MEPITEL FILM

The Effect of Mepitel Film Dressings on Acute Radiation-Induced Skin Reactions in Patients Receiving Post-Wide Local Excision Irradiation

Annie Sutherland

November 2014

A thesis resubmitted for the degree of Bachelor of Radiation Therapy with Honours at the University of Otago, Dunedin, New Zealand
Abstract

The most common malignancy for women in New Zealand is breast cancer. As part of their treatment regimen the majority of these women will receive radiation therapy. A significant number of patients will experience severe acute radiation-induced skin reactions. At the time of writing, there is no evidence-based standard treatment for these reactions, the most extreme of which is moist desquamation which has a severe effect on patient comfort and psychological well-being.

Previous studies in our department had shown that Mepilex Lite, an adhesive soft silicon dressing (Mölnlycke Health Care AB, Gothenburg, Sweden), reduced the severity of acute radiation-induced skin reaction by 40% when used to treat existing erythema. It is theorised that these soft silicone dressings prevent further mechanical damage to the radiation-damaged basal layer of the skin, allowing time for repair. Mepitel Film is another soft silicone dressing from the same company. This Film is fully breathable, transparent, very thin and with no clinically significant bolus effect; it can be left on during radiation therapy and can therefore be used prophylactically. We hypothesized that Mepitel Film would be more successful in minimizing acute radiation induced skin reactions when used in this way.

In order to test the hypothesis we conducted an intra-individual randomised controlled trial (n=80) which investigated whether the prophylactic use of Mepitel Film would be superior to aqueous cream in reducing both the incidence of moist desquamation and the severity of radiation-induced skin reactions in breast cancer patients.

The skin area to be irradiated was divided into a medial half and lateral half (which included the axilla). These two halves were then randomised to Mepitel Film (trial area) or aqueous cream (control area) from the start of radiation treatment. This trial was carried out by the author and one other radiation therapist researcher (RTR) at the Dunedin Radiation Oncology Centre (DROC) in New Zealand. Modified RTOG as well as the modified Radiation-Induced Skin Reaction Assessment Scale (RISRAS) was used to assess the visible signs (researcher component) and symptoms (patient component) of the skin reactions. Patients were reviewed three times a week during radiation therapy treatment, then once
a week post-treatment for four weeks or until reactions had completely resolved. All patients filled out an Exit Questionnaire after completion of treatment.

This thesis analyses the results of the first 10 mastectomy patients and the first 10 non-mastectomy patients who completed the trial. The results of this 20 patient cohort demonstrated that Mepitel Film, when used prophylactically, completely prevented the occurrence of moist desquamation and decreased the severity of radiation-induced skin reactions by more than 90%.

A major limitation of this trial was the fact that neither the researcher nor the patient could be blinded as it was very clear where the film was and it was important that the film remained in place for as long as possible (up to several weeks).

In conclusion, the results of this study show that using Mepitel Film prophylactically reduces the incidence and severity of radiation-induced moist desquamation in breast cancer patients.
Acknowledgements

It is a pleasure to thank the many people who made this trial and thesis possible.

First and foremost, I wish to thank all of the patients who committed their time and energy to participate in this study. You were all so positive about trialling a new product, and very keen to do anything that would help make life easier for others that may find themselves in a similar situation. I appreciate all of the feedback you provided and enjoyed spending time with you, and am humbled that you let me into your lives. Without you, none of this would have been possible. I hope you found the experience worthwhile and it goes without saying that I wish you all the very best for the future.

Thank you to all the staff at the Dunedin Radiation Oncology Department for your patience and support. I am grateful to the Radiation Oncologists (Dr Lyndell Kelly, Dr Alice Fairbairn) for supporting radiation therapist-led research.

Thank you so very much to Charge Radiation Therapist, Noelle Bennett for allowing me to combine roles of radiation therapist and researcher. Your flexibility, assistance, advice and support has been invaluable.

I offer my sincerest gratitude to my supervisor Dr Patries Herst for your encouragement, enthusiasm, energy and effort.

I am very grateful to The New Zealand Breast Cancer Foundation Post-graduate Radiation Therapy Scholarship for providing financial assistance for this thesis.

Finally, I wish to thank Mölnlycke Health Care for providing all of the Mepitel Film free of charge; without your generous donation this trial would not have been feasible.
# Table of Contents

1. **Introduction**1

   1.1. Effect of radiation on the skin .................................................................2

   1.2. Severity of Acute radiation-induced skin reactions .................................4

   1.3. Factors that affect severity of skin reactions ...........................................6
       1.3.1. Treatment construct .................................................................6
       1.3.2. Genetic Construct ........................................................................7
       1.3.3. Patient construct ........................................................................8

   1.4. Quality of Life .........................................................................................10

   1.5. Prevention and treatment of acute radiation-induced skin reaction ..........11
       1.5.1. Compounds with anti-inflammatory and wound healing activities ....11
       1.5.2. Agents that prevent friction ..........................................................12

   1.6. Aim and Objectives .................................................................................14

2. **Methodology** .........................................................................................15

2.1 Participants ..............................................................................................15

2.2. Potential confounders ..............................................................................17

2.3. Procedure .................................................................................................19

   2.3.1. Intervention arm .............................................................................19

   2.3.2. Control Arm ....................................................................................20

   2.3.3. Endpoint ..........................................................................................21

   2.3.4. Withdrawal from the study due to adverse events ..............................21

2.4. Measurements .........................................................................................23

   2.4.1. Initial skin assessment ....................................................................23

   2.4.2. Measurements of skin reaction severity ............................................23

   2.4.3. Dose Measurements .......................................................................26

2.5. Exit questionnaires ..................................................................................28

2.6. Trial timeline ............................................................................................28

2.7. Data Collection and Statistical Analysis ..................................................31

2.8. Funding .....................................................................................................31

3. **Results** ..................................................................................................32

3.1. Patient Demographics ............................................................................32
List of Tables

Table 1.1: Factors Affecting Radiation-Induced Skin Reactions ........................................6
Table 2.1: Modified Radiation-Induced Skin Reaction Assessment Scale (RISRAS)........24
Table 2.2: Radiation Therapy Oncology Group (RTOG) Toxicity Grading ......................24
Table 3.1: Patient Demographics .....................................................................................32
Table 3.2: Dose received by Mepitel Film and Control Cream skin areas at different
locations for mastectomy patients ..................................................................................34
Table 3.3: Dose received by Mepitel Film and Control Cream skin areas at different
locations for non-mastectomy patients ..........................................................................34
Table 3.4: Averages, SEM of RISRAS scores (combined researcher and patient
components) and percentage decrease in skin reaction severity of skin
areas covered with Mepitel Film and aqueous cream in mastectomy patients
(n=10), non-mastectomy patients (n=10), and entire cohort (n=20) .........................36
Table 3.5: Incidence (%) of moist desquamation (MD) in skin areas treated with
Control cream in mastectomy patients (n=10), non-mastectomy patients
(n=10), and entire cohort (n=20). ..................................................................................37
Table 3.6: RTOG scores of skin covered in Mepitel Film and control cream control
cream in mastectomy patients (n=10), non-mastectomy patients(n=10),
and entire cohort (n=20)...............................................................................................38
Table 3.7: Thematic analysis of Exit Questionnaires (n=20) .................................................39
List of Figures

Figure 1.1: Structure of the skin ................................................................. 2
Figure 2.1: Intro-individual Comparison ................................................... 17
Figure 2.2: Mepitel Film ........................................................................ 20
Figure 2.3: Schema of trial ..................................................................... 21
Figure 2.4: Placement of TLDs ............................................................... 27
Figure 2.5: Mepitel Film trial timeline ..................................................... 30
Figure 3.1: Average RISRAS scores of 10 mastectomy patients (A), 10 non-
mastectomy patients (B), and the entire patient cohort (C) ....................... 35
1. Introduction

Breast cancer is the most common malignancy for women in New Zealand. In 2010, 2797 New Zealand women were diagnosed with breast cancer [1]. The majority of these women will receive radiation therapy as part of their treatment regimen [2]. Many of these women will develop some form of acute skin reaction at some stage during or immediately after their radiation therapy treatment [3].

Acute skin reactions can vary from a light pink (erythema) to a complete loss of skin integrity, (moist desquamation). Despite the fact that moist desquamation is likely to occur in a significant proportion of breast cancer patients, there is no evidence-based standard treatment for these reactions - in fact treatments can vary not only between institutions but also within departments worldwide [4–6]. Treatment tends to be based on historical and anecdotal evidence with many departments using aqueous cream [7] in spite of a large randomised controlled clinical trial (n=357) published in 2003 showing that aqueous cream neither prevented nor decreased the severity of skin reactions [4]. In fact several studies have shown a detrimental effect of aqueous cream on the skin [8–10].

Our group in New Zealand has investigated the effect of soft silicone dressings on acute radiation-induced skin reactions in two trials over the last few years [11,12]. This thesis describes the results of the first 10 mastectomy patients and the first 10 non-mastectomy patients who took part in a third clinical trial (n=80) that investigated the effect of another soft silicone dressing, Mepitel Film, on the severity of acute radiation-induced skin reactions as well as the incidence of moist desquamation.
1.1. Effect of radiation on the skin

The skin comprises an outer layer, the epidermis, and an underlying connective tissue layer, the dermis. The epidermis is composed of five different layers, namely the stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum and stratum basale – the basal stem cell layer (Figure 1). The epidermis is continually being renewed through a balanced production of new basal cells from the stratum basale in response to the normal shedding of the cornified top layers [13]. It is the lethal damage of this stratum basale by ionising radiation that is responsible for acute skin reaction.

Figure 1.1 Structure of the skin. http://faculty.southwest.tn.edu/rburkett/A&P1_Integumentary_system.htm

Ionizing radiation affects both healthy and cancerous tissues in the same way. Radiation damage occurs either through direct ionization events or, as happens more often, through free radical damage. Although radiation damages all macromolecules, it is the damage to the DNA and in particular double stranded DNA breaks that eventually kills the cells [14]. Compromised cell function results in either immediate cell death or, more commonly, in a
series of events leading to cell death, although affected cells may go through a few more divisions before dying [15].

Tissue damage occurs immediately following the first dose of radiation [5]. Damaged basal stem cells are either repaired or replaced by cells moving from the resting phase into the active cycle (repopulation). Visible skin damage occurs when the rate of repopulation of the basal cell layer cannot match the rate of cell destruction by treatment [16]. The inflammatory response activated is a normal physiological reaction to radiation therapy damage [17]. Subsequent radiation therapy treatment interrupts repair of damaged skin cells and replacement of dead skin cells, which compromises skin integrity. It can also cause damage to local capillaries, leading to inflammation and delay in wound healing.

Patients receiving external beam radiation therapy are at risk of developing acute skin reactions particularly if the tumour is close to the skin surface, where the skin falls within the treatment field and receives a significant radiation dose, such as in breast and head and neck cancer patients.
1.2. Severity of Acute radiation-induced skin reactions

Acute radiation-induced skin reactions vary in severity from faint or mild erythema (pink and dusky colouration or rash, with possible itching or burning and mild discomfort) to dry desquamation (scaly or peeling skin often accompanied by pruritus) through to moist desquamation (where blistering and sloughing of the skin leads to open wound with pain and discomfort). The different levels of skin reaction severity are described below, based on [4,13,18–22]. The skin management booklet of the Dunedin Radiation Oncology Department (Appendix F) contains photos of the different levels of skin reaction severity.

**Erythema**

Erythema (reddening of the skin) is seen approximately 10-14 days following the first fraction of radiation. At this stage in a standard treatment regime a dose of 20 to 30 Gray (Gy) will have been delivered, and corresponds with the time it takes for the damaged basal cells to migrate to the skin surface. Initially the skin will become warm and reddened (erythema), and in some patients the area may also feel itchy. However, erythema can be seen earlier than this time-frame – at five to seven days following fraction one.

**Dry Desquamation**

As the basal layer of the skin is damaged through further exposure to radiation it tries to compensate by increasing mitotic activity in order to replace the damaged cells. However, if the new cells reproduce faster than the old cells are shed then the skin will become dry and flaky, and peel (dry desquamation). This partial loss of epidermal basal cells can also cause itching and hyperpigmentation, tenderness and discomfort.

**Moist Desquamation**

As radiation therapy continues, the basal layer cannot produce enough new cells to replace the dead cells and therefore the outer layer of the epidermis will become broken and oedematous with exudate (moist desquamation). The exudate is normal and is rich in nutrients which help the growth of new skin cells. Complete destruction of the basal cell layer results in blistering and loss of the epidermal layer.
Skin necrosis is rarely seen primarily due to the advanced techniques used in the delivery of radiation therapy. The severity of skin reactions may peak seven to ten days after radiation therapy is completed. It can take this long for the damaged cells to reach the outer epidermis. After this time side effects will gradually start to settle down and the condition of the skin will slowly improve over the ensuing few weeks. Four to six weeks after treatment has been completed skin should be healing well but may still look hyper-pigmented (darker) and will be more susceptible to UV damage [23].
1.3. Factors that affect severity of skin reactions

A number of factors appear to influence the severity of radiation-induced skin reactions. Differences in intrinsic factors (including age, skin type, breast size, and ethnicity) and extrinsic factors (prescribed dose, energy, bolus, and fractionation) may predispose a patient to severe skin toxicities. Porock et al [24] developed a conceptual framework which organises these factors into three categories: treatment construct, genetic construct, and personal construct (see Table 1.1). Each of these factors is further discussed below.

Table 1.1 Factors Affecting Severity of Radiation-Induced Skin Reactions [24]

<table>
<thead>
<tr>
<th>Treatment Construct</th>
<th>Genetic Construct</th>
<th>Patient Construct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose; presence of bolus or additional boost</td>
<td>Ethnicity (skin type)</td>
<td>Pre-disposing factors such as large breast size, high BMI, advanced age, smoking, nutritional status</td>
</tr>
<tr>
<td>Fraction regime</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site</td>
<td>Family history of cancer</td>
<td>Adjuvant chemo therapy</td>
</tr>
<tr>
<td>Technique: beam energy, orientation of beam, conformal or image guided</td>
<td>Personal history of cancer</td>
<td>Co-morbidities</td>
</tr>
</tbody>
</table>

1.3.1. Treatment construct

Dose and fractionation

The severity of radiation-induced skin toxicities is dose dependent [4,16]. The extent of cell damage increases incrementally with an increase in total dose, due to the increased number of single and double stranded DNA breaks [19]. Clinical trials have shown that a higher dose rate increases the degree of moist desquamation [25]. Late tissue complications are affected more by hypo-fractionation (higher dose per fraction) than acute tissue side effects [16]. Recent randomised trials have shown that the implementation of the advanced breast cancer treatment techniques, 3-Dimensional Conformal Radiation Therapy (3D-CRT) and
Intensity modulated radiation therapy (IMRT), is associated with significant reduction in the severity of acute radiation-induced skin toxicity, compared with the standard tangential beam arrangement [26–29].

3D planning allows more accurate dose calculations and decreases the volume in the target area that receives dose exceeding 100% of the prescribed dose. IMRT uses 3D dose calculations and ensures a more homogeneous dose distribution through the treatment volume by incorporating computer controlled modulation of the beam intensity across the target area [11,22]. Keller et al found IMRT to be beneficial, both in reducing acute skin toxicity and increasing excellence in cosmesis [30].

