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An active learning approach for stroke lesion segmentation on multimodal MRI data

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ABSTRACT

The segmentation of lesion tissue in brain images of stroke patients serves to identify the extent of the affected tissues, to perform prognosis on its recovery, and to measure its evolution in longitudinal studies. The different regions of the lesion may have different imaging contrast properties in different image modalities, making difficult the automation of the segmentation process. In this paper we consider an Active Learning selective sampling approach to build image data classifiers from multimodal MRI data to perform voxel based lesion segmentation. We report encouraging results over a dataset combining functional, anatomical and diffusion data.

1. Introduction

Stroke is the third leading cause of death in industrialized countries [18]. Patients surviving stroke suffer an strong economic and personal impact, and it is highly desirable to provide accurate prognosis and motorization of the evolution of the patient. The localization of the stroke lesion by medical imaging means is a powerful non-invasive tool to support the clinical attention to the stroke patient. The kind of imaging used encompasses several modalities of Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI), which have specific sensitivities to the diverse parts of the lesion [18]. The automated localization of the brain areas affected by the stroke lesion can be stated as a classification problem, which predicts the lesion/non-lesion character of one voxel on the basis of the imaging data. This paper is devoted to explore the predictive capacity of Random Forests (RF) trained with an Active Learning strategy, to the automated segmentation of stroke lesion from several MRI modalities.

Active Learning by selective sampling: Given a labeled training set, supervised classifier learning consists in building a map of data features into a set of classes possessing good generalization to predict the class of unseen data instances. Hence, validation processes involve simulating the existence of these future data events by cross-validation processes withholding some of the available data samples for test after training. The Active Learning approach consists in the progressive increase of the sampled data used for classifier training by some exploratory strategy. The idea of selective sampling [6] is based on the existence of an oracle that answers queries about the data which arise from an active exploration of the data domain. The active exploration takes the form of the computation of an uncertainty measure on the classification of the available data samples. Most uncertain samples are assumed to be more informative to build an accurate classifier, thus the oracle is queried about their ground truth labels and they are added to the training dataset. Testing is always reported on the data not used for train.

In general terms, Active Learning [22] soughs the simultaneous two-fold goal of maximizing the classifier accuracy generalization and using the minimal number of training samples whose ground truth label is required of the oracle, which is a human operator when dealing with image segmentation issues. Often, Active Learning starts from a small labeled data sample. The iterative process then performs the following steps: (a) train a classifier, (b) apply the classifier to unlabeled data samples computing their uncertainty, (c) select the most uncertain, (d) ask the oracle about their labels, (e) add them to the training sample. The process convergence is often measured on the accuracy of the test data. The uncertainty measure definition derives from the classifier characteristics [22]. In ensemble classifiers, it often consists in some measure of the agreement of the individual classifiers.

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Image segmentation by classification: Image segmentation can be realized as a classification process, each pixel receives a class label according to the associated image features which can be computed from the pixel neighborhood. For instance, the RF classifier [3] has been applied to delineate the myocardium in 3D ultrasounds of adult hearts [14], brain tissue segmentation [9,24,23], detection of several organs in computed tomography volumes [7,8].

Active Learning has been successfully applied to classification of remote sensing images [17,22,21], medical image segmentation such as Abdominal Aortic Aneurysm computed tomography angiography images [5,16], image retrieval based on semi-supervised Support Vector Machines [10], and the selection of a minimal collection of training images for the development of combined generative and discriminative models in the segmentation of CT scans [11].

Stroke lesion segmentation: In patients suffering a stroke, it is a common practice to perform lesion volume estimation on Diffusion Weighted Imaging (DWI) data. However, it is argued [1] that while DWI is sensitive in the acute phase, it becomes less accurate during the subacute phase (i.e. 3 months after stroke insult). Nevertheless, lesion identification is also challenging for other modalities, such as Fluid Attenuated Inversion Recovery (FLAIR), because of large variations in shape, location signal intensity, and the existence of image artifacts and pre-stroke lesions. For this reason we have considered several manual delineations as the gold standard for classifier training, although the feature vectors are always the same.

