RA-24

PREDICTING THE LOCATION AND PROBABILITY OF VIABLE TUMOR WITHIN GLIOBLASTOMA MULITFORME WITH MULTI-PARAMETRIC MAGNETIC RESONANCE IMAGING

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Introduction

➢Glioblastoma multiforme (GBM) is the most common primary malignant brain tumor.

➢GBM's infiltrative nature makes radiological tumor margin delineation challenging, which in turn affects the extent of surgical resection.

➢Contrast enhancement on MRI has traditionally been used to plot the geographic extent of tumor involvement. However, current consensus acknowledges the role of additional MRI markers in the characterization of tumor margins beyond the boundaries of contrast enhancement.

➢Our aim is to develop a rule-based multi-parametric approach which incorporates multiple MRI markers in a concerted fashion as an improved method of characterizing the extent of viable tumor within a GBM lesion.

Methods

➢**Subjects.** 7 patient subjects with a histopathological diagnosis of GBM were obtained from the COmprehensive Neuro-oncology Data Repository (CONDR), an ongoing clinical trial [NCT01124461] which includes a robust informatics and data sharing infrastructure comprised of patients from Barnes-Jewish Hospital (St. Louis, MO) and Swedish Neuroscience Institute (Seattle, WA).

➢**Manual Segmentations.** 8 MRI sequences, primary and derived [T1 pre-contrast, T1 post-contrast, T2, Fluid Attenuated Inversion Recovery (FLAIR), Susceptibility Weighted Imaging (SWI), Apparent Diffusion Coefficient (ADC), TraceW, and relative Cerebral Blood Volume (rCBV)], were co-registered and transformed to standard template space with 1 mm isotropic voxels. A board-certified radiologist manually segmented each MRI volume (Table 1) to produce a set of 6 total object maps (Figure 1).

➢**Formulation of a Multi-parametric Probability Map.** By assigning probability of active tumor to each object map and combining overlapping object maps within a voxel (according to rules summarized in Table 2), and a 3-D reformatted model of our multi-parametric tumor classification was produced (Figure 2). Tumor volumes were also calculated according to a multi-parametric approach, which were compared to volumes calculated according to contrast enhancement alone.

Results

➢In the interest of conciseness, we illustrate our method and results on a single study subject (CONDR W015).

➢3-D reformatted model of our multi-parametric tumor classification (Figure 2) illustrates expected tumor morphology wherein:

- ➢necrosis lies within the center of the tumor
- ➢the most viable, metabolically active tissue lies at the periphery of the tumor
- ➢cerebral edema or micro-invasion extends beyond the margin of viable tumor

➢This 3-D reformatted model (Figure 2) and tumor volume calculations (Table 3) also show the discrepancy between a multi-parametric assessment of tumor extent and volume compared to relying solely on contrast enhancement alone.

Conclusion

➢We show a method of integrating multiple MRI markers to produce a single composite image which predicts the probability of viable tumor within a GBM lesion.

➢We demonstrate the discrepancy between the estimation of tumor volume with a multi-parametric approach compared to relying on contrast enhancement alone. Relying on a single metric such as contrast enhancement almost certainly underestimates the extent of viable malignancy.

➢This novel method distinguishes itself from prior works in this field of research (McMillan, et al.) by weighting the importance of certain MRI markers over others.

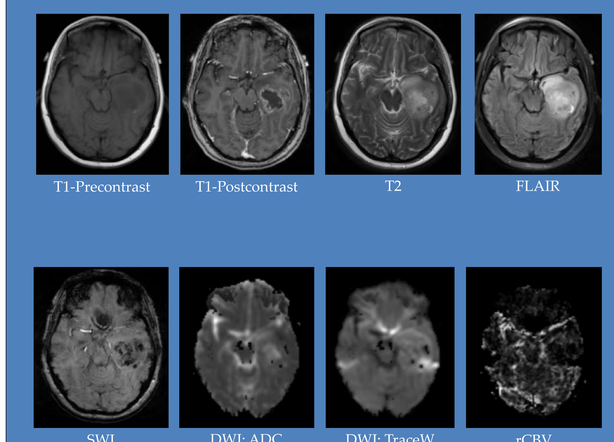
➢A multi-parametric approach in MRI may offer a more accurate assessment of GBM tumor invasion which in turn may direct more efficacious surgical resection.

Table 1. Summary of Segmentations

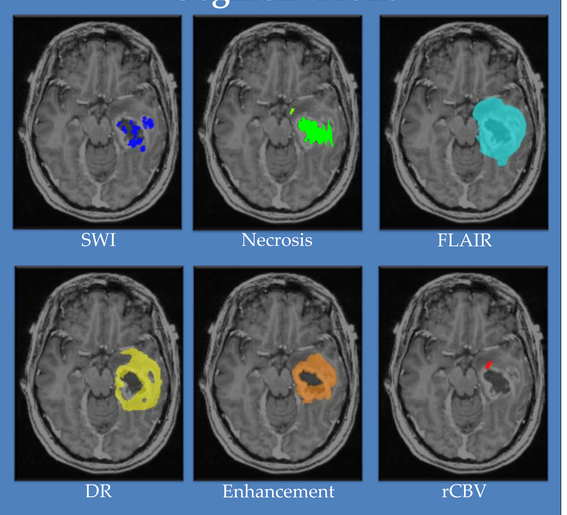
MRI parameter	Criteria for Segmentation	Positive or Negative Classification for Viable Malignancy
Susceptibility Artifact (SWI)	Discontinuous areas of signal void on SWI	Indeterminate: hemorrhage
Necrosis	T2 hyperintesity supressed on FLAIR	Negative: liquefactive necrosis
FLAIR	Hyperintensity on FLAIR	Positive: possible micro-invasion of tumor
Diffusion Restriction (DR)	Hyperintensity on TraceW suppressed on ADC	Positive: viable tumor
Elevated CBV (rCBV)	Areas demonstrated 1.75 times the cerebral blood volume compared to normal brain tissue	Positive: viable tumor
Contrast Enhancement (Enhancement)	Hyperintensity on T1 post-contrast not present on T1 pre-contrast	Positive: viable tumor

