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Literature Review: Prevention of Acute Radiation Dermatitis

Cancer Care Alberta

Literature Review SUPP-025
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Table of Contents

Table 1. Summary of Guideline and Delphi Study Recommendations (✓, strong recommendation; +, moderate or weak recommendation) for Prevention of Acute Radiation Dermatitis

Category	Recommendation	n	BCC, 2025[1]	CCM[a], 2018[2]	ScoR, 2020[3]	CDN delphi[a], 2025[4]	ESTRO, 2025[5]	MASCC delphi[b], 2023[6]	ISNCC, 2020[7]
Hygiene	Wash gently with lukewarm water, dry gently	4	✓		✓	✓	✓		
	Wash hair gently with mild shampoo	2	✓		✓				
	Skin in treatment field should be product free	1		✓					
	Use sitz bath daily if receiving RT for perineal/rectal cancer	1	✓						
Skin protection	Wear loose-fitting clothing	5	✓	✓	✓	✓	✓		
	Avoid trauma (scratching/rubbing/scrubbing)	5	✓	✓	✓	✓	✓		
	Avoid adhesive tape to treatment area	2	✓	✓					
	Avoid sun and wind exposure	5	✓	✓	✓	✓	✓		
	Avoid extreme heat and cold (heat/ice packs)	4	✓	✓	✓		✓		
	Use deodorant unless skin is broken	4		✓	✓	✓	✓		
	Avoid shaving (or use electric razor)	4	✓	✓	✓	✓			
	Shower and apply moisturizer after swimming	3	✓		✓	✓			
	Avoid wearing jewelry	2		✓			✓		
	Use sunscreen on intact skin	2		✓		✓			
	Avoid aloe vera for skin moisture	2		✓					
	Avoid hot tubs/saunas/steam rooms	2		✓		✓			
	Avoid smoking	2		✓		✓			
	Avoid products with drying agents (alcohol, alpha hydroxy acid)	1		✓					
	Avoid products with sodium lauryl sulphate free, zinc oxide	1			✓				
	Avoid swimming in pools and lakes	1		✓					
	Avoid hairdryer	1			✓				
	Avoid tanning lamps/salons	1		✓					
	Avoid aftershave, waxing, hair removal creams	1				✓			
Dermatitis prophylaxis	Use moisturizers/body lotions/creams	3				✓	✓	+	
	Use non-adherent barrier film (e.g., Mepitel, Hydrofilm)	4				✓	+	✓	+
	Use foam dressing (e.g., Mepilex Lite)	1						+	
	Use corticosteroid cream (e.g., mometasone, betamethasone)	2					✓	✓	
	Use barrier cream	1				✓			
	Use steroid cream	2				✓	✓		
	Avoid baby powder/cornstarch/talcum powder	2	✓	✓					
	Avoid hydrophobic products (petroleum jelly)	2	✓	✓					

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	Use olive oil	1						✓	
	Use silver nylon dressing	1						+	
	Products based on curcumin (turmeric), silymarin	1						+	
	Enzyme mixture (papain, trypsin, chymotrypsin)	1						+	
	Photobiomodulation/low level laser therapy	2					✓	✓	
	Avoid topical antibiotics and antimicrobials	1				✓			

[a] Breast cancer; [b] Breast, head and neck cancer

ARD, acute radiation dermatitis; BCC, BC Cancer; CCM, CancerCare Manitoba; CDN, Canada; ESTRO, European Society for Radiotherapy and Oncology; ISNCC, International Society for Nurses in Cancer Care; MASCC, Multinational Association of Supportive Care in Cancer; SCoR, Society and College of Radiographers

Table 2. White Literature for Prevention of Acute Radiation Dermatitis

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
Radiation Techniques					
Lee, 2024[8]	Systematic review & meta-analysis of RCTs ***LOE: I***	Ax of various fractionation schemes in RT for BC, w focus on side effects, cosmesis, QOL, risks of recurrence, and survival outcomes Pre-specified primary outcome grade ≥2 ARD and late RT related side effects	Inclusion criteria: RCTs w BC pts where postop EBRT directed at whole breast or chest wall, ±regional nodal irradiation 59 articles representing 35 trials (20,237 pts) assessed	Conventional fractionation (daily fx of 1.8-2 Gy, reaching total dose of 50-50.4 Gy over 5-6 wks.) Moderate HF (fx sizes of 2.65-3.3 Gy for 13-16 fx over 3-5 wks.) Ultra-HF (schedule of only 5 fx)	Moderate HF vs conventional fractionation (all pts, 20 trials): risk ratio for grade ≥2 =0.59 (95% CI 0.51–0.69), p<0.001 Moderate HF vs conventional fractionation (breast conserving therapy, 8 trials): risk ratio for grade ≥2 =0.54 (95% CI 0.49–0.61), p<0.001 Moderate HF vs conventional fractionation (mastectomy, 10 trials): risk ratio for grade ≥2 =0.68 (95% CI 0.49–0.93), p=0.02 Ultra-HF vs moderate HF (6 trials): risk ratio for grade ≥2 =0.85 (95% CI 0.47–1.55), p=0.60 Ultra-HF vs conventional fractionation (FAST trial): risk ratio for grade ≥2 =0.27 (95% CI 0.19–0.40), p<0.001 Sensitivity analysis excl. high-risk bias studies (moderate HF vs conventional fractionation, 11 trials): risk ratio for grade ≥2 =0.58 (95% CI 0.49–0.68), p<0.001
Brion, 2025[9]	Phase III RCT (HypoG-01) ***LOE: I***	Investigate early AEs in trial comparing toxicity and efficacy of adjuvant loco-regional moderately HFRT vs 2 Gy daily RT	N=1,260 T1-3 N0-3 M0 BC from 29 sites	Randomized 1:1 after surgery ± systemic therapy to: - 40 Gy/15 fx (3 wk. RT) - 50 Gy/25 fx (5wk. RT) ± tumour-bed boost	Grade ≥2 dermatitis occurred less frequently in 3 wk. RT group (45%) vs 5 wk. RT group (52%) up to 6 mos. post-randomization

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				AEs at baseline, end of Tx, and 6-mo. follow-up graded using CTCAE v4.0, LENT/SOMA and Harris 4-point scales Competing risk analysis for cumulative incidence of AEs, worst grade dermatitis according to risk factors, and cosmetic Ax performed in ITT population	Tumour-bed boost significantly increased RD risk: - Grade ≥2 RD occurred in 21% (boost) vs 9% (no boost) in 3 wk. RT group - 46% (boost) vs 17% (no boost) in 5 wk. RT group Sequential boost led to higher RD rates than integrated boost, esp. in 5 wk. RT (54% vs 29%)
Haussmann, 2023[10]	Systematic review & meta-analysis of RCTs ***LOE: I***	Investigate differences b/n PBI and WBRT in side effects and QOL	16 studies (n=19,085) incl. pts w early-stage invasive BC	PBI vs WBRT; techniques included EBRT and IORT; fractionation schedules varied (once- vs. twice-daily)	PBI associated w lower prevalence in any grade 1+acute toxicity and grade 2+skin toxicity (OR=0.12; 95% CI 0.09–0.18; p<0.001); (OR=0.16; 95% CI 0.07-0.41; p<0.001)
Brunt, 2023[11]	Acute skin toxicity substudies of phase III RCT (FAST-Forward) ***LOE: II***	Confirm safety of test schedules Primary endpoint: proportion of pts w grade ≥ 3 acute breast skin toxicity at any time from start of RT to 4 wks. after	Pts w invasive BC (pT1-3pN0-1M0) after BCS or mastectomy N=190 FAST-Forward pts included in acute toxicity sub-studies	Randomized (1:1:1): - 40 Gy in 15 fx (3 wks.) - 27 Gy - 26 Gy in 5 fx (1 wk.) whole breast/chest wall Acute reactions of skin of treated breast graded using RTOG v1 criteria for sub-study 1, n=190 Substudy 2 undertaken using standard CTCAE criteria (v4.03) (Protocol v2.1 and v2.2), n=162	Substudy 1 (RTOG): Grade 3 RD in 14% (40 Gy), 10% (27 Gy), 6% (26 Gy) Substudy 2 (CTCAE): Grade 3 RD in 0% (40 Gy), 2% (27 Gy), 0% (26 Gy)
Senyurek, 2023[12]	Phase II RCT (Istanbul R-02) ***LOE: II***	Compare pathological/ oncological outcomes, toxicity, and QOL results of long-course chemoRT vs intermediate-course chemoRT in locally advanced rectal cancer	N=60 pts w T3-4/N0+ rectal cancer	Randomized to: - Long-course chemoRT (50.4 Gy/28 fx) - Intermediate-course chemoRT (33 Gy/10 fx)	Rate of ARD significantly higher in long-course chemoRT group vs intermediate-course chemoRT (p<0.001)

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Lu, 2024[13]	Systematic review and meta-analysis of mix of RCTs and non-randomized ***LOE: II***	Conduct comparative analysis of safety and efficacy of HF and conventional fractionated RT in individuals who had undergone surgery for BC	Comprehensive analysis of 35 studies w N=18,246 pts diagnosed w BC Sample consisted of 13 RCTs and 22 retro studies Investigation of cutaneous AEs encompassed cohort of 10,185 individuals across 25 research studies	Control group: Conventional fractionation regimens of <2 Gy per day Experimental group: HF regimens of 2-5 Gy per day	RD reported in 5,478 pts across 9 studies, and skin toxicity of grade ≥2 reported in 4,253 pts from 17 studies HF significantly reduces overall skin toxicity compared to conventional fractionation (OR=0.43, 95% CI 0.33–0.55, p<0.01) HF significantly lowers RD incidence (OR=0.36, 95% CI 0.22–0.58, P<0.01) and grade ≥2 skin toxicity (OR=0.42, 95% CI 0.30–0.59, p<0.01)
Lukovic, 2023[14]	Prospective ***LOE: III***	Investigate impact of dosimetric parameters on acute and late toxicity for pts with anal squamous cell carcinoma treated w image-guided-IMRT and concurrent chemo	N=87 pts w anal squamous cell carcinoma	Standardized target and organ-at-risk contouring, planning, and imagie-guided-IMRT RT dose, based on clinicopathologic features, ranged from 45 Gy to 63 Gy to gross targets and 27 Gy to 36 Gy to elective targets Chemo concurrent 5-fluorouracil and mitomycin C (wks. 1&5) Acute and late toxicity graded by CTCAE v3 and RTOG	Grade ≥2 acute toxicity: 99% Grade ≥3 acute toxicity: 61% Dermatitis (inguino-genital): Grade ≥2: 87% Grade ≥3: 30% Dermatitis (perianal): Grade ≥2: 91% Grade ≥3: 29% Grade 4 dermatitis: 1% 38% pts required Tx break (median 8 days, range 1-25), primarily due to acute toxicity. Dose-volume correlations: anterior skin V35 and posterior skin V15 significantly associated w Grade ≥2 skin toxicity

