

TREATMENT OF RADIATION NECROSIS WITH HBO:
A RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED TRIAL

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ABSTRACT:

Background - Late radiation tissue injury is a common referral indication for hyperbaric evaluation and management. A sound physiologic basis exists, and a growing body of largely unsystematic clinical experience supports its use. Questions remain as to the absolute value of hyperbaric oxygenation for this condition and its enduring effect.

Methods - A multicenter randomized and double-blind placebo controlled trial was developed to address these "level of evidence" shortcomings. Termed HORTIS (Hyperbaric Oxygen Radiation Tissue Injury Study), this trial involves eight separate study arms. Patients are randomized to receive either oxygen at 2.0 ATA or air at 1.0 ATA. Both groups of patients undergo between 30 and 40 exposures, depending upon response. The randomization code is broken at this point and non-responding placebo group patients offered the opportunity to undergo the 2.0 ATA oxygen exposures. Data is entered into an Internet accessible password-protected database. Outcomes are assessed as clinical impression and SOMA scale improvement. Of the 68 patients enrolled, 57 completed the study protocol.

Results - An interim analysis was undertaken following the recruitment of 68 patients into the proctitis arm (HORTIS IV). The two groups were compared for pre- and post-exposure changes in both clinical findings and SOMA LENT scale. Of the 30 patients in the treatment group, 16 (53.3%) were healed or had significant improvement; only 6 of 27 (22.2%) who received placebo had these outcomes, none of whom were healed. Logistic regression indicates significance ($p = .0146$), with OR = 4.00 (1.25, 12.72). Change in LENT scale was also significant between the two groups ($p = .0015$), with a larger change in the treatment group than the placebo group (4.60 vs. 0.65). **Conclusions** - The interim results obtained from this arm of Project HORTIS indicate a statistically significant improvement in outcome. This significance is apparent upon completion of the hyperbaric exposure period. The relative benefit of an active treatment over a control is usually expressed as the relative risk, the relative risk reduction, or the odds ratio. These measures are used extensively in both clinical and epidemiological investigations. For clinical decision making, however, it is more meaningful to use the measure "number needed to treat." This measure is calculated on the inverse of the absolute risk reduction. It has the advantage that it conveys both statistical and clinical significance to the doctor. For HORTIS, the number needed to treat was 3 which means that out of every 3 patients that underwent HBO therapy, 1 patient either healed or showed significant improvement. Patient enrollment continues for HORTIS IV, in order to ensure sufficient power to ascertain comparative outcomes during the planned follow-up period.