A fully automated method for predicting glioma patient outcome from DSC imaging. A second reference to histopathology?

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Purpose: To assess whether a fully automated, multi-parametric method for predicting outcome in glioma patients from dynamic susceptibility contrast (DSC) MR imaging can be used as a second reference to pathologic findings.

Background: The added value of using multi-parametric models encompassing such MR perfusion parameters as voxel-by-voxel cerebral blood volume (CBV) values and degree of contrast agent leakage into the extra cellular space (K^{trans},) have been shown in both DSC imaging of human gliomas [1] and dynamic contrast enhanced (DCE) MR imaging of animal tumor models [2]. Since the majority of patients suspected of a glioma will undergo surgery, pre-operative glioma grading from MR perfusion imaging may have limited value. However, current histopathological methods for grading gliomas using the World Health Organization (WHO) classification may be limited by sub-optimal criteria and sampling error. Thus, accurate prediction of patient outcome may be critical with respect to treatment planning. In this study, we present a user-independent, predictive model based on analysis of CBV and K^{trans} parameters from DSC imaging and compare the results with patient outcome as suggested by histopathology.

Methods: To date, 56 adult patients (23 females, 33 males, aged 26-78 yrs, mean age 52 yrs) previously untreated patients have been included in the study. Axial T2-w image, axial T1-w images (pre- and post-contrast), coronal FLAIR images and axial gradient-echo echo-planar DSC images were acquired at 1.5 Tesla (Siemens, Germany) prior to surgery and subsequent histopathological diagnosis. CBV and K^{trans} maps were derived using established methods [3] and K^{tans} were corrected for both "negative" (T1-dominated) and "positive" (T2*-dominated) leakage effects. Multi-slice tumor regions were segmented automatically from the coregistered anatomical MR images using a knowledge-base fuzzy clustering technique [4] and macroscopic vessels were automatically removed based on clustering of multiple parameters of the DSC first-pass curve [5]. Based on the segmented tumor regions, 3D relative frequency scatter diagrams of CBV as a function of K^{trans} for each tumor pixel were derived for each patient (Figure 1). The 3D scatter diagrams were transformed into a feature vector for each patient and a predictive model [6] based on support vector machines (SVM) was used to predict outcome in each patient based on the feature vectors and survival status of the remaining patients. Kaplan-Meier survival curves of a high-risk group and a low-risk group over a 3 year span were derived based on; (a) actual survival data (alive/deceased), (b) patient outcome as suggested by histology (high-/low-grade) and (c) by DSC imaging. Here, log-rank estimations with *P*-values were used to assess differences between the survival curves. Image analysis was performed using Matlab R2008a (MathWorks, Natick, US) and nordicICE (NordicImagingLab, Norway).

Results: Of the 56 patients, 24 patients received a histopathological diagnosis of a low-grade glioma (WHO grade II). Of the remaining 32 high-grade patients, 7 were diagnosed with a grade III glioma and 25 were diagnosed with a grade IV glioma. Overall, the Kaplan-Meier survival curves from DSC imaging showed similar or better predictive values compared to histopathology (Figure 2). For the low-risk groups, the log-rank value between the survival curves derived from actual survival data (i.e. alive patients) and histopathology was 4.971 (*P*=.026). The corresponding log-rank value between actual survival data and DSC imaging was 5.46 (*P*=.019). For the high-risk groups, the log-rank value between the survival curves derived from actual survival data (i.e. deceased patients) and histopathology was 4.283 (*P*=.038). The corresponding log-rank value between actual survival data and DSC imaging was 2.901 (*P*=.089). The low-rank value between the high- and low-risk group derived from histopathology and DSC imaging was 17.153 (*P*<.001) and 19.981 (*P*<.001), respectively.

Discussion: Studies have shown that manual expert analysis of DSC parameters can predict time to progression in high-grade and low-grade glioma patients [7]. In this preliminary study, we have evaluated the use of a user-independent approach to predict patient outcome in new patients based on DSC data from previous patients. Our results suggest that the proposed method show similar or better diagnostic accuracy values to histopathology which in turn may aid in treatment planning and longitudinal monitoring of treatment response. The model is attractive in that it is user independent and that the predictive outcome is based on a 3D scatter diagram in stead if a single cut-off value. In the future, information on radiation therapy, medication and molecular biomarkers should be included in the model.

Conclusion: In this study, we have shown that a fully automated, user-independent method for predicting outcome in glioma patients provides similar diagnostic accuracy values to histopathology.

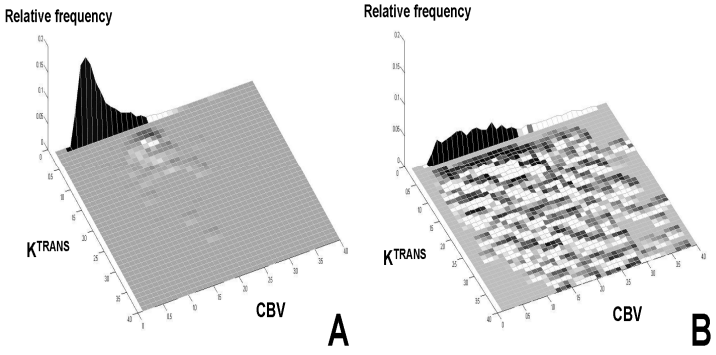

Figure 1: *3D surface plots of the scatter diagrams of a "low-risk" patient* ***(A)*** *and a "high-risk" patient* ***(B).*** *The scatter diagrams show the distribution of CBV values as a function of K^{trans} for each pixel within the tumor ROI. The black histograms illustrate the distribution of CBV at K^{trans}=0. The scatter diagrams were normalized, i.e. the area under the complete surface was equal to one.*

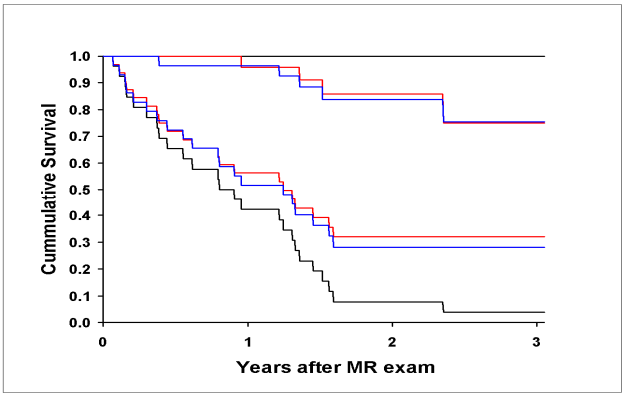

Figure 2: *Kaplan-Meier survival curves of a low-risk and high-risk group derived from actual survival data (black lines), histopathology (red lines) and predictive model based on DSC imaging (blue lines) over a 3 year span. With reference to the actual survival data, the proposed model showed similar or better diagnostic accuracy values compared to histopathology.*

References:

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