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NEWS, VIEWS, & REVIEWS

Fractional Laser for Prevention of Non-melanoma Skin Cancer

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INTRODUCTION

Non-melanoma skin cancer (NMSC) causes significant patient morbidity and healthcare costs; therefore, there is a vested interest in expanding the prevention armamentarium available for high risk patients.

Fractional lasers (FLs) are used to manage various dermatologic conditions including photoaging, scarring, and dyspigmentation, and are currently being studied in the context of NMSC prevention due to their ability to modulate epidermal turnover and signaling molecules crucial for the skin's protective response against UV.[1,2]

Herein, the mechanistic theory and evidence for use of FLs for NMSC prevention will be reviewed.

Proposed Mechanism of Effect

FL treatments are thought to reduce risk of NMSC by directly reducing burden of photodamaged keratinocytes, as well as protecting against malignant transformation of keratinocytes. FLs treat skin in a pixelated manner, creating vertical microthermal treatment zones (MTZ) with intervening spared skin.[1,3] Consequently, FL-induced injury promotes extrusion of damaged keratinocytes and stimulates epidermal regeneration by initiating the wound healing cascade, contributing to a decrease in clinical and histologic signs of photodamage.[4–9]

Further, FL may reduce risk of keratinocyte photocarcinogenesis by stimulating insulin-like growth factor (IGF-1) signaling, which is involved in UV-induced DNA damage repair.[10–13] FL resurfacing increases IGF-1 levels and decreases occurrence of proliferating UV-damaged keratinocytes.[11,14–16] One study found that FL treatment increased skin IGF-1 values by 60%, and in vivo, increased expression persisted for 2 years post-treatment.[17,18]

Fractional Lasers for Actinic Keratoses

FLs are being considered both as monotherapy and adjunctive therapy for treating actinic keratoses (AK), precancerous lesions which can progress to NMSC.[19] Both ablative and non-ablative FLs have been explored with differing treatment effects dependent on the laser type and protocol.

Ablative Fractional Lasers

Ablative FLs (AFLs) thermally ablate epidermal and dermal tissue in MTZ, causing full-thickness skin injury in treated areas of actinic damage.[3] Data currently suggests that AFLs are non-inferior to other available AK management options.[20] AFL monotherapy reduced AKs by 60-75% in studies on both forearms and scalp.[10,17,18] Further, a single AFL treatment was associated with sustained reduction of AKs for 36 months in one study (Table 1).[18]

Table 1. Fractional Ablative Laser (FAL) for Treatment of Actinic Keratoses (AKs)

Study	Methods	Study Population	Laser Used, Number of Treatments	Primary Finding
Chen et al. 2020	Intrapatient comparison: forearm AKs	30 males≥ 60yo	2790nm YSGG (1 treatment)	60% decrease in AKs on treated arm
Spandau et al. 2021	Intrapatient comparison: forearm AKs	48 adults≥ 60yo	2790nm YSGG (1 treatment)	4-fold reduction in AKs at 3 months, sustained for 36 months AFL reduced frequency of NMSC, # of individuals who developed NMSC
Trovato et al. 2023	Intrapatient comparison: scalp AKs	30 males≥ 65yo	10,600nm CO_2 (3 treatments, q21 days)	Fibroblast synthesis of IGF1 increased post-treatment by 60% AKs decreased by >75% Post-treatment reflectance confocal microscopy: reduced keratinocyte disarray and scales

YSGG= yttrium scandium gallium garnet crystal
CO_2= carbon dioxide

AFLs have also been studied as a pre-treatment to photodynamic therapy (PDT) due to their ability to improve uptake of topical drugs. AFL treatment preceding PDT was significantly more effective than conventional PDT; 92% of patients had a complete response, compared to 66% for conventional PDT, and recurrence rates were significantly lower.[21] Additionally, AFL-assisted PDT may allow for reduced incubation time with the photosensitizing agent without compromising efficacy.[21,22]

Non-ablative Fractional Lasers

In contrast to AFLs, non-ablative FLs (NAFLs) have a milder treatment effect, causing controlled dermal tissue injury without compromising the epidermis.[3] The data is less clear regarding efficacy of NAFL as monotherapy for AKs. In a study by Katz et al, NAFL clinically decreased AKs by 56%, however, 83% of follow-up biopsies had persistent dysplastic cells between MTZ and were diagnosed as AK or squamous cell carcinoma (SCC).[6] Conversely, Weiss et al. doubled the density of MTZ in their treatment protocol and found that NAFL monotherapy was efficacious, reducing AKs by 87% with 86% of follow-up biopsies demonstrating AK clearance.[7]

Delaying Development of NMSC

Preliminary research is also encouraging for use of FLs in patients with NMSC history to prevent additional NMSCs, however, data is overall limited. One in vivo study found that repeated AFL treatment in UV-exposed hairless mice delayed SCC development compared to control mice by 12, 19, and 30 days for the 1st, 2nd, and 3rd tumors.[5] Additionally, a retrospective review of patients with prior facial NMSC revealed that NAFL treatment decreased risk of subsequent NMSC development by nearly 50% (20.9% vs 40.4%) and significantly delayed timing of development compared to controls.[23]

Conclusion

FL treatment is a promising strategy for NMSC prevention; FLs injure photodamaged skin and promote a regenerative wound healing response, in addition to modulating cutaneous biologic processes contributing photocarcinogenesis, such as IGF-1 signaling. However, further research is needed to establish consensus on FL treatment protocols, as current studies utilize a variety of laser types, settings, and treatment schedules. Additional work will also be required to fully understand the role of FL relative to currently available NMSC prevention therapies.

Disclosure

The authors declare no conflicts of interest.

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