RADI-26. DOSIMETRIC EVALUATION OF 6 MV VERSUS 10 MV PHOTONS FOR HIPPOCAMPAL AVOIDANCE WHOLE BRAIN RADIOTHERAPY

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OBJECTIVE: Whole brain radiotherapy (WBRT) causes neurocognitive decline. Hippocampal avoidance WBRT (HA-WBRT) reduces hippocampal irradiation, potentially mitigating neurocognitive sequelae. We compared hippocampal and brain dosimetry with HA-WBRT with 6 megavoltage (MV) versus 10 MV photon energies. METHODS: Twenty consecutive patients treated with WBRT were retrospectively replanned with HA-WBRT techniques using 6 MV and 10 MV photons. Coplanar volumetric modulated arc therapy was employed, with a prescription dose of 3000 cGy in 10 fractions. Planning was done with Eclipse version 13.6 or 15.6. Nine patients were planned with 2.5 mm multileaf collimator leaves, with the remainder planned with 5 mm leaves. The hippocampi were contoured and a HA structure was generated using a uniform 5 mm expansion. A planning target volume (PTV) was defined as the brain parenchyma minus the HA structure. NRG-CC001 dose constraints were used. For each variable, descriptive statistics were calculated. Comparisons were made using two-tailed Wilcoxon signed rank tests or paired t-tests. RESULTS: The minimum hippocampal dose (D100%) was improved with 6 MV plans, 841 cGy compared to 914 cGy with 10 MV ($p< 0.005$). The maximum hippocampal dose (D0.03cc) was reduced with 6 MV planning, 1614 cGy versus 1676 cGy for 10 MV ($p< 0.0001$). With 6 MV photons, a greater number of plans met NRG-CC001 constraints without deviations. 6 MV photons improved PTV coverage by the 95% isodose line, 96.6% compared to 95.9% for 10 MV ($p=0.021$). 6 MV photon plans decreased the volume of PTV receiving ≥105% of the prescription, 84.2% versus 87.9% for 10 MV ($p=0.006$). The mean dose, hot spots, and cold spots did not differ by photon energy. PTV dose constraints were always met. CONCLUSION: 6 MV photon HA-WBRT plans are dosimetrically superior to 10 MV, reducing hippocampal radiation dose, without compromise in brain coverage and improved target dose homogeneity.

RADI-27. ROLE OF STEREOTACTIC RADIOSURGERY IN THE CARE OF PATIENTS WITH >/= 25 CUMULATIVE BRAIN METASTASES

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INTRODUCTION: Stereotactic radiosurgery (SRS) is an accepted treatment for multiple brain metastases. However, the upper limit of the number of brain metastases over the course of care suitable for this approach is controversial. METHODS: From a review of our prospective registry, 48 patients treated with SRS for > 25 brain metastases in either single or multiple sessions between 2013 and 2019 were identified. Patient, tumor, and treatments characteristics were evaluated. Clinical outcomes and overall survival (OS) were analyzed. RESULTS: Thirty-one females (64.6%) and 17 males (35.4%) with a median age of 56 years (25–91) were included. Primary diagnoses included lung (n=23, 47.9%), breast (n=13, 27.1%), melanoma (n=8, 16.7%), and other (n=4, 8.33%). Initial median GPA index was 2 (0.5–3). Nine patients (18.8%) had received whole brain radiation therapy (WBRT) prior to first SRS treatment, with a median dose of 35Gy (30–40.5Gy). Ten patients (20.8%) received WBRT after initial SRS, with a median dose of 30Gy (20-30Gy). Thus, only 19 patients (40%) ever received WBRT. Median number of radiosurgeries per patient was 3 (1–12). Median number of cumulative tumors irradiated was 31 (25–110). Median number of tumors irradiated at first SRS was 10 (1–35). Median marginal dose for the largest tumor per session was 16Gy (10-21Gy). Median SRS total tumor volume was 6.8cc (0.8–23.4). Median follow-up since initial SRS was 16 months (1–71). At present, 21 (43.7%) are alive. Median OS from the diagnosis of brain metastases was 31 months (2–97), and OS from the time of first SRS, 22 months (1–70). Median KPS at first SRS and last follow-up was the same (90). Sixty-three percent did not require a corticosteroid course. CONCLUSION: In selected patients with a large number of cumulative brain metastases (> 25), SRS is effective and safe. Therefore, WBRT may not be required in this population.

