

Topical Micronutrient Products Significantly Reduced Radiation
Dermatitis and Improved Patient Quality of Life Scores in a Year-
Over-Year Study of Eighty Two Patients

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Abstract

Objective: To determine if new micronutrient skin care technologies could outperform the Standard-of-Care (SOC) by reducing the incidence of radiodermatitis while improving the patient's perceived Quality-of-Life during radiotherapy. Breast cancer patients have benefited from skin sparing technologies, but remain at high risk of skin breakdown associated with radiation dermatitis. Ninety two to ninety six percent of breast cancer patients will experience skin reaction and lost Quality-of-Life. **Patients and Methods:** The study utilized validated scoring documents developed by the Oncology Nursing Society and Dermatology Life Quality Index (DLQI). Eighty two patients receiving radiotherapy were evaluated in the year-over-year study. Forty one patients received the SOC, Natural Care® Gel from Bard Medical and Aquaphor® Healing Ointment from Beiersdorf AG. The following 41 patients received Remedy™ micronutrient skin care products from Medline Industries, Inc. **Results:** Remedy micronutrient skin care products reduced radiodermatitis by 14.4% and the incidence of wet desquamation by 25% over the SOC. Significantly, over 10% of the patients receiving the SOC sustained infections during the course of their radiotherapy and one patient had to discontinue care.

No infections or discontinuation of care were reported in the Remedy group. Further, 46% of the Remedy patients reported no reduction in their quality of life due to skin related problems including product application values, resulting in higher rates of skin care compliance. Remedy patients averaged a Quality-of-Life (QL) score of 0.53 with the best possible score being 0 and the maximum score being 30, indicating the highest possible impairment of QL.

Key Words: Radiodermatitis, Skin Care, Breast Cancer, Quality-of-Life, Topical Micronutrients

Introduction

Skin is the largest organ of the human body and provides protection against the external environment. In addition, skin restores itself every 28 days and is the body's largest producer of enzymes and hormones. Skin consists of three layers; the dermis, epidermis and the protective, semi-permeable stratum corneum that permits terrestrial life¹. The stratum corneum is metabolically active and protects against excessive transepidermal water loss (e-TEWL), mechanical trauma, microbial infection, temperature variation and percutaneous toxin absorption². However, ionizing radiation commonly disturbs or damages several of the skin's protective functions. Studies have shown that 36-100% of patients receiving radiotherapy experience some degree of skin reaction 7-14 days into treatment^{3,4}. During treatment, patients may experience pruritus, erythema, edema, desquamation, necrosis, ulceration and/or hemorrhage⁵. The whole of possible skin reactions associated with radiotherapy are collectively known as radiation dermatitis.

In the past 20 years radiotherapy has experienced tremendous advances, allowing for increased tissue sparing techniques. Nevertheless, radiotherapy routinely causes severe acute and chronic damage of the skin⁶. In fact, skin injury may be the dose-limiting factor for radiotherapy⁷. Once a threshold dose has been exceeded, the severity of the radiation effect at any point on the skin increases with increasing dose. The most currently available fluoroscopic measuring systems do not provide the operator with sufficient information to perfectly minimize skin dose⁸.

During radiotherapy, vascular injury occurs, followed by leukocyte infiltration and barrier breakdown. Leukocyte infiltration is frequently observed in irradiated skin and plays a significant role in tissue damage. Cell adhesion molecules (CAMs) expressed on leukocytes and endothelial cells control the transmigration of leukocytes out of the blood vessel lumen. CAMs including platelet-, leukocyte-, and endothelial-selectins, vascular cell adhesion molecule-1, as well as β 1 and β 2 integrins are involved in the trafficking of leukocytes through the inflamed endothelium⁹. Leukocyte transmigration is also accompanied by monocyte and macrophage infiltration, causing inflammation, pruritus other symptoms associated with radiation dermatitis¹⁰. Furthermore, radiation deposition results in DNA damage manifested by single- and double-strand breaks in the sugar phosphate backbone of epidermal and dermal skin cells¹¹. Most cell types do not show morphologic evidence of radiation damage until they attempt to divide¹². Since skin cells have extraordinarily high rates of

division, symptoms associated with sub-lethal and potentially lethal damage may appear almost immediately.

