EP-1252 Brain metastases postoperative stereotactic RT

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surgical resection followed by FHSRT and 83 with FHSRT only. Most frequent histology of primary site was lung cancer in 62.72% of patients and breast cancer in 13.63%. Planning CT scans were performed with patient in supine position using high precision head mask-fixation system. Gross tumor volume (GTV) was defined using the planning CT scan registered with the diagnostic MRI. A 3 mm expansion was given to the GTV for defining the planning target volume (PTV). Treatments were performed using dynamic conformal arches (VMAT) with 6 MV energy photons. Dose prescribed was 27 Gy in 3 fractions for 67 treatments. Other dose schemes were: 24 Gy in 3 fractions for 20 treatments; 30 Gy in 10 fractions for 8 treatments; 35 Gy in 5 fractions for 7 treatments, 30 Gy in 5 fractions for 7 treatments and 30 Gy in 3 fractions for 1 treatment. Kaplan-Meier actuarial method was used for the analysis of the overall survival, disease free survival and the correlation of the dose scheme and time to progression.

Results

Local progression was observed in 54 of the 110 treatments, among these, there were 26 patients who had one single lesion and 28 who had 2 or more lesions. In the local progression group, 42 patients receive further treatment. Twenty-two receive re-irradiation using FHSRT, 13 with WBRT, 5 where treated with SRS and 2 with surgical resection. Twelve patients did not receive any further treatment. Median overall survival was 8.36 months (r: 1-45). The median disease free survival was 6.7 months (r: 1-43). Grade 2 toxicity (CTCAE v4) was observed in 3 patients, and 10 patients presented neurological symptoms during FHSRT. Radiation necrosis was confirmed in 3 patients, 2 by RMI and 1 with coline PET-TC. When analyzing by subgroups the different dose schemes used, no statistically significant differences were found with respect to the time of recurrence.

Conclusion

FHSRT is an effective alternative treatment for non-multiple brain metastases with high local control and acceptable tolerance. There were no differences regarding the prescribed doses and the time to progression. More data is needed in order to establish the optimal fractionation and dose scheme to be used.

EP-1252 Brain metastases postoperative stereotactic RT: WBRT free survival predicted by an external nomogram

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Purpose or Objective

Patients with brain metastases (BM) represent an extremely diverse group with substantial variability in risk of intra-cranial failure and survival. Patient selection for stereotactic radiotherapy (SRT) alone is complex and requires considering multiple predictive factors. Given that the ultimate goal of SRT is to prolong survival without whole brain radiotherapy (WBRT), a nomogram based on multi-institutional data was developed by another team to display 6 and 12 months WBRT-free survival (WBFS) probabilities (Gorovets, al. IJROBP 2018). The aim of this study was to externally validate this nomogram.

Material and Methods

We retrospectively reviewed the data of 70 patients treated between 2008-2017 by SRT for resected BM. The primary endpoint was the WBFS. Two subgroups of 35 patients were constructed with respect to the patient score in the nomogram (superior and inferior to the median). In each group, the observed WBFS was plotted against the predicted WBFS. The ROC curve and AUC were calculated for both 6 and 12 months time points.

Results

After a median follow up of 16.8 months, the 1-year local and distant brain failure rates were 14.3% and 35.0 %, respectively. The median time to salvage WBRT was 9.6 months. Median time to the first intracranial failure was 7.7 months. At the time of first recurrence, 90 % received local salvage therapy. We performed repeated SRT for 34% and salvage WBRT in 56%. After median time of 8.5 months, 10 patients experienced a second intracranial failure. Eight of 10 patients received further salvage therapy (5 WBRT, 3 SRT). The WBFS rates at 6 and 12 months were 87 % [IC $_{95\%}$ = 79-95 %] and 56 % [IC $_{95\%}$ = 45-69%] , respectively. In terms of calibration, the 6 months rates were overestimated while they were accurate at 12 months (Fig. 1). It is reflected by the evolution of the cumulative proportion of WBRT or death in both subgroups with observed rates inferior to expectations at 6 months while they superimpose at 12 months (Fig. 2). A ROC curve was plotted for the 6 and 12 months nomogram predictions. AUC values were 0.47 and 0.62, respectively.

