

Putting Evidence Into Practice: Evidence-Based Interventions for Radiation Dermatitis

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Radiation dermatitis, or radiodermatitis, is a significant symptom caused by radiation therapy for the treatment of cancerous and noncancerous conditions. Radiodermatitis can negatively affect patients' physical functioning and quality of life. The Oncology Nursing Society coordinated a Putting Evidence Into Practice (PEP) project team to develop a PEP resource summarizing current evidence for the management of patients with radiodermatitis. Oncology nurses play an important role in educating, assessing, and monitoring patients for this symptom. Many common nursing interventions for radiodermatitis are based on tradition or opinion and have not been researched thoroughly. In addition, evidence to support some current interventions in practice is lacking. This article presents information concerning radiodermatitis, summarizes the evidence-based review for its prevention and management, and identifies gaps in the literature, as well as opportunities for research, education, and practice.

Radiodermatitis, also known as radiation dermatitis or radiation skin reaction, is caused by the changes cells undergo in the basal layer of the epidermis and the dermis (Wickline, 2004). Cumulative daily doses of radiation to the treatment field, including doses deposited to the skin, prevent normal skin cells from repopulating immediately, which weakens skin integrity in the radiation field. In countries such as the United States, Canada, Europe, and Australia, at least 50% of patients diagnosed with cancer will receive radiation therapy during their illness (Bernier et al., 2008). Up to an estimated 95% of patients receiving radiation therapy will experience some degree of skin reaction, which may include erythema, dry desquamation, and moist desquamation (De Conno, Ventafredda, & Saita, 1991; King, Nail, Kreamer, Strohl, Johnson, 1985; Porock & Kristjanson, 1999) (see Table 1). The true incidence of radiodermatitis resulting from new technologies along with the increased use of multimodality therapy is not known (Bernier et al., 2008; Hymes, Strom, & Fife, 2006; Pignol et al., 2008). The effects of radiodermatitis can impact a patient's quality of life, cause pain and discomfort, limit activities, and delay treatment (Aistairs,

At a Glance

- ◆ Radiodermatitis is associated with the integumentary system response to a planned exposure of ionizing radiation, which depletes stem cells from the basal layer of the epidermis.
- ◆ Current evidence-based interventions recommended for practice include intensity-modulated radiation therapy and usual hygiene practices such as washing the irradiated skin and the use of mild soaps and deodorants.
- ◆ A wide variety of treatments currently in use have not demonstrated effectiveness in randomized, controlled studies, highlighting a need for research to guide evidence-based practice in this area.

2006). Radiodermatitis also may cause interruption in or cessation of treatment, depending on the severity of reaction.

Although avoidance of skin reactions caused by radiation therapy would be preferred, it often is not possible, such as

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Table 1. Potential Radiation Skin Reactions

SYMPTOM	DEFINITION	ONSET DOSAGE
Erythema	Inflammatory reaction characterized by reddened skin that may be edematous and feel hot. Redness outlines the treatment field and intensifies as treatment continues.	2,000–4,000 cGy
Dry desquamation	Inflammatory reaction to radiation characterized by dry flaky skin and pruritis	More than 3,000 cGy
Moist desquamation	Inflammatory reaction to radiation characterized by serous drainage and occurs most likely in regions of friction (e.g., inframammary folds, axilla)	More than 4,000 cGy

Note. Based on information from Baney et al., 2011; Moore-Higgs, 2005; Sparks, 2007.

in treatment for inflammatory breast cancer where an intense skin reaction is expected. Therefore, delay and reduction in severity of radiodermatitis is the goal, not total elimination (Primavera et al., 2006). Various products for prevention or management of radiodermatitis have limited evidence or consensus to support their use (Bolderson, Lloyd, Wong, Holden, & Robb-Blenderman, 2005). Although limited evidence supports the use of general measures such as washing with mild soap and water, keeping the treatment area clean and dry, wearing loose-fitting clothes, and protecting the radiation area from irritants, those measures have been found to be anecdotally effective (Omidvari et al., 2007).

Several factors can be attributed to the varying response of patients' skin to radiation therapy. Treatment-related factors such as individual fraction size, type of energy, and the use of bolus doses can impact skin reactions. Host factors also may play a role in the development of radiodermatitis; they may include genetic factors, personal factors (e.g., areas of skin friction), existing skin integrity issues, comorbid conditions, nutritional status, age, race and ethnicity, medications, sun exposure, smoking, and mobility (Ryan et al., 2007). The relationship between those factors must be considered when identifying patients at greater risk for impaired skin integrity because of radiation therapy.

Late skin changes also may be seen in patients who have received radiation therapy. The changes may appear several months to years after radiation therapy has been completed. Changes in skin pigmentation are caused by radiation's damaging effects to melanocytes. Telangectasia results from damage and stretching of the capillaries, commonly found with moist desquamation during the acute phase of radiodermatitis. Fibrosis may be one of the most debilitating late changes that can occur. Fibrosis is caused by excessive extracellular matrix and collagen deposits occurring because of the inflammatory response, with changes in the proliferative and tissue remodeling phases of wound healing following radiation therapy. Fibrosis can lead to decreased tissue flexibility causing reduced range of motion, strictures, atrophy, and reduced tissue strength. Finally, although rare, patients are at increased risk for delayed wound

healing, dehiscence, fistula, tissue graft failures, and other surgical complications within a radiation treatment field (Bentzen, 2006; McQuestion, 2010).

