

Patients Undergoing Radiation Treatment Were Clinically Evaluated for Skin Integrity, Pain and Itching in a Preliminary Trial Using RadiaPlexRx™ Gel Containing 0.2% Hyaluronic Acid

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Abstract

Objective: Acute radiation dermatitis is a side effect of radiotherapy. It has been estimated that approximately 95% of radiation therapy patients treated for cancer will experience a skin reaction (Prorock et al., 1999; Fisher et al., 2002). Peer-reviewed clinical trials are sparse and inconsistent on efficacy of topical treatments for radiation dermatitis, leaving the patient and practitioner without a solution as to an effective treatment (Wickline, 2004).

Purpose: Studies have suggested that hyaluronic acid and mannan polysaccharides reduce acute radiation-induced dermatitis. RadiaPlexRx™, a topical gel composed of these ingredients, was clinically evaluated for efficacy in radiation dermatitis. Hyaluronic acid, 0.2%, was shown clinically to significantly reduce the symptoms of radiation dermatitis as compared to placebo cream (Liguori et al., 1997). Hyaluronic acid may support skin because it is a natural component of the extracellular matrix of the dermis.

Methods: A pilot study was conducted on 20 patients who were receiving radiation treatment for breast cancer, chest wall after a mastectomy, thorax and abdomen, forehead and rectum. 60% of patients received radiation dosages of 6040cGy or higher. Patients were instructed to apply gel three times daily.

Data Analysis: Nurses assessed patient dermatitis using the NCI Common Toxicity Criteria. Patients reported their evaluations using a Patient Survey Questionnaire. Data was entered into SPSS and descriptive statistics calculated.

Findings and Implications: Results showed 90% of patients clinically evaluated experienced no dry desquamation or severe erythema. 85% of patients experienced no itching and 70% of patients experienced no painful skin problems. 75% experienced increased moisturizing effects. 100% of patients stated they would recommend it to others undergoing the same treatment. Further studies are warranted as the gel seemed to be well tolerated, non-irritating and may help prevent dry desquamation. RT nurses need to feel comfortable recommending a well-tolerated and effective treatment for their patients during the radiation treatment phase and for home care. This gel offered a potential solution for treating mild to medium dermatitis associated with most radiation protocols, bearing in mind that each case required individual assessment.

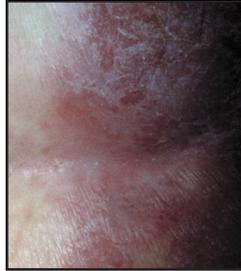
Introduction

- 87% of women receiving radiation treatment for breast cancer will develop radiation dermatitis (Fisher, et al., 2002).
- Radiation dermatitis is painful; causes itching, may interfere with treatment schedule and can create open wounds increasing likelihood of infection (Wickline, 2003).
- The use of new irradiation schedules such as hyper fractionation, accelerated fractionation or multidisciplinary approaches combining chemoradiation are known to increase significantly the risk and the severity of acute radioepithelitis (Liguori, et al., 1997).
- Patients undergoing radiation therapy for cancer and tumors experience skin reactions ranging from mild erythema to ulceration and bleeding.

Moist desquamation



Dry Desquamation



- Teaching patients how to care for irradiated skin during and after a course of radiation therapy is a major concern of oncology nurses (Sitton, 1992).
- In the U.S., United Kingdom, and Europe there is presently no known evidence-based optimal treatment for radiation dermatitis (Wickline, 2003).
- Clinical trials testing various products available are limited.

Location of Irradiated Skin Sites on Patients Preliminary Clinical Study (n=20)