Figure 1. Illustration of Segmentations

MRI Sequences Included in Segmentation Analysis



Segmentations



Segmentations have been superimposed on a T1-postcontrast image.

Table 2. Rules of Assigning Probability of Viable Tumor

Probability of Viable Tumor	Criterion
Normal brain	Voxel not included in any object map
Indeterminate	Any voxel containing susceptibility artifact
Low	Any voxel containing necrosis
Moderately low	Any voxel containing FLAIR hyperintensisty in the absence of other positive indicators (enhancement, diffusion restriction, or elevated CBV)
Moderate	Any voxel containing FLAIR hyperintensity and enhancement without additional positive indicators (diffusion restriction or elevated CBV)
Moderately high	Any voxel containing FLAIR hyperintensity and enhancement with one additional positive indicators (diffusion restriction or elevated CBV)
Highest	Any voxel containing all the positive indicators for viable tumor (FLAIR hyperintensity, enhancement, diffusion restriction, and elevated CBV)

Figure 2. 3-D Rendering of Multiparametric Predictions

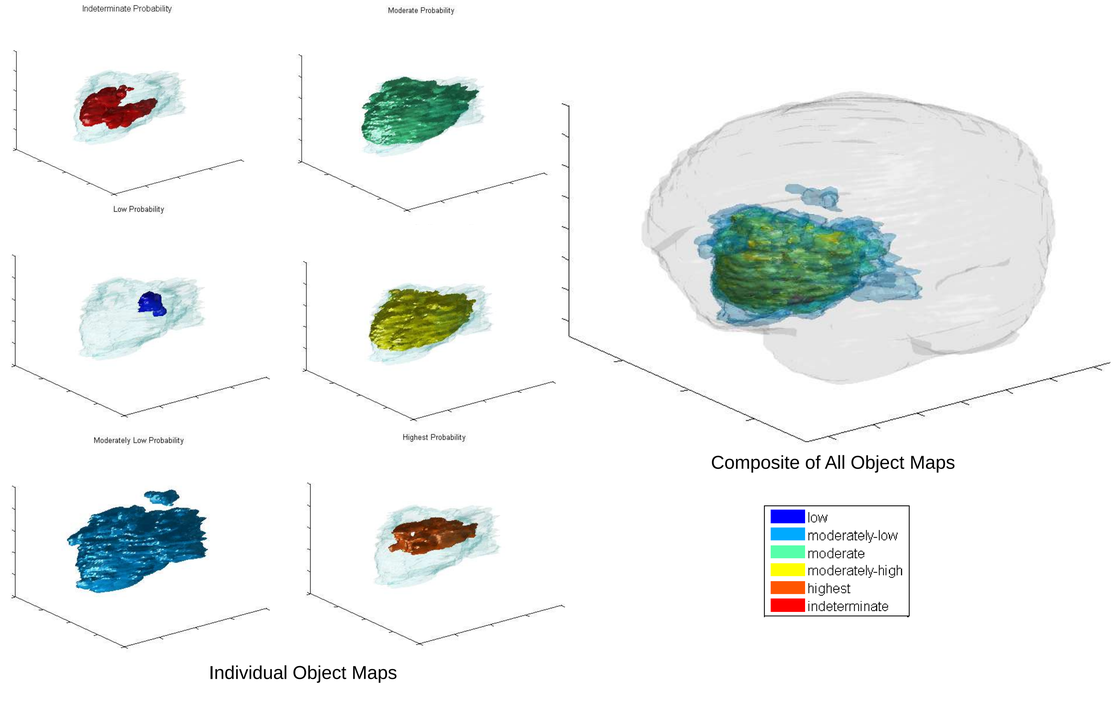


Table 3. Calculated Tumor Volumes

MRI Marker	Calculated Volume (mm^3)
Susceptibility artifact	4,377
Necrosis	1,143
FLAIR hyperintensity	75,408
Diffusion restriction	3,340
Elevated CBV	6,441
Contrast enhancement	55,062
Total tumor volume (summated volume of MRI markers listed above)	145,771
Percent difference between total tumor volume versus volume of contrast enhancement alone	+265%

References

➢ ACRIN. ACRIN 6686 (RTOG 0825) Advanced MRI Imaging Manual, American College of Radiology Imaging Network; 2009. Available from: http://www.acrin.org/Portals/0/Protocols/6686/6686%20MRmanual%2010012009.pdf

➢ McMillan, K.M., et al., *An objective method for combining multi-parametric MRI datasets to characterize malignant tumors*. Medical Physics, 2007. **34**(3): p. 1053-1061.

Acknowledgments

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➢ This research is founded on a standardized imaging protocol implemented on all clinical scanners at each of the two participating institutions. This standardized brain tumor MR imaging protocol is based on the ACRIN 6686 (RTOG 0825) protocol.