Multivariate Linear Modeling of Quantitative MR Features for Prognosis in Patients with Glioblastoma Multiforme

S. Dube[1], T. Cloughesy[2], J. Sayre[1], and U. Sinha[1]

[1]Biomedical Engineering, University of California, Los Angeles, CA, United States, [2]Neurology, University of California, Los Angeles, CA, United States

Introduction:

Patients diagnosed with glioblastoma multiforme (GBM) brain tumors treated with standard protocols have a mean survival time of 18 months. However, within the GBM tumor cases, time to survival is still highly variable. Several research groups have investigated correlations between imaging characteristics of GBM with time to survival. Imaging features that have been found to negatively correlate with survival are necrosis, edema, and contrast enhancement [1-3]. A recent study assessed the relationship between 15 imaging variables, obtained from T1 contrast-enhanced MR imaging scans, and survival in patients diagnosed with Grade 4 tumors [4]. This latter study found that for the patients with GBM, the survival was negatively correlated in the presence of the following imaging variables: edema, satellites, and multifocality. However, overwhelmingly the research performed to date uses qualitative descriptors of imaging findings or simple quantitative indices such as bi-linear measurements for tumor size. In the current work, we derive quantitative descriptors of tumor sub-region shape and texture to determine correlations of these features to time to survival. Specifically, our work uses a multivariate linear regression model to examine the efficacy of quantitative imaging features extracted from T1 post-contrast volumetric acquisitions prior to surgery in predicting survival time.

Methods:

Imaging data from 34 subjects with GBM were included in the analysis. All patients underwent gross total resection and subsequent radiation and chemotherapy. Time to survival was defined from the date of confirmation by biopsy to current date (if surviving) or to death (for deceased subjects). The imaging data used in the analysis were all pre gross total resection and were acquired at a time point close to the biopsy date. The imaging protocol included a T1 post-contrast SPGR (.47 mm x .47 mm x 1.5 mm) and a T2-weighted sequence prior to surgery. The quantitative features were extracted from only the T1 post-contrast study, but the T2 sequence was used to accurately delineate the edema region (Figure 1).

Images were pre-processed to improve image quality. The pre-processing steps were: (i) denoising (Smallest Univalue Segment Assimilating Nucleus), (ii) brain extraction (Brain Extraction Tool), (iii) image alignment (fMRIB Linear Image Registration Tool), and (iv) image intensity standardization [5]. Image intensity standardization was applied to the T1 post-contrast images to allow the image intensities to be consistent between studies and to obtain uniform measures of texture [6].

Three regions were manually segmented from the T1 post-contrast images: edema, contrast enhancement, and necrosis (Figure 1). These three regions are readily identified by an expert radiologist. In this preliminary study, we have not identified other regions such as debris, non-contrast enhancing tumor. These are, in the current study, included within the necrosis sub-region. Table 1 is a list of the shape, texture and intensity histogram features extracted for each tumor sub-region. A stepwise multivariate linear regression model was applied to the quantitative data to determine the quantitative variable (or combination of variables) that best predict time to survival.

Results:

Table 2 shows the results of the stepwise multivariate linear regression model. Each model corresponds to the number of variables used to predict survival and the respective correlation coefficient. For a given model n (where n represents the number of variables), the variables (along with their respective weighting coefficients) that gave the best correlation with time to survival are listed. Model 5 gave the highest adjusted correlation coefficient (0.848) and consisted of 3 quantitative parameters of edema and 2 parameters of contrast enhancement. The significant edema descriptors consisted of an order 2 and order 3 shape invariant moments and the correlation texture measure. The significant contrast enhancement parameters consisted of an order 3 shape invariant moments and the kurtosis feature of the intensity histogram.