**Bolus**

Bolus is a tissue equivalent material used to increase the dose to the skin or tissue immediately deep to the skin where there is risk of local recurrence post mastectomy [4]. Use of bolus increases the dose to the skin and thus the likelihood and severity of acute skin toxicities [4,5,13,18,23].

**Site**

Areas within the treatment field that are prone to increased warmth, moisture (perspiration) and friction [16] will display the highest incidence of moist desquamation compared to the rest of the treatment field. In breast cancer patients these areas are the axilla and the inframmary fold [3]. In mastectomy patients the bra line where the inframmary fold would have been is also at risk from bra friction.

**1.3.2. Genetic Construct**

Genetic make-up can influence the severity of radiation-induced skin toxicities. The majority of hereditary breast cancers arise from mutations in the BRAC1 and BRAC2 genes. Carriers of mutated BRCA1 and BRCA2 genes have an enhanced sensitivity to ionising radiation and thus an increased risk of developing breast cancer because these genes are involved in DNA repair [14,31]. Individuals with rare genetic diseases such as ataxia telangiectasia mutation (ATM), Bloom’s syndrome, Fanconi’s anaemia and Nijmegen breakage syndrome also exhibit
increased radio-sensitivity. These diseases all have gene mutations related to DNA damage or repair [32].

**Ethnicity**

Even though there is a lack of empirical data to support this, there is anecdotal evidence to suggest that patients with a dark skin type will experience less severe radiation-induced skin reactions than those with pale or fair skin. This is based on an assumption that the melanin in darker skin protects the skin from ionizing radiation in the same way as it protects the skin from UV exposure by the sun [33]. However, melanin-containing darker skin has been shown to produce more free radicals when irradiated and thus darker skin is likely to display more severe skin reactions than fair skin that does not contain much melanin [34]. Ryan and colleagues showed that African-American cancer patients (n=18) had more severe post treatment skin reactions than Caucasian cancer patients (n=393)[33]. Similarly, sun-browned skin is also more likely to experience more severe skin reactions compared with untanned skin [35]. Our previous trial [12] did not find an association between skin type and skin reaction severity using the Fitzpatrick Skin type scale (Appendix D), which may have been due to the relatively small patient numbers.

1.3.3. Patient construct

**Breast Size**

A larger breast volume has been linked to an increase in severity of skin reactions [13,16,36]. Individuals with larger breasts are prone to increased skin toxicity in the inframmary fold due to the increased friction in that area. Previous studies have suggested various reasons for this. One is that the larger treatment volume may have increased inhomogeneities compared with a smaller volume. This may result in hotspots of very high dose which could then lead to increased skin toxicities [28,36,37].

**Body Mass Index (BMI)/weight**

A high BMI can be an indicator of an increase both in weight and in breast size. An obese individual has larger skin folds in the axilla and inframmary fold. Increased severity in skin toxicity is noted in the axillary skin folds and inframmary fold due to the increase in friction
of skin against skin in these areas [24]. There is also a corresponding increase in warmth and moisture in these skin folds.

**Age**

Advanced age is generally seen as a risk factor for increased skin toxicity due to the impaired healing ability of aged skin as the epidermal cell cycle is affected by the aging process [4,16,23]. The ability of aged skin to heal is influenced by decreased levels of growth factors, diminished cell proliferation and migration, and diminished extracellular matrix secretion [38]. A decrease in collagen density and a relatively acellular and avascular dermis are age-related changes that decrease the ability of the skin to heal [39]. However, other authors have suggested that older individuals may experience less severe radiation-induced skin damage due to the decrease in turn-over rate of epidermal cells in the that cohort [24].

**Smoking**

Smoking may predispose people to having more severe skin reactions due to the adverse effects of nicotine and carbon monoxide in tobacco smoke on wound healing and cutaneous vasoconstriction. Tobacco smoke impairs collagen synthesis, decreases the function of neutrophils and restricts the oxygen-carrying capability of the haemoglobin [4,23,24,39]. Smoking has been linked to increased skin reaction severity in some [4] but not in other studies [40,41].

**Nutritional status**

Good nutrition is necessary for the healing of radiation-induced skin toxicities as poor nutrition can delay the onset of healing and tissue repair. Protein is essential in skin damage repair and insufficient protein causes both decreased collagen production and alterations in the collagen produced. A lack of carbohydrates leads to a diminished supply of energy necessary for tissue repair. A deficit in vitamins can inhibit healing. Vitamin C and B1 (thiamine) are essential in collagen repair and vitamin A in the inflammatory process [39].
Adjuvant Chemotherapy

Some chemotherapy agents (5-fluorouracil, methotrexate, adriamycin, paclitaxel and docetaxel) when administered concurrently with radiation therapy have been associated with increased skin reactions. Chemo-radiation can cause the onset of skin toxicities to occur at a lower radiation dose, be more severe and last for longer [42,43].

Co-morbidities

Diseases that may be predictors for increased severity of radiation-induced skin reactions include autoimmune disorders such as systemic lupus erythematosus (LSE) and rheumatoid arthritis as these affect overall tissue health [18,23]. Diabetes mellitus can affect tissue healing as atherosclerosis of arteries and capillaries prevents adequate oxygen and nutrient transfer between the vascular system and surrounding tissues [23].

1.4. Quality of Life

Acute radiation-induced skin reactions affect the stress level of breast cancer patients and thus their quality of life in several ways. The stress associated with dealing with the physical symptoms of severe skin reactions, such as pain, itchiness, inability to wear certain clothes or a prosthesis and/or partake in normal physical activities or attending social occasions, has been well documented [37,44,45]. However, patients also experience anxieties and emotional stress associated with the cosmetic and tactile changes of the irradiated skin. This type of stress may impact on intimate and social relationships leading to feelings of low self-esteem and the inability to cope [44–46]. Budischewski et al [47] evaluated changes in quality of life in breast cancer patients during a course of radiation therapy and reported that the maintenance of daily routine, household chores, work, hobbies and sports played an important role in the improvement of quality of life. Patients expressed low self-esteem when they were unable to fulfil their usual roles within the family or work environment [45].
1.5. Prevention and treatment of acute radiation-induced skin reaction

There are a number of recent reviews that have analysed the results of studies that have evaluated the use of topical agents for the prevention and management of acute radiation-induced skin damage [5,6,13,48].

The general consensus is that moisturising irradiated skin, by using emollients such as aqueous cream and aloe vera, minimises radiation-induced skin reactions [40,49]. However, three recent studies contra-indicate the use of aqueous cream for radiation-induced skin reactions as it causes skin thinning and enhances penetration of irritants [8–10]. Aloe vera has traditionally been used in radiation dermatitis because of its anti-bacterial and anti-inflammatory properties [50]. However, it did not exhibit any clinical effect in three randomized trials [51–53].

Several national and international guidelines exist for the prevention and treatment of acute and late radiation-induced skin toxicities. The most recent one was published in 2013 by the Multinational Association for Supportive Care in Cancer (MASCC) Skin Toxicity Study Group [48]. However, despite these existing guidelines there are still a lot of departments that base their skin care regimens on historical and anecdotal evidence [6,7,54,55].

1.5.1. Compounds with anti-inflammatory and wound healing activities

The efficacy of several topical agents in decreasing the incidence and severity of acute radiation-induced skin reactions was analysed in a systematic review published by the Supportive Care Guidelines Group of Cancer Care Ontario in 2006. This review of 28 clinical studies concluded there was a lack of proof to support the use of any topical agent [56]. A systematic literature review published in 2010 found that there was some evidence that topical corticosteroids and hyaluronidase-based creams might be beneficial for reducing radiation-induced skin reactions [5]. A later study confirmed a possible beneficial effect of the prophylactic use of corticosteroids [57]. An observational study reported that a lotion containing hyaluronic acid, urea and polidocanal may also have reduced the incidence and severity of radio-dermatitis in some instances [58]. However, this is at odds with a more recent study assessing the effectiveness of hyaluronic gel compared with petroleum-based gel on patients undergoing radiation therapy for breast cancer. The study was closed early as
patients in the hyaluronic acid arm developed a higher rate of radiation-induced dermatitis [59]. Conflicting reviews also exist for the use of the anti-inflammatory agent trolamine. Evaluation from early studies do not support the use of trolamine [60–62] but a recent trial concluded a significant reduction in intensity of radio-dermatitis was achieved with the use of trolamine [63]. Evidence published to date does not support the use of calendula cream [64], aloe vera gel, aqueous cream [4] or sucralfate cream [5] for the prevention of acute radio-dermatitis. Other agents reported to reduce the incidence of radiation-induced skin reactions are topical silver-based agents [65,66] and products containing the antioxidant plant flavonoid silymarin [67].

1.5.2. Agents that prevent friction

A recent review by Herst suggested that preventing friction may be another way of preventing or minimising skin reactions [68]. To date, two barrier products have been trialled that employ this strategy: Cavilon No-Sting barrier film and the soft silicone dressing, Mepilex Lite. The initial unblinded in-patient-controlled No-Sting barrier film (n=61) used a spray-on film. The film significantly reduced the severity of acute radio-dermatitis and rate of moist desquamation [69]. However a large double blinded trial (n=333) using this product in the form of barrier cream did not validate these findings. This large trial failed to find a difference in severity and incidence of skin reactions between patients treated with barrier cream and those treated with sorbolene cream [70]. The authors suggested that this may have been due to differences in formulation or that the Cavilon cream was not applied thickly enough to form a protective layer.

The Dunedin department took part in two trials that compared the efficacy of Mepilex Lite dressings with standard aqueous cream on the severity of acute radiation-induced skin reactions [11,12]. The hypothesis was that Mepilex Lite dressings reduced skin reactions by preventing additional mechanical damage (due to friction between damaged skin and clothing or other body parts) and chemical injury (due to perspiration trapped in the basal layer) of skin that had already been sub-lethally damaged by radiation, thus allowing for the repair of fragile skin rather than exacerbation of the damage.
The first was a single centre pilot study conducted in Dunedin [11] and the second was a multi-centre trial across four of the eight departments in New Zealand (Dunedin, Wellington, Palmerston North and Auckland Radiation Oncology)[12]. Mepilex Lite is an absorbent, self-adhesive dressing consisting of a thin flexible sheet of absorbent hydrophilic polyurethane foam bonded to a water vapour-permeable polyurethane film backing layer. The contact surface of the dressing is coated with a soft silicone adhesive layer without any added chemicals based on the patented Safetac technology. It adheres to healthy skin thus keeping the dressing in position but does not cause trauma on removal. The material does not react with chemicals in or on the skin, does not react with radiation, does not stick to open wounds and can be left on the skin for several days.

Between the two trials, a total of 104 patients were enrolled, each receiving 50Gy in 25 fractions or biologically equivalent dose. Toxicities were assessed three times a week using the Radiation-Induced Skin Reaction Scale (RISRAS) (Table 2.1) with patients doubling as their own controls to eliminate confounding patient and treatment-related factors. Both were management trials, with the dressings being applied only after faint erythema was noted. Both trials demonstrated that the dressings significantly decreased the severity of acute skin reactions by 30% and 40% respectively [11,12]. However the dressings did not affect moist desquamation rates, were not transparent and did not adhere well in the inframammary fold or axilla, both areas likely to develop moist desquamation. Lack of transparency resulted in their removal during radiation therapy sessions as the daily set-up tattoos were invisible. Visible dressings could also be awkward in social and private situations which could have affected compliance. Mepilex Lite dressings were not waterproof and did not stick to perspiring skin, which was an issue in warm weather during hot flushes or when doing sports nor could they be left on in the shower.

**Current Trial**

With these limitations in mind the next step was to test another Safetac-based dressing in a prophylactic setting. This time, the highly transparent, very thin and more adhesive Mepitel Film was used from the start of radiation treatment rather than after erythema had developed.
1.6. **Aim and Objectives**

**Aim**

The aim of this thesis is to determine whether Mepitel Film is superior to aqueous cream in decreasing the severity of acute radiation-induced skin reactions in breast cancer patients.

The entire trial will recruit 80 patients - both women and men - from across the Southern District Health Board's catchment area. This will be a fully randomized trial where the breast/chestwall area will be divided into a medial half and a lateral half (which is to contain the axilla). These two halves will be randomised to Mepitel Film (trial area) or aqueous cream (control area). Skin reaction severity will be assessed using the Radiation-Induced Skin Reaction Assessment Scale (RISRAS) [71] as well as the modified RTOG scoring system [72].

This thesis analyses and reports on the results for a 20 patient cohort consisting of the first 10 mastectomy patients and the first 10 non-mastectomy patients that enrolled in the 80 patient trial.

**Primary Objective:** To determine whether Mepitel Film reduces the severity of radiation-induced acute skin reactions in breast cancer patients.

**Primary Endpoint:** Incidence of moist desquamation
2. Methodology

This single centre, intra-individual, open, randomised controlled trial was carried out by the author and one other radiation therapist researcher (RTR) at the Dunedin Radiation Oncology Centre (DROC) in New Zealand. It compared the efficacy of Mepitel Film dressings with the standard care of aqueous cream on the severity of acute skin reactions in breast cancer patients receiving radiation treatment following either breast-sparing surgery or mastectomy. The 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 informed consent before participating in this trial.

2.1. Participants

2.1.1 Eligibility

All patients, both female and male, aged 18 years and over who had been referred for radiation therapy following either breast-sparing surgery or mastectomy for primary breast cancer and who had not had a reconstructive surgery were eligible for this RCT. However, patients who had systemic disease were to be excluded as were patients who were unlikely to be available for the once weekly post treatment follow-up skin assessments.

2.1.2 Participant numbers

This trial aimed to recruit 80 patients over a one year period. That target number of 80 was actually achieved between October 2012 and April 2013 with 78 of those patients yielding complete datasets for the trial. Only data from the first 10 mastectomy and first 10 non-mastectomy patients are included for analysis in this thesis.

2.1.3 Obtaining informed consent

Immediately following their planning CT scan, patients were given verbal as well as written information about the trial - in the form of a participant information sheet (Appendix A) - by the radiation therapists who had performed the CT scan. The patients were then afforded a
further opportunity to discuss the trial with the one of the two RTRs between the time of their CT and the start of their treatment. Written informed consent in which patients agreed to participate in the trial was obtained before their first radiation treatment following which randomisation was carried out (Appendix B).

2.1.4. Radiation treatment specifics

The radiation prescription for patients on the trial was 50Gy in 25 fractions or biologically equivalent dose at the radiation oncologists' discretion. Whilst several fractionation regimes are utilised in the department, intra-individual comparison negated this variable. Information relating to planning technique, dose, bolus application, chemotherapy and hormone therapy was recorded.

