

# Atypical Meningioma Radiotherapy Systematic Review

Data were retrieved from comparative studies of AMs undergone surgical resection alone vs. surgery+ART. Only grossly total resected AMs ([Simpson Grading System 1,2,3](#)) were included. The individual and pooled odds ratio (OR) for the crude recurrence, progression free survival (PFS) at 1, 3 and 5-years, as well as for the overall survival (OS) at 5-years were calculated by using the Mantel-Haenszel model in surgery alone vs. surgery+ART.

Evidence synthesis: 11 studies were considered eligible. 8 were included for the outcome “crude recurrence”; 6 for PFS at 1-3 years, 7 for PFS at 5-years; 6 for the OS at 5-years. Results suggest that surgery+ART might have a protective role on recurrence in gross-totally resected AMs (OR:1.66). Specifically, surgery+ART slightly improved PFS at 1-year (OR:0.92) and more consistently at 3- and 5-years (OR:0.31 and 0.35 respectively) hence favoring a combined approach.

Conclusions: Current literature on the impact of ART after gross total resection of AM are still heterogeneous and not systematically reported. The present meta-analysis suggests a possible protective role of postoperative RT against long-term recurrence as compared to surgical resection alone <sup>1)</sup>.

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PubMed, Embase, and Web of Science were searched to identify comparative studies that reported outcomes of adjuvant RT versus observation for AM patients after GTR. Local recurrence rate, progression-free survival (PFS), overall survival (OS), and toxicities related to RT were considered as outcomes of interest. Differences between two cohorts were estimated by calculating odds ratios (OR) for LR rate and hazard ratios (HR) for survival outcomes with 95% confidence intervals (CIs) for meta-analysis, using R version 4.0.3 software. Included studies were appraised with the Risk of Bias Assessment tool for Non-Randomized Studies. Outcome ratios were combined with the Mantel-Haenszel method and the inverse variance-weighted method, appropriately.

Results: Data from 30 studies involving 2904 patients (adjuvant RT: n = 737; observation: n = 2167) were eventually included. Significant reduction of local recurrence rate was seen in the adjuvant RT cohort compare to that in the observation cohort (OR 0.50; 95% CI 0.36-0.68;  $p < 0.0001$ ). Pooled HRs of PFS at 1-year, 3-year, 5-year, and > 5-year revealed that adjuvant RT was superior to observation. There was no significant difference in OS between the two cohorts during any period. Most toxicities were tolerable with grade 1 or 2. There was no documented grade 5 toxicity.

Conclusions: For AM patients who underwent GTR, evidence suggested that adjuvant RT could potentially decrease local recurrence and improve PFS better than observation <sup>2)</sup>.

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A Medline search through October 2017 using “atypical meningioma” returned 1277 papers for initial review. Inclusion criteria were as follows. We analyzed the database and included articles in which the anatomic pathological classification of atypical meningiomas was in accordance with WHO 2007 or WHO 2016 criteria, patients > 18 years of age, and there was postoperative external beam radiation to the tumor bed. Exclusion criteria were WHO grade I or III meningioma, patients who underwent whole-brain radiation, RT used as salvage therapy for recurrence, palliative dose of RT (< 45 Gy),

recurrent AMs, and multiple AMs. Papers reporting outcomes in which atypical and anaplastic meningiomas were analyzed together were rejected, as were papers with small samples that may compromise evaluation. After filtering our initial selection, only 17 papers were selected. After reviewing the seventeen articles including a total of 1761 patients (972 female and 799 male; 1.21 female/1.0 male), the difference in proportion of tumor recurrence between patients with and without radiotherapy after neurosurgical procedure was 1.0448, 95% CI [0.8318 to 1.3125], p value = 0.7062. On the basis of this review, there is no evidence to suggest that RT decreases the rate of recurrence in patients with atypical meningiomas <sup>3)</sup>.

In this study, the English-language literature was systematically reviewed for studies that reported tumor characteristics, treatment parameters, and clinical outcomes after adjuvant radiotherapy for AM and MM, including overall survival, progression-free survival, and/or time to recurrence or mortality. Clinical outcomes were further assessed in the context of resection status, timing of administration, and radiation dose. Outcomes after stereotactic radiosurgery were also examined. Treatment toxicity and other potential prognostic or confounding factors were appraised. Ten and 11 studies for AM and MM, respectively, met the inclusion criteria. The median 5-year progression-free survival and overall survival after adjuvant radiotherapy were 54.2% and 67.5%, respectively, for AM and 48% and 55.6% for MM. The complication rates were 11.1% for AM and 5.1% for MM. Incomplete resection and radiation dose <50 Gy conferred significantly poorer 5-year progression-free survival. Most studies were unable to demonstrate a statistically significant prognostic benefit for adjuvant radiotherapy in AM. In conclusion, adjuvant radiotherapy significantly improved local control of AMs and MMs, especially after subtotal resection. Study limitations, including inadequate statistical power, may underlie the studies' inability to demonstrate a statistically significant benefit for adjuvant radiotherapy in AM. Because these tumors preferentially recur within 5 years of surgical resection, future studies should define whether early adjuvant therapy should become part of the standard treatment paradigm for completely excised tumors <sup>4)</sup>.

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Zoli M, Della Pepa GM, Carretta A, Bongetta D, Somma T, Zoia C, Raffa G. Adjuvant radiotherapy in grossly total resected grade II atypical meningiomas. A protective effect on recurrence? A systematic review and meta-analysis. *J Neurosurg Sci*. 2021 Nov 11. doi: 10.23736/S0390-5616.21.05522-3. Epub ahead of print. PMID: 34763391.

2)

Chun SW, Kim KM, Kim MS, Kang H, Dho YS, Seo Y, Kim JW, Kim YH, Park CK. Adjuvant radiotherapy versus observation following gross total resection for atypical meningioma: a systematic review and meta-analysis. *Radiat Oncol*. 2021 Feb 17;16(1):34. doi: 10.1186/s13014-021-01759-9. PMID: 33596974; PMCID: PMC7890913.

3)

Pereira BJA, de Almeida AN, Paiva WS, Teixeira MJ, Marie SKN. Impact of radiotherapy in atypical meningioma recurrence: literature review. *Neurosurg Rev*. 2019 Sep;42(3):631-637. doi: 10.1007/s10143-018-0959-8. Epub 2018 Mar 19. PMID: 29552691.

4)

Kaur G, Sayegh ET, Larson A, Bloch O, Madden M, Sun MZ, Barani IJ, James CD, Parsa AT. Adjuvant radiotherapy for atypical and malignant meningiomas: a systematic review. *Neuro Oncol*. 2014 May;16(5):628-36. doi: 10.1093/neuonc/nou025. Epub 2014 Apr 2. PMID: 24696499; PMCID: PMC3984561.

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