

Grenz Ray Therapy in the New Millennium: Still a Valid Treatment Option?

Jennifer A. Warner and Ponciano D. Cruz Jr

Grenz ray therapy has declined in the United States during the past several decades with respect to availability, use, and resident training. However, it remains a simple, affordable, and effective option for managing several refractory dermatoses, especially psoriasis, hand eczema, and allergic contact dermatitis. Though high-dose grenz irradiation has been associated with the development of nonmelanoma skin cancers, grenz ray therapy is considered a safe treatment modality when administered according to the guidelines recommended herein. We review the value of grenz irradiation in contemporary dermatology.

GRENZ RAY THERAPY, once a mainstay treatment option for a variety of skin disorders, may be considered relatively obsolete, having been displaced in the past quarter century by phototherapy and immunosuppressive medications. While little has been published in the last three decades of American literature regarding grenz radiation, practitioners with access to grenz machines continue to find benefits in employing this safe, simple, and effective modality in treating patients with inflammatory skin conditions, especially those refractory to conventional therapy. In this review, we reevaluate published data and our current experience on the efficacy and safety of grenz ray therapy, reassessing its role and value in the context of modern dermatologic practice.

History and Mechanism

In 1923, Gustav Bucky constructed an apparatus that produced ultrasoft x-rays that he coined “grenz rays.” Bucky derived “grenz” from the German word for “border” because he believed these ultrasoft rays had properties interfacing between conventional x-rays and ultraviolet radiation.¹ Grenz rays (also known as Bucky

rays) emit electromagnetic radiation of very low energy in wavelengths between 0.007 nm and 0.4 nm.²

Grenz rays are subdivided into three levels of intensity based on their half-value layer (HVL), defined as the thickness of a given metal (usually aluminum) required to reduce the intensity of the original beam by 50%. “Soft” grenz rays are least penetrating and have an HVL of up to 0.02 mm aluminum (Al); “medium” grenz rays have an HVL of 0.023 to 0.029 mm Al; and “hard” grenz rays are most penetrating, having an HVL of 0.030 to 0.036 mm Al.³ The unit of tissue dosage used with grenz rays is the gray (Gy): 1 Gy is equal to 100 rads, which equal 1 joule per kilogram (1 J/kg).⁴

The administration of grenz radiation is a simple office-based outpatient procedure that takes only a few minutes per treatment session. The patient usually lies on her or his back on a treatment table, and the grenz rays are directed toward the affected area of skin at a distance of 10 to 20 cm, with or without the use of a cone to help restrict the area of exposure.⁵

Grenz rays are almost entirely absorbed within the first 2 mm of the skin, and 50% of the energy is taken up by the first 0.5 mm.⁴ The epidermis varies in thickness from 0.045 to 1.4 mm; hair roots and the vasculature lie at depths of 2 to 3 mm. Thus, the physiologic effects of grenz rays are limited predominantly to the epidermis and superficial capillaries.⁶ This shallow depth of absorption can be an advantage, sparing deeper parts of hair follicles, sebaceous and sweat glands, eyes, and gonads from the direct effects of grenz rays.⁴ Following the same line of argument, grenz rays are expected to have little or no direct benefit on inflammatory processes involving the dermis and subcutaneous tissue, yet such limitation is not always consistent with practical experience.⁷ Thus, cases of deeper

From The Johns Hopkins University School of Medicine; the Department of Dermatology, The University of Texas Southwestern Medical Center, Dallas, TX; and the Section of Dermatology (Medical Services), Dallas Veterans Affairs Medical Center, Dallas, TX.

Address reprint requests to Ponciano D. Cruz, Jr, MD, Dermatology G4.234, The University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390-9069. E-mail: Ponciano.cruz@utsouthwestern.edu

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inflammatory skin disease improved by grenz irradiation may represent indirect effects (eg, grenz ray–induced cytokine secretion by keratinocytes or Langerhans' cells).