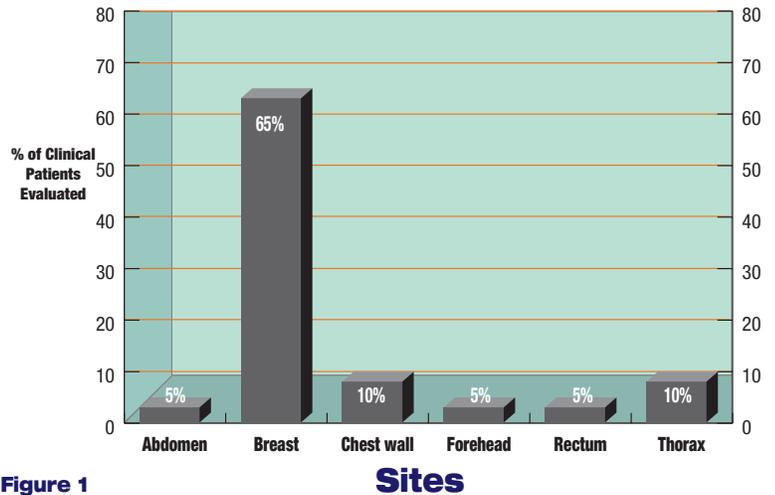


Figure 1

Patients Using RadiaPlex Were Evaluated for Skin Toxicity

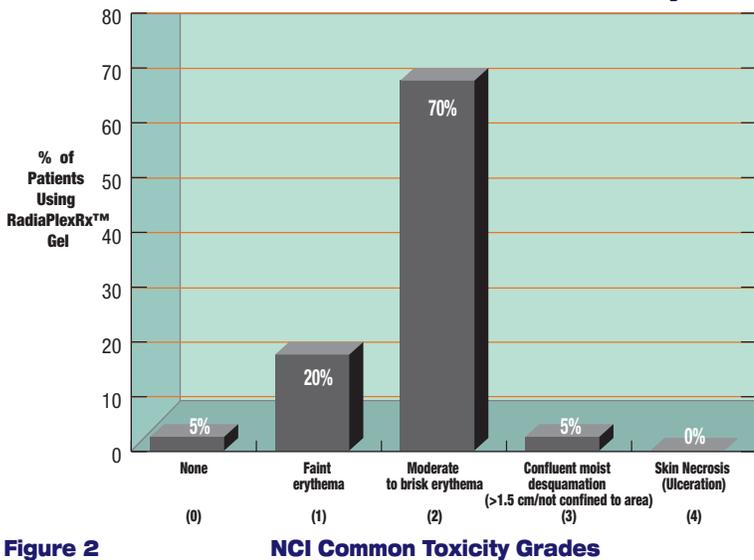


Figure 2

- Studies have indicated that moist care of irradiated skin areas during radiotherapy improves the healing time and reduces the severity of moist desquamation. Moist skin care regimes (i.e., hydrogels, bathing) seem to improve radiation tolerance and patients' acceptance (Schratte-Sehn, et al., 2001; Strunk and Maher, 1993).
- Several studies in animals have shown that components in Aloe vera enhanced collagen turnover and cross linking in granulation tissue. It was shown to help heal burned skin by influencing inflammation, fibroplasias, collagen synthesis, and maturation and wound contraction (Visuthikosol, et al., 1995; Chithra, et al., 1998).
- RadiaPlex™ gel contains two ingredients that have shown benefit in peer-reviewed literature towards supporting skin healing, repair and integrity when damaged (Chithra, 1998; Visuthikosol, et al., 1995; Liguori, et al., 2002).
- Some clinicians advise treating irradiated skin for the life of the patient due to the collateral damage.

- RadiaPlex™ gel was experimentally shown in cultured human fibroblasts to be non-toxic, showing 100% viability when incubated overnight (Gracy, et al., 2004).
- RadiaPlex™ was experimentally evaluated in human fibroblasts against two types of radical oxidative damage. RadiaPlex™ treated cells exposed to severe hydrogen peroxide damage showed 20% less cell death than untreated cells. Pretreated cells exposed to X-irradiation showed 30% less cell death (Gracy et al, 2004).
- Ingredients in RadiaPlex™ protected fibroblast cells from oxidative damage, which creates cellular membrane damage like that produced during ionizing radiation treatment (Gracy et al, 2004).

