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Management of seborrhoeic keratosis and actinic keratosis with an erbium:YAG laser—experience with 547 patients

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Abstract. Seborrhoeic keratosis and actinic keratosis are common skin lesions, and the latter is a precursor for skin malignancy. The treatment regimen can be lesion-directed or field-directed. Current lesion-directed treatments include cryotherapy, shave excision, and laser ablation. Field-directed treatment typically encompasses multiple topical agents. This article presents the authors' experience of lesion- and field-directed erbium:YAG laser treatment of 547 patients (Fotona Dualis XS Laser). In this series of patients, those who had resurfacing as field therapy showed no recurrence during the 12-month review period. However, there were six cases of recurrence in the group who underwent lesion-directed treatment over the same period. Furthermore, the results illustrated that the incidence of recurrence of actinic keratosis with malignant transformation was around 2.5%. The production of p53-negative keratin sites after laser ablation acts as a protective environment in the prevention of squamous malignancies. Thus, laser ablation not only removes lesions and resurfaces, but also protects against skin cancer. Therefore, this treatment is very worthwhile, especially in light of the increasing incidence of skin cancers.

Key words: actinic keratosis; seborrhoeic keratosis; Er:YAG; laser treatment.

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Seborrhoeic keratosis (SK) and actinic keratosis (AK) are common skin lesions affecting the Western population.

SK usually begins with the appearance of one or more sharply defined light-brown flat macules. They initially grow and develop a well-defined verrucous surface, followed by an uneven warty appearance with multiple blood follicles and a dull or lacklustre appearance. They typically look as though they have been stuck on the skin surface. On dermatoscopy, they present features of milia-like irregular crypts, fissures/ridges, grooves, grey lobules, light-brown fingerprint-like parallel structures, and fat fingers (the gyri of the cerebriform surface)[1].

These are common cutaneous lesions characterized by epidermal proliferation and are composed of basaloid cells mixed with some squamoid cells. Histologically they show an acanthotic epidermis associated with papillomatous, hyperkeratosis, and invaginations forming horn crypts. Based on architectural patterns, SK may

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be categorized as acanthotic, hyperkeratotic, reticular, or verrucous form. Irritated lesions may show a considerable amount of squamous cell proliferation that may mimic squamous cell carcinoma. On histology, there is a dense, lichenoid inflammatory infiltrate predominantly of a lymphocytic nature. SK are epidermal tumours involving atypical basaloid keratinocytes.

Multiple SK can also be a sign of internal malignancy. The most common are adenocarcinomas of the gastrointestinal tract. There is also a familial tendency of autosomal dominant presentation. The differential diagnosis of SK includes malignant melanoma, melanocytic naevus, verruca vulgaris, condyloma acuminatum, epidermal naevus, AK, pigmented basal cell carcinoma, and squamous cell carcinoma[1].

AK on the other hand presents as erythematous, scaly patches or plaques distributed in sun-exposed areas, and has the potential to change into squamous cell carcinoma, with the rate of malignant transformation being in the range of 0.25–20% over a 1-year time period[2]. The histological characteristics include abnormal keratinocytes of the basal layer, atypical enlarged nuclei, and hyperkeratosis of the epidermis[3].

AK results from the exposure of keratinized sites to ultraviolet radiation[2]. Gene mutations including mutations in p16 and p53 have been implicated in the develop ment of AK and in the progression of A to squamous cell carcinoma[4]. UV- ght is the most abundant and pene s the skin more deeply than UV-B auses the activation of oxygen cies, ch interrupt normal cell r transduc pathways and cell cell signalling resulting in altere roliferation. p53, a gene coding fo tum suppressive protein, is activate V-B lig and this activ epresc crucl tep in the path y t creat netically unst kerati ed sites . e p53 gene in nncti as been found to protec st skin cancer induction by UV light ice. In the absence of functional repair s such as p53, other DNA mutations proceed to promote carcinogenesis[4].

