Prevention of Radiation-Induced Skin Reactions in Breast Cancer External Irradiation

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PREVENTION OF RADIATION-INDUCED SKIN REACTIONS
IN BREAST CANCER EXTERNAL IRRADIATION.

A Thesis
Presented to
The Faculty of the Department of Nursing
Western Kentucky University
Bowling Green, Kentucky

In Partial Fulfillment
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Master of Science

By
Cathy Eden Ammerman

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PREVENTION OF RADIATION-INDUCED SKIN REACTIONS IN BREAST CANCER EXTERNAL IRRADIATION.

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Radiation dermatitis is a common side effect of external beam radiation therapy. The purpose of this study was to evaluate the effectiveness of applying an aloe vera based skin gel to the target area skin in preventing the development of radiation dermatitis to post-lumpectomy/mastectomy patients receiving external beam radiation therapy in an ambulatory radiation-oncology clinic in the southeastern region of the United States. In this descriptive correlational study, a convenience sample of willing participants (n=18) was followed from initial treatment through the one-month follow-up examination to assess the intensity of their skin reaction.

Five research questions were examined pertaining to the relationship between prognostic indicators and the development of radiation dermatitis when Radiacare® gel was used before and throughout external beam radiation therapy post-mastectomy or post-lumpectomy. The prognostic indicators used in this study were: Breast size ≥ C-cup, prior chemotherapeutic exposure, length of incision, age of client, and weight changes since diagnosis. Analysis of Variance (ANOVA) and Pearson’s Correlation Coefficients were used in the data analysis with a confidence of p=0.05. This study indicated that breast size and weight changes were the most prognostic of the factors studied.

The small sample size and lack of randomization or control group limit the generalizability of these findings to clinical practice; however, it does support the need for continued research in this area. Recommendations for future studies include comparing Body Mass Index (BMI) to incidence and determining a relationship between gel use and treatment breaks and if there is a difference in the length of time until the skin is restored to baseline upon completion of therapy.
PREVENTION OF RADIATION-INDUCED SKIN REACTIONS
IN BREAST CANCER EXTERNAL IRRADIATION

Chapter I

Significance

Radiation dermatitis is a common and sometimes debilitating side effect experienced by post-lumpectomy/mastectomy clients receiving external beam radiation therapy. Many factors have been identified as contributing to the development of radiation dermatitis including breast tissue greater than C-cup, size of lumpectomy/mastectomy scar, use of radiosensitive medications (including chemotherapeutic agents), age and poor nutritional status. Knowledge of these factors can be used by healthcare professionals to predict which patients could benefit from aggressive prevention of this complication.

Nurses assist women to deal with the devastating emotional, spiritual and physical effects that encompass the diagnosis and treatment of breast cancer. Since there are many changes with which the client will have to cope, the prevention of problems associated with the treatment of this disease becomes of primary importance to both the client and nurse. Many women are choosing breast conserving surgery and adjunctive irradiation of the remaining breast tissue as their treatment option when faced with the diagnosis of breast cancer (Kolcaba and Fox, 1999). Other women are choosing to receive chest wall irradiation following mastectomy. It is known that as many as 95 percent of patients receiving external beam radiation therapy will experience radiation induced skin changes known as radiation dermatitis (Porock, Nikoletti & Kristjanson, 1999). Some skin reactions are mildly irritating, while others may require interruption of treatment schedule (Williams et. al., 1996). Some reactions are so severe that ulceration,
infection and/or necrosis of tissue will occur (Archambeau, Penzer & Wasserman, 1995). Since cosmesis is often a factor when selecting lumpectomy and radiation, prevention of severe side effects are important because these complications could lead to permanent scarring and loss of affected tissue (Archambeau et. al., 1995). Archambeau and colleagues (1995) also noted that the development of the most severe chronic skin reactions were seen in those clients who developed the more severe acute skin reactions. Hoskins (1997) also noted that women who did not develop side effects from treatment reported less psychological distress and a greater perceived health status than those who did. It is also known that the psychological attitude of the clients and their perceived health status can greatly affect the outcome of the treatment. Since nursing is charged with assisting the clients to deal with and prevent problems associated with their treatment process, and external beam irradiation is known to cause irritating or debilitating skin reactions, identification of an agent that could prevent those skin reactions without adverse reactions is desirable.

Purpose Statement

The purpose of this study was to evaluate the effectiveness of applying an aloe vera based skin gel to the target area skin in preventing the development of radiation dermatitis to post-lumpectomy/mastectomy clients receiving external beam radiation therapy in an ambulatory radiation/oncology clinic located in the southeastern region of the United States.
Research Questions

1. What is the relationship between breast size and the incidence of radiation dermatitis when using Radiacare® gel before and throughout external beam radiation therapy?

2. What is the relationship between the prior use of radiosensitive agents and the incidence of radiation dermatitis when using Radiacare® gel before and throughout external beam radiation therapy?

3. What is the relationship between the length of the surgical incision and the incidence of radiation dermatitis when using Radiacare® gel before and throughout external beam radiation therapy?

4. What is the relationship between the age of the client and the incidence of radiation dermatitis when using Radiacare® gel before and throughout external beam radiation therapy?

5. What is the relationship between weight changes since diagnosis and the incidence of radiation dermatitis when using Radiacare® gel before and throughout external beam radiation therapy?

Definitions

Breast Size

Breast is a term used to describe paired mammary glands located on the anterior surface of the thoracic cage. Varying amounts of subcutaneous and retromammary adipose tissue provide a vast range in the individual's breast size and shape. Breast size is identified as a numerical and letter value placed upon the measurement of the tissue and comparing the differences in measurement.
The numerical value is recorded in inches and is obtained by measuring the circumference of the chest wall immediately inferior to the axillary fold and rounded to the nearest even whole number. The letter value is obtained by measuring around the fullest point of the bust line and recording this measurement in inches. The difference between the two numbers is calculated and a letter value is recorded based upon a the following scale:

- 1" = A
- 2" = B
- 3" = C
- 4" = D
- 5" = DD
- 6" = DDD (F)

Large breast size was classified as a measurement greater than C-cup size in the affected breast post operatively.

*Radiosensitive Agents*

Radiosensitivity is the term used to identify any pharmacological or chemotherapeutic agent that intensifies the effect of radiation especially upon the skin. A list of all current prescription and nonprescription medications including herbal supplements and vitamins was obtained from each participant. Those medications were reviewed for known radiosensitivity. A history was taken to record current or previous exposure to radiosensitizing chemotherapeutic agents; the dosage and the time lapse since last chemotherapeutic treatment was recorded.

*Surgical Scar*

Scar tissue develops when there is an interruption of skin integrity. Repair of this breech in normal skin tissue is accomplished by the formation of densely packed granular tissue commonly referred to as a scar. The length and location of each participant’s surgical scar was obtained and recorded in centimeters. The location was identified by
the quadrants of upper lateral (including tail of Spence), upper medial, lower lateral and lower medial as well as mixed lateral, medial, superior, inferior or mastectomy (Appendix 1). Clients with edema, erythema, or an open, draining wound in the treatment area at the onset of therapy were excluded from the study.

**Age**

Age is a term that reflects the cumulative existence of a person since birth. For this study, each participant’s age was recorded in years by subtracting the numerical representation of the year in which the study was conducted from the numerical representation of the year in which the participant was born.

**Weight changes**

The measured relationship between a mass of a body and the effect of gravity is conceptualized by the term weight. In this study, the participant was questioned as to their weight immediately before the diagnosis of cancer. Weights were measured on the day of the initial consultation, weekly throughout the treatment regimen, and again at the four-week follow-up appointment. Weights were recorded in pounds and rounded to the nearest one-tenth.

**Radiacare® Gel**

Aloe is identified as any number of plants within the lily family from which the sap of the spiky leaves can be applied topically to skin insults, including burns, for its therapeutic properties. Acemannan hydrogel, an extract of Aloe vera L., is the active ingredient in Radiacare® Gel, which is developed and marketed by Carrington Laboratories, Inc. It has been approved for prescription use by the Food and Drug Administration for the management of skin conditions associated with first and second
degree burns, stasis and decubitis ulcers, and superficial skin conditions including radiation dermatitis (Plemons, et. al., 1994). Acemannan has been shown to affect direct interaction of monocytes and macrophages that is believed to directly affect actions in such a manner that epithelialization and collagen deposits are hastened thus improving wound healing (McDade, Lutz and Fosmire, 1995).

Application

Application is defined as the spreading of a thin layer of a substance to the hand and transferring that substance topically to another area to disperse the substance evenly in order to receive the desired benefit from that substance.

