

## Comment on "Acute radiation dermatitis in breast cancer: topical therapy with vitamin E acetate in lipophilic gel base" by S Martella *et al* 2010 *ecancer* 190

**Sheila MacBride**

School of Nursing and Midwifery, Fife Campus, Forth Avenue, Kirkcaldy, KY2 5YS

---

Published: 13/01/2011

Received: 06/12/2010

*ecancer* 2011, 5:206 DOI: 10.3332/ecancer.2011.206

**Copyright:** © the authors; licensee ecancermedicalscience. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Competing Interests:** The authors have declared that no competing interests exist.

## Introduction

Good evidence from well-designed clinical trials remains elusive in informing radiation skin care. Morbidity from radiation skin reactions is at best distressing and at worst a dose limiting factor, and these researchers are to be commended for their interest in advancing knowledge of the topic.

## Local protocols

Local policy in this treatment centre appears to be application of steroid cream, and the authors acknowledge that best current evidence supports that albeit from a sparse research base [1,2]. Local policies in treatment centres continue to be determined by habit and preference rather than research-based evidence yet the research base continues to struggle to provide answers [3–5]. The approach taken by the group formulating the Best Practice Statement in Scotland utilized levels of evidence where experienced nurses, doctors and pharmacists offer skin care guidelines based on available evidence supported by knowledgeable, skilled and experienced clinical expertise. This level of evidence is considered to be weak and health care professionals must take responsibility for progressing the research questions.

## Interventions

Several interventions appear to have been introduced in this case study, i.e. vitamin E; tocopheral; lipophilic gel; escharectomy; antibiotics. No dressing is indicated but unless these were in-patients it is likely that some kind of wound covering was applied. The study by Macmillan *et al* [29] demonstrated that even a simple dry dressing with non-adherent properties appears to significantly impact negatively upon healing time for Radiation Therapy Oncology Group (RTOG) grade 3 skin reactions. There is a physiological basis for the choice of lotion applied, and again this is challenging given the dubiety around the cellular processes involved in radiation skin damage and repair. The physiology of radiation skin reactions is a source of debate, but there is now common belief that whether endothelial vasodilation is involved or not, the reaction is mediated by the inflammatory response Denham *et al* [27,28], Simonen [33], Tannock [34]).

The lotion appears to have been used prophylactically since first day of treatment. Use of lotions and/or dressings for prophylaxis has not been tested widely [Maiche 1994, 6–8]. Further data are, therefore, welcome.

The number of variables to be included in clinical trials for radiation skin care is ever increasing [9,10,7,11,30,12–14]. Quality of evidence grading criteria necessarily suggest the grade of current evidence is therefore 'low', as emergent research 'is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate' [15].

The use of antibiotics in this study is also interesting. While antibiotics are routinely prescribed in managing toxicities associated with radical doses of radiotherapy, the paper by Hill *et al* [16] regarding six cases where staphylococcus aureas was implicated in severe dermatitis introduced the idea that pathogens may be a more common variable in skin reactions than previously thought and early intervention may improve morbidity. Vavassis *et al* (2008) similarly report the use of silver leaf dressing for treatment of radiation dermatitis in patients receiving radiotherapy to the head and neck. While these researchers could demonstrate no reduction in RTOG grade of skin toxicity, positive outcomes suggested were diminished severity within the grade, accelerated healing and improved pain control. While this is a small study it should also be noted that the standard for comparison in this study was silver sulfadiazine (Flamazine) cream. Vuong *et al* [17] used silver leaf dressing preventively for its antimicrobial properties in a small series of consecutive patients undergoing radiotherapy to the perineum and demonstrated lower dermatitis scores for the intervention group when compared with historical controls.

