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Research article

Diagnostic value of 3DFLAIR in clinical practice for the detection of infratentorial lesions in multiple sclerosis in regard to dual echo T2 sequences

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ABSTRACT

Background and purpose: The aim of this prospective study is to investigate and evaluate in clinical practice the diagnostic impact of 3DFLAIR in regards to 2DT2/PD in terms of infratentorial lesions detection in multiple sclerosis (MS).

Material and methods: 164 MS patients from the OFSEP database were reviewed retrospectively. MR examinations were performed on 1.5T or 3T systems from four different centers. Infratentorial lesions were counted and allocated to different regions of the posterior fossa by three raters independently (junior resident, resident with an expertise in neuroradiology, and senior neuro-radiologist) on the 3DFLAIR and 2DT2/PD. Both sequences do not have the same spatial resolution but reflect what is recommended by most of the consensus and done in clinical practice.

Results: With an overall number of 528 for Rater-1 and 798 for Rater-2 infratentorial lesions, 3DFLAIR had a significantly higher number of lesions detected than 2DT2/PD (303 for Rater-1 and 370 for Rater-2). The prevalence of trigeminal lesions detected by using 3DFLAIR was also significantly higher than 2DT2/PD. ROC analysis showed 3DFLAIR to be more specific and sensitive than 2DT2/PD. An overall difference between all three Raters has been observed. The more the Rater is experienced the more lesions he detects.

Conclusion: Along with the radiologist ability to detect lesions based on his level of experience, the OFSEP optimized 3DFLAIR can significantly improve infratentorial lesion detection in MS compared to 2DT2/PD. This is important in MS follow-up that takes into account new lesions number to adapt patients' treatment.

Abbreviations: AUC, area under the curse; DIR, double inversion recovery; OFSEP, French Observatory of Multiple Sclerosis; PD, proton density; PSIR, phase-sensitive inversion recovery; ROC, receiver operating characteristic

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1. Introduction

MS is considered as an autoimmune neuro-inflammatory demyelinating disease of the CNS. It is one of the most common causes of disability in young adults. MS lesions sometimes called scars, are produced when myelin sheets are attacked by the immune system. Depending on the lesions' location and type, normal functioning is inhibited and MS symptoms and relapses are manifested. Even if in some cases scarring heals and normal functioning is restored, over time the continual scarring can cause permanent damage to motor and sensory functions [1]. MRI has become an essential tool for the establishment of a definite MS diagnosis. The identification of typical lesions on MRI remains a challenge. Indeed, lesions localization, shape and size, provide the best view yet of tissue injury, lesion activity, and disease accumulation. Moreover, MS lesion follow-up serves as a monitoring tool for their dissemination in space and time. Studies have in fact shown that patients selected with the aid of MRI for immunomodulatory-therapy benefit more from this treatment [2]. Thus, efficient tools for high sensitivity in lesion detection are necessary using MRI.

The French Observatory of MultipleSclerosis (OFSEP) aims to provide a major epidemiological tool for the scientific community in France and abroad. This tool will help answer large number of questions concerning MS causes and mechanisms, prognostic factors of disease progression, etc. The acquisition of the standardized OFSEP MRI protocol in MS [3] still vary between centers, reflecting local availability of equipment (magnet field, head coils…). Indeed, constraints related to acquisition time in a national cohort with clinical care conditions will depend on the sequences parameters, such as acceleration factor, parallel imaging or sequences type selection.

MS lesions manifest as high signal foci against the low signal background of WM on T2WI. Although important and informative, T2-hyperintensities are indistinguishable from adjacent CSF at periventricular levels. Lesions contrast can be improved with proton density (PD) because of its lower CSF signal. Nonetheless, this problem is much easily overcome with FLAIR imaging which suppresses CSF signal, while maintaining good contrast between lesions and WM [4]. For these properties, FLAIR became a standard sequence for MS imaging.

Despite this advantage, the only drawback of 2DFLAIR is its inferior lesion detection quality in the posterior fossa and spinal cord where 2DT2/PD are preferred. More recently, 3DFLAIR has become available and allowed high spatial resolution with good SNR as well as multiplanar reconstruction that improves scanning efficiency, spatial resolution, and generates a large isotropic image volume in feasible time. Hence increasing lesion detection quality in the posterior fossa and spinal cord.

