

wIRA-hyperthermia plus re-irradiation in the management of unresectable locally recurrent breast cancer

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Abstract:

Introduction: Management of locally recurrent breast cancer (LRBC) remains a therapeutical challenge, especially in cases of unresectable lesions and when prior radiotherapy was included. Re-irradiation (re-RT) combined with superficial hyperthermia (sHT) adds to options for therapeutic consideration. LRBC in pre-irradiated areas extends from microscopic disease and small lesions in patients to be treated with curative intent up to cancer en cuirasse, where palliative treatment might deliberately be restricted to areas directly affecting quality of life. Hyperthermia as a potent radiosensitizer allows for a reduction of radiotherapy dosage and opens a chance to achieve complete and partial responses even in patients where the aim of tumor control had already been abandoned.

On the basis of findings from earlier studies using hyperthermia and re-irradiation, we found that the combination with hyperthermia allowed for a reduction of the total re-irradiation dose to just 20 Gy using a hypofractionated schedule of 5×4 Gy once per week.² To our knowledge, this is the lowest total re-irradiation dose applied so far in a protocol that aims for effective tumor control. The use of a novel technique of contact-free, thermography-controlled water-filtered infrared-A superficial hyperthermia (39-43°C) allows us to cover large-size lesions and could reduce the risk of thermal skin damage to a minimum.³ In contrast to most reported protocols of radiotherapy and hyperthermia combined, we perform hyperthermia immediately before re-irradiation. Low toxicity of this protocol even allows us to repeat re-irradiation using the same dosage and schedule. This is especially crucial in the management of lymphangitis carcinomatosa, which is often recurring. Results were recently published⁴ for tumor response, local control, and overall survival of 201 patients, including a new classification of tumor size in LRR of breast cancer. There has been a lack of clear definition of tumor extension, which is a distinct criterion for prognosis. The suggested definition of five size classes of local recurrences could help with comparison of data from different protocols and studies using combined hyperthermia and re-irradiation.

The characteristics of unresectable, large-size LRR of breast cancer in pre-irradiated regions do not allow for the design of comparative studies. Randomization of hyperthermia plus re-irradiation with reduced dosages against re-irradiation alone with standard dosage is not feasible because of the expected

toxicity of the latter. Comparison of an intervention versus a nonintervention group cannot be ethically justified. The same is true for comparison with a standard treatment; thus, a standard does not exist for patients for whom the aim of tumor control has already been abandoned. Conversely, the lack of comparative studies impedes general acceptance and, in many countries, availability because of the lack of reimbursement. We are interested in remarks and suggestions from the scientific community about strategies to overcome these hurdles.

Methods: Patients (n=201) suffering from LRBC in pre-irradiated areas were treated in four centers located in Switzerland and Germany (Notter et al., *Cancers* 12: 606, 2020). Contact-free sHT was applied using water-filtered infrared-A (wIRA) radiation with thermography control, immediately followed by hypofractionated re-irradiation, consisting of 4 Gy once per week up to a total dose of 20 Gy. 141 patients had large size lesions >100 cm². Responses and local control rates were assessed using a novel size classification (Notter et al., *Cancers* 12: 606, 2020).

Results: Overall response rates ranged from 99% in small lesions to 85% in cancer en cuirasse, with lesions extending to the back. For most patients local control after CR or infield/border progression-free stabilization after PR could be achieved during lifetime. Acute and chronic toxicity was limited to grade I and a few grade II side-effects. The low toxicity allowed for one or even several repeat re-irradiation(s) in 43 patients with re-recurrences, using the same combined treatment protocol. Outcome data are presented as Kaplan-Meier estimates, stratified to size classes and tumor characteristics.

Conclusions: Superficial hyperthermia combined with re-irradiation represents a well-tolerated and effective treatment option. Contact-free, thermography-controlled wIRA-irradiation allows for safe and effective sHT-application (T=39-43°C).

Biography:

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[11th Asian Breast Cancer: Screening, Treatment & Management Summit](#), November 16-17, 2020.

Abstract Citation:

Markus Notter, wIRA-hyperthermia plus re-irradiation in the management of unresectable locally recurrent breast cancer, Asian Breast Cancer 2020, 11th Asian Breast Cancer: Screening, Treatment & Management Summit; November 16-17, 2020.