Comparison of proton density MRI and T2-Weighted Fast Spin Echo for the Detection of Cervical Spinal Cord Multiple Sclerosis Lesions

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Abstract:

Background: The prevalence of spinal cord lesions is high in multiple sclerosis particularly in the cervical cord, and their detection can assist in both the diagnosis and follow-up of the patients. For spinal multiple sclerosis, MRI is considered the first line investigation.

Objective: To evaluate the value of sagittal 1.5 Tesla proton density-fast spin echo (PD-FSE) MRI in the detecting and increasing conspicuity of multiple sclerosis lesions in cervical cord in comparison with sagittal T2 fast spin-echo (T2-FSE) MRI.

Patients and Methods: A cross sectional study carried out from 3rd of January 2017 to 1st of January 2018 in the MRI department of Al-Imamein Al-Kadhimein Medical City, and included 60 selected patients with a known diagnosis of multiple sclerosis. All patients were examined with 1.5 T sagittal PD-FSE, T2-FSE and axial gradient recalled-echo (GRE) MRI.

Results: Sixty patients with cervical multiple sclerosis were enrolled in the study, 146 (100%) lesions were detected by PD-FSE imaging, while T2 detected 105 (71.9%), 41 more lesions (28%) were detected by PD-FSE imaging, (P-value <0.001). All extra lesions were confirmed on axial imaging. In 13 patients (21.6%) one lesion or more had been detected on sagittal PD-FSE imaging while on sagittal T2-FSE imaging, no lesion were detected. On PD-FSE imaging, 17 long lesions were detected in 16 patients (26.7%) while 7 long lesions in 7 patients (11.7%) were detected by T2-FSE imaging. So, in 9 patients (16.7%) 10 lesions were detected as long in PD-FSE while short lesion in T2– FSE, the detection of long lesions by PD-FSE was significantly higher than in T2– FSE (100% vs 71.9% with p-value of 0.002). The mean lesion contrast to cord ratio was significantly higher in PD-FSE as compared to T2-FSE (PD-FSE, 79±2.0, against T2-FSE, 61± 2.6; P-value <0.001).

Conclusion: Sagittal proton density was more efficient and more accurate in the detection of cervical cord lesions than sagittal T2-FSE sequence, when used in conjunction with sagittal T2-FSE; it can raise the diagnostic assurance via improving the visualization of the lesions.

Keywords: Cervical Multiple Sclerosis, Proton density MRI, T2-Weighted Fast Echo MRI.

Introduction:

Multiple sclerosis (MS) is considered the most common acquired demyelinating disorder of the central nervous system (CNS) affecting 2.5 million people around the world. (1, 2) It is the second most common reason of neurological impairment in early adulthood, after trauma.(3) Involvement of the spinal cord is frequent in MS, predominantly in the cervical cord.(4) As silent cord lesions are uncommon in normal aging and in other neurologic diseases, therefore the detection of cord lesion is diagnostically valuable.(5) Damage of the spinal cord is thought to be the cause of the majority of clinically noticed deficits. The spinal cord is less than 1/10th of the brain size; therefore, even small lesions may cause significant impairment of all functions that are derived from the column.(6)

Clinically, magnetic resonance imaging (MRI) is considered the "gold standard" technique in the diagnosis of demyelinating lesions. MS in some patients has recently been diagnosed after a clinically isolated syndrome via new diagnostic criteria on MRI. The Study of the development of MS pathology by using MRI techniques is important to improve the understanding of the pathophysiological mechanisms that underlie the course of the disease. (7) Since the integration of MRI into the International Panel criteria,(8) there has been an increase in the global effort to standardize MRI protocols. The Consortium of Multiple Sclerosis Centers (CMSC) clinical guidelines recommend the application of sagittal T1-weighted (T1-WI) and sagittal T2-weighted (T2-WI) MRI and either short tau inversion recovery (STIR) or sagittal proton density (PD) as core sequences of the spinal cord.(9) The aim of the current study was to evaluate the value of sagittal 1.5 T proton density fast-spin echo (PD-FSE) MRI in detecting and

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increasing conspicuity of multiple sclerosis lesions in the cervical cord in comparison with sagittal T2 fast spin-echo (T2- FSE) MRI.

