

Material and Methods: Between July 2001 and July 2015, 138 patients, 66 men and 72 women, with large brain metastases from different solid tumors have been treated with HSRT, using Volumetric Modulated Arc Therapy Rapid-Arc (VMAT-RA) in flattening filter-free (FFF) beams mode. The total doses prescribed were 30 Gy in 3 fractions or 30 Gy in 5 fractions in relation to the size and site of BM or 30 Gy in 3 fractions on tumor bed in patients underwent surgical resection.

Results: At a median follow-up time of 10.6 months (range 2-53 months) 6 (4%) patients had local relapse at a median time of 8 months (range 2-53 months) and 45 (32%) patients distant brain progression at a median time of 8 months (range 2-26 months). The 1- and 2-year local control rates were 90% and 87% respectively. The 1- and 2-year survival rates were 72% and 42% respectively. At the last observation time 99 (71.7%) patients were alive and 39 (28.3%) dead. Eighty-five percent of patients succumbed to their extracranial disease and 15% died of progressive intracranial disease. During HSRS no increases of corticosteroid or AED have been needed. No symptomatic radionecrosis was observed. Factors recorded as influencing local failure and worse survival were the presence of metastases at diagnosis, NSCLC histology and impossibility to surgical resection

Conclusion: HSRS is a safe and effective treatment option for patients with large brain metastases. In our series better local control was recorded in case of metachronous BM, breast cancer histology and patients suitable for surgical resection followed by HSRT.

PO-0655

Targeted therapy and stereotactic radiotherapy in brain metastases from renal cell carcinoma

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Purpose or Objective: To retrospectively evaluate safety and brain control (BC) in patients (pts) with 1-4 brain metastases (BM) from renal cell carcinoma (RCC) submitted to radiosurgery (RS) or fractionated stereotactic radiotherapy (FSRT) with or without target therapies (TTs).

Material and Methods: 46 pts with 74 BM were treated. Male/female ratio was 31/15, median age was 62y (range, 29-76). Median KPS was 100% (range, 50-100), 14 (37%), 27 (59%) and 2 (4%) pts were in RPA class 1, 2 and 3, respectively, and 37 (80%) pts had extracranial metastases. Disease was controlled in 28 (61%) and in progression in 18 (39%) pts. Neurologic functional score was generally good (NFS=0-2) having only 5 (11%) NFS=3. Relapse was defined "in-field" when more than 95% of the recurrence volume was within the original 50% isodose, and "out-field" in the other cases. Median number of irradiated BM per patient was 1 (range, 1-4). 37 (80%) pts with 63 BM (85%) received RS at a median dose of 20Gy (range, 15-25). Remaining 9 (20%) with 11 lesions (15%) were underwent FSRT at a dose of 5x6-7Gy. 21 (46%) pts did not receive TTs, 19 (46%) received concomitant and 6 (8%) post- irradiation TTs (sunitinib, sorafenib, pazopanib, mTOR inhibitors, bevacizumab).

Results: At a median follow-up of 19 months (range, 1-51), 41 (89%) pts with 66 (89%) BM were evaluable. Local control was obtained in 96% of BM: there were complete remission in 29 (44%), partial remission in 25 (38%), stable disease in 9 (14%), and progression in 3 (4%) BM. During follow up, 21 (51%) pts had no brain progression, 4 (10%) had in-field relapse, 15 (37%) out-field relapse, and 1 (2%) in- and out-field relapse. Of 20 (49%) relapsing pts, 14 (70%) were retreated with RS, surgery, WBRT and FSRT (8, 3, 2 and 1, respectively). In-field relapse occurred after a median time of 21.5, out-field relapse after a median time of 8 months. At the time of analysis, 39/41 pts (95%) had died, 9 (22%) for brain progression, 30 (73%) for systemic progression. Global

median duration of BC was 22 months (range, 3-51) and global median OS from irradiation was 19 months (range, 4-53). No difference in outcome and toxicity was registered comparing pts receiving or not TTs. Deaths due to brain or systemic progression occurred after a median time of 12 and 20 months, respectively.

Conclusion: Effectiveness of RS and FSRT in RCC BM was confirmed. The addition of concomitant TTs, though safety, does not seem to improve outcomes.

PO-0656

Radiosurgery in brain metastases: a mono-institutional experience

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Purpose or Objective: to evaluate the local control and survival in patients with brain metastases treated with stereotactic radiosurgery (SRS) as primary treatment approach and to identify predictors of distant brain failure (DBF)

Material and Methods: from 2010 to 2014 three hundred and eleven brain metastases in 204 consecutive patients were treated with SRS at University of Turin. Patients eligible for SRS had one to five brain lesions, metastases size ≥ 3 cm, Karnofsky performance status ≥ 70 and life expectancy ≥ 3 months. A total of 172 patients with 266 brain metastases were analysed. Doses ranged from 18-24 Gy in single fraction related to lesion size. Local control (LC), overall survival (OS) and distant brain failure were estimated using the Kaplan-Meier method. Univariate and multivariate analysis were performed to determine the prognostic factors for treatment outcomes and DBF

Results: the median follow-up was 24.9 months. The 6- and 12- month local control rates were 88.5% and 75.1% respectively. 46 patients recurred locally after SRS on 55 brain metastases, with a median time to local failure of 12.1 months. The median overall survival was 12.8 months, with 6- and 12- months OS rates of 74.5% and 53.8% respectively. On multivariate analysis, no significant prognostic factors were associated with local control and survival outcome, even if RPA class (I versus II) and metastases diameter showed a trend of significance for OS ($p=0.11$ e $p=0.10$ respectively). A distant brain failure was observed in 88 patients (43.2%), with a median time to DBF of 5.5 months. 60.8% of these patients maintained an oligometastatic intracranial disease (≤ 5 brain lesions), while 39.2% of patients developed multiple brain metastases. Salvage therapy was delivered in 46.5% of DBF patients, consisting of WBRT in 28.4% of cases and SRS on metastases of new onset in 18.1% of patients. However, more than half of patients with DBF (53.5%) did not require any salvage treatment. Prognostic factors significantly associated with prolonged DBF-free survival on multivariate analysis included the number of brain metastases < 2 ($p=0.000$) and breast primary ($p=0.026$). Tumor size ≤ 10 mm, stable extracranial disease and oligometastatic brain failure were significant predictive factors for survival after DBF.

Conclusion: stereotactic radiosurgery is an effective and well-tolerated treatment option in patients with oligometastatic disease. SRS might also represent a valid salvage strategy in patients relapsing in order to delay or completely avoid WBRT.

PO-0657

Does Radiomics have prognostic value in glioblastoma?

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