Radiation induced skin reactions during and following radiotherapy: A systematic review of interventions.

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Systematic Review

Radiation induced skin reactions during and following radiotherapy: A systematic review of interventions

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ABSTRACT

Introduction: Radiation induced skin reactions (RISR) are a common adverse effect of radiotherapy that can impact on patient quality of life. The aim of this systematic review was to identify new research evidence on interventions for RISR to guide health practitioners on best practice skin care for people receiving radiotherapy.

Methods: A narrative systematic review was adopted including published research since 2014. The MESH search terms used in the 2014 College of Radiographers skin care systematic review were supplemented with terms identified through a pearl growing search technique.

Results: Thirty-three studies were identified and reviewed, 13(39.4%) were assessed as having a high risk of bias 6(18.2%) moderate risk of bias, and 13(39.4%) low risk of bias; one pilot study was not assessed. Twenty-one of the studies were randomised controlled trials, 2 feasibility studies, 9 non-randomised trials, and 1 a pilot study.

Conclusion: Evidence from well conducted studies identified prophylactic use of steroid cream for patients, at high risk of RISR, as being the most efficacious in reducing acute skin reactions. Further research is needed on photo biomodulation therapy, studied within standard dose fractionation schedules, before it is recommended for use in practice. There is insufficient evidence to support the use of barrier films or any topical emollients currently in practice to reduce RISRs. Despite the number of new studies in this area there is limited good comparative research of RISR that accounts for predictive risk and new radiotherapy techniques.

Implications for practice: Practitioners are encouraged to risk assess patients prior to radiotherapy to guide interventions and record and monitor patient skin toxicity regularly during treatment, comparing toxicity changes with scores recorded at baseline and support patient self-monitoring of skin reactions.

Introduction

Skin reactions are a common adverse effect of radiotherapy with approximately 95% of patients experiencing some skin changes during treatment.[1] Most of these skin changes are assessed by clinicians, nurses or radiographers (also known as Radiation Therapy Technologists-RTTs) and characterised by the common toxicity criteria adverse effects (CTCAE) or Radiation Therapy Oncology Group (RTOG) scale. Individuals experience mild symptoms, grade 1 (60% erythema) and grade 2 itchy flaky skin (32% dry desquamation). Serious radiation induced skin reactions (RISR) are those graded as 3, with blisters and loss of tissue (8% moist desquamation).[2] Prevalence is higher in patients receiving treatment for head and neck cancer with 25% of patients developing severe RISR.[3] RISR can delay radiotherapy and have a detrimental impact on overall patient outcomes; specifically patient experience and quality of life. Radiation adverse effects can impact on quality of life, body image, cause pain and negatively affect treatment therefore patient reported outcomes of RISR are important to capture.[4]

RISR occurs as a result of complex interplay between patient related factors such as body mass index (BMI), smoking, nutritional status, pre-existing skin disease and genetic susceptibility. Treatment factors such as total and daily dose of radiation, delivery techniques, size and location of the treatment area[5] and concurrent

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chemotherapy also impact severity.[6,7] Inflammation occurs within the first 24 h after the start of radiotherapy with generation of free radicals and reactive oxygen in the rapidly dividing cells of the basal layer and dermis,[8] this decreases the stem cells, induces change in endothelial cells and promotes inflammation. Over 2–4 weeks a sustained erythema develops with local oedema and infiltration of leukocytes.[9] Radiotherapy damage accumulates over the course of treatment leading to delayed healing of the skin and can persist up to four weeks after treatment ends.[10] Chronic effects to the skin induced by radiotherapy are changes to the vasculature and connective tissue of the cutaneous and subcutaneous layers leading to telangiectasia, atrophy and hyperpigmentation of the skin.[11]

Despite various practice recommendations and guidance[11] there is still diversity in what cancer centres recommend for RISR.[12] While the research published between 2011 and 2014 underpinning the 2015 Society and College of radiographers (SoCR) guidance was potentially valuable to the radiotherapy community, only 30% of the research reviewed for these guidelines was assessed as high quality (i.e., assessed as having limited opportunity for bias that may affect the research results). Serious skin reactions have become less common with modern skin sparing radiotherapy techniques. However, there have been recent changes to dose and fractionation regimes for example accelerated radiation dose schedules, changes in response to COVID-19[13] and the wider use of multimodality treatments such as chemotherapy and immunotherapy[14] which all impact on prevalence of RISR.

