

**OBJECTIVES:**

To review published studies evaluating interventions for the prevention and management of radiation skin reactions/dermatitis.

**DATA SOURCES:**

Research studies, review articles, and clinical practice guidelines.

**CONCLUSION:**

There is insufficient evidence in the literature to recommend specific topical or oral agents in the prevention or management of skin reactions. Recent limited evidence suggests that the use of calendula cream may reduce the incidence of grade 2 and 3 reactions in women with breast cancer. Additionally, early studies evaluating the use of barrier films or creams may improve moist desquamation.

**IMPLICATIONS FOR NURSING PRACTICE:**

Oncology nurses need to increase their awareness of the evidence or lack of evidence when recommending interventions to their patients. Further research is required to evaluate interventions in the prevention and management of radiation dermatitis.

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# EVIDENCE-BASED SKIN CARE MANAGEMENT IN RADIATION THERAPY

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MAURENE McQUESTION

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**R**ADIATION treatment may cause a variety of physical skin reactions and contributes to pain, discomfort, irritation, itching, and burning. Radiation skin changes can affect activities of daily living and quality of life. Individuals may experience difficulties with wearing or managing their usual clothing, restriction in the movement of a limb or affected area, visible reactions from others, loss of independence and self care, and incur costs in managing some skin reactions. Skin changes can be experienced by up to 95% of patients. For some, skin changes may have a dose-limiting impact.<sup>1</sup> It is imperative that nurses be knowledgeable about the assessment and management of skin reactions caused by radiation. Goals of care related to the management of radiation skin reactions include maintaining skin integrity, cleanliness, comfort, and the reduction of pain, protection from trauma, prevention and management of infection, and the promotion of a moist wound healing environment. If required, goals will also include the control of bleeding, management of exudate, and odor control.

This article addresses the normal tissue response to radiation therapy, factors that affect the degree of reaction, and evidence-based skin care management in radiation therapy. The goal is to assist nurses in making decisions about the care of patients with radiation skin reactions.

## SKIN ANATOMY AND PHYSIOLOGY

**N**ormal skin is composed of the epidermis and the dermis. The epidermis, which includes the outer cornified layer and the deeper basal layer, is continually being renewed through a bal-

anced production of new cells from the basal layer in response to the normal shedding of the cornified layer. The basal layer of the epidermis contains germinal or stem cells that divide and differentiate into mature skin cells. Approximately 10% of basal cells undergo mitosis each day. As the outer cells of the cornified layer shed or detach, they are replaced by newly differentiated cells from the basal layer. This normal process involves both the proliferation and differentiation or maturation of skin cells to completely replace the epidermal layer approximately every 4 weeks. The dermis, underlying the epidermis, contains the support structures including blood vessels, nerves, glands, and hair follicles.<sup>2,3</sup>

Following an initial dose of radiation, a fixed percentage of basal cells are destroyed.<sup>3</sup> The remaining cells become cornified and shed more quickly, thus resulting in a disruption in the balance between the normal production of cells at the basal layer of the skin and the destruction of cells at the skin surface. Although non-cycling basal cells are then stimulated into a cycling phase, continued destruction of basal cells occurs from ongoing radiation treatment. Additionally, an inflammatory response with the secretion of histamine and serotonin occurs as well as a vascular response with extracapillary cell injury and capillary dilation. Erythema begins as a result of capillary dilatation in the dermis accompanied by edema because of increased vascularity and obstruction.<sup>3,4</sup> Changes in pigmentation are caused by the migration of melanin to the more superficial layers of the epidermis. Hair growth is interrupted as hair follicles revert to a resting phase of their cell cycle and hair follicles shed new hairs. Complete hair loss can occur at doses greater than 55 Gy, with regrowth occurring approximately 2 months after the last dose of radiation. Sweat and sebaceous glands can be permanently destroyed after approximately 30 Gy in 15 treatments (ie, 2 Gy per day) over a 3-week period.<sup>3</sup> This can lead to reduced skin lubrication causing dryness and pruritus.

