AMERICAN UNIVERSITY OF BEIRUT

AN EVIDENCE BASED PROTOCOL FOR SKIN MANAGEMENT FOR BREAST CANCER PATIENTS RECEIVING RADIATION THERAPY

by
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AN ABSTRACT OF THE PROJECT OF

Aida Hassan Zaiter for Master of Science in Nursing
Major: Nursing

Title: An Evidence Based Protocol for Skin Management for Breast Cancer Patients Receiving Radiotherapy.

Radiation dermatitis (RD) is one of the most common side effects for the majority of breast cancer patients receiving external beam radiation therapy. RD affects not only the integrity of the skin but also the sense of well-being of the majority of women with breast cancer. The pain, discomfort, the itch and burning may lead to halting the treatment, thus compromising the treatment outcomes. The purpose of this project was to: 1) review the available literature on the assessment and the impact of available RD treatments on patients' outcomes; and 2) develop a protocol that can be followed with breast cancer patients treated at the American University of Beirut Medical Center who are undergoing radiation treatment.

A thorough search using the databases Academic Search Complete, MedLine and CINAHL. The key terms used for this search were: "breast cancer", "radiation therapy", "radiation dermatitis", "protocol", "guidelines", and "skin care". All articles presenting approaches for prevention, assessment and treatment of RD for breast cancer patients receiving radiation therapy were included.

Many tools are used for assessment of RD, but only a few are tested for validity and reliability. A number of investigators tested various prevention and treatment measures for RD. However, recommendations for RD management were weak as they were not based on the strongest level of evidence. One recent guideline developed by the Society and College of Radiographers (SCoR), emphasized the importance of using a standardized assessment tool for RD but did not favor one product over another for its treatment.

The proposed protocol includes an assessment tool based on two tools from the literature, and a treatment algorithm targeting each grade of RD. Plans for protocol implementation and evaluation plan for the protocol are suggested.

Radiation dermatitis is an important problem in breast cancer patients receiving radiation therapy. Applying a standardize protocol that can guide nurses in their day to day caring for those population, can lessen the complications of RD and maintain a better quality of life for those patients.

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CHAPTER I

INTRODUCTION

Breast cancer is a common major health problem among women worldwide (Tfayli, Temraz, Abou Mrad, & Shamseddine, 2010). The incidence rate of breast cancer is increasing, with an estimate of 1.35 million new cases per year "in low- and middle income countries" (Tfayli et al., 2010, p. 1). In the UK, each year 50,000 cases are diagnosed in women while 400 are recorded in men (Eccles et al., 2013). In Lebanon, breast cancer remains the most frequent type of cancer that affects Lebanese women and the leading cause of mortality. It is considered among the most commonly reported cancer site (Shamseddine et al., 2014). The treatment modalities for this common disease are multiple and include surgery, chemotherapy, hormonal therapy and radiation therapy.

Radiation therapy remains one of the most essential treatments in patients with breast cancer (Chan et al., 2014; Schnur et. al., 2011). Studies have shown that more than half of breast cancer patients will receive radiation therapy at some stage of their treatment (Grobler et al., 2010; Schnur et al., 2011). The role of radiotherapy in treating breast cancer patients is targeted not only to reduce local recurrence in early stages, but also to reduce the number of mastectomies and improve overall survival rate (Grobler et al., 2010). Despite the major technological advancement in delivering radiation therapy, this treatment is still associated with acute and long-term skin reactions. It is estimated that 95 % of breast cancer patients undergoing radiation treatment will experience skin changes (Chan et al., 2014; Laffin et al. 2015; Mcquestion, 2011). Radiation Dermatitis (RD) is the alteration of the cell division due to the exposure to ionizing radiation (Chan

et al., 2014, p. 2). RD will affect not only the physiology of the skin but also the quality of life of the patients (Chan et. al., 2014). The pain, discomfort, irritation, itching and burning associated with RD will limit the daily activities of patients. Many trials have addressed this problem in order to find ways to prevent or treat RD. However, to our knowledge, there is lack of a standardized protocol that can guide healthcare professionals in day-to-day practice. Based on the literature review, there is no one single treatment recommended for RD. Hence, this project aims to develop a skin care protocol for breast cancer patients undergoing radiation therapy based on the latest empirical evidence.

A. Background

Radiation dermatitis (RD) from external beam radiation therapy is one of the most common side effects for the majority of cancer patients receiving radiotherapy (Oddie et al., 2014). RD may cause skin toxicity and patient discomfort, which may lead the physician to reduce the radiation dose, thus jeopardizing treatment effectiveness. RD is characterized by swelling, redness, pigmentation, fibrosis, ulceration, pain, warmth, burning, and itching of the skin (Chan et al., 2014). This occurrence is due to the disruption in the cell division and regeneration of skin cells, which lead to cell damage and death. This complication occurs in up to 95 % of breast cancer patients receiving radiotherapy (Laffin et al., 2015). The development of RD might occur as early as two weeks after the initiation of the treatment, peaks in severity within the fourth week and persists up to four weeks after the end of treatment (Chan et al., 2014). As long-term side effects of radiation therapy, the patients may experience

skin fibrosis, which includes a change in skin texture such that it becomes dry, pigmentation, retraction, discomfort and telangiectasia (Schnur, et al., 2011).

B. Significance

According to Laffin et al. (2015), there are several factors that contribute to the development of RD, which are related to the radiotherapy and patient history. Therapy related factors consist of radiation dose and use of bolus materials that are applied to the skin for various purposes, such as increasing penetration of the radiation dose. Patient related factors include the patient's age, sun exposure, skin color, smoking and existence of comorbidities. Large breast size and an increased body mass index (BMI) are other pertinent intrinsic factors.

