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Patients' view of the differences in topical creams for radiation dermatitis prevention. A pilot study of cosmetic properties

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ABSTRACT

Aim: To investigate the feasibility of including patients' reports on the cosmetic properties of topical formulations for acute radiation dermatitis (ARD).

Background: No topical agent tested for acute radiation dermatitis (ARD) has proven to be better than any other, all achieving similar objective outcomes. No clear guidelines have therefore been established in clinics. Because the vehicle for such creams has shown to be an important factor in patient adherence to treatments in other dermatological diseases, patients' opinions are evaluated.

Material and methods: Seventy breast cancer patients referred for postoperative radiotherapy after conservative surgery were enrolled. Patients were assigned to use one of the 7 topical agents that are most-commonly used in the prevention of ARD. Patients' reports were assessed using continuous visual analogue scales (VAS), objective signs and symptoms produced by ARD, and were rated using the RTOG and RISRAS scales.

Results: The creams tested differed in their cosmetic properties significantly ($p = 0.044$). The performance of the agent, their absorption and any residue left over were also significantly different ($p = 0.022$, 0.014 and 0.02, respectively).

Conclusions: Topical agents for preventive ARD are reported by patients to show different cosmetic properties. Cosmetic properties are important when choosing topical agents for ARD prevention. Recommending those with better cosmetic profiles would improve patient adherence to treatments.

Abbreviations: ARD, acute radiation dermatitis; CTCAE, Common Terminology Criteria for Adverse Events; QoL, quality of life; RISRAS, Radiation-Induced Skin Reaction Assessment Scale; RT, radiation therapy; RTOG, Radiation Therapy Oncology Group; STAT, Skin toxicity assessment tool.

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1. Background

Breast cancer is the most common malignancy and the leading cause of cancer death in females worldwide.[1] Radiation therapy (RT) following conservative surgery has proved to be very effective for cancer control while avoiding mutilation.[2,3] Nevertheless, acute radiation dermatitis (ARD), which is the most common acute adverse side effect of the radiotherapy (RT) treatments, appears in virtually every breast cancer patient receiving RT.[4,5] Signs of ARD on the skin and symptoms include oedema, erythema, skin dryness, itching, pain, and, in the most severe cases, moist desquamation, bullae, ulcers or skin necrosis, which can cause patient discomfort[5] and discontinuation of the RT.[4,6] ARD has been linked to patient and radiation treatment factors, such as patient position, breast size, or body habitus, as well as the use of intensity modulated radiotherapy, dose to irradiated volume and concomitant treatments. Several scales have been used to evaluate skin toxicity.[5] The Radiation Therapy Oncology Group (RTOG) and the Common Terminology Criteria for Adverse Events (CTCAE) scales are currently the most used in practice and research. However, the RTOG scale and CTCAE scales have drawbacks.[7] To resolve these issues, the Radiation-Induced Skin Reaction Assessment Scale (RISRAS) was developed by Noble-Adams,[8,9] which links a patient-rated symptom scale with a health-care professional assessment scale. This scale also evaluates the area of the skin affected and its degree.

On one hand, some RT techniques have proven to decrease skin toxicity.[10] By the other, several agents have been tested for ARD prevention in order to reduce its severity, among them steroids, aloe vera, honey, sucralfate, hyaluronic acid or aqueous creams as well as film dressing. While RT techniques have demonstrated to decrease skin toxicity,[11,12] there is insufficient evidence to support and recommend any topical agent,[13–15] apart from steroids, that will reduce inflammation.[16] As a result, no clinical protocols have been adopted[17] and the use of steroids is not free of criticism. Several commercial moisturising creams for ARD prophylaxis have been widely adopted in RT practice worldwide, despite available data. Studies on ARD prophylaxis have often focused on the severity of the dermatitis as an objective endpoint, measured either by subjective caregiver scores, such as the RTOG or the CTCAE, or by objective assessment techniques like ultrasonography, spectrophotometry, or corneometry.[18–20] The patient's point of view is not reported in a large number of studies, some of which analyse the quality of life (QoL) related to the skin events using the RISRAS questionnaire, the Skindex-16 or the Skin toxicity assessment tool (STAT).[21]

Due to the lack of clear guidelines for ARD prevention and similar outcomes reached by the majority of commercial topical agents, we believe that patients' QoL regarding prophylactic treatments and patients' point of view on the performance of topical agent for ARD would improve the guidelines for skin interventions. Therefore, we have carried out a pilot study to explore the differences in the performance of topical treatment for ARD prophylaxis evaluated from the patients' point of view.