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Bellon, 2022[15]	Retro analysis of ATEMPT trial ***LOE: IV***	Evaluate efficacy and safety of RT among pts treated in trial receiving RT concurrently w either trastuzumab emtansine or paclitaxel + trastuzumab, across range of RT doses, targets volumes, and schedules	Protocol therapy initiated in 497 pts stage I HER2+BC	Randomized (3:1): - Adj. trastuzumab emtansine - Paclitaxel + trastuzumab after mastectomy or BCS Among 299 BCS pts, 289 received WBRT and 10 partial breast Among WBRT pts, 40% in trastuzumab emtansine arm and 42% of paclitaxel + trastuzumab pts received HF (≥2.5 Gy/fx) RT 8 mastectomy pts received RT, all conventional fractionation	Skin toxicity (grade ≥2) seen in 34% of pts in trastuzumab emtansine arm and 23% in paclitaxel + trastuzumab arm (p=0.11) In conventionally fractionated WBRT pts, 45% had grade ≥2 skin toxicity compared w 18% of pts receiving HFRT (p<0.001)
Magdy, 2025[16]	RCT, single centre ***LOE: II***	Compare ultra HFRT vs hypofractionation in terms of acute radiation adverse events according to RTOG criteria.	N=92 w pathologically confirmed diagnosis of BC w negative surgical margins (pT1–2, pN0, M0) and must have undergone BCS. Adequate axillary staging and/or dissection or sentinel lymph node biopsy required	Radiation schedules compared: - Arm1, n=45: Ultrahypofractionated RT of 27 Gy in 5 fx over 1 wk. 5.4Gy/fr ± boost to tumour bed if indicated of 0.50 Gy per fx, for total dose of 29.5 Gy - Arm 2, n=47: HFRT in form of 40.05 Gy/15 fx/3 wks. 2.67 Gy/ fraction ± boost to tumour bed if indicated of 0.53 Gy per fx, for total dose of 48 Gy Grade 1 dermatitis most common acute skin reaction Mometasone cream administered BID for 5 days to pts exhibiting skin erythema. Subsequently, beta-sitosterol cream applied for 2 wks.	End of WBRT: Arm 1 had significantly more Grade 0 reactions (85% vs 30%; p<0.0001) and fewer Grade 1 (15% vs 64%; p<0.0001) and Grade 2 reactions (0% vs 6%; p=0.097) than Arm 2 1 Mo. Post-WBRT: No significant differences b/n arms in Grade 0 (22% vs 26%; p=0.71), Grade 1 (73% vs 72%; p= 0.92), or Grade 2 reactions (5% vs. 2%; p=0.53) 3 Mo. Post-WBRT: Grade 2 reactions significantly higher in Arm 1 (13% vs 0%; p=0.01). No differences in Grade 0 (p=0.56) or Grade 1 (p=0.06) reactions

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Barrier Films and Barrier Creams					
Herst, 2025[17]	Phase III, randomized, multicentre, clinical trial (non-inferiority) ***LOE: II***	Comparison of Mepitel and StrataXRT for prevention of ARD Primary objective: moist desquamation	N=80 BC pts receiving RT postmastectomy between June 2021 and May 2024. Intra-patient randomization (medial/lateral) of Mepitel or StrataXRT. Exclusion: prior RT to chest, metastatic disease, breast reconstruction, Karnofsky <70 *Note: not all eligible pts were enrolled due to limited resources*	Both products were applied from RT start until 4wks post-RT. Mepitel was applied by radiation therapist. StrataXRT was applied twice daily by pts. RT regimen: 26Gy in 5 fractions, 40.05Gy in 15 fractions, or 50Gy in 25 fractions.	Pts were more likely to have a higher RTOG grade ARD under StrataXRT vs Mepitel patch (p=0.011). with 39% of pts higher RTOG grade under StrataXRT, 18% under Mepitel, and 44% same grade. The absolute difference in moist desquamation rates was 6% lower under Mepitel film (20%) vs StrataXRT (26%), but non-inferiority could not be determined. Mepitel film was less well tolerated, with poor skin adherence being an issue for many patients.
Lee, 2025[18]	Randomized, multicentre, clinical trial (non-inferiority) ***LOE: II***	Evaluation of StrataXRT vs Mepitel Film for ARD prevention Primary objective: average time-weighted ARD	N=44 BC pts aged ≥18y receiving RT postmastectomy in 2017 (44 analysed per prototcol Intra-patient randomization (medial/lateral) of Mepitel or StrataXRT. Exclusion: RT contraindicated, prior RT to chest wall, unsuitable skin conditions	Mepitel was applied by nurses and replaced every 1-2 weeks when necessary. StrataXRT was applied daily by pts. Both products were used from RT start until resolution of ARD or 10wks. RT dose: 50 Gy in 25 fractions, or 50.4 Gy in 28 fractions.	Maximum ARD grade observed in StrataXRT rectangles: CTCAE v4 grade 1 (30%), grade 2 (70%). In Mepitel rectangles: grade 0 (5%), grade 1 (43%), grade 2 (50%), grade 3 (3%). StrataXRT was inferior to Mepitel, with a 0.19 mean difference in average ARD grade over 10wks from RT start (95% CI 0.12-0.26, p<0.001). Non-inferiority between StrataXRT and Mepitel for mean difference in average ARD between breast halves, worst ARD grade, and

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					incidence of moist desquamation.
Corbin, 2025[19] (abstract only)	Phase III RCT (Alliance A221803), multicentre ***LOE: I***	Potential of Mepitel to mitigate RD in BC pts undergoing post-mastectomy RT Primary endpoint = difference in AUCs estimated from repeated measures (means) mixed model using pt-completed symptom scale component of modified RISRAS weekly during RT, 1-2 wks. after end of RT, and 3 mos. post-RT b/n arms controlling for stratification factors	Pts undergoing conventionally fractionated PMRT for non-inflammatory BC	N=216 randomized (2:1): - MF (n=143, ITT) - Institutional SOC (n=65, ITT) Stratification factors balanced, incl. pt BMI, planned RT bolus, planned RT boost, and ± reconstruction No specific details provided re. application (e.g., timing, method, location)	Pts in MF arm reported significantly less RD based on pt-reported mRISRAS scores AUC for mRISRAS = 33.88 in MF arm vs. 45.10 in SOC arm, w difference of -11.22 (95% CI: -19.90 to -2.54; p=0.012) Benefit consistent across all stratification factors Significant arm × timepoint interaction also showed lower RD scores w MF during wks. 4–6 of RT and 7-14 days post-Tx (p=0.027)
Valcarenghi, 2025[20]	Phase III RCT, multicentre ***LOE: I***	Compare Mepitel vs SOC in preventing RT skin toxicity onset	BCS w SLNB or axillary sampling, followed by WBRT ± boost. RT delivered as 40 Gy (hypofractionated) or 50 Gy (standard), w boost doses of 10.5 Gy or 16 Gy, respectively Inclusion: bra cup size 1 (2.5 cm) and 2 (5 cm); median volume 253 cm^3 (117-485) eligible to completely cover skin w only 1 film Exclusion: Known contraindications to film placement; prior RT or reconstruction on the	N=161 BC pts randomized, 96% evaluable: - N=79 control - N=75 experimental Film (15x20 cm) applied by trained nurses under RO supervision before CT planning to ensure consistent breast profile and assess tolerance Film replaced weekly and removed at end of RT if toxicity <Grade 1, or 2 wks. later if ≥ grade 1	Skin toxicity RTOG score ≥ 2 observed in 9.5% and 13.9% of experimental and control groups respectively (RR=0.68, 95%CI 0.28–1.66; p=0.393) RTOG scores >0 were 90.5% and 94.9% in experimental and control groups respectively (RR=0.95, 95% CI 0.87–1.04; p=0.294) Multivariable analysis, controlled for age, diabetes, BMI and smoking exposure, showed risk reduction of RTOG >0 of 38% (HR=0.62, 95% CI 0.49–0.96, p=0.028), and no statistically significant reduction is risk of RTOG >1 of 33%

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			ipsilateral breast; participation in other research protocols; or concurrent Tx w antiblastic chemo		(HR=0.67, 95 %CI 0.26–1.76, p=0.420) in experimental group Median time to recovery from RTOG grade >0 toxicity was 17 and 32 days for experimental and control groups, respectively (p=0.027) At multivariable analysis, time to recovery was 38% faster in experimental group (HR=1.38 95% CI (0.99–1.93) p=0.059)
Wong, 2024[21]	Systematic review and meta-analysis ***LOE: I***	Identify most effective barrier film or dressing to prevent ARD among BC pts	14 RCTs with 1776 pts - 3 Mepitel[22-24] - 2 StrataXRT[25, 26] - 2 Hydrofilm[27, 28] - 2 3M barrier film[29, 30] - 3 3M barrier spray film[31, 32, Graham 2014] - 1 silver leaf[33] - 1 Mepitel vs StrataXRT (abstract of ref 18)	Searched until October 2023 Inclusion: RCT, prophylaxis use, compared to SOC or other treatment, pts aged ≥18y	Compared to SOC, Hydroflm, Mepitel Film and StrataXRT reduced the incidence of moist desquamation (Hydroflm: OR 0.08 (95% CI 0.01–0.68, p=0.02); Mepitel Film: OR 0.31 (95% CI 0.14–0.68, p<0.01); StrataXRT: OR0.22 (95% CI: 0.05-0.93, p=0.04). Compared to SOC, Mepitel Film and StrataXRT reduced the incidence of grade 3 RD (Mepitel Film: OR 0.22 (95% CI 0.09–0.50, p<0.01; StrataXRT OR 0.08 (95% CI 0.02–0.29, p<0.01).
Robijns, 2023[34]	Systematic review & meta-analysis ***LOE: I***	Evaluate the efficacy of barrier films and dressings in preventing acute radiation dermatitis	11 studies included in quantitative analysis Hydrofilm: 2 BC Mepitel: 2 BC, 3 HNC StrataXRT: 1 BC, 1 HNC Cavilon film: 3 BC Sylver Nylon Dressing: 1 BC, 1 GI	Search until Sept 2020 Inclusion: comparison vs SOC, placebo, or no intervention	**Mepitel vs control** Incidence in BC pts - G1: RR 1.12 (95% CI: 0.89-1.41, p=0.35) *(the other categories had high degree of heterogeneity)* Incidence in HNC pts - G1: RR 2.99 (95% CI: 1.46-6.12; p=0.003)