Radiacare ® Gel 1.5 ounce sample tubes were given to the clients during the initial consultation and simulation visit with a prescription for a four ounce tube with five refills. The clients were instructed to apply the gel to the skin within the treatment markings two to three times daily from the date of initial consultation continuously through the four-week post-radiation follow-up appointment (Appendix 1).

External Beam Radiation Therapy

Standard External Beam Radiation (EBR) Therapy is exposure of a defined area to a concentration of X-rays with the desired purpose of interrupting the growth of neoplastic cells within that area. External Beam Radiation Therapy for post-lumpectomy or mastectomy is delivered each weekday in 200 cGy fractions over a period of twenty-five (25) consecutive treatments for a total radiation dose of 5000 cGy. An additional Boost of 1200 cGy is directed at the site of the lump for a total dose of 6200 cGy.
Radiation Dermatitis

Radiation dermatitis is a global term for any adverse skin changes that can be directly attributed to external beam radiation therapy. These changes range from erythema or bronzing of the skin within the treatment area to ulceration, infection and necrosis. This reaction may be so severe as to interrupt therapy. Many measurement scales have been suggested and tested for the accurate assessment of these skin reactions. For this study, a six-point descriptive scale was be utilized. This scale, adopted by the Oncology Nursing Society (Bruner, et.al, 1998), attempts to standardize the subjective description of radiation induced skin reactions.

Scale:

Grade I  faint or dull erythema, follicular reaction
Grade II  bright erythema
Grade III dry desquamation with or without erythema
Grade IV  small to moderate amount of wet desquamation
Grade V  confluent moist desquamation; edema
Grade VI  Ulceration, hemorrhage, or necrosis

Development of a Grade V reaction subjects the client to an interruption in therapy.

Since radiotherapeutic effects are cumulative, the goal is to avoid disruptions in the treatment plan (Archambeau, Pezner & Wasserman, 1995). There are no published reliability or validity statistics available on this scale.

Incidence

The incidence of radiation dermatitis was calculated by the summation of the total skin reaction scores in each site (incision area, inframammary fold, axilla (where
appropriate) and overall treatment field) throughout the treatment plan.

**Conceptual map**

The numbers of known and suspect factors contributing to the development of radiation dermatitis are beyond the scope of this study and were limited to five. For the questions concerning the relationship these five factors have on the incidence of radiation dermatitis when using Radiacare® gel before and throughout external beam radiation therapy, a conceptual map was drawn as follows:

It is known that EBR + these listed factors $\equiv$ Radiation Dermatitis.

\[
\begin{array}{ccc}
\text{External} & \text{Radiosensitive Agents} & \text{Radiation} \\
\text{Beam} & \text{Surgical Scar Size} & \text{Radiacare} \ ^\circ \text{ Gel} & ? & \text{Dermatitis} \\
\text{Radiation} & \text{Age} & \\
\text{+} & \text{Weight Changes} & \\
\end{array}
\]

**Contributing Factors not addressed in this study**
- Fair skin complexions
- Immunocompromise
- Prolonged Radiation Exposure
- Smoking or History of Skin Cancer
- Non-adherence to recommended skin care
- Postmenopausal state
- Co-morbidity of HPT, CVHD, or Autoimmune diseases

**Summary**

No topical agent has been shown to prevent radiation-induced skin reactions in those receiving external beam radiation therapy. Since research indicates that 95 % of these clients will develop some type of skin reaction, it is imperative that a method of preventing this complication be found. Prior studies have focused upon the treatment of such skin reactions; however, few have examined methods of prevention. Both nurses and clients are interested in preventing potentially debilitating complications and
therefore improving the outcomes of the treatment plan. A review of the relevant literature was conducted to identify both contributing factors to the incidence of radiation dermatitis and agents recommended for prophylactic use.
Chapter II

Review of Literature

In professional literature, the effects of radiation on the skin and breast tissue are described. Several studies (Appendix A-2) have been published addressing prognostic indicators for severe skin reactions to irradiation. Much has been written about the use of topical agents to treat moderate radiation-induced skin reactions while others address the most effective treatment plans and dressings for the more severe manifestations; however, very few studies have been published that specifically address the prophylaxis of radiation-induced dermatitis despite the acknowledgement of possible severe long-term effects with the development of acute skin reactions.

Effects of Radiation on the Skin and Breast Tissue

Radiation has been known to cause skin changes since 1901 when Henri Becquerel first developed ulceration while transporting radium in his pocket (Sitton, 1992a). Clients may be familiar with the skin changes seen with ultraviolet blue radiation (UVB) commonly called “sunburn”; however, the radiation used with external beam radiation therapy is quite different from other types of ionizing radiation (Noble-Adams, 1999). The rapid ability of the normal skin cells to repair themselves from ionizing radiation and the inability of the malignant cells to do so is the advantage of radiation therapy (Noble-Adams, 1999; Archembeau, Penzer & Wasserman, 1995). The reaction of the skin ranges from mild erythema to ulceration and necrosis of tissue.

Prognostic Indicators for Severe Skin Reactions

Clinicians assumed that the same skin type risks to UVB radiation would also predict those most at risk for developing radiation-induced dermatitis; however, studies have
failed to support this assumption (Lokkevik et. al, 1996; Williams et al, 1996; Maiche, Isokangas & Grohn, 1994; Sitton, 1992). Review of professional literature finds that the type of radiation employed, the length of exposure time, the strength of dose and the size and location of the treatment field are the most accurate prognostic indicator for development of severe skin changes. It was indicated that the longer the exposure time, the stronger the dose, or the larger the treatment field, the greater the risk of severe skin reaction (Porock, Nickoletti & Kristjanson, 1999; Noble-Adams, 1999; Archembeau et. al., 1995; Sitton, 1992).

An additional factor known to increase risk of severe skin reaction for women receiving post-lumpectomy or post-mastectomy irradiation was the concurrent use of radiosensitive chemotherapeutic agents (Noble-Adams, 1999; Porok et. al, 1998; Turesson et. al., 1996). Other significant prognostic factors for the development of severe skin reaction to radiation therapy were identified by Porock and colleagues (1998) as smoking, irradiation of appositional skin folds (axillary and inframammary), weight or large breast size, previous lymph aspiration or resection, wearing tightly fitting clothing, and skin-to-skin friction in the treatment field. Other studies have identified age (Turesson, et. al, 1996), poor nutritional status (Sitton, 1992) nonadherence to recommended skin care (Noble-Adams, 1999; Porock, Nicoletti & Kristjanson; 1999; Sitton, 1992), menopausal state (Porock et.al, 1998; Turesson et. al., 1996; Sitton, 1992) and that which is identified in the literature as “patient-to-patient variability” (Noble-Adams, 1999; Porock et.al., 1998; Turesson et. al., 1996; Sitton, 1992). It is this unknown factor, patient-to-patient variability, that requires prophylactic treatment be given to all clients receiving irradiation to the breast or chest wall. Co-morbid existence
of disease such as hypertension, cardiovascular disorders, history of skin cancer, and the presence of autoimmune diseases are also included as contributory factors (Turesson et al., 1996).

Use of Topical Agents to Treat Radiation-Induced Skin Reactions

Much has been written about therapeutic agents used in the treatment of radiation-induced skin reactions, although there is little empirical evidence to support their effectiveness. Mild erythema and dry desquamation have been treated with topical ointments including wax, paraffin, olive oil, and almond & chamomile creams with discouraging results (Maiche, Grohn, Maki-Hokkovien, 1991). Weak, topical corticosteroids such as 1% hydrocortisone and 0.05% clobetasone cream have been used but are known to mask signs of infection in inflamed skin (Sitton, 1992). Gleese, Mameghan-Zaheh and Sparkes (1979) saw such a severe skin reaction with the use of the 0.05% clobetasone cream that they recommended discontinuance of the use of topical steroids until the causative factor could be identified. Kolcaba & Fox (1999) and Hogan (1997) have also published the results of works with guided imagery to manage the symptoms of pain, burning, and itching that are associated with the skin reactions. When moist desquamation develops, tradition dictated cleansing the area with half-strength peroxide and saline then applying 1% gentian violet solution (Porok, Nicoletti & Kristjanson, 1999); however, current evidence discourages the use of peroxide on an open, draining wound. Both the use of hydrocolloid (Margolin et al, 1990) and moisture vapor permeable dressings (Porock, Nickoletti & Kristjanson, 1999) have been used on open draining wounds to heal and prevent infection with promising results.
**Hydrocortisone versus Clobetasone cream**

Gleese, Mameghan-Zaheh and Sparkes (1979) studied the use of 1% hydrocortisone cream or 0.05% clobetasone cream in a double blind randomized study of 54 clients receiving external beam radiation therapy for breast cancer. Once the client’s radiation dosage had reached 2000 rad, they were given one of the creams and instructed to apply a thin layer two or three times a day even if no skin reaction was seen. The reaction of the clobetasone group’s skin was so much worse than the group receiving hydrocortisone that the researchers did not recommend the use of either cream until the reason for such a reaction could be identified. Modern improvements in the delivery of radiotherapy of the radiation beam and narrowing of the irradiation field may encourage a replication study of these medications. Application of the creams at the initial treatment visit may also improve the outcome as research has identified the early part of the second week of treatment as the most frequently seen in the development of erythema (Noble-Adams, 1999; Archambeau, Pezner & Wasserman, 1995; Sitton, 1992).