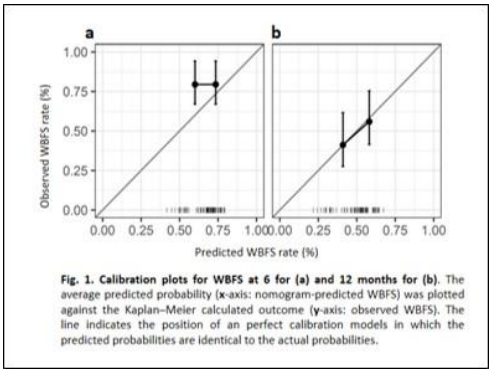

Fig. 1. Calibration plots for WBFS at 6 for (a) and 12 months for (b). The average predicted probability (x-axis: nomogram-predicted WBFS) was plotted against the Kaplan–Meier calculated outcome (y-axis: observed WBFS). The line indicates the position of an perfect calibration models in which the predicted probabilities are identical to the actual probabilities.

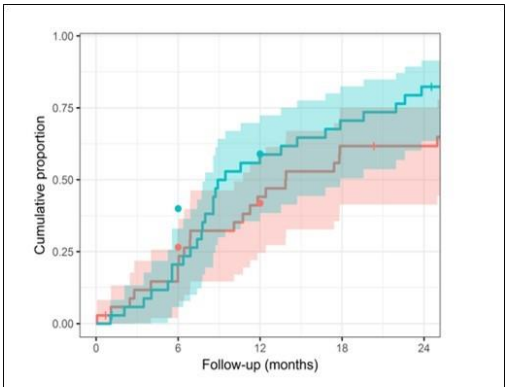

Fig. 2. Evolution of cumulative proportion of WBRT in function of the time. Patients were divided in two subgroups according to their baseline characteristics (Blue = superior to the median, red = inferior to the median). The straight line represents the Kaplan-Meier estimate of the cumulative proportions, dots indicate the predicted proportion at different time points (6 and 12 months).

Conclusion

In our population of patients with operated BM and then stereotactically irradiated, the nomogram predicted correctly the WBFS at 12 months but not at 6 months. The median time to salvage WBRT was 9.6 months in our series while it was 6.2 months in the series by Gorovets. The fact that one third of our patients were treated with SRT as first salvage treatment may have played a role. Patients were operated and this may also be a confounding factor. All in all, it reflects the inherent limitation of applying prediction models to highly heterogeneous populations. Including more patients and characteristics

(e.g. molecular data) may improve the concordance index.

EP-1253 Biological target volume using DTI-MRI in postoperative chemoradiotherapy for glioblastoma

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Purpose or Objective

Glioblastoma (GBM) is a highly aggressive malignant brain tumour with a median overall survival of only 15 months. After postoperative chemoradiotherapy, most recurrences occur within or at the margin of the treatment volume. The standard clinical target volume (CTV) is typically defined as an isotropic 2 cm expansion around the surgical cavity and the area of contrast enhancement. This isotropic margin is not taking into account the preferential tumour growth along the white matter tracts of the brain. Diffusion tensor imaging (DTI) MRI can be used to model white matter tracts. The aim of this phase 1 feasibility study is to evaluate DTI-MRI diffusion growth models in the biological CTV definition of GBM.

Material and Methods

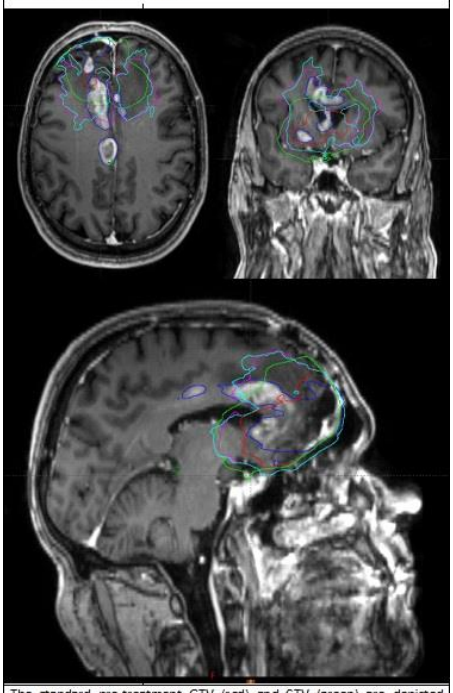
Adult GBM patients referred for postoperative RT were included, and underwent an additional pre-treatment DTI-MRI; actual treatment wasn't altered. The standard CTV was defined as described above, respecting anatomical barriers. DTI-MRI was used to create two biological CTVs, iso-volumetric to the standard CTV, using anisotropic margins based on tensor directionality of γ0 (bCTVγ0) and γ20 (bCTVγ20; higher γ meaning a higher assumed probability of tumour spread along white matter tracts). The similarity of the CTV and the bCTVs was assessed using the Dice similarity score (DSC; 0=no overlap, 1=complete overlap). Treatment effect was assessed by 3-monthly MRI and described by RANO criteria. Progression was defined as central, in-field/marginal and distant with respective ≥95%, 20-95%, or <20% of the recurrence volume (RV) located within the $D_{95\%}$. Only patients with an in-field/marginal or distant recurrence were selected for comparison of the bCTVs to the RV. The overlap or minimal distance between the bCTVs and the delineated RV was calculated.

