

# Does adjuvant radiotherapy increase survival in patients with Merkel cell carcinoma of the skin?

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The findings of a large retrospective study show that postoperative radiotherapy is associated with a significant improvement in survival, and is indicated in all patients with local or locoregional Merkel cell carcinoma.

**T**he aggressive nature of Merkel cell carcinoma (MCC), combined with high recurrence rates, frequent regional lymph-node metastases and the well-known radiosensitivity of this disease, indicate that a therapeutic regimen combining surgical excision and postoperative radiotherapy should be used to improve local control.

The optimum treatment regimen for MCC remains unclear, however, as the low worldwide incidence of this disease means that only small, retrospective series have been published.

The particular importance of the large series studied by Mojica et al. (see opposite) is that the analysis shows a significant improvement in survival

after postoperative radiation therapy. The Surveillance, Epidemiology, and End Results (SEER) programme of the National Cancer Institute, from which data were obtained for this study, did not collect information about local recurrences, so the effect of radiation therapy on this outcome could not be studied. Local recurrence rates have been reported to be as high as 80% after surgical resection alone.<sup>1</sup> The superiority of adjuvant radiotherapy over surgery alone in preventing local recurrences is supported by the findings of various smaller series that each included up to 50 patients.<sup>2</sup> Medina-Franco et al. found a highly significant improvement in local control with adjuvant radiotherapy in a literature review

of 1,024 cases.<sup>3</sup> Even the controversial study by Allen et al., who identified no significant improvement of locoregional control after adjuvant radiotherapy, showed nodal recurrence rates of 26% in the group treated with surgery alone, compared with 13% in the group with postoperative radiotherapy. It is possible that significance was not achieved because only a minority of patients (17%) received radiotherapy.<sup>4</sup> It can be supposed, however, that intensified local therapy consisting of surgical resection and postoperative radiotherapy results in better local control, which can be translated into better survival, as shown by Mojica et al.

Mojica et al. discuss the lack of information in the SEER programme

## Synopsis

Pablo Mojica, David Smith and Joshua DI Ellenhorn (2007) **Adjuvant radiation therapy is associated with improved survival in Merkel cell carcinoma of the skin.** *J Clin Oncol* 25:1043–1047

**Background.** Merkel cell carcinoma (MCC) is a relatively rare, but aggressive, skin cancer, with a high propensity for local recurrence and regional and distant metastases. Most data on MCC are from single-institution retrospective analyses, making it difficult to assess the role of adjuvant radiation therapy in the treatment of this disease. Surgical resection of the primary tumour with extensive margins is the main form of therapy.

**Objective.** To analyse the role of adjuvant radiotherapy in patients undergoing surgical excision for MCC.

**Design and intervention.** Data extracted from the Surveillance, Epidemiology, and End Results (SEER) programme of the National Cancer Institute were used to identify patients diagnosed with MCC between 1973 and 2002. Information regarding patient demographics, treatment modalities and tumour characteristics was reviewed. Tumour characteristics documented included site of primary tumour, size at presentation, nodal status of the disease and whether distant metastases were present. Information was available on what surgery was performed at the primary site and lymph nodes, and on the use of adjuvant radiation therapy, but not on the use of chemotherapy or the use of sentinel node biopsy.

**Outcome measure.** The primary end point of the trial was overall survival.

**Results.** The SEER registry contained 1,665 cases of MCC over the time period reviewed, with surgery being a component of therapy in 89% of cases ( $n=1,487$ ). The overall median follow-up was 40 months and the overall median survival was 49 months. Excision or re-excision or minor amputation without lymph-node dissection was performed in 82% of the surgical cohort ( $n=1,214$ ), and extended surgery with lymph-node dissection or major amputations was performed in 10% of this cohort ( $n=135$ ). External-beam radiation was the type of radiotherapy most frequently used (98%). Median overall survival was 63 months in patients who received adjuvant radiation therapy and 45 months in patients who did not ( $P=0.0002$ ). On multivariate analysis, the association of adjuvant radiation therapy with survival was statistically significant ( $P=0.0122$ ). The use of adjuvant radiation therapy was associated with improved overall median survival across all age groups. When the results were stratified by tumour size, adjuvant radiation therapy was associated with an improved overall median survival in patients with tumours <1 cm in size (from 48 to 93 months;  $P=0.0447$ ), in patients with tumours 1–2 cm in size (from 52 to 86 months;  $P=0.0126$ ) and in patients with tumours larger than 2 cm (from 21 to 50 months;  $P=0.0003$ ).

**Conclusion.** There was a positive association between adjuvant radiation therapy and overall survival, which remained statistically significant on multivariate analysis.

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regarding resection status, resection margins and the number of patients with lymph-node dissection. A majority of published series have the same limitations, because of the small numbers of patients and varying treatment paradigms used in different centres and regions and over long study periods. Additionally, because of problems in diagnosis of this rare tumour, patients are often administered adjuvant radiotherapy after excision of the first or second local recurrence.

The implementation of therapy standards for treatment of MCC is of even greater importance now than ever

before, because the incidence of this tumour has tripled in the last 20 years. This increase is possibly related to an enhanced awareness of the diagnostic criteria of MCC, including immunohistochemical assessments, which allow a better distinction between MCC and other skin tumours.

Nevertheless, while there is no published evidence from randomised trials to suggest otherwise, postoperative radiotherapy, which is associated with a low risk of complications, is the suggested treatment for MMC. This recommendation is supported by the important findings of Mojica et al.

### References

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