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					- G2: RR 0.81 (95% CI: 0.68-0.97, p=0.02) - G3: RR 0.68 (95% CI: 0.21-2.16, p=0.51) - Mean total RISRAS: MD -0.94 (95% CI: -1.29, -0.59, p<0.001) *Results Hydrofilm and StrataXRT not copied bc of limited evidence available.*
Dejonckheere, 2023[35]	Systematic review and meta-analysis ***LOE: I***	Review of data supporting use of barrier films for the prevention ARD after adjuvant whole-breast or chest wall irradiation	5 RCTs, with 663 pts Hydrofilm: 2 ([27, 28]) Mepitel: 3 ([22-24])	Searched until March 2023 Inclusion: RCT w ≥50 BC pts, barrier films, Exclusion: barrier forming creams or gels	Pooled effect size for developing grade 3 ARD: OR 0.18 (95% CI: 0.08-0.39). *Outcomes for meta-analysis pooled effect sizes of developing grade 0, 1, 2, ≥2, or moist desquamation not shown due to high heterogeneity.* Barrier films led to consistently better patient reported outcomes (pain, itching, burning).
Behroozian, 2023[22] ***Note***: CDN Trial	Phase III RCT, multicentre ***LOE: I***	Primary objective: compare efficacy of Mepitel in reducing RD severity Secondary tobjective: examine acute adverse events	N=376 BC pts included in modified intention-to-treat analysis Eligible: histologic diagnosis of breast malignancy or phyllodes and receiving conventional (50 Gy in 25 fractions) or hypofractionated (40-42.6 Gy in 15-16 fractions) RT to breast/chest wall ± regional LNs	Randomized Tx arm: - n=251 Mepitel - n=125 SOC Mepitel applied to entire breast or chest wall on 1st day of Tx by trained clinical research assistant Each day before start of Tx, pts seen by clinical research assistant to assess integrity of film for need of replacement In pts receiving locoregional RT, only breast or chest wall covered	Incidence of G2 or 3 RD significantly lower in Mepitel pts compared w SOC (n=39/251, 15.5%; 95% CI, 11.3 to 20.6% vs. n = 57/125, 45.6%; 95% CI, 36.7 to 54.8% respectively, odds ratio (OR): 0.20, p<0.0001) Benefits of Mepitel remained significant in pts who developed G 3 RD (n=7, 2.8%; 95% CI, 1.1 to 5.7% vs. n=17, 13.6%; 95% CI, 8.1 to 20.9%, OR: 0.19) and moist

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			Mastectomy pts eligible regardless of previous bra size or previous reconstruction. Pts receiving WBRT eligible if bra size 36" and/or ≥C cup Ineligible: brachytherapy, bilateral RT, prior RT to planned Tx site, active rash or pre-existing dermatitis, prone Tx, known prior history of silicone or adhesive sensitivity or allergy, concomitant cytotoxic chemo, current IBC or gross dermal involvement, and KPS<60	by Mepitel, while pts asked to follow SOC on supraclavicular and axillary region b/c of poor adherence of Mepitel in these areas On last day of RT, entire film replaced for all Mepitel pts to provide protection over next 2 wks. following completion of RT Pts who discontinued use of Mepitel instructed to use standard skin care, and reason for discontinuing film recorded	desquamation (n=20, 8.0%; 95% CI, 4.9 to 12.0% vs. n=24, 19.2%; 95% CI, 12.7 to 27.1%, OR: 0.36) When evaluating combined pt and health care provider score using RISRAS, Mepitel arm had significantly lower scores (p=0.0001) Individual items on RISRAS also favoured Mepitel for both pt- and clinician-reported outcomes Blistering/peeling, erythema, pigmentation, and edema significantly reduced in Mepitel arm 3 pts removed film prematurely b/c of rash (n=2) and excessive pruritus (n=1)
Lee, 2023[36]	Systematic review & meta-analysis of RCTs ***LOE: II***	Evaluate efficacy of Mepitel in preventing acute RD in pts w HNC	3 RCTs with 137 HNC pts undergoing RT (ITT, n=105 per protocol)[37-39] *Note: 2 RCTs had fewer than 50 pts[37, 39]*	Systematic search conducted in March 2023. Inclusion: RCT, preventative Mepitel, HNC pts, compared to placebo/controlled agent Exclusion: insufficient data, <18y	Mepitel reduced RD severity compared to Sorbolene or Biafine, but not mometasone Per-protocol analysis of 2 trials[37, 39] found Mepitel significantly lowered risk of grade 2/3 RD (OR 0.24, p=0.005), moist desquamation (OR 0.21, p<0.0001), and improved skin reaction scores across pt, researcher, and combined assessments Reported drawbacks included itchiness and poor adherence.

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					All 3 trials reported poor film adherence, more frequently than in BC studies. Contributing factors may include neck's irregular contours, frequent movement, exposure, beard stubble, longer Tx duration, higher RT doses, and detachment during bathing
Lee, 2023[40]	Systematic review and meta-analysis ***LOE: II***	Efficacy of StrataXRT for prevention of ARD in BC pts	3 RCTs with 200 BC pts (189 pts per protocol)[25, 26] vs SOC: 2[25, 26] vs Mepitel: 1 *Note: 1 of the included RCTs was a conference poster and had <50 pts. And 1 of the RCTs analysed <50 pts)*	Systematic search conducted in April 2023. Inclusion: RCT, StrataXRT, BC pts, compared to placebo/SOC/other treatments Exclusion: insufficient data	StrataXRT prevented grade 3 RD (OR 0.05; 95% CI, 0.01-0.22; P < 0.0001). Insufficient evidence for grades 2–3 RD (OR 0.32; 95% CI, 0.03-3.18; P = 0.33). Compared to Mepitel, no difference for grade 3 and grades 2-3 RD. 1 RCT[25] reported lower erythema index (P = 0.008) and melanin index (P = 0.015).
Shariati, 2023[41]	Systematic review & meta-analysis of RCTs ***LOE: II***	Evaluate efficacy of Mepitel in preventing or treating acute RD in pts w BC in RCTs	3 RCTs, with 738 BC pts (ITT; 681 per protocol)[22-24]	Systematic search conducted in December 2022 Inclusion: RCT, Mepitel, BC pts, compared to placebo/control agent Exclusion: non-English, pediatric population	Film significantly reduced incidence of grade 3 RD (OR 0.15 95% CI 0.06, 0.37, p<0.0001) and grade 2 or 3 RD (OR 0.16 95% CI 0.04, 0.65, p=0.01) as scored on either CTCAE or RTOG scale Additionally, film significantly reduced RISRAS mean scores assessed by pts and combined researcher and pt (SMD -7.59, 95% CI -14.42, -0.76, p=0.03; SMD -15.36, 95% CI -30.01, -0.71 p=0.04) but not researcher component of Ax tool (SMD -

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
					17.55, 95% CI -36.94, 1.84, p=0.08)
Chan, 2019[42]	Randomized, single centre, clinical trial ***LOE: I***	Effect (superiority) of StrataXRT vs Sorbolene cream in HNC pts receiving radical radiation therapy	N=172 HNC pts aged ≥18y receiving RT as primary or post-surgery - 89 StrataXRT - 83 Sorbolene cream Mean age: 64 Mean BMI: 26-28 Majority stage III-IV at baseline Male: 78% Smoking: 15% Concurrent CTx: 46% Surgery: 45% Exclusion: pre-existing skin rash, open wound, skin disease	Pts applied StrataXRT twice daily until skin reaction subsided, up to 4 wks post-RT. Pts applied Sorbolene cream twice daily or more as needed, up to 4 wks post-RT. RT as either helical tomotherapy or volumetric modulated arc, median 65 Gy in 32-33 fractions. In case of skin breakdown, application was stopped and Intraside gel dressing was applied until wound healed	Less skin toxicity in StrataXRT arm vs Sorbolene arm (CTCAE v4 score 2.4 vs 2.7, p=0.002). Lower risk CTCAE v4 grade 2 RD in StrataXRT arm (RR 0.876, p=0.031), and lower risk grade 3 RD (RR 0.648, p=0.025) vs Sorbolene arm. Longer time till grade 2 and grade 3 in StrataXRT arm (median survival of 4 and 6 wks vs 3 and 5 wks in Sorbolene arm). No difference for pain, itching, skin-related quality of life.
Laffin, 2015[29]	Randomized, clinical trial ***LOE: I***	Compare Cavilon Durable Barrier Cream and 100% Pure Sorbolene Cream at preventing moist desquamation in BC pts in a tropical setting.	N=245 BC pts aged ≥18y stratified to breast/chest wall - 119 Cavilon - 126 Sorbolene (glycerine cream) Mean age: 55.5y Current smoker: 12% Mean BMI: 29 Majority skin type III Prior CTx: 59% Exclusion: palliative RT, allergy to study creams	Creams were applied to intact skin twice daily from RT start till 4 wks post-RT. RT regimen: 42Gy in 16 fractions or 50Gy in 25 fractions to the breast (71% of pts), or 50Gy in 25 fractions to the chest wall. Bolus (26% of pts) and boost (58% of pts) if needed. For moist desquamation, application was paused and dressing applied.	Higher incidence of moist desquamation in pts w RT to chest wall (22% vs breast 12%), pts w skin type I (60% vs other skin types <15%), pts w bra size >C, pts w high BMI, and chemo. No impact of smoking or humidity. Among pts with RT to chest wall, incidence of moist desquamation was lower in Cavilon arm vs Sorbolene arm (12 vs 32%, p=0.047). No difference at new incidence at follow-up, regardless of RT site. No difference in itching (72 vs 85%, p=0.06)