AK is common in fair-skinned individuals and is particularly prevalent in areas of high-level sun exposure. In Australia, AK affects 40–50% of the Caucasian population over the age of 40 years[3]. The prevalence of AK in the USA ranges from 11% to 26%, whilst in Europe, 15% of men and 16% of women are affected. AK very commonly develops in the head and neck (balding scalp and face), dorsal forearms, and hands[5,6]. Organ transplant recipients who are on immunosuppressive medications are 250 times more likely to develop AK[7]. Human papillomavirus has also been shown to have an impact on the formation of AK[8].

The fundamental premise on which the management of AK is based is that of field cancerization. UV light affects large areas of the skin, especially in the head and neck region[7]. The area between actinic lesions is exposed to this insult and is likely to contain undetectable preclinical lesions or zones of dysplastic cells[7]. The whole of the affected area is known as the 'field'. Management is therefore divided into lesion-directed and field-directed therapy[5,6]. Current lesion-directed therapies include cryotherapy, shave excision, and forma excision. Topical field-directed thera include 5-fluorouracil (5-FU), imiq diclofenac, and ingenol mebutate cam as well as photodynamic therapy (PDT). Combining lesion- and fiel ed therapies has yielded good r ts, and several prospective therapies a currently un er investigation[6].

Australian and Europe uideline r the treatment f single lesion FU and PDT, i . For hyperkeratotic lesions, Ame n an ean guidelines recommend de br ar e, but Australi and British g nes suggest curettage, with Australian guidelines going on to include double-freeze cryotherapy and surgery. For multiple lesions there appears to be wide consensus across the continents on the use of 5-FU for field therapy. Australia, the USA, and Europe include imiquimod for multiple lesions, while the UK recommends PDT and diclofenac. For cases in which surgery or field-directed therapy are inappropriate, Australian guidelines recommend imiquimod or PDT, European guidelines suggest retinoid, an uidelines recommend persisting 5-FU[13].

It is curre not consid appropriate to make di comparison f efficacy betwee e diffe therapi or AK and SK to the va ity the studies p med. ochra iew and meta- sis ight interventions by Gupta and t indica that 5-FU treatment is the eff ve, followed by a combination ent of 5-aminolevulinic acid (ALA) PDT, imiquimod, ingenol butate, and methyl aminolevulinate ( ) PDT[14].

Table 1. Laser values.

Fluence	350–500 mJ/cm^2
Spot	3–5 mm
Mode	SP
Frequency	20 Hz

SP, short pulse.

Tabl tion of patients with actinic keratosis (AK), seborrhoeic keratosis (SK), and cted ma ancy.

Site	Total number of lesions	AK	SK	Suspected malignancy
Scalp	252	111	101	40
Forehead	66	26	40	0
Nose	46	26	20	0
Cheek	41	11	30	0
Peri-oral	16	10	6	0
Ear	46	30	16	0
Neck	20	2	18	0
Non head and neck	60	30	30	0
Total	547	246	261	40

Table 3. Parameters of patient treatment with the erbium laser (total number of patients = 547).

Site	Number	Lesion-directed (LD)	Field-directed (FD)	Response	Recurrence
Scalp	252	250	2	Complete in 248	4 (LD)
Forehead	66	60	6	Complete	
Nose	46	40	6	Complete	
Cheek	41	39	2	Complete	
Peri-oral	16	15	1	Complete	
Ear	46	42	4	Complete in 45	1 (LD)
Neck	20	20	0	Complete	
Non head and neck	60	60	0	Complete in 59	1 (LD)
Total	547	526	21	541	6

The lesion- and field-directed therapies mentioned above can prolong the recovery time and produce unpredictable results. Laser therapy, including the use of carbon dioxide (CO_2) and erbium:YAG lasers, has also been used as lesion-directed and field-directed therapy[15–17]. For the last 10 years, the present authors have been using an erbium:YAG laser as a primary treatment for symptomatic SK and AK. This article presents our experience in the treatment of 547 patients with AK and SK with an erbium:YAG laser.

