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LETTERS TO THE EDITOR

"Reirradiation: hopes and concerns of the radiation oncologist"

To the Editor: In the paper by Alongi *et al.*[1] the hope and concerns of the Italian radiation oncologist when reirradiation is needed are accurately investigated. Novel techniques have made it possible to treat patients affected by recurrences or primary tumors at previously irradiated sites, but when retreating a tumor the radiation oncologists does not refrain from delivering an effective dose even if it could be dangerous to the patient in terms of late effects. Combined treatment with hyperthermia (HT) allows administering a lower radiation dose and achieving the same radiobiological effects and better outcomes, particularly in terms of acute and late toxicity.

Dr Van Der Zee *et al.*, from Erasmus Medical Center, Rotterdam, reviewed 21 published clinical studies on 974 patients with recurrent breast cancer after previous irradiation who were treated with HT and radiotherapy (RT). The rate of complete responses following reirradiation and HT in these patients was 61%, compared to only 32% after RT alone. The authors also reviewed their clinical experience in treating patients who had recurrent breast cancer after previous irradiation[2]. They stated that, "in 74% of our patients with recurrent breast cancer treated with a reirradiation scheme of 8 fractions of 4 Gy in 4 weeks, combined with 4 or 8 HT treatments, a complete response is achieved, approximately twice as high as the complete remission (CR) rate following the same reirradiation alone. The CR rate in tumors smaller than 30 mm is 80-90%, for larger tumors it is 65%. HT appears beneficial for patients with microscopic residual tumor as well."

Dr Moros *et al.*, from the Department of Radiation Oncology of the University of Arkansas, reviewed the results of 2 consecutive clinical studies using simultaneous HT and radiation therapy to treat 119 breast cancer patients[3]. The 2 trials (60 cases) included breast cancer patients who recurred after prior therapies, including RT. The authors concluded that, "the product of radiation dose and total thermal dose was highly correlated with complete response."

Dr Jones, from the Radiation Oncology Department of Duke University, North Carolina, in a recent review on breast cancer[4] stated that, "the tremendous progress that has occurred in the role of HT for the treatment of breast cancer, has garnered broad interest at the national level, and the impact of these data led the National Comprehensive Cancer Network (NCCN) to include HT in the 2007 Breast Cancer Guidelines for recurrent breast cancer. In summary, there is a strong biological rationale for the use of HT in breast cancer, and this has been proven in clinical trials to enhance treatment outcome." This author published a randomized trial where 109 patients with superficial tumors (chest wall recurrence of breast cancer, head and neck tumors, melanoma and other tumors) were randomly assigned to receive RT alone or RT plus superficial HT; the complete response rate was 66.1% in the HT arm and 42.3% in the no-HT arm[5].

Dr Ott from the Radiation Oncology Department of Erlangen (Germany), based on previous clinical experiences, designed a phase II study for rectal cancer recurrences in previously irradiated sites by using an RT course of 45 Gy in 25 fractions combined with regional HT[6]. This trial, supported by the German Hyperthermia Study Group and the Atzelsberg Circle, has been approved by the German Krebs Liga.

In conclusion, considering these data and the important role of HT in the battle against cancer[7], we suggest that among the emerging possibilities in reirradiating patients also hyperthermia combined with lower doses of RT should be considered.

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Reply to Dr. Maluta and colleagues.

To the editor: In the comment on our recent article[1] by S. Maluta *et al.*, a potentially relevant role of hyperthermia in addition to radiotherapy for radiation retreatments is suggested.

Hyperthermia is widely considered an attractive approach to enhance the tumor-killing effects of radiotherapy and chemotherapy. While hyperthermia procedures have been proved to improve clinical outcomes after standard cancer treatments in various series of patients, several questions regarding hyperthermia remain unanswered in the oncology community. When hyperthermia is included in multimodality treatment, significant issues are: which patients, which tumor types, and which stages of cancer can really benefit in clinical practice.

Although hyperthermia has been applied during reirradiation, showing clinical benefits in selected cases (especially in breast, rectum, head and neck, and cervical cancer), very few data have been collected in the last decades[2]. Unfortunately, the adoption of hyperthermia in daily practice is limited to a few centers and this is a common reason for the poor clinical experience of medical and radiation oncologists in this field.

On the one hand, we agree with the fact that the integration of local and regional hyperthermia into cancer treatments remains particularly interesting for patients with relapse in irradiated regions, especially where it is not possible to prescribe sufficient doses to eradicate the recurrent disease because of the well-known technical and radiobiological limits of reirradiation.

On the other hand, we are convinced that the actual potential improvement for retreatments is mainly related to the continuous advances in radiotherapy technologies. Such innovations allow clinicians, more and better than in the past, to achieve good target coverage and dose homogeneity during the complex treatment planning of previously irradiated patients. Further prospective clinical trials incorporating these new technologies, with or without hyperthermia, with accurate patient selection, will hopefully help to establish the real clinical role of radiation retreatment for patients with cancer recurrence.

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