

wound healing perspectives®

A CLINICAL PATHWAY TO SUCCESS

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→ SOFT TISSUE RADIATION INJURIES

A PUBLICATION OF NATIONAL HEALING CORPORATION

Specialized care needed to heal radiation wounds

Unlike our more typical chronic wounds, soft tissue radiation injuries are usually not as visible nor do they require the same type of topical management. A simple biopsy or tooth extraction can create a wounding incident that puts an extreme metabolic and vascular demand on compromised tissue. Without proper treatment, this can have devastating impact.

Radiation creates injury to soft tissue and bone which then leads to *hypovascular*, *hypocellular*, and *hypoxic tissue*. This causes the tissue to breakdown and non-healing wounds. As time passes after radiation treatment, the tissue integrity worsens creating a pathology that is more at risk for soft tissue damage five years after radiation versus one year.

Patients with soft tissue radiation injuries require intense comprehensive wound management. Intractable pain, nutritional deficiencies, pathologic fractures, and oral and cutaneous fistulas are just some of the complications they frequently face. *The wounds that occur in the irradiated tissue constitute one of the clearest indications for hyperbaric oxygen treatment to prevent and manage problem wounds.*

One can see how the multidisciplinary approach to wound management that we provide in our centers is of extreme benefit to this patient group.



Katy Rowland
SVP Clinical Services
National Healing Corporation

Soft tissue radiation injuries

Radiation, while effective in the treatment of cancerous tumor cells, is not selective in the tissue affected. Certain cells have an increased vulnerability to radiation. Areas especially prone to tissue injury are those covering bony prominences, surgical areas, and those on the face (Sitton, 1992). Moist skin folds such as the perineum, axilla, and underside of the breast are also vulnerable areas. Areas where radiation exits in the body, the area opposite the portal of entry are prone to injury, as well.

HBO is the only therapy known to reverse the vascular compromise responsible for late radiation effects. (Warren, 1997) If a patient shows symptoms of radiation injury and/or is scheduled for surgery in the irradiated area, HBO is a key part of the treatment plan. However, HBO is only needed if evidence of radiation injury is present. Symptoms include hematuria, rectal bleeding, vaginal discharge, and pain.



RADIATION INJURIES OCCUR IN MEN AND WOMEN DUE TO THE INCIDENCE OF HEAD AND NECK, BREAST, AND PROSTATE CANCERS.

All other causes of these symptoms should be ruled out by the treating physician before assuming late radiation injury is the cause.

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Hyperbaric oxygen chambers



The Sechrist 3200 monoplace hyperbaric oxygen chamber is the most common HBO chamber used in many National Healing Wound Centers.

This HBO chamber is designed for use in clinical environments requiring critical care support. The chamber has specially designed ports that allow for respiratory support, IV lines, electrical monitoring, transcutaneous oxygen monitoring, patient air-breaks, and non-invasive blood pressure monitoring.

The Model 3200 chamber was designed with safety in mind. The chamber and stretcher are grounded. A patient grounding strap is provided. An emergency vent system can

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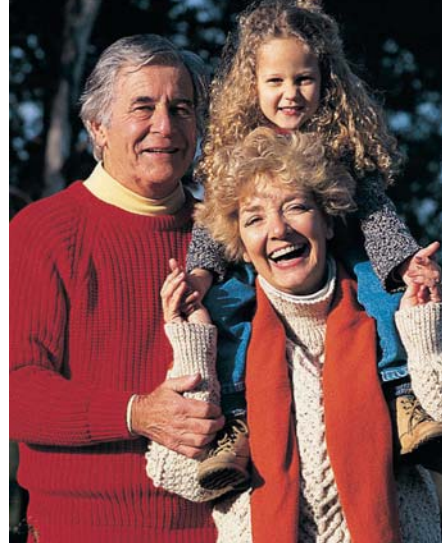
Treating soft tissue radiation injuries of the head and neck

Feldmeier's 2002 systematic literature review reports six case series and one prospective controlled but not randomized study of 160 patients about soft tissue radiation injuries to the head and neck. The reports consistently show a positive outcome for patients treated with HBO. Here are some of the results:

- In his 1999 study, Marx reported the incidence of complications in the HBO group versus the control group this way: wound infection: 6% vs. 24%; wound dehiscence: 11% vs. 48%;

and delayed wound healing: 11% vs. 55%.