Patients and methods

Study design: A Cross-sectional study was carried out from 3rd of January 2017 to 1st of January 2018. Eighty-seven patients with known diagnosis of MS were included in this study. The study was performed at the MRI department at Al-Imamein Al-Kadhimein Medical City. The diagnosis of MS was confirmed by a neurologist during a previous clinical evaluation and previous MRI findings. Informed consent was obtained from all patients. Inclusion criteria: Any patient with a definitive diagnosis of brain MS. Exclusion criteria: Patients with claustrophobia, any lesion less than 3 mm in size, patients with cervical spinal canal stenosis due to degenerative changes or any other cause leading to compression of the spinal cord and myelopathy at the level of the detected cord lesion. The local ethics committee of the Arab board of medical specialization approved this study. Diagnosis: Diagnostic criteria for MS include clinical and laboratory assessments, emphasizing the need to demonstrate dissemination of lesions in space (DIS) and time (DIT) and to exclude alternative diagnoses. The diagnosis can be made on clinical grounds by the so-called McDonald Criteria of the International Panel on Diagnosis of MS.(7) McDonald diagnostic criteria for multiple sclerosis include clinical, radiographic, and laboratory criteria. Criteria: The diagnosis of multiple sclerosis is made if there is fulfillment of either of these five categories of criteria, depending on how many clinical attacks have occurred (7).

Table 1: McDonald criteria for the diagnosis of multiple sclerosis (7).

Clinical (attacks)	Objective lesions	Additional requirements
2 or more	2 or more	None; clinical evidence will suffice (additional evidence desirable but must be consistent with MS)
2 or more	1	Dissemination in space by MRI or positive CSF* and two or more MRI lesions consistent with MS or further clinical attack involving different site
1	2 or more	Dissemination in time by MRI or second clinical attack
1(mono-symptomatic)	1	Dissemination in time by MRI or positive CSF and two or more MRI lesions consistent with MS and dissemination in time by MRI or second clinical attack
0 (progression from onset)	1	Positive CSF and dissemination in space by MRI evidence of nine or more T2 brain lesions or two or more cord lesions or 4–8 brain and one cord lesion or positive VEP† with 4–8 MRI lesions or positive VEP with less than four brain lesions plus one cord lesion and dissemination in time by MRI or continued progression for 1 year

II. Methods: MRI examination: All patients underwent MRI examination using 1.5 Tesla MR Unit (Magnetom Avanto, 2011) via 16-channel neck matrix coil. All patients underwent sagittal T2WI-TSE. Technique : All patients were examined in supine position and submitted to MRI protocol for detection of MS lesion in keeping with the clinical guideline of CMSC which included: Sagittal T1-FSE, sagittal T2-FSE, sagittal PD-FSE, and axial gradient recalled-echo (GRE) T2* along the cervical spinal cord from C1-2 to D1. Protocol :The following MRI sequences with their parameters were done for all patients: T1-WI in sagittal plane, as follows: FOV =220 mm, Matrix=256, Voxel size (0.4/0.4/3 mm), Slice Thickness=3 mm, Turbo factor=38, TR =550 msec, TE =10 msec, Number of signal averaged =2, Bandwidth=150 pixel/Hertz, Flip angle=150 degree and an acquisition time of 4 min plus 18 sec. T2-WI in sagittal plane, as follows: FOV= 220 mm, Matrix=256, Voxel size = (0.7/0.7/3 mm), Slice Thickness=3 mm, Turbo factor=18, TR =3130 msec, TE =96 msec, Number of signal averaged 2, Bandwidth =191 pixel/Hertz, Flip angle=150 degree and an acquisition time of 3 min plus 30 sec. PD-WI in sagittal plane, as follows: FOV= 220 mm, Voxel size = (0.7/0.7/3 mm), Slice Thickness=3 mm, Turbo factor =5, TR=2500 msec, TE=31msec, Number of signal averaged= 2, Bandwidth=200 pixel/Hertz, Flip angle=150 degree and an acquisition time of 2 min plus 56 sec. Axial GRE T2* in axial plane, as follows: FOV=200 mm, Matrix =256, Voxel size =0.4/0.4/3 mm, Slice Thickness=3 mm, Turbo factor=16, TR=860 msec, TE=19.8 msec, Number of signal averaged 2, Bandwidth =250 pixel/Hertz, Flip angle=150 degree and an acquisition time of 5 min plus 11 sec.

