

This is an Open Access article licensed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs 3.0 License ([www.karger.com/OA-license](http://www.karger.com/OA-license)), applicable to the online version of the article only. Distribution for non-commercial purposes only.

---

# Superficial Hyperthermia plus External Beam Radiation in the Palliation of Locally Progressive Chemoradiation-Resistant Breast Cancer

Curt Heese Pablo Lavagnini Pamela Mills Mark Lewis  
Maurie Markman

Cancer Treatment Centers of America, Eastern Regional Medical Center,  
Philadelphia, Pa., USA

## Key Words

Breast cancer · Superficial hyperthermia · External beam radiation · Locally progressive breast cancer

## Abstract

Local chest wall progression of chemotherapy/radiation-resistant breast cancer can result in substantial morbidity. In this retrospective review of 39 patients in this difficult clinical setting treated at Cancer Treatment Centers of America (Eastern Regional Medical Center), approximately one-half of the population experienced meaningful short-term palliation and improvement in quality of life when managed with local superficial hyperthermia plus external beam radiation.

## Introduction

Locally progressive breast cancer following the failure of standard radiation and chemotherapy represents a major therapeutic challenge and a potential cause of considerable morbidity and patient suffering. Worsening chest wall pain, skin ulcerations, infection, and lymph edema can have a truly profound, negative impact on an individual patient's quality of life.

Unfortunately, the large majority of clinical trials in the breast cancer arena which focus on issues of therapeutic efficacy (e.g. survival, objective response rate) almost certainly underreport the severity of this most distressing clinical feature of the malignancy. Yet, for a patient faced with this particular problem, relief of symptoms may be the single most relevant goal of therapy.

Limited published experience has suggested that the combination of local superficial hyperthermia plus external beam radiation therapy may be of clinical utility in the management of progressive chest wall involvement with breast cancer in the setting of failure of prior radiation and chemotherapy to control the disease process [1–3]. Over the past several years, in an effort to provide a meaningful degree of short-term palliation in this most difficult clinical circumstance, our group has employed this innovative palliative strategy and we report here our experience with this approach to disease management.

## Materials and Methods

An institutional review board-approved retrospective chart review of breast cancer patients was conducted at the Eastern Regional Medical Center, Cancer Treatment Centers of America; these patients had received the combination of superficial hyperthermia plus external beam radiation therapy as management of progressive chest wall involvement despite prior local radiation and standard chemotherapy.

As the specific intent of this treatment, and the focus of the current review, was on providing palliation of distressing symptoms (e.g. pain) and signs (e.g. lymph edema) of the malignancy, evidence of *'clinical benefit'* has been defined as medical record documentation of *patient-reported improvement* as well as physical exam findings or radiographic imaging (e.g. CT scan, PET scan) evidence of a decrease in the tumor volume. A second response category, *'major clinical benefit'*, has been defined as documentation within the medical record of substantial patient-reported improvement in cancer-related symptoms (e.g. pain) or objective evidence of decreases in tumor masses (e.g. CT scan findings), or both.

### *Treatment Program*

Patients undergoing reirradiation had typically received prior radiation doses to the chest wall from 45.0 to 50.4 Gy with boost to scar or tumor bed of 10.0 to 16.0 Gy. Reirradiation to clinically or radiographically involved chest areas and involved locoregional lymph nodes was typically delivered by either intensity-modulated treatment at 6 MV utilizing TomoTherapy Hi-Art equipment, or occasionally to superficial lesions utilizing en face electrons delivered via a Clinac iX at 6 or 9 MeV energies with a 0.5-cm bolus used on every other fraction. The radiation dose was 1.5 Gy per fraction delivered twice daily with a minimum of 6 h separation time between doses, for 30 fractions over a 3 week period, for a total dose of 45.0 Gy to the target area. Dose reduction to 1.2 Gy per fraction for a total dose of 36.0 Gy was occasionally used when nodes adjacent to a previously treated brachial plexus were to be treated, to help decrease dose to the brachial plexus.