## Primary and secondary outcomes

One of the principle hurdles in comparing published studies of radiation skin care lies in the dubiety over primary and secondary outcomes measured, and this study is no exception. A review of published studies reveals a variety of primary and secondary outcomes used to assess benefit. Most focus upon prevention or minimization of skin reaction, i.e. time to RTOG reaction grade 1, 2 or 3; time to healing from grade 3 reaction commencing, percentage of skin in field affected; while others focus on supportive care aspects of the experience, i.e. sleep, pain and itch. Mak *et al* [18] also measured the aesthetic appeal

of the dressing to patients as a secondary outcome and report preference due to aesthetic appearance when objective numeric assessment measures reveal no benefit. Safety and tolerance (of wound dressing) have also emerged as outcome measures [19]. These researchers also measure time to resumption of treatment, which is an interesting choice of outcome. These researchers state that after 25 days there was re-epithelialization and after 40 days the site was 'excellent' and it is difficult to estimate what was being assessed at 40 days.

## Measures

A further hurdle in comparative potential within skin care research is the range of measurement tools utilized in published studies. While the Radiation Therapy Oncology Group (RTOG) [20] remains the 'gold-standard' in terms of validity and reliability and indeed international acceptability, many authors have attempted to address its limitations [21,22,31,23,7]. These authors have tested the STAT [21], and once more data to support the ongoing development and reliability of the measure is useful. The STAT combines patient and treatment variables, observer scoring and patient reported symptoms and was tested for both research use and for utility in everyday clinical practice. The work postdates Lopez *et al*'s [24] comparison of three different scoring systems, and the accumulated data on the measure might be usefully tested in this way. Lopez *et al* [24] found the RTOG to be superior in its accuracy, but do comment that 'reporting the outcome of radiotherapy is not

satisfactory without a description of the treatment related side effects'. Wengstrom *et al* [25] tested the RTOG with reflectance spectrophotometry and digital camera. The camera measured erythema and melanin levels in the skin by measuring reflected light, and the resulting score is termed the erythema or melanin index. While the RTOG demonstrated excellent interrater reliability, the digital camera proved to be a valid and reliable objective measure. Wengstrom *et al* [25] concludes that the images taken by a digital camera can easily be arranged and take little (clinical) time. They also offer the potential to collect images in a database for scrutiny by different persons at a different time both in clinical and in research settings, across time and geography. Wengstrom *et al* [25] further state the potential of the digital camera in developing predictive capability for individual skin response to radiation but once more state the importance of collecting data on the subjective experiences of skin reactions alongside the objective photographic evidence.

## Conclusion and recommendations

Any advance in the knowledge of how best to support patients with radiation skin reactions has to be welcomed. The principle weakness in the case report is the lack of transferability. Case study research carries little weight although some authors would disagree [26]. Single report case studies almost certainly offer only a limited perspective, and it is hoped that these researchers progress this to a pilot study.

