



● *Hyperthermia Original Contribution*

**RADIOTHERAPY WITH OR WITHOUT HYPERTHERMIA IN THE  
TREATMENT OF SUPERFICIAL LOCALIZED BREAST CANCER:  
RESULTS FROM FIVE RANDOMIZED CONTROLLED TRIALS**

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**Purpose:** Claims for the value of hyperthermia as an adjunct to radiotherapy in the treatment of cancer have mostly been based on small Phase I or II trials. To test the benefit of this form of treatment, randomized Phase III trials were needed.

**Methods and Materials:** Five randomized trials addressing this question were started between 1988 and 1991. In these trials, patients were eligible if they had advanced primary or recurrent breast cancer, and local radiotherapy was indicated in preference to surgery. In addition, heating of the lesions and treatment with a prescribed (re)irradiation schedule had to be feasible and informed consent was obtained. The primary endpoint of all trials was local complete response. Slow recruitment led to a decision to collaborate and combine the trial results in one analysis, and report them simultaneously in one publication. Interim analyses were carried out and the trials were closed to recruitment when a previously agreed statistically significant difference in complete response rate was observed in the two larger trials.

**Results:** We report on pretreatment characteristics, the treatments received, the local response observed, duration of response, time to local failure, distant progression and survival, and treatment toxicity of the 306 patients randomized. The overall CR rate for RT alone was 41% and for the combined treatment arm was 59%, giving, after stratification by trial, an odds ratio of 2.3. Not all trials demonstrated an advantage for the combined treatment, although the 95% confidence intervals of the different trials all contain the pooled odds ratio. The greatest effect was observed in patients with recurrent lesions in previously irradiated areas, where further irradiation was limited to low doses.

**Conclusion:** The combined result of the five trials has demonstrated the efficacy of hyperthermia as an adjunct to radiotherapy for treatment of recurrent breast cancer. The implication of these encouraging results is that hyperthermia appears to have an important role in the clinical management of this disease, and there should be no doubt that further studies of the use of hyperthermia are warranted.

**Breast cancer, Hyperthermia, Radiotherapy, Randomized trial.**