Superficial hyperthermia was delivered utilizing the BSD 500. Clinically determined fields were placed along with cutaneous skin temperature monitors in multiple areas of the treated field to monitor temperature. Patients were typically treated with a goal temperature of 40 to 44°C for 45 to 60 min delivered twice weekly while on radiation, with the range of temperature and time dependent on patient tolerance.

Chemotherapy consisted of Xeloda 600–1,000 mg/m<sup>2</sup> twice daily at the discretion of the medical oncologist.

## Results

Between April 2008 and May 2011, a total of 39 patients (median age 46; range 27–72 years) with local progressive chest wall involvement with breast cancer after standard disease management (radiation and chemotherapy) received treatment with superficial hyperthermia plus local external beam radiation. Systemic antineoplastic drug therapy was simultaneously delivered to 17 of these individuals, at least partially, as a strategy to theoretically potentiate (chemoradiation) the effects of the local therapy.

Evidence in this retrospective chart review of *clinical benefit* (defined above) was observed in 22 (56%) of the 39 treated patients, while evidence of *major clinical benefit* was documented in 6 (17%) individuals.

Finally, while local toxicity was common (e.g. redness, skin desquamation, slow healing) in no case was this described in the medical record as being unmanageable, and hospitalization for complications of the treatment program (e.g. infection, skin breakdown, pain) was not required for any patient.

## Discussion

Few would question the statement that the development of progressive chest wall involvement following standard treatment of breast cancer is one of the most distressing and debilitating complications of this malignancy. While symptomatic options are always available (e.g. potent pain medications), strategies to directly impact the clinical course of the local process are limited and quite realistically have the potential to exacerbate the situation (e.g. extensive surgery of diffuse skin and nodal cancer in a previously radiated, poorly vascularized area).

Preclinical data provide strong support for the ability of heat to potentiate the profound biological effects of radiation against cancer [4]. Limited clinical data have revealed the combination of superficially applied hyperthermia and external beam radiation can enhance tumor cell killing and achieve therapeutic benefit in settings where the cytotoxic impact of radiation alone is anticipated to be less effective [1–3]. However, the conceptual enthusiasm for this approach must be tempered by concerns for added toxicity, especially in the setting of prior local treatment.

This report extends the previously published experience by confirming both the biological and clinical effects of combining superficial hyperthermia and radiation as a palliative management strategy in locally advanced, progressive and resistant breast cancer. Approximately one-half of the population of women in this extremely difficult setting appeared to have experienced a meaningful degree of short-term clinical benefit, with about one-fifth achieving major improvement in distressing signs and symptoms of the malignancy. Perhaps of equal relevance, the benefits achieved were associated with manageable, although clearly relevant, side effects.

Finally, these data provide important support for the clinical utility of superficial hyperthermia added to external beam radiation in the management of carefully selected patients with progressive symptomatic chest wall involvement with breast

cancer. The degree of benefit and the proportion of patients noted to have achieved these outcomes in this retrospective review may be useful in discussions with carefully selected patients being considered for this approach to palliative disease management.

## References

- 1 Li G, Mitsumori M, Ogura M, et al: Local hyperthermia combined with external irradiation for recurrent breast carcinoma. *Int J Clin Oncol* 2004;9:179–183.
- 2 Ben-Yosuf R, Vigler N, Inbar M, Vexler A: Hyperthermia combined with radiation therapy in the treatment of local recurrent breast cancer. *IMAJ* 2004;6:392–395.
- 3 Zagar T, Higgins KA, Miles EF, et al: Durable palliation of breast cancer chest wall recurrence with radiation therapy, hyperthermia, and chemotherapy. *Radiother Oncol* 2010;97:535–540.
- 4 Zagar TM, Oleson JR, Vujaskovic Z, et al: Hyperthermia combined with radiation therapy for superficial breast cancer and chest wall recurrence: a review of the randomized data. *Int J Hyperthermia* 2010;26:612–617.