StrataXRT is non inferior to Mepitel Film in preventing Radiation Induced Moist Desquamation

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INTRODUCTION

This trial was designed to compare two treatments for reducing acute radiation dermatitis (ARD) in breast cancer patients receiving post-mastectomy radiotherapy (PMRT). The treatments were:
1. StrataXRT (SX): a self-drying, non-sticky transparent silicone gel which forms a film and lightly bonds to the most superficial skin layer. It is applied daily by the patient.
2. Mepitel film (MF): a thin, transparent breathable film which is applied to the skin as a dressing. It lasts for 1–2 weeks and is re-applied by a nurse. Based on a randomised trial in New Zealand, it appeared to be the most effective available treatment for ARD[1].

A within patient, non inferiority randomised study was conducted to test whether SX is as good as MF in reducing the severity and duration of ARD and the incidence of moist desquamation in breast cancer patients receiving PMRT.

METHODS

Breast cancer patients undergoing PMRT were eligible. The prescribed doses were 50 Gy in 25 fractions (2 Gy per fraction) or 50.4 Gy in 28 fractions (1.8 Gy per fraction) to the chest wall and nodal regions as specified by the radiation oncologist. Radiotherapy was delivered one fraction per day, five days per week, for 5 – 6 weeks. Some patients received a boost of 10 Gy using electrons. Bolus was applied to half of the course of radiation therapy.

Both trial treatments were to be applied to the irradiated chest wall in each patient from day 1 of radiotherapy for 10 weeks or until ARD had completely resolved. The irradiated area was divided in half and the patients were randomised to receive MF on the medial half or the lateral half, with SX applied to the other half. ARD was assessed using the Common Terminology Criteria for Adverse Events (CTCAE) scale version 4.0, weekly for 10 weeks (see below).

Grade	Criteria
0	None
1	Faint erythema or dry desquamation
2	Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate oedema
3	Moist desquamation in areas other than skin folds and creases, bleeding induced by minor trauma or abrasion
4	Life threatening consequences; skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site; skin graft indicated Note: Moist desquamation may occur with grade 2, 3 or 4 dermatitis.

The outcome measures were occurrence of moist desquamation (MD) in each half of the irradiated area, worst grade and time weighted average (TWA) grade of ARD over 10 weeks. TWA grade of ARD was calculated by multiplying the number of days between consecutive assessments by the average grade of two assessments bounding each interval. The sum of all intervals is then divided by 70.

Statistical Analysis

No criterion for inferiority was defined for MD because the incidence was expected to be low. MD was recorded as a dichotomous variable and the presence of MD was analysed as a paired binomial variable using a 2X2 table for each arm. Analysis of MD was carried out using StatXact[2] to calculate exact confidence intervals for differences in proportions.

For worst grade of ARD, the criterion of inferiority was a mean worst grade 0.5 higher for SC than for MF within the first 10 weeks. For TWA grade, the criterion of inferiority was a mean TWA grade 0.25 higher for SX than for MF. The within patient differences (SX-MF) were analysed using the analysis of variance to estimate the treatment and location effects and their interaction, stratified by patient.

Analyses of categorical variables were performed using StatXact[2] and of continuous variables using Genstat[3].

RESULTS

A total of 44 breast cancer patients receiving PMRT were recruited between January 2017 and December 2017. Four patients were excluded: 3 had <6 weeks of assessments (1 sepsis from UTI, 1 poor compliance and 1 had an allergic reaction to MF) and 1 withdrew their consent.

Table 1 Patient Characteristics

		Arm 1 StrataXRT$_{lateral}$	Arm 2 StrataXRT$_{medial}$	All patients
Age	Median	66.5 years	56.5 years	62 years
Weight (kg)	Median	74	70	72
Body Mass Index (BMI)	Median	28	26.8	27.1
Disease Stage	2	3 (15%)	14 (70%)	17 (42.5%)
	3	16 (80%)	6 (30%)	22 (55%)
	4	1 (5%)	0 (0%)	1 (2.5%)
RT Technique	IMRT	15 (75%)	14 (70%)	29 (73%)
	VMAT	5 (25%)	6 (30%)	11 (28%)
RT Dose	50Gy /25	2 (10%)	3 (15%)	5 (13%)
	50.4Gy /28	18 (90%)	17 (85%)	35 (88%)
Electron Boost	No	18 (90%)	20 (100%)	38 (95%)
	Yes	2 (10%)	0 (0%)	2 (5%)
Duration of RT	Median	41 days	39 days	40 days
No of Assessments	6-8	4	5	9
	9	8	7	15
	10	8	8	16

REFERENCES

1. Herst PM, Bennett NC, Sutherland AE, et al. Prophylactic use of Mepitel Film prevent radiation induced moist desquamation in an intra-patient randomised controlled clinical trial of 78 breast cancer patients. Radiat Oncol 2014
2. Cytel Studio 7.0.0 (2005) Cytel Software Corporation, MA, USA
3. VSN International (2015). Genstat for Windows 18th Edition. VSN International, UK

RESULTS (Con't)

Moist Desquamation (MD)

For the 40 assessable patients (minimum of 6 weekly observations), 8 patients (20%) had moist desquamation (MD) in the halves: 3 with MF but not SX, and five with both MF and SX. No patients had moist desquamation with SX alone. (See Table 2 below)

Table 2 Comparing Treatments Both Arms

	StrataXRT		
Mepitel Film	No MD	MD	Total (%)
No MD	32	0	32 (80%)
MD	3	5	8 (20%)
Total (%)	35 (87.5%)	5 (12.5%)	

The rate of moist desquamation was 12.5% for SX versus 20% for MF, ie 7.5% lower for SX than for MF (95% CI: -20% - 3%). The difference between SX and MF was not statistically significant (p=0.099).