Unfortunately, research determining appropriate methods for prevention or treatment of late radiation skin changes is lacking. Anecdotal evidence suggests that intensity-modulated radiation therapy (IMRT) may decrease the incidence of late effects. One study reviewed the use of IMRT in patients with breast cancer and showed a decrease in severity and duration of moist desquamation (Freedman et al., 2009). One may extrapolate a potential for decreased late effect skin changes, but this was not an endpoint of the study. To date, available literature does not address interventions for late effect management, other than massage in women with fibrosis caused by breast radiation (Bourgeois, Gourgou, Kramar, Lagarde, & Guillot, 2008).

Assessment Tools and Grading Scales

Commonly used grading or scoring tools for assessment and documentation of radiodermatitis include the Radiation Therapy Oncology Group (RTOG) Acute Radiation Morbidity Scoring Criteria (Cox, Stetz, & Pajak, 1995); the RTOG/European Organization for Research and Treatment of Cancer (EORTC) toxicity criteria (Cox et al., 1995); the *Common Terminology Criteria for Adverse Events*, version 4.03 (CTCAE) (National Cancer Institute Cancer Therapy Evaluation Program, 2010); the Skin Toxicity Assessment Tool (Berthelet et al., 2004); the Oncology Nursing Society (ONS) *Radiation Therapy Patient Care Record*, using the CTCAE, version 2.0 (Catlin-Huth, Haas, & Pollock, 2002); and the Radiation-Induced Skin Reaction Assessment Scale (Noble-Adams, 1999a, 1999b) (see Table 2). Each assessment tool can be used to identify grades or ranges of skin reactions from erythema to dry and moist desquamation. Most of the tools are practitioner or observer assessments that do not capture symptoms or impact of skin reactions. A skin assessment should be completed at baseline, prior to initiation of treatment, and reassessments should occur minimally at weekly treatment appointments. Assessment should include evaluation of observed physical changes, as well as patient symptoms. Issues to assess include changes in color, appearance of erythema, patchy dry desquamation, patchy or confluent moist desquamation, drainage, odor, possible infection, and sensations of dryness, pruritis, or pain. The distress and impact associated with radiodermatitis on quality of life, daily living, self-care ability, and financial impact of caring for the skin reaction also are important areas of assessment.

Methods and Process

ONS's Radiodermatitis Putting Evidence Into Practice (PEP) Team comprised five advanced practice nurses and three staff nurses with expertise in the field of radiation oncology. The team used the problem, intervention, comparison, and outcome process for determining appropriate topics for the literature search. The evidenced-based review of literature included clinical practice guidelines, systematic reviews, and clinical research studies. Because of the small number of research studies, the

search was limited to studies done within the past 10 years, rather than five years. Studies were limited to those completed with human participants. All research was published in English. Unpublished research (e.g., abstracts, theses) was excluded. The following search engines were used: MEDLINE®, the National Library of Medicine's database, CINAHL®, CancerLit®, and the Cochrane Database. The ONS Weight of Evidence Classification was used in the review and categorization of each article (see Baney et al., 2011).

The PEP team members reviewed materials via telephone or Web conferencing from August 2009 through June 2010. Evidence tables, guideline tables, expert opinion tables, and definition lists were developed for the radiodermatitis PEP chapter (see Baney et al., 2011). Three external radiation oncology experts, as selected by the ONS PEP project coordinator, reviewed the content.

Recommended for Practice

Intensity-Modulated Radiation Therapy

Three studies demonstrated reduced skin toxicity in patients with breast cancer receiving IMRT versus conventional radiation therapy. In all studies, the National Cancer Institute Cancer

Therapy Evaluation Program's (2010) CTCAE was used to grade skin toxicity.

Freedman et al. (2009) compared 399 women treated with IMRT to 405 women treated with conventional radiation for breast cancer. The IMRT group had significantly less grade 2 or higher skin toxicity ($p \leq 0.001$) and less time spent per week with grade 2 or 3 dermatitis ($p < 0.001$) as compared to the conventional radiation group. Significant predictors ($p < 0.02$) of grade 2 or higher dermatitis were use of IMRT versus conventional techniques in the administration of radiation therapy, large bra size, treatment weeks 2–6, and receiving chemotherapy or tamoxifen before or during radiation.

Pignol et al. (2008) studied skin reactions and pain in women with early-stage breast cancer treated with IMRT ($N = 170$) versus conventional therapy ($N = 161$). Fewer patients treated with IMRT experienced moist desquamation during and up to six weeks postradiation treatment as compared to those receiving conventional treatment ($p = 0.002$). IMRT ($p = 0.003$) and smaller breast size ($p = 0.001$) were associated with decreased risk of moist desquamation in a multivariate analysis. Consistent with Freedman et al. (2009), breast size and use of technology predicted the degree of skin reaction.

Freedman et al. (2006) compared 73 women receiving breast IMRT to 60 historical controls treated with conventional radiation