Patients and methods

A retrospective study of 547 patients treated between 2006 and 2014 was performed. These patients were clinically diagnosed with SK or AK, and were treated in one centre by the same clinician using an erbium:YAG laser (Dualis XS Laser; Fotona, Ljubljana, Slovenia). The laser values are described in Table 1. Most of the patients had more than one lesion. The patients ranged in age from 42 years to 84 years (mean age 68 years). There was a male predominance, with a male to female ratio of 1.9:1. All patients fell into Fitzpatrick skin type I–IV[18].

The diagnosis was based on clinical examination using magnification loupes and a dermatoscope. Of the total 547 patients, 261 (47.7%) were diagnosed with SK and 246 (45.0%) with AK; 40 patients (7.3%) were diagnosed with a suspected malignancy. The latter group was subjected to an incisional biopsy, and t histology confirmed AK with dys ia and no invasion.

Ninety-two percent of the pa ts w treated with topical anaesth or no local anaesthetic and the re ning 8% of patients had treatmen th loc anaesthetic infiltration. ty-six rcent of the patients were trea lesion rected therap 4% rwent d-directed th y I ving areas of laser urfaci The pos eatment follow- r al cluded examinations a , 3 wee 6 months, and 1 year, and patients were followed up for over 5 s. During the recall appointments, pat nts were assessed for lesion removal, redness, scarring, and any other symptoms.

Results

The distribution of patients with AK, SK, and suspected malignancy according to the sites of the lesions are presented in Table 2. The numbers of patients in the AK and SK groups were similar. Table 3 shows the total number of patients who underwent laser ablation, the anatomical distribution of lesions, and the response to the laser therapy. More lesion-directed treatments than field-directed treatments were performed in this series.