Patients were treated in the supine position on a proprietary brand of breast board with an elevation of approximately 20 degrees. Radiation was most commonly delivered using a combination of 6MV and 18MV photon beams applied tangentially, although on occasion 6MV beams only were used. For a small percentage of patients the radiation oncologists prescribed 5mm of bolus to be applied daily. If required, the supraclavicular and axillary lymph nodes were treated using an antero-lateral oblique photon field or fields with, in most cases, a semi opposed posterior axillary field.
2.2. Potential confounders

2.2.1 Intra-patient controls and Randomisation

This trial used intra-individual methodology whereby patients acted as their own controls (Figure 2.1). This ensured the minimisation of any confounding patient-related and treatment-related factors whilst randomisation negated the effect of any small dose differences between the trial and control areas. In practice this meant that Mepitel Film was applied prophylactically to the medial or lateral half of the treatment area as dictated by the randomisation (trial area) whilst aqueous cream was applied to the other half (control area).

Figure 2.1 Intra-individual comparison.
The medial and lateral halves of the treatment area of the breast or chest wall were demarcated. Mepitel Film was randomised to either medial or lateral with the other half of the treatment field acting as the control.

The medial and lateral halves of the treatment area on the breast or chestwall were demarcated by one of the RTRs. Mepitel Film was randomised to one of the two halves using pre-determined computer generated randomisation charts created by Dr James Stanley, a biostatistician at the University of Otago, Wellington. Randomisation was carried out using a randomisation form (Appendix C) which was sent by email to the principal investigator (Dr Patries Herst) at the University of Otago, Wellington. The principal investigator had no direct involvement with the patients.
2.2.2. Blinding

Because neither the patients nor the RTRs could be blinded, this was an open trial. Blinding was impossible on two counts. Firstly, the two skin treatment regimens were very different in appearance and secondly, the RTRs were responsible for applying the Mepitel Film which stayed on the patient’s skin for several days and sometimes for longer than a week. The patients applied the aqueous cream themselves twice a day.


2.3. Procedure

On day one of treatment, Mepitel Film was applied to the trial half (intervention arm) as per randomisation whilst patients were requested to apply aqueous cream twice daily to the control half of the breast or chest wall. At this time all patients were told about the information contained within the department’s skin reaction guidelines and what routine care for would have involved had they not consented to be part of the RCT. These guidelines had been researched and written specifically for the Dunedin Radiation Oncology Centre of the Southern District Health Board (SDHB) by members of the radiation oncology team (Appendix F) to reflect best evidence-based practice as it stood at the time of writing the guidelines.

2.3.1. Intervention arm

On day one of treatment Mepitel Film was applied to the half of the breast randomised to the intervention arm, having first been templated and cut to size. Patients were supine for its application, lying in as close to treatment position as possible. This was done to make sure that there was no change in shape of the breast when the Mepitel Film was applied. Because the Mepitel Film could easily be stretched, great care had to be exercised to ensure that the breast was not distorted during application. Check measurements were taken from the couch surface to the lateral tattoo and from the medial tattoo to the supra-sternal notch before and after application as a means of verifying that no changes in their position had occurred. The treatment units were also notified when the Mepitel Film was changed so that check images could be taken pre-treatment as further verification that the shape had not been distorted. Dressings were replaced as required which could be anything from a couple of times a week to once every three weeks. The exact position of the Film was recorded photographically and stored in MOSAIQ, the electronic patient management system.

Measurements carried out on Mepitel Film by DROC’s physics team had established that there was a clinically insignificant bolus effect of 0.12mm thus validating that leaving it on
during radiation treatment would not compromise patient outcome. Furthermore, tattoo visibility was not an issue because the Mepitel Film was transparent.

Mepitel Film remained in situ throughout the duration of the radiation therapy course as well as for a follow-up period after completion of treatment. This timeframe was variable - generally less than four weeks from completion of treatment course - the endpoint being determined as full resolution of any skin reaction.

**Figure 2.2 Mepitel Film.**
Mepitel Film is a very thin, transparent, fully breathable, elastic polyurethane film with a clinically insignificant bolus effect that adheres well in the inframmary fold and axilla (www.molnlycke.com).

### 2.3.2. Control Arm

On day one of treatment the RTR applied aqueous cream to the control area and requested that subsequently the patient apply the cream twice a day unless or until they were asked to stop applying it by either of the RTRs.
2.3.3. Endpoint

The endpoint of the trial was the development of moist desquamation. Before the trial started the decision had been made that should moist desquamation develop in either the Mepitel Film arm or the aqueous cream arm, the departmental skincare protocol for addressing moist desquamation would be followed (see Figure 2.3). This meant that Mepitel Film/aqueous cream would be replaced by Mepilex Lite, which would ensure that any exudate was adequately absorbed. The Mepilex Lite would then be replaced daily until the skin had healed as per departmental protocols.

2.3.4. Withdrawal from the study due to adverse events

Mepitel Film is a diaphanous, transparent, fully breathable, elastic polyurethane film which has a thin silicon webbing backing (see Figure 2.2). As it does not contain any chemicals it is inert, and therefore does not react with any chemicals in or on the skin or with radiation. However, if it was considered necessary to discontinue the use of either Mepitel Film or aqueous cream because of an allergic reaction or any other patient-related issues, substitution with an alternative treatment would have been at the treating clinician’s discretion. Application of the agent causing the allergic reaction or other patient-related issue would cease and the patient would be withdrawn from the trial.
Figure 2.3 Schema of the trial

Eligibility criteria
- No metastatic disease
- No previous RT to breast/chest wall
- Available for follow-up assessments

Assessments - RISRAS/RTOG
- 3x weekly during treatment
- 1x weekly for up to 4 weeks after treatment completion or until healed, whichever is sooner

Outcome criteria
- % of patients with MD
- Time to MD occurring
- Time to resolution of reactions
2.4. Measurements

2.4.1. Initial skin assessment

An initial skin assessment form (Appendix D) was completed for each patient at their first treatment visit by one of the RTRs. This assessment was designed to record details of the patient's radiation construct as well as other treatment-related and personal factors that it was thought might influence or increase the likelihood of them developing a severe radiation-induced skin reaction (see Chapter One, section 1.2). Skin type was assessed using the classification of skin type known as the Fitzpatrick skin type \[73\]. The Fitzpatrick Classification Scale was developed in 1975 by Harvard Medical School dermatologist, Thomas Fitzpatrick (Appendix D). This scale classifies an individual's complexion or base colour (white, brown or black skin), plus their tolerance of sunlight and the result of exposure to ultraviolet radiation (tanning).

2.4.2. Measurements of skin reaction severity

**Modified Radiation-Induced Skin Reaction Assessment Scale (RISRAS) and RTOG**

The Modified RISRAS \[71\] was used to assess the extent of the acute radiation-induced skin reaction in both the intervention arm and the control area (Table 2.1). It had been chosen for its sensitivity to subtle changes in reaction as well as for the fact it had the added patient component which recorded reactions from the patient's perspective. However, for the sake of completeness and to allow direct comparisons to be drawn, the RTOG (Table 2.2) toxicity grading, arguably the most widely utilised assessment tool, was also used by the RTRs. Assessments occurred three times a week (Monday, Wednesday and Friday) from the start of each patient's radiation treatment and subsequently on a weekly basis after the completion of the radiation treatment course. These weekly assessments continued until the skin reaction had resolved or for up to four weeks, whichever was the sooner.
Table 2.1 Modified Radiation-Induced Skin Reaction Assessment Scale (RISRAS)[71]

<table>
<thead>
<tr>
<th>RISRAS (total scores between 0 and 36)(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Researcher Component (total scores between 0 and 24)</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Erythema (E)</th>
<th>0</th>
<th>Normal skin</th>
<th>1</th>
<th>Dusky pink</th>
<th>2</th>
<th>Dull red</th>
<th>3</th>
<th>Brilliant red</th>
<th>4</th>
<th>Deep red-purple</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry Desquamation (DD)</td>
<td>0</td>
<td>Normal skin</td>
<td>1</td>
<td>(&lt;25%)(^b)</td>
<td>2</td>
<td>(25%-50%)</td>
<td>3</td>
<td>(50%-75%)</td>
<td>4</td>
<td>(&gt;75%)</td>
</tr>
<tr>
<td>Moist Desquamation (MD)</td>
<td>0</td>
<td>Normal skin</td>
<td>1.5</td>
<td>(&lt;25%)</td>
<td>3.0</td>
<td>(25%-50%)</td>
<td>4.5</td>
<td>(50%-75%)</td>
<td>6</td>
<td>(&gt;75%)</td>
</tr>
<tr>
<td>Necrosis (N)</td>
<td>0</td>
<td>Normal skin</td>
<td>2.5</td>
<td>(&lt;25%)</td>
<td>5.0</td>
<td>(25%-50%)</td>
<td>7.5</td>
<td>(50%-75%)</td>
<td>10</td>
<td>(&gt;75%)</td>
</tr>
</tbody>
</table>

| **Patient Component (total scores between 0 and 12)** |

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Not at all</th>
<th>A little</th>
<th>Quite a bit</th>
<th>Very much</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is your skin in the treatment area tender, uncomfortable or painful?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Does your skin in the treatment area itch?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Do you feel any burning sensation on your skin in the treatment area?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Have your skin reactions and/or your symptoms affected your day to day activities?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

\(^a\) Individual scores for each item are added up to give a total score for the researcher and patient components of the scale. Adding the researcher and patient component scores together gives the total combined RISRAS score.

\(^b\) Percentage of surface area of affected skin.

Adapted from MacBride et al [74]

Table 2.2 Radiation Therapy Oncology Group (RTOG) Toxicity Grading [72].

<table>
<thead>
<tr>
<th>RTOG Acute Radiation Morbidity: Skin</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicular, faint or dull erythema; epilation; dry desquamation; decreased sweating</td>
<td>Tender or bright erythema; patchy moist desquamation; moderate oedema</td>
<td>Confluent moist desquamation other than skin folds; pitting oedema</td>
<td>Ulceration; haemorrhage; necrosis</td>
</tr>
</tbody>
</table>
The RTRs were responsible for filling out both the researcher component of the RISRAS assessments, which quantified the outward appearance of the skin reaction, as well as the RTOG evaluations. All scores were recorded under the assessments section of MOSAIQ. Both RTRs had extensive experience in the assessment and treatment of radiation toxicities - and in particular skin toxicities - having been responsible for running the on-treatment review clinics for patients at the department for several years. This ensured consistency of scoring for both the RISRAS and the RTOG grading irrespective of which RTR was carrying out the assessment. Patients were asked by the RTRs to score each of the patient components of RISRAS for both the intervention arm and control area on each assessment visit. It should be noted here that there is no patient component in the RTOG assessment tool.

In the late 1970s, a World Health Organisation (WHO) initiative facilitated collaboration between several organisations to standardise the reporting of cancer treatment outcomes. Recommendations were developed for the grading of acute radiation-induced skin toxicities – the Common Toxicity Criteria [74]. The grading system was further refined in the 1980s by the Radiotherapy Oncology Group (RTOG) and the European Organisation for Research and Treatment of Cancer (EORTC). RTOG is a widely used assessment tool by health providers in practise and research for objective evaluation of radiation-induced skin toxicities. The RTOG grading provided the basis for the development of a further tool, RISRAS, for the assessment of radiation-induced skin toxicities.

RISRAS was developed and validated by Noble-Adams [75] with later modifications being carried out by MacBride et al [71]. As alluded to earlier, this scale is sensitive to subtle changes in reaction and therefore has a number of advantages [4,76] over the more commonly used RTOG [72] acute skin toxicity scales [72,77]. By including faint or dull erythema and dry desquamation together under a Grade 1 toxicity plus bright erythema and moist desquamation together as a Grade 2 toxicity, for example, the ability to instantly recognise and differentiate the severity of reactions from the recorded RTOG toxicity grades is lost. Porrock et al [24] did advocate the inclusion of Grade 2 subsets (Grade 2a - referred to by some authors as Grade 2.5 -
representing patchy moist desquamation) but this does little to increase the sensitivity of the scale overall.

RISRAS, on the other hand, clearly differentiates between erythema, dry desquamation and moist desquamation and is sensitive enough to indicate minor variations in skin reactions. In addition, unlike RTOG, RISRAS incorporates the more subjective experience of the patient. This holistic approach to toxicity assessment seeks to address the fact that for the most part healthcare professionals consistently underestimate the severity and impact of the symptoms of radiation-induced skin toxicities [78].

Patients experience considerable distress from these toxicities principally in the form of discomfort, pruritis and parasthesia. RISRAS seeks to recognise and record that fact.

**Moist Desquamation**

The presence of moist desquamation together with the date it occurred and its location (i.e. whether it was in the intervention and/or control arm) was recorded for each patient as part of the RISRAS assessment as well as RTOG scores and in free text within the patient notes section of MOSAIQ. On completion of their radiation treatment course, patients were advised that the skin assessments would continue weekly but were asked to contact the RTRs outside the scheduled weekly post-treatment assessments if they were concerned that their skin reactions had deteriorated.

The elapsed time to healing was recorded, having been pre-defined as the time taken for complete re-epithelisation - and therefore complete resolution - of any skin reactions.

**2.4.3. Dose Measurements**

As explained previously (Section 1.3.1), the total dose received by the skin is the single most important factor to affect skin reaction severity [4,5,13,16,19,27-29,31]. In order to ensure that differences in skin reaction severity between treatment and control arms was not due to differences in dose received, one of the medical physicists at the department used thermoluminescent dosimeters (TLDs) to calculate the dose received by both the skin covered by the Mepitel Film and the aqueous cream treated skin of all patients.
Placement of the TLDs in groups was based on results of a previous trial (Digelmann). For each mastectomy patient two groups of five TLDs (one in the centre and four at the corners) were placed in a grid formation on the superior medial and inferior lateral aspects of the chest wall. In addition, two TLDs were placed in the axilla - a total 12 TLDs per patient (see Figure 2.4). For patients who had undergone breast-sparing surgery two TLDs were placed in the axilla, two in the lateral inframammary fold, two in the medial inframammary fold and three on the superior medial aspect - a total of nine TLDs per patient (see Figure 2.4). Measurements for groups of TLDs were averaged per site (axilla and superior medial aspect for all patients, inframammary fold for breast patients and inferior lateral aspect for mastectomy patients).

Figure 2.4 Placement of TLDs The placement and arrangement of the TLDs ensured that the dose was measured in both the control and the trial halves of the treated area.
2.5. Exit questionnaires

All patients were given an exit questionnaire (Appendix E) when all skin reactions had resolved. This gave them the opportunity to comment on different aspects of taking part in the trial and using the Mepitel Film. Patients were asked to comment on whether they enjoyed taking part in the trial, whether they preferred the Mepitel Film or the aqueous cream, the advantages and disadvantages of using Mepitel Film and whether they would participate in future trials.

2.6. Trial timeline

The Mepitel Film trial timeline is displayed in Figure 2.5. Breast cancer patients requiring radiation therapy were identified in MOSAIQ by the RTRs at the time of patient referral. Their eligibility was assessed by checking the information contained in the Patient Managament System as well as by looking on iSoft Clinical Intranet, the department’s electronic clinical notes system. Once eligibility had been established and the patient’s appointment for their first specialist assessment and CT planning scan had been organised, a participant information sheet (Appendix A) was placed in the patient’s treatment folder.

