

## THE EFFICACY OF HYPERBARIC OXYGEN THERAPY IN THE TREATMENT OF RADIATION-INDUCED LATE SIDE EFFECTS

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**Purpose:** We investigated the efficacy of hyperbaric oxygen therapy (HBOT) in the management of patients with radiation-induced late side effects, the majority of whom had failed previous interventions.

**Methods and Materials:** Of 105 eligible subjects, 30 had either died or were not contactable, leaving 75 who qualified for inclusion in this retrospective study. Patients answered a questionnaire documenting symptom severity before and after treatment (using Radiation Therapy Oncology Group criteria), duration of improvement, relapse incidence, and HBOT-related complications.

**Results:** The rate of participation was 60% (45/75). Improvement of principal presenting symptoms after HBOT was noted in 75% of head-and-neck, 100% of pelvic, and 57% of “other” subjects (median duration of response of 62, 72, and 68 weeks, respectively). Bone and bladder symptoms were most likely to benefit from HBOT (response rate, 81% and 83%, respectively). Fifty percent of subjects with soft tissue necrosis/mucous membrane side effects improved with HBOT. The low response rate of salivary (11%), neurologic (17%), laryngeal (17%), and upper gastrointestinal symptoms (22%) indicates that these were more resistant to HBOT. Relapse incidence was low (22%), and minor HBOT-related complications occurred in 31% of patients.

**Conclusion:** Hyperbaric oxygen therapy is a safe and effective treatment modality offering durable relief in the management of radiation-induced osteoradionecrosis either alone or as an adjunctive treatment. Radiation soft tissue necrosis, cystitis, and proctitis also seemed to benefit from HBOT, but the present study did not have sufficient numbers to reliably predict long-term response. © 2004 Elsevier Inc.

Hyperbaric oxygen therapy, Radiation late side effects, Osteoradionecrosis, Response.

### INTRODUCTION

Radiation is a therapeutic modality commonly used in the management of cancer. Although most patients experience some acute side effects, it is a rare and serious event when severe late side effects develop (1). Acute side effects during or in the immediate postirradiation period are mostly self-limiting or amenable to simple medical management. On the other hand, late side effects, occurring after this period, are slower to heal and may lead to chronic debility. For example, osteoradionecrosis is one serious late effect present in the minority of head-and-neck cancer patients treated with radiation. Although 85% of cases resolve with conservative management, the remainder become refractory and can progress to involve a more extensive area of bony and soft tissue (2).

In recent years, our understanding of the underlying mechanisms of late radiation-induced side effects has increased (3–7). Although cellular depletion and tissue devas-

ularization were originally thought of as being the predominant pathologic basis for these side effects (8), they represent merely a histopathologic marker for a far more complex and clinically diverse problem (9). Both patient- and treatment-related factors seem to contribute to this process. It is now known that the size of the radiation treatment field, dose per treatment, and total dose are important factors that are associated with the occurrence of radiation-related side effects (10, 11). Also different tissues have various levels of tolerance to radiation damage, possibly because of the structural organization of that tissue. More specifically, tissues whose functional subunits are arranged in series tend to display a lower degree of radiation tolerance than those with parallel arrangement, because serially arranged subunits depend on the well-being of all subunits before and after them (12). Patients' comorbid disease may also affect the ability to repair tissue damage caused by therapeutic radiation. Anecdotal data suggest a possible correlation between connective tissue diseases and