**Sucralfate Cream**

The use of sucralfate cream was studied on fifty breast cancer clients receiving external beam radiation post-mastectomy or lumpectomy. (Maiche, Isokangas & Groh, 1994). A double-blind study was utilized with each client acting as her own control. A thin layer of either sucralfate cream or a placebo cream was applied to either side of the scar beginning with the initial radiation treatment (up to third treatment). The skin was evaluated weekly on a five-point scale for degree of skin reaction by either the physician or oncology clinic nurse. Sucralfate was selected based on its success with mucosal membranes and the hope that the sucralfate would enhance growth of epithelial cells.
(Maiche et al., 1994). Their study found that grade I (erythematic) and grade II (dark erythema/pain) developed much later on the sucralfate treated side, that healing occurred much faster and there was a less likely chance of the development of later skin reactions. The findings of this study were encouraging. A larger sample group and replication of the use of this medication in other settings would be helpful in validating the findings.

**Dexpanthenol cream**

Lokkevik and colleagues (1996) studied the effects of dexpanthenol cream for its prophylactic properties with clients undergoing either breast or laryngeal irradiation. The active ingredient in dexpanthenol, panthenolic acid, is known to decrease the effects of dermatitis and was selected to promote epithelial formation and regeneration thus preventing severe radiation-induced skin reactions. Sixty-three breast cancer clients were included in the eighty-six total subjects studied. Twenty-one of those sixty-three were receiving concurrent low-dose chemotherapy. This study also used a subjective five-point scoring system (0 = no reaction, 1 = mild reaction, 2 = moderate reaction, 3 = severe reaction, 4 = moist desquamation). Clients were ineligible to participate if they had a history of prior skin disease, allergy to the studied agent, were unable to cooperate with the study or had their radiation therapy postponed for any reason. This study found no clinically significant difference in skin reactions with the use of this cream, and it was removed from their clinic’s routine skin care protocol.

**Biafine ® burn cream**

Szumacher (2000) reported on a study describing the results of phase two of a clinical trial in sixty patients from the Toronto area who were given the burn cream marketed as Biafine ® upon initiation of their external beam radiation treatments post mastectomy or
lumpectomy. The study used the Oncology Nursing Society scale for recording skin reactions. Although eighty-three percent of the clients still developed grade II radiation dermatitis, only six percent developed grade III and no one developed the most severe forms, grade IV and V. She indicated that while these results did not find a prophylactic benefit for the use of the cream, it did suggest that its use could benefit the client by limiting the severity of the skin reaction allowing the clients to continue their treatment plan uninterrupted and thus receive the benefits of the full cumulative effect of the radiation therapy.

Fisher and colleagues (2000) reported the results of a randomized study of 172 women receiving radiation therapy post-mastectomy/lumpectomy comparing the use of Biafine ® burn cream with the participating clinic’s choice of best supportive care product or no-treatment. Best supportive care product choices included Aquaphor ® (31%) and Aloe Vera (34%). Sixteen percent of the participants had no treatment to the treatment field (Fisher et al, 2000). While this study did not support the superiority of the use of Biafine ® over the comparative products, it did suggest that the use of this cream hastened the healing of the skin reactions in women with large breasts and in the nonsmoking (Fisher et al, 2000).

Aloe Vera

A study was found that evaluated the effects of aloe vera gel as a prophylactic agent in ameliorating radiation dermatitis. One hundred ninety-four clients were double blind randomized into groups to receive a 98% pure aloe vera gel or an inert gel (used as the base of the aloe vera gel). Both the clients and healthcare providers rated the irradiated skin field on a weekly basis with a four-point scale being used. This study found no
statistical evidence to support the use of aloe vera gel; however, some of the healthcare providers questioned the historical decrease of radiation dermatitis during the twelve-month study period. A second study was then used with one hundred eight clients randomly selected to either apply the aloe vera gel or not. The same rating scale for clients and healthcare providers was used with no clinically significant difference seen in the development or severity of radiation-induced skin changes (Williams et al. 1996).

**Acemannan**

Acemannan-containing wound gel dressings were applied to the irradiated skin fields of mice by Roberts and Travis (1995). They found that mice that were treated before the onset of skin erythema were much less likely to develop adverse skin reactions than those whose treatment was delayed until the onset of symptoms. They found the application of the gel was most effective when it was applied immediately after the irradiation of the skin. If application was delayed until manifestation of symptoms occurred, the gel did not prevent the progression of the dermatitis; however, those who continued to apply the gel healed at a faster rate than those groups who used no gel, personal lubricating jelly (K-Y), or Aquaphor® a prescription healing ointment. It was also noted that application of the gel to mice in the other groups after severe acute dermatitis had developed did not improve healing time.

**Summary**

The effects of radiation on the skin and breast tissue are known and described in the professional literature (Appendix A-2). Prognostic indicators for severe skin reactions to irradiation have been researched with encouraging results. While much has been written about the treatment of radiation-induced skin reactions, little has been done to discover an
agent that could prevent the development of these reactions despite the potentially
detrimental effects of radiation-induced skin reactions on the client’s skin, interruption of
treatment and the severe long-term effects associated with the development of acute skin
reactions including infection, necrosis and loss of healthy breast tissue.
Chapter III

Methods

In this chapter, the methods and design for the study will be described. The design, instruments, setting and sampling, data collection, ethical considerations involved and data analysis will be explained. Limitation of the study’s internal and external validity and attempts to control these factors will also be addressed.

Design

In this descriptive study, clients were instructed to apply Radiacare ® gel to the radiation treatment area at least two to three times daily from the initial consultation until four weeks after the completion of treatment. Skin reactions within the treatment area were assessed weekly and scored based upon the Oncology Nursing Society’s skin reaction scale (Bruner et al, 1998). Skin reactions were analyzed and compared to the known high risk factors of large breast size, increased length of surgical incision and recent chemotherapeutic exposure as well as suggestive factors of age and weight changes. It is known that application of this gel is effective in the treatment of radiation treatment induced skin reactions; this study was to determine if application from the start of radiation treatment may prevent the occurrence of radiation-induced skin reactions (Plemons, et. al, 1994).

Instruments

A data assessment form (Appendix 1) was used to document the skin assessment for participants throughout their treatment plan. Information about the suggestive factors of breast size, exposure to chemotherapeutic agents, length of incision, age and weight was recorded as well as a weekly assessment of the treatment skin area including the entire
breast, axillary and inframammary skin folds, and the surgical incision areas. The skin reaction was scored according to the Oncology Nursing Society’s skin assessment scale. The client’s age, weight changes, and skin complexion type, bra size and previous exposure to chemotherapeutic agents were recorded for comparison purposes.

**Breast Size**

Since the inframammary skin fold has been identified as a high-risk area for radiation induced skin reactions in women with larger breasts, clients receiving post-lumpectomy irradiation will be asked to identify their post-operative brassiere cup size. Large breast size was identified as C-cup size or larger.

**Radiosensitizing Agents**

A list of the client’s current medication regimen was obtained, and each drug will be assessed for its degree of radiosensitivity. In addition, a history was taken to determine if known radiosensitizing chemotherapeutic agents such as dactinomycin, doxorubicin, methotrexate, 5-flurouracil, and/or hydroxyurea were used (Bruner et al, 1998). The time lapse since chemotherapeutic exposure was recorded.

**Incision Length**

The length and location of each participant’s surgical scar was obtained and recorded in centimeters. The location was identified by the quadrants of upper lateral (including tail of Spence), upper medial, lower lateral, and lower medial as well as mixed superior, inferior, lateral or medial. Clients with edema, erythema, or an open, draining wound in the treatment area at the onset of therapy were excluded from the study.
Age

Age has been identified in previous studies as a contributing factor in the decreased healing time for radiation dermatitis and other skin integrity problems. It was included in this study to explore the relationship between age and the development of radiation-induced skin reactions when Radiacare® gel is applied according to the study’s protocol.

