Risk of radionecrosis in brain metastases treated with stereotactic radiotherapy and systemic therapy.

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PURPOSE

Radiation necrosis (RN) is the most common adverse event observed after stereotactic radiotherapy (SRT) of brain metastases (BMs). The main risk factors for RN are tumor volume, SRT dose, fractions and re-irradiation. However, the survival of patients who developed RN has not been properly studied until now. As the concomitant use of SRT with immunotherapy (IMT) or target therapy (TT) raises some concerns, we sought to review the characteristics of our patients who developed RN after SRT and to evaluate the factors influencing their survival.

METHODS

The data of 652 consecutive patients (p) with 1,565 BMs treated at a large European Cancer Center with Cyber-Knife or Novalis-based SRT from 2012 to 2018 were retrospectively reviewed. Risks factors for RN and survival outcomes were evaluated using Kaplan-Meier analysis and Cox regression models.

RESULTS I

After a median follow-up of 11.6 months (m), 76p (11.7%) developed post-treatment RN in 91 BMs (5.8%), and 55 of these patients (72.4%) were treated with concomitant systemic therapy (CST): 25% with IMT, 26.3% with TT and 21.1% with chemotherapy (CT). CST was not correlated with a higher risk of RN and resulted in longer mOS (33.9m vs. 19.9m in patients treated with SRT alone). Moreover, RN was associated with better post-SRT survival (Fig 1):
-in the entire cohort: 27.8 (7.9-47.7) vs.13.3 (11.2-15.4),
-in NSCLC (35p with RN): 27.8 (20.5-45.1) vs. 16.0 (11.9-20.1),
-in breast cancer (12p with RN): 42.9 (31.4-54.4) vs. 16.2 (11.9-20.4).
In the RN cohort, longer mOS was observed in patients treated with concomitant IMT or TT [43.9 (33.8-54.0) vs. 15.9 (6.6-25.3) in patients treated with CT or SRT alone] and in those with late onset of RN ≥12m after SRT [65.8 (12.9-118.6) vs.12.4 (9.8-14.8) if RN appeared in <12m after SRT].
These patients showed lower risk of death in univariate Cox regression (HR=0.53 and HR=0.24, respectively) and both factors were independent prognosticators of better survival in patients with RN. Results of Cox regression models are presenetd in Table 1 and KM analysis in Figures 1 and 2.

CONCLUSIONS

IMT and TT concomitant to SRT were safe and did not imply a higher risk of post-SRT RN. Patients with RN presented better post-SRT survival in the entire cohort and separately for NSCLC and breast cancer. Among patients with RN, IMT or TT concomitant to SRT and the RN onset ≥ 12m after SRT were associated with better survival. Both factors proved to be independent prognosticators of post-SRT survival in RN patients.

Keywords: Brain metastases, radiation necrosis, stereotactic radiotherapy

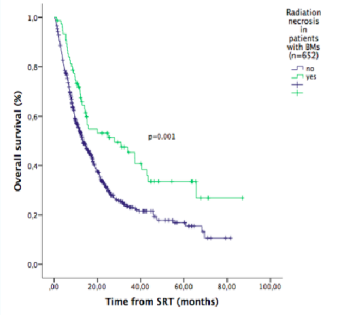
RESULTS II

Table 1. Prognostic factors for overall survival in patients with post-SRT radionecrosis (n = 76)

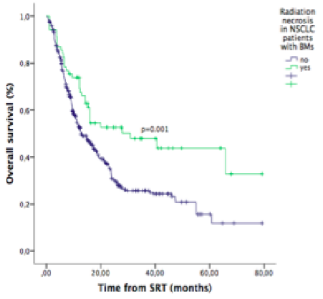
OS, *n* = 76 Variables	UNIVARIATE Cox regression		MULTIVARIATE Cox regression	
	HR (IC 95%)	p-value	HR (IC 95%)	p-value
SRT + immunotherapy or target therapy (vs. SRT alone or SRT + chemotherapy)	**0.51 (0.27-0.94)**	**0.032**	**0.47 (0.25-0.89)**	**0.020**
Time from SRT to RN development ≥ 12months (vs. <12 months)	**0.24 (0.11-0.51)**	**0.000**	**0.23 (0.10-0.50)**	**0.000**

Figure 1. Overall survival of BMs patients treated with SRT according to RN status

A) All patients included (n=652)



B) NSCLC patients (n=263)



C) Breast Cancer patients (n=71)

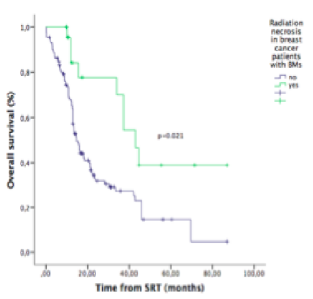
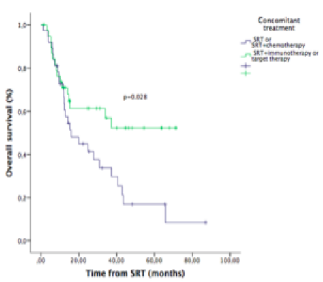
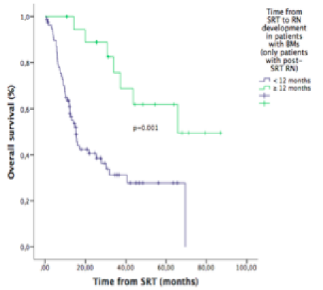


Figure 2. Factors influencing post-treatment overall survival in patients with RN after SRT (n=76)

A) SRT + IMT or TT (vs. SRT alone or SRT + chemotherapy)



B) Time from SRT to RN development ≥ 12months (vs. < 12 months)



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