Discussion:

The shape and texture of edema show strong correlations to time to survival. Edema presumably follows the white matter tracts, and a higher infiltration of the tracts may be captured in the shape indices as structures of high morphological anisotropy. The correlation texture feature is related to the inhomogeneity of intensity in the edema sub-region. Infiltration of tumor cells into edema could potentially result in inhomogeneous intensities of the edema sub-regions. Greater infiltration into the surrounding peri-tumoral edema has a poor prognosis and this could be the basis for a correlation between the edema texture feature and time to survival. The correlation of the shape of contrast enhancing tumor region to survival time may also have its origin in the infiltrative nature of tumor. Kurtosis of the intensity histogram primarily reflects asymmetry and the presence of a long tail in the high intensity end of the histogram. This heterogeneous intensity profile may arise from some voxels showing a high uptake of the contrast agent, which in turn may reflect tumor aggressiveness.

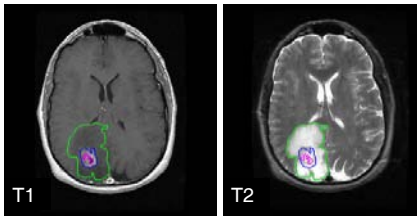

Figure 1: The left and right images are the T1 post contrast and respective T2 with the labeled regions that were segmented for quantitative analysis. The edema boundary is outlined by green, contrast enhancement by blue, and necrosis by magenta.

Category	Features
3D Texture via Co-occurrence Matrix	Correlation Contrast Homogeneity Energy
3D Shape Moments	Order 0 Invariant Moment (Volume) Order 1 Invariant Moments Order 2 Invariant Moments Order 3 Invariant Moments
Histogram	Mean Variance Skewness Kurtosis

Table 1: List of the different features extracted for each sub-region. The features consisted of texture parameters derived from 3D co-occurrence matrices, 3D shape moments, and histogram parameters.

Model	Variables	Coefficients	Adjusted R^2
1	Constant	329.54	0.648
	3rd order SM of CE	4.37E-06	
2	Constant	326.154	0.739
	3rd order SM of CE	4.27E-06	
	2nd order SM of Edema	-8.40E-06	
3	Constant	404.316	0.783
	3rd order SM of CE	4.51E-06	
	2nd order SM of Edema	6.50E-06	
	Correlation of Edema	788.71	
4	Constant	406.22	0.814
	3rd order SM of CE	4.55E-06	
	2nd order SM of Edema	-5.50E-06	
	Correlation of Edema	771.308	
	3rd order SM of Edema	6.34E-07	
5	**Constant**	**214.446**	**0.848**
	3rd order SM of CE	**4.61E-06**	
	2nd order SM of Edema	**-3.80E-06**	
	Correlation of Edema	**747.286**	
	3rd order SM of Edema	**6.85E-07**	
	Kurtosis of CE	**64.09**	

Table 2: Results of the stepwise multivariate linear regression model applied to the quantitative imaging data. Each model shows the variables involved, their weighting coefficients, and the resulting correlation coefficient to describe how well the model fits the data.

Conclusion:

We have shown that the time to survival is strongly correlated with some quantitative features of tumor sub-regions. The significant features were the shape and texture of edema as well as the shape and kurtosis of intensity histogram of contrast enhanced sub-region obtained from the volumetric T1 post-contrast sequence prior to surgery. This paper is the first to report a model to predict time to survival of patients diagnosed with GBM based on quantitative imaging features. We are currently extending the work to include more subjects as well as more features.

References:

1. Pierallini A, Bonamini M, Pantano P, et al., Neuroradiology 40, 1501-53, 1998
2. Lacroix M, Abi-Said D, Fourney DR, et al., Journal of Neurosurgery 95, 190-198, 2001
3. Pronin IN, Holodny AI, and Petraikin AV, Diagnostic Neuroradiology 39, 348-350, 1997
4. Pope WB, Sayre J, Perlina A, et al., American Journal of Neuroradiology 26, 2466-2474, 2005
5. Smith SM, Jenkinson M, Woolrich MW, et al., NeuroImage 23, 208-219, 2004
6. Nyul LG, Udupa JK, Zhang X, IEEE Transactions on Medical Imaging 19, 143-150, 2000