## References

1. Bostrom A, Lindman H and Swartling C *et al* (2001) Potent corticosteroid cream (mometasone furoate) significantly reduces acute radiation dermatitis: results from a double-blind, randomized study *Radiotherapy and Oncology* 59 257–265 [PMID: 11369066](#) [doi:10.1016/S0167-8140\(01\)00327-9](#)
2. Schmutz M, Wimmer MA and Hofer S *et al* (2002) Topical corticosteroid therapy for acute radiation dermatitis: a prospective, randomised, double-blind study *British Journal of Dermatology* 146 983–991 [PMID: 12072066](#) [doi:10.1046/j.1365-2133.2002.04751.x](#)
3. Nystedt KE, Hill JE and Mitchell AM *et al* (2005) The standardisation of radiation skin care in British Columbia: a collaborative approach *Oncology Nursing Forum* 32 (6) 1199–205 [PMID: 16270115](#) [doi:10.1188/05.ONF.1199-1205](#)
4. Bolderston A, Lloyd NS and Wong RK *et al* (2006) The Prevention and management of acute skin reactions related to radiation therapy: a systematic review and practice guideline *Supportive Care in Cancer* 14 (8) 802–17 [PMID: 16758176](#) [doi:10.1007/s00520-006-0063-4](#)
5. McQuestion M (2006) Evidence-based skin care management in radiation therapy *Seminars in Oncology Nursing* 22 (3) 163–73 [PMID: 16893745](#) [doi:10.1016/j.soncn.2006.04.004](#)
6. Szumacher E, Wighton A and Franssen E *et al* (2001) Phase II study assessing the effectiveness of Biafine Cream as a prophylactic agent for radiation-induced acute skin toxicity to the breast in women undergoing radiotherapy with concomitant CMF chemotherapy *Int J Rad Biol Physics* 51 (1) 81–86
7. Wells M, Macmillan M and Raab G *et al* (2004) Does aqueous or sucralfate cream affect the severity of erythematous radiation skin reactions? A randomised controlled trial *Radiotherapy and Oncology* 73 153–162 [PMID: 15542162](#) [doi:10.1016/j.radonc.2004.07.032](#)
8. Porock D and Kristjanson L (1999) Skin reactions during radiotherapy for skin cancer: the use and impact of topical agents and dressings *European Journal of cancer care* 8 143–153 [PMID: 10763645](#) [doi:10.1046/j.1365-2354.1999.00153.x](#)
9. Porock D, Kristjanson L and Nikoletti S *et al* (1998) Predicting the severity of radiation skin reactions in women with breast cancer *Oncology Nursing Forum* 25 (6) 1019–29 [PMID: 9679261](#)
10. Porock D, Nikoletti S and Cameron F (2004) The relationship between factors that impair wound healing and the severity of acute radiation skin and mucosal toxicities in head and neck cancer *Cancer Nursing* 27 (1) 71–78 [PMID: 15108954](#)
11. Baumann M, Holscher T and Begg AC (2003) Towards genetic prediction of radiation responses: ESTRO's GENEPI project *Radiotherapy and Oncology* 69 121–125 [PMID: 14643948](#) [doi:10.1016/j.radonc.2003.08.006](#)
12. Ambrosone CB, Tian C and Ahn J *et al* (2006) Genetic predictors of acute toxicities related to radiation therapy following lumpectomy for breast cancer: a case series study *Breast Cancer Research* 8 R40 [PMID: 16848913](#) [doi:10.1186/bcr1526](#)
13. Holscher T, Bentzen SM and Baumann M (2006) Influence of connective tissue diseases on the expression of radiation side effects: A systematic review *Radiotherapy and Oncology* 78 123–130 [PMID: 16445999](#) [doi:10.1016/j.radonc.2005.12.013](#)
14. Li-Ching L, Que J and Li-Kuei L *et al* (2006) Zinc supplementation to improve mucositis and dermatitis in patients after radiotherapy for head and neck cancers: A double-blind, randomized study *Int J Radiation Oncol Biol Phys* 65 (3) 745–750
15. Scottish Intercollegiate Guidelines Network (2010) <http://www.sign.ac.uk/pdf/gradeao.pdf> (accessed 6<sup>th</sup> October 2010)
16. Hill A, Hanson M, Bogle MA and Duvic M (2004) Severe radiation dermatitis is related to staphylococcus aureus *American Journal of Clinical Oncology* 27 (4) 361–363 [PMID: 15289728](#) [doi:10.1097/01.COC.0000071418.12121.C2](#)
17. Vuong T, Franco E and Lehnert S (2004) Silver leaf nylon dressing to prevent radiation dermatitis in patients undergoing chemotherapy and external beam radiotherapy to the perineum *Int J Radiation Oncol Biol Physics* 59 (3) 809–814 [doi:10.1016/j.ijrobp.2003.11.031](#)
18. Mak SS, Molassiotis A and Wan WM *et al* (2000) The effects of hydrocolloid dressing and gentian violet on radiation-induced moist desquamation wound healing *Cancer Nursing* 23 220–229 [PMID: 10851773](#) [doi:10.1097/00002820-200006000-00010](#)
19. MacBride SK, Wells ME and Hornsby C *et al* (2008) A case study to evaluate a new soft silicone dressing, Mepilex Lite, for patients with radiation skin reactions *Cancer Nursing* 31 (1) E8–14 [PMID: 18176123](#) [doi:10.1097/01.NCC.0000305680.06143.39](#)
20. Radiation Therapy Oncology Group (2010) Acute Radiation Morbidity Scoring Criteria <http://www.rtog.org/members/toxicity/acute.html> (accessed 3rd September 2010)
21. Berthelet E, Truong PT and Musso K *et al* (2004) Preliminary reliability and validity testing of a new Skin

