



**HAL**  
open science

## Siamese convolutional neural network for new multiple sclerosis lesion segmentation

Alexandre Fenneteau, Pascal Bourdon, David Helbert, Christine Fernandez-Maloigne, Christophe N Habas, Rémy Guillevin

### ► To cite this version:

Alexandre Fenneteau, Pascal Bourdon, David Helbert, Christine Fernandez-Maloigne, Christophe N Habas, et al.. Siamese convolutional neural network for new multiple sclerosis lesion segmentation. MSSEG-2 challenge proceedings: Multiple sclerosis new lesions segmentation challenge using a data management and processing infrastructure. MICCAI 2021, Sep 2021, Strasbourg, France. hal-03359032

**HAL Id: hal-03359032**

**<https://hal.science/hal-03359032>**

Submitted on 4 Apr 2023

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# Siamese convolutional neural network for new multiple sclerosis lesion segmentation<sup>\*</sup>

Alexandre Fenneteau<sup>1,2,3</sup>[0000–0001–7109–3548], Pascal Bourdon<sup>2,3</sup>[1111–2222–3333–4444], David Helbert<sup>2,3</sup>[2222–3333–4444–5555], Christine Fernandez-Maloigne<sup>2,3</sup>[2222–3333–4444–5555], Christophe Habas<sup>4,3</sup>[2222–3333–4444–5555], and Rémy Guillevin<sup>3,5,6</sup>[2222–3333–4444–5555]

<sup>1</sup> Siemens Healthcare, Saint Denis, France

<sup>2</sup> XLIM Laboratory, University of Poitiers, UMR CNRS 7252; Poitiers, France

<sup>3</sup> I3M, Common Laboratory CNRS-Siemens, University and Hospital of Poitiers ; Poitiers, France

<sup>4</sup> Neuroimaging Department, Quinze Vingts Hospital; Paris, France

<sup>5</sup> Poitiers University Hospital, CHU; Poitiers, France

<sup>6</sup> DACTIM-MIS/LMA Laboratory University of Poitiers, UMR CNRS 7348; Poitiers, France

**Keywords:** CNN · Segmentation · Multiple Sclerosis.

## Introduction

Multiple Sclerosis (MS) is an autoimmune and inflammatory disease causing demyelination and inflammatory lesions in the brain and the spinal cord. It generally appears near 30 years old [1]. In 2016 it was estimated to cause the disability of more than 1,000,000 persons in the world [23].

A Magnetic Resonance (MR) exam is particularly valued for the diagnosis and the monitoring of the disease as it is non invasive and is helpful to reveal lesions. In MR images lesions can be characterized and localized to deliver diagnosis with the help of the McDonald criteria [20]. The monitoring of the disease is important to orient patient medication and care since it has been shown that the lesion activity is related to the evolution of disability [21]. The activity is usually performed visually by the radiologist by comparing MR images acquired at different time (spaced by years or months). But the visual detection of new lesions is subject to inter-rater variability [2] and the definition of new or enlarged lesions is not fixed [12]. The automatic segmentation of new lesions has the potential to define a more reproducible evaluation of the lesion activity but is a difficult task due to potential registration errors, low MR resolution, partial volumes and acquisition noise and constraints.

The automatic detection of new and enlarged lesions have been conducted on intensity and deformation analysis [11]. More recently Cabezas *et al.* and Salem

---

<sup>\*</sup> Supported by Siemens Healthcare.

*et al.* took advantage of both techniques by merging intensity based activity mapping with deformation fields [4,17]. Other approaches have been proposed with the apparition of performant automated methods for White Matter (WM) lesion segmentation. Schmidt *et al.* proposed a method to revise lesion segmentation of two successive MR exams with T2-fluid-attenuated inversion recovery (FLAIR) and T1 images to produce a lesion change map [18]. McKinley *et al.* took advantages of their Convolutional Neural Network (CNN) for segmentation confidence of two time points to identify significant lesion change [12]. While these methods perform well to highlight lesion changes they are not designed to distinguish enlargement of new lesions. One type of approaches directly use CNN on MR images from two time points to obtain the segmentation of new lesion voxels. Gessert *et al.* investigated the use of a U-net [16] with two encoders (one for each time point) to segment lesion activity with attention-guided interaction between encoders [8] they also proposed a 3D temporal approach by using U-net with convolutional gated recurrent unit [7].