The duration of treatment for lesion-directed therapy was on average less than

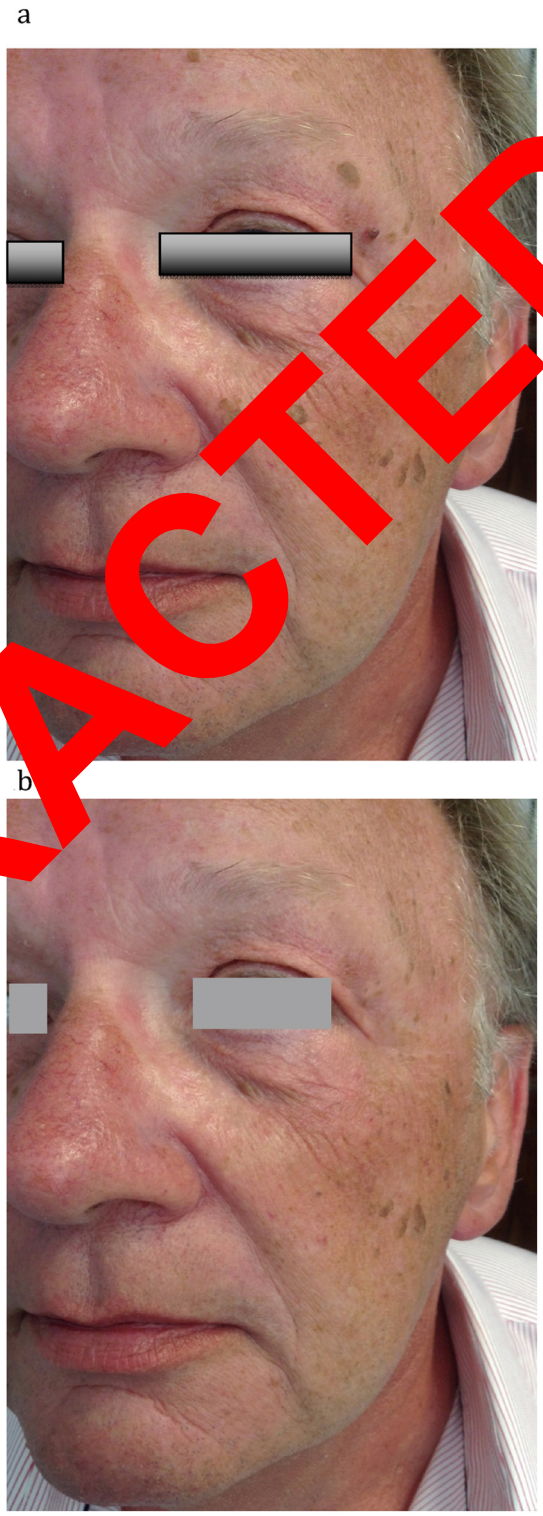

Fig. 1. (a) Multiple seborrhoeic keratoses affecting the left cheek, nasolabial, and eyebrow region. (b) The same patient 6 months after treatment of the seborrhoeic keratoses with the erbium:YAG laser.

90 seconds. Field-directed therapy included resurfacing of the forehead, peri-ocular area, and peri-oral area. The average duration for these procedures, including local anaesthetic infiltration, was 45 minutes. Petechial bleeding was stopped with the topical application of lidocaine and adrenaline soaked swabs. Thus, field-directed treatment takes a longer time to complete.

At 1 week post-surgery, the scabs had dropped off for 80% of the patients, and 93% of patients presented erythema. At 2 weeks post-treatment, the erythema had resolved in 98% of cases. For the remainder of patients, the erythema persisted for another 2 days.

At the 12-month follow-up, six patients presented with recurrence at the same site post laser ablation. All six patients underwent an excision biopsy of the lesions; four were reported as hypertrophic AK with dysplasia and two had micro-invasion.

All patients reported minimal symptoms after the laser treatment, with good to excellent outcomes. Furthermore, none of the patients presented with a loss of pigmentation or persistent redness at the 12-month recall appointment. There was no patient loss during the follow-up period.

Patients with SK had excellent aesthetic outcomes and no recurrence in the treated areas. Moreover, none of the patients had scarring as a result of lesion- or field-directed treatment. Figs 1–3 demonstrate patient cases of lesion- and field-directed treatment, including pre and post laser treatment images.

Discussion

Indications for treatment of AK and SK fall into three categories: (1) aesthetics; (2) pain and other symptoms; (3) the prevention of potential malignant transformation. Although the pathophysiology of AK and SK differ, their treatment remains somewhat similar. Management consists of either lesion-directed or field-directed therapy or a combination of the two.

The location most commonly affected by the lesions in this series was the scalp. Of the 252 patients with lesions on the scalp, 226 (90%) were male and bald.

The rationale behind laser ablation and resurfacing is based on the pathophysiology of SK and AK, the efficacy of depth-directed treatment, and the recovery of tumour suppressive gene p53 post treatment.

The most commonly reported lesion-directed treatment in the dermatology literature is cryotherapy using liquid nitrogen[7]. In spite of its extensive use, there is no widely accepted standardized method of application, thus the recommendation of cryotherapy as a treatment modality is questionable. Although the cost is low, it causes pain and redness, and results in a limited response in cases of hyperkeratotic

