

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of Grenz rays therapy for inflammatory skin conditions

Grenz rays therapy involves exposing the skin to low-energy, non-penetrative, electromagnetic radiation. It is used in several inflammatory skin conditions (including certain localised forms of eczema and psoriasis), when other therapies have failed. These conditions can severely impair quality of life with effects including redness, itching, blistering and loss of function.

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in March 2007.

Procedure name

- Grenz rays therapy for inflammatory skin conditions

Specialty societies

- British Association of Dermatologists
- Royal College of Radiologists
- Society of Radiographers

Description

Indications

Grenz ray therapy is used for certain benign inflammatory skin conditions refractory to conventional treatment.

Inflammation of the skin is associated with a large number of benign skin conditions, including eczema (synonymous with dermatitis) and psoriasis.

Conditions treated with Grenz rays include localised psoriasis (including scalp and finger nails), chronic palmo-plantar pustulosis, localised endogenous (or constitutional) eczemas including lichen simplex chronicus and hand eczemas, exogenous allergic contact hand eczema when the allergen(s) cannot be adequately avoided, and localised lichen planus.

Eczema is an inflammatory condition in which the skin becomes itchy, painful, red, dry and flaky. Affected areas may weep or bleed. The two main types of eczema are endogenous (for example, atopic eczema) and exogenous (for example, allergic contact and irritant contact eczemas). The main eczemas treated with Grenz rays are lichen simplex chronicus eczema where a small area of skin becomes very thickened and intensely itchy, and eczemas affecting the hands or feet that may cause loss of function.

Psoriasis is a chronic inflammation of the skin, characterised by an accelerated rate of turnover of the top layer of the skin and a dermal inflammation. There are several types. It usually presents as raised red patches of skin covered by silvery scales that may be itchy (plaque psoriasis). It is a chronic progressive condition characterised by flare-ups and periods of remission. Localised scalp psoriasis, hand or foot plaque psoriasis and finger nail psoriasis (of a type where the nail is not excessively thickened) are the main psoriasis indications for Grenz rays.

Chronic palmoplantar pustulosis is thought by many (although there is controversy about this) to be a variant of psoriasis. It is a chronic inflammatory skin condition characterised by crops of yellow pus spots on the palms and soles. The affected areas may be very itchy and can become red, scaly and cracked. The condition tends to run a prolonged course with intermittent exacerbations followed by partial remissions.

Current treatment and alternatives

Treatment depends on the type and severity of the inflammation and its location (for example, ultraviolet (UV) therapy is usually ineffective for treating scalp lesions as the light cannot penetrate the hair in sufficient doses).

Topical treatments for eczema include emollients, steroid creams and ointments, and non-steroid immunomodulators. UVB light therapy and psoralen and UVA (PUVA) light therapy are also used to treat severe eczema that has not responded to other treatment. Systemic treatments for more severe eczema include oral corticosteroids and immunosuppressant medication such as azathioprine, ciclosporin and methotrexate. The lichen simplex chronicus type of eczema is usually treated by potent steroid ointments under occlusion or steroid injections into the affected area. Superficial X-ray treatment has also been used.

Topical treatments for psoriasis include emollients, coal tar, keratolytics (salicylic acid), steroid creams or ointments, dithranol and ointments containing vitamin D or A derivatives. UVB light therapy and psoralen and ultraviolet A (PUVA) light therapy are also used. Systemic treatments include oral tetracyclines, retinoids or immunosuppressants such as methotrexate or ciclosporin. More recent treatments for severe plaque psoriasis that has not

responded to other treatments include subcutaneous injections of the monoclonal antibody agents efalizumab or etanercept.

What the procedure involves

Grenz rays, also known as Bucky rays, are a form of electromagnetic radiation produced at low kilovoltages. The electromagnetic waves are of relatively long wavelength, between the borderlines of ultraviolet rays and X-rays. They have a very low penetrative power, which means that they do not penetrate beneath the dermis of the skin. They are also classified as 'ultrasoft' X-ray radiation. The patient typically lies on a treatment couch and the Grenz rays are administered via the tube of a Grenz ray machine that is directed toward the affected area of skin. A cone may be used to help restrict the exposure to the designated areas and to ensure that the target to skin distance remains constant (approximately 10 to 20 cm). The operator stands about two metres away from the machine while treatment is in progress. Treatment is performed on an outpatient basis and is usually given over a number of sessions, each lasting no more than a few minutes.

Efficacy

Eczema

One randomised controlled trial (RCT) reported that 44% (11/25) of patients considered superficial X-ray treatment to be better than Grenz rays therapy at 3 weeks, in improving the severity of eczema on their hands ($p < 0.05$).¹ The difference was no longer significant at 18 weeks, with 30% (6/20) of patients reporting superficial X-ray to be better and 5% (1/20) patients reporting Grenz rays to be better. A second RCT reported that there was no significant difference between active Grenz ray treatment and placebo, with 89% (16/18) (observer's assessment) and 56% (10/18) (patient's assessment) of patients showing equal improvement 18 weeks after treatment.² In a third RCT, 87% (20/23) patients had a better response with Grenz rays than with placebo 10 weeks after the start of treatment ($p < 0.001$).³

Psoriasis

In one RCT, 88% (14/16) of patients healed completely on the side of the scalp receiving active treatment rather than placebo. No patient showed a side difference favouring placebo.⁴ At 6 months, 21% (3/14) of patients were free from relapse. In a second RCT, 36% (8/22) of patients had complete or slight recovery of nail psoriasis with active Grenz rays therapy, compared with 4% (1/22) patients receiving sham therapy ($p < 0.05$).⁵ In a third RCT, 67% (12/18) of patients reported that active Grenz rays therapy was superior to placebo and 33% (6/18) reported no preference ($p < 0.05$).⁶

Pustulosis palmoplantaris

One RCT reported that 87% (13/15) of patients responded better to Grenz rays therapy than to sham therapy according to clinical evaluation after treatment ($p < 0.01$).⁷ The decrease in disease severity score was described as moderate, however.

Safety

The Specialist Advisers stated that the main safety concern is the potential for induction of skin cancer. Other potential adverse events include erythema, pigmentation and chronic radiation damage to the skin.

