

Letter to the Editor

In Regard to Barker

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To the Editor:

Thank you for your interest in our paper¹ and abstracts^{2,3} regarding single fraction radiation therapy (SFRT) for Merkel cell carcinoma (MCC). We concur that data for SFRT in managing MCC is currently preliminary with limited sample sizes and follow-up.

Our exploration of SFRT in the adjuvant setting was built upon favorable control rates observed in treating metastatic MCC, the low toxicity of this approach, and the fact that some patients with MCC are unwilling or unable to undergo a conventional course.⁴ In this series of 12 patients with head and neck MCC,¹ we included only stage I/II patients to achieve a relatively homogenous cohort of “early stage” lymph node-negative patients.¹ Our experience suggests that, if no adjuvant radiation therapy is given, even the “lowest risk” stage I MCCs of the head and neck (resected with negative margins with a negative sentinel lymph node biopsy in a nonimmune suppressed person) have a local recurrence rate of ~25%.^{5,6} Given this historical comparative data, we analyzed an analogous head and neck cohort with localized MCC treated with SFRT in the postoperative setting. It must be noted that compared with the “lowest risk” MCC tumors, our 12 current patients included those with

worse prognostic features such as positive margins, failed or no sentinel lymph node biopsy, immunosuppression, and recurrent tumors, wherein the expected failure rate would be higher than 25%. Although we observed no in-field recurrences in this cohort, and toxicity was lower than expected for conventional therapy, these data certainly do not suggest SFRT is superior in efficacy to a conventional course of postoperative radiation therapy.

As the Letter to the Editor astutely notes, in our published meeting abstracts on SFRT for MCC,^{2,3} we have also treated patients with MCC of the trunk or extremity and lymph node positive patients (stage III). We agree that many patients with early stage MCC can be managed with surgical monotherapy, and that this is often chosen because the recurrence risk is sufficiently low, or because the toxicity or logistics of fractionated therapy are not warranted.⁶

In addition, patients with more advanced disease such as the one mentioned in the Letter to Editor might need a different approach than conventional fractionated radiation. In this case, although the patient technically had stage IIB MCC, his extensive cancer was beyond a locoregional confine, with multiple regional nodal stations involved. Such patients have very high risk for developing distant metastatic disease, and limiting toxicity from locoregional therapy is an important consideration in preserving quality of life. A conventional radiation course and SFRT were discussed with this patient, and he opted for the latter. His unfortunate outcome cautions against the indiscriminate use of SFRT in the setting of aggressive disease. However, it also remains to be established whether conventionally fractionated radiation therapy would have been more efficacious in this setting, and at what cost.

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We agree that it is of utmost importance to identify the optimal patient population that may benefit from adjuvant SFRT and that long-term follow-up is warranted. Given the rarity of MCC, a randomized controlled study does not appear to be feasible. We are considering the logistics of a prospective study and welcome collaboration in exploring the potential of this approach that may benefit a selected subset of patients with MCC.

References

1. Cook MM, Schaub SK, Goff PH, et al. Postoperative, single-fraction radiation therapy in Merkel cell carcinoma of the head and neck. *Adv Radiat Oncol.* 2020;5:1248-1254.
2. Goff P, Cook M, Schaub S, et al. Efficacy and toxicity of hypofractionated adjuvant radiotherapy in Merkel cell carcinoma. *Int J Radiat Oncol Biol Phys.* 2020;108:E46.
3. Cook MM, Schaub SK, Park S, et al. Efficacy and toxicity of hypofractionated adjuvant radiotherapy in Merkel cell carcinoma. *J Invest Dermatol.* 2019;139:S95.
4. Iyer JG, Parvathaneni U, Gooley T, et al. Single-fraction radiation therapy in patients with metastatic Merkel cell carcinoma. *Cancer Med.* 2015;4:1161-1170.
5. Takagishi SR, Marx TE, Lewis C, et al. Postoperative radiation therapy is associated with a reduced risk of local recurrence among low risk Merkel cell carcinomas of the head and neck. *Adv Radiat Oncol.* 2016;1:244-251.
6. Goff PH, Bierma M, Lachance K, et al. Primary tumor location as a potential risk factor for local recurrence in resected, low-risk Merkel cell carcinoma: Implications for postoperative radiotherapy. *Int J Radiat Oncol Biol Phys.* 2020;108:S132.