Normal tissue repair results from a homeostatic stimulus or feedback mechanism with re-epithelialization with the proliferation and differentiation of cells from the basal membrane and the migration of epithelial cells from outside the treatment field. Re-epithelialization usually begins in about 10 days.<sup>5</sup> A moist wound healing environment supports the migration of these cells across the wound area of the skin reaction.<sup>6,7</sup>

## TYPES AND SEVERITY OF SKIN REACTIONS

Early radiation skin reactions occur within 1 to 4 weeks of treatment and may persist for 2 to 4 weeks following treatment. They are identified and graded by severity along a continuum ranging from erythema and dry desquamation to moist desquamation and in more severe cases, ulceration. During the first 2 weeks of treatment, with a daily fractionated dose of 1.8 to 2.0 Gy, the patient generally does not experience any discomfort. Transient erythema may occur within 24 hours of beginning treatment and is visibly localized to the treatment field after 2 to 3 weeks of radiation. The skin appears red, warm, and may have a rashy appearance. Patients may describe their skin as feeling sensitive and tight.

Hyperpigmentation occurs after 2 to 4 weeks of treatment. With the cumulative dose reaching 20 Gy the patient may experience dryness, pruritus, or flaking of the skin or dry desquamation.<sup>8</sup> This is a result of the decreased ability of the basal layer to replace surface layers, shedding of the epidermis, and decreased functioning of the sweat and sebaceous glands. At doses of 30 to 40 Gy, extracapillary cell damage occurs with increased capillary blood flow, hyperemia, and edema. If severe, there is epilation leading to moist desquamation that can occur at doses of 45 to 60 Gy. With moist desquamation, the dermis is exposed. The treatment field is moist, tender, and red with oozing and leaking of serous fluid. It can also be accompanied by light or heavy exudate and crusting.<sup>3</sup>

### *Factors Affecting Skin Reactions*

Factors affecting the degree of skin reaction include both treatment-related factors and individual or patient-related factors. Patients at risk for skin reactions include patients receiving treatment to sites where two skin surfaces are in contact (eg, breast, perineum), areas where the epidermis is thin and smooth (eg, axilla, face, perineum) or where the skin integrity has already been disrupted from surgery, burns, or lesions. Altered wound healing may occur in situations of postoperative radiation or in surgical incisions that are in the field of irradiated tissue.<sup>2</sup> Patient risk factors also include: the individual's usual skin routine, concurrent chemotherapy, immunotherapy or targeted therapies, associated medical conditions or co-morbidities such as diabetes or renal failure, older age, compromised nutritional

status, previous lymphocele aspiration, chronic sun exposure, smoking, and environmental conditions.<sup>2,9</sup>

Treatment-related risk factors for enhanced skin reactions include the location of the tumor or treatment field (eg, chest wall, head and neck, facial, skin folds, breast, axilla, perineum), a larger treatment volume/field, a larger total dose of radiation, large fraction size (greater than 2.0 Gy per fraction), longer duration of treatment, type of energy used with lower energy photon and electrons depositing a higher skin dose, and the use of any bolus material. Megavoltage units such as linear accelerators, with higher energies delivering maximal doses of radiation to deeper tissues, 1.5 to 3.0 cm below the skin surface, depending on the energy of the particular unit (6 MV to 18 MV), thereby sparing the skin.<sup>2,9,10</sup> Electron beams deliver an increased dose to the skin because of their shorter wavelength, and are often used as a boost or way of enhancing the dose to tumors or nodes closer to the skin surface. In comparison, older treatment units such as the Cobalt-60 unit, will deposit the maximum delivery dose 0.5 cm below the skin surface.

Newer techniques of treatment can potentially affect the incidence and severity of radiation skin reactions, most notably in patients with head and neck cancer. Compared with contemporary conformal radiation delivery, traditional non-conformal external beam radiation techniques have resulted in a larger volume of normal tissue receiving high doses during a course of treatment. Conformal radiation techniques and newer intensity-modulated radiation therapy (IMRT) have resulted in small volumes of normal tissue receiving the full treatment dose. While in theory, this should result in less skin dose and improvement in skin reactions; this has not always been observed. The requirement for multiple beams tangential to skin delivered through immobilization devices (eg, in head and neck IMRT plans) can result in increased skin dose and reactions. One potential solution might be to include skin over uninvolved neck nodes as an organ at risk during treatment planning to reduce the dose to uninvolved skin and thereby reduce the degree of skin reaction.<sup>11</sup> Planning for head and neck radiation doses are often 70 Gy, with the skin over neck nodes receiving 60 to 70 Gy as well. Taking into consideration the skin as a sensitive structure and not including the uninvolved skin over neck nodes in the contour can reduce the dose to the skin by 6% to 7%,

thereby reducing the skin reaction. Many centers<sup>11</sup> now keep the uninvolved skin doses over neck nodes to 55 Gy.

