ABSTRACT

Background: Multiple sclerosis is a chronic demyelinating disease of the central nervous system, that causes permanent disabilities. Diagnostics of this disease by magnetic resonance requires the appliance of corresponding protocols with the sequences that emphasize demyelinating plaques. Standard sequences T1 and T2 sometimes cannot clearly show demyelinating plaques, and it is necessary to work on perfecting the sequences that emphasize the changes in the brain formed as demyelinating plaques.

The aim of the survey: The aim of the survey was to estimate the value of MR sequence with double inversion recovery (DIR) in discovering demyelinating lesions of the brain in multiple sclerosis (MS).

Patients and methods of the survey: 22 patients were included in the survey, they were of both genders and different age. The patients were diagnosed with multiple sclerosis. The patients underwent the scanning on MR apparatus 1.5 T. Comparison of DIR sequence to FLAIR and T2 W sequences were done.

Result: DIR sequence proved significantly more MS lesions compared to T2W or FLAIR sequence, including intracortical, juxtacortical and paraventricular zone of the brain. In the infratentorial zone of brain, T2W sequence proved significantly more plaques compared to DIR and FLAIR.

Conclusion: DIR sequence compared to T2W and FLAIR sequences discovered more demyelinating lesions in targeted regions that were examined. DIR sequence is a tool that contributes to easier and faster diagnostics of multiple sclerosis, needs to be included into the routine MR protocol of patients with MS, in order to discover more easily intracortical and juxtacortical MS lesions of the brain.

KEYWORDS Double Inversion Recovery (DIR) Sequence, Fluid–attenuated Inversion–recovery (FLAIR) Sequence, T2 weighted Magnetic Resonance Imaging (MRI), Multiple Sclerosis

Introduction

Multiple sclerosis (MS) is the most frequent chronic inflammatory demyelinating disease that impacts the central nervous system of young adult persons in western countries, that is the most significant number of cases leads to irreversible and challenging disability. [1]

MS is a chronic inflammatory disease of central nervous sys-
tem (CNS) that leads to demyelination and diffused neurodegeneration in grey and white matter of brain and spinal cord. [2] Typical syndromes that occur include, but are not limited to, monocular visual loss due to optic neuritis, limb weakness or sensory loss due to transverse myelitis, double vision due to brain-stem dysfunction, or ataxia due to a cerebellar lesion. [3]

Inflammatory demyelination is easily seen on MRI, as well as changes of the blood-brain barrier that follow the early development of disease. The therapy and care for these patients are constant, demanding and quite expensive. Thus early discovery of the disease is of the utmost importance.

Protocols of scanning by magnetic resonance are regularly being revised, and the best sequence is being looked for detection of demyelinating plaques. To find the tool for the early diagnostics of this severe disease presents big challenge. Magnetic resonance imaging (MRI) is the radiological method that presents the strongest tool for the early (differential) diagnosis of multiple sclerosis. [4] On conventional T1W and T2 W sequences for the brain examination changes sometimes cannot be clearly shown, and it is necessary to introduce other sequences that, in clearer way, can emphasize demyelinating lesions. T2 W sequence with high TR emphasizes hydrogen protons so that cerebrospinal liquor provides high intensity of signal where demyelinating processes can pass unobserved. Beside T1 and T2 W sequence the FLAIR sequence with saturation of fat and water is also used. FLAIR scanning provides the highest sensitivity in the detection of lesions close to CSF (cerebrospinal flow), such as juxtacortical and periventricular white matter, but it is less sensitive in posterior fossa. [5] Therefore it is necessary to use the sequences that can show the brain parenchyma without the limitation. One of those sequences is DIR sequence with double inversion recovery.

Inversion recovery is an MRI technique used to suppress signal from specific tissue or fluid types. DIR sequences suppress both CSF signal and normal white matter signal. This may make abnormal white matter associated with FCDs, such as signal changes at the grey-white junction and radial bands extending toward the ventricular margin, more apparent. [6]

The DIR sequence was first reported as a method to selectively image white matter (WM) or grey matter (GM). [7] DIR imaging, which selectively suppresses the signals from cerebrospinal fluid, has improved the detection of cortical grey matter lesions in MS. [8]

This study aims to determine the diagnostic value of DIR sequence compared to FLAIR and T2 sequences.

