


Long-term survivorship following stereotactic radiosurgery alone for brain metastases: risk of intracranial failure and implications for surveillance and counselling

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Abstract

Objectives: Because the vast majority of even the highly-select cohorts of brain metastases patients managed with stereotactic radiosurgery (SRS) alone die within 2 years, there is limited literature on risks of recurrence in these patients beyond 2 years. We hypothesize that, especially for the subset of patients that do not recur in the first 2 years, the risk of subsequent failure beyond 2-years is less than the commonly quoted 50-60% of intracranial failure, wherein less frequent screening may be appropriate. **Methods** As a part of our prospectively maintained institutional radiosurgery database of 1,122 brain metastases patients treated with SRS from December 2003 – September 2013, we identified 132 patients treated initially with SRS alone (\pm pre-SRS surgical resection) with at least 2 years of survival and follow-up from SRS. These patients had a sum of 218 brain metastases at the time of presentation and a total of 526 brain metastases treated with SRS over their lifetime. Patients receiving initial or prior whole brain radiotherapy were excluded. Primary study end-points were rates of actuarial intracranial progression beyond 2 years calculated using the Kaplan Meier and Cox regression methods.

Results: The median follow-up from the first course of SRS was 3.5 years [interquartile range (IQR): 2.7-4.8 years]. The median number of metastases treated at first SRS was 1 (IQR: 1-2) to a median dose of 21Gy in 1 fraction prescribed to the 80% isodose line. Salvage therapy included SRS in 66% (n=87) with a median of 1 (IQR: 0-3) salvage SRS per patient, surgery in 14% (n=18) and whole-brain radiotherapy in 26% (n=34). No salvage was required in 29% (n=38). During the first 2 years, 38% (n=50) of patients (the first 2-yr relapse-free group) had no intracranial relapse while 62% (n=82) had any intracranial relapse. Beyond 2 years, 64% (n=84) had no relapse, while 36% (n=48) had any intracranial relapse. Comparing the first 2-yr relapse-free group to those who relapsed during the first 2 years: the failure rates from 2-4 years post-initial SRS at previously-treated intracranial sites were 8% versus 24% (p=0.02), failure at previously untreated intracranial sites were 17% versus 36% (p=0.03), and any intracranial failures were 25% versus 52% (p=0.01). Total volume of brain metastases treated with SRS over the patients lifetime =5cc was a significant predictor of intracranial failure beyond 2 years, with rates of rate of any intracranial failure between 2-4 years of 51% versus 25% (p<0.01). There were no

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significant differences in failure beyond 2-years by GPA, primary site, or tumor volume of first course of SRS. Combining total SRS tumor volume =5cc and failure prior to 2-years, the 2-4 year risk of any intracranial failure if neither factor was present was 17%, either was 32%, and both was 66% ($p<0.01$). On parsimonious multivariate analysis, failure before 2-years (HR=2.2, 95%CI 1.2-4.3, $p=0.01$) and total SRS tumor volume =5cc (HR=2.3, 95%CI 1.2-4.3, $p=0.01$) remained significant predictors of intracranial relapse beyond 2-years.

Conclusions: Relapse rates beyond 2 years following SRS alone for brain metastases appear to plateau, especially in patients who do not suffer intracranial relapse within the first 2 years. Only 1/4th of patients who do not suffer relapse within the first 2 years suffer intracranial relapse at 4 years.