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Intensity based Regions Of Interest (ROIs) preselection followed by Convolutional Neuronal Network (CNN) based segmentation for new lesions detection in Multiple Sclerosis

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Abstract. Detecting new lesions is a key aspect of the radiological follow-up of patients with Multiple Sclerosis (MS), leading to eventual changes in their therapeutics. Our pipeline for new lesion detection based on two consecutive FLAIR MRIs consists in two steps. We start by a detection of potential Region Of Interest (ROI) containing new lesions using a sensitive classical image processing procedure. It detects the connected voxels which intensity increases in the second visit compared to the first one. We then apply a filtering procedure to segment voxels corresponding to new lesions in those potential ROI by applying Convolutional Neuronal Networks (CNN).

Keywords: classical image processing, CNNs, hybrid approach.

Introduction

The reduction or absence of new lesion formation over time is a key radiological endpoint in clinical trials assessing disease modifying therapies in Multiple Sclerosis. Novel lesion identification and segmentation is generally done manually, or using semi-automated procedures, by radiologists or neurologists and is time consuming. The aim of MICCAI MSSEG-2 Worskhop was to develop a new automatic method to segment new lesions based on two FLAIR MRI of the same patient.

1 Step one: MRIs post-processing for potential ROI detection

The aim of the first step (Fig. 1) is to detect the ROIs that could potentially contain a new lesion by a sensitive classical image processing procedure, so that those ROIs could be used as patches for the next step. Images were corrected for bias field with the N4 algorithm using “animaN4BiasCorrection” [1]. To enhance the quality of the registration between the two time points [3], we applied a rigid registration, using ANTs [2]. We extracted a brain mask using ‘bet’ (FSL [4]) on both images and used their intersection to restrict the analysis. Finally an affine registration of the two FLAIRs was done using ANTs.

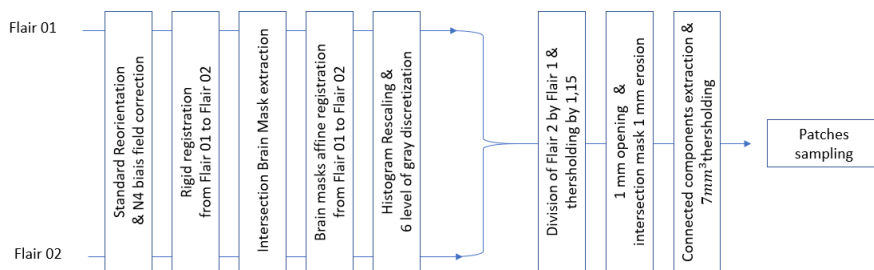


Fig. 1. Step one overview

We applied a two-step intensity matching procedure. First, we used a histogram matching from ANTs (“ImageMath”), based on landmarks intensity scaling between the two images, considering the second visit as the reference. To further reduce the small variations in the signal, intensities were discretized on 6 levels of grey.

New lesions are defined as parenchymal areas that are iso-intense at the first visit but hyperintense at the second. When considering the ratio of the two visits, as intensities have been matched, new objects should consist in areas with an intensity ratio greater than 1. By extracting ratio values in the ground truth, we chose a threshold of 1.15 to include 85% of ground truth voxels.

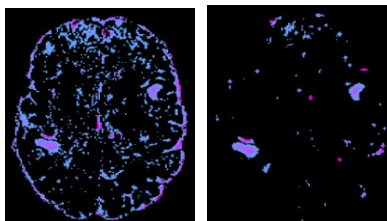


Fig. 2. map of all voxels which intensity ratio between the two visits is greater to 1.15, before (left) and after (right) connected components distinction and volume thresholding ($>7\text{mm}^3$).

Due to remaining field bias, registration inaccuracies at the interfaces, a high number of voxels external to the ground truth mask are still selected by this method (Fig. 2a). We mark them as False Positive (FP) voxels, as opposed to True Positive (TP) voxels, that are included in the ground truth mask. We added a geometrical constraint to those candidate voxels to eliminate FPs. We used an opening of one millimeter to individualize adjacent structures. Then, we proceeded to distinguish connected components (CC) (“animaConnectedComponents” [1]) and deleted those below 7mm^3 , thus eliminating isolated voxels. We eroded by 1mm the brain mask to avoid ROIs in the pial surface.