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
					Pts preferred Cavilon re application, build-up in skin creases. Sorbolene was preferred re relieving dryness
Graham, 2013[30]	Randomized, double blind, multicentre, clinical trial ***LOE: I***	Investigate the ability of an alcohol-free barrier film (Cavilon) to reduce skin reactions compared to 10% glycerine cream (Sorbolene)	N=318 BC pts w total mastectomy, aged ≥18y, ECOG 0-2 Intra-patient randomization (medial/lateral) of Cavilon or Sorbolene (glycerine) cream Mean age: 55y Mean BMI: 28.4 Concurrent CTx: 7% Prior CTx: 86% Hormones: 65% Exclusion: previous RT to chest wall, malignant cutaneous involvement, pregnant, known allergy to products	Creams were applied daily from RT start to 2wks post-RT RT regime: 45 Gy (mean 49.8Gy) in 25 fractions (mean 25fr). Bolus (96% of pts) and boost (1% of pts) as needed. For moist desquamation, hydrocolloid dressing was applied.	Worse skin reactions on lateral vs medial side. On the medial side, fewer pts had CTCAE v3 ≥grade 3 skin reactions with Cavilon vs Sorboline (18 vs 28%, OR 0.58, p=0.047). When combining medial/lateral, no difference in skin reactions w Cavilon vs Sorboline for grade 1 (6 vs 7%), grade 2 (61 vs 61%), grade 3 (31 vs 31%), moist desquamation (55 vs 56%). Also, no difference re pruritus, pain symptoms. No difference in compliance.
Simoes, 2024[43]	Randomized, single centre, clinical trial ***LOE: II***	Effectiveness of spray skin protectant 'non-burning barrier film' in the prevention ARD (moist desquamation)	N=63 anal and rectal cancer pts aged ≥18y - 34 cavilon spray - 29 moisturizer based on C. officinalis and A. barbadensis (Dnativ Revita Derm) Age 21-66: 57% Colostomy: 25% Never smoked: 56% Never alcohol: 41% RT combined: 89% Exclusion: prior RT at treatment site, preexisting	After demonstration by nurse, pts applied spray daily. Moisturizer was applied twice daily. Products were used until moist desquamation or discharge RT regime: 81% of pts received IMRT or VMAT, 19% received 3D. 70% received 45-50.4Gy total dose, 30% received 54-60Gy. Products were stopped after observation of moist desquamation.	Cavilon arm had less moist desquamation (62 vs 79%) compared to moisturizer arm. All pts developed ARD (100%). Cavilon arm had slightly lower severity (p = 0.269), 35% with grade 1 (vs 21%), 32% with grade 2 (vs 38%), and 32% with grade ≥3 (vs 41%). Cavilon arm experienced more interruptions (26 vs 14%).

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
			dermatitis, allergy to any of the products		
Omidvari, 2022[26]	Randomized, single centre, clinical trial ***LOE: II***	Investigate effectiveness of StrataXRT for prevention of ARD	N=100 BC pts receiving RT post- quadrantectomy (partial mastectomy) - 50 StrataXRT - 50 negative control (daily rinse only) Mean age: 43-45y Majority stage T1-T2 Majority node N0-N1 Exclusion: previous RT to chest wall or breast, history of systemic or cutaneous disease, systemic steroids, carcinoma in situ	Pts applied StrataXRT twice daily after washing during RT; Control arm only rinsed area daily during RT. RT regimen: 50Gy in 25-28Fr to whole breast +/- regional nodes (5d per week for 5-5.5 weeks). RT started 3 wks after CTx (doxorubicin- and taxane-based).	Pts in StrataXRT arm had lower mean size of maximum area of RD (70 vs 84 cm^2, p=0.002) compared to control arm. Pts in StrataXRT arm had more RTOG grade 2 ARD (90 vs 52% control), but less grade 3 ARD (4 vs 46%) (p <0.001)
Rades, 2019[38] RAREST-01 trial	Randomized, active-controlled, parallel-group multicenter trial ***LOE: II***	Compare Mepitel to SOC for prevention of grade ≥2 RD in pts w locally advanced SCC of head and neck	Pts w histologically proven locally advanced SCCHN receiving RT or radiochemo Excluded: N3 stage, distant mets, Tx w EGFR-antibodies, expected non-compliance RT: conventionally fractionated (5x2 Gy/wk.) VMAT. Target volume ≤50 Gy included primary tumour region and bilateral cervical and supraclavicular LNs. Sequential boosts assigned depending on Tx approach, extent of resection and extra-	At time of interim analysis, n=57 pts randomized: - 28 Mepitel - 29 SOC Mepitel started on 1st day of RT and continued until grade ≥2 moist desquamation or grade ≥3 RD occurred, otherwise until 1 wk. following RT Grade ≥2 moist desquamation and grade ≥3 RD treated w antiseptic agents followed by silicon or calcium alginate bandage until moist desquamation disappeared and/or RD improved to grade 2	Trial stopped prematurely b/c 13/28 pts did not tolerate Mepitel Grade ≥2 dermatitis: 34.8% Mepitel vs. 35.7% SOC at 50 Gy, 65.2% vs. 59.3% at 60 Gy

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
			capsular extension of LN metastasis. No bolus. Chemo: cisplatin first choice (2 courses of 20 mg/m^2/d1–5 or 25 mg/m^2/d1–4)	Mepitel changed 2x/wk. B/c film transparent, not changed it daily did not affect Ax of RD incl. desquamation Primary endpoint grade ≥2 RD (CTCAE) at 50 Gy.	
Lam, 2019[31] ***Note***: CDN Trial	Intra-patient randomized, single centre, clinical trial ***LOE: II***	Evaluate efficacy of prophylactic barrier film in post-lumpectomy patients	N=55 BC pts aged 18-90 w lumpectomy. Intra-patient randomization (medial/lateral) of Cavilon or aqueous cream like product (Glaxal Base Cream) Mean age: 62y Mean BMI: 31 Prior CTx: 16% Prior hormone Tx: 47% Majority stage T1	Cavilon was applied at RT start and continued until completion. Reapplication twice a week by RTT. RT regimen: 42.5 Gy in 16 fractions or 50 Gy in 25 fractions. No boost/bolus	Cavilon reduced ARD severity in lateral breast during treatment (mean RTOG grade 0.91 vs 1.21, p=0.041). No difference post treatment. Cavilon reduced burning in lateral breast post treatment (mean 0.92 vs 1.83, p=0.047). No difference in itching, pulling, tenderness. There was no difference between the time-to-onset. Note a low rater ICC (0.45) between 3 assessors
Møller, 2018[24]	Randomized, intra-patient controlled, multi centre clinical trial ***LOE: II***	Investigate pt-reported symptoms related to RD Examine pt preferences using Mepitel during Tx course compared to SOC	Women referred to postop adj RT for BC (n=101) Excluded: lack of compliance, not understanding Danish, inclusion in Danish HYPO PBI protocol, unable to do 2-wk. follow-up N=79 included in analyses (n=63 breast RT, n=16 chest wall RT) All pts had either lateral (n=38), or medial (n=41)	Guidelines for digital data reporting, film application instructions and pt info created to homogenize mgmt. of Mepitel Trained RTTs managed change of film q1–2 wks. or more frequent if necessary At 1st Tx fraction, film applied in Tx position to ensure shape of breast could be replicated Chest divided into medial and lateral side and according to randomization result film applied	W/n skin area covered by film, pts reported statistically significant lower level of pain (p<0.001), itching (p=0.005), burning sensation (p=0.005) as well as edema (p=0.017) and reduced sensitivity (p<0.001) Most pts (76%) would have preferred film on entire Tx area (p<0.001) and Mepitel as standard Tx option (84%) (p<0.001) Pts treated after mastectomy had significantly lower severity

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
			part of Tx area covered by film based on randomization RT: 40 Gy/15 fx, n=59 50 Gy/25 fx (n=20) Bolus, n=6 Chemo, n=42	in cranial-caudal position starting 2 cm below inframammary fold. For mastectomies this was measured according to opposite breast Mepitel has clinically insignificant bolus effect of 0.12 mm as confirmed by Herst 2014[23]	of RD w film at end of RT compared to SOC (p=0.005). However, in blinded staff evaluation, no significant differences found at follow-up
Dressings					
Perréard, 2024[44]	Randomized, multicentre, phase III, prospective study ***LOE: II***	Compare hydrogel-based skin dressing (HydroTac) with hyaluronic acid cream (Ialuset) among HNC pts	N=125 HNC pts aged ≥18 with for squamous cell carcinoma of the oral cavity, pharyngolarynx, or adenopathy without primary tumor were stratified by RT modality - 65 hydrogel dressing (48 w/o missing data) - 60 hyaluronic acid (48 w/o missing data) Mean age: 61y Male 80% Majority stage III or IV Mean BMI: 24 Definitive RT: 7% Definitive RT + CTx: 55% Post-operative RT +/- CTx: 29% Exclusion: cetuximab Tx, previous Tx other cancers, rapidly progressive disease	Hydrogel dressing was applied to cervical skin 5h per day for the duration of RT. Hyaluronic acid cream was applied twice daily for the duration of RT. RT regime: 60-70Gy in 2Gy fractions (6-7 wks).	56% of hydrogel pts took a break from local Tx, vs 38% in hyaluronic acid pts (p=0.09). No difference in deterioration of ENT pain 1-mo post-RT between arms (17 vs 27%). No difference in analgesics consumption between arms. No difference in occurrence and severity of ARD. No difference for laryngeal, salivary, and mucosal toxicities.
Schmeel, 2019[28]	Intra-patient randomized, single centre, prospective study	Benefit of prophylactic Hydrofilm application for patients receiving hypofractionated whole breast irradiation	N=74 BC pts aged >18 receiving whole-breast RT after lumpectomy	Hydrofilm was applied by RTT and replaced as needed. Pts applied the urea lotion twice daily. Both products were used until completion of RT	Hydrofilm treated areas had lower RD severity, with mean CTCAE v4 score of 0.54 vs 1.34 in control (mean difference 0.8, p<0.001), and grade ≥2