- In 1997, Neovius and colleagues found 12 of 15 patients in the HBO group healed completely with improvement in two more patients and no benefit to one. In the control group only seven of 15 patients healed; two patients developed life-threatening hemorrhage and one exsanguinated.
- Three studies (Ferguson, 1987; Feldmeier, 1993; and



WHEN HBO THERAPY IS ADDED TO YOUR TREATMENT REGIMEN, PATIENTS HEAL SOONER.

Filintisis, 2000) observed the effects of HBO on chondroradiation necrosis of the larynx. Their combined results found that only six of 35 patients underwent laryngectomy, many fewer than would typically require laryngectomy without HBO. ■

Treating radiation cystitis

There has been no known cure for radiation cystitis and all treatment has been palliative. Many treatments have been tried. Weiss, et al were the first to study hemorrhagic radiation cystitis in

1983. Based on their work and others that followed, HBO appears to be the only form of treatment that reverses the basic vascular pathophysiology induced by radiation, Kindwall reported in 1993.

The optimal treatment plan for radiation cystitis includes at least 30 treatments at 2.4 ATA.

Feldmeier's 2002 literature review found 17 published reports relating

the results of HBO interventions in the treatment of radiation-induced cystitis. All of the reports are case series and included a total of 190 patients who received HBO treatment. Of these, 145, or 76.3%, resolved completely. Many of the patients in the studies had already failed to see improvement in their conditions with conservative management techniques such as irrigation and instillation of alum or formalin. ■



HBO HAS BEEN FOUND TO BE A BENEFICIAL THERAPY IN THE TREATMENT OF RADIATION CYSTITIS, PROCTITIS, AND ENTERITIS.

Treating radiation proctitis and enteritis

There are two forms of radiation-induced proctitis. Epithelial damage occurs during or soon after the course of treatment and heals quickly. Delayed-onset proctitis, or chronic radiation proctitis (CRP), results from endothelial damage, appears months to years after radiation therapy is complete, and is often difficult to treat. Symptoms include rectal bleeding, diarrhea, tenesmus, and abdominal pain. Perforation, necrosis, stenosis, ulceration, and stricture of the intestine may occur. (Warren, 1997)

Milder cases can be treated with dietary manipulation and steroid or non-steroidal enemas are commonly prescribed. Laser therapy or electrocoagulation is often

employed in attempts to halt bleeding although it is not always successful. Surgical intervention may be required for more severe injuries, ranging from colostomy to partial or complete rectal resection. (Warren, 1997)

In Warren's study, the response to HBO in the responder group was relatively prompt. Since the prognosis for patients with bowel dysfunction is dismal, with practically no hope of symptom resolution and a 40% mortality rate, trying HBO for a short time is a reasonable humanitarian effort.

Feldmeier's 2002 literature review lists 14 published reports of experience in using HBO to treat radiation enteritis and proctitis. The results

of the studies were that HBO is likely to be beneficial in most cases. Of the 114 cases reported in nine of the publications, 41 (36%) resolved and 68 (60%) improved after HBO treatment.

Additionally, animal studies by Feldmeier in 1998 demonstrated "a decrease in fibrosis and an improvement in compliance in the small bowel of animals receiving HBO before frank necrosis was evident." To simulate the latent period observed in people with radiation injuries, these studies were constructed to allow for the vascular changes and fibrosis of late radiation injury to be established prior to autopsy. ■

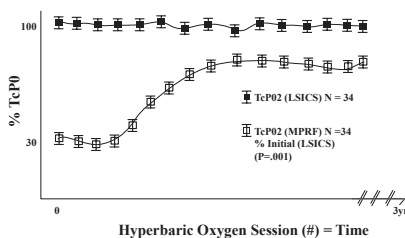
Soft tissue radiation injuries *(continued from page 1)*

Studies that compare the TcPO₂ in irradiated tissue with non-irradiated tissue show that after the 12th HBO session, the level of oxygen reaches a plateau of about 80% of normal. Repeat measurements up to four years later were in the same range which indicates that the angiogenesis is nearly permanent. This indicates that pre-surgical use of HBO produces a more vascular and cellular recipient bed. (Johnson, et al, 1994)

Based on these studies, Marx adapted his ORN treatment protocol for soft tissue injuries.

The Marx-University of Miami protocol follows:

- Twenty HBO treatments of 100% oxygen at 2.4 ATA for 90 minutes each (about one month of therapy).
- Reconstructive surgery or other elective surgery.