Peak skin reactions resulting from hyperfractionated accelerated radiotherapy (more than one treatment per day, with a smaller dose per fraction) may not be observed until the end of treatment or following treatment because of the short course of therapy. Late skin reactions are related to a larger total dose and total treatment time.<sup>3</sup>

### REVIEW OF THE LITERATURE ON MANAGEMENT INTERVENTIONS

Several studies have been conducted assessing the outcome of interventions for the prevention and management of radiation skin reactions. There continues to be a paucity of evidence to recommend many of the interventions or products that have been or are being used in clinical practice. Identified products used as interventions in the literature include lotions, creams, ointments, and specialized dressings. Most studies have been prevention trials rather than management trials, with methodologic weaknesses making it difficult to make comparisons across studies to form recommendations for specific interventions. Other methodologic weaknesses include small sample sizes, a wide variety of terms used to describe reactions, a variety of measurement tools, and differential outcomes across studies. Some studies used the Radiation Therapy Oncology Group (RTOG) acute toxicity scale or a modified version of the RTOG scale, while others report investigator-developed scales. Outcomes vary widely, including severity of skin reaction based on time to erythema, mean and maximum erythema scores, mean severity scores, mean toxicity scores, time to dry desquamation, incidence and frequency of grades of skin reaction and pain, and pruritus.

A 2002 Canadian study<sup>12</sup> involving a semi-structured telephone survey with 26 regional radiotherapy departments identified significant practice differences across organizations and within interdisciplinary teams.<sup>12</sup> Historical practices and individual opinions have often guided practice interventions. Only recently have organizations begun to develop practice guidelines based on data from randomized control trials or literature reviews with organizational consensus for practice.<sup>13,14</sup>

Many general interventions and recommendations are found in the literature. While individually these recommendations may not provide any supporting evidence, they are often recommended in practice based on clinical experience and that they do not cause harm. Patients may be advised to wear loose clothing made of cotton or soft fabrics in areas of contact with the treatment field. Tapes and adhesives are not applied to the treatment area to prevent mechanical injury. Cosmetic products (perfume, make up, or aftershave) should also be avoided in the treatment field to prevent or minimize sensitivity reactions and irritation. The use of heating pads or ice packs is also not recommended to prevent thermal injury. Electric razors should be used for any shaving in the treatment field. Patients should avoid swimming in lakes or chlorinated swimming pools or using hot tubs once dry desquamation is present or if the skin is no longer intact because of the drying and irritating potential of chemicals used in commercial pools and the risk of infections from lakes or the warm moist environment of a hot tub. A cool mist humidifier should be recommended if humidification is required for other reasons. While saline soaks are recommended in many clinical settings, they provide no proven benefit with healing, but may provide comfort with a cooling sensation with the ability to loosen and remove any crusting in the treatment field. Additionally, cost, information, and ability for self-care need to be considered when nurses make skin care recommendations to patients and family care providers.

### **Washing**

Washing with lukewarm water and a mild soap is now recommended as routine care for all patients receiving radiation therapy. While several authors make this recommendation, only two randomized trials have been conducted assessing washing routines. Campbell and Illingworth<sup>15</sup> randomized 99 women receiving adjuvant radiotherapy for breast cancer to one of three groups comparing washing practices. The groups were no washing, washing with water alone, and washing with soap and water. All women were receiving treatment to the breast (chest wall), axilla, and supraclavicular fossa for 20 fractions, with two tangential opposed fields using a 5 MV linear accelerator. Approximately half of the women received a Vaseline (Chesebrough-Ponds, Greenwich, CT) bolus with 10 to 15 of the fractions.

Skin assessments including a RTOG grading score and evaluation of itching and pain were conducted during treatment and twice following end of treatment. A significant reduction in itching scores at the end of treatment, and erythema and desquamation scores following treatment (6 or 8 weeks), was found in patients who washed with soap and water independent of any bolus dose.