Table 2. Clinical Measurement Tools for Radiodermatitis

TOOL	DESCRIPTION	BENEFITS AND/OR LIMITATIONS
Radiation Therapy Oncology Group Acute Radiation Morbidity Scoring Criteria (1985) (Cox et al., 1995)	Assesses intensity or severity of reaction Ordinal scale 0–4	No reliability or validity data published Observation of physical changes Does not address symptoms or patient perspective Commonly used in clinical trials
Radiation Therapy Oncology Group/ European Organization for Research and Treatment of Cancer toxicity criteria (Cox et al., 1995)	Assesses late complications Ordinal scale 1–4 Acute: less than 90 days after first treatment Late: after day 90 Also assesses fibrosis, induration, skin contracture, and necrosis	No reliability or validity data published Observation of physical changes Does not address symptoms or patient perspective
<i>Common Terminology Criteria for Adverse Events</i> [v.4.03] (version 2.0 incorporated into Oncology Nursing Society <i>Radiation Therapy Patient Care Record</i> for Radiation Dermatitis by Site Group) (Catlin-Huth et al., 2002)	Adverse events reporting tool Severity scale Rash: dermatitis associated with radiation Ordinal scale 0–5 Grades of desquamation	No reliability or validity data published Observation of physical changes Does not address symptoms or patient perspective
Skin Toxicity Assessment Tool (known as STAT) (Berthelet et al., 2004)	Three areas of assessment Patient and treatment factors affecting incidence and intensity of radiodermatitis Objective scoring of grades of desquamation Patient symptoms	Preliminary reliability and validity results reported (Berthelet et al., 2004) Easy to use in the clinical setting Quickly administered
Radiation-Induced Skin Reaction Assessment Scale (known as RISRAS) (Noble-Adams, 1999a, 1999b)	Weighted categories (e.g., moist desquamation weighted higher than dry desquamation) for overall score that incorporates effect on patient Symptom scale (e.g., tenderness, itching, burning, warmth, effect on activity) Observer assessment (e.g., erythema, dry desquama- tion, moist desquamation, necrosis)	Nursing assessment tool Objective observer assessment and patient's perspective of symptoms Reliability and validity scores have been reported. Has not been widely used in practice research

Note. From "Radiodermatitis" (pp. 52–53), by T. Baney, M. McQuestion, K. Bell, S. Bruck, D. Feight, L. Weis-Smith, and M. Haas in L.H. Eaton, J.M. Tipton, and M. Irwin (Eds.), *Putting Evidence Into Practice: Improving Oncology Patient Outcomes* (vol. 2), 2011, Pittsburgh, PA: Oncology Nursing Society. Copyright 2011 by the Oncology Nursing Society. Reprinted with permission.

Although research regarding intensity-modulated radiation therapy for breast radiation is promising for the reduction of radiodermatitis, use of this intervention in daily practice is not standard care.

size ($p < 0.0001$) were the only significant predictors of moist desquamation (Freedman et al., 2006).

Although research regarding IMRT for breast radiation is promising for the reduction of radiodermatitis, use of this intervention in daily practice is not considered standard care for patients with breast cancer. IMRT is not routinely covered by most insurance carriers in the United States, except in the treatment of head and neck and prostate cancers.

Usual Hygiene Practices

Washing: The practice of washing the skin and hair in the treatment field along with the use of deodorant has created controversy in the clinical setting. Preventing normal socially accepted hygiene practices distresses patients (McQuestion, 2010; Roy, Fortin, & Larochelle, 2001). Three research studies demonstrated that skin washing in the irradiated fields with mild soap and water or water alone did not increase skin toxicity. An additional study compared normal skin care practice to warm water only.

Roy et al. (2001) randomized 99 patients with breast cancer receiving radiation to washing with mild soap and water or not washing the treatment field. Those who washed had lower overall maximum skin toxicity scores (grade 2 or higher) based on RTOG scoring criteria ($p = 0.04$). Moist desquamation was significantly higher in the nonwashing group ($p = 0.03$) (Roy et al., 2001).

In a study of 107 patients receiving cranial radiation, Westbury, Hines, Hawkes, Ashley, and Brada (2000) compared usual patient scalp care practices to patients instructed not to wash their hair during treatment. Based on RTOG scoring criteria, the severity of skin reactions did not increase in the hair washing group (Westbury et al., 2000).

Meegan and Haycocks (1997) demonstrated that patients using their typical skin-care regimens did not have increased severity of skin reactions during and after radiation therapy. In the study, 94 patients used warm water only, excluding all lotion, soaps, and deodorants in the treatment fields, compared to 64 patients with no restrictions on normal skin-care practices. No significant differences were found in skin assessment scores between the two groups; however, patient self-scoring of skin reaction severity was consistently higher in patients using only warm water (Meegan & Haycocks, 1997).

Campbell and Illingworth (1992) randomized 95 women treated with radiation for breast cancer to not washing, washing with water alone, or washing with soap and water in the treated area. Comparisons showed a statistically significant reduction in itching and erythema ($p < 0.05$) with washing (water alone and

washing with soap) as compared to not washing. Women who washed had markedly smaller desquamation scores than those not washing. The findings supported allowing patients to wash (with water alone and soap) during radiation therapy (Campbell & Illingworth, 1992).

Deodorant: Two studies addressed use of nonaluminum deodorant during radiation. Concerns regarding deodorant focused on direct skin effects and potential effects on the surface dose of radiation.

In a clinical study by Theberge, Harel, and Dagnault (2009), 84 women with breast cancer receiving radiation were randomly assigned to nonaluminum deodorant versus no deodorant. Statistically significant findings favoring the use of deodorant included a reduction in grade 2 axillary dermatitis ($p = 0.02$), axillary moist desquamation ($p = 0.003$), discomfort and pain to axillary region ($p = 0.004$ and $p = 0.002$, respectively), self-reported axillary pruritis ($p = 0.0002$), grade 2 breast dermatitis ($p = 0.05$), and moderate to severe pain in the entire treatment area ($p = 0.03$) compared to those who did not use deodorant (Theberge et al., 2009).

In a nonclinical study, Burch, Parker, Vann, and Arazie (1997) examined skin surface doses with 15 products, including deodorants, powders, and creams, using an ionization chamber with large and small radiation field sizes. Very little difference was found in surface doses among products when comparing normal application thickness to five times the thickness. In addition, no differences were found between metallic and non-metallic products (Burch et al., 1997).