Patients and Methods

Objectives

- Determine if a skin care regimen using Remedy skin care products mitigates radiation-induced tissue damage in breast cancer patients receiving radiotherapy.
- Compare efficacy of Remedy skin care products to other products used to prevent skin injury.

Drug Information

The Remedy products are endermic, providing for the administration of medicine by absorption through the skin. Micronutrients with a molecular weight of less than 500 Daltons can enter or exit the skin (500 Dalton Rule). These micronutrients include amino acids, vitamins, antioxidants and polyunsaturated fatty acids (PUFAs) comprised as a balance of n-3/n-6.

- Amino acids – glycine, L- cysteine and L-proline.
- Vitamins B₃, B₆, A, C and D₃
- Antioxidants –Hydroxytyrosol and L-aurine.
- PUFAs, n-3/n/6

Patient Eligibility

Inclusion Criteria:

- Patients with newly diagnosed histologically documented breast cancer.
- Female patients greater than 18 years of age.

- Patients receiving only radiotherapy for their breast cancer.
- Four weeks post-surgical and recovered from surgical side effects.
- Not using skin care products other than those prescribed by physician.
- No skin tumor involvement.
- No rash, ulceration or open wound in the treatment field.
- Be available for follow-up.
- Have signed informed consent.

Exclusion Criteria:

- Patients with cancer other than breast cancer.
- Patients receiving concurrent immunotherapy.
- Patients using skin care products other than specified by protocol.
- Patients who previously used Remedy skin care products.
- Patients with medical conditions that prevent compliance with protocol.
- Patients unwilling or unable to give informed consent.

Treatment Regimen

Patients will follow a Remedy regimen with results being compared in a year-over-year evaluation against SOC. The Remedy regimen was as follows:

1. 4-IN-1 No-Rinse Cleansing Lotion: apply to damp cloth or directly to skin. Gently clean with moist cloth. Use twice daily, morning and bedtime.
2. Skin Repair Cream: apply to breast and back two times a day, as above.
3. Nutrashield Skin Protectant: apply to breast and back following application of Skin Care Repair Cream.

4. 4-IN-1 Antiseptic Cleanser: apply as a deodorant replacement if needed.
- Begin regimen starting with simulation and continuing for one month following the completion of therapy.
 - Avoid application of tape or adhesives directly on treatment area.
 - Avoid powder, alcohol, cologne, creams, ointment or deodorant in treatment area.
 - Avoid exposure to sunlight, any source of heat (heating pads; sun lamps), or cold (ice packs; extremely cold weather).
 - Treated area should not be shaved.

Criteria for Evaluation

The validated Oncology Nursing Society (vONS) criterion for skin evaluation was used by physician prior to treatment to document observations weekly during radiotherapy and weekly for four weeks following completion of radiotherapy. The vONC criteria are as follows:

- ONS SCORE: 0 Normal skin within the radiation field.
- ONS SCORE: 1 Faint/dull erythema, follicular reaction, epilation, dry desquamation, decreased sweating.
- ONS SCORE: 2 Bright erythema.
- ONS SCORE: 3 Dry desquamation.
- ONS SCORE: 4 Small to moderate wet desquamation.
- ONS SCORE: 5 Confluent moist desquamation.
- ONS SCORE: 6 Ulcerations, hemorrhage, or necrosis.

ONS Skin Evaluation Results

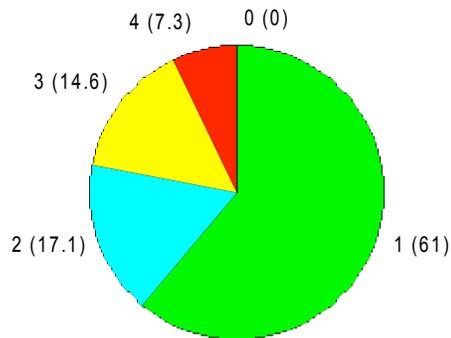
The study results found that Remedy products performed 14.4% better than the SOC. Furthermore, the incidence of wet desquamation was 25% less in the Remedy treatment group. Significantly, over 10% of the patients receiving the SOC sustained infections during the course of their radiotherapy and one patient had to discontinue care. No infections or discontinuation of care were reported in the Remedy group. Further, 46% of the Remedy patients reported no reduction in their quality of life due to skin related problems including product application values, resulting in higher rates of skin care compliance.