2. Materials and methods

This single-centre, prospective, pilot study included female breast cancer patients who had been referred for adjuvant postoperative RT after a breast conservative surgery. Women aged >18 years receiving breast cancer radiotherapy after a breast conserving surgery for pTis, pT1-2, pN0-1, M0 were recruited from February 2013 to May 2013 and assigned to one of seven groups. Each group used one of the creams commercially available in Spain for ARD prophylaxis. Exclusion criteria were Karnofsky Index <70%, previous ipsilateral breast RT, immediate or delayed breast reconstruction, inability to consent or to adhere to the directions or skin care, concomitant chemotherapy, any skin disease within the treatment area, and any skin allergy to usual cream ingredients and hypofractionated RT. With a limited sample size of 70 patients, between 9 and 11 patients were allocated to each brand.[22]

Irradiation technique has been previously described.[23] In brief, patients were irradiated in the supine position laying on a breast board. High-energy photons were delivered at a standard fractionation (2 Gy/session, 5 sessions/week). A dose of 50 Gy was delivered to the whole breast with opposing tangential fields using a field-in-field technique followed by a 10–16 Gy tumour bed boost when required. Treatment of lymph nodes was allowed as well as the use of bolus or breast cups.

Patients were instructed to use one of the 7 tested creams from the start of radiotherapy until 2 weeks after the completion of RT (COSMECLINIK Sativa Soft®, COSMECLINIK Sativa M-Tex®, AVENE Trixera®, EUCERIN Intensive urea 10%®, ISDIN Ureadin Rx Rd Locion®, DIAFARM Hialderm®, and ROTTAPHARM MADAUS Radiocrem®). Creams were kindly provided by 6 manufacturers with no involvement at any stage of the trial. Patients had to apply a homogeneous and thin layer of the assigned cream over the entire irradiated area twice a day according to the following schedule: for patients irradiated in the morning, cream was applied immediately after the RT treatment and 8 h later; for patients irradiated in the evening, the cream was applied 8 h before the radiation treatment and immediately before. Razors, deodorants and cologne were forbidden on the breast or ipsilateral axilla, as well as other creams or topical skin care products unless instructed otherwise by the attending radiation oncologist or nurse. Patients were advised to wear loose-fitting clothes and bras in cotton fabric and not to wear under-wired bras. A radiation nurse recorded the Fitzpatrick Skin Phototype Scale at baseline, as well as any other oncology treatments and demographic variables, and gave the patients their instructions for the study. During the course of irradiation, patients were seen by a clinician (MD or RN) once per week. The study outcomes were recorded at each appointment.

2.1. *Study outcomes*

Signs evaluated by a trained nurse and the patient reported symptoms associated with ARD in the irradiated area were recorded at baseline and weekly during irradiation. The RTOG scale[24] and the RISRAS modified Patient Symptom Scale were used.[25] The RTOG scale has not been formally validated but

Table 1 – Patient characteristics by cream brand.

	Overall group	Brand							*p*-value
		a	b	c	d	e	f	g	
n	67	11	8	9	9	11	9	10	
Age	58. (16)	66. (7)	50. (13)	55. (17)	51. (5)	65. (17)	60. (12)	62. (22)	0.036
BMI	27.1 (7.5)	27.7 (6.4)	24.1 (4.9)	33.7 (9)	27.6 (9.3)	26.7 (3.2)	26.1 (7.2)	27.4 (6.7)	0.529
Breast volume (cm^3)	912.8 (594)	1036.5 (825.4)	782.7 (588.5)	1216.9 (339.2)	994 (645.1)	805.7 (675.6)	779.1 (419.4)	927.2 (239)	0.274
Boost volume (cm^3)	54.9 (56.5)	56.4 (102.3)	54.9 (59.4)	88.3 (26.9)	36.9 (28.47)	39.8 (23.1)	52.8 (25)	77.3 (88.1)	0.130
Breast side									
Left	49.25%	45.45%	50%	22.22%	66.67%	18.18%	66.67%	80%	0.044
Right	50.75%	54.55%	50%	77.78%	33.33%	81.82%	33.33%	20%	
Chemotherapy									
Yes	40.3%	27.27%	62.5%	55.56%	33.33%	27.27%	66.67%	20%	0.2
No	59.7%	72.73%	37.5%	44.44%	66.67%	72.73%	33.33%	80%	
Hormonotherapy									
No	7.46%	9.09%	0%	0%	0%	0%	22.2%	20%	0.228
Yes	92.54%	90.91%	100%	100%	100%	100%	77.78%	80%	
Trastuzumab									
Yes	7.46%	0%	0%	22.22%	11.11%	0%	11.11%	10%	0.458
No	92.54%	100%	100%	77.78%	88.89%	100%	88.89%	90%	
Bolus									
Yes	10.45%	18.18%	25%	0%	0%	18.18%	0%	10%	0.383