Likely to Be Effective

Calendula

A large randomized, controlled trial demonstrated the effectiveness of calendula ointment compared to Biafine[®] topical emollient for prevention of radiodermatitis. Pommier et al. (2004) randomized 254 women with breast cancer to twice daily (or more) application of calendula or Biafine on irradiated fields. Patients applying calendula had a reduced prevalence of grade 2 dermatitis ($p < 0.001$), lower reported levels of pain ($p < 0.03$), and fewer treatment interruptions. Self-assessed prevalence of erythema and allergic reactions also were lower. Skin toxicity of grade 2 or higher was significantly increased for women whose body mass index was 25 or higher ($p < 0.001$) and for women who had received prior chemotherapy ($p = 0.01$).

Hyaluronic Acid and Sodium Hyaluronate

The literature reviewed on hyaluronic acid cream (Ialugen[®]) included a large double-blind, randomized, placebo-controlled trial and expert opinion guidelines. Bernier et al. (2008) recommended use of hyaluronic acid topical cream in the management of grade 2 or 3 skin toxicity in the absence of infection. Liguori, Guillemain, Pesce, Mirimanoff, and Bernier (1997) randomly assigned 134 patients receiving radiation therapy for head and neck, breast, or pelvic cancers to 0.2% hyaluronic acid cream or placebo twice daily, applied to the treatment field. The placebo group demonstrated significantly higher acute radiodermatitis scores ($p < 0.01$). Patients and physicians judged improved treatment efficacy with hyaluronic acid. In the subgroup of

patients with head and neck cancer, a significant difference was observed in favor of hyaluronic acid following observation at week 3 ($p = 0.0003$), week 4 ($p = 0.0001$), and week 5 ($p = 0.004$) (Liguori et al., 1997).

Benefits Balanced With Harms

No literature was found in this category.

Effectiveness Not Established

Topical and oral treatments, as well as various dressings, have been studied for effects on radiation-induced skin toxicities. A systematic review by Kedge (2009) examined results across 10 randomized, controlled trials from 1990–2008 with about 575 patients using topical agents and hydrocolloid dressings. No convincing evidence was found for any intervention studied (Kedge, 2009). The Supportive Care Guidelines Group of Cancer Care Ontario also concluded insufficient evidence to support or refute a wide variety of topical, IV, and oral agents (Bolderson et al., 2005).

Topical Agents

Aloe vera: In a systematic review, Vogler and Ernst (1999) looked at 10 controlled clinical trials involving 740 participants using aloe vera orally or topically. They concluded that topical application of aloe vera did not appear to prevent radiation-induced skin damage. However, firm conclusions could not be drawn from the review because of multiple methodologic problems (e.g., small sample size per study, variety of agents compared to aloe vera) in the research (Vogler & Ernst, 1999).

Aloe vera was studied in four randomized, controlled trials, two of which were blinded and conducted at multiple sites (Heggie et al., 2002; Williams et al., 1996). Study populations included patients receiving radiation for any field where skin reactions were expected to occur.

Merchant et al. (2007) compared aloe vera gel to an anionic polar phospholipid (APP) cream in 45 pediatric patients receiving radiation to the thorax, axilla, and craniocervical regions. Grouped common toxicity criteria scores were favorable for use of APP cream as compared to aloe vera gel ($p = 0.004$). In comparing first and last assessments, two dermatologic variables, dryness ($p = 0.04$) and peeling ($p = 0.02$), supported use of APP cream over aloe vera (Merchant et al., 2007).

Heggie et al. (2002) performed a double-blind, randomized controlled trial comparing topical aloe vera gel to a water-based moisturizing cream in 208 women treated with radiation for breast cancer. Aqueous cream was significantly more effective than aloe vera gel in reducing the incidence of dry desquamation ($p < 0.001$) and moderate to severe pain ($p = 0.03$). Only non-chemotherapy recipients using aloe vera showed a significantly reduced incidence of moderate or higher erythema ($p = 0.02$).

Olsen et al. (2001) compared use of aloe and mild soap to mild soap alone in 70 patients receiving radiation to the head and neck, chest, and extremities. Olsen et al. (2001) concluded that adding aloe seemed to have a protective effect, but did not provide definitive data to support the conclusion.

Williams et al. (1996) reported results of two randomized, controlled trials. One trial compared aloe vera gel to a placebo gel, whereas the other compared aloe vera to no treatment. Both studies included women receiving radiation for breast cancer ($N = 194$ and $N = 108$, respectively). No significant differences were found between groups in severity or prevalence of skin toxicities (Williams et al., 1996).

MAS065D: Two small trials assessed the effect of MAS065D (Xclair®) in managing radiodermatitis. Leonardi et al. (2008) randomly assigned 35 women with breast cancer receiving radiation to MAS065D or an emollient base cream with similar color and consistency to MAS065D. Results demonstrated less burning in the radiation field ($p = 0.04$), less desquamation ($p = 0.02$), and lower maximum skin toxicity grade ($p < 0.0001$) in the MAS065D group (Leonardi et al., 2008).

Primavera et al. (2006) conducted a double-blind, vehicle-controlled study in 22 women with breast cancer receiving radiation. Comparisons were made between MAS065D and a control topical agent being applied to two different sections of skin within a patient's radiation field. The mean erythema score with MAS065D was found to be significantly lower than control at the fifth treatment visit ($p = 0.03$). Patients and investigators preferred MAS065D ($p = 0.007$ and $p = 0.04$, respectively).