ONS Score	NCG/AQ (% n)	REMEDY (% n)	Percent Difference (% n)
0	0.0	2.3	2.3
1	61.0	65.9	4.9
2	17.1	17.1	0.0
3	14.6	9.8	4.8
4	7.3	4.9	2.4
5	0.0	0.0	0.0
6	0.0	0.0	0.0

Table I. Percentage of patients in each respective group along with the specified ONS toxicity scoring criteria. The Remedy™ line outperformed the Declared Institutional Preference by 14.4% overall. Incidence of wet desquamation was 25% less in the Remedy™ treatment group.

ONS Scoring of NCG/AQ Treatment Group

Chart Area Proportional to % n



ONS Scoring of Remedy Treatment Group

Chart Area Proportional to % n

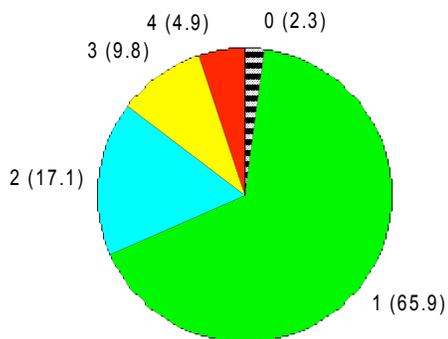


Figure I. % n that received ONS skin breakdown scores between 0 – 4 in NCG/AQ treatment group and Remedy treatment group, respectively.

Patient Quality of Life

Establishing a treatment protocol for radiation dermatitis is of importance and should take into account patient QL. The current international QL criterion for patients receiving skin care is based on the validated Dermatology Life Quality Index (vDLQI) developed by Andrew Y. Finlay, M.D. The vDLQI is the dermatology industry standard for measuring QL. The vDLQI has been cited in

more than 130 published articles and abstracts, in 17 countries and 21 languages.¹³

1. Over the last week, how **itchy, sore, painful** or **stinging** has your skin been?
2. Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?
3. Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** and **garden**?
4. Over the last week, how much has your skin influenced the **clothes** you wear?
5. Over the last week, how much has your skin affected any **social** or **leisure** activities?
6. Over the last week, how much has your skin made it difficult for you to do any **sport**?
7. Over the last week, has your skin prevented you from **working** or **studying**? If “No” over the last week how much has your skin been a problem at **work** or **studying**?
8. Over the last week, how much has your skin created problems with your **partner** or any of your close **friends** or **relatives**?
9. Over the last week, how much has your skin caused any **sexual difficulties**?
10. Over the last week, how much of a problem has the **treatment** for your skin been, for example, by making your home messy, or by taking up time?

Each question is answered either “Very much” (score 3), “A lot” (score 2), “A little” (score 1) or “Not at all” (score 0). Questions 3 – 10 also have the option “Not relevant” (score 0). The first part of question 7 has the choices “Yes” (score 3), “No”, or “Not relevant”. The second part of question 7 has the choices “A lot”, “A little”, or “Not at all”. The minimum score is 0 and the maximum score is 30, indicating the highest possible impairment of quality of life¹³.

Quality of Life Results

Twenty-six members of the Remedy treatment group completed vDLQI questionnaires during five weeks of radiotherapy. Patients using the Remedy products reported lower impairment scores and higher rates of compliance, resulting in greater vDLQI values. According to patient reviews, QL was

maintained due to the products' effectiveness against pain and pruritus, and decreased "greasiness" and "stickiness". In particular, patients reported low impairment scores for vDLQI-Question #1 throughout the entire treatment period. Question #1 asked patients to determine the degree to which their skin had been "itchy, sore, painful and/or stinging" during the previous week.

Patients being treated with Remedy products maintained an average Question #1-impairment score of 0.53. Furthermore, at the end of Week 5 when radiotherapy damage had the most time to accumulate, the mean impairment score was below 1.0. A score of 0.0 signifying impairment that is "Not at all" recognized, and a score of 1.0 indicating impairment that is recognized "A little". In fact, over 46% of the patients reported either no change in impairment or a lesser degree of impairment from Week 1 to Week 5.