Data are shown as median (iqr) or percentages. BMI: body mass index.
Cream brand: (a) COSMECLINIK Sativa Soft; (b) COSMECLINIK Sativa M-Tex; (c) AVENE Trixera; (d) EUCERIN Intensive urea; (e) ISDIN Ureadin Rx Rd; (f) DIAFARM Hialderm; (g) ROTTAPHARM MADAUS Radiocrem.

it has been widely used in clinic and trials since its publication in 1995. That scale scores ARD from 0, no signs, to 4, the highest toxicity (ulceration, haemorrhage or necrosis). Our department has used it for more than 15 years. The RISRAS scale evaluates skin reactions observed by the clinician and level of discomfort reported by the patient. Adding the scores gives the overall combined RISRAS score.[8] Patient cosmetic satisfaction was recorded by a developed questionnaire. Six items were evaluated with an 11-point Likert scale: ease of cream application, speed of skin symptom relief, permanence of the cream, freshness, scent, speed of cream absorption, residue from cream, and subjective overall assessment of the brand, which was the combined RISRAS score. Values ranged from 0, the worst cosmetic performance, to 10, the best possible performance. Treatment interruptions or the need for additional skin care due to skin reactions determined by the treating physician were documented. The need for additional skin care was rated according to the extent of the skin reaction that induced it, 0: none; 1: <25% radiation field; 2: 25%–50% radiation field; 3: 50%–75% radiation field; 4: >75% radiation field.

2.2. *Statistical methods*

Data are presented as median and interquantile range. Differences were compared using the Wilcoxon rank-sum test, Mann–Whitney *U* test, Kruskal–Wallis test, and χ^2 test. A two-sided *p*-value <0.05 was considered statistically significant. The study was approved by the institutional ethics committee and patients gave their informed consent before inclusion in the study.

3. Results

Seventy patients agreed to participate in the study. There were 3 withdrawals, from groups c, d and e, due to non-compliance with the study procedures; data for 67 patients was therefore included in the analysis. Patients and treatment characteristics are listed in Table 1. A total dose of 50 Gy was administered to 8.82% of the patients and 66 Gy was administered to the remaining 91.18% of the patients. All groups received a median dose of 66 Gy. Only age was significantly different among groups ($p = 0.036$). Notably, differences among groups on breast and boost volumes were not statistically significant. No statistically significant differences in skin phototype were observed ($p = 0.549$).

A statistically significant difference was found in the patient subjective overall cosmetic properties of the creams ($p = 0.044$). Table 2 and Fig. 1 show the cosmetic properties data. Differences in the permanence of the cream, speed of cream absorption, and the cream residue left also attained statistical significance.

No statistical significant differences in the RISRAS score were observed ($p = 0.915$). RISRAS scores are depicted in Fig. 2. None of the patients reporting symptom domains showed a statistically significant difference (pain, $p = 0.25$; itchiness, $p = 0.157$; burning, $p = 0.567$; daily activity, $p = 0.732$), nor did the signs evaluated by the carer (erythema, $p = 0.85$; dry desquamation, $p = 0.423$; moist desquamation, $p = 0.475$; necrosis, $p = 0.488$). Five patients developed necrosis, 2 cases among patients using brand a, and 1 case among patients using brands b, c, and e. Only 1 patient had to suspend her RT course, for 2 weeks, due to a very symptomatic moist desquamation after 56 Gy. No differences in needing additional skin care with corticoids or topical creams for wound healing were observed according to brand ($p = 0.364$ and $p = 0.458$, respectively) (Fig. 3).

4. Discussion

It is assumed that about 60% of patients with cancer will undergo at least one RT course at some stage during their disease[26,27] and postoperative breast RT avoids mutilation but also maintains good cosmetic results on the irradiated breast.[28] So, in a context of comparable efficacy, patient-reported outcomes are of paramount interest. This study has demonstrated that cosmetic properties of topical agents for ARD prevention differ, as rated by breast cancer patients, even though they have a similar efficacy in an objective ARD prevention.

Studies on ARD prevention have focused on the evaluation of the degree of ARD, for which there has been a myriad of scales,[5] or on the objective evaluation of physiological skin properties.[18–20] However, little attention has been paid to the cosmetic performance of the topical agents used for ARD. Few reports have addressed this issue in the context of the development of topical formulations[30] and of patient self-assessment

Table 2 – Cosmetic properties evaluated by the patients according to the cream brand.