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
	LOE: II		Intra-patient randomization (medial/lateral) of Hydrofilm and urea lotion Exclusion: Neoadjuvant/ concomitant CTx, active smoking, metastatic disease, previous radiation to ipsilateral breast, breast reconstruction, active dermatitis, dermatological disorder, topical or oral corticosteroid Tx, mastectomy, tattoos in irradiation field	RT regimen: 40.05 Gy in 15 fractions Topical corticosteroids were prescribed if needed for ARD grade ≥ 2 with moist desquamation and intense pain	occurred in 9.5 vs 36.5% (p<0.001). Hydrofilm areas did not experience moist desquamation vs 7% of areas using urea lotion. Hydrofilm areas experienced less dry desquamation (3%) compared to urea lotion (34%, p<0.001)
Schmeel, 2018[27]	Intra-patient randomized, single centre, prospective study ***LOE: II***	Compare prophylactically applied Hydrofilm dressings with SOC (moisturizing 5% urea lotion)	N=62 (ITT) BC pts aged >18 receiving whole-breast RT after lumpectomy (majority T1) Intra-patient randomization (medial/lateral) to Hydrofilm or urea lotion Exclusion: neoadjuvant/ concomitant CTx, active smoking, metastatic disease, previous radiation to ipsilateral breast, breast, reconstruction, active dermatitis, topical or oral corticosteroid Tx, mastectomy	Hydrofilm was applied by RTT on d1 and replaced as needed or q2w. Pts applied the urea lotion twice daily starting d1. Both products were used until completion of RT RT regimen: 50 Gy in 25 fractions. Pts <65y w pathology-confirmed invasive breast cancer received a sequential boost radiotherapy up to 66 Gy with 2 Gy per fraction. Topical corticosteroids were prescribed if needed for ARD grade ≥ 2 with moist desquamation and intense pain	56 pts completed protocol, 6 pts stopped hydrofilm within first 5d due to itching/redness/eczema. Hydrofilm vs urea lotion: RTOG grade 0: 48 vs 13% RTOG grade 1: 39 vs 46% RTOG grade 2: 13 vs 30% RTOG grade 3: 0 vs 10% Lower mean RTOG score w Hydrofilm (0.35) vs urea lotion (1.33, p≤0.001). Lower max erythema severity w Hydrofilm (11) vs urea lotion (16.5, p=0.0005). Less itching and pain w Hydrofilm (0.32 and 0.44) vs urea lotion (1.0, p≤0.001; and 0.83, p=0.04). No difference in burning sensation and limitations of daily activities

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
Topical Corticosteroids					
Tam, 2023[45]	Systematic review and meta-analysis ***LOE: I***	Evaluate the use and efficacy of two common topical corticosteroids for the prevention of ARD	10 RCTs w 1041pts - 6 mometasone (incl [32, 46-49]) - 4 betamethasone (incl [50-52])	Search until January 2023 Inclusion: RT to head and neck or breast areas, compared with SOC, placebo, or no intervention	*Mometasone and betamethasone combined:* Moist desquamation: OR 0.34 (95% CI: 0.25-0.47, p<0.0001) RTOG grade ≥2: OR 0.28 (95% CI: 0.17-0.44, p<0.0001) *Mometasone:* Moist desquamation: OR 0.39 (95% CI: 0.25-0.61, p<0.0001) RTOG grade ≥2: OR 0.41 (95% CI: 0.23-0.73, p=0.002)
Menon, 2020[50]	Randomized, single centre, phase III, clinical trial ***LOE: I***	To test the efficacy of 0.1% betamethasone valerate versus best supportive care in the prevention and treatment of ARD	N=150 HNC pts aged >18y w nonmetastatic carcinoma receiving either definite or adjuvant RT - 75 (ITT) betamethasone 0.1% - 75 (ITT) SOC Median age: 58y Male: 75% No comorbidities: 80% T4 stage: 42% N2-3 stage: 33% Stage IV: 56% Concurrent CTx: 49% Exclusion: rash, ulceration, or open wound in RT field, allergy to product, history of connective tissue disease, prior RT to HN, contraindication steroids.	Steroid cream applied by pts once daily from RT start until 2wks post-RT. RT regime: 66Gy in 33 fractions over 7wks (definite) or 60Gy in 30 fractions (adjuvant). Bolus allowed.	Less RTOG grade 2 or 3 ARD in steroid arm (33 vs 51%, HR 0.58, p=0.039), in favor of more grade 1 (61 vs 44%). No difference in time to healing between both arms. Steroid arm had lower peak burning score (p=0.003). No difference in itching, dry or wet desquamation.
Ho, 2018[46]	Randomized, double-blind, phase III, clinical trial	Evaluate efficacy of 0.1% mometasone furoate versus Eucerin Original	N=124 BC pts aged ≥18y w mastectomy - 64 mometasone	Product was applied twice daily from RT start until moist desquamation or 2wks post-RT.	Steroid arm had reduced moist desquamation (44 vs 67%, p=0.012), and less CTCAE v4

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
	LOE: I	cream in preventing moderate/severe ARD	- 60 aqueous cream (Eucerin) Median age: 48y BMI ≤30: 84% Hormonal Tx: 77% CTx: 86% Anti-HER2: 23% Stage III: 35% Exclusion: gross disease in RT field, prior RT to chest wall or thorax, chest wall boost, palliative or preoperative RT w CTx, grade >1 skin toxicity, cellulitis, incompletely healed wounds, uncontrolled infection, uncontrolled diabetes, connective tissue disease.	RT regime: 50Gy in 25 fractions over 5wks or 50.4Gy in 28 fractions over 5.5wks. Regional nodal irradiation was not mandated.	grade 3 ARD (19 vs 33%, p=0.036). Moist desquamation was most common in chest wall location. No difference in time till grade 2 onset. But steroid arm had longer time till grade 3 onset (46 vs 36d, p<0.001). No differences in patient reported outcomes.
Ulff, 2017[52]	Randomized, single centre, double blind, clinical trial ***LOE: I***	Efficacy of preventive topical steroid treatment instituted from start of radiotherapy to prevent ARD	N=202 BC pts >18y w lumpectomy or mastectomy - 102 betamethasone cream 0.1% - 100 moisturizer (Essex) Exclusion: pregnancy, breast feeding, concomitant CTx, previous RT to area, active dermatitis, corticosteroid Tx All pts received adjuvant CTx.	Betamethasone was applied once daily and supplemented with once daily application of moisturizer. Moisturizer pts applied product twice daily. RT regimen: either 50Gy in 25 fractions, or 42.56Gy in 16 fractions (pts >50y + breast-preserving surgery w negative lymph nodes and tumor diameter <50mm)	Less RTOG grade 3 in hypo-fractionated vs conventional fractionation RT group (3% vs 26%). Less moist desquamation: 8% RTOG grade 3 in betamethasone arm (vs 30%), regardless of BMI, skin type or breast size. High compliance (>95%), no adverse effects, all pts had ECOG 0
Kianinia, 2021[53]	Randomized, double blind, clinical trial	If use of topical corticosteroids with different potencies or	N=105 BC pts ≥18y w lumpectomy	Products were used from RT start until wk 5.	Pts with standard fractionated RT had higher ARD incidence

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
	LOE: II	moisturizing cream could prevent ARD	- 31 hydrocortisone 1% cream - 38 mometasone 0.1% cream - 36 glycol-based moisturizer Mean age: 50y Postmenopausal: 77% Stage ≥ IIC: 42% Prior CTx: 87% Exclusion: skin eczema, psoriasis, connective tissue disorder, or previous RT to the breast, progressive disease	RT regimen: 50Gy in 25 fractions (89% of pts) or 40Gy in 15 fractions (11% of pts). Bolus used as needed. Grade 3 lesions were treated with medication	vs hypo fractionated (84% vs 50%). No difference in creams for maximum ARD grade (CTCAE v4), timing of maximum ARD, but a delay in grade 1 ARD onset was noticed in the mometasone arm.
Rezaei, 2021[54]	Randomized, single centre, double blind, clinical trial ***LOE: II***	Compare the effect of alpha and hydrocortisone 1% (H1%) ointments on prevention of ARD	N=86 BC pts w lumpectomy (13% of pts) or mastectomy (87%) - 43 hydrocortisone 1% cream - 43 natural henna ointment (Alpha) Mean age: 49y Mean d between surgery and RT: 581d Mean d between CTx and RT: 87d Exclusion: advanced disease, definite or modified mastectomy, other RT, concurrent CTx, prior RT, no diabetes, no skin conditions/disease, no vascular/connective tissue disorder, diabetes,	Products were applied twice daily for 5d and once daily for 2d from RT start till 1wk post-RT. RT regimen: 45-55Gy with mean over 25-30 fractions.	Hydrocortisone arm had more ARD in wk 4 (47 vs 12% RTOG grade ≤2, p=0.001), wk 5 (84 vs 40% grade ≤2, p<0.001), and wk 6 (52 vs 14% grade ≤2, p<0.001) compared to Alpha ointment. Hydrocortisone arm had more pain and burning in wk 4 (67 vs 19%, p<0.001) and wk 5 (79 vs 42%, p=0.001) compared to Alpha ointment. More itching with Alpha ointment in wk 4 (46 vs 12%, p<0.001).

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
			interfering medication, intolerance to products		
Sunku, 2021[55]	Randomized, single centre, clinical trial ***LOE: II***	Evaluate effect of topical steroid (Betamethasone Valerate 0.1%) cream on ARD in head and neck cancer.	N=106 (ITT) HNC pts w primary squamous cell sarcoma receiving curative RT or CTx-RT - 52 betamethasone 0.1% (Betnovate) - 54 negative control Age 45-60y: 51% Male: 87% Stage IV: 52% Comorbidities: 22% BMI 18-24: 68% Tobacco yes: 83% Betel nut yes: 49% Alcohol yes: 11% Exclusion: postoperative, cutaneous disease, allergy to products, uncontrolled co-morbidities, prior RT to HN region, nasopharynx, paranasal sinus or salivary gland tumours	Betamethasone was applied twice daily during RT. RT regimen: 60-70Gy in 30-35 fractions. 65% of pts received concurrent cisplatin or carboplatin	Later RTOG grade 1 onset in betamethasone arm (6 vs 17% in wk 2, p=0.157; 29 vs 50% in wk 3, p=0.028). By wk 7, betamethasone arm had higher grade 1 (17 vs 0%), and lower grade 2 (56 vs 67%). There was no difference in incidence of grade 3 and 4 ARD. No difference in time taken to heal.
Meghrajani, 2016[56]	Randomized, double blind, clinical trial ***LOE: II***	To determine if 1% hydrocortisone cream during RT can prevent occurrence of moist desquamation	N=50 BC pts (stage I-III) aged 19-80y w modified radical mastectomy and completed CTx - 23 hydrocortisone - 27 negative control (petrolatum-based) Exclusion: connective tissue disease, concurrent CTx, systemic corticosteroids	Products were applied by pts twice daily from RT start till 1wk post-RT. RT regime: 50Gy in 25 fractions. 10Gy boost in 5 fractions when needed (34% of pts). Moist desquamation was managed with silver sulfadiazine cream.	Larger irradiated field in placebo arm. Lower mean CTCAE v3 grade for steroid arm (0.713 vs. 0.874, p=0.024). Delay in onset of ARD in steroid arm (grade 1 in wk 2 at 4 vs 26%, p=0.038; grade 2 in wk 4 at 0 vs 30%, p=0.017) compared to placebo arm.