Weight Changes

Studies have linked poor nutritional status to both loss of skin integrity and delayed wound healing. A comparison of baseline body weight and weekly weights was included. It is acknowledged that the assumption of good nutritional status before diagnosis is idealistic.

Skin Complexion Type

Although radiation-induced skin reactions affect the basal layer of skin, anecdotal data suggest that fairer complexions are more likely to experience the more severe skin reactions. This comparison was made by having the skin complexion type assigned by the client’s self-report based upon the following scale:

- Fair: burns easily with minimal sun exposure
- Medium: burns with sun exposure but rarely blisters
- Dark: rarely burns with sun exposure

Radiation Dose

Each client’s cumulative weekly radiation dosage was recorded. Differences in treatment length and area were compared. Breaks in consecutive treatments were also recorded with a rationale for its need.
Skin Assessment

In 1994, the Oncology Nursing Society adopted a six-point skin assessment scale for radiation-induced skin reactions (Bruner et al, 1998). The scale allows for standardization and improved communication between practitioners. Documentation of skin reactions were identified as

0 = No changes noted
1 = Faint or dull erythema, follicular reaction
2 = Bright erythema
3 = Dry desquamation with or without erythema
4 = Small to moderate amount of wet desquamation
5 = Confluent moist desquamation; edema
6 = Ulceration, hemorrhage, or necrosis

For this study, the entire treatment area, axillary skin fold, inframammary fold, and area adjacent to the surgical incision were assessed. Any skin reaction was graded and its location noted on the data collection form.

Setting and Sampling

The participants of this study were selected from an outpatient radiation oncology clinic in the southeastern United States. All clients who were referred for post-lumpectomy or post-mastectomy irradiation were asked to participate. Those who had a known sensitivity to aloe vera, were unable or unwilling to comply with the application of the gel, had edema, erythema or an open wound to the treatment area were excluded from the study.
**Intervention**

Each participant was given a skin care protocol (Appendix 3) that included the application of the Radiacare® gel. Sample tubes of the gel were provided along with a prescription for additional tubes. Each week, the client was asked about application of the gel and the clinic nurse, using the above-mentioned Oncology Nursing Society scale, assessed the skin for reactions.

**Data Collection**

Upon signed consent to participate (Appendix 4), the client was asked to identify her age, weight change since diagnosis, skin complexion type, post-operative bra size and exposure to chemotherapeutic agents. The clinic nurse recorded medications, herbal supplements and vitamins in use, measured and identified the location of the surgical scar and assessed the treatment area skin. A data collection sheet (Appendix 1) was placed in the chart. Each week, the client was asked to confirm continued use of the gel. The nurse assessed the treatment area skin and recorded the assessment of the breast fields, weight, medication changes and cumulative radiation dose. After the four-week follow-up appointment, the form was removed from the chart and the data was transferred to a tally sheet from which comparison to that of other participant's data was made. At the conclusion of the study, each participant's data was tabulated and reported. A comparison of skin reactions each week and between each risk factor was examined. Comparisons were made as to the influence the application of the gel may have had on the participant's skin. All results are given in grouped data to decrease the chance of individual identification of a participant.
Ethical Considerations

This study included human participants and was reviewed by the university's Human Subjects Review Board (Appendix 5) as well as the Medical Center's Research Review Committee (Appendix 6). The treatment under study has been the standard treatment protocol within this population for the clinic since February 2000 and was conducted to evaluate its clinical validity (Appendix 7).

Participants were solicited from the clients referred to the clinic for post-mastectomy or post-lumpectomy irradiation. Each client had the study explained to them by the researcher and was asked to provide a written consent to participate (Appendix 4). The participants were given a copy of the consent, which included the procedure for withdrawal from the study. Care was taken to stress that participating in the study would merely allow the data collected to be used for research purposes and would not change the skin care recommendations they received. After the participant's one-month follow-up appointment was completed, her data assessment form was removed from the chart to ensure anonymity of the data.

Data Analysis

The data analysis for this descriptive study included frequencies and the measures of central tendency including mean, median and mode. Comparisons between each suggestive factor and the degree of skin reaction were analyzed using Analysis of Variance (ANOVA). Client's use of the gel and the skin's reaction were also compared.
Study Limitations

Internal Validity

In this study, internal validity may be questioned since the selection of participants was based upon those who were referred to the clinic for irradiation during the study timeframe, those who consented to participate and those who were willing or able to continue to participate throughout the study. The lack of a control group and randomization in selection limit the ability to identify with confidence the use of the Radiacare ® gel as the influencing factor in the incidence of the development of radiation dermatitis.

Sample Size

Study participants were solicited from those clients (all women) who were referred for irradiation post-mastectomy or post-lumpectomy during the study timeframe. There was no reliable mechanism for predicting the number of referrals that would be made within that period.

Attrition

As in any study, a certain amount of attrition is expected. There are those participants who may wish to withdraw, those from the sampling pool who are not eligible to participate, and those who do not complete the treatment plan. This attrition factor will decrease the already limited sample size and will have a negative effect on the generalizability of any relationships identified.

Subjectivity of Skin Reaction Analysis

The use of the Oncology Nursing Society’s skin assessment scale, while helpful, does not eliminate the subjectivity of the skin reaction scores. To minimize this effect, the
number of persons who assessed the scores was limited to the two researchers who are
Registered Nurses, employed by the clinic and are familiar with the study and its purpose.
Further validation was provided by the medical director's independent assessment of the
skin condition.

External Validity

The external validity of this study is threatened since random selection of participants
was not used. This approach prevents generalization to the population of all clients
receiving external beam radiation therapy post-lumpectomy or mastectomy. Multiple
treatment interference may also threaten the external validity in that it is not known what
cumulative effects of prior treatments (such as chemotherapy) or other current treatments
may have had on the development of radiation dermatitis.

Setting and Sampling

It was expected that the clients for this study would be primarily female, Caucasian
and over the age of 60, thereby limiting its generalizability to the entire population;
however, it does reflect the profile of those with breast cancer that are receiving post-
surgical irradiation. This study was conducted within a mid-sized regional medical
center in the southeastern United States, which may influence the demographic reliability
of generalization to more rural or urban settings, or to those with more ethnic diversity.

Reactive Effect

While it is vital that clients be aware of and consent to participation in this study, this
requirement may not only limit the size of the sample but may also influence the
subjective data required from the participants, especially the validity of the self-reporting
of the continued use and frequency of use of the gel throughout the treatment.
Summary

The design of this descriptive study was to maximize the available data and minimize factors that could distort the validity of the findings. A review of the literature was conducted to determine those factors identified as suggestive or directly implicated in the development of radiation-induced skin reactions and were included in this study to discover the relationship between the application of the Acemannan containing Radiacare ® gel and the prevention of the development of these skin reactions. Care was taken to control those factors that could influence the data collection and analysis as well as limit the generalizability of the findings to the general population. It was the purpose of this study to determine if there is a relationship between the application of this gel and the prevention of the development of radiation dermatitis in participants with intervening factors such as large breast size, exposure to radiosensitive agents, healed surgical incisions, advanced age and weight changes since diagnosis.
Chapter IV

RESULTS

Between April 1, 2001 and October 31, 2001, 19 eligible clients were solicited for participation in the study. One declined and the remaining 18 were followed throughout their treatment regimen. Demographically, 89% of the women (n=16) were of European ancestry and 11% (n=2) were of African decent. There was no attrition. Twelve women identified their breast cup size as cup-C or larger and the affected breast was equally distributed between the right and left side. Five participants were treated with chemotherapy before the onset of their radiation. No woman in this study received concurrent chemotherapy with the external beam radiation. The incision size ranged from 2.5 cm to 12.5 cm with a mean of 5.9 cm. All but one of the participants was receiving post-lumpectomy irradiation with two thirds of the incisions being located on the lateral aspect of the affected breast. The age range of the participants was 30 - 87 with a mean age of 56.7. Five clients were aged 30 - 49; nine were between the ages of 50 - 69, and the remaining four were aged 70 - 89. Most women (n=13) claimed no weight change from the time of initial diagnosis until the onset of radiation therapy. Of those who did report a change, three cited a weight loss (-2, -5, -10 pounds) while two indicated they had experienced a weight gain (+5, +10). At the conclusion of the treatment plan, the mean weight change was a loss of 5.3 pounds. Five questions were addressed with this study and statistical data collected and analyzed to discover the degree to which the use of Radiacare gel might influence the development of radiation dermatitis.
Question One:

What is the relationship between large breast size and the incidence of radiation dermatitis when using Radiacare® gel before and throughout external beam radiation therapy?