Worst Grade of ARD

The maximum grade of ARD in the SX halves were CTCAE grade 1 (22.5%) and grade 2 (77.5%) compared with grade 0 (2.5%), grade 1 (37.5%), grade 2 (55%) and grade 3 (5%) in the MF halves.

Table 3 Arm 1 StrataXRT Lateral Half

Arm 1	StrataXRT Lateral				
Mepitel Film Medial	Grade 0	Grade 1	Grade 2	Grade 3	Total (%)
Grade 0	0	1	0	0	1 (5%)
Grade 1	0	2	6	0	8 (40%)
Grade 2	0	0	10	0	10 (50%)
Grade 3	0	0	1	0	1 (5%)
Total (%)	0	3 (15%)	17 (85%)	0	20

Table 4 Arm 2 StrataXRT Medial Half

Arm 2	StrataXRT Medial				
Mepitel Film Lateral	Grade 0	Grade 1	Grade 2	Grade 3	Total (%)
Grade 0	0	0	0	0	0
Grade 1	0	5	2	0	7 (35%)
Grade 2	0	1	11	0	12 (60%)
Grade 3	0	0	1	0	1 (5%)
Total (%)	0	6 (30%)	14 (70%)	0	20

The worst grade of radiation dermatitis in the halves within 10 weeks is 0.15 higher for SX vs MF (95% CI: -0.02-0.32). The upper limit of the CI is <0.50 (criterion for non-inferiority set in protocol), it is concluded that SX is not inferior to MF at the 95% level. The difference between SX vs MF is not statistically significant (p=0.075). The estimated location effect (Lateral-Medial) is also 0.15 (95% CI: -0.02 – 0.32) and not statistically significant (p=0.075).

Time Weighted Average (TWA) Grade of ARD

The TWA grade of ARD in the chest halves up to 10 weeks is estimated to be 0.16 higher for SX than MF (95% CI: 0.09-0.23). Because the upper limit of the CI is <0.25 (criterion for non-inferiority set in protocol), it is concluded that SX is not inferior to MF at the 95% level. The difference between SX and MF is statistically significant (p=0.0001) but not clinically significant. The estimated location effect (Lateral-Medial)is -0.02 (95% CI: -0.09 – 0.06, p=0.65).

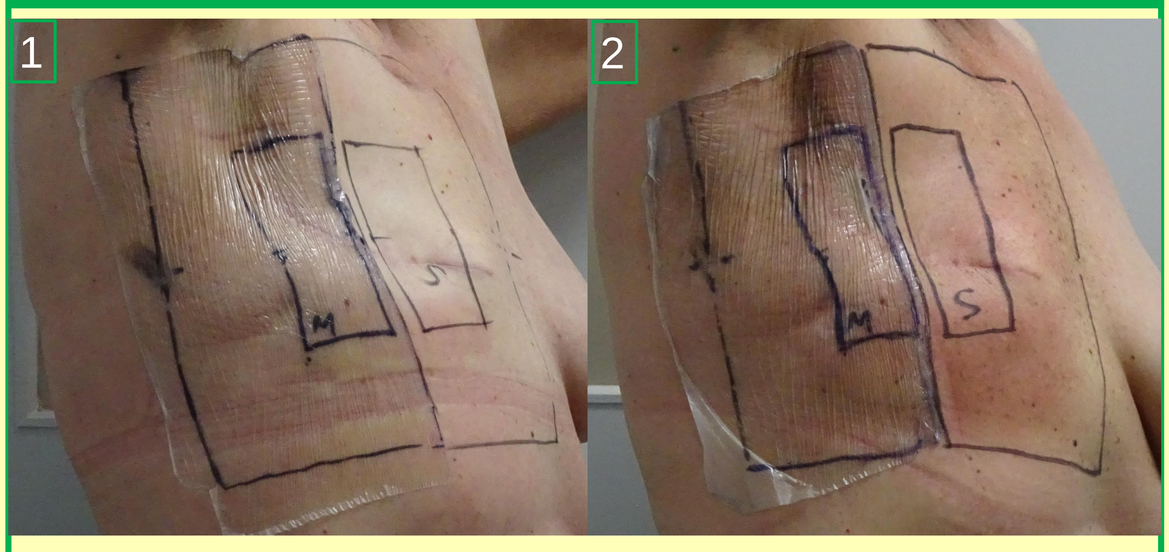
Feasibility and Patient Preference

The median duration of MF applied on the patient was 63 days (range 35-78) versus 66 days of SX application (range 38-78). The total number of MF applications was a median of 4 (range 1-17). The average time per application was a median of 15 minutes (range 7.5-50 minutes) with the total time required throughout treatment of 50 minutes (range 15-310 minutes). MF was applied and maintained by the nursing team while SX was the responsibility of the patient. Three patients developed itching from MF with early removal of MF in 1 patient.
Patients expressed no significant difference in overall preference for either product (38% preferred SX, 40% preferred MF and 22% no preference).

CONCLUSIONS

SX was not inferior to MF on the reported outcome measures of occurrence of MD, worst grade of ARD and TWA grade of ARD over 10 weeks. Patients reported no significant preference for either product. However, MF further extended the utilization of scarce nursing resource which may make SX a more pragmatic choice.

PHOTOGRAPHS



The picture on the Left is that of a patient at commencement of radiotherapy (1) with Mepitel Film of the lateral half of the right chest wall and StrataXRT on the medial half of the right chest wall (Arm 2 of study). The picture on the R is at 7 weeks after commencement of radiotherapy (2).

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