RADI-28. UP-FRONT SINGLE SESSION RADIOSURGERY FOR LARGE BRAIN METASTASES - VOLUMETRIC RESPONSES AND OUTCOMES

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OBJECTIVE: Patients presenting with large brain metastases (LBM), described in the literature as ≥2.5 cm in maximum diameter or ≥10cm^{3}in volume, pose a management challenge. For patients not compromised by mass effect, corticosteroid therapy followed by SRS allows for efficient, minimal access care that facilitates immediate institution of systemic therapy. METHODS: We performed a volumetric-based analysis in order to determine the efficacy of single-session SRS in the treatment of LBM in comparison to other treatment modalities. Thirty patients over the age of 18 with systemic cancer and brain metastases (≥2.7cm in greatest diameter or ≥10cm^{3}in volume) who underwent single session SRS were included. Serial tumor volumes, clinical outcomes, and medication requirements were studied. RESULTS: Among 30 patients, 70% of patients had either lung, melanoma, or breast cancer. Median initial tumor size (maximum diameter) was 32mm (range 28–43) and median initial tumor volume was 9.32cm^3 (range 1.09–25.31). Median marginal dose was 16Gy (range 12–18). Average percent decrease in tumor volume was 50% on imaging at 4–8 weeks, 60% at 4–6 months, 48% at 6–8 months, and 67% at >8 months compared to initial imaging. Only one patient required a subsequent craniotomy 4 years after SRS for an enlarging cyst which was granulation tissue consistent with radiation effects on pathology. There were no adverse events immediately following SRS. Median corticosteroid use after SRS was 21 days. There was no statistically significant difference in KPS score between treatment day and last follow up, suggesting relative safety and maintenance of function. CONCLUSION: Initial high dose corticosteroid therapy followed by prompt single session SRS is a safe and efficacious method of managing patients with large brain metastases (defined in our study as ≥2.7cm or ≥10cm^3), if the clinical condition of the patient is acceptable at presentation.

RADI-29. BIOLOGIC SUBTYPES OF BREAST CANCER BRAIN METS AS A PREDICTOR OF LOCAL CONTROL AFTER STEREOTACTIC RADIOSURGERY

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INTRODUCTION: Brain metastases (BM) are diagnosed in approximately 15% of breast cancer (BC) patients. Biologic subtype is predictive of loco-regional recurrence following breast conserving therapy and/or mastectomy with the highest risk in the ER-/PR-/HER2- (TN) subtype. The aim of this study is to determine whether biologic subtype is predictive of local control (LC) in BC patients with BM treated with Stereotactic Radiosurgery (SRS). MATERIALS/METHODS: All patients underwent LINAC-based SRS at our institution. Patients were subdivided into three biologic subtypes: ER+/Her2- (Luminal), Her2+, and TN (Basal). Kaplan Meier method was used to estimate the overall survival (OS). Cox proportional hazard model was used to analyze association of local failure (LF) with biologic subtypes. This is an IRB-approved single center retrospective study. RESULTS: 108 BC BM in 50 consecutive patients were included in this study with a median follow up of 11.1 months. The median disease-specific GPA was 2.0, and all patients received systemic chemotherapy and/or hormonal therapy. The 12 month LC rates for the entire cohort were 85%, 87%,49% for Luminal, Her2+ and Basal, respectively, with a significantly shorter LC for the basal sub-type ($p=0.014$). The 12 month OS rates were 83%, 88%, 80% for Luminal, Her2+ and Basal, respectively with a no significant difference in OS among the subgroups. 24% of the lesions were treated with salvage whole brain radiation therapy. CONCLUSIONS: This study shows that in BC patients with BM treated with SRS, biologic subtype impacts LC but not OS. Consideration of radiation treatment intensification or altered fractionation to improve LC may be indicated for the TN subtype. Further multi-center studies are necessary to corroborate our results.

RADI-30. TREATMENT OF MULTIPLE BRAIN METASTASES WITH CYBERKNIFE® (CK) INITIAL EXPERIENCE AT THE RADIONCOLOGY DEPARTMENT JÚLIO TEIXEIRA SA – PORTO – PORTUGAL

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Brain metastases (BM) represent an important cause of morbidity and mortality being the most common intracranial tumors in adults. Their incidence is rising for several reasons: an aging population, better systemic treatment and better diagnostic imaging techniques allowing the detection of smaller metastases in asymptomatic patients. Traditionally, the most widely used treatment for patients with multiple BM is whole brain radiation therapy (WBRT), which remains a source of debate because, although distant brain control rates have been shown to be greater with WBRT, it has no impact on overall survival and the negative effects on cognition and quality of life are higher. Radiosurgery plays a significant role in the modern management of BM. We analyzed 38 patients with multiple BM (13 with more than one treatment, totalizing 61 cases) treated with CyberKnife® (CK) in the Radioncology Department Júlio Teixeira SA, from August