Patients Using RadiaPlex Were Evaluated for Skin Appearance

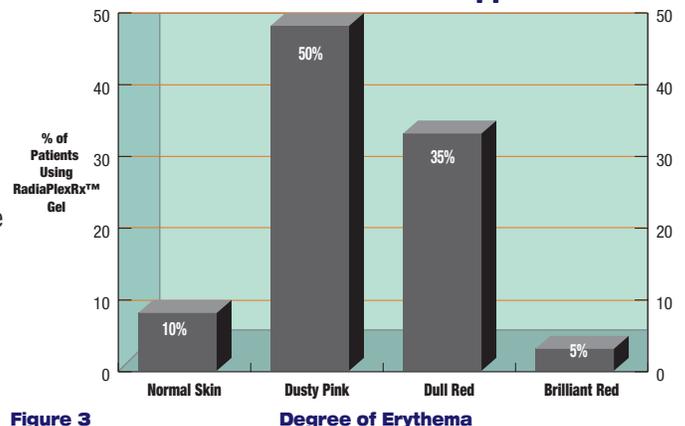


Figure 3

Background

- RadiaPlexRx™ gel contained 0.2% hyaluronic acid, a disaccharide composed of two functional sugars, glucosamine and glucuronic acid, that is the major water holding molecule in the dermis and epidermis, connective tissue, synovial fluid, and vitreous humor that fills the eye.
- Liguori and colleagues study of 134 patients treated with radiotherapy showed that 0.2% hyaluronic acid cream significantly reduced severity of skin reactions, postponed first signs of acute epithelitis, reduced the severity of skin reactions and was judged favorably by physicians and patients as compared to placebo (Liguori, et al., 2002).
- Studies have shown that hyaluronic acid was effective not only as a prophylactic treatment in humans, but also as a therapeutic measure as proven in treatment of ulcers of different origins where this compound was successfully used to accelerate granulation and the re-epithelialisation process (Liguori, et al., 1997).
- Due to an influence in signaling pathways, hyaluronic acid is involved in the wound-healing process. In clinical trials, topical application improved wound healing, in particular acute radioepithelitis, venous leg ulcers and diabetic foot lesions (Weindl, 2004).
- Many topical ointments available to oncologist are simple oil and water based formulas, have not shown clinical efficacy in radiation dermatitis, and do not contain active ingredients that indicate effect towards actual healing of dermal tissue (Prorock, et al 1999; Fisher, et al. 2000).

Objective

- The effect of a topical gel containing 0.2% hyaluronic acid and high molecular weight polymannans from aloe vera, on acute skin reactions after radiotherapy was measured using a questionnaire for patients and an NCI toxicity scale by radiation oncology nurses.

Method

- Twenty patients receiving 6-1/2 weeks of radiotherapy, participated in the study.
- Patients were instructed by nurses to wash the skin area with soap and water.
- RadiaPlexRx™ Gel was provided by MPM Medical Inc., Irving TX.
- Patients were instructed to apply a thin layer of RadiaPlexRx™ gel to the irradiated skin area three times daily and were given adequate supply of gel to last throughout the trial.
- Patients were being treated for breast cancer (65%), chest wall after a mastectomy (10%), thorax (10%), abdomen (5%), forehead (5%), and rectum (5%) (figure 1).
- The majority of cases were in the early stages of radiation therapy.
- Sixty percent of patients were receiving 6040cGy or higher.
- Nurses assessed patient dermatitis using the National Cancer Institute Common Toxicity Criteria Version 2 to determine Grade 1 through Grade 4 dermatitis reactions.
- Patients reported their reactions and evaluation of the product using a Patient Survey for Skin Care
- Data were collected on individual parameters on both nurse and patient surveys and analyzed utilizing SPSS (Statistical Package for Social Sciences).

National Cancer Institute Common Toxicity Criteria

Toxicity	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Dermatitis, focal (with high-dose chemotherapy and bone marrow transplant)	None	Faint erythema or dry desquamation	Moderate to brisk erythema or a patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	Confluent moist desquamation, ≤1.5 cm diameter, not confined to skin folds; pitting edema	Skin necrosis or ulceration of full thickness dermis; may include spontaneous bleeding not induced by minor trauma or abrasion

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Patients Using RadiaPlex Were Evaluated for Exhibiting Dry Desquamation