Steps of lesion Detection:

- Qualitative Lesion Analysis :We localized MS lesions by dividing the cervical spinal cord into 7 segments from C1 to C7. The lesions of MS were assessed separately and independently by two radiologists. Each lesion was accepted by consensus. The Trained specialist radiologists independently identified MS plaques as hyper-intense compared to normal appearing background cord in PD-FSE, T2-FSE and axial GRE images. Lesions appear on one of the mentioned sequences were included only if were detected on the axial T2WI-FSE. A long lesion is defined as contiguous involvement of more than 2 segments detected on sagittal T2WI-TSE, sagittal PD-TSE, or sagittal STIR-TSE were included. The selection of true lesions and distinction from false findings was made on biplanar basis, so if the lesion was identified by either sagittal PD-FSE or sagittal T2-FSE single sequence, it should be proved by an axial GRE thus the axial image was the reference for the sagittal sequences in each lesion; by this requirement the artifacts will be diminished. We had made changes to the window widths and levels in our sequences to improve lesion detection.
- Quantitative Lesion Analysis :Another way to improve image perception and avoid spurious

lesions was by measuring Lesion conspicuity by means of measuring lesion contrast, cord contrast and noise, this was achieved by obtaining a region of interest (ROIs) within the lesion, normal cervical cord, and background air in the nasopharynx. The mean signal intensities created in the ROIs of each one was recorded then measurement of normalized lesion to cord contrast ratio (LCCR) and a lesion contrast to noise ratio (LCNR) for each sequence (sagittal PD-FSE and sagittal T2 – FSE) were performed using the OsiriX Software. For each sequence, the LCCR estimation was reached using the average signal intensities obtained in the ROIs, as in the formula "LCCR= (S lesion _ S cord)/ (S cord)". S lesion is the signal intensity of the lesion and S cord is the signal intensity of normal cord. (10) For each sequence, the LCNR estimation was reached by measuring the difference between the S lesion and S cord against the level of background noise represented by the background of SD air in the nasopharynx as calculated in the formula: "LCNR= (S lesion _ S cord)/ (SD air)". (10)

Statistical analysis: Data analysis was performed using SPSS Version 22.0 for Windows. Continuous variables were presented as mean with standard deviation while discrete variables were presented as numbers and percentages. Significance of difference in means was tested with t-test and Wilcoxon signed ranks test as appropriate. P-values <0.05 were considered statistically significant.

Results:

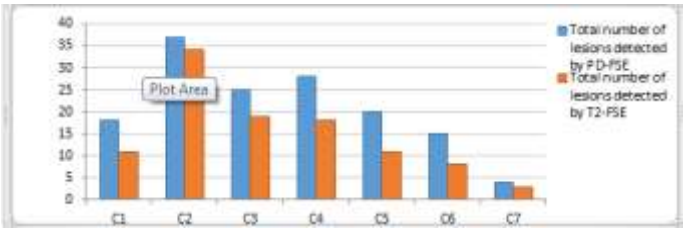
Eighty-seven patients with a known diagnosis of multiple sclerosis were included in the study. They were 29 (33.3%) males and 58 (66.7%) females. All were examined by MRI, and 27 patients were excluded due to lack of cervical MS lesions. Hence the incidence of cervical spinal cord MS was found to be 69%. Sixty patients with cervical MS were eventually included in the study; with an age range of 17 - 48 years (mean±SD: 40.6±2.7 years). There were 40 females (66.7%) and 20 males (33.3%), with a male: female ratio of 1:2. No statistically significant variations in age or gender between the 60 patients in regard to presence of cervical cord MS lesions (P-value > 0.05). Detection of lesions by PD-FSE was statistically significantly higher than sagittal T2-FSE (P-value <0.001). The number and percent of detected cervical MS lesions in each MRI sequence are shown in table 2.

Table 2: Number and percent of detected cervical MS lesions in each MRI sequence

MRI sequence	Min	Max	Total	Detection rate	P value
Sagittal PD-FSE	1	7	146	100%	<0.001
Sagittal T2-FSE	0	6	105	71.9%	
Axial GRE	1	7	146	100%	
Sagittal PD-FSE but not by sagittal T2-FSE	1	2	41	28.1%	

None of the patients with abnormal findings of T2-FSE imaging had normal findings in PD-FSE imaging. In 29patients (48.3%) PD-FSE detected more lesions than T2-FSE and in 13 patients (21.6%) one lesion or more was detected on sagittal PD-FSE imaging while on sagittal T2-FSE imaging, no lesion was detected. The number of MS lesions detected by PD-FSE was higher than the number of lesions detected by T2-FSE and this was apparent at all vertebral levels.