The side effects of radiotherapy can lead to detrimental patient outcomes. While RD can affect the patient's comfort as a result of the itching, pain, numbness, tenderness, warmth, tingling, throbbing, tightness, heaviness and burning, it will also increase the risk of infection as a result of skin break down. Furthermore, complications such as ulceration and bleeding, may also arise from RD. These problems often require surgical interventions such as breast reconstruction surgeries, among others. Moreover, the physicians are sometimes forced to reduce the radiation dose and change the treatment schedule when the severity of the skin reaction becomes severe. In addition, the consequences of RD are not limited to the patient's physical discomfort but may also affect their quality of life. For example, studies have shown that women who survive this nerve-wrecking experience, are subject to an emotional distress, sleeping problems and disturbance of body image (Chan et al., 2014; Schnur et al. 2011).

In Lebanon, there are no accurate published data about the incidence of radiation dermatitis. According to El Saghir et al. (2014), the average incidence of new breast cancer patients in Lebanon is 1700 new cases per year. The American University of Beirut of Medical Center (AUBMC) sees approximately more than 500 cases each year. The Radiation Oncology Department at AUBMC treats every year on average more than 700 patients with different types of cancer, with breast cancer patients accounting to more than 25% of those patients. Taking that into account, along with the fact that there is no protocol to guide the management of this problem at AUBMC, there is a need to create a standardized evidence based skin care protocol that includes patient assessment, preventive measures and skin care treatment. This clinical protocol will provide consistency in the care for patients; moreover, it will enhance the nurses' knowledge and guide their practice. The objectives of this project are to:

1. Review the available literature on the impact of available RD treatments on patient outcomes.
2. Develop a hospital based protocol for RD, including an assessment tool, prevention measures and a treatment algorithm.
3. Propose a plan for implementation and evaluation for the proposed protocol.

CHAPTER II

LITTERATURE REVIEW

This chapter presents an overview of the pathophysiology of the skin, the effect of radiation therapy on the skin, the factors affecting the severity of RD as well as a review of the management of RD.

A. Overview of skin structure

The skin is composed of the epidermis, dermis and hypodermis or subcutaneous layer (Bergstrom, 2011). The epidermis consists of two layers, (1) the cornified layer (the superficial) and (2) the basal layer. The basal layer undergoes mitosis and differentiation every day (McQuestion, 2011). Once the cell of the cornified layer detaches, the basal layer replaces it with new cells. The second level of the skin, known as the dermis, includes other structures; it houses the blood vessels, nerves, sweat glands and hair follicles (Bergstrom, 2011). The hypodermis contains the adipose and connective tissues. Figure 1 illustrates the structure of the skin with its different layers. In fact, the skin is considered the largest organ and the first line of defense of the body; it covers the human body completely, and hence gets very affected by any change in the environment.

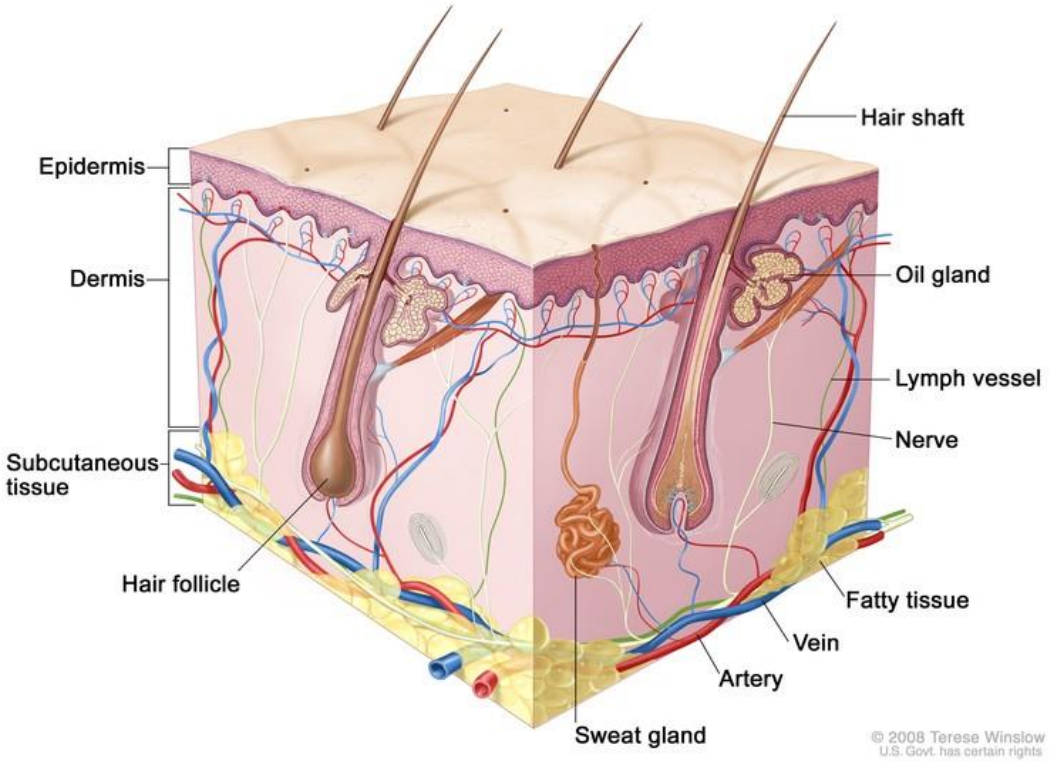


Figure 1. Different Skin Layers (Bergstrom, 2011, p. 594)

B. The Effect of Radiation Therapy on the Skin

The definition of radiation therapy is “the use of high energy x-rays or particles to treat disease" (Bruner, Haas & Gosselin – Acomb, 2005, p.12). In the treatment of breast cancer, the most commonly used form of radiation therapy is through an external beam. The radiation is emitted from a source called linear accelerator, located outside the body, where there is no direct contact with the patient’s skin. Radiation inhibits the division of cancer cells and causes their death (McQuestion, 2011). Radiation acts on the genetic material in the cell (deoxyribonucleic acid, DNA) and induces injury of the skin (Baskar, Lee, Yeo, & Yeoh, 2012). Because of free radicals’ generation, an

inflammatory reaction occurs. This leads to the release of cytokines, such as interleukins 1 and 6, Tumor Necrosis Factor α. Then the growth factor beta breaks the DNA strands, thus preventing cellular division (Bernier et al., 2008).