**Patients and method of work**

The survey was conducted as retrospective descriptive study. Twenty-two patients of both genders and different age were included in this survey. The patients were diagnosed with multiple sclerosis. The survey was conducted on the Clinics for radiology of Clinical centre of the University of Sarajevo. The patients were scanned on the apparatus Toshiba Vantage 1.5 T by standard protocol for multiple sclerosis. The comparison of DIR, FLAIR and T2 W sequences according to the visualisation of demyelinating lesions of brain was done by dividing the brain into four regions: infratentorial, periventricular, juxtacortical, intracortical. Besides that, the analysis of visualisation of motion artefacts and flow artefacts on displayed images was done.

According to the determined protocol DIR sequence was done with: slice thickness 6 mm, basic resolution 224 x224, FOV 23 mm, Number of acquisition 1, TI 2700, TR 10000, TE 110, T2 sequence was done with: slice thickness 6 mm, basic resolution 256 x256, FOV 23 mm, Number of acquisition 2, TR 5500 TE 105.

All the series of images were done in axial plane of section due to better display of subcortical and juxtacortical plane. [9] The lesions were carefully examined in order that the possibility of one lesion evaluating two or more times does not occur.

### Statistical analysis

Statistical processing of data included descriptive statistics (absolute and relative frequencies, cumulative, arithmetic means and standard deviations), parametric tests (T-test, Paired Samples Test). The processing of selected data was done by statistical software package – SPSS 20.0. The survey covered 22 examinees, 14 female (63.6%) and 8 (36.4%) male, age 16 - 58 years.

The analysis of number of lesions on different sequences was done. The number of lesions was expressed as the span between mean values, ± standard deviation and standard mistakes.

Statistic differences in both analyses were estimated by Wilcoxon test for paired samples.

The lesions are counted and classified according to anatomic regions as infratentorial, periventricular, juxtacortical, intracortical.

Besides the analysis of number of lesions and visualisation of presence of motion artefacts, the presence of flow artefacts was analysed. Two experienced neuroradiologists wrote radiological findings. According to the acquired results in an infratentorial zone of brain the visualisation of lesions was highest on T2 sequence N=15, mean 5.00, std.dev. 4.359, T2 FLAIR N=8, mean 3.63, std.dev.3.249, DIR N=8, mean 3.75, std.dev. 3.151.

In the periventricular zone of the brain, the visualisation of lesions was highest on DIR sequence N=19, mean 10.42, std.dev. 9.258, T2 N=17, mean 8.65, std.dev. 8.448, T2 FLAIR N=17, mean 8.53, std.dev. 7.930. In the juxtacortical zone of the brain, the visualisation of lesions was highest on DIR sequence N=20, mean 8.10, std.dev. 5.077, T2 N=20, mean 7.5, std.dev. 4.560, T2 FLAIR N=19, mean 7.95, std.dev. 4.648. In the intracortical zone of the brain, the visualisation of lesions was highest on DIR sequence N=9, mean 3.75, std.dev. 3.151, T2 N=8, mean 3.63, std.dev. 3.249, T2 FLAIR N=8, mean 3.63, std.dev. 3.249.

During the analysis, the flow artefacts were noticed, and they were present in highest number on DIR sequence in 18 (81.8%) patients, then on T2 FLAIR sequence in 3 (13.6%) patients, while flow artefacts were not noticed on T2 sequence (0%).