A similar study was conducted by Roy et al,<sup>16</sup> with 99 patients randomized to washing with soap and water or no washing. A higher incidence of moist desquamation was found in the no-washing group (33% vs 14%) and higher median scores for pain, itching, and burning, although these results were not statistically significant. There is insufficient evidence to recommend any particular mild soap during treatment. A study by Frosch and Kligman,<sup>17</sup> using a soap chamber method for determining the irritancy of soaps, classified Dove (Unilever, London, UK) as the only mild soap among 18 soaps tested. Washing and shampooing of the hair are socially expected hygiene practices. Preventing patients from using these normal routines may add unnecessary distress without any proven benefit.<sup>18</sup>

The use of deodorant within the treatment field has created controversy in clinical settings because of concerns about an increase in surface skin dose caused by a potential bolus effect from deodorants, creams, or powders. Burch et al<sup>19</sup> used an ionizing chamber to measure the surface dose of 15 products including six deodorants (ie, solids, roll-ons, and a spray). They compared a set of samples representing normal application thickness with a set of samples of extremely thick application and reported no increase in surface dose with normal application. The samples representing the thick application were five times the normal thickness of application and resulted in higher surface doses. Additionally, there was no difference between metallic and nonmetallic deodorant or powder products, challenging previous assumptions that products containing magnesium, aluminum, or zinc would cause an increased dose and skin reaction. The authors concluded that any enhanced skin reaction with normal product use could be related to irritating chemical ingredients in the product rather than because of an increased surface area and bolus effect with normal application of a product. Deodorant can be applied on intact skin and can be used throughout treatment.

### **Lotions and Potions**

A variety of lotions, creams, and ointments have been recommended in the literature but there is a paucity of randomized controlled trials with evidence to support one product over another.

**Aloe vera.** Three randomized trials of aloe vera gel have been conducted.<sup>20–22</sup> Aloe vera is a green fleshy cactus plant containing a gel that has been used as a complementary treatment for dry skin, cuts, and burns. While the use of aloe vera gel has been shown to be safe, none of the randomized trials showed any difference between groups that would support the use of an aloe vera product.<sup>23</sup> Williams et al<sup>22</sup> compared aloe vera gel with a placebo in 194 women receiving breast radiation. There was no difference in scores for maximum dermatitis severity or in the time to onset or duration of  $\geq$  grade 2 dermatitis. Olsen et al<sup>21</sup> randomized 73 patients receiving radiation to the head and neck, chest, or abdomen/pelvis to use aloe vera gel and washing with soap or to washing with soap alone. At higher cumulative doses ( $>27$  Gy), a significant difference was found in time to onset of skin changes. The authors concluded that aloe vera may provide a protective skin effect with increasing cumulative doses. Conversely, Heggie et al<sup>20</sup> compared aloe vera gel with a topical aqueous cream, each applied three times a day during treatment and for 2 weeks following treatment. They found that the cumulative probability of dry desquamation was higher in the aloe vera group (70% vs 41%), as was the prevalence of dry desquamation after 3 weeks of therapy. Aloe vera gel has been described as having anti-inflammatory and anti-bacterial properties, but is not a moisturizer.<sup>24</sup>

**Biafine (trolamine).** Biafine (Genmedix Ltd, France) is an oil-in-water emulsion that has been used in France for many years. It is reported to have non-steroidal anti-inflammatory properties, and heal wounds by recruiting macrophages to the wound bed and promoting the production of granulation tissue. Two randomized non-blinded studies compared trolamine with best supportive care (ie, Aquaphor [Smith & Nephew, Inc, Little Rock, AR] and aloe vera) or Lipiderm (G-Pharm Ltd, France), respectively.<sup>25,26</sup> Both studies included a no-treatment arm. Both studies included women with breast cancer receiving similar treatments of 50 Gy to the whole breast. The intervention product(s) used throughout treatment and for 2 weeks following treatment. Additionally, women in the Fenig et al<sup>26</sup> study received an additional 10 Gy

dose to the tumor bed and used the product starting 10 days before treatment. Neither study showed significant differences in the degree of skin reaction between products or no treatment, nor a prophylactic radioprotective benefit with trolamine.

A recent randomized trial compared *Calendula Officinalis* (marigold plant) with trolamine in women receiving radiation for breast cancer.<sup>27</sup> *Calendula* is a cream derived from the marigold plant. Outcome measures included the incidence of reaction by RTOG grade, pain, the relationship between pain and interference with daily living, the occurrence and reasons for any treatment disruptions, and satisfaction with the ease of product application. Results showed that calendula cream was statistically significantly better in reducing the occurrence of grade 2 or higher skin reaction, in reducing the associated pain with the skin reaction, and reducing the incidence of treatment interruption. While patients used the calendula cream (84% adherence) and were satisfied with pain relief, topical application of the cream was identified as difficult by 30% of patients. Although this study is unique in offering a potential for a product to prevent grade 2 dermatitis, a formulation that provides ease of application would encourage the uptake of this evidence into practice.

