MSMilan2023
9th Joint ECTRIMS-ACTRIMS Meeting
11–13 October 2023 | Milan, Italy

Abstract Number: [204]

Abstract Title: Deep Learning Uncertainty Quantification of Cortical Lesions in MP2RAGE for Missed Lesions Discovery

Abstract Category: Imaging and non-imaging biomarkers - 32 - Big data and artificial intelligence

Preferred Presentation Type: Oral or poster presentation

Nataliia Molchanova[1, 2, 3], Alessandro Cagol[4, 5, 6, 7], Mario Ocampo-Pineda[4, 5, 6], Xinjie Chen[4, 5, 6], Matthias Weigel[4, 5, 6, 8], Adrien Depeursinge[1], Henning Muller[1, 9], Mara Graziani[1], Cristina Granziera[4, 5, 6], Meritxell Bach Cuadra*[2, 3]

[1]University of Applied Sciences of Western Switzerland (HES-SO), Institute of Informatics, Sierre, Switzerland, [2]CIBM Center for Biomedical Imaging, Lausanne, Switzerland, [3]Lausanne University Hospital (CHUV) and University of Lausanne (UNIL), Radiology Department, Lausanne, Switzerland, [4]University Hospital Basel and University of Basel, Translational Imaging in Neurology (ThINk), Department of Biomedical Engineering, Basel, Switzerland, [5]University Hospital Basel, Department of Neurology, Basel, Switzerland, [6]University Hospital Basel and University of Basel, Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), Basel, Switzerland, [7]University of Genova, Department of Health Sciences, Genova, Italy, [8]University Hospital Basel, Division of Radiological Physics, Department of Radiology, Basel, Switzerland, [9]University of Geneva, Department of Radiology and Medical Informatics, Geneva, Switzerland

Introduction:
Cortical lesions (CL) in multiple sclerosis (MS) patients are a hallmark of MS and are associated with a progressive disease course. Deep-learning (DL) methods were proposed to facilitate lesion segmentation. However, annotation errors and data sparsity contribute to the uncertainty in predictions. Uncertainty quantification (UQ) techniques provide a measure of the trustworthiness of DL predictions.

Objectives/Aims:
To quantify CL uncertainty in MP2RAGE images and leverage this information for the dataset correction. Dataset correction is performed with the use of clinical feedback in analysing low-uncertainty CLs that have no intersection with the ground truth, i.e. false positive (FP).

Methods:
We retrospectively analysed 3T MP2RAGE images (1 mm isotropic) from **125** MS patients (69 RRMS/16 PPMS/40 SPMS, 73 female, mean age 48.1 (SD: 13.6) years, median EDSS 3.0 (IQR: 2.0-5.625)). CLs were annotated by consensus between 2 experts. We used the state-of-the-art DL segmentation model - 3D U-net, with a dataset split for training, validation, and testing as **84:10:31**. For each lesion, UQ was assessed via previously proposed detection disagreement uncertainty (DDU) expressing an increased likelihood of erroneous predictions in detection. Low-uncertainty FP lesions (DDU < 25% percentile, 164 lesions) are the ones where the model is confident that they are CLs, but they are not present in the ground truth. An experienced neurologist provided the following clinical feedback: non-lesion, CL, white matter lesion (WML).

Results:
Among 164 low-uncertainty FP lesions, 16.5% lesions were missed CLs, 64.6% - WML (25.6% were also initially missed WMLs when experts explored FLAIR), and 18.9% - non-

lesions. Analysing regions confused with WML, we identified inconsistencies in leukoCL annotations in the whole dataset. After correcting the dataset and retraining, the model segmentation quality (Dice overlap similarity) grew 14.1%.

Conclusion:

The proposed uncertainty-aware lesion-scale analysis provides a second “opinion” to clinicians helping to identify missed lesions and improve manual annotations.

Disclosures: NM: nothing to disclose.
AC is supported by the Horizon 2020 Eurostar program (grant E!113682), and received speaker honoraria from Novartis.
MOP nothing to disclose.
XC: nothing to disclose.
MW has received research funding by Biogen for developing spinal cord MRI.
AD: nothing to disclose.
MG: IBM Research Zurich employee.
HM: mandates with Roche.
CG: The University Hospital Basel (USB), as the employer of C.G., has received the following fees which were used exclusively for research support: (i) advisory boards and consultancy fees from Actelion, Novartis, Genzyme-Sanofi, GeNeuro, Hoffmann La Roche and Siemens; (ii) speaker fees from Biogen, Hoffmann La Roche, Teva, Novartis, Merck, Jannsen Pharmaceuticals and Genzyme-Sanofi; (iii) research grants: Biogen, Genzyme Sanofi, Hoffmann La Roche, GeNeuro.
MBC: nothing to disclose.

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