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Phase III randomised trial

Prophylactic use of Mepitel Film prevents radiation-induced moist desquamation in an intra-patient randomised controlled clinical trial of 78 breast cancer patients

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ABSTRACT

Purpose: Safetac-based soft silicone dressings used in a management setting decrease the severity of radiation-induced acute skin reactions but do not affect moist desquamation rates. Here we investigate the prophylactic use of another Safetac product, Mepitel Film, on moist desquamation rates.

Material and methods: A total of 80 breast cancer patients receiving radiation therapy were recruited between October 2012 and April 2013; 78 participants contributed data for analysis. Lateral and medial halves of the skin areas to be irradiated were randomised to Mepitel Film or aqueous cream; skin dose was measured using thermoluminescent dosimeters; skin reaction severity was assessed using RISRAS and RTOG scales.

Results: Overall skin reaction severity was reduced by 92% ($p < 0.0001$) in favour of Mepitel Film (RISRAS). All patients developed some form of reaction in cream-treated skin which progressed to moist desquamation in 26% of patients (RTOG grades I: 28%; IIA: 46%; IIB: 18%; III: 8%). Only 44% of patients had a skin reaction under the Film, which did not progress to moist desquamation in any of the patients (RTOG grades I: 36%; IIA: 8%).

Conclusions: Mepitel Film completely prevented moist desquamation and reduced skin reaction severity by 92% when used prophylactically in our cohort.

Moist desquamation is a clinically significant acute side effect of external beam radiation therapy particularly in breast and head & neck patients. Many studies have investigated the efficacy of topical agents on the prevention of acute radiation-induced skin reactions. A systematic review published in 2006 by the Cancer Care Ontario Supportive Care Guidelines Group concluded there was insufficient evidence to support the use of any topical agent [1]. A systematic review published in 2010 reported that topical corticosteroids and hyaluronic acid might be of some benefit [2], which was validated for corticosteroids [3], but the evidence was inconsistent for hyaluronic acid [4,5] and trolamine [6–10]. No benefit was shown for aloe vera gel [11], sucralfate cream, aqueous cream [12] or calendula cream [13]. Two barrier-forming products have been assessed to date: Cavilon and Mepilex Lite dressings. The spray-on Cavilon No-Sting barrier film significantly reduced skin toxicity, incidence of moist desquamation and pruritus in an intra-individual comparison of 61 post-mastectomy patients [14]. However, these findings were not validated in a large ($n = 333$) double-blinded multicentre follow-up RCT. This may have been due to differences in formulations and a lack of build-up of a protective layer of cream on the skin [15].

We have previously investigated the use of Safetac technology-based soft silicone dressings on the severity of acute radiation-induced skin reactions in breast cancer patients [16,17]. Like Cavilon, Safetac-based dressings provide mechanical protection from further trauma to the sub-lethally damaged basal skin layer, allowing this tissue to repair the daily damage caused by radiation therapy. Two management trials using an intra-patient controlled approach showed a significant 30–40% decrease in skin reaction severity in 24 breast cancer patients ($p < 0.001$) [16] and 74 post-mastectomy breast cancer patients ($p < 0.001$) [17]. However Mepilex Lite dressings did not affect moist desquamation rates when used to manage existing skin reactions [17]. The current trial aims to determine whether Safetac-based Mepitel Film will reduce moist desquamation rates when used prophylactically.

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Methodology

This randomised, intra-patient controlled, single centre clinical trial was approved by the University of Otago Ethics Committee in October 2012 (12/239); and is registered with the Australia New Zealand Clinical Trials Registry (ACTRN12612000949886). All participants gave written informed consent before the start of radiation therapy treatment. Based on our previous trial [17], we assumed a moist desquamation rate in our cohort of 50%. The sample size was chosen to provide a power of 80% and a p value of 0.05 to detect a reduction in moist desquamation rate from 50% (based on our previous multicentre study [17] to 25% with a drop-out rate of 10–20%.

Trial outcomes

We ascertained the effect of Mepitel Film on (1) skin reaction severity and (2) incidence of moist desquamation.

Participants

All women and men receiving radiation therapy for breast cancer at Dunedin Hospital were screened for recruitment between October 2012 and April 2013. Specific exclusion criteria were: previous radiation therapy to the ipsilateral chest wall, metastatic disease, breast reconstruction, impaired mobility and a Karnofski performance status score of less than 70. After completion of treatment, participants had to be able to return to the department weekly for follow-up assessments for up to 4 weeks.

Randomisation

At the start of radiation treatment, the breast or chest wall was divided into medial and lateral halves for randomisation to either Mepitel Film or aqueous cream. Randomisation was based on pre-prepared computer-generated randomisation charts and conducted (via randomisation fax) by the Principal Investigator (PMH), who had no patient involvement.

Blinding

Because the Film was in situ for days at a time; neither the research radiation therapist nor the patients were blinded to which skin area had been randomised to Film and which to cream.