Five RCTs reported rates of pigmentation as 0% (0/17 and 0/25), 3% (1/30), 21% (5/24) and 23% (5/22).^{1, 2, 3, 5, 7}

A cancer registry linkage study followed up over 14 000 patients receiving Grenz rays therapy, with a mean follow-up of 15 years, and reported 39 cases of non-melanoma skin cancer, compared with 26.9 cases expected (ratio between observed and expected = 1.45, 95% CI 1.03 to 1.98).⁸

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to Grenz rays therapy for inflammatory skin conditions. Searches were conducted via the following databases, covering the period from their commencement to 13/02/2007: Medline, PreMedline, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches. (See appendix C for details of search strategy.)

The following selection criteria (Table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with inflammatory skin conditions refractory to conventional treatments
Intervention/test	Grenz rays therapy
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on seven RCTs^{1–7} one large case series⁸ and one cohort study.⁹

Other studies considered relevant to the procedure but not included in the main extraction table (table 2) are listed in appendix A.

Existing reviews on this procedure

A Cochrane Review on '*Interventions for chronic palmoplantar pustulosis*' was published in 2006.¹⁰ The review identified one RCT, which is included in table 2.⁷ The authors concluded that there was some evidence of improvement, but not of clearance, in this condition, with Grenz ray therapy.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B details the recommendations made in each piece of guidance listed below.

Interventional procedures

none

Technology appraisals:

Atopic dermatitis (eczema) - topical steroids. *NICE Technology Appraisal Guidance* No. 81 (August 2004). Available from:
<http://guidance.nice.org.uk/TA81/?c=91528>

Pimecrolimus & tacrolimus for atopic dermatitis (Eczema). *NICE Technology Appraisal Guidance* No. 82 (August 2004). Available from:
<http://guidance.nice.org.uk/TA82/?c=91528>

Etanercept and efalizumab for the treatment of adults with psoriasis. *NICE Technology Appraisal Guidance* No.103 (July 2006). Available from:
<http://guidance.nice.org.uk/TA103/?c=91528>

Clinical guidelines:

Atopic eczema in children. *NICE Clinical Guideline* (expected date of issue December 2007). See
<http://guidance.nice.org.uk/page.aspx?o=265279&c=91528> for further information.

Public health

none

Table 2 Summary of key efficacy and safety findings on Grenz rays therapy for inflammatory skin conditions

Abbreviations used: CI, confidence intervals																								
Study details	Key efficacy findings		Key safety findings	Comments																				
Fairris GM (1985)¹ Randomised controlled trial (with active comparator, patient acting as own control) UK Study period: not stated n = 25 patients (50 hands) Population: patients with chronic symmetrical constitutional eczema of the hands resistant to topical therapy • Superficial X-ray = 50% (25/50) • Grenz ray = 50% (25/50) Indications: inclusion and exclusion criteria not stated. Technique: One hand received 100 rad (1 Gy) conventional superficial X-ray, the other 300 rad (3 Gy) Grenz ray (focal skin distance of 30 cm), on three occasions at 21-day intervals. Follow-up: 18 weeks Conflict of interest: none stated	Eczema was graded by the observer according to the following criteria: • Grade 0 = normal skin • Grade 1 = erythema and mild scaling • Grade 2 = erythema, moderate scaling and fissures • Grade 3 = erythema, severe scaling and bleeding fissures • Grade 4 = active pompholyx Mean grade of eczema, as recorded by the observer showed that superficial X-ray therapy was significantly better than Grenz ray therapy at all stages. Patients graded their eczema on a scale of increasing severity from 0 to 10. The mean grade of eczema showed that superficial X-ray therapy was significantly better than Grenz ray therapy at all stages. Patient preference <table><tr><td></td><td>3 weeks</td><td>6 weeks</td><td>12 weeks</td><td>18 weeks</td></tr><tr><td>Grenz ray better than X-ray</td><td>4% (1/25)</td><td>16% (4/25)</td><td>0% (0/23)</td><td>5% (1/20)</td></tr><tr><td>X-ray better than Grenz ray</td><td>44% (11/25)</td><td>56% (14/25)</td><td>61% (14/23)</td><td>30% (6/20)</td></tr><tr><td>Both equal improvement</td><td>52% (13/25)</td><td>28% (7/25)</td><td>39% (9/23)</td><td>65% (13/20)</td></tr></table> p < 0.05 for Grenz ray versus X-ray at 3, 6 and 12 weeks after starting treatment. There was no significant difference at 18 weeks.			3 weeks	6 weeks	12 weeks	18 weeks	Grenz ray better than X-ray	4% (1/25)	16% (4/25)	0% (0/23)	5% (1/20)	X-ray better than Grenz ray	44% (11/25)	56% (14/25)	61% (14/23)	30% (6/20)	Both equal improvement	52% (13/25)	28% (7/25)	39% (9/23)	65% (13/20)	The paper states “there were no side-effects from either therapy and in particular no pigmentation from Grenz ray therapy.”	Patient selection not described. One hand received superficial X-ray treatment and the other received Grenz ray treatment, according to a predetermined random code operated by the radiographer. Patients and observer were blinded to treatment allocation. However, it is not clear whether lack of blinding may have resulted by different machinery and noise properties of the two treatments.
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Abbreviations used: CI, confidence intervals

