Deep Learning for Detection of Acute Multiple Sclerosis Lesions without Gadolinium Injection

PhD proposal

Keywords Deep Learning, Multiple Sclerosis, lesions, gadolinium, segmentation, detection, data generation, GAN

Medical Context and Objectives Gadolinium (Gd) based contrast agents (GBCA) have been used for decades in clinical MRI explorations and especially to probe the blood brain barrier integrity (using Gd-enhanced T1-weighted MRI) Recently, Gd deposition within human bones and brain tissue was observed following repeated Gd based contrast agents' injections [8-9]. As the long-term toxicity of Gd accumulation in brain tissue remains unknown, the development of alternative to Gd-enhanced MRI is crucial to limit the patients' exposure to such potential toxicity. This point is especially crucial for multiple sclerosis (MS) patients, for whom Gd-enhanced MRI examination is regularly performed for monitoring of the disease course, and is a critical asset for treatment adjustment [6-7].

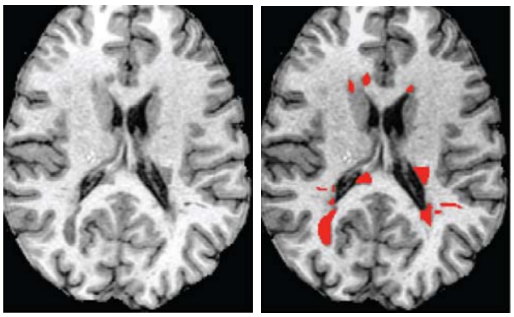

Figure 1: A T_{1w} image of an MS patient along with the segmented MS lesions.

Objectifs Our main goal is to make possible the detection on MRI images without Gd injection of the MS lesions that would have shown blood brain barrier disruption on post Gd T1 weighted MRI. The design of an approach based on deep learning able to efficiently detect/segment multiple sclerosis active lesions from MR images acquired before gadolinium injection.

Deep learning for the detection and segmentation of inflammatory lesion without Gd Our working hypothesis is that active MS lesions (i.e. Gd enhancing) can be distinguished by expert radiologists based on pre-injection conventional MRI only. Deep neural networks will be trained to detect and segment active MS lesions from these conventional images without Gd injection. Two main questions will be tackled during the phd.

Deep neural network for Gd response prediction

The challenge here is to train a sufficiently rich network that can predict Gd response from preinjection images. The difficulty will be to train this network with good generalization properties but with a from a limited amount of data.

The problem of Gd response prediction can be seen either as an image translation [17] problem (synthetize post Gd image from preinjection images) or as a pure detection or segmentation problem [18] (predict the probability of Gd enhancement from preinjection images).

We will also investigate dedicated data augmentation. We will combine pre-deep learning methods (such as 4) with deep learning approaches such as generative adversarial network (GAN) [14,15] or conditional variational auto encoder (cVAE) [16] to generate artificial annotated data that can be added to the training dataset to help the training.

Multitask learning is also an axes of investigation. We can indeed combine the question of the prediction of Gd response with the question of the segmentation of all the lesions readily visible on preinjection images. Mixing dataset and using a common network that solve several similar questions is often interesting to the resolution of both problems.

Understanding the deep neural network prediction In this axes, we will tackle the following questions: 1/ Can we quantify the uncertainties on our prediction ? 2/ What are the (combination of) preinjection modalities important for a robust prediction of Gd response. 3/ Can we reveal the pattern in preinjection images that will predict Gd response (positively or negatively).

For the first point we will based our work on variational dropout [13] that allows to estimates uncertainties on the output produced by a deep neural network. Some work proposed on the uncertainty estimation of MS lesion segmentation will be extended to our problem [12].

For question 2 and 3, our investigations will be based on approaches such as thoses described in [10] or [11] that allows, from the output of a trained network on a specific images, to identify the voxels that contribute to the classifaction of the images. The main difficulty will be to translate the method described in [11] (or a similar method) for a classification network to a segmentation network.

Data The OFSEP cohort, a large clinical national database composed by more than 1000 clinical standardized MR exams of MS patients including T2/FLAIR MRI, pre and post-Gd T1w MRI will be used. Annotated data (without Gd injection) from public challenges (MICCAI 2008, ISBI 2015, MICCAI 2016) constitute useful datasets.

The lab This work will be done at CREATIS[1] in Lyon (France) in collaboration between the "NRM and Optics" team which have a strong expertise in MRI acquisition and multiple sclerosis clinical studies and "Images et Modeles" team which have a strong expertise in medical image processing based on deep learning.

The phd student will be supervized by:

- F. Cotton, neuroradiologist, multiple sclerosis specialist, NRM and Optics team
- M. Sdika, deep learning and image processing specialist, Images et Modeles team
- T. Grenier, deep learning and image processing specialist, Images and Modeles team

Candidate & Application The candidate is expected to have a M2 in either machine learning, image processing or applied mathematics. We are seeking a serious candidate who can work semi-autonomously with:

- strong programming skills, including experience with python
- good knowledge of machine learning, deep learning
- knowledge of image processing (image segmentation, registration and warping)
- methods, writing ability

The successful candidate is expected to be autonomous and show strong motivation and interest in multidisciplinary research. He/She will need to acquire a deep understanding on the question and issues related to MS especially to inflammatory lesions process.

Interested candidates will send a cover letter, a CV, transcripts of M1 and M2 to: michael[dot]sdika[at]creatis[dot]insa-lyon[dot]fr francois[dot]cotton[at]chu-lyon[dot]fr. Other relevant documents such as letters of reference, previous internship reports, code sample,... will be appreciated.

Please note that the doctoral school requires an overall passing grade higher than or equal to 12/20 at the first session of Master 2 or an equivalent diploma.

[1] `www.creatis.insa-lyon.fr`

For the recuited applicant, this phD will open opportunities in academic research or as an expert in deep learning and medical imaging in the industry.

Application should be sent before May 15^{th} 2019.

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