Eligible patients were given a brief outline of the trial by the radiation oncologist at their FSA. This was also the time at which they signed their informed consent form for undergoing radiation treatment. However, it was at the planning CT scan, which occurred either on the same day as, or one day later than, the first specialist assessment, that a comprehensive discussion about the trial was inititated with all eligible patients by the CT radiation therapists. The offer was made to the patient for their family or other support person to be involved in the dialogue if they so wished. Included in this conversation was in-depth information about the departmental skincare advice. This discussion was augmented by written information about the trial in the form of the participant information sheet (Appendix A) which the patient then took home with them. In the intervening three to four weeks until the start of radiation treatment, the patient would have the opportunity to re-read the trial information and consider whether they would choose to participate or not. The week before the patient was due to start their treatment one of the RTRs would contact
them for further discussion about the trial, offering an additional opportunity to answer any questions about participation that the patient or their family/support network may have.

On the day of their first radiation treatment, eligible patients met with the RTRs immediately before treatment and informed consent was sought to join the trial. As soon as consent was given, a randomisation form (Appendix C) was filled in by the RTR and emailed to the Principal Investigator. The randomisation was carried out immediately and returned to the RTR. The initial skin assessment was completed following which the medial and lateral halves of the breast/chest wall treatment area were demarcated. Mepitel Film was applied as per the randomisation with aqueous cream being applied to the other half, the relative positions being recorded photographically. The digital photographs were imported to MOSAIQ for future reference. Patients then proceeded to have their first treatment.

Patients were reviewed three times a week throughout their entire treatment course by one of the RTRs during which time their skin was checked and RISRAS/RTOG assessments carried out. Any skin reactions were recorded photographically, again being uploaded to MOSAIQ, and if moist desquamation occurred departmental protocol was followed and Mepilex Lite used. The patients emotional/psychosocial well-being was also considered at each of these review sessions and any necessary actions taken.

The skin dose measurements using TLDs were done during the final 10 days of treatment for all patients. This time had been selected quite deliberately in order to allow our patients sufficient time to become familiar with the treatment process before adding in an extra procedure and an additional person in the guise of the medical physicist. The placement of the TLDs was again recorded photographically and uploaded to MOSAIQ.

Once the treatment course was complete follow-up assessments began. These occurred on a weekly basis for up to four weeks following treatment completion or until all reactions had completely resolved. The RTRs continued recording the skin reactions as before using both RISRAS and RTOG. Improvement and resolution was again recorded photographically and uploaded into MOSAIQ. Importantly, patients were asked to contact the RTRs outside the
scheduled weekly post-treatment assessments if they were concerned that their skin reactions had deteriorated.

Figure 2.5 Mepitel Film trial timeline.
2.7. Data Collection and Statistical Analysis

The RTRs used the electronic patient management system, MOSAIQ, together with the SDHB's electronic clinical records system, iSoft Clinical Intranet, to identify eligible patients who could potentially be included in the trial. RISRAS scores and participant characteristics were entered into Excel work sheets (Microsoft v 2010; Redmond Campus, Redmond, Washington, USA) which were used to calculate averages, standard deviations and standard errors as reported in the results section. SPSS 15.0 (IBM, Chicago, IL) was used for all the statistical analyses unless otherwise noted. The statistical significance between differences in Mepitel Film and control RISRAS scores was determined by student two-tailed paired Ttest. P<0.05 was considered statistically significant. Pearson Correlational analysis was performed to determine if there was a significant correlation between skin reaction severity on the one hand and BMI or breast separation on the other.

2.8. Funding

The salary of the Principal Investigator (Dr Patries Herst) was paid by the University of Otago. The salaries of the two radiation therapy researchers (Annie Sutherland and Noelle Bennett) were paid by the Southern District Health Board. Fees for the Bachelor of Radiation Therapy (Honours) programme were funded by the DROC's Continuing Professional Development fund and two scholarships from the New Zealand Breast Cancer Foundation.

The Mepitel Film dressings were supplied free of charge by Mölnlycke Health Care AB (Gothenburg, Sweden). There were no known conflicts of interest between research staff at the DROC or University of Otago and Mölnlycke Health Care AB.
3. Results

3.1. Patient Demographics

The various demographic, disease and treatment associated variables for this 20 patient cohort are shown in Table 3.1.

*Table 3.1. Patient demographics (n=20).*

<table>
<thead>
<tr>
<th>Patient Cohort</th>
<th>Total n (%)</th>
<th>Mastectomy</th>
<th>Non-Mastectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Completed</strong></td>
<td>20 (100)</td>
<td>10 (100)</td>
<td>10 (100)</td>
</tr>
<tr>
<td><strong>Randomisation</strong> (medial)</td>
<td>20 (50)</td>
<td>10 (100)</td>
<td>10 (100)</td>
</tr>
<tr>
<td><strong>Sex</strong> (F)</td>
<td>20 (100)</td>
<td>10 (100)</td>
<td>10 (100)</td>
</tr>
<tr>
<td><strong>Average age</strong> (y) (range)</td>
<td>60.3 (30-80)</td>
<td>61 (47-77)</td>
<td>59.6 (30-80)</td>
</tr>
<tr>
<td><strong>BMI</strong> (Ave, range)</td>
<td>25.2 (19.6-37.4)</td>
<td>24.5 (19.6-28.4)</td>
<td>25.8 (20-37.4)</td>
</tr>
<tr>
<td><strong>Separation</strong> (mm) (Ave,(range)</td>
<td>191.9 (158-245)</td>
<td>191.5 (182-211)</td>
<td>192.2 (158-245)</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NZ European</td>
<td>19 (95%)</td>
<td>9 (90%)</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>NZ Maori</td>
<td>1 (5%)</td>
<td>1 (10%)</td>
<td></td>
</tr>
<tr>
<td><strong>Disease Stage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DCIS</td>
<td>2 (10%)</td>
<td>2 (10%)</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>5 (25%)</td>
<td>1 (10%)</td>
<td>4 (40%)</td>
</tr>
<tr>
<td>II</td>
<td>6 (30%)</td>
<td>3 (30%)</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>III</td>
<td>7 (35%)</td>
<td>6 (60%)</td>
<td>1 (10%)</td>
</tr>
<tr>
<td><strong>Radiation Therapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50Gy/25#</td>
<td>13 (65%)</td>
<td>5 (50%)</td>
<td>8 (80%)</td>
</tr>
<tr>
<td>40Gy/15#</td>
<td>7 (35%)</td>
<td>5 (50%)</td>
<td>2 (20%)</td>
</tr>
<tr>
<td><strong>Boost</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>14 (70%)</td>
<td>8 (80%)</td>
<td>6 (60%)</td>
</tr>
<tr>
<td>9Gy/3#</td>
<td>6 (30%)</td>
<td>2 (20%)</td>
<td>4 (40%)</td>
</tr>
<tr>
<td><strong>Bolus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2 (10%)</td>
<td>2 (20%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>18 (90%)</td>
<td>8 (80%)</td>
<td>10 (100%)</td>
</tr>
<tr>
<td><strong>Chemotherapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>11 (55%)</td>
<td>7 (80%)</td>
<td>8 (80%)</td>
</tr>
<tr>
<td>Pre-RT</td>
<td>9 (45%)</td>
<td>3 (30%)</td>
<td>2 (20%)</td>
</tr>
<tr>
<td><strong>Fitzpatrick Skin Type</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>7 (35%)</td>
<td>4 (40%)</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>III</td>
<td>12 (60%)</td>
<td>6 (60%)</td>
<td>6 (60%)</td>
</tr>
<tr>
<td>IV</td>
<td>1 (5%)</td>
<td>1 (10%)</td>
<td></td>
</tr>
<tr>
<td><strong>Smoker</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>18 (90%)</td>
<td>9 (90%)</td>
<td>9 (90%)</td>
</tr>
<tr>
<td>Yes</td>
<td>2 (10%)</td>
<td>1 (10%)</td>
<td>1 (10%)</td>
</tr>
</tbody>
</table>
This thesis analyses the skin reaction severity results from a 20 patient cohort made up of the first 10 mastectomy patients and the first 10 non-mastectomy patients that enrolled in the 80 patient trial.

All patients were in the cohort were female with an average age of 60.3 years (range: 30-80) with a BMI of 25.2 (range: 19.6-37.4) and a breast separation of 191.9 mm (range: 158-245). Only one mastectomy patient identified as Maori, whilst all other patients were NZ-European. All patients were treated with a dose rate of 600cGy/min, and a dose of 50 Gy in 25 fractions over five weeks, or 40 Gy in 15 fractions over three weeks, plus or minus a boost to the tumour bed of 9 Gy in three fractions over three days.

At the initial skin assessment previous and current sun exposure, smoking, alcohol use, breast size, BMI and co-morbidities such as diabetes were recorded (Appendix D). Skin type was assessed using the Fitzpatrick skin type scale [73]. Because 19 patients were skin type II or III with only one patient having a skin type IV, a correlational analysis between skin type and skin reaction severity was not conducted. Similarly the smoking cohort (n=2) was too small to do a correlational analysis. Pearson Correlation analysis revealed a positive correlation between BMI and breast separation (Pearson Correlation 0.861) which was statistically significant (p=0.01). In contrast, BMI and breast separation were not correlated with skin reaction severity (measured by RISRAS) with p values of 0.667 and 0.259 respectively (Pearson Correlation).
3.2. Dosimetric Assessments

Total dose to the skin is arguably the biggest contributing factor to skin reaction severity. Our medical physicist measured the dose to the different locations on the breast, using thermoluminescent dosimeters (TLDs) (see Figure 2.4 for different locations). Tables 3.2 and 3.3 report the average doses to Mepitel Film and control area skin at these different locations. There was no statistically significant difference for any of the locations (p>0.05), which indicates that the differences in skin reaction severity were not likely to be due to differences in dose received by the skin covered in Mepitel Film and the skin treated with aqueous cream.

Table 3.2. Dose received by Mepitel Film and Control Cream skin areas at different locations for mastectomy patients.

<table>
<thead>
<tr>
<th>Location</th>
<th>Axilla</th>
<th>Lateral Inf</th>
<th>Superiot Med</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mepitel</td>
<td>Control</td>
<td>Mepitel</td>
</tr>
<tr>
<td>average</td>
<td>35.7</td>
<td>35.1</td>
<td>34.6</td>
</tr>
<tr>
<td>SEM</td>
<td>1.9</td>
<td>1.8</td>
<td>1.1</td>
</tr>
<tr>
<td>p-values*</td>
<td>0.930</td>
<td>0.752</td>
<td>0.488</td>
</tr>
</tbody>
</table>

*paired 2-tailed Ttest

Table 3.3. Dose received by Mepitel Film and Control Cream skin areas at different locations for non-mastectomy patients.

<table>
<thead>
<tr>
<th>Location</th>
<th>Axilla</th>
<th>IF</th>
<th>Midline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mepitel</td>
<td>Control</td>
<td>Mepitel</td>
</tr>
<tr>
<td>average</td>
<td>31.7</td>
<td>32.4</td>
<td>33.1</td>
</tr>
<tr>
<td>SEM</td>
<td>2.2</td>
<td>1.7</td>
<td>2.0</td>
</tr>
<tr>
<td>p-values*</td>
<td>0.779</td>
<td>0.521</td>
<td>0.435</td>
</tr>
</tbody>
</table>

*paired 2-tailed Ttest
3.3. **RISRAS Analysis**

A comparison of RISRAS scores (researcher, patients and combined components: § 2.3.1 Table 2.1) between the Mepitel Film and the aqueous cream areas showed that Mepitel Film decreased the skin reaction severity in both mastectomy patients (Figure 3.1.A), non-mastectomy patients (Figure 3.1.B) and in the combined cohort (Figure 3.1.C).

![Figure 3.1](image)

*Figure 3.1. Average RISRAS scores of 10 mastectomy patients (A), 10 non-mastectomy patients (B) and the entire 20 patient cohort (C). RISRAS Scores are broken down into “Combined”, “Researcher” and “Patient” components and presented as mean values ± SEM of skin patches.*
Table 3.2 reports the % decrease in skin reaction severity caused by covering the skin with Mepitel Film rather than with aqueous cream as well as the average values and SEM. A student two-tailed paired T test was used to determine whether the differences in average RISRAS scores were significant and the p values are also displayed in Table 3.2. All differences were statistically significant but for the patient scores in the non-mastectomy patient cohort (n=10), which was 0.062.

**Table 3.4. Averages, SEM of RISRAS scores (combined, researcher and patient components) and percentage decrease in skin reaction severity of skin areas covered with Mepitel Film and aqueous cream in mastectomy patients (n=10), non-mastectomy patients (n=10) and total cohort (n=20).**

<table>
<thead>
<tr>
<th></th>
<th>Mepitel</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RISRAS</strong></td>
<td>ave</td>
<td>SEM</td>
</tr>
<tr>
<td><strong>Mastectomy Patients (n=10)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>0.22</td>
<td>0.06</td>
</tr>
<tr>
<td>Researcher</td>
<td>0.18</td>
<td>0.05</td>
</tr>
<tr>
<td>Patient</td>
<td>0.04</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Non-Mastectomy Patients (n=10)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>0.34</td>
<td>0.16</td>
</tr>
<tr>
<td>Researcher</td>
<td>0.26</td>
<td>0.12</td>
</tr>
<tr>
<td>Patient</td>
<td>0.08</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Entire Cohort (n=20)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>0.28</td>
<td>0.09</td>
</tr>
<tr>
<td>Researcher</td>
<td>0.22</td>
<td>0.06</td>
</tr>
<tr>
<td>Patient</td>
<td>0.06</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*two-tailed paired T test, p<0.05 is considered statistically significant.

Moist desquamation

Our previous trial showed that although there was decrease in RISRAS, there was no change in incidence of moist desquamation [12]. However, in this prevention trial there was no moist desquamation under the Mepitel Film, whereas a total of eight out of total cohort of 20 patients (40%) developed moist desquamation in their control patches. Of these eight patients, five patients had had a mastectomy and three patients had not had a mastectomy. Interestingly, four of the five mastectomy patients developed moist desquamation in their
axilla, and one patient developed moist desquamation in the superior middle aspect of the chestwall. Of the three non-mastectomy patients, one developed moist desquamation in the inframammary fold, one in the axilla and one patient developed moist desquamation in both the axilla and the inframammary fold.

**Table 3.5** Incidence (%) of moist desquamation (MD) in skin areas treated with control cream in mastectomy patients (n=10), non-mastectomy patients (n=10) and the entire cohort (n=20).

<table>
<thead>
<tr>
<th></th>
<th># patients</th>
<th>MD</th>
<th>no MD</th>
<th>% MD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mastectomy patients</td>
<td>10</td>
<td>5</td>
<td>5</td>
<td>50</td>
</tr>
<tr>
<td>Non-Mastectomy patients</td>
<td>10</td>
<td>3</td>
<td>7</td>
<td>30</td>
</tr>
<tr>
<td>Entire Cohort</td>
<td>20</td>
<td>8</td>
<td>12</td>
<td>40</td>
</tr>
</tbody>
</table>
3.4. RTOG analysis

Several trials that have investigated the effect of various topical agents on skin reaction severity have used the RTOG scoring system [58,62–67,69–71,79,80]. In order to compare their results with those of our trial, we also scored skin reaction severity using RTOG. The results are presented in Table 3.3 and show that none of the skin patches covered with Mepitel Film developed moist desquamation (RTOG II or RTOG III). In contrast the control patches of 8 patients (5 mastectomy patients and 3 non-mastectomy patients) developed moist desquamation (40%). Almost a third (30%) of patients did not have any skin reactions underneath the Mepitel Film, whereas all of the control patches developed some form of skin reaction. The RTOG scores mirrored the researcher component of the RISRAS scores.