Study details	Key efficacy findings	Key safety findings	Comments																																																												
Cartwright PH (1987)² Randomised controlled trial (sham controlled, patient acting as own control) UK Study period: not stated n = 30 patients (60 hands) Population: patients with bilateral symmetrical constitutional hand eczema, resistant to previous treatment - Grenz ray therapy = 50% (30/60) - Sham therapy = 50% (30/60) Indications: no inclusion or exclusion criteria were described. Technique: One hand was irradiated with 300 rad (3 Gy) Grenz rays (focal skin distance 30 cm) and the other treated with sham therapy (not described). Treatments were repeated at 21-day intervals for 3 visits. Patients continued to apply tar paste or steroid ointments to both hands throughout the trial. Follow-up: 18 weeks Conflict of interest: none stated	Eczema was graded by the observer according to the following criteria: - Grade 0 = normal skin - Grade 1 = erythema and mild scaling - Grade 2 = erythema, moderate scaling and fissures - Grade 3 = erythema, severe scaling and bleeding fissures - Grade 4 = active pompholyx The patient graded the eczema on a scale of increasing severity from 0 to 10. Observer's assessment <table><tr><td></td><td>3 weeks</td><td>6 weeks</td><td>12 weeks</td><td>18 weeks</td></tr><tr><td>Grenz ray better than placebo</td><td>10% (3/30)</td><td>24% (7/29)</td><td>14% (3/21)</td><td>6% (1/18)</td></tr><tr><td>Placebo better than Grenz ray*</td><td>10% (3/30)</td><td>10% (3/29)</td><td>14% (3/21)</td><td>6% (1/18)</td></tr><tr><td>Both equally improved</td><td>47% (14/30)</td><td>59% (17/29)</td><td>67% (14/21)</td><td>89% (16/18)</td></tr><tr><td>Both equally unimproved</td><td>33% (10/30)</td><td>7% (2/29)</td><td>5% (1/21)</td><td>0% (0/18)</td></tr><tr><td>Total</td><td>30</td><td>29</td><td>21</td><td>18</td></tr></table> Patients' assessment <table><tr><td></td><td>3 weeks</td><td>6 weeks</td><td>12 weeks</td><td>18 weeks</td></tr><tr><td>Grenz ray better than placebo</td><td>33% (10/30)</td><td>38% (11/29)</td><td>29% (6/21)</td><td>28% (5/18)</td></tr><tr><td>Placebo better than Grenz ray*</td><td>23% (7/30)</td><td>28% (8/29)</td><td>33% (7/21)</td><td>6% (1/18)</td></tr><tr><td>Both equally improved</td><td>37% (11/30)</td><td>31% (9/29)</td><td>38% (8/21)</td><td>56% (10/18)</td></tr><tr><td>Both equally unimproved</td><td>7% (2/30)</td><td>3% (1/29)</td><td>0% (0/21)</td><td>11% (2/18)</td></tr><tr><td>Total</td><td>30</td><td>29</td><td>21</td><td>18</td></tr></table> *not significantly different from 'Grenz rays better than placebo' at any time point		3 weeks	6 weeks	12 weeks	18 weeks	Grenz ray better than placebo	10% (3/30)	24% (7/29)	14% (3/21)	6% (1/18)	Placebo better than Grenz ray*	10% (3/30)	10% (3/29)	14% (3/21)	6% (1/18)	Both equally improved	47% (14/30)	59% (17/29)	67% (14/21)	89% (16/18)	Both equally unimproved	33% (10/30)	7% (2/29)	5% (1/21)	0% (0/18)	Total	30	29	21	18		3 weeks	6 weeks	12 weeks	18 weeks	Grenz ray better than placebo	33% (10/30)	38% (11/29)	29% (6/21)	28% (5/18)	Placebo better than Grenz ray*	23% (7/30)	28% (8/29)	33% (7/21)	6% (1/18)	Both equally improved	37% (11/30)	31% (9/29)	38% (8/21)	56% (10/18)	Both equally unimproved	7% (2/30)	3% (1/29)	0% (0/21)	11% (2/18)	Total	30	29	21	18	"One patient developed pigmentation of the hand that had been treated with Grenz rays, but there were no other side-effects of treatment."	Patients and observers were blind to treatment allocation. Sham therapy not described. The paper states that a number of patients did not finish the full 18 weeks because they were unable to attend further, usually because their eczema had improved considerably. The authors state that the improvements in eczema previously resistant to treatment can probably be attributed to greater patient cooperation with closer supervision.
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Lindelöf B (1987)³ Randomised controlled trial (sham controlled, patient acting as own control) Sweden Study period: not stated n = 24 patients (48 hands) Population: patients with chronic symmetrical eczema of the hands, unresponsive to topical steroids - Grenz ray therapy = 50% (24/48) - Sham therapy = 50% (24/48) Indications: chronic symmetrical eczema of the hands that was unresponsive to topical steroids and that had been stable for at least 3 months (13 allergic contact dermatitis, 5 atopic dermatitis, 3 irritant eczema, 2 tylotic eczema and 1 pompholyx). Topical medication was continued unchanged during the trial. Technique: One hand was irradiated with 300 rad (3 Gy) Grenz rays (focal skin distance 10 cm) and the other was treated with sham therapy (apparatus allowed to hum without emitting radiation). Treatments were repeated at 7-day intervals for a total of 6 visits. Patients applied the same topical medication to both hands. Follow-up: 10 weeks after start of treatment Conflict of interest: none stated	The observer made a graded assessment of each hand, assessing erythema, scaling, itching, vesicles, fissures and size of affected area. A 5-grade scale was employed, where 0 denoted absence of symptoms and 4 denoted very severe symptoms. The scores for the symptoms were added together. 5 weeks after start of treatment <table><tr><th></th><th>Grenz rays better</th><th>Placebo better</th><th>No difference</th><th>p value</th></tr><tr><td>Erythema</td><td>38% (9/24)</td><td>12% (3/24)</td><td>50% (12/24)</td><td>NS</td></tr><tr><td>Scaling</td><td>67% (16/24)</td><td>8% (2/24)</td><td>25% (6/24)</td><td>< 0.01</td></tr><tr><td>Fissures</td><td>29% (7/24)</td><td>8% (2/24)</td><td>62% (15/24)</td><td>NS</td></tr><tr><td>Itching</td><td>58% (14/24)</td><td>4% (1/24)</td><td>38% (9/24)</td><td>< 0.01</td></tr><tr><td>Vesicles</td><td>42% (10/24)</td><td>8% (2/24)</td><td>50% (12/24)</td><td>< 0.05</td></tr><tr><td>Size of affected area</td><td>38% (9/24)</td><td>4% (1/24)</td><td>58% (14/24)</td><td>< 0.05</td></tr><tr><td>Total score</td><td>79% (19/24)</td><td>17% (4/24)</td><td>4% (1/24)</td><td>< 0.01</td></tr></table> 10 weeks after start of treatment <table><tr><th></th><th>Grenz rays better</th><th>Placebo better</th><th>No difference</th><th>p value</th></tr><tr><td>Erythema</td><td>48% (11/23)</td><td>4% (1/23)</td><td>48% (11/23)</td><td><0.01</td></tr><tr><td>Scaling</td><td>39% (9/23)</td><td>4% (1/23)</td><td>56% (13/23)</td><td>< 0.05</td></tr><tr><td>Fissures</td><td>35% (8/23)</td><td>4% (1/23)</td><td>61% (14/23)</td><td><0.05</td></tr><tr><td>Itching</td><td>48% (11/23)</td><td>0% (0/23)</td><td>52% (12/23)</td><td>< 0.01</td></tr><tr><td>Vesicles</td><td>43% (10/23)</td><td>0% (0/23)</td><td>56% (13/23)</td><td>< 0.01</td></tr><tr><td>Size of affected area</td><td>43% (10/23)</td><td>4% (1/23)</td><td>52% (12/23)</td><td>< 0.01</td></tr><tr><td>Total score</td><td>87% (20/23)</td><td>4% (1/23)</td><td>9% (2/23)</td><td>< 0.001</td></tr></table> Mean total score at 10 weeks (estimated from figure) = 7.5 for placebo and 4.5 for Grenz ray therapy.		Grenz rays better	Placebo better	No difference	p value	Erythema	38% (9/24)	12% (3/24)	50% (12/24)	NS	Scaling	67% (16/24)	8% (2/24)	25% (6/24)	< 0.01	Fissures	29% (7/24)	8% (2/24)	62% (15/24)	NS	Itching	58% (14/24)	4% (1/24)	38% (9/24)	< 0.01	Vesicles	42% (10/24)	8% (2/24)	50% (12/24)	< 0.05	Size of affected area	38% (9/24)	4% (1/24)	58% (14/24)	< 0.05	Total score	79% (19/24)	17% (4/24)	4% (1/24)	< 0.01		Grenz rays better	Placebo better	No difference	p value	Erythema	48% (11/23)	4% (1/23)	48% (11/23)	<0.01	Scaling	39% (9/23)	4% (1/23)	56% (13/23)	< 0.05	Fissures	35% (8/23)	4% (1/23)	61% (14/23)	<0.05	Itching	48% (11/23)	0% (0/23)	52% (12/23)	< 0.01	Vesicles	43% (10/23)	0% (0/23)	56% (13/23)	< 0.01	Size of affected area	43% (10/23)	4% (1/23)	52% (12/23)	< 0.01	Total score	87% (20/23)	4% (1/23)	9% (2/23)	< 0.001	21% (5/24) of patients showed slight pigmentation of the hand treated with Grenz rays.	Patients and observers were blind to treatment allocation. 4% (1/24) patients were lost to follow-up.
	Grenz rays better	Placebo better	No difference	p value																																																																															
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Abbreviations used: CI, confidence intervals

