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Canadian Skin Management in Oncology Group (CaSMO) Algorithm for the Prevention and Management of Acute Radiation Dermatitis

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Introduction

Up to one out of two Canadians will develop cancer in their lifetime.[1] It has been estimated that 225,800 Canadians were diagnosed with cancer in 2021.[1]

Approximately 30-40% of cancer patients receive radiotherapy.[2] A study in Ontario on breast, colorectal, lung, and prostate cancer showed that in the year following the cancer diagnosis, 96,003 patients received radiation therapy.[2]

Radiotherapy damages cancerous cells' by directly or indirectly damaging their DNA via ionization and free-radical formation.[3-5] Radiation-induced cutaneous adverse events (AEs) occur in up to 95% of cancer patients who will develop some form of radiodermatitis (RD).[3-5] Of those with breast cancer, 87% develop RD, and concurrent anti-cancer therapies may aggravate RD in 90% of head and neck patients.[4,5]

RD affects the area that received irradiation, and the severity depends on the area treated, beam energy, total dose, dose per fraction, treatment schedule, and use of concomitant systemic agents. RD varies considerably in severity, course, and prognosis and can have severe sequelae that impact the quality of life (QoL) and potentially alter cancer treatment course and outcomes.[3-7]

Radiation treatment's impact on QoL may be profound. A prospective study conducted from July 2017 to June 2018 using the Skindex-16 pre-and post-treatment included eighty-three cancer patients [breast cancer (49%), head and neck cancer (45%), and anal canal cancer (6%)] receiving radiation treatment.[7] All patients developed RD [Grade 1 – 59%, Grade 2 – 33%, and Grade 3 – 8%].[7] The median composite Skindex-16 pre-treatment was 0, and post-treatment 34, demonstrating a marked negative impact on QoL.[7]

RD is categorized as acute, occurring within 1 to 4 weeks of treatment, or chronic, manifesting beyond four weeks to years after treatment.[4]

Strategies to prevent or mitigate RD are aimed at ensuring an optimal skin condition starting before the treatment. Skincare aims to improve comfort during radiotherapy, reducing inflammation and promoting healing of skin areas affected by RD.[8-12] Patients should be educated on a daily skincare regime focusing on: hygiene, moisturization, and sun avoidance and protection measures.[8-13]

The Canadian Skin Management in Oncology Group (CaSMO) developed an algorithm for the reduction of severity and management of acute RD, which follows previous publications from this group that addressed general oncology-treatment related cutaneous AEs, prevention, and skin management.[8,13]

Scope

The CaSMO project initiated by La-Roche Posay Canada aims to improve cancer patients' and survivors' quality of life by offering tools for preventing and managing cancer-treatment-related cutaneous AEs.

The CaSMO panel of clinicians who treat cancer patients with radiation treatment-related cutaneous AEs developed, discussed, and reached a consensus on an evidence-based algorithm supporting prevention, treatment, and maintenance using OTC skin care measures for acute RD. The algorithm focuses on skincare measures to prevent and treat RD using prevention measures and a skincare regime involving hygiene, moisturization, and sun protection measures and products. The algorithm aims to improve patient outcomes and determine the best approach for oncology skin care programs for all stakeholders in the Canadian health care setting. These include oncologists, family practice/internal medicine physicians, dermatologists, oncology nurses, advanced practice providers (APPs), nurse practitioners (NP), physician assistants and pharmacists.

Methods

In the algorithm's development, the panel used a modified Delphi approach following the AGREE II instrument.[14,15] The modified Delphi method is a communication technique for interactive decision-making for medical projects.[15] The used process was adapted from face-to-face meetings to a virtual meeting to discuss the outcome of literature searches and reach a consensus on the algorithm based on the selected literature.[15,16] The virtual discussion was followed by online follow-up replacing the use of a questionnaire.[15] The process entailed preparing the project, selecting the panel, and conducting systematic literature searches followed by summarizing the literature search results, grading the literature, and drafting the algorithm. On January 23, 2021, a virtual panel meeting reviewed the systematic literature review results, discussed and adopted the algorithm using evidence coupled with the expert opinion and experience of the panel. The online process was to fine-tune the algorithm and to prepare and review the publication. (Figure 1)

The CaSMO working group's consensus on the algorithm was established as a hundred percent agreement was obtained.

Literature Review

A literature review included guidelines, consensus papers, and publications describing current best-practice in radiation-treatment related to cutaneous AEs that benefit from topical treatment using OTC skincare, clinical, and other research studies in the English language from January 2010 to December 2020. Excluded were articles with no original data (unless a review was deemed relevant), articles not dealing with skincare for prevention and treatment of RD, and publication language other than English. A dermatologist and a physician/scientist conducted the searches on January 3 and 4, 2021, on PubMed and Google Scholar as a secondary source of the English-language literature, using the terms:

RD; skincare and topical regimes for prevention, treatment, and maintenance of RD; QoL of patients with RD; adjunctive skincare use; education of staff and patients; communication strategies; adherence; concordance; efficacy; safety; tolerability; skin irritation.