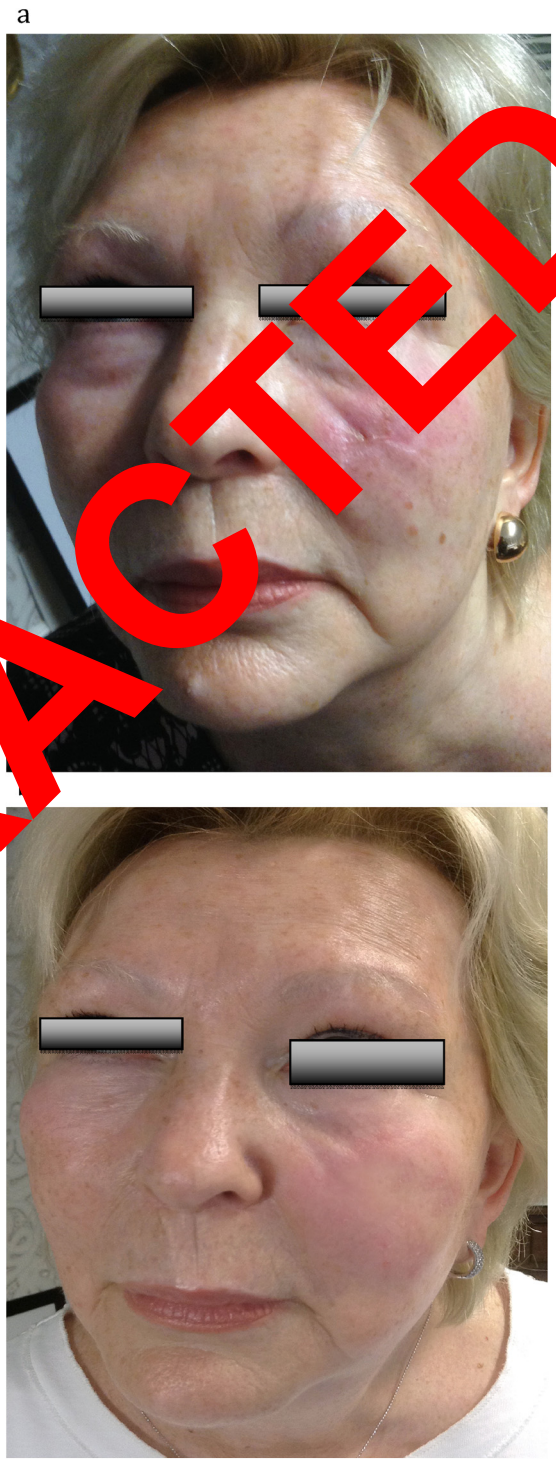

Fig. 2. (a) A patient with a scar following previous excision of squamous cell carcinoma, who developed actinic keratosis around the surgical site; image obtained 2 weeks after erbium:YAG laser ablation. (b) The same patient with actinic keratosis of the left cheek at 6 months after treatment with the erbium:YAG laser.

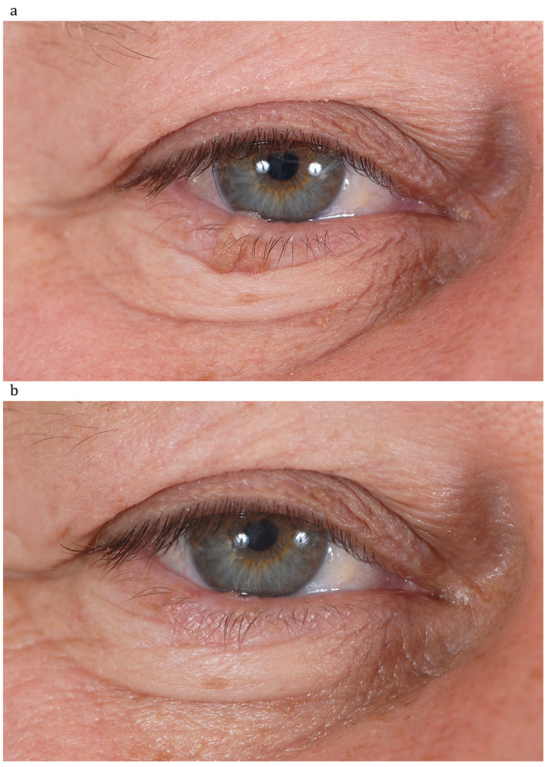

Fig. 3. (a) Seborrhoeic keratosis on the lower eyelid preoperative. (b) The same patient at 3 weeks following laser ablation of the seborrhoeic keratosis on the lower eyelid.

lesions[7]. Furthermore, aggressive therapy can cause hypopigmentation. Other lesion-directed treatments are curettage, shave excision, and formal excision with repair, which are all invasive. In the series presented here, the lesion-directed treatment resulted in complete removal of the lesion in one session. There was no associated scarring, in contrast to formal excision. Thermal injury to the surrounding areas is minimal, thus eliminating excessive patient discomfort and reducing the time to recovery.