This systematic review was undertaken to update existing knowledge and explore the efficacy of emerging interventions to inform current best practice guidance from the SCoR 2020 (https://www.sor.org/news/radiotherapy/scor-updates-radiation-dermatitis-guidelines). The aim was to assess the effectiveness of interventions and practices that may prevent, reduce (or alter) RISR in patients undergoing external beam radiotherapy for cancer; with an emphasis on research published since 2015.

Method

This review addressed two questions

1. What is the effect of preventative interventions such as topical agents in reducing acute skin reactions including radiation dermatitis, erythema, dry and moist desquamation?
2. How effective are management strategies in RISRs compared to standard care practices at the end of radiotherapy?

Data sources and searches

The review was registered on PROSPERO (CRD42019148161) and built on previous work. The search was conducted in two stages. In stage one, studies were identified via abstracts through a systematic search strategy and replicated the search MESH terms conducted in 2014 for the SCoR systematic review and guidelines. In stage 2 these terms were supplemented with terms identified through a modified pearl growing technique. Other relevant publications were retrieved by reviewing the reference lists of these studies against the eligibility criteria.

Medline (Pub med), CINAHL (with full text), Embase and Cochrane central register of controlled trials were searched (Fig. 1). The databases were chosen to identify potentially relevant published studies in the field of radiation therapy, nursing, clinical oncology and dermatology. The full search strategy and Boolean operator terms are provided in the supplementary documents (S1).

Study selection

Empirical studies published from the period October 2014 to October 2019 were included. The following were all excluded from the review; studies that combined data from previously published studies, case studies and conference abstracts.