Table 3.6. RTOG scores of skin covered in Mepitel Film and control cream of mastectomy patients (n=10), non-mastectomy patients (n=10) and the entire cohort (n=20).

<table>
<thead>
<tr>
<th>RTOG scores (%)</th>
<th>Mastectomy Patients (n=10)</th>
<th>Non-Mastectomy Patients (n=10)</th>
<th>Entire Cohort (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>I</td>
<td>IIA</td>
</tr>
<tr>
<td>Mepitel</td>
<td>2</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Control</td>
<td>0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Mepitel</td>
<td>4</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Control</td>
<td>0</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Mepitel</td>
<td>6</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Control</td>
<td>0</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>
3.5. Patient exit questionnaires

Our previous trial showed that when patients were asked about their experience using Mepilex Lite generally they reported it as a positive experience saying that the Mepilex Lite reduced symptoms of pain and irritation and afforded comfort during day-to-day activities by reducing friction from clothing and seatbelts [12]. Patients in the current trial were given the same questionnaire (Appendix E). Answers to each of the five questions were recorded and a thematic analysis of the answers was conducted (Table 3.7).

Table 3.7. Thematic analysis of exit questionnaires (n=20).

<table>
<thead>
<tr>
<th>Questions</th>
<th>Themes</th>
<th>Code</th>
<th># patients</th>
<th>% patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Taking part in trial is good experience?</td>
<td>yes</td>
<td>20</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Altruism</td>
<td>1.1</td>
<td>5</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>Better care/</td>
<td>1.2</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Continued care</td>
<td></td>
<td></td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>More information</td>
<td>1.3</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Staff interaction</td>
<td>1.5</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>2. Prefer Mepitel Film over cream</td>
<td>yes</td>
<td>19</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>3. Advantages of Mepitel Film</td>
<td>Outward Signs</td>
<td>2.1</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>Redness</td>
<td>2.1.1</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>Subjective Symptoms</td>
<td>2.2</td>
<td>9</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>Itchiness</td>
<td>2.2.1</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Pain</td>
<td>2.2.2</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Burning</td>
<td>2.2.3</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Ease of Use</td>
<td>2.3</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Comfort/soothing</td>
<td>2.4</td>
<td>14</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>Protection</td>
<td>2.5</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Nice to wear in shower</td>
<td>2.6</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>4. Disadvantages of Mepitel Film</td>
<td>Rolls up at edges</td>
<td>3.1</td>
<td>5</td>
<td>25</td>
</tr>
<tr>
<td>5. Would take part in a trial again?</td>
<td>yes</td>
<td>19</td>
<td>95</td>
<td></td>
</tr>
</tbody>
</table>
All of the 20 patients reported that taking part in the trial was a positive experience for them. Five patients took part for altruistic reasons, two patients thought they would receive better care and two patients felt they were given more information than they would have been given otherwise. All but one of the patients preferred Mepitel Film over the standard cream. They reported that the skin underneath the Mepitel Film was less red (8 patients), less itchy (2 patients) experienced less pain (4 patients) and less burning (3 patients). To 14 patients the film felt comforting to the skin and 2 patients mentioned that their skin felt better protected. In addition 4 patients mentioned they enjoyed being able to wear the film in the shower. Two patients wrote that they felt re-assured because of their skin was evaluated for four weeks after completion of radiation therapy.
4. Discussion

The overarching aim of this randomized controlled clinical trial was to evaluate the effect of Mepitel Film used prophylactically on skin reaction severity in breast cancer patients. This thesis has analysed the results for a cohort of 20 patients, made up of the first 10 mastectomy patient and the first 10 non-mastectomy patients that took part in the 80 patient trial, the results of which have now been published [81].

Key findings

1. Mepitel Film significantly decreased the severity of radiation-induced skin reactions

Mepitel Film decreased overall skin reaction severity by more than 90% in the entire non-mastectomy patient cohort when used prophylactically.

The TLD results indicated that whatever changes in the severity of the radiation-induced skin reactions were seen, these were unlikely to be due to differences in dose between Mepitel Film covered skin and skin treated with aqueous cream.

The results of the 20 patient cohort compare favourably with two previous management trials using Mepilex Lite where the severity of the radiation-induced skin reaction was reduced by 30% [11] and 40% [12] respectively. Another barrier product, Cavilon No-Sting barrier film, was initially applied as a spray-on film and this trial showed a significant reduction in the severity of skin reactions. However a further larger trial with the product in a cream formula failed to validate these findings [69,70].

Recent studies and reviews indicate that most interventions have targeted moisturising agents, anti-inflammatory agents and wound-healing agents [5,6,13,48,68,82–84]. To date, the results from these agents have been less impressive than the results with Mepitel Film. Protecting the irradiated skin from mechanical friction throughout the course of treatment may be a good alternative to other strategies [68–70].
2. **Mepitel Film prevented the occurrence of moist desquamation**

The most significant clinical finding was that Mepitel Film prevented the occurrence of moist desquamation. To date, no trial has ever demonstrated that an intervention prevented MD from developing. A recent meta-analysis by Zhang and colleagues (2013) and a systematic review by Chan and colleagues (2014) highlight this [82,83]. The previous trial using Mepilex Lite (another soft silicone dressing from the same company) to manage existing skin reactions (erythema), did not find a significant decrease in moist desquamation rates in 74 patients [12]. The current trial has used Mepitel Film in a prophylactic setting. Based on our previous experience with these dressings in Dunedin Hospital, Mepilex Lite has limitations as it does not adhere to compound curves such as the axilla or inframmary fold. Mepilex Lite is also not waterproof and does not stick to perspiring skin during hot flushes or everyday activities, thus cannot be used prophylactically but may however, play a future role in managing moist desquamation. Mepitel Film on the other hand adheres well, is transparent, fully breathable, can be left on for many days at a time and has no clinically significant bolus effect.

The results of the larger 80 patient cohort have validated these findings with a >90% decrease in skin reaction severity and an absence of moist desquamation in Mepitel Film covered skin [81]. However, there were incidents of moist desquamation occurrence in the control areas. All but one of these patches of moist desquamation occurred in the inframmary and axillary skinfolds where there is an increase in friction, moisture, and warmth, with accompanying reduced aeration [4,7,13,23,56]. Interestingly none of the inframmary and axillary skin folds covered in Mepitel Film developed moist desquamation, suggesting that the Film prevented friction of the radiation-damaged skin in these areas.

One patient developed moist desquamation on the superior sternum where previous sun damage had occurred. Sensitisation to radiation damage by previous sun exposure has previously been reported by Ryan et al [13,23,33].

Heavier patients with a larger breast size may have increased severity of skin toxicity as the potential to heal may be compromised by reduced vascularity in the adipose tissue
[39,85]. However our cohort (n=20) was too small to show a correlation between BMI, and breast separation on one side and skin reaction severity on the other side.

3. **Mepitel Film was well tolerated by the patients.**

Similar to previous trials [11,12,71,81], our patients also tolerated Mepitel Film well. The results of the exit questionnaire showed that all of our patients preferred the Film over the cream. Some patients felt that the skin underneath the Mepitel Film was less red less itchy and less painful. Almost three quarters of the patients in this cohort reported that the Mepitel Film felt comforting on their skin.

**Adverse events**

There were no adverse effects or events during this trial with Mepitel Film. The Mepitel Film did not induce any allergic skin reaction for any of the trial participants.
4.1. **Strengths and Limitations**

As with all clinical studies this trial had its strengths and its limitations.

**Strengths**

- The patients for this trial were randomised, minimising selection bias.
- This was an intra-patient controlled trial, with patients acting as their own controls thereby minimising potential confounding patient-specific factors.
- Use of a sensitive skin reaction measure (RISRAS) as well as the more commonly used RTOG. RTOG scores only the visible signs of the skin reactions (see Table 2.2). Using a widely used scoring system such as RTOG allows the results of different trials to be compared and should be incorporated in trials that use scoring scales that are less commonly used such as RISRAS. RISRAS is a more sensitive scale and measures subtle changes in skin reaction; in addition, it contains a patient component that records skin reactions from the patient’s perspective. Research into management of skin reactions is carried out with the intent of increasing patient wellness and health-related quality of life. Therefore using a scoring system that measures skin reaction severity as the patient experiences it, is very valuable. In the cohort analysed for this thesis as well as in the larger trial cohort [81], the results obtained using RTOG and RISRAS were very similar, both reported the same number of patients with moist desquamation.

**Limitations**

- **Lack of blinding**

  The most important limitation of this trial was the fact that we were unable to blind the assessors (patient and research RT). It was impossible to blind the assessors due to the obvious difference between Mepitel Film and aqueous cream. The Mepitel Film stayed in situ at all times and patients in the trial were interested to observe their own skin changes in both the intervention arm and the control area. To remove the Film before each assessment could undermine the effect of the Film which was mediated by leaving the Film on the skin for long periods of time without disturbing the skin.
• **Small Participant numbers**
  For this thesis the results of only 20 patients were analysed. It is interesting to note that even for such a small number of participants, the lack of moist desquamation and reduction in skin reaction severity was still statistically significant (with the exception of the RISRAS patient component of non-mastectomy patients). The larger trial was powered to 80% to discover a difference in moist desquamation rates from 50% to 25% with a p value of 0.05.

• **Subjective measures**
  An intrinsic limitation of both RISRAS and RTOG is the potential for researcher and patient bias, particularly as they were not blinded to which skin areas were covered in Film. It is possible that the excitement and enthusiasm of both patients and researchers for the new dressing could have led to an over estimation of the effect of the Film. However, although the severity of erythema can be open to interpretation, the presence or absence of moist desquamation is an objective measure. There are several objective skin assessment techniques, such as reflectance spectrometry, which measures skin redness [79,80,86,87] and photographic analysis [11,88]. However, we were mainly interested in moist desquamation although we did take several digital photographs of the skin of each patient at different times. This was mainly to record the presence of moist desquamation.

4.2. **Recommendations for future research**
  Future trials should use RISRAS as well as RTOG or another commonly used skin reaction severity scoring system, so that results can be compared across studies. The patients in our trial did not receive a skin dose of more than 40Gy. It is possible that patients receiving a higher skin dose or patients who receive chemo-radiation with cisplatin, such as head and neck cancer patients, may also benefit from prophylactic use of the Film.
4.3. Conclusions

Breast cancer is the most common malignancy for women in New Zealand and the majority will receive radiation therapy as part of their treatment regimen. Radiation-induced moist desquamation occurs in 45-60% of breast cancer patients and compromises patient quality of life. There is currently no solid evidence-based standard treatment to prevent or manage these reactions.

We showed in two previous skin trials that Mepilex Lite decreased skin reaction severity by 30-40% but it did not affect moist desquamation rates. The current unblinded randomized controlled trial investigated the effect of the prophylactic use of another soft silicone dressing, Mepitel Film, on moist desquamation rates and skin reaction severity. This thesis analysed the results of the first 10 mastectomy and first 10 non-mastectomy patients of a larger 80 patient trial. The results from this smaller cohort showed that Mepitel Film dressings reduced the severity of skin reactions by more than 90% and prevented the occurrence of moist desquamation. These results are clinically highly significant and we are currently in the process of modifying our departmental Skincare Guidelines (Appendix F) to include the prophylactic use of Mepitel Film to cover the entire treatment area of all our breast cancer patients.

Reduction in the severity of skin toxicity will improve the quality of life for this population of patients as they will be able to maintain their normal day to day activities in the home, at work and with sport and leisure pursuits. The findings from this study in addition to the results of the two previous skin trials have resulted in a change of skincare practice in other radiation therapy departments in New Zealand.
5. References


14. Beroukas Ernestos, Pandis Nikolaos, Giannoukakos Koulis, Rizou Eleni, Beroukas Konstantinos, Giatromanolaki Alexandra KM. Increased Chromosomal Radiosensitivity in


17. Princess T, Radiotherapy R, Team R. Managing Radiotherapy Induced Skin Reactions.


44. Halkett GKB, Kristjanson LJ, Lobb EA. “If we get too close to your bones they”ll go brittle”: women’s initial fears about radiotherapy for early breast cancer. Psychooncology. 2008 Oct;17(9):877–84.


Appendix A

Skin Reactions during Radiation Therapy

PARTICIPANT INFORMATION SHEET

You are invited to take part in a clinical trial which investigates the use of a specially designed thin film in preventing skin reactions which are normally experienced by patients who receive radiation therapy for breast cancer. All participation in this research is entirely voluntary and you are free to withdraw from the study or decline to answer any particular question or undergo assessment at any time. Please discuss your participation in this trial with family and whanau and take your time to decide whether you would like to take part in it.

1. Why are you doing this study?
Radiation therapy to the chest wall is given with the aim of getting rid of any remaining cancer cells in the area. Irradiation often causes skin reactions which can vary from a slight reddening of the skin to severe redness and itching (similar to sunburned skin). In extreme cases the skin may peel away in places and begin to weep. There is currently no best way to prevent or treat skin that has reacted to radiation therapy.

We have previously run two skin trials in this department that compared a silicone foam dressing with moisturising cream and we found that these dressings reduced the severity of the skin reactions. However, these dressings did not stay in the arm pit or underneath the breast very well and constantly needed replacing. We have since been using a thinner variety of these dressings, a type of see-through film, that is easy to shape around the breast and armpit. We have found that it will stay on for several days even when showering every day. We would like to study how well this film works in a clinical trial.

*This study compares the effect of Mepitel Film with that of a conventional moisturising cream on skin reactions in women receiving radiation therapy for breast cancer.*

2. Who will be recruited to this study?
All women who come to the department to receive radiation therapy for breast cancer will be approached with information about the trial by the research radiation therapist. However, only women who have not had previous radiation therapy to the chest and who do not have metastatic disease will be able to participate in the trial.

3. What does my participation in the study involve?
   - Once you have been accepted into the trial the area of your chest wall that needs to be treated will be visually divided into two halves. One half will be covered in Film by the research radiation therapist (RT), whilst we will ask you to put the moisturising cream, which we will supply you with, on the other half.
During the first week of your treatment, we will measure how much radiation your skin will receive each day. We will do this by placing small flat squares directly on your skin (see Figure 1 below). These small squares contain special equipment that measures the exact amount of radiation received by your skin during each treatment.

![Figure 1](image)

*Figure 1: The small white square on this finger nail is called a dosimeter and squares similar to this will be placed on your skin to measure how much radiation your skin receives each day.*

Three times a week the research RT will check your skin to see if it has reacted to the treatment and will record what she sees on an assessment form. The assessment form consists of a researcher part, which will be filled in by the research RT, and a patient part which we will ask you to fill in. This part will ask you to compare how your skin feels where the Film is with how it feels where the cream is.

After the completion of your radiation therapy course, we will ask you to come back once a week for up to four weeks so we can keep checking your skin (which is part of your normal hospital care) and we will also keep filling out the assessment forms. If you live out of town we can do this follow-up by phone possibly with the help of photographs.