The currently available field-directed agents are 5-FU, imiquimod, diclofenac, and ingenol mebutate[9–13]. These agents cause inflammation, vesiculation, scaling, crusting, erosions, photosensitivity, flu-like symptoms, and lymphadenopathy. Furthermore, they require several applications, hence prolonging the treatment time. This was not observed in the series of patients presented here. The desired clinical endpoint was achieved with a single treatment episode and the patients were able to return to normal activities within a week of treatment.

The British Association of Dermatologists (BAD) guidelines do not mention laser treatment as an option and only mention topical treatments such as cryotherapy, 5-FU, imiquimod, diclofenac, and PDT, with curettage being the only interventional treatment.

Laser resurfacing is a frequently used therapeutic modality for improving the appearance of photo-damaged skin, and it has been reported to be successful in the treatment of a number of benign cutaneous lesions[15,16]. Mutations in the tumour suppressor gene p53 are highly associated with cutaneous squamous cell carcinoma and AK. There is evidence of a consistent decrease in p53 immunostaining in the interfollicular epidermis lasting at least 6 months after CO_2 laser resurfacing of photo-damaged skin[4]. Therefore, p53-negative keratin sites should theoretically decrease the risk of malignant progression[14]. The erbium:YAG laser with a wavelength of 2940 mm has 10 to 15 times greater water absorption than the CO_2 laser and is therefore able to ablate tissue more precisely with less residual thermal damage[17,19–21]. It generates a pulse with a duration of 250 to 350 milliseconds, produces 10–40 μm of tissue ablation with each pulse, and results in 2–5 μm zones of residual thermal damage. Thus tissue damage is reduced, there are fewer side effects, and at the same time this laser has similar effects in producing p53-negative keratinized sites post treatment.

In this series, the patients who had resurfacing as field therapy showed no recurrence during the 12-month review period. In the group of patients who underwent lesion-directed treatment, there were six cases of recurrence over the same time period. All underwent formal excision and four were reported as having hypertrophic AK with marked dysplasia and two showed micro-invasion. Therefore the incidence of recurrence with potential malignant transformation and micro-invasion was about 4% in this series. If untreated the possibility of malignancy in this series would therefore be more than 4%. AK are established as direct precursors of squamous cell carcinoma with annual rates of transformation ranging from 0.25% to 20%[2].

Song et al used a fractional CO_2 laser with PDT treatment for AK[22,23]. It is reported that the fractional component allows better penetration for the PDT. The present authors believe that the erbium:YAG laser provides better control for ablation and a shorter healing period, without the need for combination therapy. The outcome is immediate and the recurrence rate, even in lesion-directed treatment, is very low.

This study has limitations. It was a single observer series. Furthermore, it was a retrospective review without randomization or control, with no histological data other than the observation of the clinical outcome during follow-up.

When adopting a treatment, the clinician should base the choice not only on the efficacy of the specific treatment modality, but also on factors such as reduced adverse reactions, good cosmetic outcomes, and good patient response. The erbium:YAG laser seems to incorporate a number of beneficial features, although the initial capital cost needs to be considered.

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Competing interests

None.

Ethical approval

Not required.

Patient consent

Patient consent was obtained.

