Computer Aided Radiological Diagnostics: Random Forest Classification of Glioma Tumor Progression using Image Texture Parameters derived from ADC-Maps.

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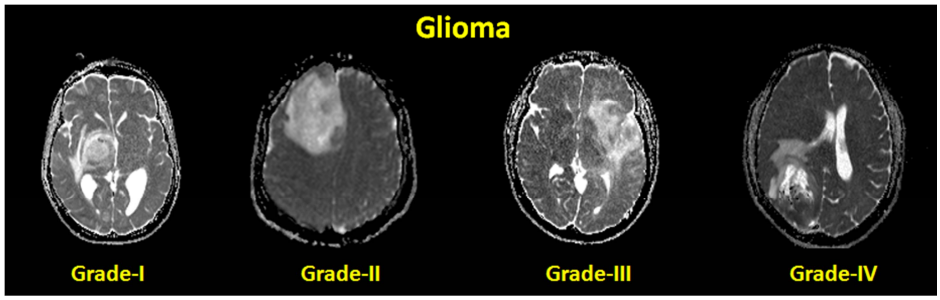
Target audience – Neuroradiologist and scientist interested in methods for computer aided diagnostics (CARD).

Purpose – Despite the huge amount of information provided by an MR-examination, the initial diagnosis and grading of frequently extremely heterogeneous brain tumors by *visual inspection* remains a difficult task. A diagnostic text often lists a number of most likely diagnoses, e.g. anaplastic astrocytoma or glioblastoma multiforme. Here we discuss how texture parameter analysis in combination with advanced statistical classification algorithms can offer an important advantage for the differential diagnosis problem for *individual* diagnostics.



Methods – In tumor diagnostics the apparent diffusion coefficient (ADC) maps are used to differentiate regions with high cellular density from regions with tissue edema and normal tissue. Figure 1 above shows ADC-maps of grade I to IV glioma (recorded at 1.5T), illustrating the difficulty to diagnose the correct grade from this type of images. There are multiple papers on patient *group* studies investigating the tumour's *mean* ADC-values only as predictor that show significant *group differences* between glioma of different grade[1]. However, there are also papers that conclude the opposite[2]. Apparently is the *mean* ADC-value only not a robust predictor for glioma grade. It was hypothesized here that the *quantification* of the *heterogeneity* of glioma might be useful for brain tumor grading. For quantification of the tumors *heterogeneity*, histogram as well as cooccurrence based texture parameters were computed. For 84 patients suffering from glioma (10 grade-I, 23 grade-II, 20 grade-III, and 30 grade-IV) patients a total of 108 texture parameters were computed, each quantifying another aspect of the tumors heterogeneity, and stored into a database. This database was used to compute a predictive statistical models using the random forest classification algorithm as proposed by Breiman and implemented in the statistical programming language R[3]. Random forest is a so called *ensemble* classifier method that builds multiple decision trees (the forest). A tree is known to be able to model non-linear structures with potential complex local interactions with very small bias but considerable variation. By combining different tree predictions the variance is averaged out and leading to an accurate prediction which outperforms a single classification tree, as long as the single tree-classifiers are reasonably independent and better than random guessing. The independence of the trees is achieved by using different bootstrap samples for the training of the trees and by randomly selecting features subset - in this case texture parameters – to find the optimal split at each position of a tree. A classification (patient diagnosis) is performed by entering the tumor texture parameter dataset into all decision trees (i.e. the forest). The final classification result is obtained by majority voting (one tree one vote).

Results – Table below shows cross-validated classifier performance obtained for the 6 differential diagnoses for glioma of four grades:

Performance measure	**Grade-I vs II**		**Grade-I vs III**		**Grade-I vs IV**		**Grade-II vs III**		**Grade-II vs IV**		**Grade-III vs IV**	
	Grade-I	Grade-II	Grade-I	Grade-III	Grade-I	Grade-IV	Grade-II	Grade-III	Grade-II	Grade-IV	Grade-III	Grade-IV
Sensitivity	0.900	0.957	0.900	0.950	0.900	1.000	0.696	0.600	0.870	1.000	0.650	0.900
Specificity	0.957	0.900	0.950	0.900	1.000	0.900	0.600	0.696	1.000	0.870	0.900	0.650
Accuracy	0.939	0.939	0.933	0.933	0.975	0.975	0.651	0.651	0.943	0.943	0.800	0.800
Matthews correlation	0.865	0.865	0.860	0.860	0.933	0.933	0.541	0.541	0.889	0.889	0.580	0.580

Discussion – The information contained in the tumor heterogeneity of ADC-maps is such that it allows for glioma grading with a high level of accuracy (see Table). An interesting aspect of the results presented above is the fact that the more benign grade II gliomas can be distinguished from the malignant gliomas grade III and IV without the need of contrast agent. Another interesting aspect is that grade-I gliomas, although benign show frequently contrast enhancement making it difficult to distinguish this tumor type from the malignant grade III and IV gliomas can be discriminated by the proposed method. The method proposed in this abstract shows however, that the discrimination of the enhancing grade-I gliomas from grade-III and IV can be performed with classification accuracies between 93.3% and 97.5% on individual basis. Additionally, our study also showed that taking the ADC-map *mean* value alone did *not* allow for discrimination of grade-II, III and IV gliomas from each other and was therefore in accordance with reference[2]. However, taking textural parameters that quantify subtle heterogeneities of the gliomas enable reliable glioma grading. It is likely that taking also other MR-imaging modalities into account will further improve the classification performance.

Conclusion – The quantification of brain tumor heterogeneity by means of histogram and cooccurrence based texture parameters and their higher order statistics can be used to perform glioma tumor grading of individual patients with sensitivity and specificity between 60% and 100%, accuracies between 0.651 and 0.975, and Matthews correlation between 0.541 and 0.889. The combination of texture parameters derived from ADC-maps with random forest classification enables glioma grading on individual base, and can therefore be regarded as a step towards computer aided radiological diagnostics (CARD) of individual patients.

References – 1. K. Kono, Y. Inoue, K. Nakayama, et al., "*The role of diffusion-weighted imaging in patients with brain tumors.* ", AJNR Am J Neuroradiol, 22(6):p. 1081–1088, 2001. **2.** WWM Lam, WS Poon, et al. "*Diffusion MR-imaging in glioma: does it have any role in the pre-operation determination of grading of glioma?*", Clinical radiology, 57(3):219–225, 2002.; **3.** Leo Breiman, "*Random forests*", Machine Learning, 45(1):5–32, 2001.