Multiparametric MR analysis of temporal evolution of abnormality in MS

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INTRODUCTION. Multiple sclerosis (MS) is chronic decease which affects patient's central nervous system, leading to a gradual destruction of myelin which manifests itself not only as lesions but also as abnormality in the normal appearing brain tissue (NABT). Although lesions can be seen easily in modalities like T2 and FLAIR, it is difficult to measure the extent of damage in the NABT. Various modalities, like FLAIR, T2 and magnetic transfer ratio (MTR), have been used individually to quantify damage in the NABT; however, there are very few studies combining these modalities to derive better information about tissue abnormality, with most methods concentrating on lesion segmentation rather than tissue abnormality characterization. In this work, we combine several MR modalities into a probabilistic pattern classification method to determine a voxel-wise probabilistic tissue abnormality score. This score can then been correlated with clinical and cognitive scores to study temporal WM changes. The proposed method is applicable to studying treatment effects and can help physicians determine the extent of abnormality in the NABT beyond the conventional visual symptoms like lesions.

METHOD. For each patient, we create a tissue profile consisting of seven MR modalities, including six structural images, namely, FLAIR, T1-weighted (pre-, and post Gadolinium), T2-weighted, Magnetic Transfer Ratio (MTR), B0 and two scalar maps computed from the DTI, namely, Fractional Anisotropy (FA) and trace of diffusion matrix (Trace). First, images of all modalities of each patient are registered to the FLAIR image of corresponding patient. In order to eliminate magnetic field inhomogeneities, bias correction and histogram matching steps are applied. A neuro-radiologist delineated lesion ground truth (ROI's) based on FLAIR modality, with only regions of high certainty being chosen (Fig.1.b). For healthy tissue profile, ROI's were defined on brains of healthy controls in such a way that they include portions of healthy gray matter (GM), white matter (WM), and CSF. For each voxel, a tissue signature is built by concatenating intensities from each modality (except FLAIR) into a feature vector. As FLAIR biases the feature towards high-intensity regions we exclude that from the feature vector. The feature vector is now more sensitive to the tissue abnormality outside of the lesions. These features computed from the lesions and healthy tissue are then incorporated into a probabilistic Support Vector Machine [1] to generate tissue classifiers for the lesion and healthy class. Within training process of classifier, some parameters are calculated in order to estimate the pseudo-probability of a voxel belonging to either lesion or normal class. These probability maps (called Tissue Abnormality maps) characterize the degree of abnormality in the tissue. Estimated probability assists us to derive additional information about tissue from combination of modalities. Given probability maps for each patient, we define some ROI's (Fig.1.c) which show a high level of abnormality. Then, we investigate percent wise changes of each tissue type (lesion, healthy and intermediate abnormal tissue) over time as a new measure to assess temporal tissue changes. Additionally, correlations between baseline cognitive scores and probabilistic score derived from our algorithm are calculated to validate our method.

RESULTS. In our study, there are 11 patients diagnosed with MS, with each patient followed longitudinally. Tissue abnormality maps are computed for each of the patients. We achieved classification performance rates of 89.3% in the lesions. Fig. 1.a shows an example for one dataset; in the second column, ROI examples are provided to show how training samples are collected (Fig1.b) and how some regions are delineated for longitudinal study (Fig1.c). Fig.2 shows a sample of probabilistic map; appearance and disappearance of lesion is shown in the probabilistic map. Fig.3 represents changes in average of intensities on defined ROIs, example of which is shown in Fig.1.c, in three different modalities. It shows how different probabilistic intervals on defined ROIs behave over time in three modalities and how it relates to clinical scores. The sharp change in the second time point which can be seen in all modalities can be attributed to improvement of the tissue. In addition, we found significant correlation between some cognitive scores (e.g. facial memory accuracy score) and amount of abnormality in various WM brain structures (e.g. corpus Callosum: (corr=-0.85,p<0.05)).

DISCUSSION. The results show that a multi-parametric combination of MR modalities, when incorporated into a pattern classification framework produces a tissue abnormality map that can be used to characterize and quantify the degree of tissue abnormality outside of the lesions. The correlation with clinical scores determines the applicability of these tissue abnormality measures in study of temporal evolution of MS pathology in the brain.

REFERENCES.

[1] C.-C. Chang and C.-J. Lin, LIBSVM: a library for support vector machines, 2001. Software available at http://www.csie.ntu.edu.tw/~cjlin/libsvm

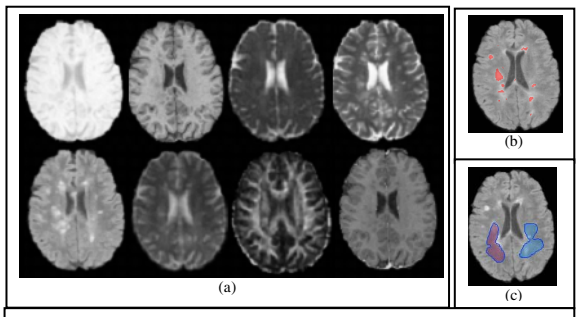

Fig.1. (a) multi-parametric data sample for one of the patients. (b) Sample of regions which is used for training of the classifier. (c) Sample of regions used for longitudinal follow up.

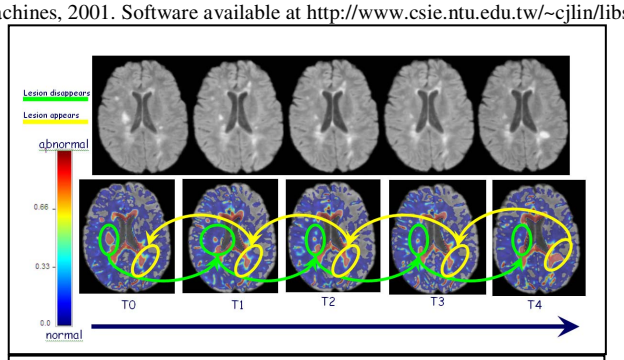

Fig.2. Probabilistic map: The more reddish, the more abnormal. Big blue arrow in the bottom with T1 through T4 symbols show time evolution. Green arrow points out disappearance of a lesion; yellow one depicts gradual appearance of a lesion. Although abnormality of tissue is not very clear from FLAIR modality, our method picks up part of the area which converts to full fledge lesion at T4.

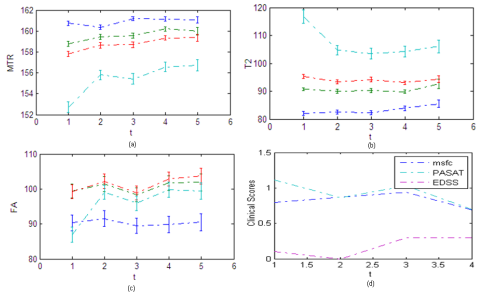

Fig.3. (a),(b),(c) show changes of MTR, T2, FA modalities over time for patient whose probability map depicts in Fig1,2 and for various probability intervals. It shows how various tissue types defined by probability map behave differently over time. Abrupt change from first time to the second time point shows drug effect (d) shows clinical scores (MSFC, PASAT, EDSS for the same patient).