Study details	Key efficacy findings	Key safety findings	Comments																		
Johannesson A (1985)⁴ Randomised controlled trial (sham controlled, patient acting as own control) Sweden Study period: not stated n = 16 patients Population: patients with symmetrical scalp psoriasis Age range: 27–71 years Duration of disease: 1–44 years Indications: Patients had been untreated for at least 4 weeks before the start of the study. All lesions were located in hair-bearing areas. Technique: Each patient received 4 Gy Grenz rays (focus-skin distance 20 cm) given on 6 occasions at intervals of 1 week. One side of the scalp was given active treatment and the other was treated with placebo (allowing the apparatus to hum without irradiation). No treatments other than topical oils containing salicylic acid were permitted. When greater than 50% difference in disease severity was noted during follow-up, active treatment was then administered to the whole scalp. Follow-up: 6 months Conflict of interest: none stated	Clinical evaluation was performed before Grenz ray therapy and 1 week after the sixth treatment. The observer made a graded assessment of each side of the scalp, assessing erythema, scaling, itching and size of affected area. A 5-grade scale was employed, where 0 denoted absence of symptoms and 4 denoted very severe symptoms. Patients estimated itching using a visual analogue scale: the observer converted the score to a 5-grade scale. The scores for the symptoms were added together. <table><tr><th>Severity score</th><th>Before treatment</th><th>After treatment</th></tr><tr><td>0 – 2</td><td>0</td><td>14</td></tr><tr><td>3 – 5</td><td>0</td><td>1</td></tr><tr><td>6 – 8</td><td>3</td><td>0</td></tr><tr><td>9 – 11</td><td>5</td><td>1</td></tr><tr><td>12 – 16</td><td>8</td><td>0</td></tr></table> 87.5% (14/16) patients healed completely on the half of the scalp receiving active treatment. No one showed a side difference favouring placebo. Sequential analysis showed that treatment with Grenz rays was significantly better than placebo (p < 0.0001). After the last treatment, each patient was asked to contact the authors when relapse occurred on the first healed side. (Relapse was defined as the need for treatment more active than the usual scalp and hair wash twice a week). 64% (9/14) patients were still free from relapse 3 months after treatment. 21% (3/14) patients were still free from relapse at 6 months after treatment.	Severity score	Before treatment	After treatment	0 – 2	0	14	3 – 5	0	1	6 – 8	3	0	9 – 11	5	1	12 – 16	8	0	No safety data were reported in the paper.	Patient selection not described. Active or placebo treatment was administered according to a randomised predetermined code. The patients and evaluating doctors were blinded to treatment allocation. When the patient and the nurse giving the treatment noted a profound difference between the two sides, a clinical evaluation was made. In all patients a score difference of at least 50% was noted between the two sides and, at this point, active treatment was given to the whole scalp. When the trial was completed, the irradiated side was identified and the results were analysed sequentially.
Severity score	Before treatment	After treatment																			
0 – 2	0	14																			
3 – 5	0	1																			
6 – 8	3	0																			
9 – 11	5	1																			
12 – 16	8	0																			