Average Reported Impairment Score
Based on DLQI Question #1

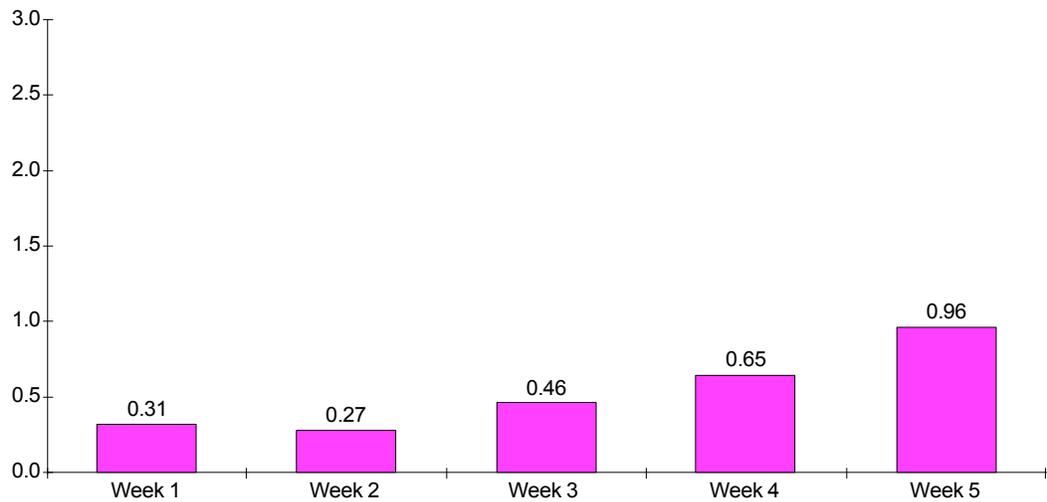


Figure II. During five weeks of radiotherapy, patients being treated with the Remedy™ skin care line averaged a Question #1-impairment score of only 0.53. Over 46% of the patients self-reported either no change in impairment or a lesser degree of impairment from Week 1 to Week 5.

Discussion

Antioxidants

The outermost layer of the skin, the stratum corneum, is metabolically active and requires antioxidants and specific nutrients to maintain its integrity and proper function^{14,15}. Topically applied antioxidants reduce free radicals in skin cells and substantially inhibit the biochemical cascades responsible for infected and inflamed skin¹⁶. There is an expressed concern in the scientific community that oral antioxidants may reduce oxidizing free radicals created by radiotherapy¹⁷. However, there is significant evidence that exogenous antioxidants produce beneficial effects in numerous cancer cell lines. Multiple animal and human

studies have demonstrated an increased effectiveness of cancer therapeutic agents, as well as decreased adverse effects, when given concomitantly with topical antioxidant application^{18,19}.

One of the most effective antioxidants in the terms of free radical scavenging is 3,4-dihydroxyphenyl ethanol or hydroxytyrosol (HT)^{20,21}. HT is a simple phenol found predominantly in the aqueous fraction of olive pulp. HT application has been found to prevent both radiation-induced protein damage and radiation-induced oxidative DNA damage^{22,23}. The protective effects provided by HT are relevant to the radiation-induced DNA damage manifested by single- and double-strand breaks in epidermal and dermal skin cells. Furthermore, several studies have shown that HT inhibits leukocyte and macrophage activation, as well as their subsequent infiltration into epidermal and dermal skin cells^{24,25}. HT's modulation of immune function helps reduce the inflammatory processes associated with radiation dermatitis.

n-3 and n-6 Polyunsaturated Fatty Acids (PUFAs)

The stratum corneum is composed of epidermal cell remnants surrounded by a combination of biological lipids. The epidermal cells producing these remnants require certain amino acids to sustain stratum corneum formation, while the lipid barrier requires specific PUFAs to maintain stratum corneum integrity²⁶. A mixture of sphingolipids, cholesterol, and free fatty acids forms the intercellular membrane bilayers of the stratum corneum which regulate barrier function²⁷. PUFAs have also been shown to reduce or prevent numerous side effects associated with radiotherapy, including radiation dermatitis.