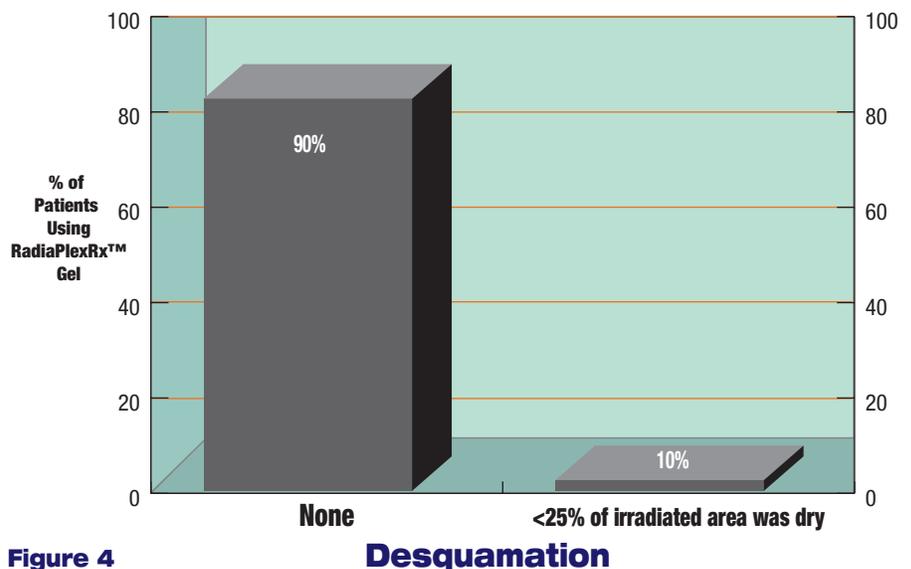


Figure 4

Results

- Patients were receiving aggressive dosages of radiotherapy.
- 70% of patients washed the area with soap and water and 30% used water only.
- Nurses evaluated skin toxicity showing that 95% of patients did not develop moist desquamation with the use of the gel (figure 2).
- Nurses evaluated degree of erythema in patients applying gel to irradiated skin area showing only one patient (5%) developed brisk erythema (figure 3).
- Nurses' evaluations showed that 90% of patients in the clinical study did not experience dry desquamation while using the gel on irradiated skin (figure 4).
- Patients' participation and usage of the gel during the clinical study was high (figure 5).
- Patients' perceptions indicated a high degree of satisfaction with comfort and ease using the gel (figure 6).

