

# COMPARISON OF RADIOGRAPHIC AND HISTOPATHOLOGICAL RESPONSE TO NEOADJUVANT CHEMOTHERAPY COMBINED WITH REGIONAL HYPERTHERMIA (RHT) IN PATIENTS WITH SOFT TISSUE SARCOMAS (STS)

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## Background

Evaluation of tumor size modifications in response to treatment is important in the management of advanced malignancies. This is usually determined by serial measurements of tumor size in radiographic examinations before and after neoadjuvant chemotherapy. Since the early 1980s, WHO criteria have been widely used. They are based on bidimensional measurement of target lesions and calculation of the product of the maximum diameter and its longest perpendicular diameter. Due to some problems with this way of measurement, in 1999 RECIST was established, based on unidimensional measurement instead of the bi-dimensional approach. A further approach is the determination of the change of the tumor volume during the treatment with anticancer drugs.

## Purpose

In this work, the comparability of the above-mentioned three radiographic approaches after neoadjuvant chemotherapy combined with regional hyperthermia (RHT) in patients with soft tissue sarcomas (STS) was studied. The corresponding histopathological response was also evaluated, since the histopathological evaluation of the resected tumor after the therapy could be seen as the gold standard. Additionally, the correlation of the tumor response with the achieved time-averaged intratumoral temperature and the applied intratumoral thermal dose was assessed.

## Methods

In our RHT-91, RHT-95, and EORTC-62961 studies, patients with STS were treated preoperatively with the same scheme of chemotherapy combined with RHT. 15 patients histopathologically responding to therapy (complete response, pCR) and, as a matched-pair group, 15 patients not histopathologically responding to therapy (no response, NR) with comparable age, sex, localization of tumor, and entity were selected from the quoted studies. The images of the staging examinations before and after preoperative therapy were digitized and the tumor size criteria according to RECIST, WHO, and volume were determined. The latter was done by encycling the tumor on all axial slices and multiplying the slice thickness with the area. Of all 30 patients investigated, 13 patients were assessable for intratumoral temperature measurements. For each patient, the time-averaged intratumoral temperature ( $T_{90}$ ) and the intratumoral thermal dose (CEM 43°C  $T_{90}$ ) according to the Sapareto-model were calculated.

## Results

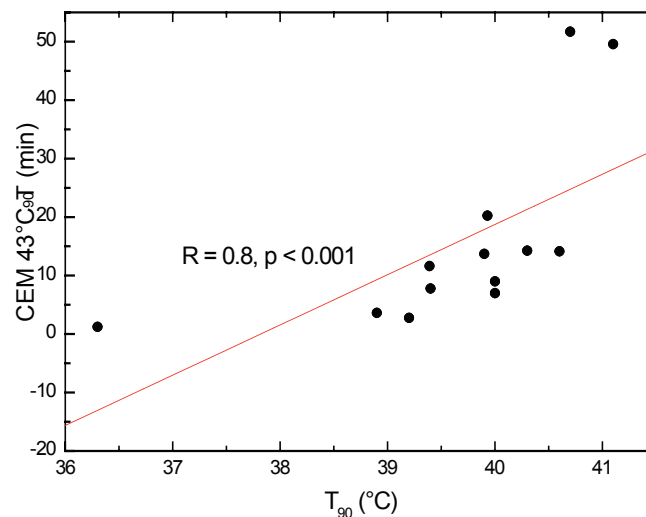
The evaluated radiographic responses, partial response (PR) and no change (NC), of all 30 patients were summarized in Table 1. In the pCR-group, 15 patients were classified according to the applied criteria as follows: 5 PR and 10 NC (RECIST), 7 PR and 8 NC (WHO), 6 PR and 9 NC (volume). In the NR-group, the results were 6 PR and 9 NC (RECIST), 5 PR and 10

NC (WHO), 4 PR and 11 NC (volume). The concordance of these criteria was 73% in the pCR-group and 80% in the NR-group ( $\kappa > 0.64$ ,  $p < 0.001$ ).

	PR (RECIST)	NC (RECIST)	PR (WHO)	NC (WHO)	PR (volume)	NC (volume)
pCR (histopathological)	5	10	7	8	6	9
NR (histopathological)	6	9	5	10	4	11

**Table 1**

The calculated CEM 43°C  $T_{90}$  against  $T_{90}$  for each of 13 assessable patients was plotted in Figure 1. Using linear regression, a good nonparametric correlation of CEM 43°C  $T_{90}$  with  $T_{90}$  was depicted with  $R = 0.8$  and  $p < 0.001$ . In addition, the patients who received higher thermal dose responded both radiographically and histopathologically to therapy.



**Figure 1**

### Discussion

No significant correspondence between the radiographic response and the histopathological response to neoadjuvant chemotherapy combined with RHT in patients with STS was shown in this work. This agrees with previous findings reported in the literature and is caused presumably by underestimation of the treatment effects because of the well-known effects creating tissue-oedema and coagulation necrosis within the field of the heat-treated tumor. Nevertheless, the comparison of RECIST, WHO, and volume criteria yielded a good agreement among the three methods of measurement, suggesting the use of the easiest RECIST for assessment of radiographic response. Although the number of assessable patients with intratumoral temperature measurements is low ( $n = 13$ ), the fact that the prescription of higher thermal dose could lead to better tumor response to neoadjuvant chemotherapy combined with RHT in patients with STS might define qualitatively the important roll of RHT within this multimodality approach which has to be confirmed in further analysis.