonthermal atmospheric pressure plasma: A case series

To the Editor: The treatment of actinic keratoses (AKs) represents a daily challenge for dermatologists: the available modalities all have significant downsides, such as pain, inflammation, treatment-site reaction, incomplete response, and frequent recurrences. We have studied the usefulness of uniform nonequilibrium, nonthermal atmospheric pressure plasma (NTAP) in the treatment of AKs. NTAP was shown to selectively induce apoptosis in cancer cell lines in vitro, including squamous cell carcinoma cells. Our prior studies suggest that NTAP may also up-regulate local and tumor-specific systemic immune response,[1-3] possibly leading to immunologic advantage against AKs.

We have conducted a single-treatment, short-term follow-up, case series trial as proof of concept for the use of NTAP in the treatment of AKs. The protocol was approved by the Western Institutional Review Board (2/8/2016; 20130084; ClinicalTrials.gov registration number: NCT02759900).

Five patients were enrolled after obtaining informed consent with 5 biopsy-proven and 12 clinically diagnosed AKs. The treatment protocol called for a single treatment using a NTAP device (described in detail by the authors previously[4]) on the target lesions and 1 month follow-up without interval evaluation. The 1-month posttreatment results were evaluated clinically and by comparing pretreatment and follow-up photographs. The outcome was categorized as fully resolved when no visible or palpable lesions remained except minimal site erythema, significantly improved when there was at least 50%

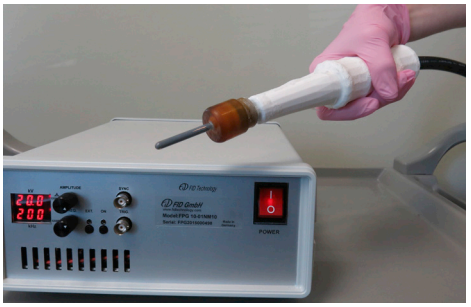


Fig 1. Custom-made nonthermal atmospheric pressure plasma device with hand-held electrode.

improvement of the lesion and minor or no improvement when the improvement was less than 50% in the clinician assessment based both on examination and photograph comparison.

To create plasma, we used a pulse generator supplying 20-kV pulse of 20-ns pulse width at 200 Hz (FPG10-01NM10, FID GmbH, Burbach, Germany) to a 5-mm diameter quartz-covered copper electrode of 10-cm length and 1-mm quartz thickness. These nanosecond pulse parameters were chosen to provide sufficient treatment dose at the high level of plasma uniformity required to avoid any tissue damage[5] (Fig 1). We treated the lesions for approximately 1 to 2 minutes each, moving the electrode gently over the treatment area.

In total we treated 17 lesions. Nine lesions showed full clinical resolution 1 month after the treatment. Three lesions significantly improved and 5 showed minor or no improvement (Fig 2). None of the patients experienced any adverse effects related to the treatment: no pain, inflammation, site reaction during the treatment, or report of delayed adverse effects at 1-month follow-up.

Our results are encouraging as they demonstrate that NTAP may serve as an effective, well-tolerated treatment for AKs. Further studies are needed to optimize treatment parameters, provide histologic confirmation of treatment effect, and evaluate the long-term benefits of this modality. Although the value of our preliminary results is limited by the small number of patients treated and the short follow-up period limiting recurrence evaluation, our efficacy numbers are comparable with the reported numbers of other, currently widely used modalities. Given its very impressive tolerability, NTAP may be an excellent alternative for our current treatment options for AKs, especially if its efficacy and treatment procedure time can be improved and if further, long-term studies demonstrate lasting effects.

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Fig 2. Actinic keratoses: photographs taken before (*top*) and 1 month after (*bottom*) treatment with nonthermal atmospheric pressure plasma demonstrating full resolution (*solid arrows*) and partial improvement (*dotted arrow*) of some lesions.

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REFERENCES

1. Miller V, Lin A, Fridman G, et al. Plasma stimulation of migration of macrophages. *Plasma Process Polym*. 2014;11:1193-1197.
2. Lin A, Truong B, Pappas A, et al. Uniform nanosecond pulsed dielectric barrier discharge plasma enhances anti-tumor effects by induction of immunogenic cell death in tumors and stimulation of macrophages. *Plasma Process Polym*. 2015;12:1392-1399.
3. Miller V, Lin A, Fridman A. Why target immune cells for plasma treatment of cancer. *Plasma Chem Plasma Process*. 2016;36:259-268.
4. Fridman G, Peddinghaus M, Balasubramanian M, et al. Blood coagulation and living tissue sterilization by floating-electrode dielectric barrier discharge in air. *Plasma Chem Plasma Process*. 2006;26:425-442.
5. Fridman G, Friedman G, Gutsol A, et al. Applied plasma medicine. *Plasma Process Polym*. 2008;5:503-533.

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