

Hyperbaric Oxygen Therapy for Radiation Necrosis

Introduction

Radiation induced soft-tissue and bone necrosis, while rare, presents a challenge to the treatment team. High radiation doses, previous surgery and trauma all increase the risk of the necrosis. When it develops, pain, disability, progression, or even death due to loss of protective barriers may result.

Response to antibiotics and/or conservative debridement can be poor. This is largely due to chronic hypoxia which is characteristic of the necrotic tissue ([Marx](#)). Superimposed infectious processes can further compromise the situation.

Roughly 1/3 of osteoradionecrosis occurs spontaneously with soft tissue breakdown over nonviable bone. Trauma such as tooth extraction, biopsy, or placement of dental appliances initiates the other 2/3.

Hyperbaric oxygen therapy (HBO), the administration of 100% oxygen under high pressure, can improve the situation. Such therapy greatly increases the amount of oxygen available to tissue. This is due to the gaseous/fluid (oxygen/plasma) interface that enhances oxygen absorption and transportation into the liquid phase of the blood. Under such circumstances, repair of tissue damaged by high doses of ionizing radiation is facilitated. Mechanisms of repair can be explained on the following bases;

- **Stimulation of Angiogenesis:**

HBO-induced angiogenesis and fibroplasia have been studied by sequential biopsies and transcutaneous monitoring. Myers and Marx in 1990 compared the transcutaneous oxygen (TcO₂) measurements of patients in a resting state breathing room air to measurements breathing hyperbaric oxygen on the same day. Measurements were taken at two sites: one in the center of the radiation field, and the second in non-irradiated tissue. Plotting these measurements produces a [characteristic curve](#) with three phases: lag, rapid rise, and plateau. The lag phase shows no measurable angiogenesis but reflects capillary budding. The rapid rise phase shows an increase to 82% of the non irradiated tissue level. The geometric rise is due to capillary budding from preexisting vessels in adjacent tissues. Neovascularisation is accomplished, converting the hypovascular tissue to a more vascular tissue. In the plateau phase, the TcO₂ measurement levels off at 80%-85% of the level in nonirradiated tissue. Here maximum angiogenesis was seen and has been shown to be long lasting by long term follow up of the plateau phase. Repeat measurements made between 1 and 4 years after hyperbaric oxygen exposure have shown that the TcO₂ values remain elevated.

- **Stimulation of Neovascularization:**

[Ketchum et al.](#) and [Manson et al.](#) showed that new blood vessels develop as a consequence of HBO. A microangiographic technique demonstrated greater numbers of new blood vessels

developing in animal burns subjected to HBO compared with control animals not subjected to HBO. Furthermore, histochemical staining showed that lactate levels were reduced and glucose levels were elevated along the flaps treated with HBO compared with the control animal flaps.

APPLICATIONS OF HBO:

1. **THERAPEUTIC:** Reports of early administration of HBO alone without appropriate aggressive surgical debridement were very disappointing, with a response rate of only 8%. HBO was thus used as an adjunct to conservative therapy, with excellent response rates and TcO₂ measurements reflecting 80%-85% neovascularization of soft tissue. An increase in the success rate for bone grafts to irradiated tissues was sought by Marx and Johnson in 1985. They performed a prospective randomized trial involving 104 patients. Following exposure to 6,400 cGy, patients were randomized into air breathing control groups and groups treated with HBO at 2.4 ATA (atmospheres absolute), for 90 minutes daily for 20 sessions. A complication rate of 11% and success rate of 92% were found in the HBO group, compared with a complication rate of 26% and a success rate of 66% in the control group.
2. **PROPHYLACTIC:** Marx et al. (Marx, 1985) reported a group of 74 high risk irradiated patients. Prior to dental surgery, each had received at least 6,800 cGy to the mandible. In the penicillin control group, 11 patients (29.9%) developed osteonecrosis, whereas only two patients (5.4%) in the HBO treated group developed it, and actually both were salvaged by sequestrectomy and 10 additional treatments.

DELIVERY OF HBO THERAPY TO CHILDREN:

1. PREPARATION OF THE CHILD:

- Chamber orientation.
- Puppet or doll pre-enactment.
- Standard fire hazard precautions.
- Consideration of ventilating tubes especially if upper respiratory infection.
- Consideration of accompanying adult.