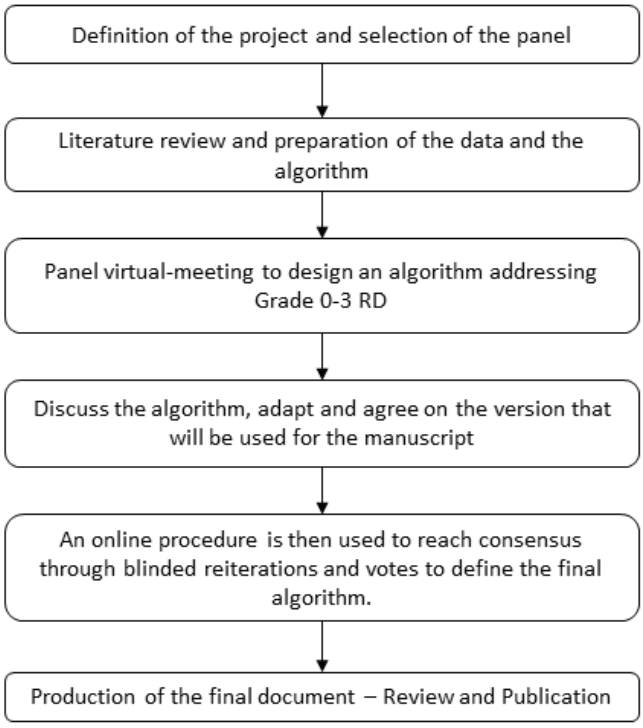


Figure 1: Process used for the development of the algorithm

The results of the searches were evaluated independently by two reviewers, resolving discrepancies by discussion. The searches yielded one hundred and twenty-two publications. After excluding duplicates and articles deemed not relevant for the algorithm ([n = 52] other subjects, low quality, a small number, case studies), seventy papers remained. Twenty-five review articles (including one guideline, one algorithm and, eighteen systemic literature reviews), and forty-five were clinical studies (including eighteen randomized controlled trials, eighteen clinical evaluations, and cohort studies, four randomized trials, and five other).

Radiation Dermatitis, Prevention, and Treatment

The goal of radiation therapy is either curative or palliative.[3,4] It can be delivered in the neoadjuvant or adjuvant setting, or can be the main treatment, with or without combined systemic treatment.[3,4] The multidisciplinary team guiding the patient through the radiation treatment process comprises the radiation oncologist, the radiation oncology nurse, the radiation therapist, medical physicist, and dosimetrist.[3,4]

Radiation therapy can be external [i.e. 3-D conformal radiation therapy, intensity-modulated radiation treatment, image-guided, Thomotherapy, and stereotactic radiosurgery] or internal, such as brachytherapy, radioisotope therapy, radioimmunotherapy, and radioembolization (Table 1).[17] RD is defined as a cutaneous inflammatory reaction induced by exposure to biologically effective levels of ionizing radiation.[17] The mechanisms associated with a radiation induced AE include an inflammatory response and oxidative stress, which interact and promote each other.[18] Inflammatory markers involved in acute inflammation secondary to ionizing radiation including IL-1, IL-6, TNF-alpha and TGF-Beta, can be expressed within hours after receiving the first

External beam radiation therapy
2D and 3D external radiation therapy
Intensity-modulated radiation therapy
Volumetric-modulated arc therapy
Image-guided radiation therapy
Stereotactic radiosurgery
Stereotactic body radiation therapy
Proton therapy
Total body irradiation

Table 1: External beam radiation therapy

radiation treatment.[18] Radiation treatment exhibits biological effects within hours to weeks of exposure, through irreversible breaks of the nuclear DNA strands that cause extensive genetic damage and inhibit cells' ability to divide and replicate.[3,18] Further damage comprises structural tissue destruction, generation of reactive oxygen species, a decrease in functional stem cells, initiation of epidermal and dermal inflammation, and skin cell necrosis.[3,18] Radiation damage is complex, and a variety of factors influence its severity.

RD is generally limited to the irradiated area and depends on several factors, including the target area, dose and fractionation schedule, patient's condition, and the use of other concomitant cancer treatments (e.g. platinum-based regimens, cetuximab, 5-fluorouracil).[3,4-6,18-22]

Intrinsic factors that influence the occurrence and severity of RD include demographic or patient-related characteristics.[6] These include age, ethnic origin, skin type, smoking, obesity, breast size, hormonal status, presence of infection, and co-existing diseases, such as diabetes or cardiovascular disease.[6,17-22]

Extrinsic factors include treatment-related characteristics such as technique, dose, volume, fractionation, beam energy, use of bolus, immobilization devices, and the use of combined systemic anti-cancer therapies. Further factors comprise the clinical site of treatment, e.g., areas with skin folds [head and neck, breast and axilla].[17-22]

Certain drugs (e.g. platinum-based regimens, cetuximab, 5-fluorouracil) increase sensitivity to radiation treatment, causing increased cellular damage and delayed tissue repair.[22] Conventional chemotherapy agents and cancer treatment with EGFR inhibitors increase the risk for severe RD (Box 1).[22,23]

RD is categorized as acute, occurring within 1 to 4 weeks of radiation treatment, or chronic, manifesting beyond four weeks to years after treatment (Table 2).[3,4,6,18-23]

Cutaneous effects of radiotherapy vary considerably in severity, course, and prognosis and can have severe sequelae that impact the quality of life and disrupt cancer treatment.[7,8] The two most prevalent grading systems of RD are the RTOG (Radiation Therapy Oncology Group) and CTCAE v5 (Common Terminology Criteria for Adverse Events) systems. The RTOG assessment tool classifies RD from 0 [no visible signs of RD] to 4 [ulceration, bleeding, necrosis].[20,21] For the present algorithm, the CTCAE v5 grading system for acute RD from the National Cancer Institute (NCI) is used. This tool has five classes from 1 [faint erythema and dry desquamation] to 5 [death] (Table 3).[19,22]