Radiation therapy affects the body cells that undergo the most rapid division and multiplication such as the cells of the skin. Radiation destroys the cancer cells as well as the healthy rapidly dividing cells. The healthy cells repair the damage caused by radiation therapy since they proliferate slower than the cancer cells; thus, they have enough time to repair themselves. After the first session of radiation treatment, a substantial percentage of basal layer cells are damaged. The remaining healthy cells become weakened, and thus, are easily removed from the skin. Consequently, this will result in an imbalance between the normal production of the cells at the basal layer and the damage of the cells at the superficial layer of the skin (Bernier et al., 2008; Schnur, et al., 2011).

Hence, an inflammatory process begins. The release of cytokines, serotonin, histamine and other inflammatory mediators occurs with capillary dilatation in response to cellular injury. At the same time, an increase in the expression of the epidermal growth factor receptor (EGFR) is noted in the keratinocytes of the skin. As a reaction to the radiation damage, erythema, edema and changes in skin pigmentation begin. The destruction of the cells at the basal layer starts after the initial dose of radiation. The severity of the reaction depends on the total radiation dose, the dose per fraction, the overall treatment time, beam type and its energy, and lastly, the field of radiation treatment. After two weeks of administering 1.8 to 2 gray (Gy) of radiation therapy daily to the patient, the RD will appear (Glover & Harmer, 2014). Moreover, the

addition of chemotherapy will increase the severity of the skin reaction because of the toxic effects of chemotherapy agents (Bernier et al., 2008).

C. Risk Factors for Radiation Dermatitis

Factors affecting skin reactions' severity to radiotherapy are of two types: intrinsic and extrinsic. Intrinsic factors are related to the patient's general health condition and age. Older victims are at higher risk to develop skin dermatitis compared to those of the younger generation because the presence of health comorbidities such as uncontrolled diabetes mellitus can delay wound healing during the radiation therapy treatment and can make the patient more prone to acquire infections.

Moreover, the ethnicity of the patients is also an important factor; darker skinned patients are at higher risk of developing RD compared to lighter skinned patients (Kodiyan et al., 2015; Rayan et al., 2007; Wright et al., 2014). Skin pigmentation depends on the amount of melanin present. Darker skin contains larger amounts of melanin than lighter skin. In a correlational study conducted by Ryan et al. (2007) in a sample of 656 patients including 33 Black patients and 623 White patients receiving radiation treatment, black patients were more likely to develop severe RD (56 %) compared to white patients (23%), $p = 0.0001$. However, the sample size of the Black group was considered small in comparison to that of the White group, which limits the generalizability of the findings. Similarly, a prospective cohort study of 110 breast cancer patients by wright et al. (2014) showed that black patients have a higher risk to develop skin toxicity than white patients. It is worth noting that in this study also the number of the black patients was small in comparison to the nonblack patients (26 versus 84). Therefore, the statistical results might be affected by this

underrepresentation of the black subjects. Other intrinsic factors might affect the onset and intensity of RD, which include hormonal status, tumor site, UV exposure and genetic factors.

On the other hand, extrinsic factors include first the ones related to radiation therapy such as the dose, volume, fraction of radiation and the field of treatment. Secondly, other extrinsic factors are related to the use of chemotherapy as radio-sensitizer. Thirdly, the use of chemical, thermal or mechanical irritants such as products containing metal, such as some creams or deodorants, can affect the severity of RD. Finally, the exposure to extreme temperatures such as direct exposure to cold or heat, for instance applying ice on the skin to soothe the pain and irritation, can also have a detrimental effect on the skin (Chan et. al., 2014). Subsequently, the skin reaction can range from a minimal erythema like that caused by a suntan to a more severe grade of RD (Chan et al., 2014).

D. Assessment of radiation dermatitis

The progress of skin damage due to radiation therapy leads to specific manifestations that develop over time into distinct stages. Recently, the Radiation Therapy Oncology Group (RTOG) experts have classified RD into five grades (Huang et al., 2015). Grade I is characterized by faint/dull erythema; Grade 2 involves tender or bright erythema; Grade 2.5 is characterized by patchy moist desquamation/ moderate edema; Grade 3 involves moist desquamation (blistering/sloughing of skin); and finally, Grade 4 includes the ulceration and skin necrosis. The erythema will appear gradually within one to four weeks of the start of treatment; initially, the skin becomes warm and itchy (McQuestion, 2011).

Patients may complain of discomfort and tightness of their skin. The severity of the reaction will increase gradually until the end of the treatment. Patients may experience pain, pruritus, infection, bleeding and ulceration throughout the course of radiation. Two weeks after the end of the treatment, skin reactions will decrease gradually. Patients recover within one to two months after completion of the treatment (Ruppert, 2011). In addition, chronic skin damage might appear within 90 days after the end of the treatment (Wong et al., 2013). Chronic skin damage includes telangiectasia, skin fibrosis, delayed wound healing and necrosis, among others (Schnur et al., 2011).

A number of assessment tools were developed for the assessment of RD. The following tools are commonly used to assess skin toxicity: the Radiation Therapy Oncology Group grading system Acute Radiation Morbidity Scoring Criteria (RTOG), the European Organization for Research and Treatment of Cancer toxicity criteria (EORTC), the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), the World Health Organization Criteria (WHO), the Radiation-Induced Skin Reaction Assessment Scale (RISRAS) and the Skin Toxicity Assessment Tool (STAT) (Feight et al., 2011).