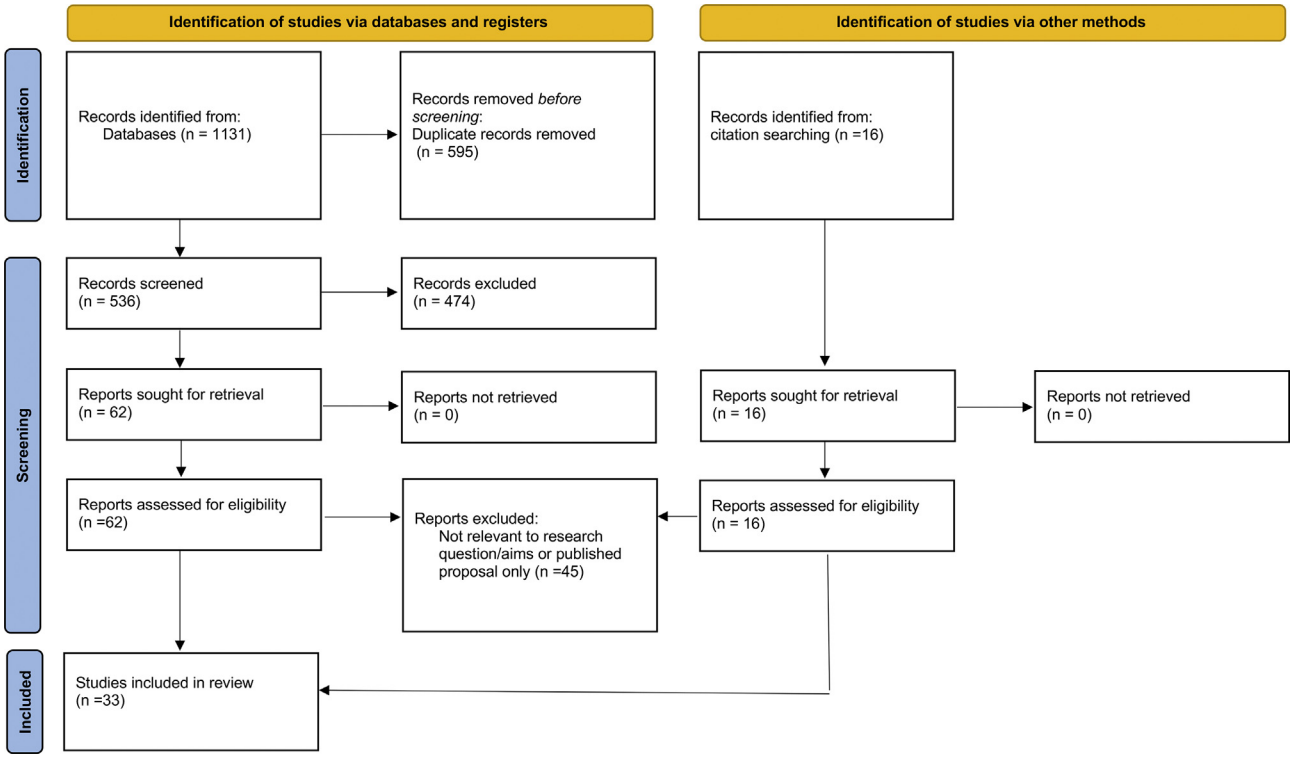

Figure 1. PRISMA fowchart.

Population included cancer patients who were treated with and received any form of external beam photon, proton or electron beam radiotherapy. *Interventions* were preventative measures including the use of topical applications, use of barrier films and deodorant guidance. Management measures included dressings, topical and medical applications.

Comparison groups were defined as standard skin care practice including normal washing and use of non-specific moisturisers. Identification of objective *outcomes* of RISR were identified through RTOG/CTCAE and patient reported outcome measures (PROM) at the end of radiotherapy delivery.

Quality assessment

Risk of bias was assessed by an interdisciplinary research team (GB, HP and SF). Depending on the study design either the Cochrane Collaboration RoB2 or ROBINS-I tool were used. Our data extraction tool can be found in the supplementary materials (S2). Fig. 1 indicates the number of studies identified for review through the search process. Following exclusion of duplicates, and studies not meeting the search inclusion criteria a total of 33 studies were included for review and quality assessment.

Results

Of the 33 studies reviewed 13(39.4%) were assessed as having a high risk of bias 6(18.2%) assessed as having a moderate risk of bias, and 13(39.4%) as low risk of bias. There was one pilot study not assessed. 21 of the studies were RCTs, 2 feasibility studies, 9 non-randomised trials, and 1 pilot study (S3 in the Supplementary Materials presents the summary of all articles reviewed).

The results of the review are presented in four sections. These sections represent suitable groupings of research on the same or similar interventions for the prevention or treatment of RISRs as follows: (i) steroid creams, (ii) low level laser therapy (LLLT) or photo biomodulation therapy (PBMT), (iii) barrier films and (iv) topical emollients. In each section a summary table is presented showing the studies reviewed on that topic highlighting whether the research resulted in statistically significant improvements in RISR, or patient reported measures of discomfort. Results are classified into; significant results at $p \leq 0.05$ and not significant results in terms of RISR at end of radiotherapy. Studies were classified into low, moderate and high risk of bias.

Steroid cream intervention studies

Four studies reported positive outcomes in relation to the use of topical steroid creams in reduction of RISR compared to controls at end of therapy (Table 1). Erridge,[15] Ho[16] and Ulff[17] all showed significant reductions in RISR on CTCAE or RTOG scores. Sio[18] reported positive PROMs. Fenton-Kerimian[19] and Ulff[20] reported non-significant results, and also undertook additional post radiotherapy evaluations at a variety of time points with Fenton- Kerimian assessing RISR measurements extending up to 3 months post treatment and Ulff a mean of six years post radiotherapy.

LLLT or PBMT intervention studies

Three studies investigated the use of PBMT to reduce or prevent the incidence of moist desquamation or radiation dermatitis; studies involved samples of patients treated for breast cancer (Table 2). All[21–23] demonstrated a statistically significant reduction

Table 1
Steroid cream intervention and prevention of RISR studies evaluating risk of bias and providing a summary of study outcomes on clinician and patient reported outcomes.