- Ten post-surgical HBO treatments of 100% oxygen at 2.4 ATA for 90 minutes each (about two weeks of therapy).

As of 1994, the protocol had been used in 407 bony reconstructions with a success rate of 92% and a complication rate of 9%. ■

Hyperbaric oxygen chambers

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depressurize the chamber in 60 seconds or less. Each chamber has a patient-activated call system in addition to continuous audio monitoring via the two-way communication system.

All Wound Healing Center clinical staff are specially trained at the National Healing Institute's Wound Care and Hyperbaric Oxygen course in the theory and practice of using HBO chambers. Contact your Wound Healing Center today to arrange a tour of the center. ■

Treating post-radiation wounds

HBO Therapy: Does it promote growth or recurrence of malignancy?



For some time, practitioners of hyperbaric medicine have had concerns that the therapeutic modality could also lead to proliferation of malignant cells and angiogenesis in a malignant tumor. Since cellular and vascular proliferation are promoted by HBO in a healing wound, one might assume that it would have the same effect in a tumor. This line of reasoning is indeed understandable at first glance, but it fails to recognize important differences between the complex physiology of wound healing and the equally complex and unique pathophysiology of malignant transformation, tumor growth, and metastases.

A recent study by Feldmeier (2003) reviews clinical reports, animal studies, and cell culture including putative mechanisms whereby HBO would have carcinogenic effects. The process

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Radiation, while effective in the treatment of cancerous tumor cells, is not selective in the tissue affected. Because radiation generates free radicals and reactive oxygen intermediates that can damage rapidly proliferating areas, the skin, due to its continuous cellular renewal, is highly predisposed to tissue injury (Bryant, 1992). Areas especially prone to

surface any time from 2 weeks post treatment until as many as 20 years later. A 10-year retrospective study conducted by Landthaler (1992) revealed the mean period for ulceration occurrence to be 8 years, 7 months. The frequency of wound ulcerations was found to increase with the total dose of radiation, and decrease with the increasing age of the

irradiated area and generally are very painful. These late ulcerations usually occur in the chest wall, the head and neck regions, and the perineum (Belcher and Selekof, 2001). These ulcers present clinically with ragged borders and non-viable tissue present in the base of the ulcer. Cellular level changes contributing to delayed wound healing include

TREATING THE CHRONIC NON-HEALING ULCERATIONS POST RADIATION INVOLVES IMPLEMENTATION OF WOUND-HEALING PRINCIPLES.

tissue injury are those covering bony prominences, surgical areas, and those on the face (Sitton, 1992). Moist skin fold areas, such as the perineum, axilla and underside of the breast, are also vulnerable areas. Areas where the radiation exits the body, the area opposite the portal of entry, are also prone to injury. The greater the area of treatment by radiation, the greater the risk of tissue injury (Belcher and Selekof).

Patients who are currently receiving radiation in combination with chemotherapy, are especially prone to tissue injury because the tissue reaction created by the radiation, then reacts to the chemotherapeutic agents. These complications to the skin may

patient in this study. Skin that has been irradiated heals with thinner, smoother epithelium. Loss of hair follicles and sebaceous glands, elasticity, and decreased healing capacities provide an increased susceptibility to trauma and infection.

Clinical presentation of post-irradiated skin initially may resemble early skin changes consistent with thermal injuries. Erythema, itching, excoriation, alterations in pigmentation, changes in superficial blood flow and pain may be found. Ulcerations that develop may occur spontaneously or in response to a traumatic injury or infection, and initially may be superficial. The ulceration may progress to encompass the complete

epidermal atrophy, loss of epidermal accessory structures, micro-vascular occlusions, increased amounts of connective tissue, reduced fibroblast reproduction, and massive cellular damage. (Rudolph, 1983).

Treating the chronic non-healing ulcerations post radiation involves implementation of wound-healing principles. Providing an optimal wound environment to promote granulation utilizing the most appropriate dressing is the first step in addressing these ulcerations. Pain often accompanies these ulcerations, therefore, pain management is a crucial component of the treatment plan. The pain associated with these ulcerations is often the reason a patient seeks

treatment in the first place. Dressing choices to reduce the pain associated with these ulcerations must be incorporated. Often, dressings that need to be changed every few days or longer may be selected to minimize the pain associated with dressing changes. Use of a hydrogel in dry wound beds will promote wound healing as well as decrease the pain. Other dressing considerations include anatomical location of the ulceration, topical antibacterial control, and protection of the fragile peri-wound skin areas.