The RTOG Criteria were designed by a multidisciplinary team and revised several times to objectively measure different levels of skin reactions that vary between erythema and ulceration. The RTOG is composed of four individually scored criteria rated between zero and four (refer to Table 1), where zero representing no change over baseline and four representing ulceration, hemorrhage and necrosis. This tool is the most preferred to be used in clinical research and the most “clinically useful” (Huang et al., 2015, p.231). Yet, the RTOG does not differentiate between erythema and patchy desquamation, which are considered grade two-skin reaction. The RTOG scale was later

revised. In its new version, grade two was further divided into: a score of two for "tender or bright erythema "and a score of 2.5 for "patchy moist desquamation" (Table 2) (Huang et al., 2015, p.231). Validity testing was performed for the RTOG. Filling the RTOG grading system takes a maximum of five minutes by the physician; therefore, the RTOG was considered the most useful tool for health care providers in identifying the four grades of RD. However, the old and the modified RTOG grading system still have some limitations. The reliability testing data was not reported and both versions of the tool do not address the patient's perception in terms of comfort and dysfunction, among others (Oddie et al., 2014).

Table 1. RTOG criteria (original version)

0	1	2	3	4
No change over baseline	Follicular, faint or dull erythema/epilation/dry desquamation/decreased sweating	Tender or bright erythema, patchy moist desquamation/moderate edema	Confluent, moist desquamation other than skin folds, pitting edema	Ulceration, hemorrhage, necrosis

Table 2. RTOG criteria (modified version)

0	1	2	2.5	3	4
No change over baseline	Follicular, faint or dull erythema/epilation/dry desquamation/decreased sweating	Tender or bright erythema	Patchy moist desquamation/ moderate edema	Confluent, moist desquamation other than skin folds, pitting edema	Ulceration, hemorrhage, necrosis

On the other hand, the European Organization for Research and Treatment of Cancer toxicity criteria (EORTC) assess late complications on an ordinal scale from one

to four. Yet, there is no published data about the reliability and validity testing of this scale. In addition, the EORTC does not assess the patient's symptoms (Feight et al., 2011).

The National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) is an adverse event-reporting tool that measures skin toxicity induced by radiation on an ordinal scale from zero to four. The data about the reliability and validity testing are limited (Wong et al, 2013). Furthermore, the CTCAE does not address the patient's concern (Feight et al., 2011). Table 3 shows the CTCAE criteria.

Table 3. CTCAE criteria

0	1	2	3	4
None	Faint erythema or dry desquamation	Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	Moist desquamation in areas other than skin folds and increases; bleeding induced by minor trauma or abrasion	Life-threatening consequences; skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site; skin graft indicated

In addition, the World Health Organization (WHO) established criteria that rate the skin toxicity on an ordinal scale from zero to four (Table 4), but no data were reported about their validity and reliability (Feight et al., 2011;Huang et al., 2015).

Table 4. WHO criteria

0	1	2	3	4
None	Erythema	Dry desquamation, vesiculation, pruritus	Moist desquamation, ulceration	Exfoliative dermatitis, necrosis requiring surgical intervention

Furthermore, the Radiation-Induced Skin Reaction Assessment Scale, known as RISRAS, has weighted categories for the physical changes, such as moist desquamation and dry desquamation. RIRAS includes a symptom scale like tenderness, itch, burn, warmth and effect on activity. Also, observer assessment criteria such as erythema, dry desquamation, moist desquamation and necrosis are included in the grading of the skin toxicity (Noble-Adam, 1999). RISRAS is a nursing assessment tool that combines the objective observer assessment and the patient's perspective of their symptoms. The reliability and validity testing were reported. The overall intrarater reliability coefficient was 0.76. Face, content and construct validity were examined for RISRAS. The 13 experts who examined RISRAS agreed that this tool measures what is supposed to measure. Yet, the RISRAS is not widely used in clinical practice (Feight et al, 2011).

Finally, the Skin Toxicity Assessment Tool, known as STAT, reports three areas of assessment. These areas include (1) “patient and treatment parameters affecting the incidence and intensity of radiodermatitis” such as the radiation energy used and the size of the field; (2) “observer scoring of the skin changes”; and (3) “patient reported symptoms” such as itching, pulling, tenderness, burning (Berthelet et al., 2004, p.626). The STAT evaluates subjective and objective components of the radiation induced skin toxicity. The reliability testing of this scale showed inter-observer agreement while recording skin changes ranging from 65.0% to 97.5%, with ƙ 0.46–0.81, and validity

testing results were acceptable. Berthelet et al. (2004) confirmed the criterion related validity of the STAT tool after examining the percent agreement between the objective and the subjective toxicity scores, with agreements ranging between 72% tom 92%, with a CI = 63–96%; Ƙ =0.33–0.68 and a P <0.05 (Berthelet et al., 2004). When patients were scored higher on the objective scale, they reported a higher degree of discomfort. Moreover, this tool is easy to use in clinical settings, since it allows health care providers to assess patients within few minutes (Berthelet et al., 2004).

E. Treatment of radiation dermatitis

As defined in Chapter I, RD is the alteration in cellular division due to the exposure to ionizing radiation (Chan et al., 2014). The treatment of RD is based upon two aspects: the (1) physical factor, i.e. severity of the skin reaction, and (2) psychological factor, i.e. the patients' degree of pain and discomfort (Huang et al., 2015). In this vein, the health care givers' role is very important in terms of RD prevention. Preventing the onset of RD is much more beneficial and cost effective than the treatment thereof; hence, going through the journey of the repetitive sessions of radiotherapy with no side effects is an advantage in itself; this being said, health care givers would ensure the maintenance of both the physical and the psychological health statuses of the patient.