In particular, linolenic (n-3) and linoleic (n-6) PUFAs were found to protect against radiation dermatitis while potentiating radiation treatment via lipid peroxidation. The fatty acids' effect on tumor growth depends on the balance between n-3 and n-6 PUFAs and antioxidants. The proper formulation of potent antioxidants, n-3 and n-6 PUFAs significantly enhances radiotherapy while preventing fatty acid-induced oxidative stress on epidermal and dermal skin cells²⁸. PUFAs play important roles as regulators of the complex inflammatory processes established shortly after radiation-induced skin injury²⁹. PUFAs exert their functions in the form of protective phospholipids anchored in epidermal cell membranes or as soluble lipoic mediators of the inflammatory response³⁰. Linolenic n-3 fatty acids specifically inhibit proinflammatory interleukin-1, interleukin-6 and tumor necrosis factor-alpha (TNF α) production^{31,32}. Modulating the balance of lipid inflammatory mediators is an extremely valuable treatment for inflammatory skin disorders such as radiation dermatitis³³. Both n-3 and n-6 PUFAs balance lipid mediators and improve the reconstitution of epithelial integrity following skin injury³⁴. There exist numerous n-3 and n-6 PUFA sources, several of which significantly protect against radiation-induced tissue damage. Canola oil has been reported as being one of the most potent antimutagenic compounds available for topical administration³⁵. Canola oil induces intracellular oxidative stress and apoptosis in human cancer cells while inhibiting inflammatory leukocyte activity and subsequent skin irritation^{35,36}. Similarly, safflower oil protects against normal

cell damage³⁷. Olive oil is another PUFA that has been shown to exhibit substantial anticancer and antioxidative effects²³. In addition, olive oil specifically prevents radiation-induced skin injury by protecting normal DNA and sustaining skin cell homeostasis²². Altogether, the proper balance of certain PUFAs provides important protection against radiation dermatitis.

Fatty Acid	Beneficial Anticancer Effects Synergistic with Radiotherapy	Protective Functions Against Tissue Damage and Radiation Dermatitis
Canola Oil (n-3 PUFA)	Acts as a potent antimutagenic compounds ⁴⁸	Inhibits inflammatory leukocyte activity and subsequent skin irritation ^{48,49}
Olive Oil (n-3 PUFA)	Substantially limits tumor growth ^{32,37}	Prevents radiation-induced skin injury ³¹ ; protects normal DNA and maintains skin cell homeostasis ⁵²
Safflower Oil (n-6 PUFA)	Suppresses tumor growth in mammary gland, colon and pancreas epithelial cells ⁵¹	Protects against normal cell damage ⁵⁰

Table II. Beneficial anticancer effects and protective skin care functions of topical n-3 and n-6 PUFAs. The proper balance of the specified oils substantially limits tumor growth while protecting against tissue damage and radiation dermatitis.

Vitamins and Vitamin Derivatives

In addition to antioxidant application, specific micronutrients, including vitamins and vitamin derivatives, have been deemed invaluable for nourishing skin and protecting against radiation dermatitis. Moreover, micronutrient deficiency

actually mimics radiation damage by causing DNA single- and double-strand breaks and oxidative lesions in normal skin cells³⁸. Supplementing micronutrients via the topical application of vitamin precursors and vitamin derivatives protects against radiation-induced skin injury. Accordingly, retinyl palmitate, the precursor to retinoic acid and a biological form of vitamin A, has been shown to prevent radiation-induced DNA damage and erythema in normal skin cells³⁸. The topical application of retinyl palmitate counteracts vitamin A depletion caused by radiotherapy and promotes recovery⁴⁰. Retinyl palmitate also helps treat radiation-induced skin ulcerations by nourishing the migratory epithelial cells responsible for closing the wound⁴¹. Overall, retinyl palmitate has been found to increase radiation's effect on tumor cells *in vivo*, while decreasing symptoms associated with radiation dermatitis¹⁸.

Ascorbyl palmitate is another important vitamin derivative that nourishes human skin and helps prevent radiation dermatitis. The micronutrient is a lipid-soluble derivative of ascorbic acid capable of penetrating the stratum corneum to target sites of cell-signaling pathways that are not accessible to water-soluble molecules^{42,43}. Ascorbyl palmitate has been found to maintain tissue integrity while protecting against erythema and desquamation via its potent moisturizing effect⁴⁴. Furthermore, ascorbyl palmitate is an effective free radical scavenger and guards well against radiation-induced DNA damage in epithelial cell lines⁴⁵. Ascorbyl palmitate may play a critical role in preventing radiation-induced tissue damage by providing proper cell nourishment and antioxidative protection.