Steroids: Four randomized, controlled studies were conducted to determine the effectiveness of various topical steroids for the prevention or management of radiodermatitis. All reviewed studies had small sample sizes and methodologic issues, including a variety of treatment delivery methods (i.e., different radiation techniques or doses and concentrations of steroid), lack of randomization, comparison to cohort groups, and investigator-developed assessment tools that lacked proven validity and reliability. No study demonstrated a clear benefit for use of topical steroids.

Omidvari et al. (2007) randomized 51 women receiving radiation for breast cancer to three arms: bethamethasone, petrolatum, and no treatment. Use of bethamethasone demonstrated no clear benefits (Omidvari et al., 2007).

Shukla, Gairola, Mohanti, and Rath (2006) randomly assigned 60 women undergoing radiation therapy for breast cancer to the use of beclomethasone spray versus no intervention. Patients using beclomethasone had less prevalence of axillary wet desquamation than the control group ($p = 0.04$). Whether differences in skin toxicity were associated with topical treatment or method of radiation delivery was unclear (Shukla et al., 2006).

Bostrom, Lindman, Swartling, Berne, and Bergh (2001) examined the use of mometasone furoate versus emollient cream in 50 women treated with radiation for breast cancer. Erythema was calculated using spectrophotometry, with a significantly lower maximal score reported for those treated with mometasone furoate ($p = 0.01$) (Bostrom et al., 2001).

Schmuth et al. (2002) randomly assigned women with breast cancer receiving radiation to 1% methylprednisolone aceponate

Evidence is insufficient to support or refute a wide variety of topical, IV, and oral agents currently used in the management of radiodermatitis.

cream (N = 10) or dexpanthenol (N = 11). The experimental arms were compared to a historical cohort of 15 patients. Women treated in the steroid arms had fewer high-grade skin reactions, but the finding was not statistically significant (Schmuth et al., 2002).

Dexpanthenol: In four clinical trials, a specific steroid, dexpanthenol (Bepanthol®), was compared to other treatments for management of radiodermatitis. The study by Schmuth et al. (2002) was summarized in the previous section. In two studies (Roper, Kaisig, Auer, Mergen, & Molls, 2004; Schreck, Paulsen, Bamberg, & Budach, 2002), dexpanthenol was the institutional standard of care and used as the control arm. The fourth study (Lokkevik, Skovlund, Reitan, Hannisdal, & Tanum, 1996) compared dexpanthenol to no topical treatment. All four studies had small sample sizes.

Roper et al. (2004) compared dexpanthenol to theta cream in a randomized, controlled study of 20 women receiving radiation treatment for breast cancer. No differences were found between study groups, and neither topical treatment demonstrated benefit (Roper et al., 2004).

Schreck et al. (2002) completed a quasiexperimental-design study in 12 patients treated with radiation for head and neck cancer, applying dexpanthenol cream or azulon powder at onset of

dry desquamation. Azulon powder was used on both sides of the neck from the start of treatment until onset of dry desquamation, then used as control for comparison to

dexpanthenol. Because of the small sample size, no statistical analysis was completed. Descriptive findings indicated no differences between treatments (Schreck et al., 2002).

Lokkevik et al. (1996) completed a quasiexperimental study in 79 patients treated for head and neck or breast cancer receiving radiation therapy. Patients used dexpanthenol on one side of the treatment field, and no topical treatment on the opposite side. No differences were found in erythema, moist desquamation, pruritis, or pain (Lokkevik et al., 1996).

Glutathione and anthocyanin: One randomized, placebo-controlled trial (Enomoto et al., 2005) evaluated the effectiveness of RayGel® (glutathione and anthocyanin) in 30 women given radiation therapy for treatment of breast cancer. Women were randomized to glutathione and anthocyanin versus a water-based gel. Although some results appeared to favor glutathione and anthocyanin, they were not statistically significant. In addition, all women were instructed to use aloe vera and vitamin E, compromising findings (Enomoto et al., 2005).

Sucralfate: Falkowski, Trouillas, Duroux, Bonnetlanc, and Clavere (2011) studied 21 women with breast cancer receiving radiation, using a quasiexperimental design. Different skin zones inside and outside of the radiation treatment field were compared using spectrophotometry and RTOG scoring. No differences were found between sucralfate-treated and nontreated areas (Falkowski et al., 2011).

Wells et al. (2004) conducted a randomized, double-blind controlled trial in 357 patients with head and neck, breast, or anorectal cancer receiving radiation therapy. Participants

were randomized to one of six treatment combinations using an aqueous cream, sucralfate cream, or no cream. Within each group, further randomization occurred to either a dry or hydrogel dressing. No differences were found among groups in time to moist desquamation, severity of skin reaction, or discomfort. The sucralfate cream group had lower erythema readings via spectrophotometry than the aqueous cream group, but lowest readings were with the no cream group (Wells et al., 2004).

Maiche, Isokangas, and Grohn (1994) completed a quasiexperimental study in 44 women undergoing radiation treatment for breast cancer. Patients applied sucralfate or a base cream to either side of the surgical scar. The development of grade 1 or 2 skin reactions over the course of treatment tended to occur later in the sucralfate group. Recovery time of skin reaction was faster and the severity of grade was lower in the sucralfate group postradiation ($p = 0.05$) (Maiche et al., 1994).

Moisturizing cream: A prospective, randomized, three-arm controlled trial compared the use of Lipiderm® to trolamine (Biafine) to no prophylactic treatment for the prevention of radiodermatitis in 74 women with breast cancer. The study did not refute or support either product in terms of radioprotection (Fenig et al., 2001).