Each resulting CC was used as a target to crop a patch with a padding of two voxels, defining our potential ROI (Fig. 2 right). In all patches we sampled the processed FLAIR from the first and second visit after discretization, the ground truth, and three distance maps: from pial surface to brain depth (DM), from vertex to neck (DMz) and from occiput to nose (DMx). Those distance maps will be inserted into convolutional layers in later steps to give anatomical references for segmentation.

2 Step two: Filtering of true positive voxels in previously found ROIs by CNN

2.1. Batch constitution: infratentorial imbalance

We used the torchIO [5] to generate batches. Each training batch included 32 patches as described above. We identified infratentorial patches based on a threshold in the DMz. The fewer number of infratentorial new lesions, smaller volume of this area and the high complexity of the brain anatomy in this region, lead us to imbalance our training toward infratentorial regions. In the training set, we selected with a uniform probability, as many FP patches as TP patches. To increase the specificity of the segmentation and decrease the number of FP voxels, notably in infratentorial areas, we added to the training set 30% of extra patches with a higher probability of being infratentorial and FP patches. In detail, those extra patches were constituted by 85% of infratentorial patches (33% TP and 67% FP infratentorial patches) and 15% of supratentorial FP patches. We used the data augmentation methods provided by the torchIO library, applying random noise and random bias field with, each, a 30% probability.

2.2. Network architecture

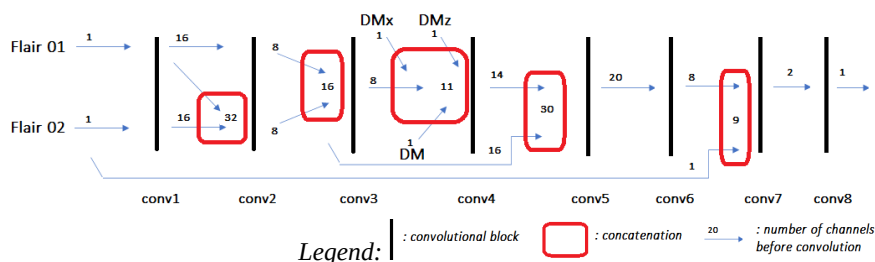


Fig. 3. CNN architecture for patch segmentation

The architecture shown in fig. 3, was implemented with Pytorch [7]. Each convolutional block was formed by a 3D convolutional layer (in and out channels described in Fig. 3) without striding and with a padding of one, followed by a 3D batch normalization, and finally a Rectified Linear Unifier activation function. Due to the variable patch sizes, no pooling layers were added [6]. Between conv3 and conv4, we added the three distance maps created in step one. There are two recurrent connections: at short distance between conv2 and conv5, and at long distance between Flair 02 input image and conv7. This second long-distance recurrent connection was given to help segment at the last steps by concatenating conv6's output to the input Flair 02, on which the final segmentation has to be based on.

2.3. Training

The absence of pooling layers in our architecture (fig. 3) is known to increase the risk of over-fitting [6]. In consequence, we limited our training to 20 epochs, with a

decreasing learning rate using an ADAM optimizer, beginning from a learning rate of 0.001 at the first epoch and decaying it by 0.1 every 4 epochs.

2.4. Inference

As patches could overlap, for each voxel of the global image, we kept only the value from the output patch where this voxel was the closest to the patch's center. Indeed, as each patch was cropped around its own potential ROI, peripheral voxels are more at risk of belonging to an adjacent ROI caught in the field of view. Moreover, as we observed that bigger patches contained more FP voxels, taking the distance from center as a discriminator is in favor of smaller patches in the final prediction. We applied a sigmoid to the prediction and binarized the final image with threshold of 0.75.

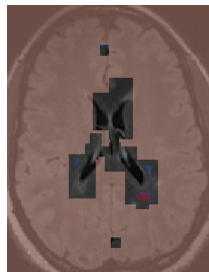


Fig. 4. Inference with all patches overlaid on Flair 02 image, before sigmoid, with low probabilities (in blue) and high probabilities (in red), the only ones kept in the final binarized image.

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