References		Outcomes +Ve significance at P≤.05, NS= not significant																
Author and risk of bias assessment	Tumour site	Clinician Reported Outcomes									Patient Reported Outcomes							
		RTOG	CTCAE	RISRAS	CTC	EORTC	Digital Imaging	10-point Catterall	WHO Criteria	Other	SKINDEX 16 Overall	VAS	Symptom Inventory	McGill Pain Questionnaire	Likert Scales	Dermatology QoL Index	Skin Experience Diary (SED)	Other PROMS
Erridge et al 2016	H+N, Brain, Breast, Pelvis, Other	+Ve																+Ve
Fenton-Kerimian 2015	Breast Cancer		NS														NS	
Ho 2018	Breast Cancer	+Ve									NS							
Sio 2016	Breast Cancer		NS															+Ve
Ulff 2017 (late toxicity)	Breast Cancer	NS																
Ulff 2017	Breast Cancer	+Ve										+Ve						
		Risk of bias: green low risk, orange moderate risk, red high risk of bias																
		Abbreviations: Radiation Therapy Oncology Group =RTOG, Common Terminology Criteria for Adverse effects=CTCA/E, Common Terminology Criteria=CTC, European Organisation for Treatment of Cancer=EORTC, Radiation Induced Skin Reaction Assessment Scale=RISRAS, Visual Analogue Scale=VAS																

Table 2
Laser therapy and PBMT intervention studies risk of bias and summary of study outcomes for RISR in clinician and patient reported outcomes.

References		Outcomes +Ve significance at P≤0.05, NS= not significant																
Author and risk of bias assessment	Tumour type	Clinician Reported Outcome Measures									Patient Reported Outcome Measures							
		RTOG	CTCAE	RISRAS	CTC	EORTC	Digital Imaging	10-point Catterall	WHO Criteria	Other	SKINDEX 16 Overall	VAS	Symptom Inventory	McGill Pain Questionnaire	Likert Scales	Dermatology QoL Index	Skin Experience Diary (SED)	Other PROMS
Censabella et al 2016	Breast cancer			+ve							NS							
Robijns et al 2019	Breast Cancer	+Ve																
Strouthos et al 2016	Breast Cancer		+Ve				+Ve					+Ve						
		Risk of bias: green low risk, orange moderate risk, red high risk of bias Abbreviations: Radiation Therapy Oncology Group =RTOG, Common Terminology Criteria for Adverse effects=CTCA/E, Common Terminology Criteria=CTC, European Organisation for Treatment of Cancer=EORTC, Radiation Induced Skin Reaction Assessment Scale=RISRAS, Visual Analogue Scale=VAS																

in radiation dermatitis when compared to either a placebo intervention[21] or no intervention at all.[22,23]

Barrier film intervention studies

Six studies[24–29] were identified that investigated the use of a barrier film to reduce skin reactions; three were conducted with patients diagnosed with a primary breast cancer, one with patients treated for a head and neck cancer, and one with patients treated for prostate cancer (Table 3). Three of the studies reported positive reduction in RISR scores in relation to the use of barrier films but we noted a high number of participant withdrawals from these studies due to sensitivity of patients to the barrier film resulting in a risk of bias in the analysis.

Topical emollients

A total of fifteen studies (Table 4) investigated the use of a topical cream or gel for RISR. Across the studies 14 different products were investigated, including boron gel,[30] heparinoid,[31–33] essential oil[34,35]; emu oil,[36] flavonoid extract,[37] hydrocolloid gel (Censabella et al.) camellia sinensis nonfermantatum extract,[38] urea lotion,[39] aloe vera,[40] Boswellia cream,[41] melatonin[42] and an olive oil-based product.[43] Ten of the studies were assessed as having either a moderate or high risk of bias, with only four rated as low risk; one study was not assessed as it was a pilot study. Only two studies of Melatonin and flavonoid extract creams showed significant results on RTOG scores for RISR and demonstrated a low risk of bias.[37,42]

The summary of studies (supplementary papers S2) demonstrates the breadth of choice and timing of outcome measurements across all the studies, description of controls used and assessment tools. Few of the studies used a PROM; fourteen in total. The concordance of clinical rating and patient reported is well known to under estimate the impact of RISR on quality of life[44] and should be included in future research. Future research studies of RISR should consider improving design features to reduce risk of bias, such as intention to treat analysis, multivariate analysis to control for confounding variables and inclusion of modern fractionation regimes (these are detailed in the supplementary materials S4).