Infratentorial lesions have been considered as clinically eloquent sites that may have major impact on clinical disability in MS [5]. Indeed, they might be related to long-term prognosis for MS patients and thus help identify high risk patients for earlier occurrence of clinically relevant disability [6]. Better outcomes for infratentorial lesion detection were obtained when routinely applying dual T2/PD [7]. However, the application of 3DFLAIR significantly increased detection quality and efficiency of whole-brain lesions [8]. Thus, acquiring both sequences might be redundant and time consuming in routine exams [3,8]. The aim of this prospective study is therefore to investigate and evaluate the diagnostic impact of 3DFLAIR compared to 2DT2/PD in terms of infratentorial lesions load.

2. Materials and methods

2.1. Patients

Through the systematic longitudinal follow-up of patients with MS and combination of clinical data with biological samples and neuro-images, the OFSEP aims to foster clinical, basic and translational research in MS. OFSEP's neuro-imaging working-package have implemented an optimal and standardized MRI protocol [3] for MS patients follow-up. Acquired MR data are anonymized and saved in a centralized database along with the patients anonymized clinical records and biological samples. For the purposes of this study, 164 patients with clinically definite MS according to the McDonald's criteria [9] (108 women, mean age 41.5 ± 11.0 years; 56 men, mean age 41.0 ± 10.8 years) were selected from the OFSEP imaging database. These patients were followed at four different neuroradiology centers in France: Center-1 (21 patients), Center-2 (58 patients), Center-3 (2 patients) and Center-4 (83 patients). All patients signed an informed consent form approved by the national commission on informatics and liberty (CNIL:DR-2015-212).

2.2. Data acquisition

The OFSEP MRI brain protocol was implemented, tested and validated on seven MRI machines in four French centers. It comprised recommended conventional MR sequences (3DT1WI with and without gadolinium injection, axial DWI, axial dual-TSE 2DT2/PD or 3DT2, and 3DFLAIR (or 2DFLAIR if 3D is not available)) and some optional sequences (DTI and 2D gradient echo T2 for a first diagnosis). In this study, only patients that have both 2DT2/PD and 3DFLAIR sequences acquired were included (164 MS patients; 139 at 1.5T and 25 at 3T). Sequences parameters for each MRI and center are detailed in Supplementary Table 1. Within the framework of MRI recommendations, centers had a certain freedom of choice of the MR sequences parameters including the possibility to use multichannel coils and parallel imaging. By doing so, MRI data acquired within the OFSEP framework could be performed routinely in clinical and private centers; it is therefore a national clinical cohort and not a research study.

2.3. Image analysis

The selected anonymized MR data were first downloaded from the OFSEP database, after the OFSEP scientific committee approval. Quality of images (artifacts and image homogeneity) was assessed for each sequence. MITK-3M3 (Mint Medical, Germany) was used for analysis and visualization of radiological data. Image analysis was independently performed by three raters in consensus (Rater-1, junior resident with 3-years of experience; Rater-2, resident with 5-years of experience; and Rater-3, senior neuro-radiologist with 20-years of experience). Rater-3 performed the analysis on 30 patients whom lesion count differences between the first and the second raters were the highest. Raters were blinded to patients' number and never checked both sequences one after the other. 3DFLAIR images were analyzed in the three orthogonal planes while 2DT2/PD images were only analyzed in axial slices. For each subject and for each sequence, infratentorial lesions were counted based on their anatomical location: cerebral peduncle, tegmentum of midbrain, tectal plate, pons, floor of the 4 ventricle, superior, middle and inferior cerebellar peduncles, and cerebellum. Raters gave special and careful attention to lesions in the trigeminal nerves in both its intra-pontine and trancisternal parts.

2.4. Statistical analysis

Statistical analysis was performed using the Data Analysis and Statistic Software (STATA, v9.2, stataCorp, Texas, USA). The matched-pairs Mann-Whitney test (two-sample Wilcoxon rank-sum) for non-parametrical data was first applied to compare infratentorial lesions' number in 2DT2/PD vs 3DFLAIR images in all previously mentioned anatomical regions for both Raters-1 and -2, and to test the difference between both sequences when separating patients' MRIs acquired at 1.5T and 3T. The same test was also used to compare lesions count between all three Raters for the 30 MS patients. The receiver operating characteristic (ROC) curve analysis was then applied to test the specificity and the sensibility of 2DT2/PD compared to 3DFLAIR. ROC