Enhancing Fraction and Survival in Glioblastoma Multiforme

S. J. Mills[1,2], C. Soh[2], G. Thompson[1], G. Buonaccorsi[1], C. McBain[3], S. Zhao[1], G. J. Parker[1], and A. Jackson[1,2]
[1]Imaging Science and Biomedical Engineering, University of Manchester, Manchester, Greater Manchester, United Kingdom,
[2]Department of Neuroradiology, Salford Royal Foundation Trust Hospital, Salford, Greater Manchester, United Kingdom,
[3]Department of Clinical Oncology, Christie Hospital, Manchester, Greater Manchester, United Kingdom

Purpose: Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI) has shown prognostic potential in glioblastoma multiforme (GBM). Enhancing Fraction (EnF) is a recently described DCE-MRI derived measure [1-3]. This quantifies the proportion of a tumour that enhances and in GBM has been shown to correlate with K^{trans} (contrast agent transfer coefficient) derived from DCE-MRI [3]. The objective of this study was to evaluate the prognostic value of EnF in GBM.

Materials and Methods: 15 patients with GBM were recruited. All underwent standard radiotherapy with adjuvant & concomitant temo-zolamide. All imaging was performed prior to surgery on a 3 tesla MR scanner. Imaging included T_1-weighted DCE-MRI (3 pre-contrast spoiled fast field echo sequences with different flip angles (2^o, 10^o, 16^o) for calculation of baseline T_1 maps (TR 3.5ms, TE 1.1ms, slice thickness 4.2mm, 128x128) and a dynamic, contrast enhanced acquisition series with identical acquisition parameters as the variable flip angle baseline T_1 measurement, consisting of 100 volumes with temporal spacing of approximately 3.4 seconds, with gadolinium-based contrast agent injected as a bolus of 3ml, at 15 mls^{-1}, at a dose of 0.1$mmolkg^{-1}$ of body weight after acquisition of the fifth image volume) and anatomical sequences (pre and post contrast geometrically matched T_1 weighted images, TR 9.3 ms, TE 4.6 ms, slice thickness 4.2mm, 128x128). Voxels were classified as enhancing if the initial area under the contrast concentration curve (*IAUC*) was positive ($EnF_{IAUC60>0}$). A threshold of $IAUC > 2.5$ mMol.s was used to generate thresholded EnF ($EnF_{IAUC60>2.5}$). Parametric maps of $IAUC_{60}$, K^{trans}, v_p (blood plasma volume per unit volume tissue), and v_e (volume of the extravascular extracellular space per unit volume tissue) were generated. The prognostic value of patient age, sex, tumour volume, $EnF_{IAUC60>0}$, $EnF_{IAUC60>2.5}$, median $IAUC_{60}$, median K^{trans}, median v_p, and median v_e were assessed using a multivariate Cox regression analysis.

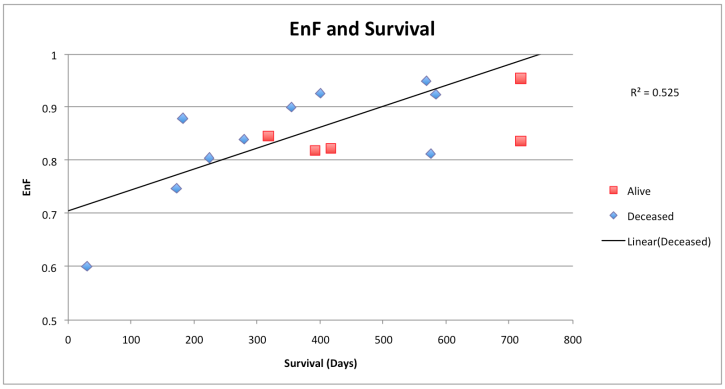

Figure 1. *Scatter plot of $EnF_{IAUC60>0}$ and patient survival. Linear regression analysis shows increased survival with increased $EnF_{IAUC60>0}$*

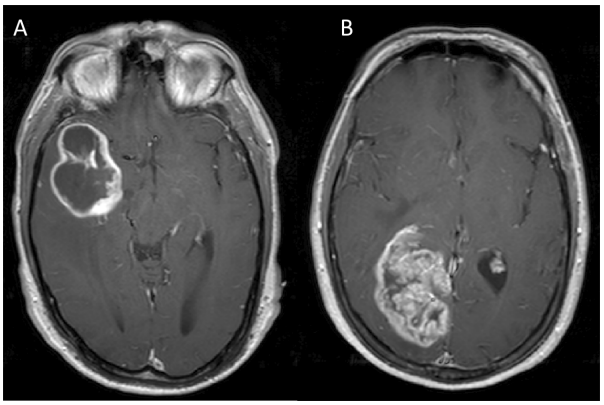

Figure 2 *Illustrative examples of post contrast T_1 weighted images for two patients with low and high $EnF_{IAUC60>0}$ and corresponding short and long survival times.* ***Patient A*** *(55 year old male) demonstrates a necrotic tumour within the right temporal lobe, $EnF_{IAUC60>0} = 0.75$ and survival 172 days.* ***Patient B*** *(58 year old female) has a more solid tumour within the right posterior parietal/occipital lobes; $EnF_{IAUC60>0} = 0.95$ and survival 568 days.*

Results: Examination of survival data from deceased patients demonstrated a linear relationship between $EnF_{IAUC60>0}$ and patient survival ($p<0.05$, $R^2=0.525$, Figure 1). Only $EnF_{IAUC60>0}$ was identified as an independent prognostic factor ($p<0.05$). Illustrative patient examples are shown in Figure 2.

Conclusion: This preliminary study suggests a possible relationship between EnF and length of survival in patients with GBM. We hypothesised that this relationship reflects the effect of increasing intracranial pressure in the face of failing physiological compensation mechanisms, resulting in a fall in enhancing proportion.

Grant Support: This research was funded by a Cancer Research UK Clinicians Training Fellowship ref: C21247/A7473 (S Mills). G Buonaccorsi is funded on a Cancer Research UK Program Grant ref: C237/A6295. G Thompson is funded by a Cancer Research UK Clinicians Training Fellowship ref: C30033/A9809

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