Algorithm for the Prevention and Management of Acute Rd

The CaSMO algorithm for acute RD used the mnemonic RECUR (Reliable, Efficient, Clear instructions, Understandable, Remember easily).[24]

A clinical algorithm's function is to standardize and support medical decision-making, such as regulating the selection and use of treatment regimens, thereby improving adherence to evidence-based guidelines.[14] The algorithms have inputs and outputs, precisely defined specific steps, and uniquely defined results that depend on the preceding steps.[24] The current algorithm for the prevention and management of acute RD focused on preventing or reducing and managing RD using OTC skincare and topical treatment (Figure 2). Detailed information on the various grades of RD is given in Figure 3.

The algorithm details measures to be taken before radiation treatment which include education, avoidance of skin irritants, preventative skincare, and sun avoidance and sunscreen use; it also describes prophylactic measures to be taken when radiation starts. Finally, it describes how treatment assessment of skin condition and grading of RD should take place during treatment while the preventative measures continue.

Each section is discussed in the order as they appear in the algorithm.

Education on Prevention and Treatment of RD

Education on the type of radiation treatment, on preventive and on treatment measures for RD is essential for both clinicians and patients.[13,25] Before starting the treatment, a therapeutic relationship with the patient should be built, supporting the patients' active participation in their cancer treatment.[13] As outlined in two previous publications by the CaSMO group, a detailed discussion between the patient, treating physician, and nurse or other team members includes explaining the radiation treatment protocol, potential side effects, hospital visits, diagnostic tests, management of AEs, and prophylactic and preventative measures.[8,13] It is recommended to provide the patients with details on who to contact in the early stages of RD to enable addressing the AEs as early as possible.[8,13] It is recommended to support education given to patients verbally by printed or online information (Box 2).[8,13]

Education on general measures include avoiding skin irritants, products with an elevated pH (>7), scented products and temperature extremes.[8,13] Further skin trauma should be avoided such as the use of adhesive bandages and tape, rubbing, scratching and massaging the skin within the treatment area. The patient should be recommended to wear loose fitting cotton clothing which may help avoid traumatic shearing and friction injuries.

Location of the treatment field	RD may be more severe depending on the location of the treatment field i.e. sites with intertriginous skin folds such as the breast or buttocks
Chemotherapeutic agents	Bleomycin, cisplatin, dacarbazine, docetaxel, doxorubicin, etoposide, 5-fluorouracil, gemcitabine, methotrexate, temozolomide. Any radio-sensitizers or drugs that cause immune suppression
Antibiotics and anti-tuberculosis medication	-
Comorbidities	Anemia, diabetes mellitus, cardiovascular disease, suppression of the immune system, connective tissue diseases, radiosensitive disorders, ataxia telangiectasia, xeroderma pigmentosa
Other factors	Advanced age, female sex, obesity, tobacco use, chronic sun exposure, previous breast reconstruction/implants, nutrition and hydration status, mobility status

Box 1: Contributing factors to radiodermatitis (RD)

Acute – ~1 to 4 weeks	Chronic – weeks to years	Chronic – 5 to 10 years
*Grade 1 and 2 • Dry desquamation • Moderate erythema • Pruritus *Grade 3 and 4 • Moist desquamation • Bleeding • Severe pain • Ulceration	• Cetuximab • Panitumumab • Erlotinib • Gefitinib	• Head and neck, colorectal • Colorectal • Lung, pancreatic • Non-small cell lung

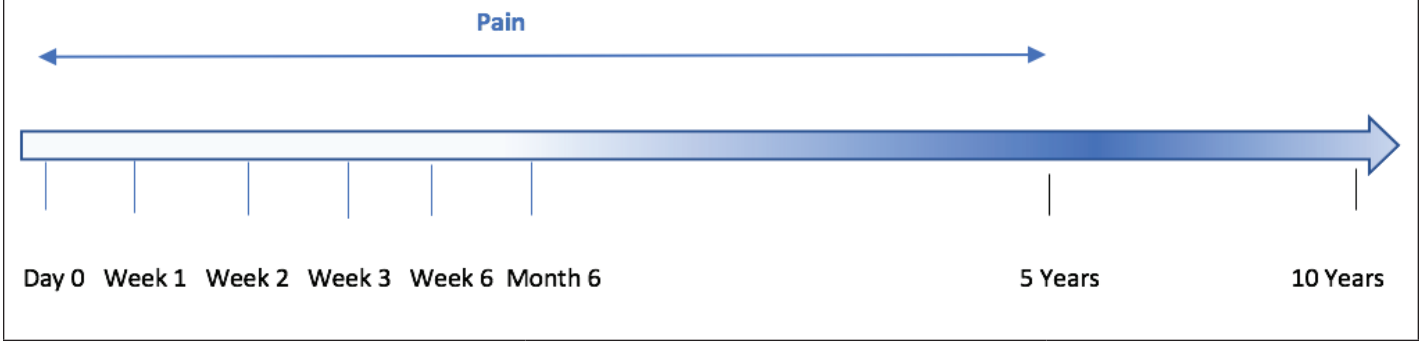


Table 2: Acute and chronic radiation dermatitis[20]

