AN ALTERNATIVE APPROACH FOR THE AUTOMATIC PREDICTION OF THERAPY RESPONSE FROM MRI DATA SETS IN SMALL COHORTS OF EXPERIMENTAL HIGH GRADE GLIOMAS

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Purpose

Clinical management of High Grade Gliomas (HGG) often involves antiangiogenic therapies using monoclonal antibodies, mainly against VGEF. Responses to this treatment are highly heterogeneous, with similar cohorts of patients behaving as "*responders*" or "*non-responders*". It would be then very useful to discriminate by non invasive criteria the two populations as early as possible, to tailor treatment accordingly. Magnetic Resonance Imaging (MRI) is presently one of the most important non-invasive methods to investigate and diagnose HGG. Similarly, the automatic classification of medical images into different pathological categories is currently an active area of research in developing diagnostic support environments. A common problem to both areas is the relatively small size of experimental observations available to establish robust classifications. Although the sample size is small, the data set about each subject is normally very big: several MRIs types, slices, pixels and many times, longitudinal days of treatment. Thus, automatic processing of all this information adequately entails vital relevance. Here we propose an alternative protocol to classic approaches, implementing the automatic classification by selecting patterns and attributes from MRI data set using Pixel-Pattern Analysis (P-PA). Moreover, we present a pilot study on the discriminant power of the method as compared to the classical approach in predicting the outcome of the treatment to anti-VGEF therapy in mice bearing implanted GL621 tumors.

Methods

Treatment response was evaluated in 13 mice bearing implanted GL261 tumors receiving antiangiogenic bevacizumab treatment (RECIST criteria [1], mAb against VEGF B20-4.1, 5mg/Kg twice weekly for 8 weeks) followed on a 7T MR scanner. MRI studies included T2w and DWI performed sequentially at 3/4 day intervals until completion of treatment or obvious, treatment independent, tumor growth. The problem is modeled in three different ways before applying a classification method: classical modeling, classical modeling using Principal Components Analysis (PCA) [2] and P-PA modeling. Classical modeling transforms the complete data set in a matrix where each row corresponds to a subject to be classified, and each column with DWI and T2w slices. Whereas in P-PA modeling each mouse is represented by a matrix where rows represent the pixels and the columns represent the different intensity values of DWI and T2w slices. Linear Discriminant Analysis (LDA) [2] was then applied to Day-1 and Day-2 of treatment data set, using the three modeling approaches, in order to find the linear projection that best discriminates the pixels as belonging to "*responder*" or "*non-responder*" animals to anti-VGEF treatment.

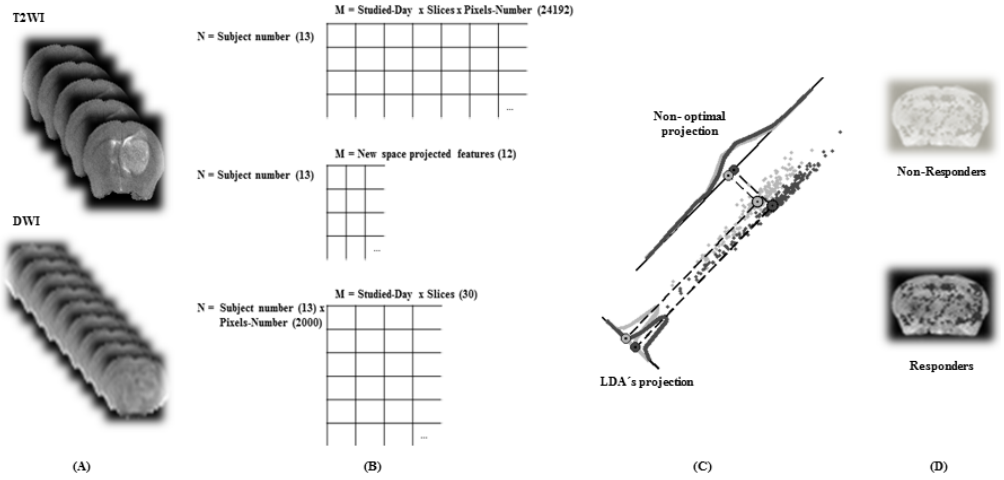

Figure 1. (A): MRIs data set. **(B):** Three different ways modeling of MRIs data set. Top: Classical, Middle: Classical with PCA, Bottom: P-PA. **(C):** LDA application. **(D):** Images showing classification results.

Results

Figure 1 illustrates the complete data processing approach. Using the three mentioned methods, LDA and a leave one out strategy [2], we obtained the following error rate of prediction (**Table 1**).

Modeling	Error (%)
Classical	46.15
PCA	30,77
P-PA	23,08

Table 1. Comparative prediction error rate.

Conclusion

We provide an effective approach the problem of classifying therapy response in small samples of MRI examinations, considering only the first two days of treatment to HGG animal models. The P-PA approach in combination with LDA was able to predict therapy response with the lowest error, as compared to the Classical and PCA approaches, classifying among "*responders*" and "*non-responders*" more precisely.

References

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