Heterogeneity in brain metastases - advanced MRI at the leading edge relates to recurrence, survival and aggressive growth patterns

Mr Rasheed Zakaria MA · Supervisors Prof PS Rudland, Mr MD Jenkinson, Dr V Sluming
Department of Neurosurgery · Walton Centre NHS Foundation Trust & Institute of Integrative Biology · University of Liverpool

Background

Secondary brain tumours are common and we are seeing more of them

The prognosis has remained dismal (median c. 2-3 months for all-comers) despite advances in treating primary cancers and patients are dying of brain metastases not with them.

WE DO NOT UNDERSTAND HOW LOCALLY INVASIVE THESE TUMOURS ARE

However, there are significant rates of local recurrence and we have shown that diffusion MRI changes at the brain-tumour boundary can predict survival and recurrence, as shown below.

Methods

Pre-operative 3T MRI was obtained with 32 direction DTI and T1 with gadolinium. Image guided sampling was performed as shown at the leading edge of the tumour as it was removed. Histogram analysis of regions of interest were matched to tissue locations. Growth pattern was assessed by a pathologist using a previously described classification and CD34, Ki67, necrosis and cellularity were scored semi-automatically using NIH ImageJ software. Survival and brain recurrence were recorded.

Results

The mean diffusivity (MD) values recorded at the edge of metastases were significantly different in distribution, median and mean from those at the core (Wilcoxon matched pairs, p=.001).

There was significantly higher necrosis (p=.026) and a trend to higher CD34 density at the leading edge versus the core. MD and the change in MD across the leading edge correlated with cellularity (p=-.41, p=0.047) but did not predict clinical outcomes nor pathological growth pattern.

Metastases which appeared more diffusely invasive pathologically (above right H&E,Ki67) had a significantly lower peritumoral fractional anisotropy (FA) (p=0.039) suggesting more tract white matter disruption (above and left FA map). These tumours also had more dense CD34 staining (r=-.55, p=0.041) at their leading edge and a trend to lower survival and more rapid intracranial recurrence.

Conclusions

There is significant intra-tumoral heterogeneity among brain metastases and assessment of the brain-tumour interface radiologically and biologically may yield more useful information about behaviour and prognosis than assessing the whole metastasis.