Urea lotion: Momm, Weibenberger, Bartelt, and Henke (2003) investigated whether moist skin care with urea lotion (Eucerin®) would reduce acute radiation skin toxicity in a study of 88 patients given radiation for head and neck cancer. A 3% urea lotion was compared to conventional dry skin care; results showed higher skin toxicities in patients using the dry skin care protocol versus patients using the moist skin care protocol with urea lotion ($p < 0.05$) (Momm et al., 2003).

Anionic polar phospholipid cream: As discussed previously, Merchant et al. (2007) tested APP cream versus aloe vera gel in 45 pediatric patients with various cancers. Overall results suggested APP cream was more effective than aloe vera gel by grouped common toxicity scores ($p = 0.004$). However, the sample size of 45 was small (Merchant et al., 2007).

Vitamin C: Halperin, Gaspar, George, Darr, and Pinnell (1993) studied 65 patients receiving cranial irradiation for metastatic disease. A 10% ascorbic acid solution was applied to one side of the radiation field, and a vehicle control solution was applied on the opposite side. No benefit was found from use of ascorbic acid lotion (Halperin et al., 1993).

Chamomile cream and almond ointment: Maiche, Grohn, & Maki-Hokkonen (1991) compared the use of chamomile cream (Kamillosan®) to almond ointment in 48 women receiving radiation treatments to the breast. Participants served as their own control by applying chamomile cream or almond ointment to randomly determined sections of their radiation field twice daily during treatment. Overall, no significant differences were observed among use of chamomile cream, almond ointment, or no topical treatment.

Sodium sucrose octasulfate: Evensen, Bjordal, Jacobsen, Lokkevik, and Tausjo (2001) tested sodium sucrose octasulfate as prevention for radiation-induced skin damage in 60 patients receiving radiation for head and neck cancer. Patients served as their own controls by applying sodium sucrose octasulfate to one side of the neck and a placebo to the opposite

The interventions currently showing the most potential are calendula, hyaluronic acid, silver leaf nylon dressings, and no-sting barrier films.

side. Mean skin reaction values were slightly higher on the placebo side ($p = 0.02$) (Evensen et al., 2001).

Dressings

Hydrocolloid dressings: Evidence for use of hydrogel and hydrocolloid dressings was mixed in a systematic review by Kedge (2009) of randomized, controlled studies. The review observed patient comfort in some studies, whereas others showed no differences. One study demonstrated increased healing time with hydrogel dressings (MacMillan et al., 2007).

Gollins, Gaffney, Slade, and Swindell (2008) randomly assigned 30 patients with head and neck or breast cancer who developed moist desquamation during radiation to receive hydrogel dressings or gentian violet. The study showed a progressive reduction in moist desquamation in the hydrogel group ($p = 0.003$) over 14 days. A difference was observed in median time to healing of 12 days in the hydrogel group as compared to 30 days in the gentian violet group. The study was weakened by the withdrawal of 62% of patients in the gentian violet group and a lack of a nontreatment arm for definitive comparisons (Gollins et al., 2008).

The use of hydrogel in patients with moist desquamation also was studied by MacMillan et al. (2007). Hydrogel and nonadherent dressings were compared in 100 patients with head and neck, breast, or anorectal cancer treated with radiation. Patients were randomly assigned to treatment of moist desquamation at the start of radiation, beginning the assigned treatment only when moist desquamation occurred. Skin reactions of patients assigned to hydrogel had a prolonged period of moist desquamation ($p = 0.03$). Because of the higher costs for hydrogel and the lack of supportive evidence of superior action, hydrogel was not recommended (MacMillan et al., 2007).

Mak et al. (2005) studied use of nonadherent dressings versus gentian violet in 142 patients postradiation with unhealed wounds. Participants were randomly assigned to dressing or gentian violet. No significant differences were found between groups in healing, healing time, sleep, mood, and restriction of neck movement (Mak et al., 2005).

In a trial by Mak, Molassiotis, Wan, Lee, and Chan (2000), hydrocolloid dressings were examined for management of moist desquamation postradiation. In the study, 39 patients with various radiation treatment areas who developed moist desquamation were randomly assigned to receive gentian violet or hydrocolloid dressings. No differences were found between groups for healing time or pain (Mak et al., 2000).

Silver leaf dressings: Two studies investigated the effectiveness of silver leaf dressings, and both were limited by very small sample sizes. Vavassis, Gelinas, Chabot Tr, & Nguyen-Tan (2008) studied 12 patients treated with radiation for head and neck cancer. Silver leaf dressings were applied to one side of the neck and silver sulfadiazine was applied to the opposite side for treatment of radiodermatitis. No difference was found in improvement between the silver leaf dressing and the control groups. However, the silver leaf dressing reduced severity of reaction among those with the same dermatitis grade, accelerated healing, and improved pain control (Vavassis et al., 2008).

Vuong et al. (2004) compared 15 patients with anal or gynecologic cancers receiving radiation using silver leaf dressing versus historical controls using silver sulfadiazine at occurrence

of symptomatic dermatitis. All study participants used silver leaf dressings from day 1 of radiation until two weeks after completion of treatment. The mean dermatitis score among those using silver leaf was significantly lower than control ($p < 0.001$). Vuong et al. (2004) concluded that silver leaf dressing is effective in reducing radiodermatitis.

No-sting barrier film: Graham et al. (2004) compared the use of no-sting barrier film (Cavilon®) versus glycerin cream in relation to skin toxicity and rates of moist desquamation. The study sample consisted of 58 women treated with radiation for breast cancer. Participants applied control cream to one portion of the radiation field and no-sting barrier to the alternate half of the field. In the presence of moist desquamation, treatment was switched to a hydrocolloid dressing. No-sting barrier was associated with a lower total skin toxicity score ($p = 0.005$) and lower prevalence of pruritis ($p = 0.01$) (Graham et al., 2004).