**Hyaluronic acid cream.** Only one human study has been conducted assessing the prophylactic use of hyaluronic acid (HA) cream.<sup>28</sup> Patients receiving radiation treatment for head and neck cancer, breast, or pelvic carcinomas were randomized to receive either HA 0.2% cream (Ialugen; IBSA, Lugano, Switzerland) or placebo, applied to the skin twice daily at the start of radiation. HA is a polymer that has been shown to stimulate fibroblasts and fibrin development, thereby accelerating the granulation phase of healing. In animal models, it has been hypothesized that HA destroys the oxygen free radicals associated with impairing wound healing.<sup>29</sup> An institution-based rating scale for skin reaction was used with outcome measures including skin reaction score, patient tolerability, and a subjective efficacy score by physician and patient. Results indicated a statistically significant improvement in delaying the onset of skin reaction by the third week as well as reducing the intensity and duration of reaction in the group using the HA cream. No other studies have been conducted to replicate and support or refute this finding. Although not

significant, the mean dose of radiation was lower in the group receiving the HA cream.

**Corticosteroids.** Corticosteroids have often been prescribed in both the prevention and management of radiation skin reactions caused by the anti-inflammatory effect in general dermatological conditions. The effects in radiation skin reactions are thought to be a result of vasoconstriction, reduced capillary permeability, and inhibition of leukocyte migration.<sup>30</sup> Although the studies have generally not found any significant differences or benefits with a particular steroid cream, all have compared different formulations of corticosteroid creams to each other or to an emollient cream.

Two randomized, double blind trials compared the prophylactic use of corticosteroid creams for the prevention of acute skin reactions in women with breast cancer.<sup>31,32</sup> Bostrom et al<sup>31</sup> randomized 49 women receiving radiation for node-negative breast cancer to receive either mometasone furoate (MMF) or an emollient cream twice daily from the start of radiation treatment until the twelfth treatment and then once daily until 3 weeks following treatment. Outcomes measured included the degree of erythema and pigmentation using reflectance spectrophotometry, visual skin assessment scores using a six-point investigator-developed scale, and subjective symptom experience. The patients receiving the emollient cream had significantly higher skin reactions scores compared with those in the MMF group (60% grade IV reaction vs 25%, respectively;  $P = .011$ ) but no significant difference in symptoms of pruritus or pain. While Schmuth et al<sup>32</sup> suggested that the topical corticosteroid cream may be beneficial to patients receiving radiation for breast cancer, no significant differences were found in the trial.

Two earlier studies evaluated the use of steroid creams in the management of skin reactions in patients with breast cancer, head and neck, chest wall, and abdominal cancers, respectively.<sup>33,34</sup> Glees et al<sup>33</sup> reported a significant difference in intensity of skin reaction favoring a 1% hydrocortisone cream compared with clobetasone butyrate cream. Despite this finding, these authors did not recommend either cream as a first choice treatment because 96.4% of the patients using the hydrocortisone cream and 88.5% of the patients using the clobetasone cream had a moderate to maximum skin reaction. Potera et al<sup>34</sup> reported no significant differences in the duration or intensity of skin reactions with the prophylactic use of a

0.2% hydrocortisone cream and a placebo in patients with a variety of cancer diagnoses.

**Sulcralfate.** Studies investigating sulcralfate have included both prevention and management trials as well as oral and topical routes of administration. Sulcralfate has been shown to stimulate cell growth in rats and has been reported to have an anti-inflammatory effect on gastrointestinal mucosa.<sup>35,36</sup> Two intraindividual prevention trials were conducted using patients as their own controls.<sup>37,38</sup> Evensen et al<sup>37</sup> assessed skin reactions in patients with head and neck cancer randomized to receive either sodium sucrose octasulfate (Na SOS) or a placebo. These authors reported no difference in erythema, but the placebo group had less moist desquamation resulting.

Maiche et al<sup>38</sup> randomized women with breast cancer to apply sucralfate cream or a base cream twice daily during 5 weeks of radiation therapy and reported a significant reduction in the development of grade 2 skin reactions with more rapid healing with the sucralfate cream. The conflicting results between these two trials may be related to the different patient groups and treatment doses and the different formulations of the sucralfate cream used.