Abbreviations used: CI, confidence intervals

Study details	Key efficacy findings	Key safety findings	Comments
Lindelöf B (1989)⁵ Randomised controlled trial (sham controlled, patient acting as own control) Sweden Study period: not stated n = 24 patients (48 hands) Population: patients with psoriasis of the nails of both hands - Grenz ray therapy = 50% (24/48) - Sham therapy = 50% (24/48) Age range: 29–75 years Duration of disease: 1–15 years Indications: psoriasis of the nails of both hands, untreated for at least 6 months before the start of the study. The psoriatic nails of the patients had various degrees of severity, ranging from nails of normal thickness with pits to very thickened hyperkeratotic nails. Technique: Treatment parameters were: 10 kV, focus skin distance 10 cm. The treatment was given at weekly intervals for a total of 10 sessions. One hand was irradiated with Grenz rays and the other treated with sham therapy (apparatus allowed to hum without emitting radiation). Follow-up: 6 months Conflict of interest: none stated	Clinical evaluation after 10th treatment session Almost complete recovery - Grenz rays = 4% (1/22) - Sham = 0% (0/22) Slight improvement - Grenz rays = 32% (7/22) - Sham = 4% (1/22) No improvement - Grenz rays = 64% (14/22) - Sham = 95% (21/22) $p < 0.05$ All the nails that responded were of normal thickness. None of the hyperkeratotic nails responded. Six months after treatment, the treated psoriatic nails of 2 patients had improved moderately and the nails of 2 patients had become slightly worse. The nails of the remaining 18 patients were unchanged.	23% (5/22) of patients showed slight pigmentation of the Grenz-ray-treated nail fold. “No other local or systemic adverse reactions were noted.”	Patients and the evaluating doctor were blind to treatment allocation. After the initial 10 sessions, active treatment was given to the former placebo-treated hand. Two patients failed to participate in the study because of illness in their families.

Abbreviations used: CI, confidence intervals

Study details	Key efficacy findings	Key safety findings	Comments												
Brodersen (1981)⁶ Randomised controlled trial (sham controlled, patient acting as own control) Denmark Study period: not stated n = 20 patients (40 sides of the body) Population: patients with symmetrical psoriasis - Grenz ray therapy and topical steroids = 50% (20/40) - Sham irradiation and topical steroids = 50% (20/40) Indications: inclusion criteria were symmetrical psoriasis and age 20–60 years. Exclusion criteria were guttate psoriasis, recent Grenz ray treatment (3 months), pregnancy. Technique: Voltage = 12 kV. The treatment was given at weekly intervals for a total of 3 sessions. One side was irradiated with Grenz rays and the other treated with sham therapy (apparatus allowed to hum without emitting radiation). All patients used steroid ointments, applied twice a day throughout the study to lesions on both sides. Follow-up: 4 weeks Conflict of interest: none stated	Effect of Grenz rays on psoriasis treated with local steroids (patient preference) <table><tr><td></td><td>2 weeks</td><td>4 weeks</td></tr><tr><td>Grenz rays superior to placebo</td><td>10</td><td>12</td></tr><tr><td>Placebo superior to Grenz rays</td><td>0</td><td>0</td></tr><tr><td>No side difference</td><td>10</td><td>6</td></tr></table> Sequential analysis showed that treatment with Grenz rays and local steroids was significantly better than local steroids alone (p < 0.05).		2 weeks	4 weeks	Grenz rays superior to placebo	10	12	Placebo superior to Grenz rays	0	0	No side difference	10	6	No safety data were presented.	Treatment allocation was done by drawing lots: even numbers indicated Grenz ray treatment on the right-side lesions and uneven numbers indicated treatment on the left-side lesions. The patient and the evaluating doctor were blind to treatment allocation. 10% (2/20) patients were lost to follow-up.
	2 weeks	4 weeks													
Grenz rays superior to placebo	10	12													
Placebo superior to Grenz rays	0	0													
No side difference	10	6													

Abbreviations used: CI, confidence intervals

Study details	Key efficacy findings	Key safety findings	Comments
Lindelöf B (1990)⁷ Randomised controlled trial (sham controlled, patient acting as own control) Sweden Study period: not stated n = 17 patients (34 hands and/or feet) Population: patients with pustulosis palmoplantaris - Grenz ray therapy = 50% (17/34) - Placebo therapy = 50% (17/34) Median age: 54 years (range 26–84) Median duration of disease: 3 years (range 0.5–35) Indications: moderate to severe pustulosis palmoplantaris untreated for at least 3 weeks before the start of the study, except for 2% salicylic acid in petroleum. Patients were encouraged to use this emollient throughout the study but no other treatments were allowed. Nine patients had lesions both on feet and palms and 8 patients had lesions only on feet. Technique: Treatment parameters were: 10 kV, focus skin distance 10 cm. 4 Gy Grenz rays given on 6 occasions at intervals of 1 week. One hand and/or foot was irradiated with Grenz rays and the other with sham therapy (apparatus allowed to hum without emitting radiation). Follow-up: 6 weeks after treatment Conflict of interest: none stated	The observer assessed erythema, scaling, itching and size of affected area on a 5-grade scale, where 0 denoted absence of symptoms and 4 denoted very severe symptoms. Patients estimated itching using a visual analogue scale; the observer converted the score to a 5-grade scale. The scores for the symptoms were added together. Clinical evaluation after treatment - Grenz rays better than placebo = 87% (13/15) - Placebo better than Grenz rays = 7% (1/15), $p < 0.01$ - No difference = 7% (1/15) The mean total scores were lower on the hands and/or feet receiving Grenz rays than on those receiving placebo at 6 weeks. However, the decrease in score after treatment was moderate. (From figure in paper, score for placebo = approximately 15 and score for active treatment = approximately 11.)	“No local or systemic adverse reactions were noted. Particularly, no pigmentation of the soles or palms was observed.”	The patient and the evaluating doctor were blind to treatment allocation. After the initial 6 sessions, active treatment was given to the lesions of the former placebo-treated side. The side first treated was followed up. Two patients failed to participate throughout the study, 1 because of a severe flare up reaction of psoriasis on other parts of the body and 1 because of illness. 11 patients also received treatment on the previously placebo-treated side and 4 patients withdrew after the initial treatment period.