Discussion

Steroid Creams are an important preventative agent for reducing risk for patients at higher risk of RISR but need appropriate dosing and use early in radiotherapy. The rationale for using steroid creams is based on the known anti-inflammatory properties of steroids. Studies[16,18] reported positive outcomes when using steroid creams and scored low for potential bias; these studies were conducted on patients undergoing radiotherapy for breast cancer. Studies found a lower rate of grade 2 or 3 (moist desquamation) using 0.1% mometasone furoate than in controls. Ho et al.[16] reported 43.8% vs 66.7% intervention vs control respectively ($P = 0.012$) and a lower incidence of maximum grade radiation dermatitis, reporting 18.8% vs 33.3% ($P = 0.036$) in their intervention arm.

Steroid creams have often been discouraged because of potential late effects to the skin. Research[17,20] reported not only reduced acute toxicity following administration of betamethasone 17-valerate cream to women with breast cancer but also no detrimental late effects. Starting steroids at the beginning of radiotherapy ameliorated acute radiation dermatitis compared to a control moisturiser. Women in the intervention (steroid cream) arm developed fewer skin reactions than those treated with a normal moisturiser ($P < 0.001$) and this was regardless of the radiotherapy fractionation regimen used.[17] However, women with a hypofractionated (2.67Gy/fraction) course of radiotherapy had lower acute RISR than those treated with a conventional fractionation (2Gy/fraction). Fractionation regime is therefore also important to consider in those individuals who are at a higher risk of RISR.

Outcomes with steroid cream are slightly confounded by the use of conventional dose fractionations (50Gy in 25 fractions) compared with hypofractionated regimens (40Gy in 15 fractions) where it is known that acute skin toxicity is lower[45] but steroid therapy shows potential for use as a preventative for those patients at higher risk.

PBMT is a relatively new therapy providing low-power infrared light to the skin to stimulate the natural healing process that may be interrupted by the impact of RISR by reducing inflammation and pain. Studies by Robijns et al.[21] and Strouthos et al.[22] demonstrated a reduction in moist desquamation and/or radiation dermatitis. The

Table 3
Barrier film intervention studies risk of bias and summary of study outcomes for RISR in clinician and patient reported outcomes.

Reference		Outcomes +Ve significance at P≤0.05, NS= not significant															
Author and risk of bias assessment	Tumour type	Clinician Reported Outcome Measures								Patient Reported Outcome Measures							
		RTOG	CTCAE	RISRAS	CTC	EORTC	10-point Catterall	WHO Criteria	Other	SKINDEX 16 Overall	VAS	Symptom Inventory	McGill Pain Questionnaire	Likert Scales	Dermatology QoL Index	Skin Experience Diary (SED)	Other PROMS
Arimura et al 2016	Prostate				+Ve												
Chan et al 2019	Head and Neck		+Ve														
Lam et al 2019	Breast	NS															
Moller et al 2018	Breast				NS												+Ve
Rades et al 2019	Head and Neck		NS														
Shmeel et al 2018	Breast	+Ve				+Ve											
	Risk of bias: green low risk, orange moderate risk, red high risk of bias Abbreviations: Radiation Therapy Oncology Group =RTOG, Common Terminology Criteria for Adverse effects=CTCA/E, Common Terminology Criteria=CTC, European Organisation for Treatment of Cancer=EORTC, Radiation Induced Skin Reaction Assessment Scale=RISRAS, Visual Analogue Scale=VAS																

study by Robijns et al. demonstrated a higher incidence of RISR in the control arm at the 66Gy time point compared to the intervention arm ($p = 0.004$). Strouthos also reported a lower incidence of radiation dermatitis in the PBMT group compared to control ($p = 0.0211$). In addition, Strouthos recorded pain level and intensity using a weekly patient reported visual analogue scale (VAS) reporting pain intensity in the PBMT group was significantly lower ($p = 0.003$).

The use of PBMT is an emerging area, with several ongoing trials that are currently recruiting (S4 supplementary material). There are some potential concerns about the long-term impact of PBMT and further research on this is needed. It is not clear whether the benefits from PBMT presented from these two studies would be replicated in patients receiving radiotherapy with hypofractionated schedules or in other patient groups.