Numerous studies were conducted on the prevention and treatment of RD (D'haese et al., 2010; Kodiyan et al., 2015; McQuestion, 2011; O'Donovan et al., 2014; Wong et al., 2013). The investigators found that early skin assessment and application of a skin moisturizer before the start of radiation sessions play an important role in decreasing the severity of skin reactions (Di Franco et al., 2013). Haddad, Hashemi,

Samsemi, Chinishian and Oghabian (2013) evaluated the effectiveness of Aloe Vera in the prevention and treatment of RD. The trial included 60 patients who were applied Aloe Vera to half the area exposed to radiation and nothing to the other half. Thirty-eight percent of the patients were diagnosed with breast cancer, 32 % with pelvic cancer, 22% with head and neck, and 8% other types of cancer. The mean of radiation dose was 54 Gray (Gy). The patients were assessed weekly from the beginning of radiation treatment, then during the second and fourth week after treatment completion. The results showed that application of Aloe Vera lotion has a protective effect against RD, reducing skin reaction, especially for patients treated with larger field and higher dose of radiation. There were significant differences in the grade of dermatitis ($p < 0.001$) between the areas treated with Aloe vera and the areas not treated at all. However, Wong et al. (2013) in their systematic review found in three other studies that Aloe vera was not effective in reducing radiation dermatitis, and so did not recommend it for the prevention of the skin reaction. Similarly, Kodiyan et al. (2015) reviewed studies done on various complementary medicine products and pointed out that Aloe Vera had an inferior benefit in reducing acute radiation dermatitis compared to other agents.

On the other hand, numerous randomized trials showed that the application of barrier films, for example a skin protector such as Cavilon No-Sting barrier film, reduced the incidence of moist desquamation more than Sorbelene, a moisturizer cream, in patients receiving chest wall radiation treatment (Breslow : $\chi 2= 3.93$, $P = .047$) (McQuestion , 2011). Another favorable outcome was found in Laffin et al's. trial (2015), where the application of Cavilon was more accepted by breast cancer patients

in comparison to the application of Sorbolene (95.8% for Cavilon versus 85.7% for Sorbolene). Yet, the result was not statistically significant with P= 0.05.

Along the same lines, Shaw et al., (2015) examined the effect of 3M Cavilon and topical corticosteroids (mometasone furoate) on 39 post-operative breast cancer patients receiving radiation therapy in a randomized controlled trial. The patients were divided into three groups and in each group the skin to be irradiated was divided into two parts, one part treated and the other not treated. Group one included 13 patients who were receiving Cavilon barrier cream versus no treatment. In group two, nine were receiving the topical corticosteroids versus no treatment and 17 patients in group three were receiving steroids versus 3M Cavilon. The investigators found that Cavilon delayed the onset of grade 1 pruritus longer than topical steroids, with 3 M Cavilon pruritus occurring on day 32.4 from first treatment day vs. on day 28.4 with topical steroids" (Shaw et al, 2015, p. 409). In group one, 3M was also found to delay the onset of pruritus with3M at day 32.5 days versus at day 29.4" in the untreated skin (Shaw et al, 2015, p. 409). However, both above results were only marginally significant with P= 0.072 for group three and P= 0.079 for group one. In contrast, the occurrence of RD grade two was significantly less in the group using topical steroids compared to the 3M Cavilon group (P= 0.002). Therefore, Shaw et al. (2015) suggested the use of Cavilon the barrier film for the prevention of RD, especially for the skin folds areas and the axillae. Moreover, the authors recommended the use of topical corticosteroids once hyperemia appears, since steroids ointment delays the onset of grade 2 RD.

Furthermore, Chan et al. (2014) reviewed 47 randomized controlled trials testing six interventions for prevention and treatment of RD. In their review, they identified other skin care treatments that might contribute to the prevention of RD. The

interventions included oral systemic medications named Wobe-Mugos E; skin care practices; steroidal topical therapies including 1 % hydrocortisone, 0.05% clobetasone burtrate, betamethasone cream, 0.1% mometasone furoate cream; non-steroidal topical therapies such as Aloe Vera and Biafine, dressings and others. The authors reported four meta-analyses, each one based on two studies only. The use of systemic oral therapy Wobe-Mugos E , which is made up of proteolytic enzymes containing 100 mg papain, 40 mg trypsin, and 40 mg chymotrypsin, was associated with 87% reduction in the incidence of RD compared to no oral therapy (odd ratio [OR] = 0.13, 95% confidence interval [CI] = 0.05, 0.38). Another result was a significant mean difference in the severity of RD of −0.92, 95% CI −1.36 to −0.48 with the use of Wobe-Mugos E compared to the control group. (Dale, 2001 and Gujral, 2001 cited in Chan et al., 2014). On the other hand, no significant difference was found in the development of RD by use of deodorant (OR = 0.8, 95% CI = 0.47, 1.37) (Bennett, 2009 and Gee, 2000 cited in Chan et al., 2014). Moreover, the authors found that the use of Trolamine, a skin emollient, had no effect on skin toxicity compared to placebo (Elliott 2006 and Fisher 2000, cited in Chan et al., 2014). The other products were compared in single studies with varying sample sizes and some were more than 20 years old. Considering all these variations, the authors concluded that there were no particular agents with superior benefit in treating RD (Chan et al., 2014).

Also, Chan et al. (2014) reported two small randomized control trials (RCT) with fewer than 40 subjects each that studied the effect of using gentian violet dressing in comparison to hydrogel dressing or non-adherent dressing to treat RD. In one trial of 20 patients hydrogel dressing had a significant effect with hazard ratio (HR) 7.95, 95% CI 2.20-28.68, p = 0.002 favoring hydrogen dressing (Gollins 2008 cited in Chan et al.,

2014). However, in the other trial of 39 subjects, no significant difference was found between gentian violet and non-adherent dressing, HR = 0.73,95% CI 0.52-1.03, p = 0.07 (Mak 2005 cited in Chan et al., 2014).

Finally, Chan et al. (2014) noted in their review that the use of steroidal ointments did not show benefit in prevention of RD compared to placebo (P=0.2). However, there was a benefit for steroids in the treatment of RD, as evidenced by significant reduction in pain and itching (Miller 2011, Omidvari 2007 cited in Chan et al., 2014).

Interestingly, O'Donovan et al. (2014), D'haese et al. (2010) and Kumar et al. (2010) noted that there is convincing evidence that gentian violet is harmful in treating RD because of its carcinogenic effect. Along these lines, the authors recommended further research on the effect of using hydrogel dressing in moist desquamation. On the other hand, the use of a soft silicone dressing, Mepilex Lite, was assessed. Paterson et al. (2012) showed in their randomized controlled trial that Mepilex Lite dressing decreased the severity of RD more than aqueous cream dressing (P= 0.001).

