Adapting a white matter lesion segmentation algorithm for large cohort studies

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Target audience: Radiologists and neurologists interested in lesion mapping with MRI

Purpose: The vast majority of the elderly present white matter lesions (WML) in T2-weigthed images[1], likely due to cardiovascular pathologies (e.g. small vessel disease), while primarily inflammatory events represent another category of lesion evolution. WML can affect numerous functions such as cognition, mood and motor functions[2]. Therefore it is of high importance to account for the lesion-deficit relationship. Furthermore WML will corrupt the analysis of DWI and fMRI[3]. As lesion load increases with age, large datasets with elderly subjects require automated lesion segmentation and mapping methods. Here we present the adaptation of a multiple sclerosis (MS) lesion segmentation algorithm for the application in the general population with approximately 1200 subjects with moderate (Faz1), medium (Faz2) and high (Faz3) lesion load.

Methods: We obtained imaging data of over 2500 participants, representative for the general population (age ranges between 19 and 80 years) acquired for the LIFE study (Leipzig Research Centre for Civilization Diseases). All participants provided informed consent. The acquisition was performed at 3 Tesla on a MAGNETOM Verio scanner (Siemens, Erlangen, Germany). The body coil was used for RF transmission, and a 32-channel head coil was used for signal reception. FLAIR and MPRAGE were acquired as part of a standardized protocol: 3D-T1w MPRAGE (FA=9°, TR=2300ms, TI=900ms, TE=2.98ms, 1mm isotropic resolution, AT=5.10 min), and T2w 3D-FLAIR (TR=5000ms, TI=1800ms, TE=395ms, 1mm isotropic resolution, AT=7.02 min). Lesion amount was visually assessed by two trained neuroradiologists according to the Fazekas Scale[4]. Approx. 1000 subjects were classified as lesion-free (Faz0), presenting either no or one minimal lesion smaller than 0.5 mm. In contrast, more than half of all subjects did show lesions. Due to an increase in WML of the aging brain the majority of the subjects were over 60 years old. Approx. 1000 subjects showed focal lesions (Faz1). Around 240 subjects presented confluent lesions (Faz2). About 40 subjects exhibited severe leukoariosis (Faz3). To further quantify the lesion load, we used a lesion segmentation method previously aimed at segmenting MS lesions[5] and adjusted it to the specific requirements of WML in the normal aging brain. WML in the general population differ in pattern, intensity and extent. To best account for the large variety of lesions we iteratively re-normalized the contrast of the input FLAIR images to better separate lesions from healthy tissues, based on previous segmentation results. Three iterations were necessary to achieve an improved stable result on five test subjects (Fig.1 and Tab.1). The algorithm also computes full brain segmentation (Fig.2), which allowed us to separate the detected lesions into periventricular hyperintensities (PVH), deep white matter hyperintensities (DWMH), and pericortical hyperintensities (PCH) (Tab. 2).

Results/Discussion: The dice overlap for the test subjects (Tab.1) shows lesion segmentation improvement within three iterations. An average dice coefficient of 0.63 demonstrates the performance of the algorithm. Of note, the five subjects were selected for their variability in lesion pattern, extent and intensity, representing difficult lesions for segmentation algorithms. The lesion segmentation results for the entire cohort shows a large variety in lesion load (Tab.2). As expected the calculated lesion load was highest for Faz3 subjects compared to the smallest lesion load in Faz1 subjects. The increase of PVH in the Faz2/3 subjects is due to the confluence of PVH and DWMH. Interestingly the PVC is higher in Faz2 subjects over Faz3 subjects most likely at the cost of the high PVH in Faz3 subjects.

Conclusion: Especially when dealing with large datasets automated methods are indispensable for data analysis. The large standard deviation in lesion load explicitly shows the advantage of automated segmentation algorithms over visual rating scales, first by providing a quantitative measure and second by compensating for subjective rating differences.

References: 1. De Leeuw FE et al., JNNP (2001); 2. Bennet IJ et Madden DJ, Neuroscience (2013); 3. Schaefer A et al., J.Cereb. Blood Flow Metab. (2014); 4. Fazekas F et al., AJR (1987); 5. Shiee N et al., Neuroimage (2010)

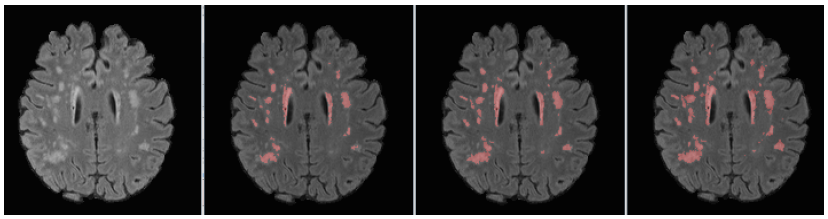

Figure 1: FLAIR, lesion segmentation (first iteration), lesion segmentation (third iteration), and manual delineation

	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5
Iteration 1	0,576	0,583	0,717	0,471	0,571
Iteration 2	0,620	0,613	0,783	0,464	0,575
Iteration 3	0,632	0,617	0,796	0,464	0,573
Iteration 4	0,633	0,621	0,796	0,453	0,575
Iteration 5	0,631	0,615	0,799	0,461	0,575
Iteration 6	0,634	0,621	0,797	0,454	0,575

Table 1: Dice coefficient over six iterations

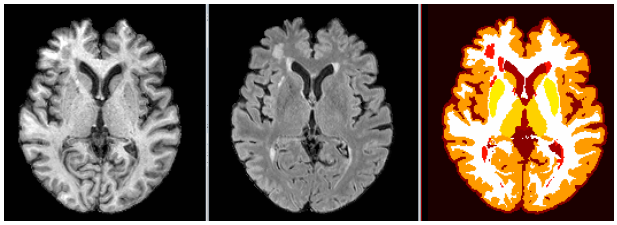

Figure 2: MPRAGE, FLAIR, and segmentation

	Mean PVH	StDev PVH	Mean DWMH	StDev DWMH	Mean PCH	StDev PCH	Mean Overall	StDev Overall
Fazekas 1	1687	1727	178	214	316	1205	727	1399
Fazekas 2	3231	5318	504	555	12990	31910	5575	19397
Fazekas 3	31731	18703	674	491	7586	19837	13331	20553

Table 2: Calculated lesion volume (mm^3) of 1200 subjects