2016 to February 2019, for a total of 178 lesions. The average volume was 9,2cc (0,01-73,2). Total dose ranged 18-30Gy delivered in 1–5 fractions. The average nCI was 1,23 (0,19-1,69). Tumor coverage of at least 95% was obtained by prescribing the therapeutic dose to isodose lines ranging from 69–90%. Whole brain tissue was outlined as a critical structure. The average volume of 14Gy (single fraction) and 23Gy (multiple fractions) for normal brain tissue was 6,35cc and 12,4cc, respectively. The treatment was well tolerated, with improvement or resolution of the initial neurological symptoms. Among all radiosurgical platforms the CK offers the advantage of delivering with stereotactic precision high doses of radiation without the invasive attachment of a localizing frame. As a result, in many cases, became the method of choice for treating multiple brain metastases. The attractive therapeutic profile of CK radiosurgery is reflected by a high tumor control and low toxicity allowing retreatment for recurrent metastases.

RADI-31. MULTI-INSTITUTIONAL VALIDATION OF BRAIN METASTASIS VELOCITY, A RECENTLY DEFINED PREDICTOR OF OUTCOMES FOLLOWING STEREOTACTIC RADIOSURGERY

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INTRODUCTION: Brain metastasis velocity (BMV) is a prognostic metric that describes the recurrence rate of new brain metastases after initial treatment with radiosurgery (SRS). We have previously risk stratified patients into high, intermediate, and low-risk BMV groups, which correlates with overall survival (OS). We sought to externally validate BMV in a multi-institutional setting. METHODS: Patients from nine academic centers were treated with upfront SRS; the validation cohort consisted of data from eight institutions not previously used to define BMV. Patients were classified by BMV into low (< 4 BMV), intermediate (4–13 BMV), and high-risk groups (>13 BMV). Time-to-event outcomes were estimated using the Kaplan-Meier method. Cox proportional hazards methods were used to estimate the effect of BMV and salvage modality on OS. RESULTS: Of 2829 patients, 2092 patients were included in the validation dataset. Of these, 921 (44.0%) experienced distant brain failure (DBF). Median OS from initial SRS was 11.2 mo. Median OS for BMV < 4, BMV 4–13, and BMV > 13 were 12.5 mo, 7.0 mo, and 4.6 mo ($p < 0.0001$). Compared to initial salvage with WBRT, salvage SRS was associated with improved OS following DBF for BMV < 4 ($p = 0.05$), BMV 4–13 ($p = 0.002$) and BMV > 13 ($p = 0.0001$). CONCLUSIONS: This multi-institutional dataset validates BMV as a predictor of OS following initial SRS. BMV is being utilized in upcoming multi-institutional randomized controlled trials as a stratification variable for salvage whole brain radiation vs salvage SRS after DBF.

RADI-32. INTRACRANIAL CONTROL AND RADIONECROSIS IN MELANOMA PATIENTS WITH BRAIN METASTASES TREATED WITH STEREOTACTIC RADIOSURGERY

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PURPOSE/OBJECTIVE(S): Melanoma commonly metastasizes to the brain and is radioresistant. Stereotactic radiosurgery (SRS) confers durable local control of brain metastases (BM) while maintaining neurocognitive function. These advantages are increasingly important as survival among these patients improves secondary to advances in systemic therapies. This study investigated the local control (LC), intracranial PFS (iPFS), freedom from radionecrosis (FFRN), and overall survival (OS) among melanoma patients receiving SRS for BM. MATERIALS/METHODS: We retrospectively reviewed clinical outcomes of melanoma patients with brain metastases treated with SRS between October 2008 and January 2017 in a large academic centre. Post-SRS, patients were followed in a multidisciplinary clinic with clinical examination and brain MRI every 3 months. Survival outcomes were estimated using the Kaplan-Meier method. RESULTS: In total, 97 patients with 283 brain metastases (including 12 surgical cavities) treated with SRS were identified. Median age was 60.5 (24.4–90.7). Median follow-up was 9.6 (2.2–74.7) months after first SRS. Median prescription dose was 21 (10–24) Gy delivered in a single fraction. Thirty (30.9%) patients had WBRT post-SRS, 36 (37.1%) patients had BRAF-positive disease. Per lesion (N=283), 1-year LC and FFRN were 84.4%, and 90.1%, respectively; medians were not achieved for either LC or FFRN. Radionecrosis (RN) occurred in 20 (7.1%) lesions. Per patient (N=97), median OS and iPFS were 16.0 and 5.3 months, respectively; 1-year OS and iPFS rates were 62.0%, and 30.1%, respectively. CONCLUSION: SRS resulted in excellent rates of LC, with a low risk of RN. However, most patients developed intracranial progression within 1 year. Further analyses to establish correlates (lesion size, SRS dose, and molecular status) to LC, FFRN, OS, and iPFS will be performed prior to the final presentation.

