Baseline total brain volume predicts for poorer QoL and reduced OS after cranial radiotherapy in older patients with glioblastoma (GBM): results from the prospective UK BRITER study

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Introduction

GBM is the commonest primary malignant brain tumour amongst the adult population, incidence rates peak in the 65-75 age group.

Short-course partial brain radiotherapy, +/- chemotherapy, extends survival compared to supportive care but there is no validated evidence for prediction of individual risk of acute radiotherapy related side effects.

We aimed to consider putative MRI markers of brain resilience and their relationship to change in QoL amongst older patients being treated for GBM with cranial radiotherapy.

Method

Prospective multicentre observational trial, recruited patients with newly diagnosed GBM aged ≥ 65 planned for cranial radiotherapy.

Baseline MRI scans were analysed for:

- relative total brain volume (ratio of cerebrospinal fluid (CSF)
- volume to total intracranial volume (TIV))
- contralateral medial temporal lobe volume
- number and volume of T1 white matter hypointensities
- Fazekas' scale of white matter change
- Radiotherapy treatment volumes were obtained from planning software

EORTC QoL questionnaires completed at baseline, 4 weeks and 8 weeks after completing radiotherapy alongside survival and toxicity data

Results

126 patients were enrolled from 12 UK centres; mean age 72 years (range 65-83)
68% were men, 32% women.

ECOG performance status at baseline was 0-1 in 75%, 2 in 23% and 3 in 2%. Baseline MoCA was impaired in 58% of participants.

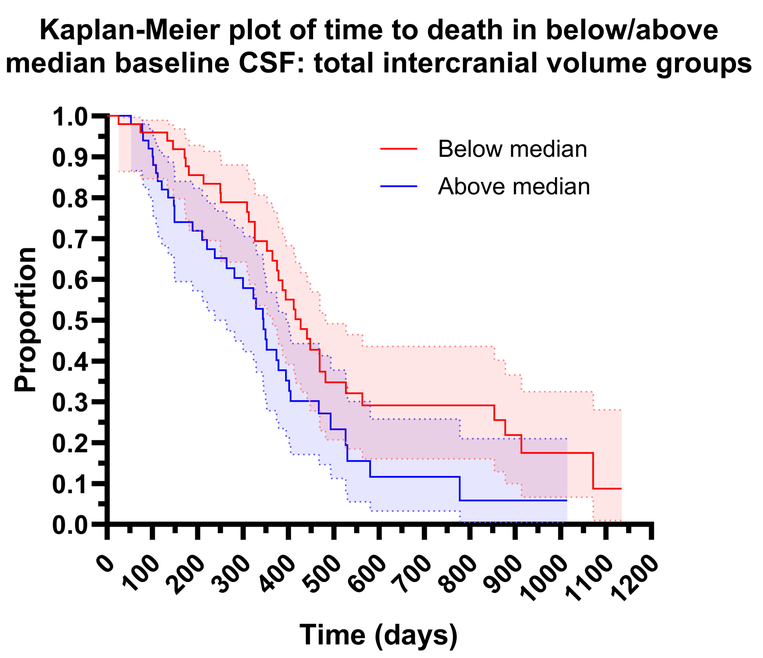
Median overall survival was 11.3 months.

After accounting for age, sex, treatment and baseline MoCA score, there was a meaningful relationship between baseline CSF:TIV ratio and change in QoL score.

For each $1*10^{-4}$ unit increase in CSF:TIV ratio, there was a corresponding decrease in QoL score of 1.72 (coefficient -1.72, 95% CI -3.24 to -0.19 p=0.03)

35 participants were too unwell to complete questionnaires or had died by the 8 week follow up visit. In this subgroup, post hoc logistic regression showed baseline CSF:TIV ratio was related to risk of non-attendance (OR 1.35, 95% CI 1.01-1.80, p=0.04).