Barrier films have been widely used and are thin, self-adhesive sheets that provide a protective layer to the surface layers of the skin. The rationale for them is that they prevent further trauma or risk of infection. Recent studies that have investigated the use of Mepitel® film in patients with head and neck cancer and breast cancer respectively.[27,28] Neither study reported statistically significant improvements in reaction when using the Mepitel® film. In the study by Rades et al.,[28] the trial was halted at interim analysis (when some patients had received a total dose of 50Gy). The premature closure of the study was due to a high proportion of the particpants being unable to tolerate the product (46.4% n = 13). Common toxicity criteria (CTC) scores in the Møller et al. (2018) trial showed no significant difference between intervention and control in the incidence of grades 1 to 3 skin toxicity at the end of treatment or at 14 days post treatment. However, the PROMs showed significant differences in favour of the barrier film, with patients stating that the film was comfortable. At 14 days, pain was reduced ($P = 0.001$), and sensitivity of the skin, as well as itching, was also reduced ($P < 0.01$). The high level of patients withdrawing from these studies due to reaction to the barrier film is of note and raises important issues of sensitivity.

Barrier film wound dressings (e.g. StrataXRT® or alternative product) have also been used in patients undergoing radiotherapy for head and neck cancer, lung cancer and breast cancer.[25,26] In the study by Chan et al.,[25] at the end of treatment grade 2 skin reactions were identified in 80% of patients in the StrataXRT® arm and grade 3 in 28%, compared with 91% and 45% respectively in the control arm. After controlling for the cancer drug cetuximab, the StrataXRT® arm had a 12% lower risk of experiencing grade 2 skin toxicity (RRR = 0.876, 95% CI 0.778–0.987) and a 36% lower risk of developing a grade 3 reaction (RRR = 0.648, 95% CI 0.442–0.947). Creams used as control comparators could potentially have influenced the results of these studies. In the study by Lam et al.,[26] patients with breast cancer in the sample were treated with either a conventional fractionation (50Gy in 25 fractions) or a hypofractionated biologically equivalent dose.

There was no difference in PROMs for burning, pulling and tenderness for those where the barrier film was applied to the medial half of the chest, except for itching, where a significant improvement was seen (1.14 vs 2.06 barrier film vs control cream $P = 0.035$). For cases where the barrier film was applied to the lateral half, only for burning was there a difference in patient reported scores, 0.92 vs 1.83 ($P = 0.047$, no confidence intervals presented). There was no significant difference seen between barrier film and standard local care for time taken to develop grade 2 radiation dermatitis. In those patients where the barrier film was applied to the lateral half of the chest, a grade 2 or more radiation dermatitis was reported in 17.3% of cases compared with 27.6% in the no film half ($P = 0.041$). For those where the barrier film was applied to the medial half, a grade 2 dermatitis was reported in 17.2% of cases and 9.6% for no film ($P = 0.76$). Post treatment, no difference was seen in grade 2, or above, scores for barrier film vs no film.

Hydroactive colloid gels form another barrier method[46] and have been used in patients undergoing radiotherapy for breast cancer in a non-randomised single centre study design that used two historical control groups as comparators. Significant reductions

Table 4
Emollients and cream intervention studies in preventing and managing RISR evaluating the risk of bias and summary of study outcomes for RISR in clinician and patient reported outcomes.

References		Outcomes +Ve significance at P≤0.05, NS= not significant																
Author and risk of bias assessment	Tumour type	Clinician Reported Outcome Measures									Patient reported outcome measures							
		RTOG	CTCAE	RISRAS	CTC	EORTC	Digital Imaging	10-point Catterall	WHO Criteria	Other	SKINDEX 16 Overall	VAS	Symptom Inventory	McGill Pain Questionnaire	Likert Scales	Dermatology QoL Index	Skin Experience Diary (SED)	Other PROMS
Aysan et al 2017	Breast	+Ve																NS
Ben-David et al 2016	Breast	+Ve																
Eda et al 2016	Breast	+Ve																
Halm 2014	Breast	NS																
Chan 2014	Breast, Lung, H&N		NS								NS							
Karbasdorooshan et al 2018	Breast (Post surgery)	+Ve	+Ve															
Náf et al 2018	Breast				NS													
Ogita et al 2019	Breast									NS								
Sekiguchi 2015	Breast									NS	+Ve							
Sekiguchi 2018	Breast									NS	+Ve							
Togni et al 2015	Breast	NS																
Hoopfer 2015	Breast							NS										
Cui et al 2015	Nasopharynx	+Ve															NS	
Manas et al 2015	Breast & H&N			+Ve	+Ve													
Censebella 2017	Breast								+Ve									
	Risk of bias: green low risk, orange moderate risk, red high risk of bias Abbreviations: Radiation Therapy Oncology Group =RTOG, Common Terminology Criteria for Adverse effects=CTCA/E, Common Terminology Criteria=CTC, European Organisation for Treatment of Cancer=EORTC, Radiation Induced Skin Reaction Assessment Scale=RISRAS, Visual Analogue Scale=VAS																	

