Estimation of Tissue at Risk of Infarction using a Support Vector Machine on multimodal Stroke MRI Data

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INTRODUCTION: Acute ischemic stroke is a frequent cause of neurological disability in the developed world. A clinical tool for the differentiation of reversible from irreversible damaged tissue would be valuable for acute treatment decisions. This requires accurate prediction of the extent of the final infarction. Typically, the damage estimation relies on models derived from perfusion and diffusion weighed data (e.g. perfusion-diffusion mismatch, MTT, CBF, CBV etc). In this feasability study we introduce a new data-driven prediction method without deploying any model using a statistical learning approach: the Support Vector Machine (SVM) classification [1]. The input data, the feature vector, for the SVM consists of acute diffusion and perfusion information. The labelled training data set is created with knowledge gained from a follow up scan in the chronic stage. The reversible damaged part of the ischemic lesion is found by subtracting the chronic lesion from the acute lesion. This classification method was applied to two patient data sets: 8000 selected voxels of the first patient were used for training and the second data set was used for testing. The goal was to differentiate seven classes: noise, cerebrospinal fluid (CSF), grey matter (GM), white matter (WM), reversible GM (GMrev), reversible WM (WMrev), damaged GM (GMchronic) and damaged WM (WMchronic).

METHODS: Patients were scanned on a 3 T Magnetom TRIO (Siemens, Erlangen, Germany) using a multimodal stroke MRI protocol including a perfusion scan (TE = 40 ms, TR = 1800 ms, voxel size = 1.8 x 1.8x 5 mm^3, matrix = 128 x 128 pixel, slices = 13) and a diffusion weighted scan in six diffusion encoding directions (TE = 81 ms, TR = 3100 ms, voxel size = 1.8 x 1.8 x 5 mm^3, matrix = 128 x 128 pixel, slices = 23, b = 0 and 1000 s/mm^2, 3 averages) four hours post stroke. We used scanner-generated trace and ADC images and calculated averaged diffusion-weighted images (averDWI). Coregistration was performed with SPM8. A follow up scan was acquired after three months and included a three-dimensional fluid-attenuated inversion recovery turbo spin echo (3d-FLAIR) with variable flip angle (TE = 408 ms, TR = 6000 ms, TI = 2100 ms, voxel size = 0.98 x 0.98 x 1 mm^3, matrix = 256 x 240 x 176 voxel). Final lesion, as well as acute perfusion and diffusion lesions, were delineated by an expert. The acute lesion was defined by union of the perfusion and diffusion lesion. We determined noise, CSF, GM and WM masks by thresholding with manual correction. The SVM C++ library libSVMtl [2] was employed, which has a number of internal algorithmic options. We used the radial basis function as kernel for mapping the feature vector into feature space and investigated the results for the two possible multi-class algorithms: one versus one and one versus rest. In addition, we compared two scaling methods "minmax" (scaling of each feature the way that the minimum becomes -1 and the maximum +1) and the "stddev" approach (scaling of each feature the way that the mean becomes 0 and the standard deviation becomes 1). The input feature vector for each voxel consists of a trace value, ADC value, the signal value of the non-diffusion weighted scan and averDWI, as well as the perfusion time series including the first and the second bolus passage.

RESULTS: The sensitivity and specificity results of the two best performing algorithms are listed in table 1. It can be seen that there is a trade-off for the detection of healthy and reversible tissue versus ischemic tissue. Also, many false positive voxels for GM were reversible damaged GM voxels and respectively for WM. Since WM and GM is not differentiable in the follow up scan we combined the GMchronic and WMchronic results for better evaluation.

algorithm		noise	CSF	GM	WM	GMrev	WMrev	Lesion Chronic
1 ("stddev" scaling, one versus one multi-class comparison)	sensitivity	99.0	81.5	75.2	87.6	18.2	17.6	54.8
	specificity	99.9	98.3	98.3	98.5	99.8	99.8	99.9
2 ("minmax" scaling, one versus rest multi-class comparison)	sensitivity	99.0	91.7	18.9	93.2	14.6	3.8	71.0
	specificity	94.3	98.1	98.5	97.4	99.7	99.9	99.8

Table 1: Results of the segmentation of multi-modal acute stroke patient data in percentage for each tissue class an SVM algorithmic options.

The figures 1a and b show the acute lesion in the averDWI and perfusion image mapped by an expert. Those images were logically added and the chronic lesion was subtracted resulting in the mapped reversible lesion (figure 1c). Figure 1d illustrates the SVM result of this reversible regions. The chronic lesion mapped by an expert is shown in 1e and classification results of the SVM in 1f.

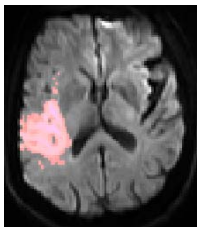

Fig. 1a: Acute lesion Acute averDWI, expert

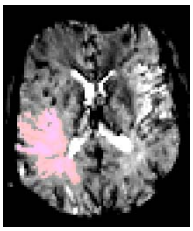

Fig. 1b: Acute lesion perfusion, expert

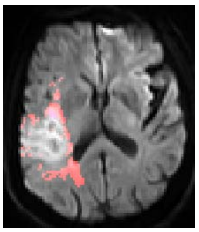

Fig. 1c: Reversible lesion, averDWI, subtraction

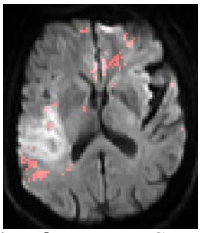

Fig. 1d:.WMrev + GMrev, algorithm 3, averDWI

Fig. 1e: Chronic lesion, 3d-FLAIR, expert

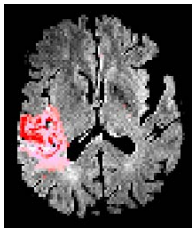

Fig. 1f: WMchronic, algorithm 3, averDWI

DISCUSSION AND OUTLOOK: A new model-free method for the prediction of reversible versus irreversible damage from acute ischemic stroke data was developed and applied to one example dataset for the first time. For the prediction of irreversible damaged tissue our method performed well with 71 percent sensitivity for the best performing algorithm (highlighed in green in table 1). If segmentation of healthy tissue is the main objective one would rather chose a different algorithm (here algorithm 1). Our method lacked for the prediction of recoverable tissue: hardly voxels with reversible damage were found and on the other hand many false positive results for WM and GM were reversible tissue. We suggest a way to proceed without classification of reversible tissue: once the SVM classified the chronically affected tissue, the reversible tissue can be determined by subtracting the chronical tissue mask from the acute mask.

The precise evaluation of the results is difficult, since first, the ground truth is unknown in respect to the determination of GM and WM in the lesion and its degree of damage. Secondly, the multimodal coregistration of the follow up scans with the acute scans needs improvement. In addition, the results highly depend on the investigator's expertise in lesion mapping and the prospects of *in vivo* imaging. An expert can only segment a lesion with visual guide control, which is not enough for gliosis and non-full necrosis of GM. Future effort will be put into optimisation of the preprocessing of the perfusion time series, as well as the creation of a training dataset from a large collective and application to acute stroke MRI data in a prospective study. An interesting point would be, how the sensitivity depends on the advance of the infarction and if it improves for a large perfusion-diffusion mismatch, since the investigated case here only had a small mismatch.

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