*Grades of Acute Dermatitis (CTCAE V5– common terminology criteria for adverse events (National Cancer Institute)[19]

CTCAE v5 - DCTD Grading		RTOG Grading	
Grade	Definition	Grade	Definition
1	Faint erythema or dry desquamation	0	No visible change to skin
2	• Moderate to brisk erythema; • Patchy moist desquamation mostly confined to skin folds and creases; • Moderate edema	1	• Faint or dull erythema. • Mild tightness of skin and itching may occur
3	• Moist desquamation in areas other than skin folds and creases; • Bleeding induced by minor trauma or abrasion	2	• Bright erythema / dry desquamation. • Sore, pruritus, and tight skin
4	• Life-threatening consequences; • Skin necrosis or ulceration of full-thickness dermis; • Spontaneous bleeding from the involved site; • Skin graft indicated	2.5	• Patchy moist desquamation • Yellow/pale green exudate. Soreness with edema
5	Death	3	• Confluent moist desquamation. • Yellow/pale green exudate • Soreness with edema
		4	• Ulceration, bleeding, necrosis (rarely) seen

Table 3: CTCAE and RTOG grading for acute RD

Division of Cancer Treatment & Diagnosis Dermatitis Radiation Grading (DCTD); Radiation Therapy Oncology Group (RTOG)
Grades of Acute Dermatitis (CTCAE – common terminology criteria for adverse events (National Cancer Institute)19
A-B – Grade 1 – faint erythema and dry desquamation
C-D – Grade 2 – moderate erythema and/or edema; patchy desquamation confined to folds
E-F – Grade 3 – moist desquamation in areas other than folds and bleeding from minor trauma
Grade 4 – Life-threatening consequences; full-thickness necrosis, spontaneous bleeding; skin graft indicated

Question	Website/Documentation
Cancer Care Ontario: The Prevention and Management of Acute Skin Reactions Related to Radiation Therapy	https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/846
NCI: Radiation Therapy Side Effects	https://www.cancer.gov/aboutcancer/treatment/types/radiation-therapy/side-effects
Questions to ask your doctor about your cancer treatment	https://www.cancer.gov/about-cancer/treatment/questions
Questions on how radiation therapy works	https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy
Questions about How, why and what to do during radition treatment	https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy#RTCCSE
Information on skincare from CDA websites	https://dermatology.ca https://dermatology.ca/recognized-products/skincare/
Information on cancer treatments, cutaneous AEs, and treatments	Ruth C. The Dermatology World//December 2019
Glossary and review on cutaneous AEs	Support system. www.aad.org/dw/
Algorithm on skincare for cutaneous AEs	Sauder M, et al. Skin Ther Letter 2021;S(3):1-10