in the onset of radiation induced moist desquamation using the hydroactive colloid gel were reported, an incidence of 6.9% in the intervention arm vs 35.1% and 12.6% in the historical control arms. Patients undergoing breast irradiation, particularly where hypofractionated dose schedules are employed, or for patients receiving radiotherapy to the head and neck the use of a barrier film is not recommended as evidence is lacking.

Topical emollients are most used to prevent RISRs in practice, or to provide comfort for patients once a reaction has occurred. As radiation damages the basal cell layer of the skin, the normal desquamation of cells and growth of replacement cells are both interrupted, and dehydration of the skin occurs. Topical emollients are considered to hydrate the skin and ameliorate itching and soreness. Newer agents show promise Karbasforooshan et al.[37] studied the use of silymarin, herbal medicine (dried extract of *Silybum marianum*, also known as milk thistle). At week 5 grade 1 radiation dermatitis was reported as 100% in the silymarin group, while in the control group grade 1 was reported as 55%, grade 2 as 40% and grade 3 as 5% ($P = 0.003$). While these results look promising, a larger study is needed to replicate this data before the results and this product could be recommended for use in practice. Ben-David et al.[42] investigated a melatonin-containing emulsion in patients treated for breast cancer. During treatment, no significant differences were observed between the two groups for clinician assessed skin toxicity. At weeks 5–7 the melatonin emulsion group ($P = 0.049$) had significantly lower RISR. At two weeks follow-up (week 7) the melatonin group 59% had grade 0, 41% grade 1 or 2, compared with 11% grade 0 and 90% grade 1 or 2 in the placebo group ($P = 0.03$). Patients in this study received a conventional fractionation (50Gy in 25 fractions) and further research is needed to identify whether the benefits reported in this study could be replicated in cases where a hypofractionated regimen is adopted. There is no strong evidence to support or recommend any of the emollients reviewed. There are some promising interventions identified in the studies, but further research is required to replicate the results in wider populations

or in samples using modern dose fractionation schedules before recommendations for use in practice can be made.

Conclusion and recommendations

The evidence review has led us to the following conclusions:

- Steroid creams should be used prophylactically on individuals identified as high risk of developing a RISR i.e. a grade 3 skin reaction.
- Prophylactic use of steroid cream should not be used for patients with breast cancer receiving adjuvant hypofractionated regimens (i.e., 40Gy in 15 fractions or equivalent).
- There needs to be more high-quality research to identify the hazard ratios for identified risk variables for RISR, to inform the development of an evidence-based risk stratification algorithm to support the appropriate use of steroid creams in the preventative setting.
- PBMT shows promise, but further research is needed confirming the benefits using hypofractionated dose fractionation schedules (i.e. 40Gy in 15 fractions or shorter equivalent regimens) for patients undergoing breast or chest wall irradiation.
- Barrier films are not recommended for patients receiving hypofractionated radiotherapy for adjuvant breast or chest wall irradiation or currently for those undergoing radiotherapy for head and neck cancer based on currently available evidence.
- There is insufficient evidence to recommend any specific topical emollient for use during radiotherapy.
- Assessing skin toxicity consistently is recommended to ensure accurate reporting and auditing of RISRs.

Data sharing

Research data are stored in an institutional repository at Sheffield Hallam University and will be shared upon request to Prof Heidi Probst.

Ethics statement

This research was a review of secondary data sources and so no ethical approval was required. The Systematic review proposal was registered with the Prospero database (CRD42019148161)

Conflict of interest statement

The College of Radiographers funded a member of the project team to support completion of the literature review. There are no other conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radi.2021.09.006.

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