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
					Lower incidence of pruritus in steroid arm at wk 4 (~28 vs 48%, p=0.022) and wk 5 (~48 vs 55%, p=0.032).
Natural and Miscellaneous Agents					
Robijns, 2023[57]	Systematic review and meta-analysis ***LOE: I***	Review of natural and miscellaneous agents for ARD prevention	17 RCTs Aloe vera: 6 (833 pts, mostly BC) Oral enzymes: 2 (219 pts, cervical, HNC) Olive oil: 2 (156 pts, BC, nasopharyngeal) Calendula: 4 (725 pts, BC) Topical curcumin: 2 (175 pts, BC) Oral curcumin: 3 (609 pts, BC, HNC	Search until January 2023 Inclusion: one or more RCTs, prevention of ARD, natural or miscellaneous agents, compared to standard skin care, placebo or no intervention, reporting quantitative outcomes	**Aloe vera:** No impact on incidence and severity of RD (moist desquamation, erythema, pruritus) - Olsen, 2021: At cumulative RT dose of >27Gy, the addition of aloe vera to the soap regimen delayed the onset of RD symptoms vs soap-only arm (5 vs 3 weeks) - Tungkasamit, 2022: less moderate to severe erythema in wk4 and wk6 and moderate to severe moist desquamation in wk7. Less burning sensation in wk7. **Oral enzymes:** positive effect - reduced incidence moist desquamation (RR 0.52, 95% CI 0.31, 0.85) - reduction in grade 2+ (RR 0.42, 95% CI 0.30, 0.58) - reduction in maximum RTOG grading (SMD -1.02, 95% CI -1.41, -0.63) - Gujral, 2001: delay in time to onset, shorter duration **Olive oil**: reduction incidence of grade 2+ RD (RR 0.66, 95% CI 0.51) - Cui, 2015: reduction in grade 3+ RD and itch, pain and burning

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
					- Chitapanarux, 2019: lower severity and better HRQoL **Calendula:** no impact moist desquamation in BC pts (RR 0.93, 95% CI 0.69, 1.25) - Pommier, 2004: reduced the incidence of RD grade 2+ vs trolamine, less frequent RT interruptions and reduced RT-induced pain - no differences for Sharp, 2013; Fenton-Kerimian, 2015; Siddiquee, 2021 **Curcumin (oral)** - Ryan, 2013: reduced severity, less moist desquamation at RT-end - Ryan, 2017: no impact on severity **Curcumin (topical)** - Palatty, 2014; Rao, 2017: delay and reduction of RD - Ryan Wolf, 2020: no impact on severity
Ngan, 2025[58]	Randomized, blinded, clinical trial ***LOE: II***	Evaluate effectiveness of Calendula w Chinese herbal ointment	N=50 HNC pts aged 20-80y receiving definitive or adjuvant RT - 25 Calendula cream - 30 Bao Yuan Gao Exclusion: pre-existing sin conditions, allergy to products, use of glucocorticoids, immunosuppressants, amifostine, prior HN RT, pregnancy, lactation,	Products were applied three times daily from RT start till 2 weeks post-RT. RT regimen: external beam RT, 60-70Gy in 33-35 fractions.	No difference in incidence CTCAE v4 grade ≥2 ARD. Bao Yuan Gao arm had reduced erythema and improved skin moisture at wk3 (p=0.02).

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
			concurrent primary malignancies.		
Fatima, 2023[59]	Systematic review and meta-analysis ***LOE: II***	Use of topical non-steroidal agents in prevention of ARD	6 RCTs w 627 BC pts Trolamine: 2 Biafine: 2 Hyaluronic acid/hyaluronan: 2	Systematic search conducted in December 2022. Inclusion: >2 RCTs, non-steroidal agent, compared to SOC, placebo or no intervention Exclusion: insufficient information	Only Biafine prevented RTOG grade 4 and 3+ ARD (OR=0.07, 95% CI 0.01–0.63, p=0.02, and OR 0.11, 95% CI 0.03–0.41, p<0.01). trolamine alone and hyaluronic acid/hyaluronan did not significantly prevent the occurrence of RD
Robijns, 2023[60]	Randomized, single centre, clinical trial ***LOE: II***	Efficacy of anti-oxidative cream with *Calendula* in preventing and managing ARD in BC pts undergoing moderate hypo-fractionated RT	N=100 BC post lumpectomy or mastectomy, stratified by RT modality and planned target volume - 50 anti-oxidative cream with *Calendula* and hyaluronate - 50 hydroactive colloid gel (Flamigel) Median age: 58y Median BMI: 24.6 Current smoker: 56% Prior CTx: 43% Exclusion: previous irradiation to the breast or chest wall, immunotherapy, metastatic disease, pre-existing skin conditions in the irradiated area	Anti-oxidative Calendula cream and Hydroactive colloid gel were applied by pts twice daily during RT. RT regimen: 40.05-42.56Gy in 15-16 fractions. Inclusion of regional lymph nodes if needed. Boost of 13.3-13.35Gy in 5 fractions if indicated. Mepilex was used to treat moist desquamation. Topical corticosteroid and/or antihistaminic was prescribed for inflammatory skin reaction.	ARD severity was lower (p=0.003) in *Calendula*/hyaluronate arm compared to hydroactive colloid gel arm, with mod-RTOG grade 1 in 82% of pts (vs 50%), grade 2 in 16% of pts (vs 48%), and grade 3 in 0% of pts (vs 2%). No difference in severity of pruritus between study arms (p=0.066). With similar local or mild pruritus (CTCAE v5 grade 1) in *Calendula*/hyaluronate arm (56%vs 60% in hydroactive colloid arm; and higher widespread and intermittent pruritus (grade 2) in hydroactive colloid arm (12% vs 2%). Frequency and severity of xerosis was higher in hydroactive colloid arm at final RT vs *Calendula*/hyaluronate arm. No differences in pruritus, erythema, burning, and pain at final RT between arms. No difference in Skindex-29 between arms.

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
Ryan Wolf, 2018[61]	Randomized, multicentre, phase II, clinical trial ***LOE: I***	Assess the efficacy of oral curcumin to reduce RD severity	N=578 BC pts aged ≥18y receiving RT after lumpectomy or mastectomy - 283 oral curcumin capsules (Curcumin C3; 500mg) - 295 placebo capsule Mean age: 58y Mean BMI: 29.8 Prior chemo: 37 vs 45% Exclusion: Concurrent chemo, breast reconstruction, implants, expanders, prior chemo, hormone treatment, herceptin, prior RT to breast, anticoagulant therapy, EGFR therapy, radiosensitivity, collagen vascular disease, unhealed wounds or infections to area	Products were taken orally three times daily (6.0g daily dose) from RT start till 2wk post-RT. Conventional RT: 89% Hypofractionated RT: 11% Mean radiation dose (whole breast): 51Gy Mean sessions: 30	No difference between arms for RDS score, incidence of moist desquamation (9 vs 12%), and Skindex-29 score at RT end. No difference between arms for RDS score and incidence of moist desquamation (17 vs 15%) at 1-wk post RT.
Deantonio, 2025[62]	Randomized, double-blind, clinical trial ***LOE: II***	If prophylactic hyaluronic acid cream can prevent or delay ARD and mitigate severity	N=86 stage I-III BC pts w lumpectomy - 43 hyaluronic 0.2% acid (Ialuset) - 43 placebo cream Median age: 65y Median BMI: 66.5 Never tobacco: 55% Concurrent hormonal therapy: 62%	Creams were applied TID to whole breast, from 2wk prior to RT, to 2wk post-RT. RT: 50Gy in 25 fractions (w/wo additional 10-16Gy boost), or 40Gy in 15 fractions (no boost)	"Although the HA cream's positive benefit and risk profile was apparent, a significant difference between the HA-containing cream and the neutral comparator could not be demonstrated"
Heydari, 2025[63]	Randomized, double-blind, clinical trial	Efficacy of topically applied curcumin in preventing ARD	N=52 BC pts aged 18-65 receiving RT (any chemo	Products were used twice daily.	Curcumin arm had less pain (30 vs 72%), irritation (63 vs 84%) and redness under (96 vs

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
	LOE: II		needed to be terminated 2-wk prior to RT) - 27 curcumin 2% gel - 25 placebo gel Mean age: 50.6y Exclusion: pregnancy, concurrent chemo, bilateral BC, prior RT to breast, breast reconstruction, radiosensitivity, collagen vascular disorder, vasculitis, unhealed wounds, derma issues, no systemic diseases, no hypersensitivity to product	RT (3D-CRT): 50Gy + 10 Gy boost in 2Gy fractions	100%) or on skin (93 vs 100%) in first four weeks of RT. No difference in itching.
Meneses, 2025[64]	Randomized, double-blind, clinical trial ***LOE: II***	Compare liposomal gels with and without chamomile extract for prevention of ARD	N=100 BC pts aged ≥18 receiving RT - 50 liposomal gel w chamomile (chamomile glycolic extract 8.35%) - 50 liposomal gel Median age: 51-56y Skin type III: 53% Never smoked: 70% Exclusion: broken skin in RT area, history of hypersensitivity or allergy to products	Products were applied twice daily. RT: hypofractionated (83% of pts) or conventional fractionation (7% of pts). Median total dose: 44Gy in 2.6Gy fractions.	No difference between the arms for dry desquamation (6 vs 12%), erythema (72 vs 74%), moist desquamation (6 vs 8%), and global RD (72 vs 76%). No differences in median cumulative dose of radiation for first occurrence of dry desquamation (45 vs 44Gy), moist desquamation (46 vs 43Gy), global RD (33 vs 33Gy).
Meneses, 2024[65]	Randomized, double-blind, clinical trial ***LOE: II***	Compare liposomal gels with and without chamomile extract for prevention and management of ARD	N=53 HNC pts aged ≥18 receiving RT	Products were applied twice daily. RT: 60-70 Gy in 2Gy fractions	No difference between groups for dry desquamation (77 vs 89%), moist desquamation (35 vs 52%), erythema (92 vs