	a	b	c	d	e	f	g	*p*-Value
Application	8. (3)	9.5 (1)	10. (3)	9.(1)	10.(2)	10. (2)	9 (1.75)	0.689
Relief	8. (3)	7.5 (3.25)	9. (3)	8. (2)	9. (2)	9 .(2)	7.5 (1.75)	0.417
Permanence	8. (2)	6.5 (2.5)	8. (1)	9. (2)	9. (3)	9. (2)	7 (1.5)	0.022
Freshness	8 (2.5)	8 (1.25)	8. (3)	8. (5)	8. (2)	8 .(5)	7 (3.5)	0.922
Smell	8 (2.5)	8 (3.25	9. (3)	8 .(5)	8 .(4)	8 .(5)	7. (3)	0.633
Absorption	8 (2.5)	9.5 (2)	9. (1)	8. (4)	7. (1)	10. (1)	7 (2.5)	0.014
Residue	8 (2.5)	7. (10)	7. (4)	8. (2)	8 (4.5)	10. (0)	5. (5)	0.020
Overall	8 (2.5)	7.5 (1.25)	9. (2)	8. (3)	8. (2)	10. (1)	7.5 (1.75)	0.044

Data are shown as median (iqr).
Cream brand: (a) COSMECLINIK Sativa Soft; (b) COSMECLINIK Sativa M-Tex; (c) AVENE Trixera; (d) EUCERIN Intensive urea; (e) ISDIN Ureadin Rx Rd; (f) DIAFARM Hialderm; (g) ROTTAPHARM MADAUS Radiocrem.

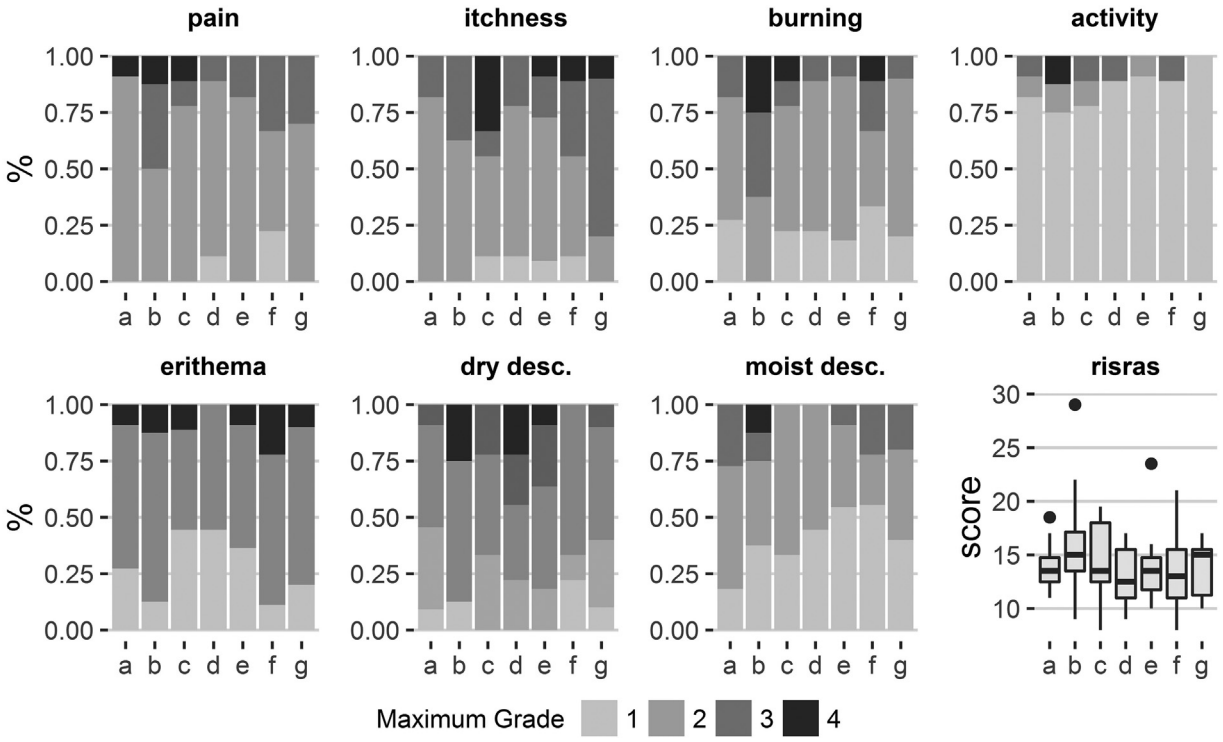

Fig. 1 – Plots of the cosmetic properties evaluated by the patients according to brand. Cream brand: (a) COSMECLINIK Sativa Soft; (b) COSMECLINIK Sativa M-Tex; (c) AVENE Trixera; (d) EUCERIN Intensive urea; (e) ISDIN Ureadin Rx Rd; (f) DIAFARM Hialderm; (g) ROTTAPHARM MADAUS Radiocrem.