Surgical options in the treatment of irradiated tissue include removal of the non-viable tissue and bone and reconstructive repair. Surgical procedures should be performed once past the acute or inflammatory phase. Wound debridement to healthy bleeding tissue may not be ade-



PATIENTS WHO ARE CURRENTLY RECEIVING RADIATION IN COMBINATION WITH CHEMOTHERAPY, ARE ESPECIALLY PRONE TO TISSUE INJURY.

quate as fibrosis may prevent contracture of arterioles. Debridement to tissue exceeding the wound margins may be necessary to promote optimal wound healing in post-radiated ulcerations.

Nutrition is an important aspect of the comprehensive treatment protocol. A thorough nutritional evaluation will provide critical information in treating patients with post-radiated ulcerations. Identification of patients with inadequate albumin and pre-albumin levels and overall poor nutritional status is essential. Coordinating services with a nutritionist may be necessary to provide patients with optimal

health for the greatest healing potential.

In summary, treating post-radiated ulcerations involves all of the key aspects of good wound healing principles. Identification of the underlying etiology, promotion of a healthy wound base, control of pain, proper wound covering, and adequate nutrition are essential in the attainment of wound healing. Utilizing these principles, along with coordination of wound services, promotes an optimal clinical course, decreasing time to healing and increasing patient satisfaction. ■

Stages of radiation-induced tissue injury

ACUTE (FIRST SIX MONTHS)	Organ damage accumulates. This period may be clinically silent, unless tissue-tolerance limits are exceeded.
SUBACUTE (SECOND SIX MONTHS)	Recovery from acute damage ends. Persistence and progression of permanent residual damage is evident. Clinical changes may become apparent, depending on the degree of vascular impairment.
CHRONIC (SECOND TO FIFTH YEAR)	Progression of permanent residual damage occurs. The most significant problems arising during this period result from hypoperfusion because of progressive deterioration of the involved microvasculature.
LATE (AFTER THE FIFTH YEAR)	Clinical conditions similar to chronic phase, but progression is slower.

HBO Therapy

(continued from page 4)

of angiogenesis in wound healing and in cancer growth were compared and contrasted. In vitro, in vivo, and clinical studies strongly suggest no more than a neutral effect of HBO on tumor growth. In fact some studies suggest a negative impact of HBO on malignant progression or formation. For angiogenesis, similarities in wound healing and cancer are striking but significant differences were found including the relative importance of angiogenic factors and the process of cessation of angiogenesis. Tumors that grow in hypoxic environments are more prone to metastases and more lethal to the patient. They are also more likely to mutate toward resistant genotypes.

The authors conclude that the published evidence suggests that intermittent HBO does not enhance primary or metastatic cancer growth. Likewise, there is no credible evidence HBO initiates or promotes cancer de novo. Patients for whom HBO treatments are likely to be useful for the treatment of radiation injuries should not have this therapy denied to them because of concerns that HBO might cause a higher likelihood of tumor recurrence or metastases. ■

Questions and answers with

Indications for HBO



Medicare has approved reimbursement for HBO therapy when the following diagnoses are made:

- Actinomycosis
- Acute carbon monoxide intoxication
- Acute peripheral arterial insufficiency
- Acute traumatic peripheral ischemia
- Chronic refractory osteomyelitis
- Crush injuries and suture (reattachments) of severed limbs
- Cyanide poisoning
- Decompression illness
- Diabetic wounds of the lower extremities
- Gas embolism
- Gas gangrene
- Osteoradionecrosis
- Preparation and preservation of compromised skin grafts
- Progressive necrotizing infections
- Soft tissue radiation injury ■

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He is board-certified in both hyperbaric and emergency medicine. He is also a Certified Independent Medical Examiner and a Diving Medical Officer with the National Oceanic and Atmospheric Administration. Dr. Bartlett has over 15 years of wound care experience and considerable management experience through the creation and direction of several health care companies and one health care foundation.

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Q: Why should we use HBO on radiation patients?

A: There are no alternative therapies that correct the problems these patients have. Narcotics and antidepressants have been used to control the pain associated with these injuries with limited success and significant side effects, including drug addiction. HBO is the only therapy that reverses the effects of radiation on healthy tissue.