Figure 1: Distribution of MS cervical cord lesions, detected by PD-FSE imaging and T2-FSE imaging.



In 16 patients (26.7%), 17 long lesions were detected on PD-FSE imaging while 7 long lesions in 7 patients (11.7%) were detected on T2-FSE imaging. All of the long lesions detected on PD-FSE were shown by axial GRE as continuous lesions. So, in 9 patients (16.7%) 10 lesions were detected as long on PD-FSE while they were either absent, short or interrupted lesions in T2 – FSE. PD-FSE detected 59% (10/17) more long lesions than T2-FSE, making the detection of long lesions by PD- FSE significantly higher than T2 – FSE (p value 0.002) as shown in table 3.

Table 3: Total number and significance of long cervical cord lesions

MRI sequence	Min	Max	Total	P value
Sagittal PD-FSE	0	2	17	0.002
Sagittal T2-FSE	0	1-	7	
Axial GRE or axial T2-FSE	0	2	17	
Sagittal PD-FSE, not via T2-FSE	0	1	10	

The mean value for the estimated LCCR for PD-FSE was 0.29 and for T2-FSE was 0.30 so they had approximately similar LCCR (P-value 0.33) but the mean LCNR was significantly higher in PD-FSE as compared to T2-FSE (PD-FSE, 79±2.0, versus T2-FSE, 61±2.6; P value <0.001) as shown in table 4.

Table 4: Mean value of LCCR and LCNR for PD-FSE and T2-FSE

LCCR and LCNR	Mean	SD	P value
LCCR PD-FSE	0.29	0.01	0.33
LCCR T2-FSE	0.30	0.01	
LCNR PD-FSE	79	2.0	<0.001*
LCNR T2-FSE	61	2.6	

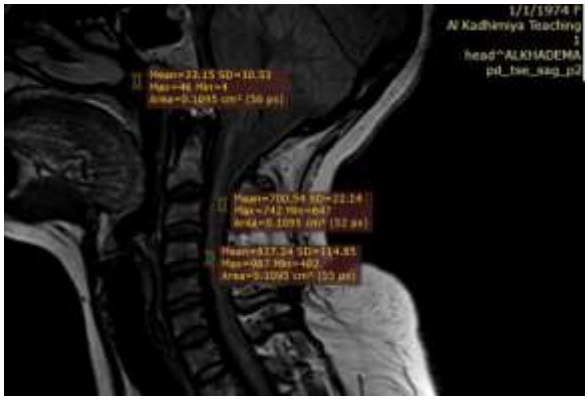


Figure 2: Quantitative method of lesion analysis

Sagittal PD-FSE imaging illustrates the method of measuring mean lesion contrast (817), mean cord contrast. (700) and noise represented by standard deviation of air in the nasopharynx (SD air =10.5) for estimation of LCNR and LCCR respectively.

Discussion:

MS is an inflammatory disorder of the CNS which affects both the brain and the spinal cord. MRI findings in the spinal cord are essential to create an accurate diagnostic and prognostic information of MS.(11) The CMSC Guidelines have recommended PD, T2 WI in standard imaging protocol of MS of the spinal cord. (12) In the current study, PD-FSE MR sequence detect 41 more lesions than T2-FSE; In 13 (21.6%) patients, one lesion or more were detected on sagittal PD-FSE imaging which is better than sagittal T2-FSE imaging. Better performance of PD-FSE imaging was obvious at all vertebral segmental levels. PD-FSE imaging detected 10 long lesions (16.7% patients) which were either absent or reported as small multiple lesions on sagittal T2-FSE imaging. These results agree with those of Chong, et al (13) who found that PD-FSE imaging could detect more lesions (32%) than T2-FSE. On PD-FSE imaging, Long lesions were detected in 27% of the patients while on T2-FSE imaging they were detected in 13% of the patients. The better identification of long lesion in this study is in agreement with Darin et al (14) who stated that diffuse or long lesions are particularly better detected in PD-WI sequence rather than other sequences, in addition to its accuracy in identifying focal lesions. However, theses result are in discordance with the findings of study of fourteen Australian institutes published by Curley et al (15), who concluded that 75% of spinal cord MRI examinations had not followed the CMSC guidelines and depended only on T2-WI. These results can be attributed to the smaller number of examined patients in their study, where PD- WI was done in only two out of 79 cord examinations (2.5%), and STIR imaging was performed in 18 out of (79) spinal cord examinations (23%). Different study designs had compared T2-WI with other novel sequences. In all of these previous studies, T2-weighted sequence was constantly outperformed by other MR sequences. (16,17) Furthermore, there are valuable histopathological results that support the usage of PD-MRI. A post-mortem study evaluated the association between both 4.7 Tesla and 1 Tesla PD-FSE MR imaging and histopathological results for 19 patients with MS where all spinal cord regions labelled as abnormal by neuropathologist which were also assessed as abnormal in PD-WI. (18) The higher detection rate of MS cord lesions by PD could be attributed to the good delineation of the central grey matter and white matter of the spinal cord afforded by PD-WI, and by its long TR produced a T1 effect made the CSF to appear hypo-intense relative to the cord so it offered a well-defined outline of the anatomy of the spinal cord and was not distorted by CSF artefacts. (19)The superior lesion detection in PD MRI is aided by the higher lesion conspicuity in that sequence due to the greater LCNR of PD-FSE in the current results. The mean LCNR was significantly higher in PD-FSE as compared to T2-FSE (PD-FSE, 79 ± 2.0, versus T2-FSE, 61±2.6), providing greater diagnostic confidence, whereas lesion contrast was not significant statistically from background cord contrast so the LCCR was nearly similar between PD-FSE and T2-FSE (for PD-FSE was 0.29 and for T2-FSE was 0.30, P-value = 0.33). Similar results were reported by Chong et al (12). Karavasilis et al. (20) had noticed on comparison between two sequences: Proton density combined with fat suppression sequence (SPAIR) and T2-FSE combined with spectral adiabatic inversion recovery sequence for fat suppression (SPAIR) in the detection of cervical MS plaque. LCCR and LCNR were calculated, they found that lesions on PD combined with SPAIR had a statistically significant higher contrast for both LCCR and LCNR. Bot et al (21) on the other hand, found that PD-CSE had a greater contrast to noise ratio when compared with T2- CSE sequence but the end result was not statistically significant. The increased LCNR in PD-FSE can be explained by the high spin density of MS lesions at this sequence as they detect lesions of MS which are associated with an increase in PD, also the additional T1 effect of PD-FSE yielded good contrast between CSF and spinal cord. (19) However, T2-WI by its long TEs and long echo trains was more capable in displaying extramedullary and extradural disorder than PD-FSE. (22) In the present study, we evaluated the images by comparing axial image to linked sagittal images. Weier et al. (23) found that biplanar imaging enhances the accuracy of detection of the lesion and minimizes the possibility that artefacts could interfere with interpretability of the study. However, sagittal acquisition, rather than axial sections, permitted spinal cord coverage in the least time without changing of matrix acquisition in size of the subject– dependent manner. (22) In this study the use of axial GRE T2 * WI sequence rather than axial T2 WI as the reference for sagittal sequences could confirm the 146 MS cervical lesions that were detected by sagittal PD-FSE. Usually GRE-based sequences are not involved in

the protocols of MS spinal cord imaging (24), but previous studies reported their value for assessment clinically. A recent study has appreciated other recent axial sequences (GRE-based) for the detection of MS lesion, giving similar findings. (25,26) This can be attributed to the brilliant discrimination between the butterfly shaped grey matter and contiguous white matter of spinal cord by the T2*-weighted sequence. (27) It must be noticed that total scan time for the GRE sequences in the current study is equivalent to that of the conventional T2- FSE, so it does not require an increase of the total scan-time. The strength of the current study includes using both quantitative and qualitative analyses and the use of fast imaging sequences in addition to spinal phased-array coils, all of which cause a reduction of image noise and scan time and avoid ghost artefacts from the large vessels and heart seen on the CSE images. The limitations of this study are the use of 1.5T MRI scanner, which was selected to raise the generalization of the research findings to smaller institutes and clinical applications when 3T MRI scanners are unavailable. Though 3T MRI improves the detection rate of PD lesion volume in the brain in comparison with 1.5T MRI, till now no such data are existing for the spinal cord. (28) Moreover, in this study, STIR sequences had not been examined. The current study protocol, which is consistent with the guidelines of CMSC (9), as sagittal proton density or STIR may be achieved as core spinal cord sequences. Another limitation of the current study is the lack of pathological confirmation, which requires a radiologic standard reference and a technique that depicts the greatest number of lesions.

