

## THE PALLIATIVE EFFECT OF RADIOTHERAPY AND HYPERTHERMIA IN RECURRENT SUPERFICIAL MELANOMA

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**Background:** Radiotherapy combined with hyperthermia is the standard treatment for recurrent melanoma in the Academic Medical Center of Amsterdam. Two randomized studies reported response rates of  $\geq 80\%$  in a selected group of patients (Overgaard 1995, Jones 2005). Question was whether this high response rate could also be achieved in an unselected group of patients in daily clinical practice.

**Patients and Methods:** Between 1997 and 2005 59 patients with 94 lesions of superficial and recurrent melanoma were treated with radiotherapy and hyperthermia and analyzed retrospectively. All patients had either multiple skin lesions, bulky lesions (skin or lymphnodes  $> 3$  cm) or a combination of both. Hyperthermia was applied in the majority of lesions (86%) with a 434 MHz microwave antenna and in 14% with a 70 MHz antenna. Mostly three sessions were applied (range 1-4). Temperature was measured interstitially in 40 lesions and in 47 lesions the thermal probes were superficially attached to the affected skin. Several radiation schedules were used, but most used schemes were 3 x 8, 3x 9 Gy, 7 x 5 Gy and 8 x 4 Gy. Radiation schedules were converted into their biological equivalent dose with an  $\alpha/\beta$  of 4 Gy. Median follow up time was 4 months (range 1-64). Response was evaluated by regression of the tumor size and by regression of the symptoms (palliative response) and was evaluable for 87 lesions. In six lesions the treatment was interrupted because of tumor progression or clinical deterioration. Regression was scored as Complete (CR), nearly Complete (nCR,  $> 95\%$  remission), partial (PR), stable (SD) or progression (Progr). The following patient and tumor characteristics were evaluated for prognostic value on response and survival: Performance, sex, symptom type, tumor size and localization, presence of lymphnodes or distant metastasis, pre-treatment types, radiation dose and hyperthermia dose.

**Results:** Overall median survival after start of treatment was 13 months. Tumor regression occurred in 44%, SD in 39% and progression in 17%. A palliative response (CR/PR) occurred in 54%. Significant factors for response were clinical performance, tumor size and radiation dose: 51% of the patients with a WHO performance of I/II (n=74 lesions) showed tumor regression versus 0% for patients with a performance of III/IV (n=11). There is no linear trend for a size-effect relationship: A tumor size of 15-30 mm showed a response of 67% (n=25), versus 24% (n=24) and 43% (n=37) for size  $< 15$  mm and  $> 30$  mm respectively. The highest radiation doses (3 x 9 and 7 x 5 Gy) showed a higher response rate compared to the lower dose group (3 x 8 Gy or less): 58% versus 35%, respectively (p=0.038). No correlation was found between thermal dose and response rate.

**Conclusion:** Response rates of recurrent melanomas after radiotherapy plus hyperthermia were lower compared to those from the randomized trial by Overgaard et al. Prognostic factors for response were clinical performance and radiation dose.