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
			- 26 liposomal gel w chamomile (chamomile glycolic extract 8.35%) - 27 liposomal gel Median age: 62y Skin type IV: 55% Oropharyngeal: 45% Laryngeal: 33% Exclusion: broken skin in RT area, history of hypersensitivity or allergy to products		100%), and global RD (96 vs 100%). Chamomile group required higher median cumulative dose of radiation for first occurrence of dry desquamation (28 vs 40Gy), erythema (34 vs 30Gy), and global RD (34 vs 30Gy).
Chang, 2024[66]	Systematic review & meta-analysis of RCTs ***LOE: II***	Effectiveness of glutamine for Tx of RD in cancer pts	5 RCTs, N=218 BC (2 RCTs) and HNC (3 RCTs) pts receiving RT or chemo RT Radiation dose approx. 50 to 70 Gy, and pts also received CT w cisplatin or carboplatin weekly or once q 3 wks	Oral glutamine (various doses) vs. placebo - 2 trials: 10 g, TID (total 30 g/day) - 1 trial: 15 g/day in three divided doses - 1 trial: 0.5 g/kg/day - 1 trial: Combination supplement (arginine 7 g, glutamine 7 g, HMB 1.2 g) twice daily 2 RCTs used RTOG grading and 3 used CTCAE	Any-grade RD: RR 0.90 (95% CI, 0.81–1.00; p=0.05; I^2=7%) Moderate to severe RD: RR 0.49 (95% CI, 0.32-0.76; p=0.001; I^2=52%) Subgroup: 20-30 g/day glutamine: RR 0.60 (95% CI, 0.41-0.87; I^2=0%)
Que, 2024[67]	Systematic review and meta-analysis ***LOE: II***	Clinical efficacy of herbal agents for RD in breast cancer	N=16 for qualitative review N=10 for meta-analysis (1465 pts) Calendula: 3 Aloe vera: 5 Silymarin: 2 Henna: 1 Nigella sativa: 1 Boswellia: 1 Adley bran: 1	Systematic search from 2000 till 2022 Inclusion: BC pts, herbal agents, randomized trials, placebo controlled	Calendula: OR 0.73 (95% CI 0.53-1.01; I^2 80%) Silymarin: RD -0.43 (95% CI -0.56, -0.30; I^2 0%) Aloe vera: MD -0.15 (95% CI -0.32, 0.01; I^2 0%)

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
Long, 2023[68]	Randomized, clinical trial ***LOE: II***	Understand prophylactic effect of Sanyrene cream for ARD in BC and HNC pts	N=99 BC and HNC pts aged ≥18y - 50 linoleic acid + linolenic acid cream (Sanyrene) - 49 vitamin E + hyaluronic acid cream Median age: 51y BC: 55% Concurrent CTx: 13% Exclusion: prior RT, palliative RT, lumpectomy (BC), anti-EGFR Tx (HNC), pre-existing grade >1 skin toxicity, cellulitis, autoimmune skin disease, wound, allergic to any product.	Both creams were applied twice daily until 2wk post-RT. RT for BC: 50Gy in 25 fractions w 5mm bolus RT for HNC: 50-55Gy in 25-27 fractions if post-resection, and ≥66 Gy in 2Gy fractions if radical (concurrent with cisplatin-based chemotherapy.	Hyaluronic acid arm had higher incidence of grade ≥2 ARD (67 vs 22%, p<0.001) and grade 3 ARD (20 vs 8%, p=0.076). Both groups had a similar median time to reach grade 1 (28 vs 29d), but hyaluronic acid had a shorter time to reach grade ≥2 (HR 4.3, p<0.001). Hyaluronic acid arm had higher mean Skindex-16 score at end of RT (25 vs.8.3), 2 weeks after RT (22.9 vs. 0.5) and 4 weeks after RT (4.2 vs.0).
Mirzaei Dahka, 2023[69]	Systematic review & meta-analysis of RCTs ***LOE: II***	To assess effect of curcumin on RD severity in pts w BC	BC pts receiving RT (n=882 across 4 RCTs)	Curcumin supplementation vs. placebo or standard care Curcumin doses ranged from 500 mg to 2 g per administration, given TID, either PO or as 500 mg topical gel applied TID Radiation Dermatitis Severity score	Curcumin supplementation significantly reduced radiation dermatitis severity score in intervention group vs. control group (weighted mean difference -0.50; 95% CI -0.72 to -0.27, p<0.001) Significant heterogeneity observed b/n studies (I^2=95.7%, p<0.001)
Vasconcelos, 2023[70]	Systematic review ***LOE: II***	Evaluate efficacy and safety of oral supplementation to prevent and manage ARD	Oral curcuminoids: 3 RCTs (BC) Glutamine: 3 RCTs (HNC, BC) Enzyme: 3 RCTs (cervix, HNC, pelvic)	Search conducted in May 2022 Inclusion: RCTs; cancer pts w RT; oral supplementation to manage, prevent, reduce severity of ARD; compared to none or any intervention	**Oral curcuminoids (BC pts)**: no impact moist desquamation, **Glutamine**: no impact grade 2+ **Enzyme**: no impact grade 2+ *Note that each analysis had high heterogeneity.* From the reported table:

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
				Exclusion: age <18y, animal studies, non-RCT, posters, guidelines, insufficient data, no full text	**Glutamine:** - Eda, 2016 (BC): Reduced severity, more grade 1, less grade 2+ ($p<0.05$) - Huang, 2019 (HNC): Increased severity, less grade 1, more grade 2+ ($p<0.10$) - Lopez-Vaquero 2017 (HNC): Reduced severity, more grade ≤1, less grade 2+ ($p<0.05$) **Enzyme:** - Dale, 2001 (cervix): Reduced severity, more grade 0, less grade 1+ ($p<0.01$) - Gujral, 2001 (HNC): Reduced severity, more grade 1, less grade 2+ ($p<0.01$) - Martin, 2002 (pelvic): no impact
Ryan Wolf, 2020[71]	Randomized, multicentre, phase II, clinical trial ***LOE: II***	Compare the prophylactic effectiveness of Curcumin gel, HPR Plus™, or Placebo for reducing radiation dermatitis and associated pain	N=169 BC pts - 59 curcumin gel (Psoria Gold) - 58 HPR Plus lotion - 52 placebo gel Mean age: 60y Prior chemo: 47% Hormone Tx: 22% Herceptin Tx: 10% Exclusion: concurrent chemo, pregnancy, bilateral BC, hypofractionated RT, prior RT to breast/chest, radiosensitivity, collagen vascular disorder,	Products were applied three times daily from RT-start will 1-wk post-RT. RT: 1.8 to 2.0 Gy fractions for 22 to 36 sessions (total radiation dose of 44 to 66 Gy) with or without boost	No difference between arms for RDS score, incidence of moist desquamation, Skin-Pain Inventory, Pain-Dairy scores.

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
			vasculitis, unhealed wounds or derma issues in Tx area		
Chitapanarux, 2019[72]	Randomized clinical trial ***LOE: II***	Effect of prophylactic use of one particular emulsion in preventing acute skin reactions in patients receiving adjuvant hypofractionation PMRT	N=62 BC pts aged ≥18y receiving hypofractionated PMRT w ECOG 0-1 - 31 SOC + olive oil & calcium hydroxide emulsion - 31 SOC Exclusion: inflammatory carcinoma, allergy to product, pre-existing loss of skin integrity in Tx area	Product was applied twice daily from RT start till 2-wk post-RT RT (3D-CRT): 2.65Gy per fraction, total dose 42.4Gy	Olive oil arm had reduced incidence of grade 1 dermatitis throughout the 2nd (16 vs 42%), 3rd (30 vs 90%) and 4th (71 vs 90%) week of RT, as well as at 6wk post-RT (58 vs 90%, p=0.002). Olive oil arm had also reduced Skindex-16 scores.
Ogita, 2019[73]	Randomized, open-label, single centre, clinical trial ***LOE: II***	Efficacy of heparinoid moisturizer	74 BC pts aged 30-65 w lumptectomy - 14 preventative heparinoid moisturizer (Hirudoid) - 30 management heparinoid moisturizer (after WBRT) - 32 negative control Median age: 45-50y Median BMI: 21-22 Never smoked: 78% CTx prior to RT: 85% Endocrine Tx prior to RT: 5% Exclusion: bilateral BC, previous RT to thorax, skin disease, collagen vascular disease, sensitivity to product	Moisturizer was applied twice daily from start RT until study completion. RT: WBRT 48-50Gy in 24-25 fractions w/wo supraclavical region and boost (10-18 Gy in 5-9 fractions).	Moisturizer use kept or returned sebum content at pre-RT levels. - baseline: 10 vs 11 vs 12 μg/cm^2 - 2 wk post-RT: 16 vs 1.5 vs 0.5 μg/cm^2 - 3-mo post RT: 12 vs 5 vs 0.4 μg/cm^2

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
Cui, 2015[74]	Randomized, clinical trial ***LOE: II***	Effect of olive oil on radiodermatitis	N=94 HNC (nasopharyngeal, stage III or IV) pts - 47 SOC + olive oil - 47 SOC Exclusion: prior RT, allergy to product	Product was applied three times daily from RT start till 2wk post-RT RT (IMRT): 70Gy in 2Gy fractions w concurrent weekly cisplatin (25-30 mg/m2) and docetaxel (25-30 mg/m2).	Olive oil arm had less severe dermatitis, with more grade 1-2 (94 vs 72%) and less grade 3 (6 vs 38%) ($p<0.01$), and lower VAS scores during RT and follow-up ($p<0.01$). Olive oil arm had also longer time till onset of ARD
Low-Level Laser Therapy (Photobiomodulation)					
Lin, 2025[75]	Systematic review & meta-analysis of RCTs and non-randomized ***LOE: II***	Examine effectiveness of PBMT for ARD in pts w cancer	8 studies (5 RCTs and 3 non-RCTs) involving BC or HNC pts Included clinical trials w pts w cancer undergoing RT, PBMT, placebo or usual skin care, and outcomes incl. different grades of ARD, RT interruption, pain, and quality of life in different subgroups Excluded if involved pts w chronic RD, metastatic disease, or preexisting skin condition or open wound, provided no grading of ARD, involved no comparison group in single-arm study	6 studies investigated efficacy of PBMT in prevention of ARD, and 2 studies in Tx of ARD	Compared w control group, PBMT group exhibited significantly lower ARD incidence at grades 2 and 3 (risk difference= - 0.36, 95% CI= - 0.53 to - 0.19, I^2=85%, $p<0.00001$) Subgroup analysis by cancer type: Grades 0/1 ARD: PBMT increased incidence in both BC (RD=0.31, 95% CI: 0.10–0.52, I^2=88%, p=0.004) and HNC (RD=0.52, 95% CI: 0.37–0.67, I^2=0%, $p<0.00001$). Grades 2/3 ARD: PBMT reduced incidence in both BC (RD=–0.31, 95% CI: –0.52 to –0.10, I^2=88%, p=0.004) and HNC (RD=–0.52, 95% CI: –0.67 to –0.36, I^2=0%, $p<0.00001$). PBMT vs control: Grades 0/1 ARD: Higher incidence w PBMT in both prevention (RD=0.35, 95% CI: 0.12–0.58, I^2=88%, p=0.003) and Tx