4. Are there any risks to me if I participate in this study?

- Our experience with using the Film on patients so far has shown us that it is very comfortable to wear and makes the skin reactions less severe.

- In the unlikely event of an adverse reaction to the Film we will ask you to stop using it and we’ll treat the affected skin with the moisturising cream instead.

- On the other hand, if the uncovered area has a much more severe skin reaction than the area with the Film on, we will ask you to stop using the moisturising cream and will use the Film on that instead.

- In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue
the investigators. If you have any questions about ACC, contact your nearest ACC office or the investigator.

5. Are there any costs involved if I participate in this study?
There are no costs involved if you participate in this study.

6. What will you do with the information?
Information that may identify you, such as your name, address and date of birth, will be kept together with your medical records, skin reactions and the exit questionnaire in your patient file in the oncology department.

The Principal Investigator, Dr Patries Herst, who will collate and analyse all the information will receive your information in a form that is no longer linked to your name, address or date of birth. You will be given a special trial number which will link all your trial information together.

This ‘de-identified’ information will be stored in a lockable metal filing cabinet in the office of the Principal Investigator at the University of Otago, Wellington for a period of 10 years. Only the research RTs will be able to link the de-identified data to patient files.

When the study is completed we will collate and analyse the information from all the participants in the study. This will tell us whether the Film is better than the moisturising cream in preventing skin reactions. If the Film is better we aim to conduct a larger trial and we would like to incorporate the data from this trial into that larger future study.

We anticipate that this will lead to a standardised treatment for radiation-induced skin reactions in New Zealand.

Reporting

- We will report on the results of this study in scientific reports and publications but NO material will be published which can identify you personally.

- You will be informed of the results of the study by letter from the Principal Investigator, Dr Patries Herst.

- You may be asked if we can use photos of parts of your chest wall to illustrate our findings. The photos will only show a small part of your chest area and no other parts of your body. You will in no way be able to be identified by these photos. The photo below gives you an idea of the area of the chest that is likely to be photographed.

![Figure 2: This is an example of a photo taken of one of our patients from a previous skin trial.](image)
7. Do I have to take part in this study?
No, there is absolutely no pressure on you to take part in this study.

8. Can I withdraw from the study if I change my mind?
If you do agree to take part, you are free to withdraw from the study at anytime without having to give any reason and this will in no way affect your future health care.
If you wish to withdraw, please contact the research RTs and let them know that you have decided to withdraw. We will then make sure that all information and data that have been collected about you will be deleted from our database.

9. What if I have more questions or concerns about this study?
If you have any questions or concerns about your rights as a participant in this research study you can contact an independent health and disability advocate. This is a free service provided under the Health and Disability Commissioner Act. Local (03) 479 0265; Telephone: (NZ wide) 0800 555 050; Free Fax (NZ wide): 0800 2787 7078 (0800 2 SUPPORT); Email (NZ wide): advocacy@hdc.org.nz. If there is a specific Māori issue/concern please contact Linda Orennell at 0800 37 77 661.

If you have any questions or concerns about your skin reactions or any other aspects of this study, at any time, please call the research RTs, Noelle Bennett or Annie Sutherland (telephone 03 474 7047).

This study has been approved by the University of Otago Human Ethics Committee. If you have any concerns about the ethical conduct of the research you may contact the Committee through the Human Ethics Committee Administrator (ph 03 479 8256). Any issues you raise will be treated in confidence and investigated and you will be informed of the outcome.
Skin Reactions during Radiation Therapy

INFORMED CONSENT

This form is to obtain your agreement to participate in our study which aims to find out whether Mepitel Film decreases skin reactions caused by radiation treatment.

REQUEST FOR INTERPRETER

<table>
<thead>
<tr>
<th>Language</th>
<th>Request</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>English</td>
<td>I wish to have an interpreter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deaf</td>
<td>NZ Sign Language interpreter.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maori</td>
<td>E hiahiaanaahaukitetahikaiwhakamaori/kaiwhaka pakeha korero</td>
<td>Ae</td>
<td>Kao</td>
</tr>
<tr>
<td>CookIsland</td>
<td>Ka inangaro au i tetai tangata uri reo</td>
<td>Ae</td>
<td>Kare</td>
</tr>
<tr>
<td>Fijian</td>
<td>Au gadreva me dua e vakadewa vosa vei au</td>
<td>Io</td>
<td>Sega</td>
</tr>
<tr>
<td>Niuean</td>
<td>Fia manako au ke fakaaoga e taha tagata</td>
<td>E</td>
<td>Nakai</td>
</tr>
<tr>
<td>Language</td>
<td>Sentence</td>
<td>Translation</td>
<td></td>
</tr>
<tr>
<td>----------</td>
<td>----------</td>
<td>-------------</td>
<td></td>
</tr>
<tr>
<td>Samoan</td>
<td>Ou te mana’oia i ai se fa’amatalaupu</td>
<td>Ioe Leai</td>
<td></td>
</tr>
<tr>
<td>Tokelaun</td>
<td>Ko au e fofoukihetinokafakaliliu te gaganaPeletaniakin a gagana o na motu o te Pahefika</td>
<td>Ioe Leai</td>
<td></td>
</tr>
<tr>
<td>Tongan</td>
<td>Oku oufiema’u ha fakatonulea</td>
<td>Io Ikai</td>
<td></td>
</tr>
</tbody>
</table>

**Informed Consent**

- I have read and I understand the information sheet dated October 2012 for volunteers taking part in the study designed to investigate whether Mepitel Film decreases the extent of radiation-induced skin reactions.
- I have had the opportunity to discuss this study with whanau and friends. I am satisfied with the answers I have been given.
- I understand that taking part in this study is voluntary (my choice), and that I may withdraw from the study at any time, and this will in no way affect my future health care.
- I understand that my participation in this study is confidential and that no material that could identify me will be used in any reports on this study.
- I understand that the treatment, or investigation, will be stopped if it should appear harmful to me.
- I have had time to consider whether to take part in the study.
- I know who to contact if I have any side effects from the study.
- I know who to contact if I have any questions about the methods used in this study or about the study in general.

**I would like to participate in this research study and I give consent to participate in the study assessment which includes:**

- A general skin-risk assessment by the research radiation therapist.

- Regular skin reaction assessments by the research radiation therapist, which will be carried out three times a week during treatment as well as once a week after the completion of treatment until the final check-up four weeks after treatment. For out of town patients, this can be done by phone with the possible use of photographs. The skin
assessment form has a patient part to be filled in by myself and a researcher part to be filled in by the research radiation therapist.

- Use of photographs that may be taken of parts of my chest wall for publication purposes as long as I can in not be identified from these photos.

- An exit questionnaire that will allow me to describe my experience in taking part in this trial and using the Film on my skin.

I consider my ethnicity to be:

- New Zealand European
- Māori
- Samoan
- Cook Islands Maori
- Tongan
- Niuean
- Chinese
- Indian
- Other (such as Dutch, Japanese, Tokelauan). Please state.

I, ....................................................... (full name) hereby consent to taking part in this study.

Date: __________________________

Signature: ______________________

Full names of researchers: ______________________

Contact phone number for researchers: ______________________
This study has been approved by the University of Otago Human Ethics Committee. If you have any concerns about the ethical conduct of the research you may contact the Committee through the Human Ethics Committee Administrator (ph 03 479 8256). Any issues you raise will be treated in confidence and investigated and you will be informed of the outcome.
Appendix C

Randomisation coversheet

Mepiltel Film for radiation-induced skin reactions trial

Date:
To: PatriesHerst
Email: patries.herst@otago.ac.nz
Phone: 04 385 5475

From: Annie Sutherland
Email: annie.sutherland@southerndhb.govt.nz
Phone: 03 474 7047

Randomisation (B)

Patient initials:

Patient date of birth:

Mepitel Film: Lateral

Medial

Patient randomisation number:

Randomisation date:

Randomisation completed by:

Signature:
### Appendix D

#### Initial assessment

<table>
<thead>
<tr>
<th>Patient no: B</th>
<th>Randomisation:</th>
<th>Medial</th>
<th>Lateral</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Personal construct

<table>
<thead>
<tr>
<th>Personal construct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Height (cm)</td>
</tr>
<tr>
<td>Weight (kg)</td>
</tr>
<tr>
<td>BMI</td>
</tr>
<tr>
<td>Bra size (cm)</td>
</tr>
<tr>
<td>Sepn</td>
</tr>
<tr>
<td>Nutritional status</td>
</tr>
</tbody>
</table>

#### Pre-disposing factors/co-morbidities

<table>
<thead>
<tr>
<th>Pre-disposing factors/co-morbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoker?</td>
</tr>
<tr>
<td>Alcohol/week?</td>
</tr>
<tr>
<td>Sun exposure?</td>
</tr>
<tr>
<td>Sun bed use?</td>
</tr>
<tr>
<td>Skin type (Fitzpatrick)</td>
</tr>
<tr>
<td>Diabetes?</td>
</tr>
<tr>
<td>High blood pressure?</td>
</tr>
<tr>
<td>If yes, type</td>
</tr>
<tr>
<td>If yes, on medication?</td>
</tr>
<tr>
<td>Allergies?</td>
</tr>
</tbody>
</table>

#### Medications list

#### Genetic construct

<table>
<thead>
<tr>
<th>Genetic construct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity</td>
</tr>
<tr>
<td>Family history of breast ca?</td>
</tr>
<tr>
<td>If yes, relatives affected</td>
</tr>
</tbody>
</table>

#### Day-to-day issues

<table>
<thead>
<tr>
<th>Day-to-day issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family at home</td>
</tr>
<tr>
<td>Out of town?</td>
</tr>
<tr>
<td>Still working?</td>
</tr>
<tr>
<td>Regular exercise?</td>
</tr>
<tr>
<td>Generally sleeps well?</td>
</tr>
<tr>
<td>Night sweats?</td>
</tr>
<tr>
<td>Appetite</td>
</tr>
<tr>
<td>Hydration</td>
</tr>
<tr>
<td>Bath/shower</td>
</tr>
<tr>
<td>-------------</td>
</tr>
<tr>
<td>Uses spa pool?</td>
</tr>
</tbody>
</table>

**Cancer construct**

<table>
<thead>
<tr>
<th>Breast affected</th>
<th>L</th>
<th>R</th>
</tr>
</thead>
</table>

**Diagnosis**

<table>
<thead>
<tr>
<th>Tumour site</th>
<th>Upper</th>
<th>Lower</th>
<th>Inner</th>
<th>Outer</th>
<th>Central</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Stage</th>
<th>0</th>
<th>IA</th>
<th>IIA</th>
<th>IIIA</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IB</td>
<td>IIB</td>
<td>IIIB</td>
<td></td>
<td>IIIC</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grade</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Size</th>
<th>mm</th>
</tr>
</thead>
</table>

**Receptor status**

<table>
<thead>
<tr>
<th>ER</th>
<th>+ve</th>
<th>-ve</th>
<th>strong</th>
<th>weak</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR</td>
<td>+ve</td>
<td>-ve</td>
<td>strong</td>
<td>weak</td>
</tr>
<tr>
<td>HER2</td>
<td>+ve</td>
<td>-ve</td>
<td>strong</td>
<td>weak</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infection/Seroma?</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>

**RT Construct**

<table>
<thead>
<tr>
<th>Starting date</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Starting day</td>
<td>Mon</td>
</tr>
<tr>
<td>Machine</td>
<td>iX</td>
</tr>
<tr>
<td>Prescription</td>
<td>50Gy/25#</td>
</tr>
<tr>
<td>Energy</td>
<td>6MV</td>
</tr>
<tr>
<td>Fields</td>
<td>Tangent</td>
</tr>
<tr>
<td>Bolus?</td>
<td>Yes</td>
</tr>
<tr>
<td>If yes, how much</td>
<td>0.5cm</td>
</tr>
<tr>
<td>Boost?</td>
<td>Yes</td>
</tr>
<tr>
<td>If yes, prescription</td>
<td>10Gy/5#</td>
</tr>
</tbody>
</table>

**Adjuvant therapy**

<table>
<thead>
<tr>
<th>Surgery?</th>
<th>Yes</th>
<th>No</th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>If yes, type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Axillary dissection</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sentinel node?</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chemotherapy</th>
<th>Yes</th>
<th>No</th>
<th>Pre</th>
<th>Post</th>
<th>Concurrent</th>
</tr>
</thead>
<tbody>
<tr>
<td>If yes, type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hormone therapy?</th>
<th>Yes</th>
<th>No</th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Alternative/complementary?</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Perceived risk</th>
<th>High</th>
<th>Medium</th>
<th>Low</th>
</tr>
</thead>
</table>

64
<table>
<thead>
<tr>
<th>BMI result</th>
<th>Underweight</th>
<th>Healthy</th>
<th>Overweight</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>NZ European</td>
<td>Less than 18.5</td>
<td>18.5 to 25</td>
<td>25 to 30</td>
<td>&gt;30</td>
</tr>
<tr>
<td>Maori/Pacific Islanders</td>
<td>Less than 18.5</td>
<td>18.5 to 26</td>
<td>26 to 32</td>
<td>&gt;32</td>
</tr>
</tbody>
</table>
# Fitzpatrick skin-type chart

## Patient no: B

### Randomisation: Medial

<table>
<thead>
<tr>
<th>Lateral</th>
<th>Genetic disposition</th>
<th>Eye colour</th>
<th>Hair colour</th>
<th>Skin colour</th>
<th>Freckles</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Light blue</td>
<td>Light blue</td>
<td>Sandy red</td>
<td>Reddish</td>
<td>Many</td>
</tr>
<tr>
<td>1</td>
<td>Light grey</td>
<td>Light grey</td>
<td>Blonde</td>
<td>Very pale</td>
<td>Several</td>
</tr>
<tr>
<td>2</td>
<td>Light green</td>
<td>Blue</td>
<td>Lt brown</td>
<td>Pale</td>
<td>Few</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>Blue</td>
<td>Dark blonde</td>
<td>Beige tint</td>
<td>Incidental</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>Dark brown</td>
<td>Black</td>
<td>Light brown</td>
<td>None</td>
</tr>
</tbody>
</table>

### Total score

#### Reaction to sun exposure

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Too much sun?</td>
<td>Sore, red, blister, peel</td>
<td>Blister then peel</td>
<td>Burn sometimes then peel</td>
<td>Rarely burn</td>
</tr>
<tr>
<td>Turn brown?</td>
<td>Not at all</td>
<td>Light colour tan</td>
<td>Reasonable tan</td>
<td>Tan very easily</td>
</tr>
<tr>
<td>Turn brown within several hours?</td>
<td>Never</td>
<td>Seldom</td>
<td>Sometimes</td>
<td>Often</td>
</tr>
<tr>
<td>Reaction of face to sun</td>
<td>V. sensitive</td>
<td>Sensitive</td>
<td>Normal</td>
<td>Very resistant</td>
</tr>
</tbody>
</table>

### Total score

#### Tanning habits

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last exposed to sun (or sunbed)?</td>
<td>&gt;3 months ago</td>
<td>2-3 months ago</td>
<td>1-2 months ago</td>
<td>&lt;1 month ago</td>
</tr>
<tr>
<td>Last exposed area to be treated?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Often</td>
</tr>
</tbody>
</table>

### Skin type score

<table>
<thead>
<tr>
<th>0-7</th>
<th>8-16</th>
<th>17-25</th>
<th>26-30</th>
<th>&gt;30</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>II</td>
<td>III</td>
<td>IV</td>
<td>V-VI</td>
</tr>
</tbody>
</table>

- Highly sensitive - always burns - never tans
- Very sun sensitive - burns easily - tans minimally
- Sun sensitive skin - sometimes burns - slowly tans light brown
- Minimally sun sensitive - burns minimally - tans mid brown
- Sun insensitive skin - rarely/never burns - deeply pigmented
Appendix E: Mepitel Film Trial Exit Questionnaire

1. Was taking part in this trial a positive experience for you?  
   Yes / No  
   Please add any comments you'd like to make below

2. Do you think the Mepitel Film was better than the cream for helping with your skin reactions?  
   Yes / No  
   Please add any comments you'd like to make below

3. What were the advantages of the Mepitel Film dressings for you - for example were they easy to use, comfortable, did they help with symptoms etc  
   Please write your comments below
4. What were the disadvantages of the Mepitel Film dressings for you - for example were they easy to use, comfortable, did they help with symptoms etc

Please write your comments below

5. Thinking about how you found taking part in this trial, would you be willing to take part in other clinical trials in the future?  
Yes / No

Please add any comments you’d like to make below

Would you like the results of this trial sent to you?  Yes / No

Thank you for taking part in this trial. This valuable research would not have been possible without your help.