- Toxicity Assessment Tool (STAT) in breast cancer patients undergoing radiotherapy *American Journal of Clinical Oncology* 27 (6) 626–31 PMID: 15577442 doi:10.1097/O1.coc.0000138965.97476.0f
22. Munro AJ and Potter S (1996) A qualitative approach to the distress caused by symptoms in patients treated with radical radiotherapy *British Journal of Cancer* 74 640–647 PMID: 8761383
  23. Nystrom J, Geladi P and Lindhol-Stethson B *et al* (2004) Objective measurements of radiotherapy-induced erythema *Skin Research and Technology* 10 242–250 PMID: 15536655 doi:10.1111/j.1600-0846.2004.00078.x
  24. Lopez E, Nunez A and Guerrero R *et al* (2002) Breast cancer acute radiotherapy morbidity evaluated by different scoring systems *Breast Cancer Research and Treatment* 73 (2) 127 PMID: 12088115 doi:10.1023/A:1015296607061
  25. Wengstrom Y, Forsberg C and Naslund I *et al* (2004) Quantitative assessment of skin erythema due to radiotherapy-evaluation of different measurements *Radiotherapy and Oncology* 72 191–197 PMID: 15376368 doi:10.1016/j.radonc.2004.04.011
  26. Flyvberg B (2006) Five misunderstandings about case-study research *Qualitative Inquiry* 12 (2) 219–245 doi:10.1177/1077800405284363
  27. Denham JW, Hamilton CS and Simpson SA *et al* (1995) factors influencing the degree of erythematous skin reactions in humans *Radiotherapy and Oncology* 36 107–120 PMID: 7501808 doi:10.1016/0167-8140(95)01599-C
  28. Denham JW, Hamilton CS and O'Brien M *et al* (1997) Letter to the editor: Erythema: Goodbye LQ *Radiotherapy and Oncology* 44 191–193 doi:10.1016/S0167-8140(97)00086-8
  29. Macmillan M, Wells M and MacBride S *et al* (2007) Randomized comparison of dry dressings versus hydrogel in management of radiation-induced moist desquamation *Int J Rad Oncology Biol Physics* 68 (3) 864–872 doi:10.1016/j.ijrobp.2006.12.049
  30. Maiche A, Isokangas O and Grohn P (1994) Skin protection by 'Sucralfate' cream during electron beam therapy *Acta Oncologica* 33 (2) 201–203 PMID: 8204277 doi:10.3109/02841869409098406
  31. Noble-Adams R (1999) Radiation-induced skin reactions3: evaluating the RISRAS *British Journal of Nursing* 8 (19) 1305–1312 PMID: 10887808
  32. NHS Quality Improvement Scotland (2004) *Best Practice Statement: Skincare of Patients receiving Radiotherapy* NHS Quality Improvement Scotland
  33. Simonen P, Hamilton C and Ferguson S *et al* (1998) Do inflammatory processes contribute to radiation-induced erythema observed in the skin of humans *Radiotherapy and Oncology* 46 (1) 73–82 PMID: 9488130 doi:10.1016/S0167-8140(97)00115-1
  34. Tannock IF Ed. (2005) *The Basic Science of Oncology* London McGraw Hill 4th Ed
  35. Twardella D, Popanda O and Helmbold I *et al* (2003) Personal characteristics, therapy modalities and individual repair capacity as predictors of acute skin toxicity in an unselected cohort of breast cancer patients receiving radiotherapy *Radiotherapy & Oncology* 69 145–153 doi:10.1016/S0167-8140(03)00166-X