



Immunotherapy, Conformity Index and Overall BM Volume but not a number of lesions are related to efficacy of Multiple-Metastases SRS

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Purpose

Our study aim was to assess the safety and efficacy of a linac-based single-isocenter SRS (SI-MM-SRS) for multiple brain metastases in relation to various clinical factors.

Materials and Methods

The analysis included a group of 123 patients with MBM treated at the Department of Neurooncology and Radiosurgery at Franciszek Lukaszczyk Oncology Center in Bydgoszcz between 02.08.2018 r. and 15.09.2020 r. A total of 560 brain metastases were treated. The minimum follow-up was 12 months and the median follow-up was 23 months. The median sum of PTV volume was 9.95 cm³. All patients were treated with the BrainLab Elements MultiMets software using single isocenter Dynamic Conformal Arcs (Fig 1.). The ExacTrac system was used to monitor the position during SRS. 36 patients with 195 metastatic lesions had follow-up MRI 6 months after treatment, 13 of them (36%) received immunotherapy within 4 months of SRS. Local control was analyzed with RANO criteria. Clinical characteristic of this group are presented in table 1.

Characteristic	
Number of lesions	3 (2-11)
GTV volume (mean, cm ³)	0,96
PTV volume (mean, cm ³)	2,14
Margins (median, mm)	1 (0-2)
Dose (median, Gy)	20 (12-24)
Conformity Index (range)	1,09-2,97
Gradient Index (range)	2,43-5,78
Distance to isocenter (median, mm)	45 (7-85)

Table 1. The clinical characteristics of the analyzed group



Figure 1. BrainLab Elements MultiMets software for planning single isocenter multiple metastases Stereotactic Radiosurgery

Results

Sixteen percent of patients was still alive in time of analysis (>3 years of fu). The 6- and 12-months rate was 60% and 33%. In the multivariate analysis **the sum of PTV volumes (p=0.0007)** but not a number of lesions was related to survival. Every increase by 1 cm³ of total brain metastatic volume increased the risk of death by 2%. A diagnosis of squamous cell carcinoma of the lung was related to worst outcomes.. The reported neurological symptoms were stabilized or improved in 79% of patients after SRS in 6 months. There was no relationship between the neurological deterioration and total whole brain V12 dose (p = 0.319). Local control was achieved in 93% of the lesions, as shown in Table 2. Lesions with a margin of at least 0.5 mm had better local control 6 months after treatment (p=0,049). A better response was also associated with a **conformity index below 1.42 (p=0,0006)** and with the use of **immunotherapy within 4 months of SRS (p=0,026)**. the impact of margins and CI on local control are shown in Figure 2.

Treatment response after 6 months	N of lesions (Percentage)
Stable	22 (11%)
Partial response	110 (56%)
Complete response	50 (26%)
Unequivocal progressive Disease	1 (<1%)
Increase in size but stable in subsequent MRI	12 (6%)
Overall lesions analyzed	195

Table 2. Response after 6 month of treatment

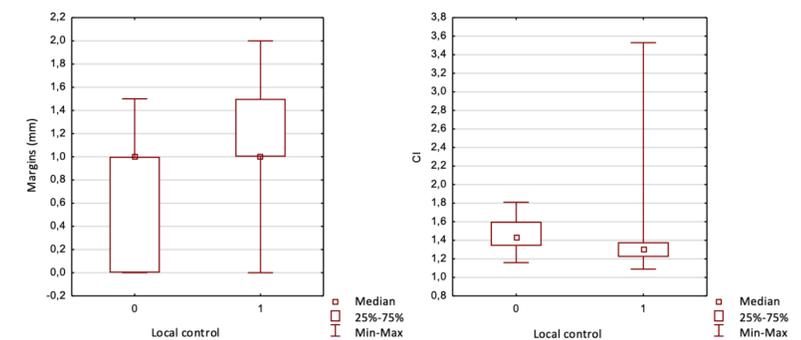


Figure 2. Relationships of margins, CI and 6 months local control of brain metastases

Conclusion

The number of long term survivors after MBM SRS is encouraging but depends on histopathology and total PTV volume. The early diagnosis seems crucial. Other parameters than overall V12 dose to whole brain should be further analyzed to optimized safety. Squamous cell carcinoma should be included in dedicated clinical trials to decrease the risk of bias. Treatment plan quality assessed to optimize CI improves lesions response.