2. HYPERBARIC OXYGEN PROTOCOLS FOR OSTEORADIONECROSIS:

- Pressure 2.0 - 2.4 ATA.
- Frequency of therapy = Daily.
- Prophylaxis = 20 pre-op, 10 post-op.
- Active ORN = 30 pre-op, 10 post-op.

PATHOGENESIS OF OSTEORADIONECROSIS:

Ionizing radiation causes an obliterative endarteritis to the main endosteal blood supply of the relevant bone in the radiation therapy field. Histologically there is osteoblasts and osteocytes with fatty marrow

degeneration.

- **RISK FACTORS:**

1. **ANATOMIC SITE:** Patients receiving radiation to tumors related the mandible develop osteoradionecrosis at five times the rate of patients with tumors of other sites.
2. **DOSE OF RADIATION:** The risk of osteoradionecrosis is increased significantly at dosages of 6000 cGy or more, the risk is increased twofold for patients receiving greater than 8000 cGy compared to 5000 cGy to 6000 cGy, and is almost five times as great as when the patient receives 4000 cGy to 5000 cGy.
3. **DENTAL STATUS:** Dentulous patients are more prone to develop osteoradionecrosis than are edentulous patients. Furthermore, patients with dental disease are at twice the risk of dentulous patients patients without dental disease.

- **CONTRIBUTING FACTORS:**

- Implanted sources
- Large fraction size
- Fields with poor vascularity
- Large field size
- High total dose
- Smoking
- Diabetes
- Infection
- Hypertension

- **CONTRAINDICATIONS TO HBO:**

- **ABSOLUTE:**

- Untreated pneumothorax
- Extreme claustrophobia
- Concomitant use of adriamycin, cisplatin, or bleomycin

- **RELATIVE:**

- Severe COPD with CO₂ retention
- Respiratory tract infection
- Chronic sinusitis
- Uncontrolled high fever
- History of spontaneous pneumothorax
- History of thoracic surgery
- History of reconstructive ear surgery
- Pulmonary lesions on routine CXR/CT
- Viral infections

- Seizure disorder
- Congenital spherocytosis
- History of optic neuritis

• RT-RELATED SEQUELAE RESPONSIVE TO HBO:

- Osteoradionecrosis
- Soft tissue radionecrosis
- Radiation cystitis
- Severe hemorrhagic proctitis
- Radionecrosis of the larynx
- Radiation-induced optic neuropathy
- Radiation-induced retinopathy
- Vesicocutaneous fistula
- [Prophylaxis for dental procedures](#)

• ADVERSE EFFECTS OF HBO:

1. Barotrauma:

- The most common problem during hyperbaric oxygen treatment is failure of pressure to equalize on the two sides of the eardrum. This results in squeezing of the delicate vessels of the eardrum, with pain and bleeding into the middle ear.
- Patients with upper respiratory tract infection or congested mucous membranes are usually placed on prophylactic nasal or systemic decongestants. Myringotomies or pressure-equalizing tubes are resorted to if there is an urgent need for pressurization.
- Another ill effect of pressurization is development of mucous plugs in patients with partly occluded or congested sinuses, asthma, or obstructive airway disease.
- In the sinuses, excruciating pain can result. In the alveoli, rupture may ensue resulting in tension pneumothorax or even air embolism in severe cases.
- With careful patient selection this complication can be avoided.

2. Oxygen toxicity:

- If 100% oxygen at 3 atmospheres were used for two to three hours, CNS toxicity would be produced in a large number of patients.
- Present protocols for radiation induced necrosis call for use of pressures equal to 33 to 45 ft of sea water (2 to 2.4 atm) for 60 to 120 minutes. CNS toxicity is very unusual at pressures less than 2.4 atm . Pulmonary toxicity is also uncommon with fractionated

regimens, allowing time for the pneumocytes to recover from the toxic effects of oxygen.