Analysis of Variance indicated that there was no relationship between the incidence of radiation dermatitis within the entire treatment field (p=0.741) between large-breasted women and small-busted; however, there was a statistically significant difference noted between those groups at both the area around the incision site and the inframammary skin fold. Women with size C-cup breasts or larger were likely to have a more intense skin reaction along the incision line (p=0.0249) or the inframammary fold (p=0.0180) than those who were smaller busted. Since this finding has been reflected in prior studies, the application of Radiacare® had no influence on the incidence of radiation dermatitis.

(Figure 1)

<table>
<thead>
<tr>
<th></th>
<th>Breast</th>
<th>Incision</th>
<th>IMF</th>
<th>Axilla</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; C-cup</td>
<td>5.3</td>
<td>5.2</td>
<td>4.3</td>
<td>5.2</td>
<td>20</td>
</tr>
<tr>
<td>&gt; C-Cup</td>
<td>7.4</td>
<td>7.6</td>
<td>9.7</td>
<td>7.6</td>
<td>32.3</td>
</tr>
</tbody>
</table>

Figure 1: Comparison of incidence of radiation dermatitis between large-breasted and small-breasted women throughout treatment field (incidence), and at the breast, incision, inframammary skin fold, and axillary sites.
Question Two

What is the relationship between prior exposure to chemotherapeutic agents and the incidence of radiation dermatitis when using Radiacare® gel before and throughout external beam radiation therapy?

No relationship was seen between the women who had prior exposure to chemotherapeutic agents and those who did not (figure 2). Incidence was determined by calculating the total of the skin severity reactions at each site (entire breast, incision line, inframammary fold and axilla, where applicable) throughout the treatment period then compared by groups (chemo and non-chemo) with no statistical difference found.

![Comparison of Incidence and Chemotherapeutic Exposure](image)

*Figure 2. Comparison of total incidence of skin reaction by entire breast, area surrounding the incision, the inframammary skin fold and mean incidence between those who were exposed to chemotherapeutic agents prior to irradiation and those who were not.*
Question Three

What is the relationship between the length of incision and the incidence of radiation induced dermatitis when using Radiacare® gel before and throughout external beam radiation therapy?

Using the Pearson's Correlation Coefficients, the length of the scar was able to account for less than 1% of the skin reaction of the total treatment field ($R^2=0.616$) and for less than 2% of the reaction seen around the incision line ($R^2=0.02$). Of interest, a negative correlation ($r=-0.08141$) was seen between the incision length and the incidence of skin reaction at the inframammary skin fold (Figure 3). This end result could indicate a positive relationship between the use of Radiacare® gel and the decrease in the skin reaction at the inframammary skin fold.

![Incidence by Incision Size](image)

*Figure 4.* Total incidence of skin reaction by site (axilla, inframammary skin fold, area surrounding the incision, and entire breast) for each participant.
Question Four

What is the relationship between the age of the client and the incidence of radiation dermatitis when using Radiacare® gel before and throughout external beam radiation therapy?

*Figure 4.* Incidence of skin reaction totals by age of client.

The relationship between age of the client and the incidence of radiation dermatitis (figure 4) in this study was mixed. The data indicated a positive correlation between age and the skin reaction incidence over the entire treatment field ($r=0.01841$). The data also showed a negative correlation between incidence and the area around the incision line ($r=-0.03169$) and the inframammary fold ($r=-0.039331$) that is, as age increased, a lower incidence of radiation dermatitis occurred in each of these observation sites (figure 5). The study findings indicate the possibility that a favorable relationship exists between the use of Radiacare® gel and the incidence of radiation dermatitis at the incision line and inframammary fold in older women.
Figure 5. Comparison of the incidence of skin reaction and age of the client by contrasting reaction at the inframammary skin fold and incisional area.
Question Five.

*What is the relationship between weight changes since diagnosis and the incidence of radiation dermatitis when Radiacare® gel before and throughout external beam radiation therapy?*

A positive relationship between the weight changes and the incidence of radiation dermatitis was seen with the use of Radiacare® gel (figure 6). By Pearson's Correlation Coefficient, 14% of the skin reaction over the entire treatment field was correlated to weight changes ($r = -0.37524$), 8% of the reaction seen around the incision site ($r = -0.28978$) and 3.7% of the inframammary skin fold reaction ($r = -0.19274$). As weight decreased, the skin was less likely to react. The suggestion is that the Radiacare® gel may have positively affected the degree of skin reaction in this group of participants.

*Figure 6. Comparison of total skin reaction to amount of weight change since breast cancer diagnosis by participant.*
Summary

The overall goal of this study was to determine if the use of Radiacare® gel before and throughout treatment with external beam irradiation following a mastectomy or lumpectomy for breast cancer would alter the expected skin reaction. A review of literature identified factors that could be used to identify persons or areas most at risk for intense skin reactions from the treatment. The use of Radiacare® gel did not change the skin reaction intensity from that which was expected in women with larger than C-cup breasts; however, results showed a positive relationship among women who had undergone chemotherapy before radiation therapy, who were older or who had lost weight since breast cancer diagnosis and decreased skin reaction.
Chapter V

Discussion

In this descriptive study, the effects of the application of Radiacare® gel before and throughout external beam radiation therapy post-lumpectomy or post-mastectomy were evaluated to determine if there was a difference in skin reactions from those described in the literature. Many prognostic indices were suggested as factors that negatively influenced the development of radiation dermatitis during therapy. Five risk factors were selected from these to be used in this study and were identified as follows: breast size of C-cup or larger, previous exposure to chemotherapeutic agents, length of surgical incision, age, and weight change since diagnosis with breast cancer. The small sample size and lack of a control group limit the generalizability of the findings; however, these risk factors should be used to guide future studies since the use of the Radiacare® gel may have positively influenced the degree to which the skin reacted during treatment.

Breast size

When assessing the skin reaction of women with C-cup or larger breasts receiving external beam radiation therapy post-lumpectomy, there were more intense skin reactions noted at the incision line and the inframammary skin fold than those seen with smaller breasted women in the group. However, there was no statistically significant difference in the overall treatment field when compared with the smaller breasted women receiving treatment. It was expected that the larger breasted women would have significantly more intense reactions in every assessed area (when compared with the smaller breasted women under treatment); therefore, the possibility that Radiacare® gel positively affected the skin in the larger breasted group can be considered. Of note, during this study, only
one woman (size EEE) required a break in the treatment plan due to radiation dermatitis. This factor is one that should be included in future studies of this nature, as the cumulative benefit of irradiation has long been documented as most effective in treating tumors and interruption in treatment may decrease the effectiveness of the irradiation.

Prior chemotherapeutic agent exposure

The prior exposure to chemotherapeutic agents was expected to increase the incidence of skin reaction; however, in this study, there was no statistically significant difference found when assessing the treatment field, axillary, inframammary fold, or incision areas. While the study’s design and sample size cited previously prevent generalizability, it is possible to speculate that the use of the Radiacare® gel may have had a positive influence on this factor. Future studies using control groups and random assignment to treatment modalities should identify the role Radiacare® gel application plays in the decreased incidence of radiation dermatitis.

Length of surgical incision

It was expected that those with larger surgical incisions would have greater skin reactions due to the breech of skin integrity before the insult of irradiation. Each participant was required to have a well-healed incision without a break in the skin to be eligible for participation in this study. The length of surgical incision was able to account for less than two percent of the skin’s reaction in this study. It is possible that a larger, more randomly selected population would reflect a different correlation. In this study, a negative correlation was seen between the larger surgical incisions and skin reaction incidence at the inframammary fold. This finding could be a serendipitous one, or, could suggest that the Radiacare® gel applied to this area afforded some skin protection.
**Age of client**

As with the increased incidence of skin reaction expected with a breech in the integrity of the skin, it was expected that older skin would have more intense skin reactions due to the loss of elasticity, moisture and slower recovery time from insults. When assessing the overall treatment fields, the incidence of skin reaction did rise with the age of the client; however, the areas of the inframammary skin fold and surgical incision had a negative correlation suggesting that the application of the Radiacare® gel may have had beneficial effect on these treatment areas. A larger, more comprehensive study should investigate this phenomenon.

**Weight change since diagnosis**

The final prognostic factor evaluated in this study was the relationship between weight change and the incidence of skin reactions when using Radiacare® gel before and throughout treatment. Prior studies have indicated that poorly nourished skin is less pliable and slower to heal than well-nourished skin and that the nutritional status of the client before the onset of treatments will influence how well the skin is able to protect and repair itself from the damage caused by the radiation. This study utilized a self-report of the amount of weight change since diagnosis combined with the actual beginning and ending weights to define weight changes. Future studies may consider the use of other determinations of nutritional status or Body Mass Index (BMI) to estimate this factor. In this sample few clients reported a weight change, and the mean weight change throughout the twenty-five consecutive treatments was a loss of five pounds. The assumption that the women were nutritionally healthy at the time of diagnosis was unrealistically ideal. Even within the small sample size of this study, there were women
who were grossly underweight as well as those who were morbidly obese. This ideal weight assumption negates any correlations identified in this group.