Best wishes for the future.
Appendix F

Care of radiation-induced skin reactions
Departmental guidelines

A radiation oncology resource

Care of radiation-induced skin reactions
Authors: Noelle Bennett & Jo Tuaine. April 2011
SECTION 1 - General Information

Purpose
The purpose of this document is to provide a consistent framework for decision-making in the care of radiation-induced skin reactions. This framework has been developed by an interdisciplinary team from the Oncology Department in Dunedin.

Presently, there is inadequate evidence in the literature to recommend specific topical agents in the prevention or management of radiation skin reactions. Recommendations in this document are based on available literature, clinical expertise, theory and knowledge about moist wound healing.

Definition
Radiation skin reactions are a common side effect of radiation treatment. Stem cells in the skin’s basal layer are particularly sensitive to radiation and subsequently become less able to divide and repair as treatment progresses. Radiation repeatedly interrupts the repopulation of the skin’s cells, weakening the integrity of the skin within the treatment field.

While some patients may not experience skin changes, more commonly the reaction progresses from erythema to dry desquamation to moist desquamation and rarely to ulceration. Necrosis would not be expected with current technology and treatment delivery. Subjectively, patients may complain of tenderness, discomfort, pain, or a burning sensation in the affected skin area.¹

Document intent
The intent of this document is to provide common guidelines for the care of radiation-induced skin reactions whilst on treatment and for three weeks after. It does NOT apply to skin cancers and their treatment.

The framework has been developed for use by health professionals who are providing care for individuals receiving radiation therapy. It is not intended as a patient handout although it is acknowledged that its contents can be used to develop patient education material.

Any questions or concerns about signs and symptoms of radiation-induced skin reactions, the management of those reactions, or suspicion of bacterial or fungal infections should be raised with a member of the patient’s multidisciplinary care team.

Disclaimer
Products listed in this framework document are examples of identified product classifications. These products have been cited in the literature and identified as causing no harmful effects to the patient. The examples are based on practice within the Radiation Oncology Department in Dunedin. The products listed are often used to promote patient comfort.

Unless stated otherwise, use packaging directions for any example products. There have been no clinical trials completed to provide evidence of effectiveness or safety with respect to radiation-induced skin reactions.
SECTION 1a - Goals and principles

Radiation causes damage to the intracellular components of living cells resulting in disruption of cell division and cell death. A cell’s DNA is particularly sensitive to damage during cell division and hence cell populations with a high mitotic rate are more prone to radiation damage. As well as in malignant cells, these rapidly dividing cells are also found in a number of body sites including the mucous membranes, bone marrow and skin.

Goals of these guidelines
- To minimise radiation-induced skin reactions
- To preserve skin integrity whenever possible
- To control symptoms, promote comfort, and enhance quality of life
- To provide optimum conditions for healing

Principles
- Early radiation-induced skin reactions result from the depletion of actively proliferating cells in the basal layer of the epidermis (stratum basale) which prevents the normal process of replacing the outer, keratinised cells taking place
- Radiation may also cause damage to local capillaries. Compromising the capillaries will, in turn, delay wound healing
- Typically, reactions are evident approximately two weeks after beginning treatment and can persist for several weeks post treatment
- Expected radiation-induced skin reactions are multifactorial and complex
- Well hydrated skin promotes healing and comfort as well as reducing the potential for trauma

• A moist environment promotes healing in damaged skin
• Individualised care is based on a particular patient’s unique set of circumstances
• Skin reactions are dependent on treatment factors such as:
  ✓ total dose
  ✓ fractional dose
  ✓ type and energy of treatment modality – electrons or lower energy photons generally produce higher skin doses
  ✓ location of treatment field – tends to be exacerbated in sites where two skin surfaces are in contact (for example infra-mammary fold; natal cleft; groins)
  ✓ use of bolus which increases the dose to the skin
• Skin reactions are also dependent on patient factors such as:
  ✓ Areas where the skin is thin and smooth such as the face, axilla, groin or perineum
  ✓ Compromised skin integrity (e.g surgery, scars, lesions)
  ✓ Existing inflammation
  ✓ Skin care routine
  ✓ Chemotherapy
  ✓ Pre-disposing medical conditions such as diabetes or renal failure
  ✓ Age - older patients are at increased risk
  ✓ Compromised nutritional status
  ✓ Compromised lymph drainage
  ✓ Chronic sun exposure
  ✓ Smoking
  ✓ Limited self-care abilities
SECTION 2 - Erythema

Clinical Presentation
- Pink to dusky coloration
- May be accompanied by mild oedema
- Burning, itching and mild discomfort

Reaction Assessment
Assessment should include:
- Location
- Size of area
- Colour
- Discomfort (burning, itching, pulling, tenderness)
### Erythema: Care objective - to promote cleanliness

#### Accepted, appropriate actions
From the first day of treatment, wash/bathe/shower using lukewarm water and mild, unscented soap. Use palm of hand to gently wash affected skin. Rinse well and pat dry gently with a soft towel.

** Rationale
- Soothes skin, reduces erythema and itching
- Subjectively, washing is associated with stress reduction and patient well-being

** Example products
- Mild, unscented soap
- Baby soap
- Simple® soap
- Aqueous cream
- Non-perfumed Dove® soap

---

#### Additional actions for pelvic patients (particularly gynaec, rectum and anus pts)
Salt baths from the beginning of their treatment course.

** Rationale
- Soothes skin, reduces erythema and itching
- Subjectively, washing is associated with stress reduction and patient well-being

** Example products
- Mild shampoo
- Some baby shampoos (avoid Johnson & Johnson’s which has been shown to contain 1,4-dioxane and formaldehyde)

---

#### Appropriate actions specific to brain patients
Wash hair using lukewarm water and mild, non-medicated shampoo

** Rationale
- Shown not to significantly increase scalp reaction nor to be detrimental to the scalp
- Subjectively, washing is associated with stress reduction and patient well-being

---

** Additional information**
- **Recommended intervention** (see pages 20, Section 6 - Appropriate washing/bathing regime during treatment)
- **Recommended intervention** (see pages 21, Section 6 - Salt baths)
Erythema: Care objective - to promote comfort

Accepted, appropriate actions

- Apply hydrophilic (water-based) creams to the affected area. Apply gently at least twice a day with clean hands. Do NOT rub the skin in that area.
- Apply absorbent hydrophilic polyurethane foam dressing

Rationale

- Maintains skin integrity whilst keeping the skin hydrated and supple
- Helps maintain skin integrity; slows down skin reaction; reduces friction, trauma and irritation; no significant bolus effect has been demonstrated 4,11,12

Example products

- Hydrophilic lotions, moisturisers or creams* 4,4
- Aqueous cream
- Absorbent hydrophilic polyurethane foam dressing
- Mepilex Lite® 10

* recommended intervention (see page 18, Section 6 - Application of Topical Products)
† recommended intervention (see page 19, Section 6 - Mepilex Lite)

Acceptable actions but check rationale before proceeding

Aloe Vera gel (at least 95% pure) can be used on the skin in the treated area 12

Rationale

- It is not harmful and may cool and soothe the skin. However, it does NOT moisturise

Example products to be used with caution

- Any topical Aloe Vera - minimum 95% pure. Lesser concentrations NOT to be used

Actions which must be avoided

Use of (in the treatment area):

- Cornstarch
- Talc or baby powder
- Petroleum Jelly based products (hydrophobic/water repelling)
- Products containing alcohol, perfume or additives
- Products containing Alpha Hydroxy Acids (AHA)

Rationale

- Cornstarch, talc and baby powder can create an environment for bacterial and fungal infections if applied to moist areas 4,4,15 such as skin folds, axilla or buttocks
- Petroleum products are poorly absorbed, provide minimal hydration and are difficult to remove
- All can increase skin reaction

Example products to avoid

- Vaseline® Petroleum Jelly
- All brands of baby powder
- All brands of talcum powder
- Perfumes, most deodorants (although rock crystal, aluminium-free and alcohol-free deodorants are OK)
- Ordinary soaps, shower gels, moisturisers etc
Erythema: Care objective - to reduce inflammation / pruritus

**Accepted, appropriate actions**
Apply absorbent hydrophilic polyurethane foam dressing

**Rationale**
Helps maintain skin integrity; slows down skin reaction; reduces friction, trauma and irritation; no significant bolus effect has been demonstrated.

**Example products**
Absorbent hydrophilic polyurethane foam dressing
- Mepilex Lite®
+ recommended intervention (see page 19, Section 6 - Mepilex Lite®)

**Acceptable actions but check rationale before proceeding**
- Alleviate pruritus
- Alleviate inflammation

**Rationale**
- Predominantly local anti-inflammatory effect - must be used sparingly and only on intact skin

**Example products but use with caution**
- Corticosteroid creams
  - Betamethasone cream*
  - Hydrocortisone cream*
  Both to be used sparingly and only on intact skin
  3,7,14,17
  + recommended intervention (see page 18, Section 6 - Application of Topical Products)

Erythema: Care objective - to prevent trauma to the treated area

**Specific actions for head and neck or breast patients**
Use an electric razor for facial and underarm shaving but keep shaving to a minimum

**Rationale**
- Minimises friction
- Prevents cuts

**Example products**
Any brand of electric razor
Erythema: Care objective - to prevent trauma to the treated area (cont)

Accepted, appropriate actions

- Wear loose, non-binding, natural fibre clothing around the treated area
- Protect skin in treated area from direct sunlight
- Protect skin in treated area from direct wind exposure
- Apply absorbent hydrophilic polyurethane foam dressing

Rationale

- To promote comfort
- To avoid added trauma to the skin in the treated area
- To avoid added irritation to the skin in the treated area
- Helps reduce friction and trauma

Example products

- Soft, breathable fabrics e.g. cotton
- Wear a wide brimmed hat/protective clothing (e.g., long sleeved shirt) as dictated by the treated area
- Absorbent hydrophilic polyurethane foam dressing
- Mepilex Lite® 12

* recommended intervention (see page 19, Section 6 - Mepilex Unit)

Actions which should be avoided

- Avoid extremes of heat or cold to the treated area
- Avoid use of adhesive dressings in the treated area. Extend dressings outside the treated area and adhere to intact skin with hypoallergenic tape

Rationale

- Avoids thermal injury to the treated area
- Prevents epidermal tears and shearing
- Prevents additional trauma to the treated area

Example products to avoid

- Heating pads
- Ice packs
- Any adhesive tapes including paper tapes.

Specific actions to be avoided by head and neck or breast patients

Avoid wet shaving for facial and underarm shaving

- Minimises friction
- Prevents cuts
- Minimises irritation

Any brand of wet shaver.
SECTION 3 - Dry desquamation

Clinical presentation
- Partial loss of epidermal basal cells
- Dryness, itching, flaking, scaling, peeling
- Pain
- Hyperpigmentation

Reaction Assessment
Assessments should include the following:
- Location
- Size of affected area
- Colour
- Discomfort (dryness, itching, flaking, scaling, peeling)
- Pain
- Monitor closely for any sign of drainage or open area (indicating...
**Dry desquamation: Care objective - to promote cleanliness**

**Accepted, appropriate actions**

From the first day of treatment, wash/bathe/shower using lukewarm water and mild, unscented soap. Use palm of hand to gently wash affected skin. Rinse well and pat dry gently with a soft towel.

---

**Rationale**

- Soothes skin, reduces erythema and itching.
- Subjectively, washing is associated with stress reduction and patient well-being.

**Mild, unscented soap**
- Baby soap
- Simple
- Aqueous cream
- Non-perfumed Dove soap

---

**Additional actions for pelvic patients (particularly gynaec, rectum and anus pts)**

Salt baths from the beginning of their treatment course.

---

**Rationale**

- Soothes skin, reduces erythema and itching.
- Subjectively, washing is associated with stress reduction and patient well-being.

---

**Appropriate actions specific to brain patients**

Wash hair using lukewarm water and mild, non-medicated shampoo.

---

**Rationale**

- Shown not to significantly increase scalp reaction nor to be detrimental to the scalp.
- Subjectively, washing is associated with stress reduction and patient well-being.