Cholecalciferol (CF), or vitamin D₃, is hydroxylated in the kidney to produce 1,25-dihydroxyvitmain D, which is an active metabolite and hormone that sustains proper cell function by binding to vitamin D receptors^{46,47}. In particular, the derivative demonstrates strong immunoreactivity in skin and hair follicle vitamin D receptors, thereby protecting against radiation toxicity and preventing radiation dermatitis⁴⁸. The topical application of certain micronutrients and subsequent uptake by the stratum corneum, epidermis and dermis, has a synergistic effect with radiotherapy. Altogether, CF, ascorbyl palmitate and retinyl palmitate have been shown to increase tumor response during radiation treatment while protecting against radiation dermatitis.

Micronutrient	Beneficial Anticancer Effects Synergistic with Radiotherapy	Protective Functions Against Tissue Damage and Radiation Dermatitis
Ascorbyl Palmitate (Vitamin C)	Invasively inhibits tumor growth and cancer cell reproduction ⁶²	Moisturizes and reduces erythema and desquamation ⁶⁰ ; guards against DNA damage in epithelial cell lines ⁶¹
Cholecalciferol (Vitamin D ₃)	Displays potent anticancer effects ^{67,68} ; promotes cell death and inhibits tumor growth ⁶⁹	Demonstrates strong immunoreactivity in skin and hair follicle vitamin D receptors ⁶⁶
Niacinamide (Vitamin B ₃)	Moderates the induction of tumors by established carcinogens ⁸⁰	Reduces erythema and hyperpigmentation ⁸¹
Pyridoxine (Vitamin B ₆)	Deficiency mimics radiation damage ⁵³	Protects against chromosome breaks in normal skin cells ⁵³

Retinyl Palmitate (Vitamin A)	Increases radiations effect <i>in vivo</i> ²⁷ ; deficiency mimics radiation damage ⁵³	Prevents DNA damage and erythema in normal skin cells ⁵⁴ ; inhibits inflammatory macrophage activity ⁵⁶
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Table III. Beneficial anticancer effects and protective skin care functions of topical vitamins and vitamin derivatives. Specified micronutrients may work synergistically with radiotherapy while preventing symptoms associated with radiation dermatitis.

Amino Acids

Symptoms associated with radiation dermatitis are a result of tissue breakdown involving a decline in both collagen and glycosaminoglycans, as well as from changes in their chemical structure and 3-dimensional organization⁴⁹. The transdermal delivery of certain amino acids has been shown to restore collagen synthesis and deposition, while thickening the epidermal skin layer⁵⁰. Selected amino acids have been shown to inhibit the genotoxicity of reactive oxygen species in dermal and epidermal skin cells during radiotherapy. In particular, N-acetyl-l- cysteine (NAC) exhibits significant protective effects on skin, including the extracellular inhibition of mutagenic agents from exogenous sources such as irradiation⁵¹.

NAC modulates reactive metabolic pathways, protects normal DNA and nuclear enzymes, and prevents the formation of carcinogen-DNA adducts⁵². The amino acid exerts its effects via its potent antioxidative properties, as well as its unique ability to sequester nitric oxide (NO) and reverse TNF α toxicity in human

cells^{53,54}. NO production was found to be significantly increased in cancer patients, especially in individuals being treated for breast cancer. Breast cancer patients are known to exhibit increased levels of both nitrate and nitrite, which may be in response to the inflammation characteristic of breast tumor growth⁵⁵. Since radiotherapy further increases NO activity and induces inflammation, the topical application of amino acids such as NAC should be considered. NAC reacts directly with NO to reduce the increased NO generation while reversing harmful glutathione depletion⁵⁶.

Amino Acid	Beneficial Anticancer Effects Synergistic with Radiotherapy	Protective Functions Against Tissue Damage and Radiation Dermatitis
L-cysteine	Protects normal DNA while allowing damage to cancerous genetic material ^{72,73}	Sequesters nitric oxide (NO) and reverses TNF α toxicity in skin cells ^{74,75}
L-proline	Induces apoptosis of cancer cells via intrinsic mitochondrial pathway and extrinsic death receptor pathway ⁷⁹	Restores collagen synthesis and glycosaminoglycan production ⁷¹ ; involved in extracellular matrix turnover ⁸²
L-aurine	Modulates cell proliferation and exerts potent antioxidative effects ⁸³	Eliminates the negative effects of oxygen free radicals, reduces inflammation and induces collagenogenesis ⁸³

Table IV. Beneficial anticancer effects and protective skin care functions of altered amino acids delivered transdermally. Specified amino acids may enhance radiotherapy while preventing symptoms associated with radiation dermatitis.