Treatment received	
	%
Surgery	
None	3
Biopsy	19
Debulking	78
Oncological	
30Gy in 6# alone	6
40Gy in 15# alone	14
40Gy in 15# with concurrent TMZ	42
60Gy in 30# with concurrent TMZ	38



Below median represents a lower atrophy score which indicates less baseline atrophy

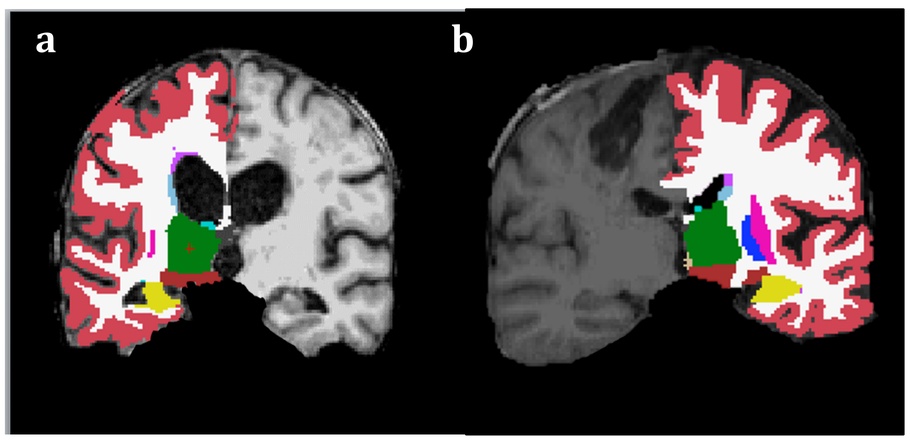
Discussion

First prospective study of this kind shows routine baseline imaging parameters can independently predict changes in QoL and overall survival following cranial radiotherapy for a GBM

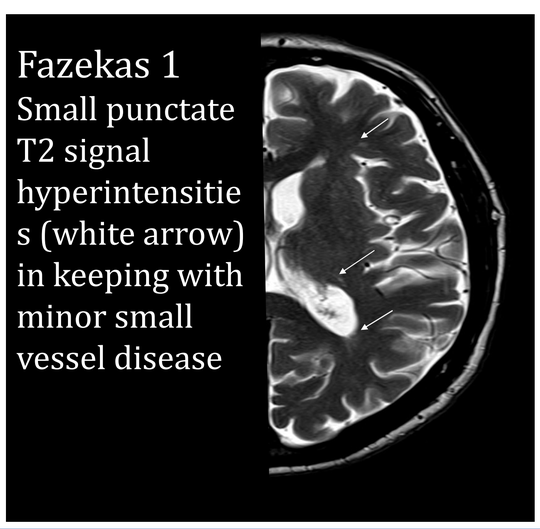
This cohort of patients were predominantly ECOG PS 0-2 and 38% were planned for full Stupp protocol therapy. Despite this 28% of them were too unwell to attend or had died by the 8 week post radiotherapy follow up appointment

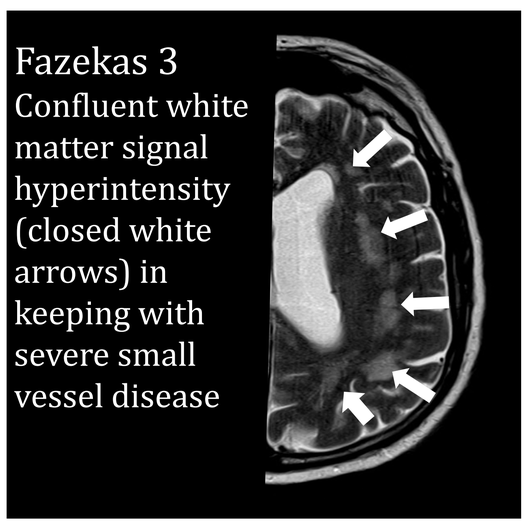
Better assessment of patient fitness prior to starting treatment is essential to maximise the quality of life.

Baseline measures of global cortical atrophy alongside geriatric assessment techniques should be used to guide discussions around the benefits versus expected toxicities of treatment amongst older patients with a GBM



Freesurfer segmented brain overlays for coronal views of a) Patient with high atrophy score CSF:total (contralateral hemi)brain volume $1.12^{-3}$and b) Patient with low atrophy score CSF:total (contralateral hemi)brain volume 2.36^{-4}.
Patient a) overall survival 11 weeks
Patient b) overall survival 142 weeks
Medial temporal lobe volume segmentation is depicted in yellow





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