---

**Mild shampoo**

- Some baby shampoos (avoid Johnson & Johnson’s which has been shown to contain 1,4-dioxane and formaldehyde)
Dry desquamation: Care objective - to promote comfort

**Accepted, appropriate actions**
- Apply hydrophilic (water-based) creams to the affected area. Apply gently at least twice a day with clean hands. Do NOT rub the skin in that area.
- Apply absorbent hydrophilic polyurethane foam dressing

**Rationale**
- Maintains skin integrity whilst keeping the skin hydrated and supple
- Helps maintain skin integrity; slows down skin reaction; reduces friction, trauma and irritation; no significant bolus effect has been demonstrated 4,11,12

**Example products**
- Hydrophilic lotions, moisturisers or creams* +
- Aqueous cream
- Absorbent hydrophilic polyurethane foam dressing
- Mepilex Lite®

* recommended intervention (see page 15, Section 6 - Application of Topical Products)  + recommended intervention (see page 19, Section 6 - Mepilex Lite®)

**Acceptable actions but check rationale before proceeding**
- Aloe Vera gel (at least 95% pure) can be used on the skin in the treated area 13

**Rationale**
- It is not harmful and may cool and soothe the skin. However, it does NOT moisturise

**Example products to be used with caution**
- Any topical Aloe Vera - minimum 95% pure. Lesser concentrations NOT to be used

**Actions which must be avoided**

**Use of:**
- Cornstarch
- Talc
- Baby powder
- Petroleum jelly based products (hydrophobic/water repelling)
- Products containing alcohol, perfume or additives
- Products containing Alpha Hydroxy Acids (AHA)

**Rationale**
- Cornstarch, talc and baby powder can create an environment for bacterial and fungal infections if applied to moist areas 4,6,15 such as skin folds, axilla and buttocks 4,6,15
- Petroleum products are poorly absorbed, provide minimal hydration, are difficult to remove
- All can increase skin reaction

**Example products to avoid**
- Vaseline® Petroleum Jelly
- All brands of baby powder
- All brands of talcum powder
- Perfumes, most deodorants (although rock crystal, aluminium-free and alcohol-free deodorants are OK)
- Ordinary soaps, shower gels, moisturisers etc
Dry desquamation: Care objective - to reduce inflammation/pruritus

<table>
<thead>
<tr>
<th>Accepted appropriate action</th>
<th>Rationale</th>
<th>Example products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apply absorbent hydrophilic polyurethane foam dressing</td>
<td>Helps maintain skin integrity; slows down skin reaction; reduces friction, trauma and irritation; no significant bolus effect has been demonstrated 9,11,12</td>
<td>Absorbent hydrophilic polyurethane foam dressing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mepilex Lite® 10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ recommended intervention (see page 19, Section 6 - Mepilex Lite®)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acceptable actions but check rationale before proceeding</th>
<th>Rationale</th>
<th>Example products to be used with caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Alleviate pruritus</td>
<td>• Predominantly local anti-inflammatory effect - must be used sparingly and only on intact skin</td>
<td>Corticosteroid creams</td>
</tr>
<tr>
<td>• Alleviate inflammation</td>
<td></td>
<td>• Betamethasone cream*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hydrocortisone cream*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Both to be used sparingly and only on intact skin 9,7,11,17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>* recommended intervention (see page 18, Section 6 - Application of Topical Products)</td>
</tr>
</tbody>
</table>

Dry desquamation: Care objective - to prevent trauma to the treated area

<table>
<thead>
<tr>
<th>Specific appropriate actions for head and neck or breast patients</th>
<th>Rationale</th>
<th>Example products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use an electric razor for facial and underarm shaving but keep shaving to a minimum</td>
<td>• Minimise friction</td>
<td>Any brand of electric razor</td>
</tr>
<tr>
<td></td>
<td>• Prevent cuts</td>
<td></td>
</tr>
</tbody>
</table>
Erythema: Care objective - to prevent trauma to the treated area (cont)

**Accepted, appropriate actions**
- Wear loose, non-binding, natural fibre clothing around the treated area
- Protect skin in treated area from direct sunlight
- Protect skin in treated area from direct wind exposure
- Apply absorbent hydrophilic polyurethane foam dressing

**Rationale**
- To promote comfort
- To avoid added trauma to the skin in the treated area
- To avoid added irritation to the skin in the treated area
- Helps reduce friction and trauma

**Example products**
- Soft, breathable fabrics e.g. cotton
- Wear a wide brimmed hat/protective clothing (e.g. long sleeved shirt) as dictated by the treated area
- Absorbent hydrophilic polyurethane foam dressing
- Mepilex Lite® †

† recommended intervention (see page 19, Section 6 - Mepilex Lite®)

**Actions which should be avoided**
- Avoid extremes of heat or cold to the treated area
- Avoid use of adhesive dressings in the treated area. Extend dressings outside the treated area and adhere to intact skin with hypoallergenic tape

**Rationale**
- Avoids thermal injury to the treated area
- Prevents epidermal tears and shearing
- Prevents additional trauma to the treated area
- Minimises friction
- Prevents cuts
- Minimises irritation

**Example products to avoid**
- Heating pads
- Ice packs
- Any adhesive tapes including paper tapes.

**Specific actions to be avoided by head and neck or breast patients**
- Avoid wet shaving for facial and underarm shaving

**Any brand of wet shaver**
SECTION 4 - Moist desquamation

Clinical presentation
- Complete destruction of basal cell layer
- Blister or vesicle formation
- Nerve exposure and pain
- Serous drainage

Reaction Assessment
Assessments should include the following:
- Location of
  - moist areas
  - dry areas
- Size of area
- Exudate
  - amount
  - odour
- Discomfort (burning, itching, pulling, tenderness, swelling, pain)
- Signs of clinical infection
  - Fever
  - Yellow or green sticky exudate
  - Foul odour
## Moist desquamation: Care objective - to promote cleanliness

### Accepted appropriate actions
- Cleanse the area with room temperature normal saline
  or alternatively
- Gently wash with warm tap water
- Pat dry with soft, disposable facecloth (as supplied by Department)

- Monitor area carefully for signs of infection. Swab area only if considering antibiotic cover

### Rationale
- Cools and soothes skin
- Subjectively, washing is associated with stress reduction and patient well-being
- Soft facecloth less likely to irritate inflamed skin

There is a high risk of infection when skin is not intact. Signs of clinical infection are:
- Exudate which is yellow or green and sticky
- Exudate which is malodorous
- Signs of spreading cellulitis beyond the treatment field

### Example products
- Recipe for saline
  - Heat one (1) litre of water to boiling point. Remove from heat
  - Add 1.5 - 2 teaspoons table salt. Stir until dissolved
  - Pour solution into clean one (1) litre container
  - Make a fresh solution each evening. Cover and leave out overnight to cool to room temperature

### Additional actions for pelvic patients
(perticularly gynaec, rectum and anus pts)
- Salt baths from the beginning of their treatment course?!

- Soothes skin, reduces erythema and itching
- Subjectively, washing is associated with stress reduction and patient well-being

---

1. Recommended intervention (see page 21, Section 6 - Salt baths)
**Moist desquamation: Care objective - to promote protection and comfort and to prevent trauma**

<table>
<thead>
<tr>
<th>Accepted, appropriate actions</th>
<th>Rationale</th>
<th>Example products</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Apply absorvent hydrophilic polyurethane foam dressing</td>
<td>• Acts as barrier protection to moisture loss. Cools, soothes and comforts</td>
<td><strong>Hydrophilic polyurethane foam dressing</strong>&lt;br&gt;• Mepilex Lite®&lt;sup&gt;10&lt;/sup&gt;</td>
</tr>
<tr>
<td>• Apply non-adherent dressings</td>
<td>• Promotes comfort and maintains a moist environment. Can be removed without damage.</td>
<td><strong>Appropriate non-adherent dressings</strong>&lt;br&gt;• Mepilex®&lt;br&gt;• Cuticell®&lt;sup&gt;®&lt;/sup&gt;</td>
</tr>
<tr>
<td>• Apply absorvent dressing over low adherent dressing. Change as exudate warrants</td>
<td>• To absorb exudate</td>
<td><strong>Appropriate absorvent dressings</strong>&lt;br&gt;• Mepilex®&lt;br&gt;• Exu-dry™&lt;br&gt;• Mekolin™&lt;br&gt;• Mersorb™&lt;br&gt;• Gamgee</td>
</tr>
<tr>
<td>• Secure products with appropriate secondary dressing</td>
<td>• Prevent epidermal tears and additional trauma</td>
<td><strong>Appropriate secondary dressings</strong>&lt;br&gt;• Opsite&lt;br&gt;• Hypafix</td>
</tr>
<tr>
<td>• Secondary dressing to be secured with appropriate fixator - paper tape must be extended out of treatment area and adhered to intact skin</td>
<td></td>
<td><strong>Appropriate fixators</strong>&lt;br&gt;• Tubitac&lt;br&gt;• Mepitac - OK to adhere to treated skin&lt;br&gt;• Micropor - must be extended out of treatment area and adhered to intact skin</td>
</tr>
<tr>
<td><strong>Additional actions for pelvic patients</strong>&lt;br&gt;(particularly gynae, rectum and anus pts)</td>
<td>• Cools and soothes the skin</td>
<td><strong>Recommended amorphous hydrogel</strong>&lt;br&gt;• Intralite gel (+ Xylocaine)</td>
</tr>
<tr>
<td>• Apply amorphous hydrogel (+ topical local anaesthetic) thickly PRN</td>
<td>• Promotes comfort</td>
<td></td>
</tr>
</tbody>
</table>
Moist desquamation: Care objective - to promote protection and comfort and to prevent trauma

<table>
<thead>
<tr>
<th>Actions which must be avoided</th>
<th>Rationale</th>
<th>Example products to avoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of adhesive tapes on treated skin</td>
<td>Prevents epidermal tears and shearing</td>
<td>Any adhesive tapes including paper tapes.</td>
</tr>
</tbody>
</table>

Prevents additional trauma to the treated area
SECTION 5 - Immediate post treatment assessment and care

Clinical presentation
- Brittle erythema
- Dry desquamation
- Moist desquamation

Reaction Assessment
Assessments should include the following:
- Location
- Size of affected area
- Colour
- Discomfort (dryness, itching, flaking, scaling, peeling)

Procedure
Ask patient to:
- Smear cream thickly on the treated area [do NOT rub in] twice a day for 10 to 14 days. Can be used on moist desquamation
- Wash daily and pat area dry but without rubbing or trying to wash cream off
- After 14 days clean area with Secura® moisturising cleanser (to be supplied by Department) - the cream will gently wash off

Action
Use of:
- Zinc and Caster Oil cream
- Secura® Protective cream

Purpose
To promote comfort and cooling; to prevent friction and trauma

Contraindications
None - but not to be used during treatment

*Note: An exhaustive literature review has failed to produce any radiation therapy based evidence to fully support the use of zinc oxide (ZnO) based products in our field. Anecdotal evidence and local experience, however, have shown that it works. Zinc itself helps maintain the integrity of skin and mucosal membranes whilst the fine particles of the ZnO have been shown to have both a deodorizing and an antibacterial/antiinflammatory action. Most studies involve acute cutaneous inflammatory reactions in infants where damage to the stratum corneum is triggered by frictional damage and increased inflammmation. In these studies, the use of zinc oxide has been shown to be an effective treatment. However, in one study adult skin was exposed to ZnO prior to an irritant challenge and demonstrated a substantial reduction in skin barrier damage and skin irritation. • RJ, 169
SECTION 6 - Recommended intervention *

Application of topical products

Purpose

To promote comfort, and keep the skin in the treatment area hydrated and supple

Use of hydrophilic cream (Aqueous cream)

Indications for use

- Use from onset of treatment to maintain integrity of skin (breast + head and neck patients) - Aqueous cream is generally provided for patients by the department
- For sites other than breast or head and neck, use when skin appears dry or mild erythema becomes visible

Contraindications

- Increased irritation or rash

Rationale

- Maintains skin integrity in treatment area
- Hydrates skin in treatment area

Procedure

Ask patient to apply cream gently to the treatment area at least twice a day with clean hands. They must NOT rub the skin in that area

Use of corticosteroid cream (Hydrocortisone; Betamethasone)

Indications for use

To alleviate pruritus. To be used with caution (see contraindications below).

Contraindications

- Not to be used on broken skin
- Not to be used if a skin infection is suspected as it may mask signs and symptoms of infection and increasing severity.
- Not to be used on a long-term basis as it may cause problems resulting from reduced blood flow to the skin.

Procedure

- Ask patient to apply gently with clean hands
- Tell patient to wash hands thoroughly after application
- Only a very thin layer to be applied up to four times per day
- Continue to apply to skin in the treatment area until discomfort decreases. If the skin begins to tear or break, application MUST stop
- Discontinue use if there is any exudate from the affected area.
Recommended intervention +

Mepilex Lite®

Description and purpose
Highly conformable, absorbent, thin, soft silicone dressing which promotes comfort, whilst reducing radiation induced erythema

Indications for use
- From the onset of erythema
- Can be used prophylactically to delay the onset of erythema

Contraindications
- Irritation and itching after application of Mepilex Lite® (although generally settles within 24 hours if dressing is left undisturbed)

Rationale
- Helps maintain skin integrity
- Slows down development of erythema
- Reduces friction, irritation and trauma
- No significant bolusing effect so can be left on during treatment. This means the dressing can be left undisturbed for several days
- Provides moist wound healing environment
- Absorbs exudate
- Adheres to dry tissue only; will not adhere to moist wound bed
- Atraumatic to wound and surrounding skin on removal
- Able to be fitted and replaced without losing adherent properties

Procedure
- Wash treated area gently using warm water ensuring there is no aqueous cream residue still present, then pat dry
- Apply dressing, cutting to size as necessary
- Advise patient to remove dressing when they shower or bathe (tell them to place the dressing white side uppermost on a dry surface once it has been removed). It should then be replaced once they have dried their skin thoroughly
- Renew dressing when it ceases to adhere or becomes soiled - generally after four or five days
- If the patient experiences any irritation, ask them to leave the dressing undisturbed and dry for 24 hours (not to be removed for showering or bathing) and then re-assess. The irritation should subside
- **When Mepilex Lite® is used on broken skin, the dressing MUST be kept dry. Patients are to be asked NOT to remove the dressing for any reason - not even for showering and bathing. If the dressing is covering treatment set-up marks, it will be removed by the RTs to allow them to access the marks but then will be replaced again as quickly as possible**
Recommended intervention**

Appropriate washing / bathing regime during treatment

Purpose
To promote cleanliness, reduce irritation and promote feeling of well-being for the patient

Indications for use
- Instructions to be followed from onset of treatment for comfort and cleanliness
- Continue following instruction for up to two weeks post treatment

Contraindications
- None

Rationale
- Soothes skin
- Reduces erythema and itching
- Lukewarm water will increase vasoconstriction and may decrease itching
- Subjectively, can be a stress reliever and potentially increases patient’s feeling of well-being

Procedure
The following advice should be given:
- Ask patient to wash / shower / bathe using lukewarm water
- Bath oils and other products must not be added to bath water
- Most soaps contain irritants, such as alcohol and metals, that can increase skin reactions so advise patients only to use mild soaps such as
  - Any brand of baby soap
  - Simple® soap
  - Aqueous cream
  - Dove® unscented soap
- Shower gels and liquid soaps should not be used
- Patients should use the palm of their hand to gently wash the skin in the treated area and then rinse that area well
- Gently pat the treated area dry with a soft towel - the area must not be rubbed
Recommended intervention †

Salt baths

Purpose
Perineal and peri-rectal hygiene both during and post RT when the area is tender and inflamed.

Indications for use
- Use at onset of treatment for comfort and cleanliness
- Use at any time for any skin reaction in the perineal or peri-rectal area
- Discomfort with defaecation
- Continuous discomfort due to perineal inflammation, haemorrhoids, radiation-induced diarrhoea

Contraindications
- Increased discomfort during salt bath

Rationale
- Normal saline is more soothing than water
- Water or saline should be lukewarm (40°C - 43°C)
- Hot water can cause increased drying of skin
- Lukewarm water will increase vasoconstriction and may decrease the itching

Procedure
- Bath oils and other products must not be added to water
- A hand held shower with a gentle spray or a bidet may be appropriate alternatives
- Use for a maximum 10 - 15 minutes, repeat up to QID and/or after each bowel movement
- Gently pat area dry with a soft towel

"Recipe" for saline bath
- Quarter fill a bath with lukewarm water (only needs to be sufficient water to sit in)
- Add 1 to 2 cups of table salt and swirl the bath water around until the salt is dissolved
- Use up to four times a day and / or after every bowel movement (if possible)