Conclusion

The response of skin to radiotherapy is highly complex and is dependent on numerous radiation-related, treatment-related, and patient-related factors.

Establishing an effective treatment protocol for radiation dermatitis is of great significance and should take into account patient QL. The current SOC for skin during radiotherapy may be insufficient. Remedy products were found to be 14.4% more effective against radiation-induced tissue damage than the SOC. Patients treated with the Remedy products self-reported lower symptomatic impairment scores and higher rates of compliance, resulting in greater vDLQI values.

Breast cancer patients being treated with radiotherapy should benefit from topical adjunctive care that provides tissue protection from radiation dermatitis.

Currently, the products preferred for skin care during radiotherapy provide no micronutrient benefits. The skin is a complex organ that requires specific balances of antioxidants, PUFAs, vitamins and amino acids in order to maintain homeostasis. Current stands-of-care regimens should be reevaluated based upon these findings.

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ONS Score	NCG/AQ (% n)	REMEDY (% n)	Percent Difference (% n)
0	0.0	2.3	2.3
1	61.0	65.9	4.9
2	17.1	17.1	0.0
3	14.6	9.8	4.8
4	7.3	4.9	2.4
5	0.0	0.0	0.0
6	0.0	0.0	0.0

Table I. Percentages of patients in each respective group that sustained the specified ONS toxicity scoring criteria. The Remedy™ line outperformed the Declared Institutional Preference by 14.4% overall. Incidence of wet desquamation was 25% less in the Remedy™ treatment group.

Fatty Acid	Beneficial Anticancer Effects Synergistic with Radiotherapy	Protective Functions Against Tissue Damage and Radiation Dermatitis
Canola Oil (n-3 PUFA)	Acts as a potent antimutagenic compounds ⁴⁸	Inhibits inflammatory leukocyte activity and subsequent skin irritation ^{48,49}
Olive Oil (n-3 PUFA)	Substantially limits tumor growth ^{32,37}	Prevents radiation-induced skin injury ³¹ ; protects normal DNA and maintains skin cell homeostasis ⁵²
Safflower Oil (n-6 PUFA)	Suppresses tumor growth in mammary gland, colon and pancreas epithelial cells ⁵¹	Protects against normal cell damage ⁵⁰

Table II. Beneficial anticancer effects and protective skin care functions of topical n-3 and n-6 PUFAs. The proper balance of the specified oils substantially limits tumor growth while protecting against tissue damage and radiation dermatitis.

Micronutrient	Beneficial Anticancer Effects Synergistic with Radiotherapy	Protective Functions Against Tissue Damage and Radiation Dermatitis
Ascorbyl Palmitate (Vitamin C)	Invasively inhibits tumor growth and cancer cell reproduction ⁶²	Moisturizes and reduces erythema and desquamation ⁶⁰ ; guards against DNA damage in epithelial cell lines ⁶¹
Cholecalciferol (Vitamin D ₃)	Displays potent anticancer effects ^{67,68} ; promotes cell death and inhibits tumor growth ⁶⁹	Demonstrates strong immunoreactivity in skin and hair follicle vitamin D receptors ⁶⁶
Niacinamide (Vitamin B ₃)	Moderates the induction of tumors by established carcinogens ⁸⁰	Reduces erythema and hyperpigmentation ⁸¹
Pyridoxine (Vitamin B ₆)	Deficiency mimics radiation damage ⁵³	Protects against chromosome breaks in normal skin cells ⁵³
Retinyl Palmitate (Vitamin A)	Increases radiations effect <i>in vivo</i> ²⁷ ; deficiency mimics radiation damage ⁵³	Prevents DNA damage and erythema in normal skin cells ⁵⁴ ; inhibits inflammatory macrophage activity ⁵⁶

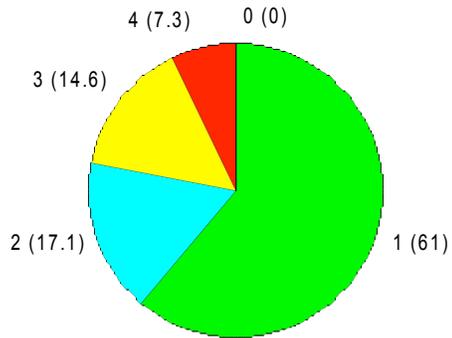
Table III. Beneficial anticancer effects and protective skin care functions of topical vitamins and vitamin derivatives. Specified micronutrients may work synergistically with radiotherapy while preventing symptoms associated with radiation dermatitis.