While the scope and limitations of this study, as previously identified, limit its usefulness, the results are encouraging in the potential of Radiacare® gel in preventing or minimizing the incidence of radiation dermatitis in women receiving external beam radiation therapy post-lumpectomy or post-mastectomy. This study’s data analysis did indicate that of the factors under consideration, forty percent of a women’s degree of skin reaction could be accurately predicted based upon knowing her breast cup size and the amount of weight change she had experienced since her diagnosis. Incidentally, the data also supported previous findings stating that fair skin complexion is not an accurate prognostic factor for intensity of skin reactions while receiving external beam irradiation.

Suggestions for future studies

Suggestions for future studies include the use of a larger sample size with a control group and more ethnic diversification of the population. In addition, the use of BMI or other measure of nutritional status rather than weight change since diagnosis is recommended. An objective means of recording a comparison of the number of and amount of applications applied daily would assist researchers in evaluation of data. Additionally, studies should analyze the frequency and duration of treatment breaks caused by acute skin reactions, as well as time of healing of the skin back to baseline.

The participants in this study were primarily middle-aged Caucasian women of middle- to upper-middle class socioeconomic status. A larger, more diverse population may illicit significantly different results or may confirm those suggested in this study. As noted previously, a more accurate measure of nutritional status is needed to better
evaluate the degree to which the skin’s nutritional health influences the incidence of skin reactions during irradiation therapy.

The daily use of the gel and number of applications per day were self-reported and were, therefore, subject to reactive effect. A study to compare the amount of gel applied and/or the number of applications per day would be useful in guiding skin care protocols using this product if further research indicates its usefulness in the prevention of or decreased incidence of skin reactions.

Future studies should include an indication of the number of participants who are required to have a break in the treatment regime due to severe skin reactions when compared to a control group. If the use of this gel can prevent a break in treatment, then, women who use this product would be able to gain the full benefit of the cumulative effects of their therapy.

Summary

This descriptive study identified and evaluated five prognostic indicators of radiation dermatitis in women receiving external beam radiation therapy post-lumpectomy or post-mastectomy. While the small sample size and lack of a control group limits the usefulness of the findings, there were indications that the use of Radiacare® gel may have positive outcomes in preventing the occurrence radiation dermatitis or alleviating the symptoms which promote treatment adherence and improved quality of life for the client receiving treatment.

The nurse working within the radiation/oncology clinic may also use this study’s findings to reinforce skin care protocols with those women with large breasts.

Additionally, the oncology nurse should identify those with weight changes since breast
cancer diagnosis because this factor has been identified as putting the individual at significant risk of more severe skin reactions. Those women with both risk factors would be especially encouraged to adhere to the skin care protocols.

Future studies should include these factors when comparing the use of this gel to another or a control group with no treatment to assist in evaluating its effectiveness. They should also include a more ethnically diverse population and a better mechanism for identifying nutritional status. It is also recommended that the number of breaks in treatment required due to severe skin reaction be compared.

Nurses assist women in dealing with the devastating emotional, spiritual, and physical effects that encompass the diagnosis and treatment of breast cancer. It is imperative for a product to be found that will prevent or alleviate the uncomfortable and sometimes debilitating skin side effects experienced by women receiving external beam radiation therapy for their cancer. Knowledge of the prognostic factors for more severe skin reactions will be useful to the oncology nurse only if a product can be identified to offer prevention or palliation of those symptoms. Nurses must encourage participation in future studies to assist in the continued search for help for the suffering of the clients entrusted to our care.
Reference List


APPENDIX
Appendix A-1

Radiacare Project Form

Thank-you for agreeing to participate in this study. Please identify the following information. Remember that once your treatment is completed, this form will be removed from your chart and no one will be able to tell it was yours.

Personal Information:

Age: _______ Bra Size: _______ Amount of weight change since diagnosis: _______ Gain

Loss

Have you taken, or are you now taking, chemotherapy? Yes No

If so, how long since treatment completed? ____________________________

Would you rate your skin complexion as?

Fair: burns easily with minimal sun exposure

Medium: burns with sun exposure but rarely blisters

Dark: rarely burns with sun exposure

For Nurse to complete:

List of current prescription and over the counter medications: ____________________________________________

________________________________________________________________________________________

________________________________________________________________________________________

________________________________________________________________________________________

Initial weight: _______ Surgical scar measurements: _______

Data Collection

<table>
<thead>
<tr>
<th>Date</th>
<th>Weight</th>
<th>Use of gel?</th>
<th># times/day</th>
<th>Breast</th>
<th>Axilla</th>
<th>Scar</th>
<th>Inframammary fold</th>
<th>Rad. Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

Scale: 0 = no changes noted 4 = small to moderate wet desquamation

1 = faint or dull erythema, follicular reaction 5 = confluent moist desquamation; edema

2 = bright erythema 6 = ulceration, hemorrhage, or necrosis

3 = dry desquamation with or w/o erythema
## Appendix A-2

**Literature Relevant to the use of Topical Agents to Treat Radiation Dermatitis**

<table>
<thead>
<tr>
<th>Source</th>
<th>Agent</th>
<th>Sample</th>
<th>Design</th>
<th>Instrument</th>
<th>Results</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>hydrocortisone vs. clobetasone</td>
<td>54 Breast Cancer</td>
<td>Prophylaxis Double-blind, Exp.</td>
<td>Weekly scale 1 – 4</td>
<td>clobetasone skin reacted severely to radiation</td>
<td>Discouraged use of either until cause of reaction to clobetasone identified</td>
</tr>
<tr>
<td>1994</td>
<td>sucralfate cream</td>
<td>50 Breast cancer</td>
<td>Double-blind Own control</td>
<td>Weekly 5 pt skin rating</td>
<td>Slower developing reaction, faster healing</td>
<td>Needs replication for validation—encouraging</td>
</tr>
<tr>
<td>1996</td>
<td>dexpanthenol cream (panothenic acid)</td>
<td>63 breast cancer</td>
<td>Exp. Own control</td>
<td>Weekly scale 0 – 4</td>
<td>No sign diff w/use of cream</td>
<td>Removed from clinic's protocol</td>
</tr>
<tr>
<td>2000 Fisher</td>
<td>Biofine® vs. Aquaphor®, aloe vera, or pt choice OTC</td>
<td>172 ½ Biafine® 1/6 ea others</td>
<td>NE Random assignment to groups</td>
<td>Weekly 4 point scale</td>
<td>No prophylaxis Biafine® group healed faster in high-risk</td>
<td>Encouraging for Biafine®, Discouraging: Aquaphor®, Aloe vera, or OTC remedies</td>
</tr>
<tr>
<td>1996 Williams</td>
<td>aloe vera</td>
<td>194 clients</td>
<td>Double-blind; randomized</td>
<td>4 pt scale weekly AND Client self-assessment questionnaire</td>
<td>No statistical difference in groups</td>
<td>Aloe vera not supported in prophylaxis</td>
</tr>
<tr>
<td>1996 Williams</td>
<td>aloe vera</td>
<td>108 clients</td>
<td>Random assignment</td>
<td>Weekly 4 pt scale</td>
<td>No diff in development or severity</td>
<td>Aloe vera not supported for prophylaxis</td>
</tr>
<tr>
<td>2000 Szumacher.</td>
<td>Biafine®</td>
<td>60 Br Ca w/concurrent low dose chemo</td>
<td>NE</td>
<td>0 – 4 point scale &amp; pt questionnaire weekly</td>
<td>Only 3% developed Grade III None developed Grade IV</td>
<td>Reduction in severity seen from expected</td>
</tr>
<tr>
<td>1995 Roberts</td>
<td>Acemannan Gel</td>
<td>Laboratory mice</td>
<td>Random assignment</td>
<td>Skin assessment</td>
<td>Best if applied immediately after Tx. Reactions healed better w/ continued use</td>
<td>Encouraging for use in humans Not useful after severe reaction develops</td>
</tr>
</tbody>
</table>
Skin Care Instructions for Breast Cancer Radiation Therapy

Radiation therapy works by exposing the cancerous area to high-energy x-rays. While both the diseased and healthy cells are affected, the healthy cells possess a better ability to recover and the diseased cells are damaged or destroyed.

There are many things you can do to help make your treatment a success!