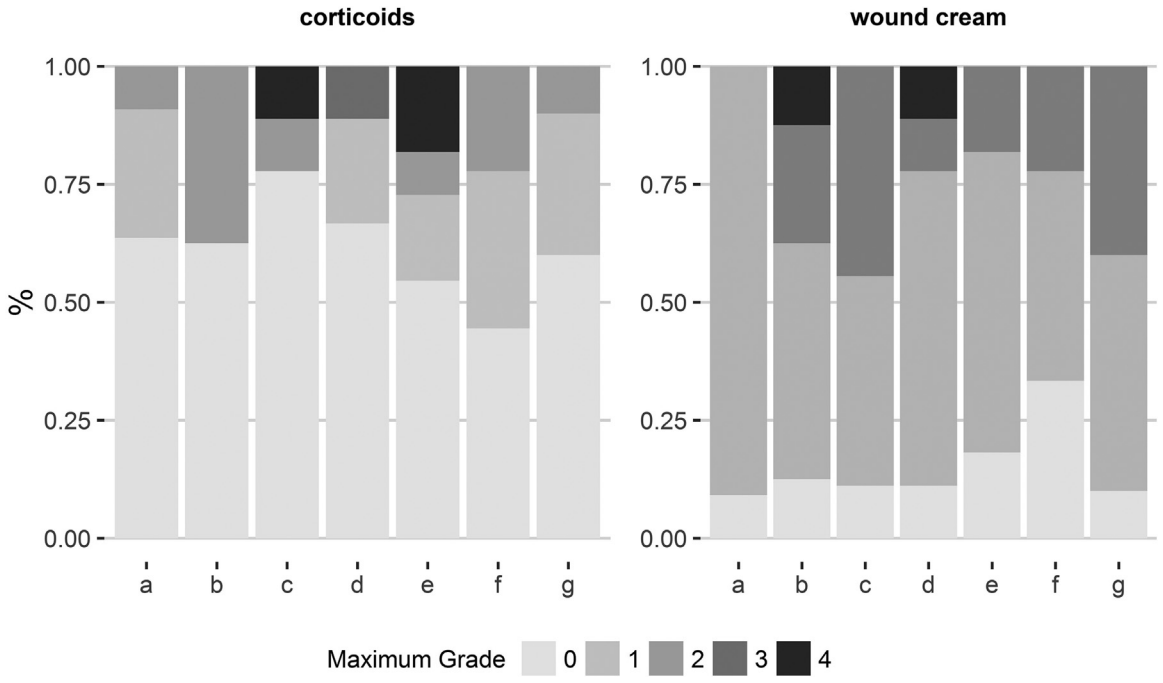

Fig. 2 – Maximum scores of the dimensions evaluated by RISRAS according to the cream brand and box plots showing the overall RISRAS score. (Dry desc.: dry desquamation: Moist desc.: moist desquamation; RISRAS: Radiation-Induced Skin Reaction Assessment Scale). Cream brand: (a) COSMECLINIK Sativa Soft; (b) COSMECLINIK Sativa M-Tex; (c) AVENE Trixera; (d) EUCERIN Intensive urea; (e) ISDIN Ureadin Rx Rd; (f) DIAFARM Hialderm; (g) ROTTAPHARM MADAUS Radiocrem.