Results

Between 10/2016 and 06/2018 38 patients were included. One patient went off-study and one was lost to follow-up, leaving 36 for analyses. Gross total resection was performed in 42% of patients, and 89% completed irradiation to 60 Gy in 30 fractions (Table). At a median follow-up of 9.5 (range 3-21) months, 23 patients had disease progression; 2 clinical, 19 central, 1 in-field/marginal, 2 distant. The median PFS was 7.0 (range 4.5-9.5) months. The mean DSC between CTV and bCTVγ0 was 0.75 (range 0.65-0.85), and CTV and bCTVγ20 was 0.72 (range 0.62-0.81) (bCTVγ0 vs bCTVγ20 p<0.001). For patient 1 with a non-central recurrence the CTV/bCTVγ0/bCTVγ20 overlapped with the RV by 87/90/89% (Figure). For patient 2 the CTV/bCTVγ0/bCTVγ20 overlapped with the RV by 19/21/25%.

For patient 3 (no overlap) the shortest distance from the CTV/bCTVγ0/bCTVγ20 to the RV was 4.6/3.6/3.3 cm.

Figure. DTI-MRI based biological target volume in postoperative chemoradiotherapy for GBM.



The standard pre-treatment GTV (red) and CTV (green) are depicted together with the bCTVγ0 (magenta) and bCTVγ20 (cyan) at the co-registered follow-up MRI at time of progression (blue). This example shows the improved overlap of the bCTVs to the recurrence volume at the corpus callosum compared to the standard CTV.

Table. Patient and treatment characteristics for the total study population, patients with a central recurrence and patients with a non-central recurrence.

	Total (n=36)	Central recurrence (n=19)	Non-central recurrence (n=3)
Characteristic	No. (%)	No. %	No. %
Age			
Median (range)	64 (25–76)	63 (44–75)	55 (52–63)
Gender			
Male	26 (72)	13 (68)	2 (67)
Female	10 (28)	6 (32)	1 (33)
KPS			
100	14 (39)	9 (47)	0
80-90	19 (53)	8 (42)	3 (100)
60-70	2 (6)	1 (5)	0
Unknown	1 (3)	1 (5)	0
Tumour localization			
Frontal	7 (19)	3 (16)	1 (33)
Temporal	15 (42)	7 (37)	1 (33)
Parietal	3 (8)	3 (16)	1 (33)
Occipital	3 (8)	2 (11)	0
Multiple areas	7 (19)	4 (21)	0
Extent of resection			
Biopsy only	9 (25)	4 (21)	0
Partial resection	12 (33)	5 (26)	1 (33)
Gross total resection	15 (42)	10 (53)	2 (67)
MGMT status			
Methylated	20 (56)	9 (47)	1 (33)
Non-methylated	14 (39)	9 (47)	2 (67)
Unknown	2 (6)	1 (5)	0
Radiation dose			
40 Gy in 15 fractions			
completed	2 (6)	1 (5)	0
60 Gy in 30 fractions			
completed	32 (89)	18 (95)	3 (100)
stopped preliminary*	2 (6)	0	0
Temozolomide			
Concurrent			
never started	1 (3)	1 (5)	0
completed	30 (83)	17 (89)	3 (100)
stopped preliminary	5 (14)	1 (5)	0
Adjuvant			
never started	7 (19)	5 (26)	0
completed	11 (31)	5 (26)	1 (33)
stopped preliminary	15 (42)	9 (47)	2 (67)
ongoing	3 (8)	0	0

*one patient received 50 Gy in 25 fractions, and one patient received 54 Gy in 27 fractions.

Conclusion

Biological DTI-MRI based CTV showed marginal improvement in a limited number of GBM patients with non-central recurrence. Further investigation in a larger cohort including non- iso-volumetric approaches is needed for further improvement in CTV definition.

EP-1254 When could we spare hippocampus in the WB radiation for the primary central nervous system lymphoma?

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