A meta-analysis by Kumar et al. (2010) did not show a benefit for sucralfate cream in reducing RD or intensity of associated pain. With respect to the use of Silver sulfadiazine cream, studies revealed a limited benefit in treating RD (Hemati et al., 2012; Wong et al., 2013). Furthermore, other agents such as the hyaluronic acid, petroleum-based ointments (aquaphor) and calendula, among others, were examined in recent studies. There was limited evidence to support or refute the effectiveness of these agents in the management of RD; so further studies were recommended with more rigorous methodology (Hemati et al., 2012; Kumar et al., 2010; Wong et al., 2013).

Three studies reviewed by Chan et al. (2014) that compared washing with water and/or ph-mild soap to no washing, have shown that washing decreased the symptoms, itching and pain significantly. On the other hand, there were disparities regarding the use of antiperspirants; while evidence showed that the use of deodorants did not increase the intensity of skin reaction, in many radiation oncology departments in Europe and the US patients are often advised against using these products (O'Donovan et al., 2014; Watson et al., 2012; Wong et al., 2013).

A set of clinical guidelines was proposed recently in February 2015 by the Society and College of Radiographers (SCoR) to guide the radiographers, radiotherapy nurses and other health care providers while caring for patients receiving external beam radiation. Twenty-four studies formed the basis of this review. The SCoR did not support or refute any specific product since the evidence is not strong enough. However, the group focused on the education of patients and the health care team on how to prevent RD by reducing the friction and the irritation. Moreover, the society recommended the use of a standardized skin assessment tool. Documentation of the patient acceptability of and compliance with the skin care instruction provided by the institution was also strongly advised. Finally, the team proposed the use of a suitable dressing on a broken skin to reduce further injury (SCoR, 2015).

After reviewing the current literature, we conclude that keeping the skin well hydrated with moisturizers can reduce or delay the onset of RD. Barrier films could also protect the skin from trauma and retain moisture, which promotes healthy skin and reduces the severity of RD. Moreover, there is no strong evidence to support or refute the use of any specific product. Only gentian violet dressing is not recommended, as it was found to have carcinogenic effects. On the other hand, early prevention, such as

avoidance of sun exposure, skin irritant products and the abrasion of the affected skin, is essential to optimize the treatment outcomes. Moreover, it is important to keep the skin clean and treat any suspected infection with local or systemic antibiotics.

As a result, the multidisciplinary team needs to address these solutions and intervene earlier in order to prevent further skin toxicity from RT. The team needs to educate the patients and the family about the various ways to prevent and reduce RD and associated pain such as through washing with water and mild soap and using topical steroids. The healthcare team also needs to consider the effectiveness of the oral therapy, promote adaptation, coping, and pain management. The strength of recommendations to treat or prevent RD is limited by the quality of empirical evidence in terms of the number of studies, sample size and rigor of design. Therefore, future studies are needed to create a gold standard protocol for RD management.

CHAPTER III

THE PROPOSED PROTOCOL FOR SKIN MANAGEMENT DURING RADIATION THERAPY FOR BREAST CANCER PATIENTS

Radiation dermatitis is a common side effect for breast cancer patients undergoing radiation therapy. The erythema, the itch and the pain may affect the quality of life of the patients and lead to halt the treatment. Radiation oncology nurses play an important role in the care of breast cancer patients undergoing radiation therapy. In the absence of standardized evidence based guidelines to guide nurses in the prevention and management of radiation-induced dermatitis, a protocol is proposed based on the literature.

The protocol is divided into three parts: Assessment, prevention and treatment.

A. Assessment

Before the initiation of the first session of radiotherapy, baseline assessment of skin integrity should be performed. The assessment should include the condition of the skin and the care used. The nurse should document the assessment findings in the patient's chart. There are different tools for skin assessment that are used. However, the modified version of the RTOG is the most commonly used and was revised several times to objectively measure the different levels of skin reactions that vary between erythema and ulceration. The tool is composed of four criteria rated between 0 and 4 where 0 represents no change over baseline and 4 represents ulceration, hemorrhage and

necrosis. In addition, the STAT tool measures the subjective and the objective components of the skin toxicity and includes four parameters rated on a scale from 0 to 5. In this proposed protocol, a combination of the RTOG and the STAT tool will be used in order to measure the objective components of the RD and assess patient reported outcomes.

Table 5. Proposed Assessment Tool

0	**1**	**2**	**2.5**	**3**	**4**
No change over baseline	Follicular, faint or dull Erythema epilation dry Desquamation decreased sweating	Tender or bright erythema	Patchy moist desquamation/ moderate edema	Confluent, moist desquamation other than skin folds, pitting edema	Ulceration, hemorrhagenecrosis
Discomfort	Item	Score			
	Burning (0-5)				
	Itchiness (0-5)				
	Pulling (0-5)				
	Tenderness (0-5)				
	Other……..(0-5)				

After the skin assessment, pain assessment should be performed by the nurse. The assessment should include the type, frequency, severity, quality and intensity of pain. The nurse should document the findings of the assessment in the patient's chart. There are several pain assessment tools to assess the pain in adult patients such as, the 0 - 10 Numeric Rating Scale (NRS), the Verbal Descriptive Scale (VDS), the Visual Analogue Scale (VAS), among others (Asiato et al., 2015, AUMC policy on Pain

Assessment Management_4th Ed_0165, 2015). One of the commonly used tool is the NRS which is a rating scale from zero to ten, where zero indicates no pain, five indicates moderate pain and ten indicates worst possible pain (refer to figure 1).

The result of the pain assessment will be documented in tandem with the result of the RD assessment. For the subjective components and the pain, the physician will be informed about the assessment result and a case-by-case approach will be applied, for example an analgesic can be prescribed among other interventions.