1. Protect the treatment area from rubbing, pressure, or irritation.
   - Wear loose, soft cotton, comfortable clothes. (Old ones that can get ink on them!)
   - Do not wear a bra or tight clothing that will rub the treatment area.
   - Do not starch your clothes.
   - Do not rub or scrub the treatment area. Use your hands to gently cleanse the area.
   - Do not use adhesive tape on the treatment area. If you must bandage the area, use paper tape and try to apply it to an untreated part of the skin.
   - Try to keep your underarm from rubbing skin to skin—stand with your hand on your hip to keep the skin from your arm from rubbing your underarm.

2. Protect the treatment area from irritants such as:
   - Soaps, perfumes, heating pads, ice packs, or talcum powder.
   - Use only the deodorant provided by the Radiation Oncology Nurse.
   - Avoid shaving the underarm of the treated side. If you MUST shave, use an electric shaver and DO NOT apply preshave lotions or hair remover products to the treatment side.

3. Protect the treatment area from the sun during treatment and after the treatment is completed. During your treatment time, keep the area covered from sun exposure with light colored clothing. After treatment, we recommend using a PABA sunscreen with at least a 15 rating as well as covering the treated area with light colored clothing.

4. Do not wash off the marks applied by the Radiation Therapists to outline the treatment area.

5. Apply a thin layer of Radiacare gel to the inside of the outlined area FOUR TIMES A DAY beginning on the day the outline marks are made. Continue to apply the gel throughout the treatment until your one-month follow-up visit. The gel will protect the healthy cells from damage during treatment. It will supply the healthy cells with moisture and help them heal after treatment is complete.
   - On treatment days, do not apply the gel within TWO hours of treatment and apply the gel as soon as possible after your treatment to get the most benefit.
   - If itching or drainage develops, see the physician or nurse for the gel in a cooling or absorbent formula.

6. Eat a healthy, balanced diet and drink plenty of fluids.

7. Avoid people with colds or other infections until your treatment is over.

8. Ask questions! Write them down and bring them with you to your treatment sessions and follow-up visits. You will see the Radiation Oncologist each week, usually on Wednesday, but please let us know if you have questions or concerns before then.
Appendix A-4

INFORMED CONSENT DOCUMENT

Project Title: Prevention of Radiation-Induced Dermatitis in Breast Cancer Irradiation.

Investigator: Cathy Eden Ammerman, Nursing, 615.451.2817

You are being asked to participate in a project conducted through Western Kentucky University and Sumner Radiation Oncology. The University requires that you give your signed agreement to participate in this project. Mrs. Ammerman or Mrs. Rippy will explain to you in detail the purpose of the project, the procedures to be used, and the potential benefits and possible risks of participation. You may ask her any questions you have to help you understand the project. A basic explanation of the project is written below. Please read this explanation and discuss with Mrs. Ammerman or Mrs. Rippy any questions you may have.

If you then decide to participate in the project, please sign on the last page of this form in the presence of the person who explained the project to you. You will be given a copy of this form to keep.

1. **Nature and Purpose of the Project:**
The purpose of this study is to determine if the gel marketed under the name of Radiacare is effective in preventing the skin reactions that are sometimes seen in women who are having radiation therapy after their mastectomy or lumpectomy.

2. **Explanation of Procedures:**
You will be given a copy of the clinic’s skin care guidelines including applying the Radiacare Gel to the treatment site two or three times a day beginning today and continuing to apply the gel to that area for one month after your treatments have ended. Each week (usually on Wednesdays) you will be asked how many times a day you are applying the gel and your skin will be checked for signs of redness and swelling.

3. **Discomfort and Risks:**
If using aloe vera in the past has caused you to develop hives or caused redness or swelling to your skin or you have had a previous adverse reaction to Radiacare Gel, you should not use this product. There is a slight chance that you may develop redness, swelling, or hives to the treatment area if you develop an allergy to the gel. If you do, you will be advised to stop using the gel and your information will not be used in the study except to say one person was not able to complete the study due to an adverse skin reaction to the gel.

4. **Benefits:**
It is anticipated that the application of this gel will prevent skin damage from your radiation treatments similar to the way sunscreens prevent skin damage from sunburn.
5. **Confidentiality:**
A form like the one attached to this one will be placed in your chart upon which the nurse will track your skin response each week. This form will also have your age, bra cup-size, size of surgical scar, and list of your current medications. This information has been included to determine whether these factors change the effectiveness of the gel in preventing skin reactions. No one except the persons employed by the radiation clinic will be able to view the form. Once you have completed your one-month post-treatment appointment, that form will be removed from your chart, the skin reaction scores and above-mentioned information will be placed on an anonymous form and the one in your chart will be destroyed. No one will be able to determine your individual results once your follow-up appointment is completed.

6. **Refusal/Withdrawal:**
Refusal to participate or withdrawal from the study does not alter the skin care guidelines for you. If you do not wish to continue your participation in the study, you may withdraw from the study at anytime during your treatments until the time of your one-month follow-up appointment. Once your information has been transferred to the anonymous group form, it cannot be removed. Withdrawal may be done in person by informing the nurse of your decision to withdraw any day during your treatment or upon your one-month follow-up visit. Refusal to participate in this study will have no effect on any future services you may be entitled to from the University or the Radiation Oncology Clinic. Anyone who agrees to participate in this study is free to withdraw from the study at any time with no penalty.

*I understand also that it is not possible to identify all potential risks in an experimental procedure, and I believe that reasonable safeguards have been taken to minimize both the known and potential but unknown risks. I also understand that my participation in this study is voluntary.*

______________________________  __________________________
Signature of Participant        Date

______________________________  __________________________
Witness                      Date

**THE DATED APPROVAL ON THIS CONSENT FORM INDICATES THAT THIS PROJECT HAS BEEN REVIEWED AND APPROVED BY THE WESTERN KENTUCKY UNIVERSITY HUMAN SUBJECTS REVIEW BOARD**
**TELEPHONE: (270) 745-4652**
**YOU MAY CONTACT THE HUMAN PROTECTIONS ADMINISTRATOR AT THIS NUMBER**
**SHOULD YOU HAVE COMMENTS OR CONCERNS**
Appendix A-5  
APPLICATION FOR APPROVAL OF INVESTIGATIONS INVOLVING THE USE OF HUMAN SUBJECTS

Submit by the first working Monday of the month for screening prior to the HSRB meeting. Please add additional space between items as needed to describe your project.

1. Principal Investigator's Name: Cathy Eden Ammerman, RN  
   Email Address: cathyea@home.com  
   Mailing Address: 811 Harden Street Gallatin, Tennessee 37066  
   Department: Nursing  
   Phone: (615) 451-2817  
   Co-Investigator: Carol B. Rippy, RN, C  
   Email Address: rippyc@sumner.org  
   Mailing Address: 300 Steam Plant Road, Suite 150 Gallatin, Tennessee 37066  
   Department: Sumner Radiation/Oncology  
   Phone: (615) 451-6080  

2. If you are a student, provide the following information:  
   Faculty Sponsor: Dr. Beverelv E. Holland, Nursing  
   Phone: (270) 745-3489  
   Faculty Mailing Address: AC 108-A 1 Big Red Way Bowling Green, KY 42101  
   Student Permanent Address (where you can be reached 12 months from now):  
   811 Harden Street Gallatin, Tennessee 37066  
   Is this your thesis or dissertation research? Yes  

3. Title of project: Prevention of Radiation-Induced Dermatitis in Breast Cancer Irradiation.  

4. Project Period: Start: May 1, 2001  
   End: October 31, 2001  

5. Has this project previously been considered by the HSRB? NO  

6. Do you or any other person responsible for the design, conduct, or reporting of this research have an economic interest in, or act as an officer or a director of, any outside entity whose financial interests would reasonably appear to be affected by the research? NO  

7. Is a proposal for external support being submitted? NO  

8. You must include copies of all pertinent information such as, a copy of the questionnaire you will be using or other survey instruments, informed consent documents, letters of approval from cooperating institutions (e.g., schools, hospitals or other medical facilities and/or clinics, human services agencies, individuals such as physicians or other specialists in different fields, etc.), copy of
external support proposals, etc. **Attached:** Informed consent document, Letters of approval from Sumner Regional Medical Center, and Dr. Robert T. McClure, Radiation/Oncology.

I. **PROPOSED RESEARCH PROJECT**

A. Provide a brief summary of the proposed research. Include major hypotheses and research design.

Descriptive study of the effects of applying Acemannan (Radiacare Gel) in the prevention of the development of radiation-induced skin reactions in women receiving post-lumpectomy/mastectomy external beam radiation therapy at an outpatient radiation oncology clinic.