Grenz rays are absorbed predominantly through a photoelectric effect. Each low-energy photon is small and is absorbed within one cell, but the combined effect of thousands of photoelectron collisions leads to the production of large numbers of ionized and excited molecules that combine with other molecules or free radicals to form new structures with unpredictable biologic effects.⁸

Mechanistically, grenz rays are thought to work by modulating immunologic pathways, including those originating from epidermal Langerhans' cells (LCs) and keratinocytes. A consistent difference between grenz-irradiated and unirradiated human skin is a reduction in the number of LCs within the epidermis.^{9,10} The remaining LCs appear normal, and there is no apparent morphologic damage on the stratum corneum, keratinocytes, and other epidermal cells.⁹ Grenz ray treatment has been shown to suppress the elicitation of allergic contact dermatitis (ACD) from nickel in sensitized individuals, which may or may not be related to the reduction in the number of epidermal LCs.¹¹ By contrast, grenz ray treatment has little effect on irritant contact

dermatitis (ICD) despite the same degree of reduction in epidermal LCs.¹² Radiobiologic mechanisms for the antiinflammatory effects of low-dose radiation therapy have begun to attract study with modern techniques. Using several in vitro models, recent investigators revealed that low-dose ionizing radiation (single fractions below 1.0 Gy and total dose below 12 Gy) reduces inflammation by a variety of mechanisms, in particular, (1) the modulation of cytokine and adhesion molecule expression on activated endothelial cells and leukocytes and (2) the alteration of nitric oxide production and oxidative burst in activated macrophages and native granulocytes.¹³ Further studies may reveal that identical or similar mechanisms are involved in the antiinflammatory effects of grenz ray therapy.

Efficacy

According to expert opinion, grenz ray therapy can be used effectively in the treatment of psoriasis, chronic eczemas, lichen simplex chronicus, and pruritus ani.¹⁴ Support for the efficacy of grenz ray treatment in cases of psoriasis and chronic eczemas is provided by several randomized controlled clinical trials (Tables 1 and 2) but is limited

Table 1. Grenz Ray Therapy in Psoriasis

Study	Condition	Study Design	Key Results	Conclusions
Harber (1958) ¹⁶	Psoriasis involving the trunk and extremities	76 subjects. On each subject, one lesion was treated with four weekly 2 Gy doses of grenz rays, one lesion was treated with four weekly 160 rad doses of x-rays, and one lesion was untreated and observed as a control. Relative clinical improvement was subjectively assessed on a weekly basis every 7 days through day 28.	Lesions treated with either conventional x-rays or grenz rays were more improved than nonirradiated control sites in at least 80% of cases. In 70% of cases, there was no statistically significant difference between the two types of radiation; in 20% of cases, grenz ray–treated lesions were significantly more improved; and in 8% of cases, x-ray–treated lesions were significantly more improved.	Grenz ray therapy and conventional x-ray therapy both lead to clinical improvement in psoriasis.
Broderson and Reymann (1981) ¹⁷	Psoriasis involving the trunk and extremities	20 subjects. The full body was treated with betamethasone ointment. Half of the body received three weekly 12 kV treatments of grenz rays while the other half received sham therapy. Patients were followed for 4 weeks.	Treatment with grenz rays plus topical steroids was significantly better than with topical steroids alone ($p < .05$), with 67% (12/18) of subjects reporting that grenz rays were superior to placebo and 33% (6/18) reporting no preference.	Patients perceive greater improvement in their psoriasis when grenz ray therapy is added to their topical steroid regimen.