Abbreviations used: CI, confidence intervals

Study details	Key efficacy findings	Key safety findings	Comments
Lindelöf B (1986)⁸ Case series (cancer registry linkage study) Sweden Study period: 1949–1975 n = 14,140 patients Population: patients receiving therapeutic doses of Grenz rays for the treatment of benign skin disorders such as chronic eczema, psoriasis and warts. Male = 54% (n = 7615) Mean age = 40.8 years (range 1–90) Indications: inclusion and exclusion criteria not stated. Technique: Treatment parameters were: 10–11kV, focus skin distance 10–20 cm, beryllium window. The standard regimen was one treatment per week for 4–6 weeks. No area of skin should be subjected to > 10,000 rad (100 Gy) in a lifetime. Mean follow-up: 15 years Conflict of interest: none stated	No efficacy data were presented.	19 cases of melanoma were observed, vs 17.8 expected (ratio between observed and expected = 1.07) 39 cases of skin tumours excluding melanomas were observed, vs 26.9 expected (ratio between observed and expected = 1.45, 95% CI 1.03 to 1.98) For the lower leg, 10 cases of malignant skin tumours (excluding melanoma) were observed, vs 1.6 were expected (ratio between observed and expected = 6.00, 95% CI 3.00 to 11.00) 8 patients with non-melanoma skin tumours had received Grenz ray therapy at the site of the tumour; 6 of these patients had also received treatment with other carcinogens such as arsenic, conventional X-rays, ultraviolet light or tars. No malignancies were found in the 481 patients who had received an accumulated dose of Grenz rays $\geq$ 10,000 rad ($\geq$ 100 Gy) on the same area.	During the study period, a total of 14237 patients were treated with therapeutic doses of Grenz rays for benign skin disorders such as chronic eczema, psoriasis and warts; 97 (< 1 %) of these patients could not be followed up. The authors noted that many patients had received considerably higher doses than recommended; 481 patients had received a total high dose of Grenz rays $\geq$ 10,000 rad ($\geq$ 100 Gy). The frequency of other risk factors such as exposure to arsenic and ultraviolet radiation in this population made it difficult to verify whether treatment with Grenz rays is an independent carcinogenic factor. The first five years after first Grenz ray treatment were excluded from analysis.

Abbreviations used: CI, confidence intervals

Study details	Key efficacy findings	Key safety findings	Comments
Frentz (1989)⁹ Cohort study Denmark Study period: 1976–1985 n = 82 patients Population: patients with non-melanoma skin cancer of the scalp and neck Distribution of carcinogenic factors: • UV-related = 24% • Nevi = 11% • Grenz rays = 2% • X-ray = 1% • Tar = 1% • Scarring = 1% • Combined = 12% • Unknown = 46% 15% (12/82) of patients had previous exposure to Grenz ray therapy: • 1 man, 11 women • Age range: 40–76 years • Skin disorder: 8 patients had psoriasis and 4 had pityriasis rosea • Tumour type: 11 basal cell carcinoma, 1 squamous cell carcinoma; 8 patients had multiple skin cancers. • Dose administered to tumour site ranged from > 14 to > 124 Gy. Four were just described as 'high'. Conflict of interest: none stated	No efficacy data were presented.	Patients previously exposed to Grenz ray therapy (n = 12) Presumed latency period (between exposure and skin cancer diagnosis) ranged from 20 to 36 years. The presumed latency period was unknown for 4 patients. 83% (10/12) of patients had been exposed to at least one additional relevant skin carcinogen (thorium, tar, arsenic or UV). In 2 patients with multiple basal cell carcinomas on previously irradiated scalp, no skin carcinogen other than exposure to Grenz rays could be implicated.	The authors conclude that different individuals may have different sensitivity to ionizing radiation with regard to development of cancer. The authors note that the hyperproliferative skin disorder for which the treatment was given may predispose to skin cancer. The ratio of men to women in the 82 patients with non-melanoma scalp cancers was 1.1. Women were significantly overrepresented in these cases of Grenz-ray related scalp cancers.

Validity and generalisability of the studies

- All the RCTs are small, with little or no follow-up. None of the RCTs has a long enough follow-up to assess the potential risk of induction of skin cancer.
- Some patients treated with Grenz ray therapy will also have had other potentially carcinogenic treatments, such as tar and UV light, which makes it hard to assess the carcinogenic risk of Grenz ray therapy.
- Different treatment parameters, such as number of doses and dosing intervals, were used in different studies.
- One study included children⁸ and five studies included only adults.^{4,5,6,7,9} Three studies did not specify the ages of the patients.^{1,2,3}
- In two studies, topical treatments (including steroids) were continued unchanged during the study. It is likely that there may be better treatment compliance for local treatments while patients are under medical supervision within a trial, which may enable improvements in previously refractory conditions, even with sham therapy.^{2,3}
- Most of the presented evidence relates to two Scandinavian countries.

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

Dr R Dawe, Mr A Flynn, Ms T Gilleece, Dr S Morris, Dr H Smedley

- Three Specialist Advisers described the procedure as established practice and no longer new. They all stated that its use in the UK had been superseded by other therapies. One Specialist Adviser considered that if the procedure is to be used again in the UK, it should be regarded as novel and of uncertain safety and efficacy.
- Two Specialist Advisers stated that the main indication for Grenz ray therapy is when no appropriate standard practice alternative is available in the UK (because alternatives have not worked or are not indicated for an individual). Two Specialist Advisers described appropriate comparators to include topical steroids, vitamin D analogues, retinoid applications, UVB, UVA, PUVA, methotrexate and cyclosporin. Superficial radiotherapy may be used for severe palmer plantar psoriasis.
- Patient selection is important.
- Grenz rays therapy is used more widely in other countries, including Sweden and Denmark.
- Potential adverse events include non-melanoma skin cancer, erythema, pigmentation of the skin, and chronic radiation damage to the skin.
- One Specialist Adviser noted that other treatments for these conditions are also carcinogenic.
- Uncertainty remains about aspects such as optimal doses, number of exposures, dosing intervals and other aspects of treatment methodology.

- The potential impact of this procedure on the NHS is minor, in terms of numbers of patients eligible for treatment and use of resources.

Issues for consideration by IPAC

- Grenz ray therapy has been in use since the 1920s and is still widely used in some countries other than the UK. It has not been used in the UK since the 1980s.