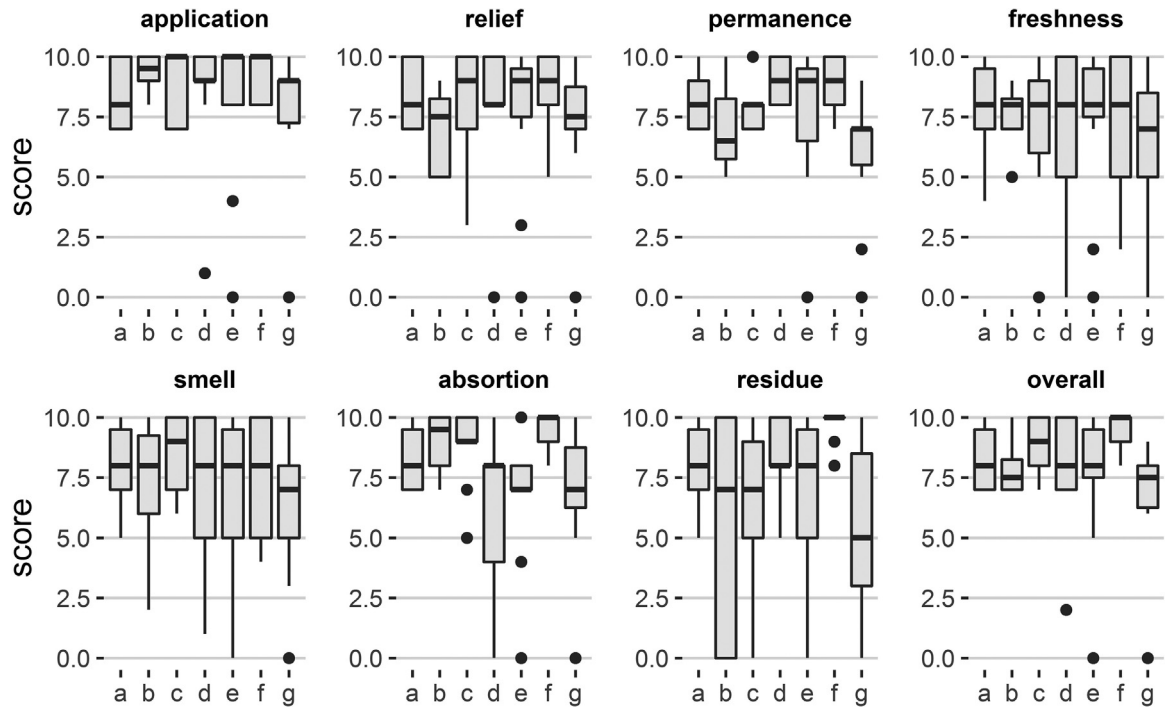

Fig. 3 – Steroids and wound creams for radiodermitis treatment. Graphs show the maximum grade scores related to the use of steroids and wound creams for radiodermitis treatment according to brand. Their use was rated by taking into account the extent of the foliculitis and radiodermitis: 0: none; 1: <25% radiation field; 2: 25%–50% radiation field; 3: 50%–75% radiation field; 4: >75% radiation field. Cream brand: (a) COSMECLINIK Sativa Soft; (b) COSMECLINIK Sativa M-Tex; (c) AVENE Trixera; (d) EUCERIN Intensive urea; (e) ISDIN Ureadin Rx Rd; (f) DIAFARM Hialderm; (g) ROTTAPHARM MADAUS Radiocrem.

of the overall study.[31] Patients preferred a cream-based product that was easy to apply rather than a thick ointment or a gel product that made the skin feel tight after it dried. Recent studies on patient-reported measures have, to some extent, begun to include analyses of the cosmetic properties of the topical products.[32,33] Nevertheless, this is not a standard practice yet. The randomised trial reported by Sharp et al. compared topical preventive Calendula officinalis to aqueous. However, they were unable to demonstrate any significant differences in severe ARD development or differences between patient reported symptoms.[32] The study did find patient-reported differences in the application and absorption of the products but no differences in smell, relief of redness, tightness, tenderness, pain or burning were observed. The preventive use of Mepitel Film showed a reduction in moist desquamation for breast cancer patients.[33] No clear cosmetic evaluation was described, but the authors reported that 92% of the patients preferred it over the cream. A similar overview is found in the ARD treatment scenario.[25]

The significant differences in the cosmetic properties of the products for ARD have to be linked to patient adherence to treatment. In other areas of dermatology, such as the use of sunscreen by outdoor workers[34] or topical products for acne, atopic dermatitis and plaque psoriasis,[35] it has been recognised that usability and acceptance of the topical formulations is an important issue for patient adherence to treatments due to its relationship with absorption and tolerability.[36] It is important not to forget that the main part of any topical formulation is the vehicle; therefore, its cosmetic properties are essential for patient preference. In the ARD setting, the ease of application on painful and irritated skin is valuable. On top of that, vehicles can influence the development of moist desquamation. A recent study found a moist desquamation with the use of a hydroactive colloid gel compared with dexpanthenol. This was ascribed, to some degree, to differences in vehicles, as they compared a gel vs. an oil-in-water emulsion.[37] In our study, cosmetic properties proved important to the breast cancer patients' preferences. Patients rated the f cream (DIAFARM Hialderm) as the best option due to the ease of application, speed of absorption, and residue from cream (Table 2) in spite of the lack of objective differences.

While our study points to the value of a cosmetic properties analysis in ARD, the data needs to be considered in the light of the study limitations, the main one being the small sample size for each of the topical products tested. This will limit the generalizations of the findings together with the fact that different countries may have different products commercially available. This is further magnified by the single-site study design, but counterbalanced by a lack of generalised protocols for ARD, which are local.[17,38] Despite not recording all the factors involved in ARD, such as smoking,[39] all the patients included in the study underwent the same RT protocol with the most recognised variables in ARD being recorded, in particular anthropometric parameters. Notably, there were no statistically significant differences in breast size and body habitus across the groups. These parameters are some of the variables that have been more frequently related to skin

toxicity.[40] Concern could also arise from the ad-hoc cosmetic questionnaire, which was not previously validated.

We would like to stress that this is a pilot study addressing the feasibility of establishing recommendations and guidelines for clinics and for further research. Generalisation of the approach implies addressing in advance its reliability and validity. In spite of the limitations, we believe that the use of patient-reported symptoms needs to be highlighted in ARD trials because there has never been a parallel ARD assessment by carers and patients.[16] We believe that our results will prompt radiation departments to evaluate cosmetic properties of their own products, which, in turn, will improve clinical practice and patient well-being.