Patients' Participation Using RadiaPlex

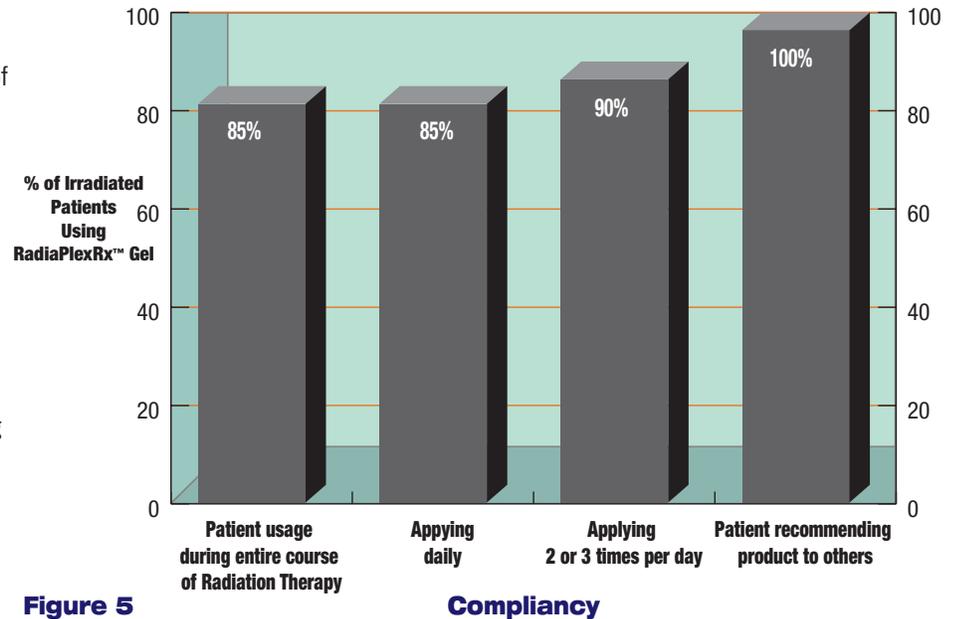


Figure 5

Compliance

Conclusions

- 1.) Severe skin toxicities did not occur in this patient population.
- 2.) According to nurses' assessments, patients predominantly developed faint to brisk erythema and very few developed moist desquamation.
- 3.) Hyaluronic acid is known to demonstrate remarkable rheological, viscoelastic and hygroscopic properties, relevant for dermal tissue function as may be indicated by nurse evaluations in this study (i.e. only one patient developed moist desquamation; 90% of patients did not develop dry desquamation).
- 4.) The pilot study showed positive reactions and overall acceptance by patients (100% would recommend gel to others, 85% used gel throughout treatment period, 75% experienced moisturizing effect, 75% reported it was not painful, 80% experienced no itching during use).
- 5.) Both clinical and patient perception scoring during the study resulted in a greater number of beneficial than non-beneficial responses.
- 6.) None of the patients discarded or refused to apply the product even if they made their own application schedule.
- 7.) The results of this preliminary trial tend to confirm and support prior investigations (both *in vivo* and *in vitro*) that the active ingredients in the gel may be effective in treating radiation dermatitis (Liguori, et al., 2002; Weindl, et al., 2004; Gracy, et al., 2005)

Implications

- 1.) Research regarding product ingredients should be evaluated to determine optimal treatments for radiation dermatitis. It is important for nurses to become aware of newly developed products. (Olsen, et al., 2001; Liguori, et al., 1997).
- 2.) Future studies warrant the investigation of quality of life issues regarding self-care and skin integrity among radiation therapy patients utilizing the gel containing 0.2% hyaluronic acid.
- 3.) While this preliminary study supports use of RadiaPlexRx™ gel, increasing the number of patients and expanding different clinical skin sites should be explored to ascertain possibility of universal application.
- 4.) If patients are allowed to apply a moisturizing, skin repairing, supportive gel on the first day of radiation treatment, the patient may have some control over the outcome of their skin health and comfort.

Patients' Perceptions of Comfort and Ease Using RadiaPlex on Irradiated Skin

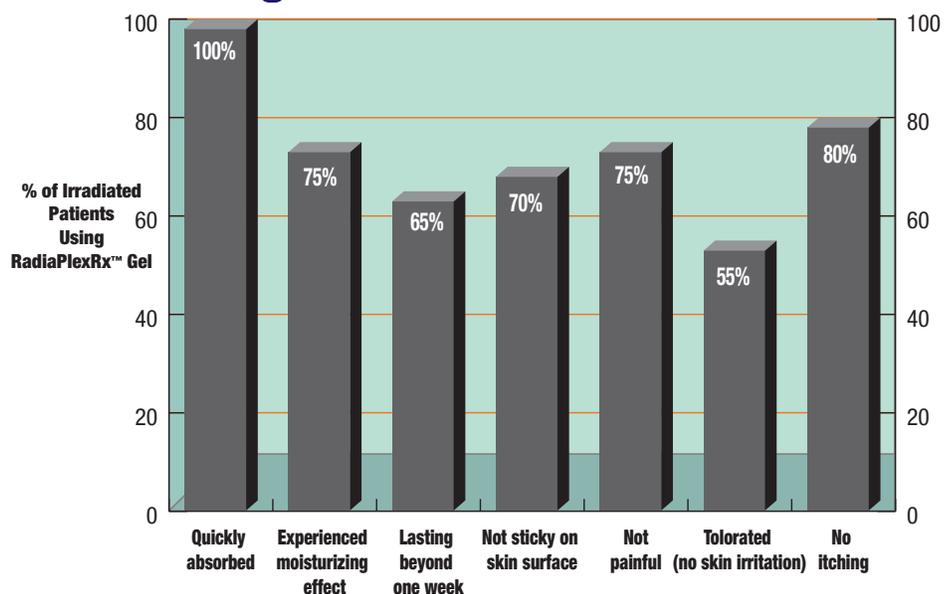


Figure 6

Patient Responses

Products for study provided by:

MPM Medical, Inc., 2301 Crown Ct., Irving, Texas 75038 • www.mpmmedicalinc.com • Phone: 800-232-5512 • FAX: 972-893-4092