A later study by Wells et al<sup>39</sup> randomized 357 patients with head and neck, breast, or anorectal cancer to receive either aqueous cream, sucralfate cream, or no cream from the start of treatment. Outcome measures included the measurement of acute skin toxicity or grade (modified RTOG score), erythema readings using reflectance spectrophotometry, a quality-of-life score, and symptoms including pain, itching, burning, and sleep disturbance. No significant differences were found between the treatment arms. The researchers concluded that there was no benefit from a prophylactic application of a cream to the treatment area. More significantly, the authors identified several risk factors related to more severe skin reactions, suggesting the need for further study in patients at higher risk.

Two studies assessing the effectiveness of oral sucralfate found no benefit of the prophylactic use of sucralfate in reducing the degree of skin reactions in patients receiving head and neck cancer or in reducing any late toxicity on the rectum in patients receiving radiation for prostate cancer.<sup>40,41</sup> Delaney et al<sup>42</sup> stratified patients by cancer diagnosis and randomized patients to receive 10% sucralfate in sorbolene cream or sorbolene alone for the management of  $\geq$  grade 3 (RTOG

criteria) moist desquamation. Sorbolene is a cream composed of water and oils often containing 10% glycerin. No differences were found in the measurement of pain or in time to healing between the two products, although the study was closed early because of limited accrual. The researchers also identified that significant heterogeneity existed between the two treatment groups.

**Barrier films.** The use of barrier films or creams as a skin protector has been hypothesized to reduce trauma and retain moisture in the maintenance of intact skin, thereby reducing radiation injury. Cavilon No-Sting barrier film (3M, St Paul, MN) was evaluated as a prophylactic treatment in the prevention of moist desquamation.<sup>43</sup> No-Sting was compared to sorbolene in women receiving 50 Gy in 25 fractions of radiation for breast cancer. An internal control method was used randomizing the products to either the medial or lateral aspect of the chest wall, applied from the start of radiation to 2 weeks following treatment. No-Sting was applied twice weekly as it is designed to last several days, whereas the sorbolene cream was applied twice daily based on standard practice. Irrespective of the frequency of application of the two products, the No-Sting showed a statistically significant improvement in frequency and duration of moist desquamation, but no difference in pain or pruritus.

An earlier pilot study by See et al<sup>44</sup> evaluated the use of Dermofilm (Innovatec, Australia Pty Ltd), a micro-thin emollient skin protector, containing hydrophilic and lipophilic agents, in 50 patients receiving radiation to a variety of treatment sites. Although favorable results were reported in reducing pain and skin irritation, a larger randomized trial comparing Dermofilm with other products was recommended.

Table 1 describes trials on ointments and creams for the prevention and management of acute radiation skin reactions.

**Antimicrobials.** Silver sulfadiazine (Silvadene; King Pharmaceuticals Inc, Bristol, TN) and other antibacterial agents have been used with radiation skin reactions because of their ability to reach a high concentration of the drug in the local area with minimal systemic absorption. Silver sulfadiazine, a sulfa drug, is a bacteriocidal agent active against most gram-positive and gram-negative bacteria. It has generally been used in patients with burns or mild infections.<sup>45</sup> While other drugs have been shown to be more effective in burns, silver sulfadiazine has been shown to have

a low toxicity and hypersensitivity as well as a low incidence of resistance. It should be avoided in patients with sensitivity to sulfa drugs. No studies exist that assess the use and benefit of silver sulfadiazine ointment in radiation skin reactions. Antimicrobials should not be used as prophylactic management because of concerns about sensitivity or resistance with overuse.<sup>8</sup>

### Dressings

The use of dressings in the management of radiation skin reactions is based on the understanding that a moist wound-healing environment promotes the rate of re-epithelialization and the migration of epithelial cells across the wound bed and that wounds kept moist heal 50% faster.<sup>6,7</sup>

**Hydrophilic dressings.** While a number of authors have cited the use of dressings in the management of moist desquamation, few studies exist evaluating the effects of hydrocolloids, semi-permeable dressings, or hydrogels in the management of radiation skin reactions. Further, the variety of dressings on the market varies in thickness, fluid handling or retention ability, permeability, and conformability. The most commonly cited study evaluating moisture vapor permeable (MVP) dressings assessed the rate of healing and patient comfort in 16 patients with dry and moist desquamation.<sup>46</sup> Patients were randomized to use either a MVP (Tegaderm, 3M) dressing or hydrous lanolin gauze dressing to manage skin reactions during radiation treatment.<sup>46</sup>