Amino Acid	Beneficial Anticancer Effects Synergistic with Radiotherapy	Protective Functions Against Tissue Damage and Radiation Dermatitis
L-cysteine	Protects normal DNA while allowing damage to cancerous genetic material ^{72,73}	Sequesters nitric oxide (NO) and reverses TNF α toxicity in skin cells ^{74,75}
L-proline	Induces apoptosis of cancer cells via intrinsic mitochondrial pathway and extrinsic death receptor pathway ⁷⁹	Restores collagen synthesis and glycosaminoglycan production ⁷¹ ; involved in extracellular matrix turnover ⁸²
L-taurine	Modulates cell proliferation and exerts potent antioxidative effects ⁸³	Eliminates the negative effects of oxygen free radicals, reduces inflammation and induces collagenogenesis ⁸³

Table IV. Beneficial anticancer effects and protective skin care functions of altered amino acids delivered transdermally. Specified amino acids may enhance radiotherapy while preventing symptoms associated with radiation dermatitis.

ONS Scoring of NCG/AQ Treatment Group

Chart Area Proportional to % n



ONS Scoring of Remedy Treatment Group

Chart Area Proportional to % n

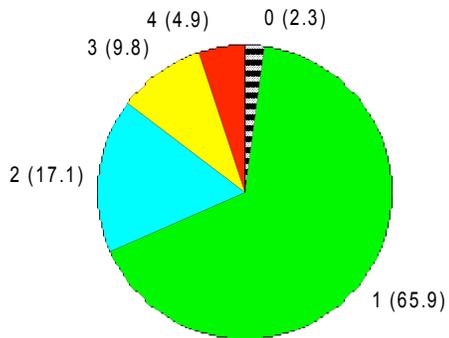


Figure I. % n that received ONS skin breakdown scores between 0 – 4 in NCG/AQ treatment group and Remedy treatment group, respectively.

Average Reported Impairment Score

Based on DLQI Question #1

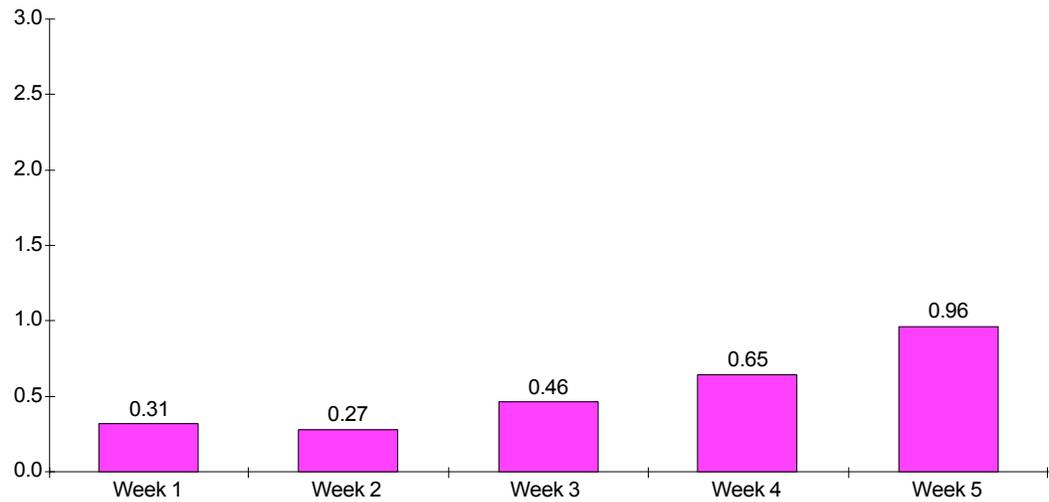


Figure II. During five weeks of radiotherapy, patients being treated with the Remedy™ skin care line averaged a Question #1-impairment score of only 0.53. Over 46% of the patients self-reported either no change in impairment or a lesser degree of impairment from Week 1 to Week 5.