Table 1. Continued

Study	Condition	Study Design	Key Results	Conclusions
Johannesson and Lindelof (1985) ¹⁸	Scalp psoriasis	16 subjects. Half of the scalp was treated with six weekly 4 Gy treatments of grenz rays while the other half received sham therapy. Patients were followed for 6 months.	Grenz rays were significantly better than placebo in terms of improvement of psoriasis, based on a 5-grade scale ($p < .0001$), 87.5% (14/16) of subjects healing completely with grenz ray treatment, 64% remaining free of relapse 3 months after treatment, and 21% still free from relapse 6 months after treatment.	Grenz ray therapy is a useful treatment modality for scalp psoriasis, with healing rates from 70–85%, with 50–70% of patients still healed at 3 months and 20–50% still healed at 6 months after treatment.
Johannesson and Lindelof (1987) ¹⁹		17 subjects. The full scalp was treated with betamethasone solution once a day for 2 weeks and then biweekly for 4 months. Half of the scalp was treated with six weekly 4 Gy treatments of grenz rays while the other half received sham therapy. Patients were followed for 6 months.	Grenz rays plus topical steroid treatment showed faster clearing than with topical steroids alone ($p < .001$): 88.2% (15/17) healed almost completely, 68% remained free of relapse 3 months after treatment, and 53% remained free of relapse 6 months after treatment. In comparison with the previous study (Johannesson and Lindelof 1985), the combination of grenz rays plus topical steroids gives a longer remission time than with grenz rays alone.	Grenz therapy combined with topical steroids leads to faster clearing than with steroids alone but the same rate as with grenz rays alone. The combination of grenz rays and steroids leads to longer remission than with grenz rays alone.
Lindelof and Johannesson (1988) ²⁰		40 subjects. Half of the subjects received six weekly 4 Gy treatments with grenz rays while the other half received the same grenz ray treatment plus topical betamethasone solution. Patients were followed for 6 months.	There was no significant difference in healing rates between subjects treated with grenz rays alone and those treated with grenz rays plus topical steroids. 84% (16/19) of subjects in the grenz ray group and 72% (13/18) of the subjects in the combination group healed. The remission rate did not differ significantly between the two groups at 6-month follow-up (31% for both groups).	
Lindelof (1989) ²¹	Psoriatic nails	22 subjects. One hand was treated with 10 weekly 10 kV doses of grenz rays while the other hand received sham therapy. Patients were followed for 6 months.	There was a moderate but significantly better effect with grenz rays ($p < .05$). After treatment, 4% (1/22) had almost complete improvement, 32% (7/22) had slight improvement, and 64% had no improvement. None of the hyperkeratotic nails responded. At 6-month follow-up, 18 patients reported no change in their nails since treatment, 2 reported moderate improvement, and 2 reported slight worsening.	Grenz rays are moderately useful in treating psoriatic nails but only when applied to nails of normal thickness.

Table 2. Grenz Ray Therapy in Chronic Eczemas

<i>Study</i>	<i>Condition</i>	<i>Study Design</i>	<i>Key Results</i>	<i>Conclusions</i>
Lindelof et al (1985) ¹¹	Allergic contact dermatitis (nickel sensitivity confirmed by patch test)	6 subjects. Nickel-sensitive subjects received three weekly 3 Gy treatments with grenz rays on a defined area on the back; 24 hours after the last treatment, serial dilution nickel patch tests were applied to the treated area and an untreated control area on the other side of the back. The patch tests were read 72 hours later.	Grenz ray treatment suppressed the patch-test response to nickel in 5 of 6 patients (83%). The sixth patient, who was strongly sensitive to nickel, developed two follicular papules at the site of a 1.25% nickel sulfate test on the grenz ray-treated area but no edema, redness, or vesiculation.	Grenz rays inhibit the clinical expression of ACD almost completely.
Lindelof and Lindberg (1987) ¹²	Irritant contact dermatitis (induced in healthy volunteers)	11 subjects. Healthy volunteers received three weekly 3 Gy treatments with grenz rays on a defined area on the back; 24 hours after the last treatment, serial dilution sodium lauryl sulfate patch tests were applied to the treated area and an untreated control area on the other side of the back. The patch tests were read 48 hours later.	There was a tendency toward a weaker expression of the irritant reaction in grenz ray-treated skin, but this difference was not statistically significant.	Grenz rays do not have a marked effect on the elicitation of ICD.
Fairris et al (1985) ²⁴	Chronic hand eczema resistant to topical therapy	25 subjects. One hand received 1 Gy of conventional superficial x-rays while the other hand received 3 Gy of grenz rays. Treatment was given on three occasions separated by 21-day intervals, and subjects were seen at weeks 3, 6, 12, and 18 after the first exposure.	Conventional superficial x-rays were better than grenz rays in terms of subjects' perceptions and clinical improvement based on a severity scale of 0–10 ($p < .05$). Though superficial x-rays were more efficacious, grenz ray therapy did result in clinical improvement, with a mean improvement in severity from 7 to 2.5 by 18-week follow-up.	Grenz ray therapy does result in improved hand eczema although conventional superficial x-ray therapy is superior.
Cartwright and Rowell (1987) ²³	Hand eczema refractory to previous treatments	30 subjects. One hand received 3 Gy treatments with grenz rays while the other hand received sham therapy. Treatment was given on three occasions separated by 21-day intervals, and subjects were seen every 3 weeks through week 18 following the initial treatment. Patients continued to apply tar paste or steroid ointment to both hands throughout the trial.	From both the patients' and the observers' perspectives, there was no statistically significant difference in the degree of improvement of hand eczema on a severity scale of 0–10 between grenz ray-treated and placebo-treated hands at any of the posttreatment visits. Both grenz ray-treated and placebo-treated hands had a mean improvement in severity from 5.5 to 2 by week 18.	Grenz ray therapy does improve the severity of hand eczema but does so no better than placebo.