Q: What is the problem with radiation injury?

A: Radiation is designed to kill tumor cells; however, the secondary effect is an injury to blood vessels which leaves the tissue hypoxic with a limited ability to recover from daily trauma or surgical procedures.

Q: How does HBO help?

A: HBO has been demonstrated in all tissues to date to induce angiogenesis and restore capillary density and oxygen values to 80% of normal.

Q: What groups of radiation patients should we consider HBO for?

A: The classic indication for HBO has been tooth extraction for patients with prior radiation therapy. Since that time, treatment guidelines have been expanded to include soft tissue injury to pelvic organs as the second most common area. Specifically, these are patients who have received radiation to treat GYN, prostate, and colon cancers. The most common presentations are hematuria, bladder spasms, proctalgia, and rectal bleeding.

Q: What are the common complications of operating in irradiated tissue?

A: Dehiscence, infection, and delayed healing.

Q: How would HBO be used to reduce surgical complications?

A: Patients receive a pre-operative prep of one month of therapy during which time the angiogenesis effect occurs. Following surgery the patient receives one to two weeks of treatment because the tissue will always have some residual disease.

h Dr. Bartlett



Q: Are there any drug interactions with HBO?

A: Patients who are receiving chemotherapy must have a thorough review by a hyperbaric physician as there are some drugs that may have adverse effects. Three drugs to specifically watch for are cisplatinium, bleomycin, and adriamycin.

Q: Do you need a biopsy to substantiate the diagnosis of radiation injury?

A: A biopsy is often desirable; however, it may

not always be practical. It is important that the differential diagnosis has excluded other possible causes prior to referral.

Q: Is there a relationship between HBO and tumor growth?

A: No.

Q: Is there a relationship between HBO and tumor recurrence?

A: No, however, it should be kept in mind that all cancer patients have a higher baseline risk of recurrence with the primary tumor as well

as an increased risk for secondary cancer types.

Q: Can HBO be used for pain management in these radiation patients?

A: Yes, if there is reasonable confidence that pain is due to radiation injury and not recurring cancer or other causes. ■

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working with hyperbaric oxygen

Hyperbaric physicians take no chances with patients in these circumstances:

- Untreated pneumothorax
- History of spontaneous pneumothorax
- Recent use of cisplatinium or adriamycin for chemotherapy
- Any use of bleomycin for chemotherapy
- Current use of disulfiram (Antabuse) if your patient needs >1 treatment

Common side effects from HBO therapy are:

- Idiosyncratic cataract growth
- Transient deterioration of far vision as near vision improves. Effect is commonly noticed after 30 treatments. Vision generally returns to baseline after 2-3 months.
- Paresthesia, tingling of the fingertips, can be noticed after 30 treatments. Effect disappears about one month after completing treatment.

Inherent risks are barotraumas, transient visual changes, and oxygen seizures. The Wound Healing Center has policies and procedures in place to limit these risks while providing the highest quality care. ■

QUESTIONS OR COMMENTS?

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Working with your Wound Healing Center

Over one million new cases of cancer will be diagnosed this year, half of those will undergo radiation therapy, and 5% of them will develop long-term radiation injury. Until recently, there has been no satisfactory treatment of radiation damage. HBO therapy fills this long-standing need. Radiation damage causes *hypoxia*, or a lack of oxygen in the body's tissues. HBO helps fight this damage by increasing the amount of oxygen within the tissues, which aids in recovery. Like any therapy, HBO treatment is not a panacea; however, approximately 60-80% of patients will experience either improvement or complete resolution of soft tissue radiation injury.

Wound Healing Center physicians will work with you to rule out all other causes of the symptoms of patients with soft tissue radiation injuries. The common symptoms that suggest radiation injury are:

- Hematuria
- Rectal bleeding
- Vaginal discharge
- Pain

HBO treatment from a qualified wound center will put your patient back on the right track, and will extend your expertise without expanding your office. ■

SYMPTOMS OF RADIATION INJURIES

Osteoradionecrosis: Dental caries requiring extraction, non-healing wound in oral cavity (usually from dental extractions), non-healing wound under jaw

Radiation cystitis: Urinary frequency, urgency, nocturia, gross hematuria, pain

Radiation proctitis: Diarrhea, rectal bleeding, tenesmus, abdominal pain, constipation, pain.

