Predictive factors for local and distant brain control and survival after SRT of brain metastases

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PURPOSE

Brain metastases (BMs) are the most common adult intracranial tumors with the growing prevalence. Stereotactic radiotherapy (SRT) has greatly improved their local control (LC), but scores to predict distant control (DC) and overall survival (OS) after SRT are lacking. This study aims to investigate the factors related with local and distant brain progression free survival (LPFS, DPFS), OS and survival limited by neurological death in patients with BMs treated with upfront or post-surgical SRT.

METHODS

Data of 652 consecutive adult patients with 1565 newly diagnosed BMs from histologically confirmed solid tumors, treated with SRT between 2012 and 2018 in a large European cancer centre were retrospectively reviewed. In order to evaluate the predictive factors of LPFS, DPFS and OS, the following variables were evaluated: primary tumor histology, time to BMs diagnosis (≥ 6 months), BM location, gross tumor volume (GTV), planning target volume (PTV) and single BM (vs. multiple). Survival outcomes of patients with upfront and postoperative SRT were analysed separately. All statistical tests were two-sided ($p<0.05$), Kaplan-Meier's and Cox regression models were used applied (SPSS v.23).

RESULTS I

SRT was administrated to 567 patients as an upfront treatment of 1399 BMs and to 156 patients with 166 postoperative cavities; 83 patients received both post-surgical and upfront SRT to different lesions.
Median age at SRT was 60.3 years old. Most frequent histologies were NSCLC (267p, 40.9%), melanoma (130p, 19.9%), breast (70p, 10.7%), renal (48p, 7.4%) and colorectal cancer (21p, 3.2%).

In patients treated with **upfront SRT**, shorter LPFS was observed in melanoma [mLPFS 36.6m (20.0-53.3) vs. 53.2m (47.2-59.2) for other histology] and GTV≥1.5cm3 [55.5m (50.7-60.4) vs. 36.3 (20.7-52.6) for smaller lesions]. In terms of DPFS, single BM determined better DC [22.3m (16.6-27.8) vs. 9.3 (8.1-10.4) in case of multiple BMs].See Fig 1. Better mOS was observed in patients with single BM [16.2 (14.3-18.0) vs. 12.0 (10.7-13.3) in multiple BMs], with control of extracranial disease at the time of SRT [20.0m (16.8-23.1) vs. 10.0 (8.6-11.6) in uncontrolled extracranial tumor] and time from cancer diagnosis to BMs diagnosis ≥ 6m [17.4 (13.9-20.8) vs. 12.5 (11.3-13.5) if BMs were diagnosed earlier], see Figure 2.

In patients with **postoperative SRT**, LC was better in small lesions (PTV<30.0cm3, p=0.033), while DPFS was nearly 5 times longer in single BM compared with multiple BMs (36.7m vs. 7.7m, p=0.000). Infratentorial BM location was associated with worse mOS [9.8 months (6.3-13.2) vs. 19.0m (11.5-26.4) in patients with supratentorial BMs], see Figure 3.
In a cohort of **patients whose death was determined by brain progression**, single BMs (p=0.012) and smaller lesions (PTV < 30.0cm3, p=0.000) were associated with better mOS.

CONCLUSIONS

Our results on the impact of primary tumor histology, number, size and location of BMs on the local and distant control and survival after SRT may help to establish the predictive scores evaluating the risk of brain progression after SRT.

Keywords: Brain metastases, stereotactic RT, local/distant control.
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RESULTS II

Figure 1. Factors influencing local and distant control in BMs treated with upfront SRT (melanoma histology and large GTV correlated with worse LPFS, single BM correlated with better distant control)

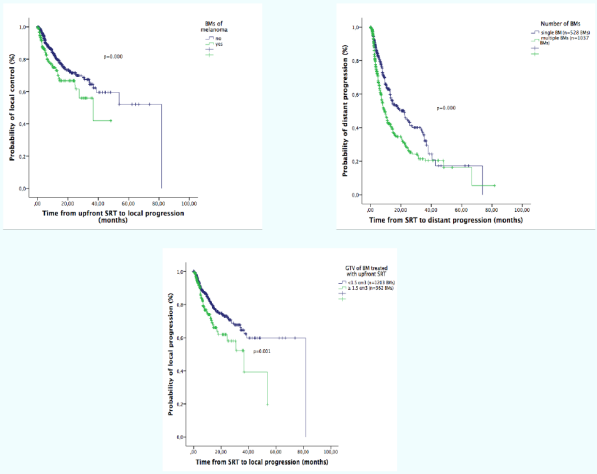

Figure 2. Factors influencing median OS of patients with BMs treated with upfront SRT (better survival if single BMs, controlled extracranial disease and time from cancer diagnosis to BMs diagnosis ≥ 6 months).

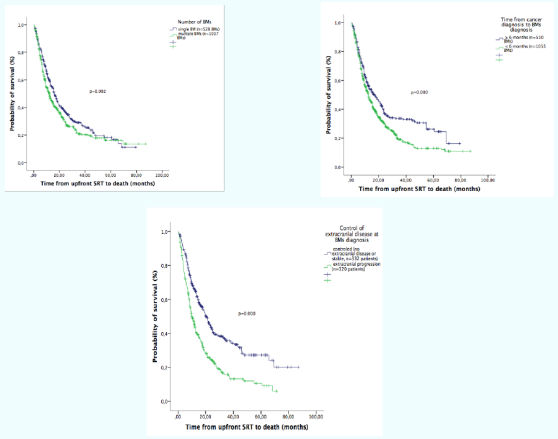

Figure 3. Factors influencing median OS (better in supratentorial location), local (worse in larger BM) and distant control (better in single BM) in patients with BMs treated with postoperative SRT.