Conclusion:

Sagittal PD-FSE is more efficient and more accurate in the visualization of cervical spinal cord MS lesions than sagittal T2-FSE sequence at 1.5T MRI scanners; it detected lesions that T2-FSE missed.

Authors' Contributions:

All authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication.

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في الكشف عن أضرار FSE-T2 مقارنة التصوير بالرنين المغناطيسي من خلال تسلسل كثافة البروتون وتسلسل التصلب المتعدد التي تصيب الحبل الشوكي العنقي

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الخلاصة :

خلفية الدراسة: آفات الحبل الشوكي منتشرة بشكل كبير في مرض التصلب العصبي المتعدد على وجه التحديد في الحبل العنقي، ويمكن أن يساعد اكتشافها في التشخيص ومتابعة المريض.
هدف الدراسة: الغرض من هذه الدراسة هو تقدير دور التصوير بالرنين المغناطيسي باستخدام تسلسل كثافة البروتون بالمقطع السهمي 1.5 تسلا لزيادة كشف ووضوح آفات الحبل الشوكي لمرضى التصلب المتعدد بالمقارنة مع تسلسل FSE-T2 بالمقطع السهمي.
الطريقة: أجريت هذه الدراسة على مدى سنة واحدة من يناير 2017 إلى يناير 2018 في قسم التصوير بالرنين المغناطيسي في مدينة الإمامين الكاظمين (ع) الطبية، وشملت 60 مريضا مشخصين بمرض التصلب العصبي المتعدد. تم التصوير بالرنين المغناطيسي لجميع المرضى باستخدام تسلسل كثافة البروتون بالمقطع السهمي 1.5 تسلا، وتسلسل FSE-T2 بالمقطع السهمي واستخدام تسلسل GRE بالمقطع المحوري كمرجع لتصوير الحبل الشوكي العنقي.
النَتائِج: تم شمل ستين مريضا مصاب بآفات الحبل الشوكي، عدد الآفات التي تم الكشف عنها من قبل تسلسل كثافة البروتون كان 146 (100٪)، بينما في T2 كان 105 (71.9٪)، تم الكشف عن 41 آفة أخرى (28٪) من قبل التصوير بواسطة تسلسل كثافة البروتون، (P value <0.001). تم تأكيد جميع الآفات الإضافية على التصوير المحوري. في 13 مريضا (21.6٪) تم الكشف عن واحد أو أكثر من الآفة على التصوير بتسلسل كثافة البروتون السهمي في حين لم يتم الكشف عن اي آفة على التصوير السهمي بتسلسل FSE- T2. تم الكشف عن 17 آفة طويلة في 16 مريضا (26.7٪) على التصوير تسلسل كثافة البروتون و7 آفات طويلة في 7 مرضى (11.7٪) على التصوير تسلسل .FSE- T2 في 9 مرضى (16.7٪) تم الكشف عن 10 آفات طويلة في تسلسل كثافة البروتون كانت عل شكل آفة قصيرة في T2 -FSE، الكشف عن الآفات الطويلة من قبل تسلسل كثافة البروتون كان أعلى بكثير مما كانت عليه في T2 -FSE (p value 0.002)، بينما كان معدل نسبة تباين الآفة إلى الحبل الشوكي أعلى بكثير في تسلسل كثافة البروتون بالمقارنة مع تسلسل FSE- T2 تسلسل كثافة البروتون، (2.0 ± 79)، مقابل تسلسل FSE- T2 (2.6±61)؛ (P <0.001).
الاستنتاج: التصوير بالمقطع السهمي باستخدام تسلسل كثافة البروتون كان أكثر كفاءة وأكثر دقة في تقدير آفات الحبل الشوكي مقارنة مع تسلسل FSE- T2بالمقطع السهمي، عندما تستخدم بالاشتراك مع تسلسل FSE- T2 يمكن أن يزيد من الثقة التشخيصية من خلال الرؤية الأفضل لهذه الآفات.
مفتاح الكلمات: مرض التصلب العصبي العنقي، كثافة البروتون بالمقطع السهمي، FSE-T2 بالمقطع السهمي