We decided to propose a solution designed for the segmentation of only new MS lesions based on the use of U-net like architecture driven by the success of Gessert *et al.* methods. Inspired by the work of Schmidt *et al.* and McKinley *et al.* we wanted to decompose both time point images segmentation and analysis of those segmentation since it is a relevant process. We selected the light Minimally Parameterized U-net (MPU-net) [6] architecture as a basis architecture and extended it. We improved the MPU-net architecture and integrated it in a siamese model processing both time point images in the same way followed by a refinement block. It combines the lesion segmentation and segmentation refinement in an fully supervised way with a light CNN architecture.

## 1 Material and methods

### 1.1 Task and data

The work performed is an attempt to the MSSEG-2 challenge (<https://portal.fl-iam.irisa.fr/msseg-2/>). The challenge task is to identify only new lesions and not enlarging ones from two co-registered FLAIR images acquired at different time separated by 1 to 3 years.

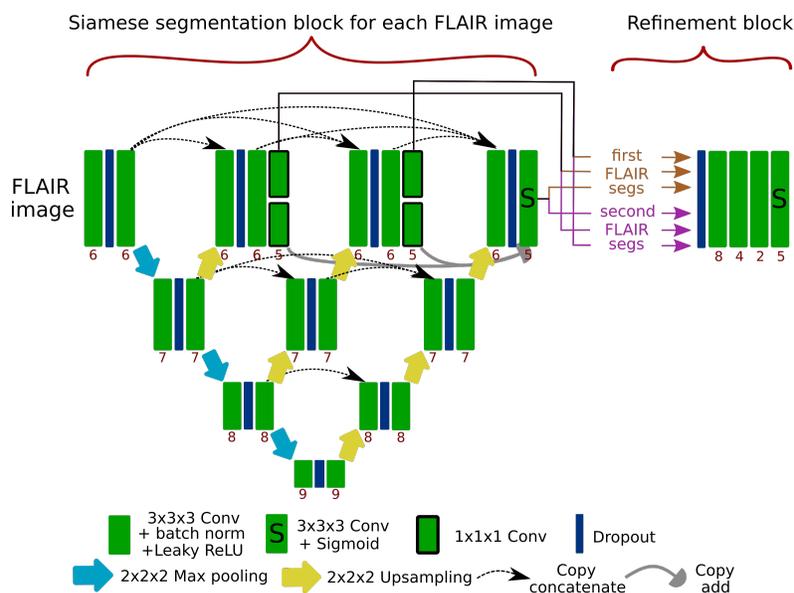
The FLAIR images were acquired by different French health centers with different scanners brands, magnetic field strength and specifications in the framework of the French MS registry OFSEP [22] collected prospectively in the EDMUS software [5] and made anonymous.

The training data-set consists of 40 patients with the two time-point images along with 4 segmentations performed by different neuroradiologist experts and 1 consensus segmentation.

The only preprocessing performed on images is a rigid co-registration bringing both FLAIR images to a middle point. In addition to that the Anima pre-processing script proposed by the challenge organizers was used. It extracts the union of the brain mask of both FLAIR images, then mask both FLAIR images and applies MR bias field correction.

### 1.2 Architecture

To segment new lesions, the architecture is conceived to integrate two parts: one segmentation block and one refinement block see Fig.1. The segmentation block performs segmentation on both FLAIR images in the same way without interactions. The refinement block concatenates segmentations produced for each FLAIR images to produce the final segmentation of new lesions. In practice, we can not be sure that the neural network works as described because of the complexity of such models.



**Fig. 1.** Proposed architecture with the Siamese improved MPU-net in the segmentation block on the left and the convolutional refinement block on the right

#### Segmentation block

To produce segmentation, the MPU-net [6] has been selected. It is a U-net [16]

like architecture with only 3D convolutions, max-pooling and upsampling with approximately 30,000 learnable parameters. The high nature of this architecture is interesting since the number of learnable parameters is subject to the curse of dimensionality [3]. The restricted number of parameters also limits the training and inference costs in time and energy. Big and complex models can fit random labels [24], and so, can over-fit a whole dataset. We expect light models to have a reduced capacity of memorizing a whole data set and thus can be constrained to generalize by this fact. While it produces reasonable segmentation performances, it can be improved and adapted for the task of new lesion segmentation.