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
					subgroups (RD=0.39, 95% CI: 0.13–0.66, I^2=78%, p=0.004). Grades 2/3 ARD: Lower incidence w PBMT in both prevention (RD=–0.35, 95% CI: –0.58 to –0.12, I^2=88%, *p*=0.003) and Tx (RD=–0.39, 95% CI: –0.66 to –0.13, I^2=78%, p=0.004).
Gobbo, 2023[76]	Systematic review & meta-analysis of RCTs ***LOE: II***	Investigate efficacy of PBMT in RD prevention	4 studies evaluated BC pts and 1 evaluated HNC pts 5 studies included in qualitative analysis and 1 in quantitative	Studies met criteria for inclusion in review if (1) consisted of RCTs that examined efficacy of intervention in RD prevention, and (2) investigated PBMT vs placebo, SOC, or no intervention	Pts receiving PBMT experienced less severe RD than control groups after 40 Gy of RT (grade 3 toxicity: OR: 0.57, 95% CI 0.14–2.22, p=0.42) and at end of RT (grade 0+1 vs. 2+3 toxicity: OR: 0.28, 95% CI 0.15–0.53, p<0.0001) RT interruptions due to RD severity more frequent in control group (OR: 0.81, 95% CI 0.10–6.58, p=0.85)
Robijns, 2022[77]	RCT (LABRA) ***LOE: II***	Evaluate efficacy of PBMT in BC pts post-lumpectomy undergoing HF-WBRT for prevention and mgmt. of ARD	N=71 BC pts planned to undergo HF-WBRT ± chemo Excluded if prior irradiation to same breast, bilateral BC, metastatic disease, bolus use, pre-existing skin condition or wound in Tx area, or medical/ psychosocial issues interfering w participation or evaluation	Randomized 1:1 to: - Control group (n=32) - PBMT group (n=39) RT delivered using 6 MV photons on IMRT-capable linear accelerator. Whole breast ± nodal RT: 42.56 Gy in 16 fx; tumour bed boost: 13.3 Gy in 5 fx PBMT group received standard institutional skincare combined w PBMT (2×/wk.) using class IV MLS M6 laser (ASASrl) during complete RT course	At wk. 3 of RT, 1 pt presented grade 2 and 1 pt a grade3 skin reaction in control group, while in PBMT group, all pts still presented grade 1 ARD At final RT session 28% of pts presented w grade 2–3 ARD, while in PBMT group 10% presented grade 2 and no grade 3 ARD PBMT reduced incidence of severe ARD by 18%. Difference not significant (p=0.053)

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
				Patients in control group received standard skincare combined w placebo Tx (2x/week) Pts' skin reactions evaluated weekly during RT Tx using modified RTOG criteria	
Zhang, 2021[78]	RCT ***LOE: II***	Observe effect of red-light phototherapy on RD caused by RT in pts w HN cancer	N=60 pts with HN cancer (52, nasopharyngeal; 4 laryngeal) Inclusion: pathologically diagnosed, received chemo and RT for 1st time Exclusion: communication disorders	Randomly divided (1:1) into: - Red-light phototherapy - Control Control: Routine nursing care during RT, incl. health edu, skin self-care, application of skin protective agents, and wound cleaning w 0.9% normal saline using cotton balls to remove necrotic tissue, followed by drying w sterile gauze Experimental: Same wound cleaning protocol as control group + red-light phototherapy. Pts received red-light PT while in supine position w radiation field skin fully exposed Tx delivered BID for 10 mins., w lamp 15-20 cm from wound surface, maintaining wound temp of 30°C Pain and conditions of pts' skin assessed daily, and skin pain and dermatitis grades compared	RD severity: Experimental group had significantly less severe RD than control group. In experimental group, 60% had grade 0/1 RD and 40% had grade 2; no pts had grade 3. In contrast, control group had 63% w grade 2 RD, 30% w grade 3, and only 7% w grade 0/1 ($p<0.05$) Skin pain: Experimental group reported significantly less skin pain than control group at wks. 2, 3, and 4 ($p<0.05$). No significant differences observed at wks. 5 and 6. W/n both groups, pain increased over time, w significant linear trends (experimental group $\chi^2=65.083$; control group χ^2 27.091; $p<0.05$)
Robijns, 2018[79]	RCT (TRANSDERMIS)	Evaluate effectiveness of PBMT in prevention of ARD in BC pts undergoing RT	N=120 BC pts who underwent lumpectomy, and scheduled to undergo RT regimen of 25 fx of 2	Pts stratified based on PTV to small (<450 cc), medium (450–800 cc), large breasts (>800 cc)	At RT dose of 40 Gy, no significant difference b/n groups in distribution of RTOG grades.

Author, Year	Study Type, *LOE*	Objective	Patients	Intervention	Results
	LOE: II		Gy to whole breast and 8 fx (2 Gy/fraction) to tumour region (total RT dose 66 Gy) Excluded: pts w previous irradiation to same breast, mastectomy, metastatic disease, concomitant chemo, and infection of to-be-irradiated zone	Followed by random allocation (1:1): - PBMT - Placebo from day 1 of RT (2×/wk.) Topical skin care Tx: Hydroactive colloid gel applied to irradiated area 3x daily, starting on first day of RT For pts who developed painful skin reactions and/or moist desquamation, a foam, absorbent, self-adhesive silicone dressing applied to affected area PBMT: 14 sessions (2x/wk.) using class IV MLS M6 laser combining 2 synchronized laser diodes in infrared range (808-905 nm) w fixed energy density (4 J/cm^2) Skin reactions scored based on RTOG and RISRAS criteria. Pts completed Skindex-16 questionnaire to evaluate QOL. All measurements collected at first day, at RT dose of 40 Gy, and at end of RT (total dose 66 Gy)	At end of RT severity of skin reactions significantly differed b/n groups (p=0.004), w larger percentage of pts experiencing RTOG ≥grade 2 (e.g. moist desquamation) in placebo group (30% vs 6.7%, for placebo and laser group, resp.) Objective RISRAS score confirmed results Skindex-16 and RISRAS subjective score demonstrated pts' QOL significantly better in PBMT vs control group

AE, adverse event; APBI, accelerated partial breast irradiation; ARD, acute radiation dermatitis; AUC, area under the curve; Ax, assessment; BC, breast cancer; BCS, breast conserving surgery; BID, twice a day; CI, confidence interval; CTCAE, Common Terminology Criteria of Adverse Events; CTx, chemotherapy; DIBH, deep inspiration breath hold; EBRT, external beam radiation therapy; Gy, Gray; HF, hypofractionated; HNC, head and neck cancer; HR, hazard ratio; RTOG, Radiation Therapy Oncology Group; RTT, radiation therapist; SCC, squamous cell carcinoma; SMD, standardized mean difference; SOC, standard of care; SGR; IBC, inflammatory breast cancer; IMRT, intensity modulated radiation therapy; ITT, intention-to-treat; KPS, Karnofsky performance status; LN, lymph node; LOE, level of evidence; NCI-CTCAE, National Cancer Institute-Common Terminology Criteria for Adverse Events; OLCs, Online Corrections; OR, odds ratio; PBMT, photobiomodulation therapy; PMRT, post-mastectomy radiation therapy; PRO, patient-reported outcomes; PRN, as needed; PTV, planning target volume; QOL, quality of life; RCT, randomized controlled trials; RD, radiation dermatitis; RDS, Radiation Dermatitis Severity Scoring Scale; RISRAS, Radiation-Induced Skin Reaction Assessment Scale; RO, radiation oncologist; ROI, region of interest; RR, risk reduction; RT, radiation therapy T; surface-guided radiation therapy; Tx, treatment; VAS, visual analog scale; VMAT, volumetric modulated arc therapy; WBRT, whole-breast RT.

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Appendix A: Search Strategy

Database	Date	Search Terms	Results
Medline ***Note:*** Rows 1-16 are replica of MASCC 2023 systematic review	5/22/2024 (update 9/23/2025)	1. exp Neoplasms/rt [Radiotherapy]	203395
		2. exp Neoplasms/	4120612
		3. (cancer* or neoplasm* or carcinoma*).mp.	4442742
		4. exp Radiotherapy/	217922
		5. (radiotherap* or radiation therap*).mp.	443727
		6. 1 or ((2 or 3) and (4 or 5))	391809
		7. exp Radiodermatitis/	2723
		8. (radiation dermatitis or radiodermatitis or dermatitis).mp.	115093
		9. ((skin or dermatol*) adj3 (toxic* or react* or burn* or rash* or damage* or injur* or irritat*)).mp.	55451
		10. or/7-9	164562
		11. th.xs.	8641221
		12. pc.fs.	1545775
		13. ((manag* or treat* or alleviat* or avoid* or lessen* or prevent* or prophyla* or control*) adj5 (skin or dermatol* or dermatitis or radiodermatitis)).mp.	81145
		14. or/11-13	8681271
		15. 6 and 10 and 14	4465
		16. limit 15 to english language	3989
		17. limit 16 to ed=20230120-20250522	399
		18. limit 17 to (english language and humans and (clinical trial, all or comparative study or controlled clinical trial or guideline or meta analysis or multicenter study or network meta-analysis or observational study or practice guideline or randomized controlled trial or "systematic review"))	157
		19. remove duplicates from 18	156
Oncology-Based Health Organizations and Guideline Developers	5/22/2024	Search terms: “radiation dermatitis”, “dermatitis”, “radiodermatitis”	ASTRO (0) BCC (1) CCM (1) CCO (0) EANM (0) ESTRO (1) ISNCC (1) NCCN (0) NICE (0) ScoR (1)

ASTRO, American Society for Radiation Oncology; BCC, BC Cancer; CCM, CancerCare Manitoba; CCO, Cancer Care Ontario; EANM, European Association of Nuclear Medicine; ESTRO, European Society for Radiotherapy and Oncology; ISNCC, International Society for Nurses in Cancer Care; NCCN, National Comprehensive Cancer Network; NICE, National Institute for Health and Care Excellence; SCoR, Society and College of Radiographers

Appendix B: Levels of Evidence

- Level I – evidence from at least one large randomized controlled trial (RCT) of good methodological quality with low potential for bias or meta-analyses of RCTs without heterogeneity
- Level II – small RCTs, large RCTs with potential bias, meta-analyses including such trials, or RCTs with heterogeneity
- Level III – prospective cohort studies
- Level IV – retrospective cohort studies or case-control studies
- Level V – studies without a control group, case reports, or expert opinions