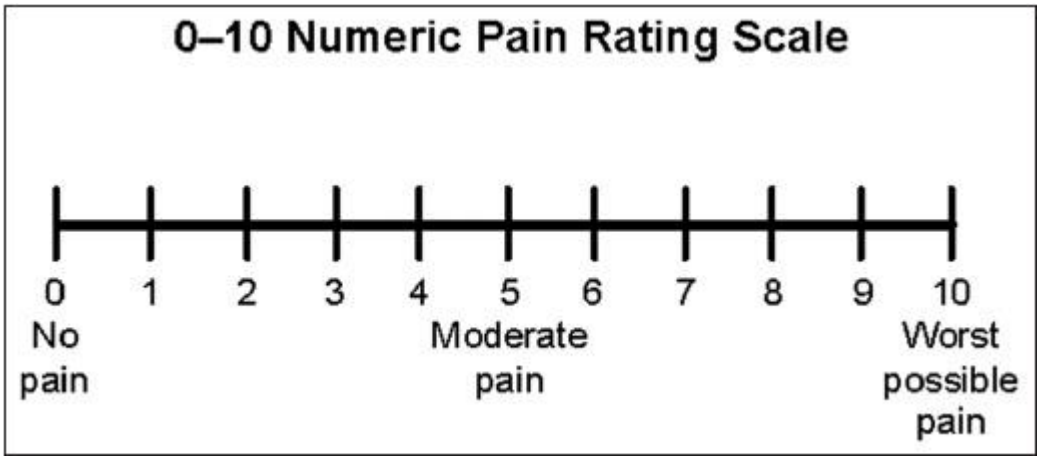


Figure 2. The Numeric Pain Rating Scale (Aziato et al., 2015, p.6)

B. General Measures for Prevention

The radiation Oncology nurse will educate the patient about the general skin care measures to be taken at start, during the whole treatment period and three months later. The patients should be instructed about:

- Keeping the irradiated area clean
- Washing softly with water, with or without mild non-perfumed soap. Pat and dry.

- Applying a barrier film such as Cavilon twice per week to the area to be treated. The application of the film can be Monday and Thursday or Tuesday and Friday or Wednesday and Saturday. The film resists water for three days.
- Or alternatively
- Using hydrophilic agents such as aquaphor
- Application of the moisturizer at least twice per day, after the receiving the radiation session and at bedtime.
- Avoiding skin injuries such as the use of a razor or tight clothes
- Wearing cotton clothes
- Allowing the use of antiperspirant
- Avoiding baby powder in the skin folds, Eosin or gentian Violet solution
- Avoiding direct sun exposure to the irradiated skin
- Avoiding the exposure to extreme temperature such as direct application of hot water or ice on the affected area.

C. Management of the Different Grades of RD

The treatment of RD should be based on the assessment scores as described below. For patients who score zero, which is no change over baseline, standard care is recommended that includes application of the prevention measures described in the previous section. The nurse should assess the patient's skin on weekly basis.

Patients with RD grade 1, which is faint or dull erythema, will:

- Receive standard care
- Be assessed for pain using the " Numeric Rating Scale""
- Be assessed weekly.

The management of patients with grade 2 RD, which is tender or bright erythema, includes:

- Pain assessment
- Advising the patient to apply hydrophilic cream
- Low to medium potency steroid or cortisone creams such as Mometasone or Hydrocortisone 1% can be started. It can be applied twice per day for a one-week period. The steroid creams should not be used on broken skin because they will delay the healing process and could cause thinning of the skin if used for a long time. If the skin breaks, the steroids cream should be stopped.
- The nurse should assess the patient daily.

The management of patients with grade 2.5, patchy moist desquamation, moist edema, includes:

- Cleaning of the moist desquamation with hydrogen peroxide 3 % followed by normal saline solution twice per day
- Advising the patient to use non or low adherent dressing such as the hydrogel dressing
- Advising the patient to use hydrophilic agents or barrier film to the other treatment area of the unbroken skin
- The nurse should assess the patient daily.
- Assess the patient for pain.

The patients with grade 3 RD, confluent moist desquamation, will receive the following care:

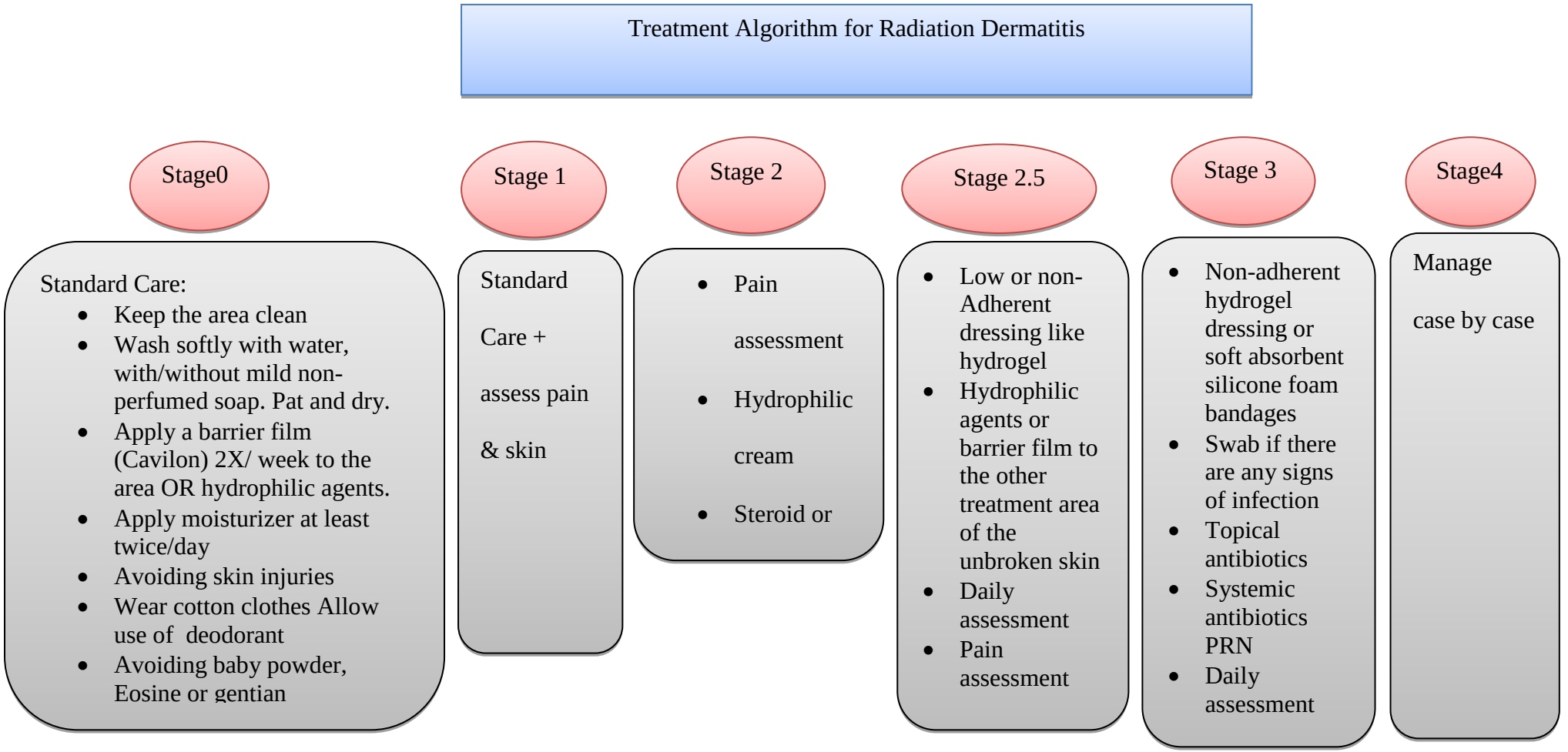
- Cleaning of the broken skin with hydrogen peroxide 3 % followed by normal saline solution rinse twice per day.

- Application of wound dressing such as non-adherent hydrogel or soft absorbent silicone foam bandages.
- No use of adhesive dressing.
- Taking a swab for culture if there are any signs of infection.
- Asking the patient to apply topical antibiotics such as fucidin ointment or silver sulfadiazine among others, twice per day.
- A systemic antibiotic can be added, for bacterial superinfection, based on the infectious doctor's assessment.
- Pain assessment.
- Daily assessment of the patient's treated skin area including the location, and the size.

For the patients with grade 4 RD, which is ulceration, hemorrhage and necrosis, a multidisciplinary approach to treatment should be applied case by case.

At the end of the treatment, the radiation oncology nurse should reinforce patient education about the skin care. She/he should make sure that the patient adheres to the above instructions. The figure below summarizes treatment by stage.

Figure 3. The treatment algorithm for radiation dermatitis



CHAPTER 4

IMPLEMEENTATION AND EVALUATION

Providing high quality and effective care through the incorporation of the protocol into practice mandates the cooperation of all members in the health care team including and not limited to the radiation oncology physicians, the nurses, the therapists and the skin experts.

First, a multidisciplinary task force will be formed. The task force shall include a representative from the: nursing team working in the radiation oncology, radiation oncology physicians, skin experts such as a wound care specialist or a dermatologist, and radiation oncology therapist. The oncology clinical nurse specialist and the research assistant in the radiation oncology department will also be involved. The task force will have the responsibility to review the protocol and suggest any further refinements. After the review, a proposal will be submitted to the Chairman of Radiation Oncology and a meeting held with him to gain his support in the protocol implementation, before sending it to the hospital administration for approval. A detailed description of the protocol including the related evidence on skin care, the protocol and related documentation, as well as any expenses related to its implementation, will be sent to the hospital administration.

Following the administrative approval, a revision of the protocol will be performed based on the feedback. After the final changes are made to the protocol, staff education on the assessment tool will follow. At the same time, all the documentation forms will be processed for approval by the Medical Records Committee. As soon as the assessment tool gets approved, collection of data is done over six months to evaluate

patients' skin status with the current treatment of RD, using the protocol assessment tool. The data shall include:

- Incidence of skin dermatitis
- Documentation of RD assessment, care and related patient education
- Pain scores of patients related to RD
- Presence of complications with RT treatment documented such as in infection or bleeding
- Use of antimicrobial agents to treat skin dermatitis
- Delay in RT treatment related to the skin toxicity
- Patient information including age, existence of comorbidities, smoking, body mass index (BMI), skin color, tumor site, presence of mastectomy, presence of breast implants

When data collection is over, the staff will be educated about the protocol and given the opportunity to voice their concerns about protocol implementation. Then, the protocol implementation will follow. The protocol will be pilot tested on 20 patients. Staff satisfaction questionnaires will be distributed in order to evaluate the protocol in terms of feasibility of implementation and ease of use, as well as patients' acceptance of it. Based on the results, barriers and / or problems will be identified and the protocol will be further modified. Six months later, a prospective study on skin dermatitis incidence after the protocol implementation will be conducted. The same data shown above will be gathered after the protocol implementation, in addition to patient satisfaction with RD management. Then the pre and post data will be compared to evaluate whether patient outcomes improved with the new protocol. The protocol will be updated every three to five years based on the latest literature.

As seen, the establishment of a skin care management protocol for radiation dermatitis is a challenge that needs a concerted effort of the multidisciplinary team in the Radiation Oncology Department. The nurses at all levels play a pivotal role in the management of one of the major side effects of radiation therapy that affects the patients' quality of life, which is radiation dermatitis (RD). Standardizing the care for breast cancer patients treated with RT is the main aim of this protocol. Implementing pertinent skin care guidelines that illustrate evidence-based intervention guide the nurses in their practice. For breast cancer patients, the pain, itching, infection and bleeding can compromise their daily activities and sense of well-being. By applying a standardized care for patients, their quality of life will be better maintained.

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