To improve the MPU-net, batch normalization [9] has been added after each convolution to regularize feature map outputs and dropout layers [19] has been added in each blocks to avoid over-fitting. Those changes improved both stability and performance of the model.

We wanted the refinement block to work with different level of abstraction for a better analysis. The implementation of this idea has been made by fusing the MPU-net architecture and the U-net++ architecture [25] which consists in adding intermediate decoders with skip-connections between them making the model deeply supervised. To limit the number of convolutional layer in the model to keep it light, we decided to reduce the number of consecutive convolution in one level of encoder and decoder to 2.

### Refinement block

The refinement block takes as input the segmentations of all decoders from the segmentation block on each FLAIR images. The segmentation block is applied over each FLAIR images at the time making the whole neural network siamese. The inputs are concatenated and followed by a dropout layers and 4 convolution-Batch normalization layers couples.

The architecture is trained over all given segmentation maps to train to take benefit of all supervision.

### 1.3 Pre-processing

The data provided did not have the same resolution. To get comparable convolution analysis, the resampling of subject at the same resolution was needed. As the neural network is designed for volume, we wanted to provide it isotropic voxels resolution to avoid spatial preference of bias. To have a compromise on volume size and resolution we opt for a resampling at the  $0.8 \times 0.8 \times 0.8$  resolution. The FLAIR image histograms were then standardized [13] and each image intensity were normalized by subtracting mean and dividing by standard deviation.

#### 1.4 Learning specifications

The architecture has been trained with FLAIR volumes from two time points to reconstruct each given segmentation (the consensus and 4 different radiologist segmentation of new lesions). We found that training with all 5 segmentations helped the neural network to converge and to find its own consensus. In practice, as observed in [6] the different segmentation predictions are almost the same.

The volumes sent were  $56 \times 56 \times 56$  patches randomly extracted from brain areas with a probability of 80% to contain new lesion voxels for patient with new lesions and all over the brain with same probability for patient with no new lesions.

The batch size was set to 40 and epochs were defined to contain 872 patches from each patient. The model was trained with the Adam optimizer [10] and a learning rate of 0.004 for 40 epochs. We found that even with the Adam optimizer, the gradual decreasing of the learning rate helped convergence. We gradually decrease it by 10% after each epoch. The batch dice loss Eq.1 is used as loss function.

$$BatchDiceLoss = -2 \frac{10^{-5} + \sum_{c=1}^C \sum_{b=1}^B \sum_{h=1}^H \sum_{w=1}^W \sum_{d=1}^D P_{c,b,h,w,d} \hat{P}_{c,b,h,w,d}}{10^{-5} + \sum_{c=1}^C \sum_{b=1}^B \sum_{h=1}^H \sum_{w=1}^W \sum_{d=1}^D P_{c,b,h,w,d} + \hat{P}_{c,b,h,w,d}} \quad (1)$$

where  $P$  is the ground truth,  $\hat{P}$  is the prediction,  $C$  is the number of ground truth segmentation,  $B$  is the patch in the batch,  $H$  the height,  $W$  the weight and  $D$  the depth.

#### 1.5 Testing

On testing time, after preprocessing the neural network predicts 5 segmentation maps (one for each radiologist involved in the study and the consensus) for each patch, only the consensus prediction is kept. Patches are regularly extracted all over the volume with an overlap of **14 MAYBE CHANGE** and the final prediction map consists in spatial averaging of all overlapping patches. The prediction map is then resampled at the original resolution and thresholded to keep only voxels [VISUALLY > 0.5 SHOULD BE BETTER] > 0.6 as new lesion voxel.

#### 1.6 Implementation details

The model was trained on a 4GPU machine with PyTorch [14] for the CNN conception and training. The TorchIO library [15] were used to perform data loading, online data preprocessing and patching.

## Conclusion

The segmentation of new MS new lesion relies on the comparison of two acquisitions of the same patient but at different time. It is a challenging task since enlarging lesions are not taken into account and both acquisition have to be aligned and perfect match does not exist. The comparison is not a simple subtraction of lesion segmentation but a careful analysis robust to registration errors and able to identify what is a new lesion and not an enlarging one.