References

1. Fairris GM, Jones DH, Mack DP et al. (1985) Conventional superficial X-ray versus Grenz ray therapy in the treatment of constitutional eczema of the hands. *British Journal of Dermatology* 112: 339–41.
2. Cartwright PH, Rowell NR. (1987) Comparison of Grenz rays versus placebo in the treatment of hand eczema. *British Journal of Dermatology* 117: 73–76.
3. Lindelöf B, Wrangsjö K, Lidén S. (1987) A double-blind study of Grenz ray therapy in chronic eczema of the hands. *British Journal of Dermatology* 117: 77–80.
4. Johannesson A, Lindelöf B. (1985) The effect of grenz rays on psoriasis lesions of the scalp: a double blind bilateral trial. *Photodermatology* 2: 388–91.
5. Lindelöf B. (1989) Psoriasis of the nails treated with Grenz rays: a double-blind bilateral trial. *Acta Dermato-Venereologica* 69: 80–2.
6. Brodersen I, Reymann F. (1981) Effect of Grenz rays on psoriasis treated with local corticosteroids. *Dermatologica* 162: 327–9.
7. Lindelöf B, Beitner H. (1990) The effect of Grenz ray therapy on pustulosis palmoplantaris. *Acta Dermato-Venereologica* 70: 529–31.
8. Lindelöf B, Eklund G. (1986) Incidence of malignant skin tumours in 14140 patients after Grenz ray treatment for benign skin disorders. *Archives of Dermatology* 122: 1391–5.
9. Frentz G, Sørensen JL, Flod K. (1989) Non melanoma skin cancer of the scalp. *Acta Dermato-Venereologica* 69: 142–6.
10. Marsland AM, Chalmers RJG, Hollis S et al. (2006) Interventions for chronic palmoplantar pustulosis. *Cochrane Database of Systematic Reviews* Issue 1. Art. No.: CD001433. DOI: 10.1002/14651858.CD001433.pub2.

Appendix A: Additional papers on Grenz rays therapy for inflammatory skin conditions not included in summary table 2

The following table outlines studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article title	Number of patients	Direction of conclusions	Reasons for non-inclusion in Table 2
Dabski K, Stoll HL. (1986) Skin cancer caused by Grenz rays. <i>Journal of Surgical Oncology</i> 31: 87–93.	n = 1	Patient with 5 squamous cell carcinomas after 16-year period of repeated Grenz irradiations to psoriasis. Estimated cumulative dose was approximately 3000 rad to each treated area.	Case report
Ek L, Lindelof B, Liden S. (1989) The duration of Grenz ray-induced suppression of allergic contact dermatitis and its correlation with the density of Langerhans cells in human epidermis. <i>Clinical & Experimental Dermatology</i> 14: 206–9.	n = 28	Patch test reactions for nickel were initially suppressed and Langerhans cell density was decreased. The effect of Grenz rays on eczematous reactions extended to a maximum of 3 weeks.	Small case series
Frentz G. (1989) Grenz-ray induced nonmelanoma skin cancer. <i>Journal of the American Academy of Dermatology</i> 21: 475–8.	n = 28	In 28 patients, non-melanoma skin cancers developed in areas previously exposed to Grenz rays. In 17 patients, no other relevant carcinogenic exposure could be identified. Women were more often affected than men and most of the tumours were basal cell carcinomas. Median latency time = 18 years. "Grenz rays are capable of causing skin cancer, but only in those persons who are abnormally sensitive to X-rays"	Small case series
Johannesson A, Lindelof B. (1987) Additional effect of Grenz rays on psoriasis lesions of the scalp treated with topical corticosteroids. <i>Dermatologica</i> 175: 290–2.	n = 17	RCT Combination of Grenz ray treatment and topical steroid showed a faster clearing than topical steroid alone.	The focus of the study was to clarify whether Grenz rays give any additional therapeutic advantage to treatment with topical corticosteroids.
Lindelof B, Johannesson A (1988) Psoriasis of the scalp treated with Grenz rays or topical corticosteroid combined with Grenz rays. A comparative randomised trial. <i>British Journal of Dermatology</i> 119: 241–4.	n = 40	RCT 84% (16/19) of patients in Grenz ray group and 72% (13/18) patients in Grenz ray plus corticosteroid group healed. "Grenz ray therapy is a useful treatment modality for scalp psoriasis, but the addition of a topical corticosteroid has only a minor effect"	The focus of the study was to assess the effect of corticosteroid as an adjunct to Grenz ray therapy.

Article title	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in Table 2
Lindelof B, Johannesson A. (1991) Treatment of scalp psoriasis with topical selenium sulphide alone or in combination with Grenz rays. <i>Journal of Dermatological Treatment</i> 2: 47–9.	n = 52	RCT There may be a longer remission time with selenium sulphide shampoo in combination with Grenz rays compared with placebo shampoo and Grenz rays, but the difference is not statistically significant.	The focus of the study is to test efficacy of selenium sulphide rather than Grenz rays.
Mortensen AC, Kjeldsen H. (1987) Carcinomas following Grenz ray treatment of benign dermatoses. <i>Acta Dermato-Venereologica</i> 67: 523–5.	n = 5	5 cases of carcinoma occurring in skin on sites previously treated with Grenz ray therapy. Doses between 10,000 rad (100 Gy) and 29,300 rad (293 Gy) plus one described as 'very extensive'. None of the patients had been exposed to other known carcinogens.	Small case series
Yoshizawa K, Kakinuma H. (1997) Verrucous trichilemmal tumour arising on chronic grenz ray dermatitis. <i>European Journal of Dermatology</i> 7: 589–92.	n = 1	Patient developed at least two verrucous trichilemmal tumours in an area of chronic radiodermatitis caused by irradiation with Grenz rays administered for psoriasis 20 years earlier.	Case report
Zachariae H, Zachariae R, Blomqvist K et al. (2001) Treatment of psoriasis in the Nordic countries: a questionnaire survey from 5739 members of the psoriasis associations data from the Nordic Quality of Life Study. <i>Acta Dermato-Venereologica</i> 81: 116–21.	n = 5739 patients with psoriasis	24% of all psoriasis patients had been treated with Grenz rays; 5% had been given Grenz rays therapy within the last week. 70% of all Danish patients with psoriasis had previously been treated with Grenz rays (14% within the last week).	Study focuses on different treatment regimens in Nordic countries.