5. Conclusion

There is a reported lack of consistency in ARD skin care, which varies greatly and depends on local practices that can often be outdated or wrong[14,17,38] and no superiority of one topical agent over the others for ARD prevention has been demonstrated. So, individual evaluation of the cosmetic properties of the products used in each department is paramount if we are to recommend those that are more user-friendly and accepted by our patient population. Our results have shown different patient-reported cosmetic properties among the different products for ARD prevention. Results suggest the need to introduce this evaluation in the clinical setting in order to recommend the best accepted products by patients taking into account that they produce similar objective reductions of ARD. Development of reliable, consistent and standardised tools analysing cosmetic properties have to be built previously to be included as a goal on trials. Additionally, our results stress the importance of including analyses of cosmetic properties in future ARD trials.

Conflict of interest

None declared.

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REFERENCES

1. Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. *CA Cancer J Clin* 2015;**65**:87–108.
2. Offersen BV, Boersma LJ, Kirkove C, et al. ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer. *Radiother Oncol* 2015;**114**:3–10.
3. Montero A, Sanz X, Hernanz R, et al. Accelerated hypofractionated breast radiotherapy: FAQs (frequently asked questions) and facts. *Breast* 2014;**23**:299–309.
4. Mikeljevic JS, Haward R, Johnston C, et al. Trends in postoperative radiotherapy delay and the effect on survival in breast cancer patients treated with conservation surgery. *Br J Cancer* 2004;**90**:1343–8.
5. Noble-Adams R. Radiation-induced reactions. 1: An examination of the phenomenon. *Br J Nurs* 1999;**8**:1134–40.
6. Arenas M, Sabater S, Gascon M, et al. Quality assurance in radiotherapy: analysis of the causes of not starting or early radiotherapy withdrawal. *Radiat Oncol* 2014;**9**:260.
7. Porock D, Kristjanson L, Nikoletti S, et al. Predicting the severity of radiation skin reactions in women with breast cancer. *Oncol Nurs Forum* 1998;**25**:1019–29.
8. Noble-Adams R. Radiation-induced skin reactions. 2: Development of a measurement tool. *Br J Nurs* 1999;**8**:1208–11.
9. Noble-Adams R. Radiation-induced skin reactions. 3: Evaluating the RISRAS. *Br J Nurs* 1999;**8**:1305–12.
10. Di Franco R, Sammarco E, Calvanese MG, et al. Preventing the acute skin side effects in patients treated with radiotherapy for breast cancer: the use of corneometry in order to evaluate the protective effect of moisturizing creams. *Radiat Oncol* 2013;**8**:57.
11. Donovan E, Bleakley N, Denholm E, et al. Randomised trial of standard 2D radiotherapy (RT) versus intensity modulated radiotherapy (IMRT) in patients prescribed breast radiotherapy. *Radiother Oncol* 2007;**82**:254–64.
12. Pignol JP, Olivotto I, Rakovitch E, et al. A multicenter randomized trial of breast intensity-modulated radiation therapy to reduce acute radiation dermatitis. *J Clin Oncol* 2008;**26**:2085–92.
13. Wong RK, Bensadoun RJ, Boers-Doets CB, et al. Clinical practice guidelines for the prevention and treatment of acute and late radiation reactions from the MASCC Skin Toxicity Study Group. *Supp Care Cancer* 2013;**21**:2933–48.
14. Kumar S, Juresic E, Barton M, et al. Management of skin toxicity during radiation therapy: a review of the evidence. *J Med Imaging Radiat Oncol* 2010;**54**:264–79.
15. Zhang Y, Zhang S, Shao X:. Topical agent therapy for prevention and treatment of radiodermatitis: a meta-analysis. *Supp Care Cancer* 2013;**21**:1025–31.
16. Ulff E, Maroti M, Serup J, et al. A potent steroid cream is superior to emollients in reducing acute radiation dermatitis in breast cancer patients treated with adjuvant radiotherapy. A randomised study of betamethasone versus two moisturizing creams. *Radiother Oncol* 2013;**108**:287–92.
17. O'Donovan A, Coleman M, Harris R, et al. Prophylaxis and management of acute radiation-induced skin toxicity: a survey of practice across Europe and the USA. *Eur J Cancer Care (Engl)* 2015;**24**:425–35.
18. Yoshida EJ, Chen H, Torres MA, et al. Spectrophotometer and ultrasound evaluation of late toxicity following breast-cancer radiotherapy. *Med Phys* 2011;**38**:5747–55.
19. Liu T, Zhou J, Yoshida EJ, et al. Quantitative ultrasonic evaluation of radiation-induced late tissue toxicity: pilot study of breast cancer radiotherapy. *Int J Radiat Oncol Biol Phys* 2010;**78**:811–20.

