No Universally Applicable Thermal Dose Descriptor

To the Editor: We would like to congratulate Thrall et al. for their study on combining radiotherapy with hyperthermia at a prospectively prescribed thermal dose, showing that a high dose results in a higher complete response rate than a low dose and, after correction for other prognostic factors, better local control as well (1). The problem with the earlier retrospective studies is that the achieved temperature distribution, of which control as well (1). The problem with the earlier retrospective and, after correction for other prognostic factors, better local control, the authors speculate that this longer duration of negative correlation of a cumulative treatment duration with local control. With regard to the other retrospectively derived thermal dose variables, will be

certainly when combined with radiotherapy, the achievement of effects may contribute to the desired eventual effect which is, enhancement of the effects of radiotherapy, improvement of observed effect of hyperthermia can be explained. Several effects have been described: direct cell kill at higher temperatures, enhancement of the effects of radiotherapy, improvement of oxygenation, and stimulation of the immune system (3). These effects become apparent at different temperatures, and all these effects may contribute to the desired eventual effect which is, certainly when combined with radiotherapy, the achievement of local control.

The difference in local control only becomes apparent after correction for other prognostic factors, among which, the cumulative duration of all hyperthermia treatments. This cumulative duration is a confounding factor, because it, like other retrospectively derived thermal dose variables, will be strongly influenced by tumor characteristics. With regard to the negative correlation of a cumulative treatment duration with local control, the authors speculate that this longer duration of heating due to a low T90 may have been accompanied by higher temperatures elsewhere in the tumor, which then would have resulted in a worse oxygenation status of the tumor. We assume that all data are available for evaluation and would like to ask the authors whether they have looked at the correlation between treatment duration and T10, and if yes, to share these data with us, as such information would contain valuable information for further studies.

The authors recommend that the procedure of applying a prospectively prescribed dose should be used during clinical treatments. In practice, however, this will be difficult to realize. In their study, the overall duration per treatment session varied by a factor 10. In a hyperthermia unit where patients are treated to the full capacity of equipment and personnel, it will be a problem to schedule treatments with such a large variability of duration, and moreover, not many patients would tolerate treatments of such an uncertain duration.

The authors further recommend that all patients should first be given a test treatment to determine the heatability of their tumor. We find that such a test treatment can only be recommended after showing that hyperthermia has no effect in these so-called unheatable tumors, and after finding which thermal dose is required for specific patient groups. If we had used the definition of "unheatable" for cervix cancer patients in whom a tumor T90 of 40.1°C was not achieved during their first treatment, we would have excluded the majority of patients from our randomized deep hyperthermia trial. T90 was 40.1°C or higher during the first treatment in only 25% of the patients. Fortunately, we did not exclude patients on the basis of low temperature achievement and we did show considerably better local control plus overall survival from the addition of hyperthermia to radiotherapy (4).

The authors refer to our study on the use of interstitial thermometry in patients with intrapelvic tumors and state that their findings justify the use of invasive thermometry—leaving it unclear if they meant interstitial thermometry. In our report on interstitial thermometry, we have argued that intratumorally placed catheters caused complications and that intratumor temperature measurements did not add to the quality of treatment, as small-scale steering is not possible with the presently available equipment. Higher temperatures were only achieved by steering the power away from painful hotspots in normal tissues—which were reported by the patient. Since we have abandoned interstitial thermometry for pelvic tumors, we measure intraluminal temperatures which reflect the overall temperatures in the area well (5). According to published results, this procedure is not different from that used at Duke University for human patients (6). The introduction of thermometry catheters is much less problematic in superficially located tumors or sarcomas of the extremities, and certainly in anesthetized patients, than in intrapelvic tumors in human patients.

Finally, we agree with the authors that the optimal fractionation of hyperthermia in addition to radiotherapy is unknown. However, our approach of applying three to five treatments of fixed duration with maximum achievable temperatures has been shown to be effective in randomized comparative trials of radiation alone versus radiation plus hyperthermia in, among others, melanoma, breast, and cervical cancers (3). In order to get the maximum achievable temperatures, thermometry, within or near the tumor, is important.

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References


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