Box 2: Resources and information

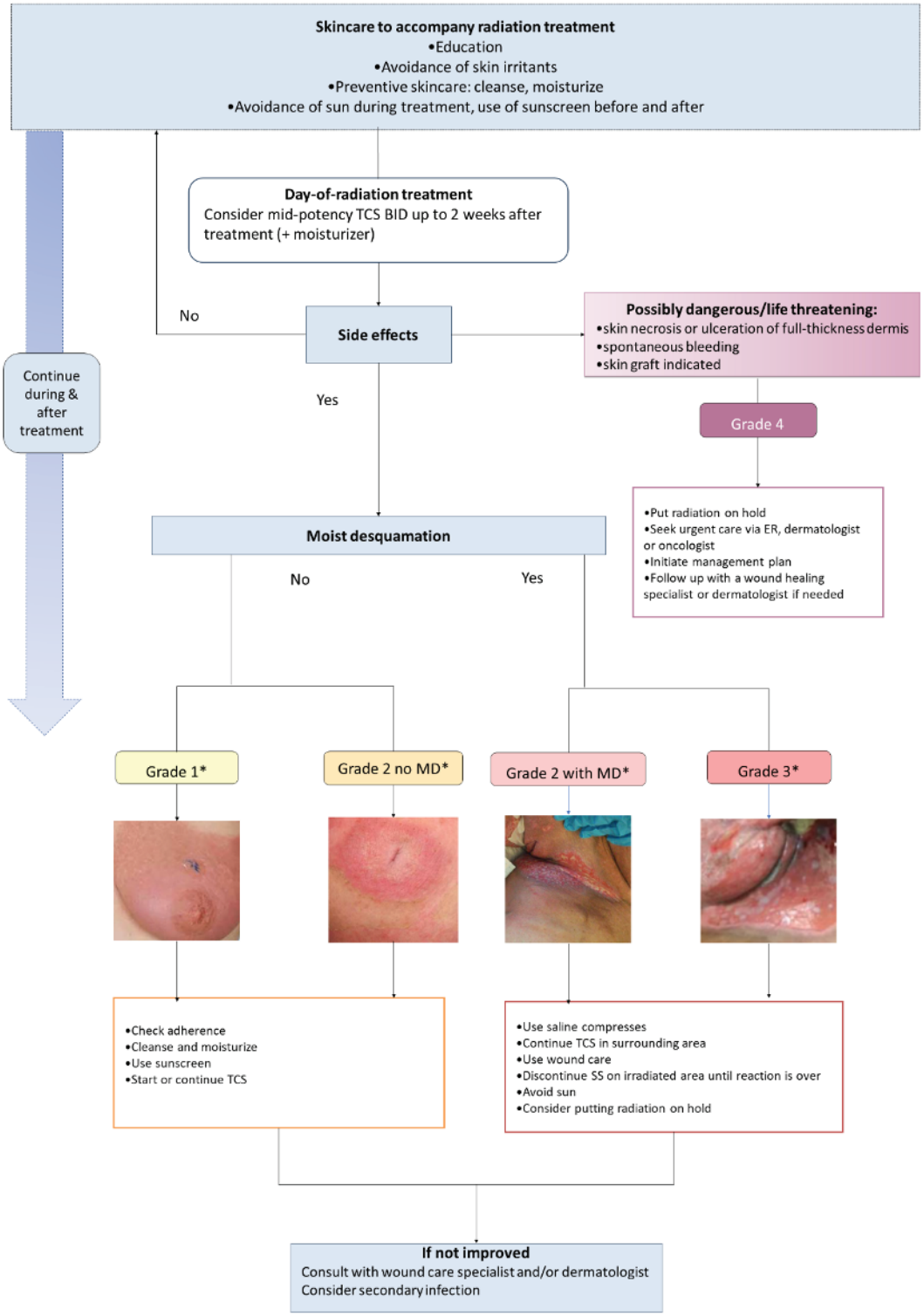


Figure 2: CaSMO radiation dermatitis algorithm

Moist desquamation (MD); Sunscreen (SS); Topical corticosteroids (TCS); Radiation dermatitis (RD); Twice/day (BID) Grade 0: No visible RD; Grade 1: Faint erythema or dry desquamation; Grade 2: Moderate to brisk erythema; Patchy moist desquamation, mostly confined to skin folds and creases; moderate edema; Grade 3: Moist desquamation in areas other than skin folds and creases; Bleeding induced by minor trauma or abrasion; Grade 4: Life-threatening consequences; Skin necrosis or ulceration of full-thickness dermis; Spontaneous bleeding from the involved site; Skin graft indicated.

*Photograph grade 1: RD on the left breast showing erythema during radiation therapy for breast cancer.

*Photograph grade 2 no MD: RD on the neck showing erythema and dry desquamation

*Photograph grade 2 with MD: Vulva-sarcoma RD with erythema and moist desquamation

*Photograph grade 3 with MD: RD with erythema, moist desquamation, and bleeding from minor trauma

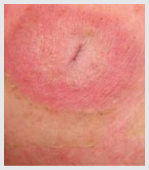
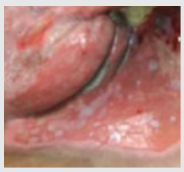
Grading	Prevention, skincare and treatment
Grade 1: Faint erythema or dry desquamation, possible pain  Erythema  Dry desquamation	• Check adherence to treatment. • Cleanse the skin and use a moisturizer. • Avoid sun exposure and use sunscreen. • For dry desquamation start or continue with low to mid potency TCS to decrease progression and severity of itching, burning and irritation.[3]
Grade 2: Moderate to brisk erythema; Patchy moist desquamation mostly confined to skin folds and creases; Moderate edema, pain  Moist desquamation in the groin	• Check adherence to treatment. • Cleanse the skin and use a moisturizer. • Avoid sun exposure and use sunscreen. • Use saline compresses for cooling. • Continue TCS in the surrounding area of moist desquamation.
Grade 3: Moist desquamation in areas other than skin folds and creases; Bleeding induced by minor trauma or abrasion, severe pain  Moist desquamation and bleeding	• Check adherence to treatment. • Cleanse the skin and use a moisturizer. • Avoid sun exposure and discontinue sunscreen on irradiated area until the reaction is over. • Use saline compresses on the areas with moist desquamation. • Continue TCS in the surrounding area of moist desquamation • Use a wound dressing for bullae and erosions, and select the type of dressing according to the wound bed condition and the exudate production. • Consider putting radiation treatment on hold.

Figure 3: RD Treatment according to presentation (to show the position of the photos)

Patients should also be recommended to use electric shavers for hair removal. Wax or other depilatory creams and pre-shave liquids and aftershave are discouraged, as they can irritate the irradiated skin.

Patients should be asked not to shave the axilla if it is within the treatment field but may continue to use antiperspirants or deodorants during radiation therapy on dry intact skin.

Sun Avoidance and Sun Protection

Patients should be educated on radiation treatment-induced photosensitivity which can result in symptoms such as severe sunburn, pruritus, erythema, or edema. It should be explained that phototoxicity may occur, primarily induced by UVA exposure.[8,13]

Phototoxicity symptoms may appear on the exposed area within a few minutes to several hours after exposure to UV light.[3-5,8,13]

Patients should be educated on sun avoidance as part of a healthy lifestyle, and the use of sun-protective clothing [e.g., brim hats and sunglasses].[8,13] During the course of radiation and while skin is healing the patient should keep the treatment field out of direct sunlight.[3-5,8,13] After the skin has healed, it may be more sun sensitive and therefore requires diligent protection from sunlight and tanning beds should be avoided.[8,13]

Most dermatologists recommend daily sunscreen of SPF 30 or higher, especially for sun-exposed areas. Special populations that are at higher risk for sun-induced toxicities and neoplasms are advised to avoid sun exposure by using para-aminobenzoic acid (PABA) free UVA and UVB protection as well as sun-protective clothing.[8,13] Sunscreen should be reapplied as needed (e.g. after swimming or heavy perspiration) (Box 3).