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References

1. Lee GS, At KJ, Kim JM, Lee ES. A histopathologic study of seborrheic keratosis. *Korean J Dermatol* 1992;**30**:76–80.
2. Marks R, Jolley D, Dovrevitch AP, Selwood TS. The incidence of non-melanocytic skin cancers in an Australian population: results of a five-year prospective study. *Med J Aust* 1989;**150**:475–8.
3. Frost CA, Green AC. Epidemiology of solar keratosis. *Br J Dermatol* 1994;**131**:455–64.
4. Orringer JS, Johnson TM, Kang S, Karimipour DJ, Hammerberg C, Hamilton T, Voorhees JJ, Fisher GJ. Effect of carbon dioxide laser resurfacing on epidermal p53 immunostaining in photodamaged skin. *Arch Dermatol* 2004;**140**:1073–7.
5. Brodsky J. Management of benign skin lesions commonly affecting the face: actinic keratosis, seborrheic keratosis and rosacea. *Curr Opin Otolaryngol Head Neck Surg* 2009;**17**:315–20.
6. Dodds A, Chia A, Shumack S. Actinic keratosis: rationale and management. *Dermatol Ther (Heidelb)* 2014;**4**:11–31.
7. de Berker D, McGregor JM, Mohd Mustapa MF, Exton LS, Hughes BR. British Association of Dermatologists' guidelines for the care of patients with actinic keratosis. *Br J Dermatol* 2017;**2017**(176):20–43.
8. Hufbauer M, Akgul B. Molecular mechanisms of human papillomavirus induced skin carcinogenesis. *Viruses* 2017;**9**. pii: E187.
9. Lebwohl M, Swanson N, Lawrence L, Anderson MD, Melgaard A, Xu Z, Berman B. Ingenol mebutate gel for actinic keratosis. *N Engl J Med* 2012;**366**:1010–9.
10. Klein A, Babilas P, Karrer S, Landthaler M, Szeimies RM. Photodynamic therapy in dermatology: an update 2008. *J Dtsch Dermatol Ges* 2008;**6**:839–45.
11. MacCormack MA. Photodynamic therapy in dermatology: an update on applications and outcomes. *Semin Cutan Med Surg* 2008;**27**:52–62.
12. Goldberg DJ. Photodynamic therapy in skin rejuvenation. *Clin Dermatol* 2008;**26**:608–13.
13. Spelman L, Rubel D, Murell DF, See JA, Hewitt D, Foley P, Salmon R, Kerob D, Pascual T, Shumack S, Fernandez-Pen… Treatment of face and scalp solar … keratosis with daylight mediated … otody… namic therapy is possible throughout the year in Australia: evidenc… clinical and meteorological stud… *Australas J Dermatol* 2016;**57**:24–8.
14. Gupta AK, Paquet M. …work meta-a… sis of the outcome '… ipant com… clearance' in nonimmuno… ssed … ci… pants of … erventions f… kera… tosis: a fo… -up … chrane review. *Br J Dermatol* …;**169**:…
15. Hantash B… S… rt DB, Cooper ZA, …us WE… RJ, Swetter SM. Facial re… cing fo… melanoma skin cancer pr… ylaxis. *Arch Dermatol* …82.
16. Sherry SD, Miles BA, Finn RA. Long-term efficacy of carbon dioxide laser resurfacing for facial actinic keratosis. *J Oral Maxillofac Surg* 2007;**65**:135–9.
17. Riggs K, Keller M, Humphreys TR. Ablative laser resurfacing: high-energy pulsed carbon dioxide and erbium:yttrium–aluminum–garnet. *Clin Dermatol* 2007;**25**:462–73.
18. Sachdeva S. Fitzpatrick skin typing: applications in dermatology. *Indian J Dermatol Venereol Leprol* 2009;**75**:93–6.
19. Jiang SB, Levine VJ, Nehal KS, Baldassano M, Kamino H… A. Er:YAG laser for the trea… of acti… ratosis. *Dermatol Su…* 00;**26**:437–40.
20. Tanzi EL, … TS. Sing… ass carbon dio… versus … ple-pas… :YAG laser … resurfacing: a… n of postoperative wo… healing … side-effect rates. *…rm… Surg* 2003;**29**:80–4.
21. … NB. Fac… esurfacing: an overview. *Op… ch … aryngol Head Neck Surg* 2007;… 0.
22. Tannus Z… fraction resurfacing. *Clin Dermatol* 2007;**25**:480–6.
23. …ng HS, Jung SE, Jang YH, Kang HY, Lee …, Kim YC. Fractional carbon dioxide laser-assisted photodynamic therapy for patients with actinic keratosis. *Photodermatol Photoimmunol Photomed* 2015;**31**:296–301.

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