Radiation therapy treatment

Patients were treated supine with their arms supported above their head. Radiation therapy to the breast or the chest wall included conventional and hypo-fractionation regimens using 6 MV or a combination of 6 and 18 MV tangential photon beams. Segmented fields were used to reduce areas of high dose. A small number of mastectomy patients had daily bolus (5 mm) applied to the chest wall (or scar). Supraclavicular and axillary lymph nodes were treated with anterior (or near anterior) and posterior photon beams when required (see Table 1 for differences in treatment regimens).

Application of film and aqueous cream

Patients doubled as their own controls to eliminate confounding patient- and treatment-related factors. Mepitel Film was applied at the start of radiation treatment by the research radiation therapist on either the entire lateral or the entire medial part of the breast or chest wall to be irradiated whilst aqueous cream was applied twice daily to the control area by the patients. It was important that the Film was not stretched during application; neither was it to overlap other pieces of Film. Gentle digital pressure was used to ease the Film neatly into all skin folds. Patients were supine for Film application not only to maximise patient comfort but also to replicate treatment position. This ensured that breast shape was as consistent as possible. If small areas of Film curled, these were carefully removed with scissors leaving the rest of the dressing in place. Film was replaced by the RRT when it curled up too much (every 1 or 2 weeks). Mepitel Film was generously donated by Molnlycke Healthcare LTD; aqueous cream was obtained from AFT pharmaceuticals (Auckland, NZ) and contained 9 g emulsifying wax, 10 g white soft paraffin, 6 g, liquid paraffin, 1 g phenoxyethanol in boiled and cooled purified water to 100 g.

Table 1
Patient demographics.

	Breast (%)	Chest wall (%)	Combined (%)
Total enrolled	46	34	80
Total completed	44 (56.4)	34 (43.6)	78 (100)
Randomisation (medial)	22 (50.0)	16 (47.1)	38 (48.7)
Sex (F)	44 (100)	32 (94.1)	76 (97.4)
Average age (y) (range)	61.2 (30–88)	58.4 (34–93)	59.9 (30–94)
BMI (Ave ± SD)	27.1 ± 6.3	27.1 ± 5.6	27.1 ± 6.0
Ethnicity			
NZ European	39 (88.6)	33 (97.1)	72 (92.3)
NZ Maori	1 (2.3)	0 (0)	1 (1.3)
Pacific Islander	2 (4.5)	0 (0)	2 (2.6)
Asian	0 (0)	1 (2.9)	1 (1.3)
Hispanic	1 (2.3)	0 (0)	1 (1.3)
Turk	1 (2.3)	0 (0)	1 (1.3)
Disease stage			
DCIS	6 (13.6)	0 (0)	6 (7.7)
I	22 (50.0)	2 (5.9)	24 (30.8)
II	13 (29.5)	18 (52.9)	31 (39.7)
III	1 (2.3)	12 (35.3)	13 (16.7)
Recurrence	0 (0)	1 (2.9)	1 (1.3)
Missing data	2 (4.5)	1 (2.9)	3 (3.8)
Radiation therapy			
50 Gy/25[#]	18 (40.9)	19 (55.9)	37 (47.4)
40 Gy/15[#]	26 (59.1)	10 (29.4)	36 (46.2)
45 Gy/20[#]	0 (0)	1 (2.9)	1 (1.3)
46 Gy/20[#]	0 (0)	2 (5.9)	2 (2.6)
50.4 Gy/25[#]	0 (0)	1 (2.9)	1 (1.3)
54 Gy/27[#]	0 (0)	1 (2.9)	1 (1.3)
Boost			
None	23 (52.3)	27 (79.4)	50 (64.1)
10 Gy/5[#]	5 (11.4)	3 (8.8)	8 (10.3)
9 Gy/3[#]	15 (34.1)	4 (11.8)	19 (24.4)
12 Gy/6[#]	1 (2.3)	0 (0)	1 (1.3)
Bolus			
0.5 mm	0 (0)	6[*] (17.6)	6 (7.7)
None	44 (100)	28 (82.4)	72 (92.3)
Chemotherapy			
None	7 (15.9)	26 (76.5)	33 (42.3)
Pre-RT	37 (84.1)	8 (23.5)	45 (57.7)
Fitzpatrick skin type			
I	3 (6.8)	2 (5.9)	5 (6.4)
II	10 (22.7)	7 (20.6)	17 (21.8)
III	20 (45.5)	17 (50.0)	37 (47.4)
IV	10 (22.7)	8 (23.5)	18 (23.1)
V	1 (2.3)	0 (0)	1 (1.3)
VI	0 (0)	0 (0)	0 (0)
Smoker			
Yes	4 (9.1)	4 (11.8)	8 (10.3)
No	40 (90.9)	30 (88.2)	70 (89.7)

[*] One patient had bolus over the scar only and one patient had bolus removed after 10 fractions.
[#] Number of fractions.