[state of the art to continue after introduction revision] Multiple attempts have been made to identify lesion change with intensity and deformation analysis.

We propose here, a light fully convolutional siamese and deeply supervised architecture and training method to segment new MS lesions. The architecture is light with 40,465 learnable parameters and have 28 convolutional layers. It is expected to segment separately both FLAIR images at different time points and then compare and refine those segmentations to output new lesions segmentation map. It is trained and test on small overlapping patches extracted from brain.

This method requires few preprocessing and post-processing steps and takes advantage of the 3D nature of the MR image data. The light nature of the model is expected to limit the training cost in time, energy and infrastructure and we expect it to have a great generalization power.

## References

1. Acheson, E.D.: Epidemiology of multiple sclerosis. *British Medical Bulletin* **33**(1), 9–14 (01 1977). <https://doi.org/10.1093/oxfordjournals.bmb.a071407>, <https://doi.org/10.1093/oxfordjournals.bmb.a071407>
2. Altay, E.E., Fisher, E., Jones, S.E., Hara-Cleaver, C., Lee, J.C., Rudick, R.A.: Reliability of classifying multiple sclerosis disease activity using magnetic resonance imaging in a multiple sclerosis clinic. *JAMA neurology* **70**(3), 338–344 (2013)
3. Bengio, Y., LeCun, Y., et al.: Scaling learning algorithms towards ai. *Large-scale kernel machines* **34**(5), 1–41 (2007)
4. Cabezas, M., Corral, J., Oliver, A., Díez, Y., Tintoré, M., Auger, C., Montalban, X., Lladó, X., Pareto, D., Rovira, À.: Improved automatic detection of new t2 lesions in multiple sclerosis using deformation fields. *American Journal of Neuroradiology* **37**(10), 1816–1823 (2016)
5. Confavreux, C., Compston, D., Hommes, O., McDonald, W., Thompson, A.: Edmus, a european database for multiple sclerosis. *Journal of Neurology, Neurosurgery & Psychiatry* **55**(8), 671–676 (1992)
6. Fenneteau, A., Bourdon, P., Helbert, D., Fernandez-Maloigne, C., Habas, C., Guillevin, R.: Investigating efficient cnn architecture for multiple sclerosis lesion segmentation. *Journal of Medical Imaging* **8**(1), 014504 (2021)
7. Gessert, N., Bengs, M., Krüger, J., Opfer, R., Ostwaldt, A.C., Manogaran, P., Schippling, S., Schlaefer, A.: 4d deep learning for multiple sclerosis lesion activity segmentation. *arXiv preprint arXiv:2004.09216* (2020)