Table 2. Continued

Study	Condition	Study Design	Key Results	Conclusions
Lindelof et al. (1987) ²²	Chronic hand eczema unresponsive to topical steroids	24 subjects. Both hands were treated with an unspecified topical steroid. One hand received six weekly 3 Gy treatments of grenz rays while the other hand received sham therapy. Clinical evaluation with a 5-grade scale was performed at weeks 5 and 10 after starting therapy.	A significantly greater improvement in grade of eczema, as well as individual symptoms, was seen on the grenz ray-treated hand ($p < .01$). Of the 13 of 24 subjects with allergic contact dermatitis, 10 (77%) responded better with grenz rays plus topical steroids than with topical steroids plus placebo.	Patients with chronic hand eczema that is not improving with topical steroids alone will likely benefit from the addition of grenz ray therapy. Specifically, ACD responds well to grenz rays.

ACD = allergic contact dermatitis; ICD = irritant contact dermatitis.

by small sample sizes, the lack of long-term follow-up, and differences in dosing between studies. By contrast, support for the usefulness of grenz ray treatment in other conditions is mostly anecdotal, consisting of case reports and few (if any) controlled trials.

Psoriasis

Grenz ray treatment is useful in psoriasis.^{14,15} Psoriasis of the scalp and trunk responds well to grenz rays,¹⁶ and patients perceive greater improvement when grenz ray therapy is added to their topical steroid regimen.¹⁷ For psoriasis of the scalp, resolution rates vary from 70 to 85%; 50 to 70% of patients are improved at 3 months, and 20 to 50% experience sustained improvement at 6 months after treatment.^{18–20} Grenz ray therapy combined with topical steroids leads to faster clearing than is achieved with steroids alone¹⁹ but clears at the same rate as that of grenz ray therapy alone.²⁰ The combination of grenz ray therapy and topical steroids leads to longer remission than can be achieved with grenz ray therapy alone.¹⁹ To improve the absorption of grenz rays, thick scales may be reduced by pretreating the scalp with keratolytics.¹⁴ Keeping the grenz ray dose below erythemogenic levels may help prevent a Koebner reaction, which has been a proposed cause of rapid recurrence of psoriasis in some studies.¹⁴ Finally, grenz rays may be useful in treating nail psoriasis cases in which the nails are of normal thickness; by contrast, they may have no effect on thickened nails, likely owing to inadequate penetration (see Table 1).²¹