Patients may continue to swim in chlorinated pools but should rinse afterwards with a gentle cleanser followed by immediately applying a moisturizer. If RD has progressed beyond dry desquamation (CTCAE grade 1) swimming should be avoided.

Assessment of Skin Condition

Upon presentation of a patient with RD, it is important to check the location, size of the affected area, erythema, dry desquamation, moist desquamation, exudate, signs of infection, and discomfort (burning, pruritus, pulling, tenderness, dryness, scaling, flaking, peeling).[3-5,8,13,19] Similarly, the healthcare provider should check for the presence of fever, pain, mucosal involvement and if there are significant blood laboratory abnormalities. The clinician must establish whether the AE is possibly dangerous or life threatening such as in the case of skin necrosis, ulceration of the full thickness dermis or spontaneous bleeding,[13,19] and seek urgent care via a dermatologist, or emergency room for these patients.[13,19]

Phototoxicity and photoallergy	**Photosensitivity** can result in symptoms such as severe sunburn, pruritus, erythema, or edema. The two types of reactions that may occur are phototoxicity and photoallergy. UVA is primarily responsible for triggering these effects and is present throughout the day and year and is readily transmitted through window glass. **Phototoxicity** symptoms may appear on the exposed area within a few minutes to several hours after exposure to UV light. **Photoallergic reactions** are less common and usually occur due to topically applied medications. They involve the immune system, and symptoms can appear immediately after sun exposure or may take longer to develop. These reactions may look like eczema and can spread to areas of the body not exposed to sunlight.
Sun avoidance and protection	Some anticancer drugs may cause photosensitivity reactions making certain precautions necessary: 1. Avoid unnecessary exposure to UV light including sunlight, tanning beds, and sun lamps. 2. When outside, cover up with a long-sleeved shirt, long pants or skirt and a broad-brimmed hat made out of tightly woven, dark coloured fabric. If light shines through the fabric, then UV can also go through it. 3. Use a broad-spectrum sunscreen (protects against both UVA and UVB) that has SPF of at least 30.
Sunscreen application	• Apply at least 15 to 30 minutes before sun exposure to allow time for the product to diffuse into the skin. • Apply generously to all exposed areas, including tops of ears, under chin, and balding areas. Avoid eye area. • Reapply at least every 2 hours and after swimming. • Discontinue use if erythema or irritation occur.

Box 3: Information on photoprotection and sunscreen application

The patient must be asked about the duration of the AE and what products were used for cleansing, moisturizing, or dressings for erosions or bullae.[3-5,8,13,19]

Finally, the impact of RD on the patients' daily activities, sleeping, eating or drinking must be verified. In the context of the assessment, the date of the last radiation or chemotherapy treatment, as well as concurrent medication use (analgesic, antibiotic, antifungal) and efficacy must be verified.[3-5,13,19]

Skincare Using Cleansers and Moisturizers

Skincare using OTC products comprises cleansers and moisturizers (Box 4).[8,13] Although evidence is lacking on the best choice of product, basic recommendations on supportive measures using OTC skincare are given in various cancer treatment guidelines and consensus papers (Table 4).[3,9-13,22,23,25-33]

Rosenthal and colleagues recommended a treatment algorithm for RD that included basic hygiene measures using mild soap and lukewarm water.[3] A consensus paper and skincare algorithm by the CaSMO group recommended a daily skincare regime focusing on: hygiene, moisturization, sun protection, and, if applicable, camouflage products.[8,13] They recommended to encourage patients to keep their skin moisturized using gentle products to prevent pruritus and xerosis.[8,13]

The skincare formulations used for patients with RD should be safe, effective, free of additives, fragrances, perfumes, sensitizing agents, and should have a near physiologic stratum corneum (SC) pH.[8,13] To support adherence to the skincare regime, products should be cosmetically pleasant and easy to use.[8,13]

Evidence levels of components of topical treatments is shown in Table 5.[3,8,13,26-28,34-59] A systematic review[3] of topical agents for the treatment of RD reported no benefits from formulations containing aloe vera[26], chamomile[3,37], ascorbic acid, pantothenic acid, and trolamine.[49] However, benefits or potential benefits were shown when using formulations containing hyaluronic acid (HA)[27,28,34,54] epidermal growth factor EGF3,[39,51] granulocyte-macrophage colony stimulating factor (GM-CSF), topical corticosteroids (TCS) 40-45 or statins.[58]

Topical agents that have common ingredients known as soothing may be beneficial for the reduction of symptoms such as niacinamide, panthenol, squalene, glycerin, and allantoin.[8,13] A skincare kit including all the products needed may be easy to use for the patients supporting adherence to the regimen.[8,13] A thermal water containing skincare regime (La Roche-Posay) comprising two types of cleansers, a moisturizer, a healing baume, and an SPF50+ sunscreen was shown to be beneficial for RD prevention and treatment.[8] The regimen was evaluated in two-hundred-fifty-three women with mostly stage I (International Union Against Cancer (UICC) /American Joint Committee on Cancer (AJCC)) breast cancer undergoing radiotherapy. The frequent users who daily used the total skincare regime showed significantly ($p \leq 0.0001$) less severe RD than those who used parts of the skincare regimen infrequently.[8]