Additionally, patients in the gauze-dressing group who had more severe reactions had the skin cleansed with a one quarter strength hydrogen peroxide solution followed by a saline rinse. Healing time in the MVP group was 19 days versus 24 days for patients using the gauze dressing. Patient discomfort scores varied in both groups and were associated with dressing changes. Despite no statistical difference being found between the two types of dressings, these authors suggest the potential for MVP dressings to be used in the management of radiation skin reactions.<sup>46</sup>

Two studies evaluated the use of hydrocolloid dressings in patients who had completed radiation treatment.<sup>47,48</sup> Margolin et al<sup>47</sup> evaluated the use of Duoderm (ConvaTec, Princeton, NJ) in a non-comparative study with 18 patients who completed radiation. Mean healing time was 13 days without any documented wound infections. Mak et al<sup>48</sup> compared the effect of a hydrocolloid dress-

**TABLE 1.**  
**Descriptions of Trials on Ointments and Creams for the Prevention and Management of Acute Radiation Skin Reactions**

Intervention	Study	Study Design	No. of Patients Per Treatment Arm	Outcomes Measured	Findings
Aloe vera	Dudek et al <sup>23</sup> (2000)	Non-randomized controlled	109 (3 different commercial products of aloe vera gel) - 25, 25, and 59 in each group	RTOG toxicity score, Acute Skin Reaction Index (ASRI)	No difference between groups; Aloe vera shown to be safe
	Heggie et al <sup>20</sup> (2002)	RCT	107 - aloe vera 101 - aqueous cream	Skin toxicity, pain, itching	Higher probability of dry desquamation in aloe group; higher prevalence of dry desquamation in aloe group
	Olsen et al <sup>21</sup> (2001)	RCT	33 - mild soap + aloe 40 - mild soap	Skin change and RTOG toxicity (erythema, skin texture, skin itch, tanning)	69% pf patients receiving aloe + soap had skin changes at < 27Gy vs 43 % of soap only ( $P < .034$ )
	Williams et al <sup>22</sup> (1996)	RCT	194 - aloe vs placebo 108 - aloe vs no treatment	Maximum dermatitis severity, time to onset of $\geq$ grade 2 dermatitis, duration of $\geq$ grade 2 dermatitis	No difference in scores for all measures
Trolamine	Fisher, et al <sup>25</sup> (2000)	RCT	66 - biafine 74 - best supportive care	RN and RT grading of skin reaction	No difference in degree of skin reaction between groups
	Fenig et al <sup>26</sup> (2001)	RCT	25 - biafine 24 - lipiderm 25 - no treatment	Maximum skin reaction score, time to grade 2 toxicity, duration of dermatitis	No difference in degree of skin reaction between groups
Calendula cream	Pommier et al <sup>27</sup> (2004)	RCT	126 - calendula 128 - trolamine (biafine)	Incidence, RTOG score, pain, pain and interference with ADL, treatment interruptions, product satisfaction	Reduced grade 2 or higher skin reactions ( $P < .001$ ); reduced pain ( $P = .03$ ) with calendula cream
Hyaluronic acid cream	Liguori et al <sup>28</sup> (1997)	RCT	76 - hyaluronic acid 0.2% 76 - placebo	Skin reaction scale (institution based), patient tolerability, efficacy score by physician and patient	Delayed onset of skin reaction by week 3; reduced intensity and duration of skin reaction with hyaluronic acid weeks 3-7, 8 and 10
Corticosteroids	Bostrom et al <sup>31</sup> (2001)	RCT	25 - MMF 25 - emollient cream	Degree of erythema, pigmentation, visual skin assessment (investigator developed tool), symptom rating	60% grade IV skin reaction in emollient group vs 35% MMF group, $P = .011$ ; no difference in pain or pruritis

**TABLE 1.**  
**Descriptions of Trials on Ointments and Creams for the Prevention and Management of Acute Radiation Skin Reactions (Cont'd)**