Chronic Eczemas

As cited, grenz ray therapy is highly effective in suppressing ACD¹¹ but has little effect on ICD.¹² With respect to chronic hand eczema, one study showed that the addition of grenz ray therapy to a topical steroid regimen produced results superior to those obtained with unirradiated controls²² whereas another study revealed no difference relative to placebo.²³ In the former study, more than half of the subjects had ACD of the hands; 77% of these subjects responded to grenz rays, which is consistent with previous findings of strong efficacy in controlling ACD. By contrast, in the latter study, the subtypes of hand eczema were not specified; thus, it is conceivable that the study population may have consisted predominantly of subjects with diagnoses other than ACD of the hands. Conventional superficial x-rays have been shown to be more efficacious for chronic eczemas than grenz rays are²⁴ but carry a considerable risk of carcinogenesis (see Table 2).²² Of note, none of the chronic eczema studies followed patients beyond 18 weeks. Considering that the length of remission is an important outcome with grenz irradiation, the lack of long-term follow-up limits our assessment of the results of this therapy.

Safety

The most common potential side effects of grenz ray therapy are relatively minor; these include erythema (typically asymptomatic) and dyspigmentation (usually temporary).⁶ The latter can be accentuated by close

shielding, which may create a sharp demarcation of pigmentary change at the edge of a treatment area.¹⁴

The most serious adverse effect associated with irradiation with grenz rays is the risk of malignancy, which overall appears to be relatively small. The first reported case of skin cancer associated with grenz rays occurred in 1959, when a dermatologist who had been accidentally overexposed to grenz radiation ($> 40,000$ R)³ developed a squamous cell carcinoma on a distal phalynx.⁶ An epidemiologic cancer linkage study of 14,140 patients treated with grenz rays with a mean follow-up of 15 years²⁵ found no significant excess risk of melanoma but found a statistically significant excess risk of nonmelanoma skin cancer (NMSC) (with a standardized incidence ratio of 1.45). However, of the 39 patients who developed NMSC, only 8 had received grenz ray therapy at the site of the tumor, and 6 of these 8 patients had also been exposed to other known carcinogens, including tar, arsenic, conventional x-rays, methotrexate, and hydroxyurea. There was no increased risk of cancer development in 481 patients who had received at least 10,000 rads of grenz rays on the same body area. The authors of this epidemiologic study concluded that grenz ray therapy cannot be excluded as a risk factor in the development of NMSC, but the risk is quite small.²⁵ In a separate epidemiologic study, it was found that most of the grenz ray-exposed individuals were women and were likely to develop multiple tumors, mostly basal cell carcinomas.²⁶ In one particularly striking case, a woman who received a cumulative dose of 3,000 rads to each of seven treated areas developed five squamous cell carcinomas within 7 years.²⁷ These results suggest that the usual therapeutic doses of grenz rays are capable of causing NMSC but only in a few persons who are abnormally sensitive to x-rays.²⁶ Higher doses of grenz rays (10,000–29,300 rads) have been associated with the development of NMSC and therefore should be avoided.²⁸

Recommendations

Table 3 summarizes the recommendations of the Food and Drug Administration and other experts in regard to the use of grenz radiation for benign dermatoses.^{29–34} By carefully following these guidelines, clinicians can use grenz radiation safely as therapy in refractory cases of inflammatory skin conditions. Grenz radiation is especially recommended in the treatment of (1) psoriasis of the trunk, extremities, or scalp; (2) hand eczemas; and (3) ACD, all of which are conditions for which the greatest quantity and quality of evidence exist in support of efficacy. A variety of dosing schedules have been proposed,

including 150 to 300 rads weekly or twice monthly for three to four exposures, repeated after 6 months if necessary, with total exposure limited to 5,000 rads.³⁵ In the clinic of one author (PDC), patients are routinely treated with 500 rads weekly for 3 weeks, with a “ceiling” of 12 treatments per year.

Availability and Use

The study and use of ionizing radiation therapy in the United States (including US academic dermatology training centers) has declined substantially in the past several decades. Indeed, most of the literature cited herein was written by European authors. Based on a 2005 survey of 78% of US dermatology residency programs, only 10% of programs have and use soft x-ray or grenz ray equipment as compared to 22% of programs in 1986 and 44.3% of practicing dermatologists in 1975.³⁶ However, 80% of programs include the theory and practice of radiation therapy in their curriculum. Interestingly, only 5% of program directors thought grenz irradiation ineffective, and several commented that they miss grenz ray therapy, especially for recalcitrant hand dermatitis.