Contrary to the advice some cancer patients may receive when undergoing radiation treatment, skincare does not interfere with or increase the radiation dose to the skin and can be used in moderation before daily radiation treatments.[60] Even if applied shortly before radiation treatment, thin or moderately applied skincare may have minimal influence on skin radiation dose regardless of beam energy or beam incidence.[60] Patients are frequently concerned about toxic effects on the skin.[60,61] Allowing patients to apply skincare throughout their radiation treatment period will simplify patient instructions and reduce patient confusion and anxiety.[60,61] Allowing patients to apply skincare daily and liberally without restrictions on application timing is likely to improve patient quality of life and adherence to the prevention and management of cutaneous AEs using skincare.[60-62]

Topical Pharmaceuticals

Topical corticosteroids (TCS) have anti-inflammatory effects and may be used for the prevention and treatment of RD.[3,4,25,28,40-45,59] A meta-analysis confirmed that TCS, ranging from mild to potent, significantly prevented the incidence of wet desquamation and reduced the mean RD score.[28] Various studies confirmed the efficacy of mild TCS decreasing moist desquamation, lowering the incidence of severe RD and delaying time to development of grade three RD.[41-44] Extensive and inappropriate use especially of high

Cleansers[8,13]	• Encourage to wash the irradiated skin daily using lukewarm water. • Wash cloths may cause friction and are therefore discouraged. • Use a soft towel to pat the skin to remove water but not completely dry. • Use gentle cleansers such as those with a near-physiological skin pH (4.0 – 6.0).[8,13] • Avoid the use of soap and cleansers with an alkaline pH (> 7), which may excessively remove skin lipids, elevating skin surface pH, and compromise the skin barrier function further.[8,13]
Moisturizers[8,13]	• Apply moisturizers to the face, hands, feet, neck, and back liberally and daily. • Moisturizers should be applied at room temperature. • Formulations should be safe, effective, free of additives, fragrances, perfumes or sensitizing agents and should have a physiologic skin surface pH (4.0 – 6.0).[8,13] • Skincare product choices depend on the skin condition, availability, costs, and individual preferences. • Moisturizer effectiveness depends on the formulation, the vehicle, frequency, and compliance of applications. • Choose a moisturizer vehicle based on skin condition, level of xerosis, and patient preference.

Box 4: Criteria and application of cleansers and moisturizers

Subject	Type	Reference
Management of acute RD: a review of the literature and proposal for a treatment algorithm	Systematic review and algorithm	Rosenthal A, et al. J Am Acad Dermatol. 2019;81(2):558–567.[3]
The role of skincare in oncology patients.	Systematic review	Sauder MB et al. Skin Ther Letter; 2020 S Oct(10):1-12.[8]
Management of acute RD	Systematic review and meta-analysis	Chan RJ, et al. BMC Cancer 2014;14:53.[9]
Prophylaxis and management of acute RD	Systematic review	Salvo N, et al. Curr Oncol 2010;17:94–112.[10]
Evidence in RD management	Critical appraisal of systematic reviews	Chan et al. Int J Radiat Oncol Biol Phys 2012;84:e357–62.[11]
Topical interventions to prevent acute RD in head and neck cancer patients	Systematic review	Ferreira EB, et al. Support Care Cancer. 2017;25 (3):1001–1011. doi: 10.1007/s00520-016-3521-7.[12]
Canadian skin management in oncology (CaSMO) algorithm	Algorithm	Sauder MB et al Skin Ther Letter; 2021 S (3):1-10.[13]
Topical treatment of RD	Systematic Review	Iacovelli NA,et al Drugs Context. 2020 jun 12;9:2020-4-7. 10.7573/dic.2020-4-7. eCollection 2020.[22]
Prevention and treatment of RD in head and neck cancer patients	Systematic review	Iacovelli NA, et al. Future Oncol. 2018;14(3):291–305.[23]
Clinical practice guidelines for the prevention and treatment of acute and late RD from the MASCC Skin Toxicity Study Group	Guidelines	Wong RK, et al. Support Care Cancer. 2013;21(10):2933–2948.[25]
The use of aloe vera in cancer radiation: an updated comprehensive review.	Review	Farrugia CE, et al. Complement Ther Clin Pract. 2019;35:126–130.[26]
Hyaluronic acid for treatment of RD	Systematic review	Cosentino D, Piro F. Eur Rev Med Pharmacol Sci. 2018;22(21):7562–7572.[27]
Topical management of acute radiation dermatitis in breast cancer patients: a systematic review.	Systematic review and meta-analysis	Haruna F, et al. Anticancer Res. 2017;37(10):5343–5353. doi: 10.21873/anticanres.11960.[28]
Acute RD in head and neck cancer patients treated with radiotherapy and chemotherapy or EGFR inhibitors	Review and consensus	Russi EG, et al. Crit Rev Oncol Hematol. 2015;96(1):167–182.[29]
Evidence-based skin care management in radiation therapy: clinical update.	Systematic review	McQuestion M. Semin Oncol Nurs. 2011;27:e1–e17.[30]
Patient-rated measures of RD in breast cancer radiotherapy.	Systematic review	Schnur JB, et al. Am J Clin Oncol. 2011;34(5):529–536.[31]
RD treatment overview	Review	Hegedus F, et al. Int J Dermatol. 2017;9:909–914.[32]
Wound healing after radiation therapy	Review	Haubner F, Ohmann E, Pohl F, Strutz J, Gassner HG. Radiat Oncol. 2012;7:162.[33-]

Table 4: Systematic literature reviews, consensus papers, guidelines and algorithms