In the past, some attempts have been made on anatomical T1 weighted MRI data [19] to perform lesion identification using standard segmentation processes followed by a fuzzy clustering approach to detect outlier signal values in the segmented volume. The interactive segmentation of stroke and tumor lesions on FLAIR images is reported in [1]. The process includes the clustering of FLAIR signal into foreground and background classes. Lesions are extracted as hyperintense outlier voxels on the segmented foreground regions. The segmentation applying a Markov Random Field model on the fusion of multi-sequence MRI images is reported in [12]. The work is closely related to the elaboration of an atlas of brain territories which provides the topological background for the segmentation process. A *z*-score based test is applied to diffusion images to produce lesion identifications which are then used to build a map of lesion incidence in the occipital lobe [15] for the use in clinical studies. A comprehensive review containing a critical appraisal of computational methods applied on MRI and CT image data to identify lesions in brain tissues and perform prognosis of its recovery is given in [18].

Paper contributions: The work reported in this paper follows a classification approach to automated stroke lesion segmentation, where the classifier is trained by an Active Learning selective sampling strategy. The classifier model chosen is the Random Forest (RF). A trained RF classifier is applied to each voxel independently to predict the class of the pixel, lesion versus no lesion. The voxel features which are the input of the classifier are the values of the scalar MRI data volumes and the scalar measures extracted from multidimensional data, described in Section 2. Compared with other algorithms reported in the literature, the main advance of our approach is that it combines heterogenous information from diverse MRI modalities, while other algorithms work on a single image modality. Further contribution to the state of the art is the Active Learning approach to sample selection, which allows an enhanced interactive work in clinical environments. Different from other reported works is the consideration of the construction of the gold standard for classification validation, given by manual delineations of the lesion ground truth. We explore the effect of the source data used by the expert neuroradiologist to carry out the manual delineation, finding quite different gold standards in some cases. The computational experiments carried out explore the effect of the variability in the provided the gold standard. To this end, we consider four different gold standards obtained from different image modalities.

Structure of the paper: Section 2 provides the explanation of the multimodal MRI data acquisition and pre-processing. Section 3 gives a description of the classification learning methods, including a detailed Active Learning algorithm. Section 4 presents the experimental design. Section 5 presents the experimental results. Section 6 contains a discussion of the results. Finally, Section 7 gives the conclusions of our work.

2. Multimodal MRI data and its preprocessing

The details of MRI signal acquisition for each modality are given elsewhere. The pre-processing pipeline is specific for each kind of image modality. Hence a careful process has been carried out for each of them to ensure anatomical alignment and to remove noise sources. Most pre-processes have been carried out using FSL software library (FMRIB Centre, Department of Clinical Neurology, University of Oxford, www.fmrib.ox.ac.uk/fsl [20]. Besides, the multidimensional signal, such as fMRI and DWI are subjected to some feature extraction processes that produce scalar measures for each voxel. These pipelines are as follows:

- *T1* weighted MRI preprocessing consisted of the removal of non-brain structures, linear registration of the skull stripped image to the 2 mm resolution MNI152 template, nonlinear registration of the volume created from the previous linear registration to compensate the local changes around ventricles and sulci caused by atrophy, and, finally, we applied the estimated warps to the skull striped volume.
- *T2* and Flair image preprocessing consisted of the removal of non-brain structures, rigid linear co-registration of image to the subject's T1 skull striped volume (6DOF) and affine (12DOF) linear registration to the 2 mm resolution MNI152 brain template.
- *fMRI*: Functional magnetic resonance imaging (fMRI) preprocessing consisted of the removal of the first 6 volumes to ensure saturation and adaptation of the subjects to the environment leaving 234 volumes for further analysis, removal of non-brain structures, motion correction, low-pass and high-pass temporal filtering, spatial smoothing using a Gaussian kernel of full-width half-maximum of 5 mm, intensity normalization, rigid linear co-registration to the main structural image with 6 Degrees of Freedom (DOF), and posterior affine linear registration algorithm to the MNI152 standard template (12 DOF). Absolute head movement was below 1.5 mm
  - Amplitude of Low Frequency Fluctuations (ALFF) [25] and fractional Amplitude of Low Frequency Fluctuations (fALFF) [27] are low frequency oscillation measures of amplitude of the BOLD signal. ALFF is defined as the total power within the frequency range between 0.01 and 0.1 Hz. fALFF is defined as the power within the low-frequency range (0.01–0.1 Hz) split by the total power in the entire detectable frequency range [28].
  - Regional Homogeneity (ReHo) estimates the similarity between the time series of a given voxel and its (27) nearest neighbors [26], computed as the Kendall's coefficient of concordance (KCC) [13]. The KCC values are standardized and smoothed (4 mm