Various reasons were cited for discontinuing the use of grenz or ionizing radiation, including concerns about equipment licensing (47%) and skin cancer risk (46%) and a belief that better therapies are available (46%).³⁶ The most common reason reported for discontinued use of grenz irradiation was problems with grenz ray machine maintenance (70%),³⁶ which is related to the machine's commercial unavailability in the United States. Our extensive search for American companies that manufacture the grenz ray machine yielded nothing. A sole company in Sweden (whose Web site can be accessed at www.progressusmedica.se) confirmed that it manufactures “a new and improved” grenz ray machine that the Food and Drug Administration has approved for sale in the US market for \$28,000 (US) (Bernt Lindelof, Director, personal communication, September 2007).

Conclusion

Given the limited availability and use of grenz radiation in the United States, this therapeutic modality may be well on its way to extinction there if action is not taken soon. We believe this would be an unfortunate loss because grenz radiation is an effective and safe treatment of refractory dermatoses such as psoriasis and hand eczema. It is also relatively affordable; Medicare reimburses at \$63.00 (US). Finally and perhaps most important, the majority of

Table 3. Recommendations for Safe and Effective Administration of Grenz Ray Therapy

Grenz ray therapy should be used only when the diagnosis is clearly established, preferably by biopsy. ²⁹
Grenz ray therapy should only be used in refractory cases in which the consequences of treatment failure are unacceptable. ³⁰
Grenz ray therapy should be used only when there is a reasonable expectation that radiotherapy will lead to clinical improvement. ²⁹
Grenz ray therapy should be avoided in children. ³⁰
Grenz ray therapy should be administered only by trained personnel. ³⁰
Meticulous radiation protection techniques should always be used. ³⁰
It is safest for the operator to stand 4 m or more from the machine, where air absorption of radiation is practically nil. ³¹
At a distance of 2 m from the unit, the operator can be exposed 100 hours per year ³¹ ; at a distance of 1 m from the unit, the operator can be exposed for only 3 hours per year. ³¹
All patients should be questioned about previous radiation exposures prior to grenz irradiation. ²⁹
For patients such as those with severe psoriasis who have been previously exposed to multiple carcinogenic agents such as radium, thorium, tar, large amounts of ultraviolet light, and oral arsenic, dermatologists should be cautious in considering the addition of grenz ray therapy and should carefully screen for skin cancers prior to initiation of treatment. ³²
No topical agents should be applied to the area prior to irradiation, to avoid irritation or reduced treatment efficacy. ²⁹
The dosage of radiation should be adjusted, based on the radiosensitivity of the treatment area. ³⁰
For palms, soles, and scalp (the least sensitive), one can safely administer 4 Gy per treatment; For the anogenital area (the most sensitive), reduce the dose to 0.5 to 2 Gy per treatment. ¹²
Because hair tends to absorb a portion of the grenz ray dose, one author suggests that the thickness of hair should be assessed and the dose of grenz rays adjusted accordingly: multiply the dose by 1.5 for thin hair, 2 for medium, and 3 for thick hair. ³³
While the US literature recommends 5,000 rads (50 Gy) as the total lifetime cumulative dose per treatment area, ³⁴ the authors of the only large-scale study of the carcinogenic effects of grenz ray therapy believe that higher doses can be safely tolerated and recommend the following:
The maximum cumulative dose for a certain skin area should not exceed an arbitrary limit of 10,000 rads (100 Gy) ⁴
In situations in which it is necessary to go beyond this limit, the patient should be monitored closely, and the treatment areas should be examined for malignancy every 10,000 rads ¹⁴
The dose must be fractionated; one treatment per week for 4 to 6 weeks should be administered, followed by at least 6 months of rest before resuming therapy. ⁴
The palms, soles, and scalp can safely tolerate more than 10,000 rads of grenz rays in a lifetime. ¹⁴

patients receiving grenz ray therapy perceive it to be worthwhile, and most would choose it again if needed, especially those with chronic eczema.³⁷

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