Granulocyte macrophage-colony-stimulating factor: Kouvaris, Kouloulis, Plataniotis, Balafouta, and Vlahos (2001) examined the effectiveness of GM-CSF-impregnated gauze in 61 women treated with radiation for vulvar cancer. All participants used steroid cream. When the treatment group reached 20 Gy, they began using GM-CSF-impregnated gauze. Patients treated with GM-CSF had overall lower pain results ($p = 0.001$) and less severe skin toxicity ($p = 0.008$) as compared to historical controls who used only steroids. However, the study had a small sample size and lacked a prospective control group (Kouvaris et al., 2001).

Honey-impregnated gauze: Robson and Cooper (2009) reported a small case series with four patients in which honey was used as a primary dressing for managing radiation skin toxicity with impaired healing. The use of honey for chronic wound healing prompted this study in patients with radiation-induced skin damage. In all cases, the change from conventional dressings to topical application of honey was followed by anecdotal noticeable improvement in healing (Robson & Cooper, 2009).

Oral Treatments

Zinc: Lin, Que, Lin, and Lin (2006) used zinc supplements versus placebo capsules in a randomized, double-blind controlled study of 97 patients with head and neck cancer receiving radiation. Grade 2 ($p = 0.14$) and grade 3 ($p = 0.009$) dermatitis were less prevalent in those taking zinc across all weeks of therapy. In patients receiving concurrent chemotherapy, zinc did not show any benefit (Lin et al., 2006).

Red wine: Morganti et al. (2009) completed a retrospective analysis of 348 women given radiation for breast cancer to evaluate potential protective effects of red wine. The incidence of grade 2 or higher acute skin toxicity was greater in patients without red wine intake ($p = 0.002$). In addition, the risk of high grades of skin toxicity in patients who reported drinking one glass of red wine per day was lower than in nondrinkers ($p = 0.006$) (Morganti et al., 2009).

Sucralfate: Lievens et al. (1998) conducted a randomized, placebo-controlled double-blind study in 83 patients receiving radiation for head and neck cancer to determine whether oral sucralfate could reduce acute radiation-induced toxicities. However, Lievens et al. (1998) found no evidence that sucralfate reduced side effects.

Proteolytic enzymes: Gujral et al. (2001) studied the use of oral proteolytic enzymes (papain, trypsin, and chymotrypsin) (Wobe-Mugos[®]) versus no oral intervention in the prevention of acute radiation side effects. The prospective, randomized, open-label trial examined 98 patients receiving radiation for head and neck cancers. Maximum skin toxicity was significantly lower in the enzyme group ($p < 0.001$). Based on the results, additional studies in larger, more rigorously controlled trials would be beneficial (Gujral et al., 2001).

Effectiveness Unlikely

Trolamine

Five studies reported on the use of trolamine (Biafine) for the prevention and management of radiodermatitis. As discussed earlier, Pommier et al. (2004) compared calendula to trolamine. Patients treated with trolamine had less effective results than those treated with calendula (Pommier et al., 2004).

In a multicenter phase III trial, Elliott et al. (2006) compared trolamine with supportive care in 547 patients receiving radiation for head and neck cancer. Participants were randomly assigned to prophylactic trolamine, trolamine as the specific intervention for dermatitis, or best supportive care (1 of 14 products) preferred and used by the individual institutions participating in the trial. Results demonstrated no advantage for trolamine or differences across groups in rates of grade 2 or higher radiodermatitis (Elliott et al., 2006).

As discussed previously, Fenig et al. (2001) conducted a randomized, prospective trial of 74 patients with breast cancer receiving radiation. Patients were randomized to Biafine, Lipiderm, or no treatment. The results showed no advantage for either preparation compared to the nontreatment arm (Fenig et al., 2001).

In an exploratory phase II intervention trial, Szumacher et al. (2001) assessed the efficacy of Biafine in the prevention of grade 2 acute radiodermatitis. Sixty women treated with radiation for breast cancer were included in the trial. All women received concomitant chemotherapy. Most women developed grade 2 radiodermatitis during the course of treatment; however, no control group existed for comparing effects (Szumacher et al., 2001).

Fisher et al. (2000) conducted a multicenter trial with 172 analyzable patients with breast cancer receiving radiation. Biafine was compared to best supportive care. The study showed no difference in maximum skin toxicity or prevalence of grade 2 or higher skin toxicity between treatment arms. In addition, no differences were found between the treatment arms when reviewing prevention of, time to, or duration of radiodermatitis. Biafine appeared to have a slight advantage in women with larger bra cup size (Fisher et al., 2000).

Not Recommended for Practice

Gentian Violet

Gentian violet was discussed as a control for prevention or management of radiodermatitis in several studies and a systematic review (Gollins et al., 2008; Kedge, 2009; Mak et al., 2000, 2005). Despite its use in practice and as a control in past trials, gentian

violet is no longer recommended by the Department of Health in the United Kingdom because of its carcinogenic potential in animals (Kedge, 2009). The tissue-damaging potency of crystal violet dyes was demonstrated in experimental models of rats and rabbits. In addition, the tissue-irritating effect of gentian violet also has created controversy regarding its use on radiation-induced moist wounds (Eriksson & Mobacken, 1977; Mobacken & Zederfeldt, 1973). In vitro, crystal violet was cytotoxic at low concentrations to HeLa cells and fibroblasts (Norrby & Mobacken, 1972). For those reasons, gentian violet is not recommended for practice.