Topical	Proposed mechanism of action	Clinical efficacy	Level of evidence
Gentle cleansers[8,13]	Cleansing, antimicrobial, hydrating	Proven useful, reduced RD symptoms	A2
Thermal water containing skincare regimen[8]	Prevention and treatment of RD, anti-inflammatory, supports a balanced skin microbiome	Potentially useful for prevention and treatment	B2
Calendula[3,38,50]	Anti-inflammatory, antibacterial, antifungal, and antioxidant properties; stimulates angiogenesis	Potentially useful, reduced symptoms	B2
Catechins	Anti-inflammatory, antibacterial, and antioxidant properties	Potentially useful, reduced symptoms	C3
Aloe vera[26]	Anti-inflammatory; rich in vitamins, enzymes, minerals, sugars, and other active constituents	Not proven useful	A2
Chamomile[3,37]	Anti-inflammatory, spasmolytic, antibacterial	Not proven useful	B2
b-Sitosterol	Herbal formulation thought to be antibacterial with analgesic, anti-inflammatory, antiedema, and antithrombotic effects	Potentially useful	C2
Ascorbic acid	Antioxidant, free radical scavenging	Not proven useful	B2
Pantothenic acid	Antioxidant, incorporated into CoA and increases glutathione levels, promotes epithelial growth	Not proven useful	C2
HA[27,28,34,54]	Antioxidant, involved in epidermal moisture retention	Potentially useful	A2
EGF3,39,51	Stimulates proliferation of human fibroblasts and keratinocytes, promotes epithelialization	Potentially useful	C4
GM-CSF	Promotion of chemotaxis of monocytes into tissues, stimulating macrophage maturation and activation	Potentially useful	C3
Corticosteroids[40-45]	Anti-inflammatory; inhibits radiation-induced cytokines	Proven useful, reduced grade of RD	A1
Statins58	Anti-inflammatory, immunomodulatory, antioxidant, metabolic, and antibacterial activities	Potentially useful	A2
Silicone-based film or dressing[35,36,46-48]	Anti-inflammatory, promotes epithelialization	Potentially useful	A3
Trolamine[49]	Nonsteroidal anti-inflammatory; promotes macrophages recruitment and stimulates of granulation tissue	Not proven useful	A2
Silver sulfadiazine[53]	Antimicrobial	Potentially useful	A2
Silver nylon dressings[56]	Anti-inflammatory, barrier-enhancing	Proven to be useful	A2
Barrier cream[52]	Prophylactic management	Not proven useful	A3
Oil-in-water emulsion[55]	Reduction of RD symptoms	Potentially useful	A3

Table 5: Evidence levels of components of topical treatments

potency TCS on the face, neck or genitalia can cause AEs including skin atrophy, permanent striae, hematomas and tearing of the skin, telangiectasia, hypertrichosis, local and systemic infections, and rarely adrenal suppression.[8,13]

Although the efficacy of TCS is established in RD such as in breast cancer[28], it is currently under evaluation in head and neck cancer where the use of TCS is frequently associated with the onset of clinically relevant adverse events.[22,42,59] In particular, the prolonged use of TCS leads to skin atrophy, which may be particularly contraindicated in this condition.[59]

Topical use of statins may be beneficial for RD as the product may display some anti-inflammatory, immunomodulatory, antioxidant, metabolic, and antibacterial properties.[48]

Although topical trolamine (doxepin) is extensively used for the management of RD, its efficacy for RD has not been established.[49]

Wound Healing Products

Wound healing products and barrier films are widely used, as well, in oncology for cracked skin, erosion, bullae and more severe RD healing by secondary intention. Depending on the wound bed condition and exudate levels, various dressings may be used, such as a foam dressing or a non-adherent wound contact layer, including silicone-coated dressings. The frequency of dressing changes depends on exudate level and are typically twice weekly. The evidence supporting the efficacy of various dressings is scarce. Silicone based agents may have anti-inflammatory properties and are available as a gel or as coated wound dressings.[35,36,46-48]

Prophylactic topical antibiotics should be avoided to comply with antimicrobial stewardship preventing antibiotic resistance.

The Multidisciplinary Team

Prevention and treatment of RD is a multidisciplinary effort involving radiation oncologists, dermatologists, nurses, and advanced practitioners (APPs). Collaboration and an interprofessional approach between oncology and dermatology is effective in connecting cancer patients with dermatological care from the start of their radiation treatment through to completion.[8,13,63-68]

Timely intervention by a radiation-oncologist or dermatologist trained in supportive dermatology for oncology patients is critical to preventing avoidable treatment interruptions.[8,13,63-68] Moreover, almost equally important is an oncology specialists' ability to improve quality of life-related to RD and may be able to preserve cancer treatment through managing RD early.[8,13]

Limitations

Statements used and recommendations given in the algorithm were based on a mix of data and expert opinion. While it is possible that alternatives for RD could exist, the recommendations are suggestions for best practice developed from a panel of expert clinicians that are supported by peer-reviewed literature.

A small panel of physicians developed the algorithm, representing a few centers, and did not include patients in the development. Although limited evidence was available to guide the development, the project will hopefully encourage more skincare studies to prevent, treat and maintain RD.

Conclusions

A multidisciplinary team treating and guiding the cancer patient who receives radiation treatment may improve cancer treatment tolerance. The CaSMO algorithm on acute radiation dermatitis and general preventive measures, including cleansers and moisturizers to prevent or reduce the severity of acute radiation dermatitis, may increase awareness and help improve cancer patient outcomes.

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