Self-learning predictive modeling in glioma grading

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Purpose: To develop and evaluate four self-learning predictive models in glioma grading based on histogram analysis of MR-derived cerebral blood volume heterogeneity.

Background: Several studies have shown that cerebral blood volume (CBV) maps derived from dynamic susceptibility contrast (DSC) analysis can improve differentiation between high-grade (WHO grade III-IV) and low-grade (WHO grade I-II) gliomas [1]. Based on normalized (n)CBV maps, viable malignant tumor tissue can be identified as regions of elevated microvascular blood volume ('hot spots'). Recent studies have further shown that histogram analysis of nCBV values from total glioma volume may improve differentiation between these two cohorts [2,3]. In the latter method, each tumor can be represented by a histogram 'signature' which can readily be compared to a database of histologically confirmed cases representing average signatures for each tumor grade. It is therefore hypothesized that the tumor histogram analysis approach can be used to develop self-learning predictive models – an important step towards MR-based automated glioma grading.

Methods: Eighty-seven patients with histologically confirmed gliomas, (aged 8-77 yrs, mean age 46; 47 males, 40 females) have so far been included. The study has been approved by the local ethics committee and an informed consent was obtained from all patients. Imaging was performed at 1.5 T (Siemens Sonata or Avanto, Siemens AG, Germany) prior to surgery. Relative (r)CBV maps were generated using established tracer kinetic models [4] applied to the first-pass data obtained by i.v. bolus injection of 0.2 mmol/kg of Gadovist (Schering AG, Germany). The time resolution of the first-pass gradient echo (GRE)-EPI sequence was 1.5s and the voxel size was 1.8x1.8x6.5mm^3. Normalized (n)CBV maps were created by voxel-vise division of rCBV values with an unaffected white matter rCBV value in each slice. The nCBV maps were coregistered with conventional T2-w FSE and T1-w SE post-contrast images. The predictive models were developed based on histologically confirmed tumors in 63 patients, analyzed independently by three neuroradiologists. Each neuroradiologist determined the total glioma volume based on the nCBV maps overlaid on the anatomical MR images, taking care to avoid large vessels. The glioma grade for each patient was determined from the maximum normalized peak height of nCBV distribution from the total glioma volume, under the hypothesis that a low peak implies a wide distribution of nCBV values due to the vascular heterogeneity of high-grade gliomas. The final histogram signature for each patient was an average sum of the result from each of the three neuroradiologists.

Four predictive models were evaluated for their ability to correctly grade new gliomas. For all models the reference database was divided into a high -grade and a low-grade group; (A) Comparison of histogram peak height of new case with the mean peak height ± 1.96*standard error (SE) of the reference groups. (B) The frequency at which the value of each histogram bin in the new case was within the mean value ± 1.96*SE of the equivalent bin in the reference groups. (C, D) Comparison of the 'godness-of-fit' in terms of chi-square (C) or RMS (D) between the histogram distribution for the new case and the distributions for the reference groups. To evaluate the accuracy with which the four predictive models correctly predicted glioma grade in a new patient, a cross validation test was performed. Here, the tumor grade for each patient in random order was predicted based on the data from the 62 other patients. Using histopathology as a reference, the percent of correct predictions was obtained. To evaluate whether the predictive models improved as the number of patients in the database increased from 20 to 63, the models was tested on completely independent data from the remaining 24 patients analyzed by a fourth neuroradiologist. Here, the Pearson correlation (r) between the predicted grades of the 24 patients and histopathology was assessed, and linear regression was used to evaluate how the predictive models improved as a function of the number of subjects included in the database. Image analysis was performed using Matlab R2007a (MathWorks, Natick, US) and nordicICE (NordicImagingLab, Norway).

Results: Forty-one patients had high-grade gliomas and 46 patients had low-grade gliomas. The results of the cross-validation showed that the predictive models correctly predicted glioma grade in (A) 79.37%, (B) 80.95%, (C) 73.02% and (D) 76.19% of the 63 patients (Figure 1). All four predictive models converged to a stable prediction level at about 40 reference cases, with evenly distributed cohorts. For all four models, the Pearson correlation between predicted grade and histopathology increased as the number of subjects in the predictive models increased (Figure 2, R-square value: (A) = 0.402, (B) = 0.412, (C) = 0.7206, (D) = 0.626). The predictive models (A) and (D) had the highest correlation between predicted grade and histopathology in the 24 independent (i.e. new patient, new radiologist) patients (r=0.58).

Discussion: We propose four self-learning predictive models for grading gliomas based on histogram analysis of MR-derived nCBV maps. Our preliminary results show that the four models are able to correctly predict glioma grade in 7-8 out of 10 patients. The ability to correctly grade new glioma cases increases with the number of cases in the reference database for all models investigated. The strongest correlation with database size was observed for the chi-square estimation of goodness-of-fit between histogram distributions (C).

Conclusion: Self-learning predictive models can be developed as a diagnostic aid for improved glioma grading based on tumor histogram analysis derived from DSC MRI. With the models tested in this study, at least forty histologically confirmed tumors independently analyzed by several radiologists needed to be included in the reference database to obtain a robust predictive model.

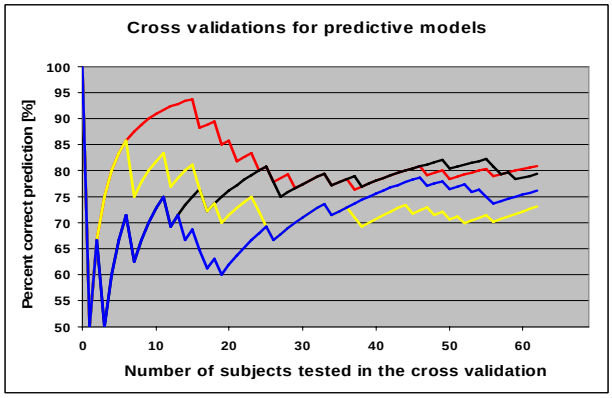

Figure 1: *Percent correctly predicted glioma grades as a function of the number of subjects tested for the four predictive models The plots represent predictive models (A) black, (B) red, (C) yellow and (D) blue.*

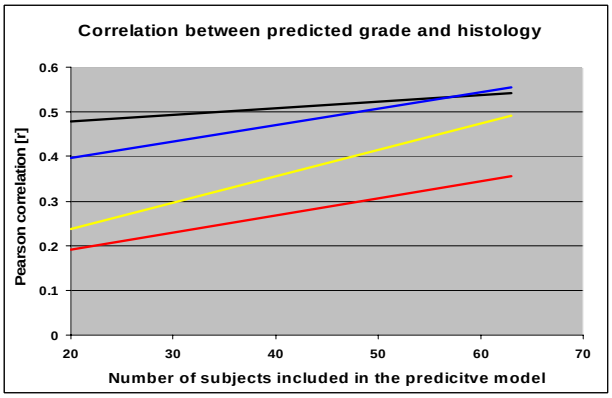

Figure 2: *Linear regressions illustrating the effect of including more patients in the database of the predictive models. The plots represent predictive models (A) black, (B) red, (C) yellow and (D) blue. As the number of patients in the database increase, the models continuously improve their ability to grade new gliomas.*

References:

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