20. Tanaka E, Yamazaki H, Yoshida K, et al. Objective and longitudinal assessment of dermatitis after postoperative accelerated partial breast irradiation using high-dose-rate interstitial brachytherapy in patients with breast cancer treated with breast conserving therapy: reduction of moisture deterioration by APBI. *Int J Radiat Oncol Biol Phys* 2011;**81**:1098–104.
21. Neben-Wittich MA, Atherton PJ, Schwartz DJ, et al. Comparison of provider-assessed and patient-reported outcome measures of acute skin toxicity during a Phase III trial of mometasone cream versus placebo during breast radiotherapy: the North Central Cancer Treatment Group (N06C4). *Int J Radiat Oncol Biol Phys* 2011;**81**:397–402.
22. Julious SA:. Sample size of 12 per group rule of thumb for a pilot study. *Pharma Stat* 2005;**4**:287–91.
23. Arenas M, Hernandez V, Farrus B, et al. Do breast cups improve breast cancer dosimetry? A comparative study for patients with large or pendulous breasts. *Acta Oncol* 2014;**53**:795–801.
24. Cox JD, Stetz J, Pajak TF:. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). *Int J Radiat Oncol Biol Phys* 1995;**31**:1341–6.
25. MacBride SK, Wells ME, Hornsby C, et al. A case study to evaluate a new soft silicone dressing. Mepilex Lite, for patients with radiation skin reactions. *Cancer Nurs* 2008;**31**:E8–14.
26. Delaney G, Jacob S, Featherstone C, et al. The role of radiotherapy in cancer treatment: estimating optimal utilization from a review of evidence-based clinical guidelines. *Cancer* 2005;**104**:1129–37.
27. Arenas M, Sabater S, Biete A, et al. Radiation oncology teaching programmes as part of the undergraduate degree in medicine in Spanish universities: the need for an update of the contents and structure. *J Cancer Educ* 2018;**33**:352–8.
28. Arenas M, Sabater S, Hernandez V, et al. Cosmetic outcome of breast conservative treatment for early stage breast cancer. *Clin Transl Oncol* 2006;**8**:334–8.
30. Primavera G, Carrera M, Berardesca E, et al. A double-blind, vehicle-controlled clinical study to evaluate the efficacy of MAS065D (XClair), a hyaluronic acid-based formulation, in the management of radiation-induced dermatitis. *Cutan Ocul Toxicol* 2006;**25**:165–71.
31. Gosselin TK, Schneider SM, Plambeck MA, et al. A prospective randomized, placebo-controlled skin care study in women diagnosed with breast cancer undergoing radiation therapy. *Oncol Nurs Forum* 2010;**37**:619–26.
32. Sharp L, Finnila K, Johansson H, et al. No differences between Calendula cream and aqueous cream in the prevention of acute radiation skin reactions – results from a randomised blinded trial. *Eur J Oncol Nurs* 2013;**17**:429–35.
33. Herst PM, Bennett NC, Sutherland AE, et al. Prophylactic use of Mepitel Film prevents radiation-induced moist desquamation in an intra-patient randomised controlled clinical trial of 78 breast cancer patients. *Radiother Oncol* 2014;**110**:137–43.
34. Bauer A, Hault K, Puschel A, et al. Acceptance and usability of different sunscreen formulations among outdoor workers: a randomized, single-blind, cross-over study. *Acta Derm Venereol* 2014;**94**:152–6.
35. Eastman WJ, Malahias S, Delconte J, et al. Assessing attributes of topical vehicles for the treatment of acne, atopic dermatitis, and plaque psoriasis. *Cutis* 2014;**94**:46–53.
36. Piacquadio D, Kligman A:. The critical role of the vehicle to therapeutic efficacy and patient compliance. *J Am Acad Dermatol* 1998;**39**:S67–73.
37. Censabella S, Claes S, Orlandini M, et al. Retrospective study of radiotherapy-induced skin reactions in breast cancer patients: reduced incidence of moist desquamation with a hydroactive colloid gel versus dexpanthenol. *Eur J Oncol Nurs* 2014;**18**:499–504.
38. Harris R, Probst H, Beardmore C, et al. Radiotherapy skin care: a survey of practice in the UK. *Radiography* 2012;**18**:21–7.
39. Sharp L, Johansson H, Hatschek T, et al. Smoking as an independent risk factor for severe skin reactions due to adjuvant radiotherapy for breast cancer. *Breast* 2013;**22**:634–8.
40. Mery B, Vallard A, Trone JC, et al. Correlation between anthropometric parameters and acute skin toxicity in breast cancer radiotherapy patients: a pilot assessment study. *Br J Radiol* 2015;**88**, 20150414.