Expert Opinion

McQuestion (2010) and the Supportive Care Guidelines Group (Bolderson et al., 2005) have provided clinical recommendations for general skin care for patients receiving radiation therapy based on literature, systematic review, and guidelines review (see Figure 1). In addition, Bernier et al. (2008) included guidelines for care during radiation with concurrent epidermal growth factor receptor inhibitors (see Figure 2).

Healthcare Provider Precautions

- Establish that the skin reaction is not caused by concomitant medication or the patient's condition.
- Ensure correct verification of radiation therapy dose and distribution.

Moist Desquamation

- Consider dressings for bleeding, exudates, and drainage.
- Consider topical or systemic antimicrobials if positive cultures or documented infections are present.

Patient Personal Hygiene

- Patients should continue to practice personal hygiene habits before and during treatment.
- Use an electric razor if necessary.
- Use deodorant only on intact skin.
- Gently wash with mild soap or a pH-neutral detergent or cleanser and water.
 - Use mild shampoo if receiving cranial radiation therapy.
 - Pat dry and use a soft towel.
- Do not use topical moisturizers, gels, or emulsions before treatment.
- Follow institutional policies for skin preparation.
- Use plain, nonscented, lanolin-free hydrophilic cream; discontinue with skin breakdown.
- Use calendula ointment for breast radiation.
- Use low-dose corticosteroid cream for itching or irritation, but do not overuse.

Patient Safety

- Avoid swimming in lakes or pools and the use of hot tubs or saunas.
- In treatment fields,
 - Avoid tapes and adhesives.
 - Avoid ice or heating pads.
 - Avoid lifetime sun exposure (use sunscreen with a sun protection factor higher than 30).
 - Cover for sun or cold protection.

Figure 1. Expert Opinion and Consensus Guidelines on Management of Radiodermatitis

Note. Based on information from Bernier et al., 2008; Bolderson et al., 2005; McQuestion, 2010.

Grade 1

- Follow general institutional guidelines and management.
- Moisturizer is optional.
- May use anti-infectives (triclosan or chlorhexidine-based cream)

Grade 2 or 3

- Follow general institutional guidelines and management.
- No infection: use topical approaches.
- If infection occurs, consider culture to identify the infectious agent and use topical antibiotics. Doxycycline is not recommended.
- Integrate team management.

Grade 4

- Treat case by case.
- Refer patient for wound care or wound specialist management.

Figure 2. Expert Opinion on Management of Reactions to Concurrent Radiation and Epidermal Growth Factor Receptor Inhibitors

Note. Based on information from Bernier et al., 2008.

Implications for Nursing Practice and Research

The review of the evidence indicates that ongoing research in prevention and management of radiodermatitis is warranted. The literature generally lacks support for products being used in practice today. Basic skin care is rooted largely on anecdotal experiences, institutional and patient preferences, and product availability. Wide variations and inconsistencies exist between practitioners in the same institution or department because no widely accepted standardized skin-care protocols exist. That results in conflicting information being provided to patients and their families. The evidence to date is insufficient to support any interventions, with the exceptions of IMRT and basic skin care hygiene (e.g., washing the irradiated skin). Despite lack of evidence, practitioners recognize the need to intervene, making radiodermatitis and its associated symptoms an area warranting additional nursing research. Advanced practice oncology nurses have a critical role, possessing the skills necessary to conduct research and develop the evidence base for the prevention and management of radiodermatitis.

Future research should use larger sample sizes with varied patient populations receiving radiotherapy to different treatment sites. More research also is needed in diverse ethnic populations. Study endpoints should be clearly defined: Is the goal to prevent, delay, or facilitate healing of radiodermatitis? Use of valid and reliable skin grading scales and measurement tools should be consistent. The RTOG scale (Cox et al., 2005) is used commonly in many radiation clinics. Unfortunately, reliability or validity data has not been published, and the tool does not have the sensitivity to identify practical clinical differences. Standardization with the timing of interventions and assessment points should be identified clearly in the research. In addition, consistency in assessment will allow for better comparisons of interventions.

IMRT is the only treatment-related management strategy with sufficient evidence for practice. Intervention studies in patients receiving IMRT are needed because most research related to radiodermatitis has been done in groups receiving therapy

with older technologies. As radiation treatment changes, studies of interventions aimed at the prevention or management of radiodermatitis must be conducted to identify the impact of newer technology. Treatment effectiveness trials also could include symptom outcomes such as radiodermatitis, in addition to focusing on the evaluation of products to prevent or manage this skin reaction.

Interventions that have shown promise should be replicated in other cancer or radiation treatment areas with larger sample sizes so the results can be generalized more widely. The interventions currently showing the most potential are calendula, hyaluronic acid, silver leaf nylon dressings, and no-sting barrier films.

Conclusion

To date, no gold standard exists for the prevention or management of radiodermatitis. Attempted interventions to manage this significant side effect of radiation therapy have been lacking in evidence. Future researchers should consider the pathophysiologic process of radiodermatitis. Assessment tools require validation, incorporation of patient-reported outcomes, and inclusion of patient experiences with associated symptoms resulting from radiodermatitis (e.g., pain, pruritis).

Oncology nurses are crucial to the delivery of quality cancer care. Nurses should be aware of the evidence-based interventions, or lack thereof, in the management of radiodermatitis and use that information to guide decision making in clinical practice. In their role as educators, nurses must provide patients and families with information on general skin care, when to expect skin reactions to occur, signs and symptoms of infection, and the need to report those significant findings to their healthcare team.

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