Intervention	Study	Study Design	No. of Patients Per Treatment Arm	Outcomes Measured	Findings
Sulcrafate	Schmuth et al <sup>32</sup> (2002)	RCT	11 - 0.5% dexpanthenol cream 10 - 0.1% MPA 15 - control group	Mean severity score, adverse effects (itching, burning), Skindex	No differences between groups
	Evensen et al <sup>37</sup> (2001)	RCT (patients as own control)	60 - Na SOS vs placebo	Erythema, desquamation, pain, itching	No significant differences
	Maiche et al <sup>38</sup> (1994)	RCT (internal control method)	44 - sulcrafate vs base cream	Incidence of grade 2 reaction	Significant reduction in grade 2 skin reaction, more rapid healing with sulcrafate cream
	Wells et al <sup>39</sup> (2004)	RCT	120 - Aqueous cream 122 - Sulcrafate cream 124 - No cream	Skin toxicity, (modified RTOG), erythema, quality of life, symptoms (itching, pain, sunburn, sleep disturbances, erythema, desquamation)	No difference in treatment arms
	Delaney et al <sup>42</sup> (1997)	RCT	20 - 10% sulcrafate in sorbolene cream 19 - Sorbolene cream	RTOG toxicity, pain, healing	No difference in pain or healing of moist desquamation
Barrier Films	Graham et al <sup>43</sup> (2004)	RCT (internal control method)	61 - No-Sting vs sorbolene (30 medial application, 30 lateral)	RTOG score, pain, pruritis	Reduction in frequency and duration of moist desquamation and pruritis in No-Sting group

Abbreviations: RCT, randomized controlled trial; MMF, mometasone furoate; MPA, methylprednisolone aceponate cream; Na SOS, sodium sucrose octasulfate; RTOG, Radiation Therapy Oncology Group; RN, registered nurse; RT, radiation therapist; ADL, activities of daily living.

ing changed every 2 days with the twice-daily application of gentian violet, an antifungal and antiseptic agent, on moist desquamation in 42 patients. The study was conducted despite evidence in animal models indicating that gentian violet interfered with wound healing. Although the effect on human wound healing was not known, toxicities were reported when gentian violet was used on blisters in mucosal tissue. No significant differences existed between the two groups in wound healing time, although dressing comfort and aesthetics was statistically significant for the hydrocolloid dressing.

Several other dressings have been used in clinical practice or described in the literature, including hydrogels for wound hydration, absorbent dressings for exudates management, foam dressings, and alginates, among others, but none have been studied in patients with radiation skin reactions.<sup>6</sup> Although one study was conducted evaluating Mepitel (Mölnlycke Health Care, Göteborg, Sweden), a non-adhering dressing, the study evaluated the potential bolus effect to the skin rather than the effect on wound healing.

**Silver dressings.** Silver dressings have been used in the treatment of burns, venous ulcers, and

chronic wounds requiring an antibacterial.<sup>49,50</sup> The dressing is a non-adherent rayon and polyester material coated with manocrystalline silver. In patients with burns, silver leaf nylon dressings (SLND) have been shown to be more effective than topical agents, including silver sulfadiazine. SLND have only been recently considered in the management of radiation skin reactions. Vuong et al<sup>51</sup> evaluated the dressings with 15 consecutive patients receiving radiation to the perineum for anal canal or gynecologic cancers. Patients wore the dressing from the beginning of treatment and for 2 weeks post-treatment. Historical controls were used for comparison. All patients received radiation and chemotherapy. While the incidence of grade 3 and 4 reactions in this group of patients is typically 43% to 78%, the SLND reduced this incidence significantly, with only three grade 3 scores and no grade 4 scores in patients using the SLND compared with 92 grade 3 and 4 scores in the control group. This study highlighted the role and benefit of using an antibacterial dressing in patients receiving radiation for anal canal and gynecologic cancers.

### RECOMMENDATIONS FOR FUTURE RESEARCH

There remains a paucity of literature and well-designed studies evaluating the effectiveness of interventions for the prevention and

management of radiation skin reactions. Early data supports the use of calendula cream to decrease the incidence of moist desquamation. Further evaluation is required with consideration to the formulation for ease of application. Barrier films or creams may also be an intervention that will prove beneficial, but further research is also required. Because of limited evidence for prevention and management, secondary outcomes such as comfort, symptom relief, ease of application, and cost may be more important. Larger, multi-site trials need to be conducted using consistent and validated outcome measures. Outcomes directed at reducing the onset and duration of skin reactions in addition to incidence need to be considered.

Several trials evaluating topical agents have raised the question whether any product will actually prevent or promote the healing of radiation skin reactions. Given that radiation skin reactions are a result of damage to the dermal layer of the skin and the resultant imbalance between the normal production of cells at the basal layer of the skin and the destruction of cells at the skin surface, other interventions may need to be developed aimed at affecting the underlying physiologic mechanisms.

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