RADI-33. DISTRIBUTED FRAMELESS GAMMA KNIFE RADIOSURGERY: A NEW TREATMENT PARADIGM FOR PATIENTS WITH BRAIN METASTASES

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INTRODUCTION: Stereotactic radiosurgery (SRS) has excellent efficacy for patients with limited intracranial disease. Its use in patients with >10 brain metastases remains controversial. Nonetheless, cancer patients are living longer due to advancements in systemic therapeutics and avoiding the neurocognitive toxicities of whole brain radiation therapy is critical. Recent reports suggest that SRS may be effective in patients with ≥10 metastases. Treating large numbers of brain metastases in a single Gamma Knife radiosurgery (GKRS) treatment session poses several challenges. Treatment of metastases in close proximity to one another leads to an increased dose to normal brain, potentially increasing the risk of necrosis. Furthermore, single session treatment of multiple metastases may last several hours, causing significant patient discomfort. Here, we describe a novel treatment paradigm to address these issues: distributed frameless GKRS. Patients with ≥6 brain metastases undergo multi-session frameless GKRS with both temporal and spatial distribution over 2–5 sessions, decreasing treatment time per day and not treating adjacent metastases simultaneously. METHODS: We evaluated all patients with brain metastases who underwent distributed frameless SRS, using the Gamma Knife ICON, between January 2017 and November 2018. Fifty-one patients with 1097 unique lesions were included in this analysis. RESULTS: Mean patient age was 58.8 (range 29–89) years. Median follow-up was 4.1 (range: 0–20.4) months. The median number of metastases treated was 5 (range: 1–19) per treatment session and 11.5 (range: 3–82) per treatment course. The median number of treatment sessions per treatment course was 3 (range: 2–10). The median number of treatment courses, per patient, was 1 (range: 1–4). The median margin dose was 15 Gy. The median overall survival was 5.9 (range: 0.2–20.9) months. CONCLUSIONS: Distributed frameless Gamma Knife radiosurgery is technically feasible and should be considered in lieu of single session GKRS for patients with ≥6 brain metastases.

RADI-34. USE OF LOW-DOSE STEREOTACTIC RADIOSURGERY FOR ADVANCED BRAIN METASTASES

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BACKGROUND: Gamma knife stereotactic radiosurgery (GKSRS) is commonly used to treat brain metastases. However, treatment time significantly increases as a function of increasing dose and number of lesions treated. In patients with large number of brain metastases, advanced disease, and poor performance status, low-dose GKSRS may be better tolerated and allows for safer re-treatment with radiotherapy should tumors recur. METHODS: We queried our institutional GKSRS database and identified patients treated with low-dose GKSRS for brain metastases as defined by a prescription of 12–15 Gy margin dose. Overall survival was measured from time of initial low-dose GKSRS to death or study exit. A composite endpoint of time to additional GKSRS, whole brain radiotherapy (WBRT), craniotomy, or death was used to examine disease progression. RESULTS: We identified 30 patients treated with low-dose GKSRS at a single institution between 2008 to 2018. A total of 428 brain metastases were treated, with a median of 12 (IQR=4–20) brain metastases per patient. Thirteen patients received immunotherapy concurrent with low-dose GKSRS, and 23 patients received mutation-targeted therapy or immunotherapy. Median overall survival was 238 (IQR 91–580) days, and median composite time to disease progression was 121 (IQR = 33–371) days. The two longest survivors in our cohort are alive at over three years. One had testicular cancer, and the other had melanoma. The metastatic melanoma patient had a BRAF V600E tumor and received mutation-targeted systemic therapy. He received standard-dose GKSRS and WBRT prior to low-dose GKSRS, as well as immunotherapy prior to and concurrent with low-dose GKSRS. CONCLUSIONS: A heterogenous population with large number of brain metastases was treated with low-dose GKSRS, with acceptable but varied results in terms of survival and tumor control. Further study with larger cohorts is warranted to optimize selection criteria and timing of low-dose GKSRS with other radiotherapy and systemic agent.