Women will be asked to participate in the study and will be given a skin care protocol that includes the application of Acemannan to the skin within the treatment area. The skin will be assessed and assigned a reaction score weekly throughout treatment and at the one month follow-up appointment.

B. Describe the source(s) of subjects and the selection criteria. Specifically, how will you obtain potential subjects, and how will you contact them?

All clients receiving post-lumpectomy/mastectomy irradiation at Sumner Radiation/Oncology between May 1, 2001 and October 31, 2001 will be asked to participate. The clients will be solicited for participation at the time of initial consultation and simulation at which time the nurse will review the skin care protocol and explain the study.

C. Informed consent: Describe the consent process and attach all consent documents.

A written consent which explains the study and skin care protocol will be given to each prospective client. Emphasis will be placed upon the fact that participation does not alter the plan of care. See Appendix.

D. Procedures: Provide a step-by-step description of each procedure, including the frequency, duration, and location of each procedure.

1. Clients will be identified from new client referral list by nurse and request for participation consent will be placed in chart with usual educational materials. Once the clients have been deemed appropriate candidates for the ERBT, their participation in the study will be solicited.

2. Clients who consent to EBRT will then be advised of skin care protocol including the application of Acemannan (Radiacare Gel) and will be solicited to participate in the data collection study. Care will be taken to emphasize that the treatment plan will not be altered by their participation or their decision not to participate.
3. Clients will be given sample tubes of the gel and a prescription for the gel by the medical director with instructions to apply a thin layer to the treatment area two to three times daily beginning with the initial consultation and continuing until the four-week follow-up visit.

D. Procedures (cont.)
4. Skin within the treatment area will be assessed on a weekly basis and again at the four week post-treatment follow up appointment and assigned a score based upon a six-point scale from 0 (no reaction) to 6 (necrosis).
5. In addition data regarding, age, weight, bra cup size, size of surgical scar, skin complexion, and a list of current medication (including chemotherapy) will be collected to compare skin reaction severity within sub-groups. Each of these factors has been implicated in influencing skin reactions to EBRT.

E. How will confidentiality of the data be maintained? (Note: Data must be securely kept for a minimum of three years on campus.)

Information will be collected on a form that will include the client’s initials during treatment and follow-up and kept in the client’s treatment record. Once the follow-up visit is completed, the form’s data will be transferred to a central tabulation form and the individual’s form will be destroyed. Only healthcare personnel with legal access to the chart and the investigator will have access to the form during treatment.

F. Describe all known and anticipated risks to the subject including side effects, risks of placebo, risks of normal treatment delay, etc.

Acemannan has no known side effects. It has been FDA approved in the healing of radiation induced skin reactions. Since there is no approved prophylactic treatment for radiation induced skin reactions, the standard treatment is to treat the skin symptomatically.

G. Describe the anticipated benefits to subjects, and the importance of the knowledge that may reasonably be expected to result.

Acemannan has been shown to significantly reduce the radiation skin reactions in laboratory mice. It is anticipated that similar benefits will be obtained in human subjects. Acemannan is thought to support the monocytes and phagocytic action to improve the skin’s ability to repair itself from the damages of irradiation. The hydrogel properties of the gel are also thought to support retention of moisture within the skin (Roberts and Travis, 1995).
II. SIGNATURES

A. I certify that to the best of my knowledge the information presented herein is an accurate reflection of the proposed research project.

   Principal Investigator
   ____________________________  3/29/01
   Date

   Co-Investigator
   ____________________________  3/29/01
   Date

B. Approval by faculty sponsor (required for all students):

   I affirm the accuracy of this application, I accept the responsibility for the conduct of this research, the supervision of human subjects, and maintenance of informed consent documentation as required by the HSRB.

   ____________________________  3/29/01
   Faculty Sponsor
   Date

C. Approval by Department Head (required for all applications)

   I confirm the accuracy of the information stated in this application. I am familiar with, and approve of the procedures that involve human subjects.

   ____________________________  3/29/01
   Department Head
   Date

D. Advising Physician*:

   I certify that I am a duly licensed physician in the State of Tennessee and that, acting as advising physician; I accept the procedures prescribed herein.

   ____________________________  3/29/01
   Physician’s Name and Signature
   Date

*Physician signature is needed only if the project involves medical procedures and the investigator is not a licensed physician.
To Whom It May Concern:

The purpose of this letter is to let you know that Cathy Eden Ammerman has Sumner Regional Medical Center’s permission to conduct her study as outlined in her “Prevention of Radiation-Induced Skin Reactions In Breast Cancer External Irradiation” proposal dated December 11, 2000.

Sincerely,

Nicole Brashear
Vice President of Ancillary Services
March 30, 2001

RE: RESEARCH PROJECT

To Whom I May Concern:

This letter is in support of the Cathy Ammerman proposed research project on prevention of radiation induced dermatitis in breast cancer radiation. I am a radiation oncologist at Sumner Regional Medical Center. I have had the opportunity to work with Cathy when she filled in as our nurse during the maternity leave for our usual nurse. I think this would be an excellent research project and we would be glad to support Cathy in this endeavor.

If I can be of any further assistance, please feel free to call.

Sincerely yours,

Robert McClure, M.D.
Radiation Oncologist, Sumner Regional Medical Center

/wsj
Cathy Eden Ammerman, RN
811 Harden Street
Gallatin, TN 37066

Dear Cathy:

Your research project, "Prevention of Radiation-Induced Dermatitis in Breast Cancer Irradiation," was reviewed by the HSRB and it has been determined that risks to subjects are: (1) minimized and reasonable; and that (2) research procedures are consistent with a sound research design and do not expose the subjects to unnecessary risk. Reviewers determined that: (1) benefits to subjects are considered along with the importance of the topic and that outcomes are reasonable; (2) selection of subjects is equitable; and (3) the purposes of the research and the research setting is amenable to subjects' welfare and producing desired outcomes; that indications of coercion or prejudice are absent, and that participation is clearly voluntary.

1. In addition, the IRB found that: (1) written informed consent will be required of subjects. (2) Provision is made for collecting, using and storing data in a manner that protects the safety and privacy of the subjects and the confidentiality of the data. (3) Appropriate safeguards are included to protect the rights and welfare of the subjects.

Your research therefore meets the criteria of Expedited Review and is approved.

2. Please note that the institution is not responsible for any actions regarding this protocol before approval. If you expand the project at a later date to use other instruments please re-apply. Copies of your request for human subjects review, your application, and this approval, are maintained in the Office of Sponsored Programs at the above address. Please report any changes to this approved protocol to this office. A Continuing Review protocol will be sent to you in the future to determine the status of the project.

Sincerely,

Phillip E. Myers, Ph.D.
Director, OSP and
Human Protections Administrator

c: Human Subjects File0195R
Dr. Beverly E. Holland, Department of Nursing
FOR HSRB USE ONLY:
Application Number: HS0195
Date of Original IRB Approval: 04/16/01
Level of Approval (please check one): □ Exempt □ Expedited □ Full Board
Was the project approved above or below minimum risk?: □ Below □ Above
(If "Above" HSRB Chair and one other HSRB reviewer may determine whether the PI needs to appear before the HSRB).
Name of Project: Prevention of Radiation-Induced Dermatitis in Breast Cancer Irradiation
Name of Researcher: Cathy Eden Ammerman
Department: Nursing

Is your data collection with human subjects complete? □ Yes □ No
(If "Yes", please sign below and return to the Office of Sponsored Programs, Room 106, Foundation Building. If "No", please respond to the questions below, sign and return).

Thank you.

Continuing Review Checklist

1. Has there been any change in the level of risks to human subjects? (If "Yes", please explain changes on a separate sheet).
   □ Yes □ No

2. Have informed consent procedures changed so as to put subjects above minimal risk? (If "Yes", please describe on a separate sheet).
   □ Yes □ No

3. How many subjects have participated in the project in the past year? 
   □ _______
   Have any subjects withdrawn from the research due to adverse events or any unanticipated problems? (If "Yes", please describe on a separate sheet).
   □ Yes □ No

4. Have there been any changes to the source(s) of subjects and the Selection criteria? (If "Yes", please describe on a separate sheet).
   □ Yes □ No

5. Have there been any changes to your research design that were not specified in your application, including the frequency, duration and location of each procedure. (If "Yes", please describe on a separate sheet).
   □ Yes □ No

6. Has there been any change to the way in which confidentiality of the Data is maintained? (If "Yes", please describe on a separate sheet).
   □ Yes □ No

Signature of Principal Investigator
Signature of Reviewer
Signature of Reviewer
HSContinuingReviewFormRevised01/22/02
SK/02/18/02