8. Gessert, N., Krüger, J., Opfer, R., Ostwaldt, A.C., Manogaran, P., Kitzler, H.H., Schippling, S., Schlaefer, A.: Multiple sclerosis lesion activity segmentation with attention-guided two-path cnns. *Computerized Medical Imaging and Graphics* **84**, 101772 (2020)
9. Ioffe, S., Szegedy, C.: Batch normalization: Accelerating deep network training by reducing internal covariate shift. *arXiv preprint arXiv:1502.03167* (2015)
10. Kingma, D.P., Ba, J.: Adam: A method for stochastic optimization. *arXiv preprint arXiv:1412.6980* (2014)
11. Lladó, X., Ganiler, O., Oliver, A., Martí, R., Freixenet, J., Valls, L., Vilanova, J.C., Ramió-Torrentà, L., Rovira, À.: Automated detection of multiple sclerosis lesions in serial brain mri. *Neuroradiology* **54**(8), 787–807 (2012)
12. McKinley, R., Wepfer, R., Grunder, L., Aschwanden, F., Fischer, T., Friedli, C., Muri, R., Rummel, C., Verma, R., Weisstanner, C., et al.: Automatic detection of lesion load change in multiple sclerosis using convolutional neural networks with segmentation confidence. *NeuroImage: Clinical* **25**, 102104 (2020)
13. Nyúl, L.G., Udupa, J.K., Zhang, X.: New variants of a method of mri scale standardization. *IEEE transactions on medical imaging* **19**(2), 143–150 (2000)
14. Paszke, A., Gross, S., Massa, F., Lerer, A., Bradbury, J., Chanan, G., Killeen, T., Lin, Z., Gimelshein, N., Antiga, L., Desmaison, A., Kopf, A., Yang, E., DeVito, Z., Raison, M., Tejani, A., Chilamkurthy, S., Steiner, B., Fang, L., Bai, J., Chintala, S.: Pytorch: An imperative style, high-performance deep learning library. In: Wallach, H., Larochelle, H., Beygelzimer, A., d'Alché-Buc, F., Fox, E., Garnett, R. (eds.) *Advances in Neural Information Processing Systems* 32, pp. 8024–8035. Curran Associates, Inc. (2019), <http://papers.neurips.cc/paper/9015-pytorch-an-imperative-style-high-performance-deep-learning-library.pdf>
15. Pérez-García, F., Sparks, R., Ourselin, S.: TorchIO: a Python library for efficient loading, preprocessing, augmentation and patch-based sampling of medical images in deep learning. *arXiv:2003.04696 [cs, eess, stat]* (#mar# 2020), <http://arxiv.org/abs/2003.04696>, *arXiv: 2003.04696*
16. Ronneberger, O., Fischer, P., Brox, T.: U-net: Convolutional networks for biomedical image segmentation. In: *MICCAI. LNCS*, vol. 9351, pp. 234–241. Springer (2015), <http://lmb.informatik.uni-freiburg.de/Publications/2015/RFB15a>, (available on *arXiv:1505.04597 [cs.CV]*)
17. Salem, M., Cabezas, M., Valverde, S., Pareto, D., Oliver, A., Salvi, J., Rovira, À., Lladó, X.: A supervised framework with intensity subtraction and deformation field features for the detection of new t2-w lesions in multiple sclerosis. *NeuroImage: Clinical* **17**, 607–615 (2018)
18. Schmidt, P., Pongratz, V., Küster, P., Meier, D., Wuerfel, J., Lukas, C., Bellenberg, B., Zipp, F., Groppa, S., Sämann, P.G., et al.: Automated segmentation of changes in flair-hyperintense white matter lesions in multiple sclerosis on serial magnetic resonance imaging. *NeuroImage: Clinical* **23**, 101849 (2019)
19. Srivastava, N., Hinton, G., Krizhevsky, A., Sutskever, I., Salakhutdinov, R.: Dropout: a simple way to prevent neural networks from overfitting. *The journal of machine learning research* **15**(1), 1929–1958 (2014)
20. Thompson, A.J., Banwell, B.L., Barkhof, F., Carroll, W.M., Coetzee, T., Comi, G., Correale, J., Fazekas, F., Filippi, M., Freedman, M.S., et al.: Diagnosis of multiple sclerosis: 2017 revisions of the mcdonald criteria. *The Lancet Neurology* **17**(2), 162–173 (2018)
21. Tintore, M., Rovira, À., Río, J., Otero-Romero, S., Arrambide, G., Tur, C., Comabella, M., Nos, C., Arévalo, M.J., Negrotto, L., et al.: Defining high, medium

- and low impact prognostic factors for developing multiple sclerosis. *Brain* **138**(7), 1863–1874 (2015)
22. Vukusic, S., Casey, R., Rollot, F., Brochet, B., Pelletier, J., Laplaud, D.A., De Sèze, J., Cotton, F., Moreau, T., Stankoff, B., et al.: Observatoire français de la sclérose en plaques (ofsep): A unique multimodal nationwide ms registry in france. *Multiple Sclerosis Journal* **26**(1), 118–122 (2020)
  23. Wallin, M.T., Culpepper, W.J., Nichols, E., Bhutta, Z.A., Gebrehiwot, T.T., Hay, S.I., Khalil, I.A., Krohn, K.J., Liang, X., Naghavi, M., et al.: Global, regional, and national burden of multiple sclerosis 1990–2016: a systematic analysis for the global burden of disease study 2016. *The Lancet Neurology* **18**(3), 269–285 (2019)
  24. Zhang, C., Bengio, S., Hardt, M., Recht, B., Vinyals, O.: Understanding deep learning requires rethinking generalization. arXiv preprint arXiv:1611.03530 (2016)
  25. Zhou, Z., Siddiquee, M.M.R., Tajbakhsh, N., Liang, J.: Unet++: Redesigning skip connections to exploit multiscale features in image segmentation. *IEEE transactions on medical imaging* **39**(6), 1856–1867 (2019)