The analysis of results was done by t-test for paired samples whereby it was determined that there is a statistically significant difference (p<0.01) between the DIR sequence compared to FLAIR and T2 sequence in showing demyelinating plaques.

| Region          | DIR        | FLAIR      | T2         |
|-----------------|------------|------------|------------|
| Infratentorial  | 3.75±3.151 | 3.63±3.249 | 5.00±4.359 |
| Periventricular | 10.42±9.258| 8.53±7.930 | 8.65±8.448 |
| Juxtacortical   | 8.10±5.077 | 7.95±4.648 | 7.50±4.560 |
| Intracortical   | 3.75±3.151 | 3.63±3.249 | 3.63±3.249 |
Table 2: Analysis of results for paired samples

| Pair | Region | Sequence 1 | Sequence 2 | N  | Correlation | Sig.(p) |
|------|--------|------------|------------|----|-------------|---------|
| 1    | Infratentorial zone | T2 & DIR |           | 15 | 0.799       | 0       |
| 2    | Infratentorial zone | FLAIR & DIR |       | 15 | 0.929       | 0       |
| 3    | Periventricular zone | T2 & DIR |           | 16 | 0.959       | 0       |
| 4    | Periventricular zone | FLAIR & DIR |       | 16 | 0.958       | 0       |
| 5    | Juxtacortical | T2 & DIR |           | 20 | 0.943       | 0       |
| 6    | Juxtacortical | FLAIR & DIR |       | 19 | 0.979       | 0       |
| 7    | Intracortical | T2 & DIR |           | 8  | 0.994       | 0       |
| 8    | Intracortical | FLAIR & DIR |       | 8  | 0.994       | 0       |

Discussion

Standard sequences of magnetic resonance T1 weighted and T2 weighted sometimes do not show sufficiently clearly demyelinating plaques on the patient’s brain. High signal of cerebrospinal fluid on standard T2 w sequence can mislead the radiologist in the interpretation of the radiological image so that the lesions stationed near the liquor space are poorly visible. For those reasons it is necessary to use the sequences that enable the signal attenuation of fat and water, for demyelinating changes to be more visible. In DIR imaging, normal appearance of white matter and signal of cerebrospinal fluid are completely repressed that brings to better demarcation of MS lesions. In our survey the main aim was to compare the possibility of detection of demyelinating plaques on DIR sequence compared to T2 W and FLAIR sequences.

According to acquired results in an intracortical zone of brain the visualisation of lesions was highest on DIR sequence with mean value 3.75, compared to T2 with mean value 3.151 and T2 FLAIR with mean value 3.63 with statistical significance on the level p<0.05.

In the survey of Zahra Abidi and ass. DIR sequence showed significantly more lesions compared to T2 and FLAIR sequence. [9] Gulhan Ertan and associates have also cited that DIR sequence showed more lesions in intracortical zone compared to T2 and FLAIR sequences. [10]

In the juxtacortical zone of the brain, the visualisation of lesions was the highest on DIR sequence with mean value 8.10, on T2 sequence 7.5, T2 FLAIR 7.95. According to the survey of Abdelaziz M., in the detection of juxtacortical zone DIR sequence had the highest number of displayed lesions compared to T2 and FLAIR sequences. [11]

In the periventricular zone of the brain, the visualisation of lesions was the highest on DIR sequence 10.42, T2 8.65, T2 FLAIR 8.53. According to the acquired results in infratentorial zone of brain the visualisation of lesions was the highest on T2 sequence with mean value 5.00, T2 FLAIR 3.63, and on DIR 3.75. In the infratentorial zone, there were also flow artefacts, that made the analysis on DIR and FLAIR sequences more difficult, while on T2 sequence such artefacts were not noticed. Favareto and ass. conducted a similar survey where PSIR and DIR images were compared, and DIR sequence failed to detect some plaques, especially small lesions located near the sigmoid sinus, in the region where flow artefacts interfere with the tissue signal. [12]

Conclusion

From this study, we concluded that the DIR sequence is superior in detecting the demyelinating lesions of brain compared to standard sequences T2 and FLAIR. DIR sequence is a valuable tool for the detection of demyelinating lesions that should be a standard part of every MRI protocol for multiple sclerosis. Its disadvantage is the appearance of flow artefacts in infratentorial zone of brain.

Conflict of Interest

There are no conflicts of interest to declare by any of the authors of this study.

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