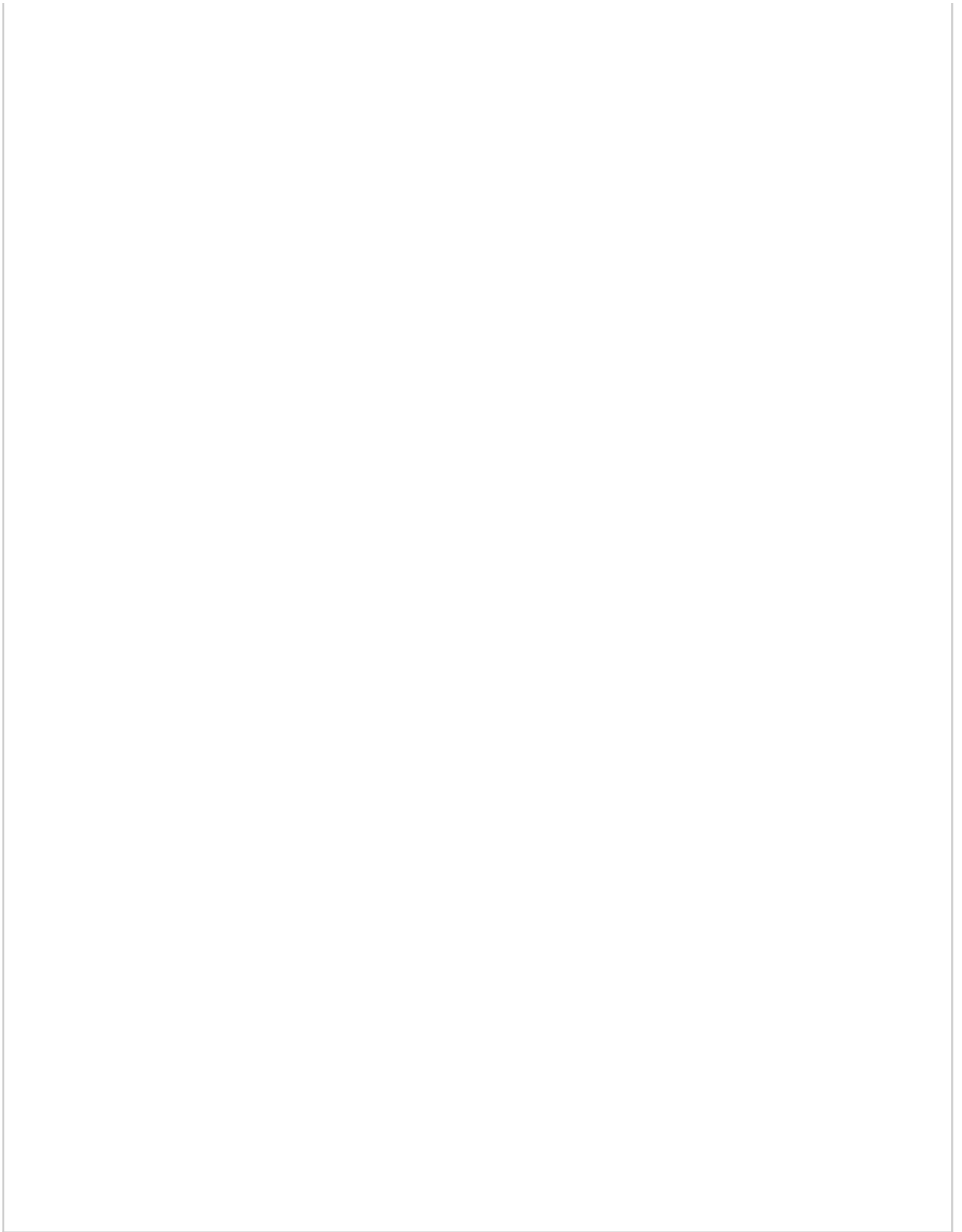
3. Fire hazards:

- Fire is less likely to occur in a multiplace chamber (where compression is applied to 21% oxygen) than in a monoplace chamber (where the compression is applied to 100% oxygen).

• RELATIONSHIP OF HBO TO CANCER:

- To date there is no evidence linking HBO therapy with increased risk of tumor formation. Davis and Hunt in 1988 studied 75 animals treated with HBO and found no increase or progression of tumors in HBO group compared with controls.

• RADIONECROSIS COST ANALYSIS:



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