Appendix B: Related published NICE guidance for Grenz rays therapy for inflammatory skin conditions

Guidance programme	Recommendation
Interventional procedures	None applicable
Technology appraisals	<i>Atopic dermatitis (eczema)- topical steroids. NICE Technology Appraisal Guidance No. 81 (2004)</i> 1.1 It is recommended that topical corticosteroids for atopic eczema should be prescribed for application only once or twice daily. 1.2 It is recommended that where more than one alternative topical corticosteroid is considered clinically appropriate within a potency class, the drug with the lowest acquisition cost should be prescribed, taking into account pack size and frequency of application. <i>Pimecrolimus & tacrolimus for atopic dermatitis (eczema). NICE Technology Appraisal Guidance No. 82 (2004)</i> 1.1 Topical tacrolimus and pimecrolimus are not recommended for the treatment of mild atopic eczema or as first-line treatments for atopic eczema of any severity. 1.2 Topical tacrolimus is recommended, within its licensed indications, as an option for the second-line treatment of moderate to severe atopic eczema in adults and children aged 2 years and older that has not been controlled by topical corticosteroids (see Section 1.4), where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy. 1.3 Pimecrolimus is recommended, within its licensed indications, as an option for the second-line treatment of moderate atopic eczema on the face and neck in children aged 2 to 16 years that has not been controlled by topical corticosteroids (see Section 1.4), where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.

	1.4 For the purposes of this guidance, atopic eczema that has not been controlled by topical corticosteroids refers to disease that has not shown a satisfactory clinical response to adequate use of the maximum strength and potency that is appropriate for the patient's age and the area being treated. 1.5 It is recommended that treatment with tacrolimus or pimecrolimus be initiated only by physicians (including general practitioners) with a special interest and experience in dermatology, and only after careful discussion with the patient about the potential risks and benefits of all appropriate second-line treatment options. <i>Etanercept and efalizumab for the treatment of adults with psoriasis. NICE Technology Appraisal Guidance No. 103 (2006)</i> 1.1 Etanercept, within its licensed indications, administered at a dose not exceeding 25 mg twice weekly is recommended for the treatment of adults with plaque psoriasis only when the following criteria are met. • The disease is severe as defined by a total Psoriasis Area Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10. • The psoriasis has failed to respond to standard systemic therapies including ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet radiation); or the person is intolerant to, or has a contraindication to, these treatments. 1.2 Etanercept treatment should be discontinued in patients whose psoriasis has not responded adequately at 12 weeks. Further treatment cycles are not recommended in these patients. An adequate response is defined as either: • a 75% reduction in the PASI score from when treatment started (PASI 75) or • a 50% reduction in the PASI score (PASI 50) and a five-point reduction in DLQI from when treatment started.
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	1.3 Efalizumab, within its licensed indications, is recommended for the treatment of adults with plaque psoriasis under the circumstances detailed in section 1.1 only if their psoriasis has failed to respond to etanercept or they are shown to be intolerant of, or have contraindications to, treatment with etanercept. 1.4 Further treatment with efalizumab is not recommended in patients unless their psoriasis has responded adequately at 12 weeks as defined in section 1.2. 1.5 It is recommended that the use of etanercept and efalizumab for psoriasis should be initiated and supervised only by specialist physicians experienced in the diagnosis and treatment of psoriasis. If a person has both psoriasis and psoriatic arthritis their treatment should be managed by collaboration between a rheumatologist and a dermatologist. 1.6 Patients who have begun a course of treatment with efalizumab at the date of publication of this guidance should have the option of continuing to receive treatment until the patients and their clinicians consider it is appropriate to stop.
Clinical guidelines	<i>Atopic eczema in children</i>. NICE Clinical Guideline (expected date of issue December 2007). Grenz rays therapy is not included within the scope of the guideline.
Public health	None applicable

Appendix C: Literature search for Grenz rays therapy for inflammatory skin conditions

IP: 394 Grenz ray therapy for inflammatory skin conditions		
Database	Date searched	Version searched
Cochrane Library	13/02/07	2007, Issue 1
CRD databases (DARE & HTA)	13/02/07	2007, Issue 1
Embase	13/02/07	1980 to 2007 Week 06
Medline	13/02/07	1950 to January Week 5 2007
Premedline	13/02/07	February 13, 2007
CINAHL	13/02/07	1982 to February Week 1 2007
British Library Inside Conferences	14/02/07	-
NRR	14/02/07	2007 Issue 1
Controlled Trials Registry	14/02/07	-

Search strategy used in Medline

The search strategy was adapted for use in the databases above

1	((grenz or bucky or bucki or border) adj3 ray\$).tw.
2	(ultra-soft adj3 (radiation or x-ray\$ or x-radiation)).tw.
3	(ultrasoft adj3 (radiation or x-ray\$ or x-radiation)).tw.
4	(ultra adj3 soft adj3 (radiation or x-ray\$ or x-radiation)).tw.
5	(low adj3 (energy or kilovoltage) adj3 x-ray\$).tw.
6	(soft adj3 roentgen\$).tw.
7	(infra adj3 roentgen\$).tw.
8	(roentgen\$ adj3 ray\$).tw.
9	(x-ray\$ adj3 therap\$).tw.
10	exp X-Rays/
11	exp x-ray therapy/
12	or/1-11
13	(inflam\$ adj3 dermat\$).tw.
14	dermatitis.tw.
15	eczema\$.tw.

16	psoriasis.tw.
17	(papulosquamous adj3 (disease or disorder\$)).tw.
18	(skin adj3 disorder\$).tw.
19	(hives or urticaria).tw.
20	rosacea.tw.
21	(pyoderma adj3 gangrenosum).tw.
22	acne.tw.
23	((lyell's or stevens) adj3 syndrome).tw.
24	(epidermal adj3 necrolysis).tw.
25	((palmar or plantar or palmar-plantar or palmoplantar) adj3 (dermatos\$ or erythema or pustulosis)).tw.
26	exp Dermatitis/
27	exp Eczema/
28	exp Psoriasis/
29	exp Urticaria/
30	exp Rosacea/
31	exp Acne Vulgaris/
32	exp Epidermal Necrolysis, Toxic/
33	exp Hand Dermatoses/
34	exp Foot Dermatoses/
35	or/13-34
36	12 and 35