

BALANCE REHABILITATION UNIT (BRU™) POSTUROGRAPHY IN RELAPSING-REMITTING MULTIPLE SCLEROSIS

Natália Kessler¹, Maurício Malavasi Ganança², Cristina Freitas Ganança³, Fernando Freitas Ganança⁴, Sabrina Chiogna Lopes⁵, Ana Paula Serra⁵, Heloisa Helena Caovilla⁶

1. Master of Sciences, Human Communication Disorders, Federal University of São Paulo, São Paulo, Brazil;
2. PhD, Head Professor of Otorhinolaryngology, Federal University of São Paulo, Brazil;
3. PhD, Human Communication Disorders, Federal University of São Paulo, São Paulo, Brazil;
4. PhD, Adjunct Professor of Otology-Neurotology, Federal University of São Paulo, Brazil;
5. Master of Sciences, Otorhinolaryngology Head and Neck Surgery, Federal University of São Paulo, São Paulo, Brazil;
6. PhD, Associate Professor of Otology-Neurotology, Federal University of São Paulo, São Paulo, Brazil;

Natália Kessler - Rua Martiniano de Carvalho 629 / apto 22 – 01321-001 Bela Vista - São Paulo SP – Brasil. (E-mail: natalia_kessler@hotmail.com)

Received 22 June 2010, received in final form 15 December 2010. Accepted 29 December 2010.

Abstract- Objective: To evaluate balance control with Balance Rehabilitation Unit (BRU™) posturography in patients with multiple sclerosis (MS). **Method:** A cross controlled study was performed including 39 relapsing-remitting multiple sclerosis patients with scores less than or equal to 4 in the Expanded Disability Status Scale (EDSS), and a homogeneous control group consisting of 65 healthy individuals, matched by the age and gender. The experimental group was distributed according to the EDSS scale scores in 0-2.5 and 3-4. To assess the vestibular system function, the patients underwent a neurotological evaluation, including posturography of the Balance Rehabilitation Unit (BRU™). **Results:** Statistically significant differences were observed when comparing the values of the sway velocity and the ellipse area of the MS 0-2.5 group with the control and the MS 3-4 group with the control. A statistically significant difference was verified between the MS 0-2.5 and the MS 3-4 groups in the condition 3 ellipse area values. **Conclusion:** The evaluation of the balance control with posturography of Balance Rehabilitation Unit (BRU™) enables the identification of abnormalities of the sway velocity and confidential ellipse in patients with relapsing-remitting multiple sclerosis.

Key Words: multiple sclerosis, dizziness, vestibular system evaluation.

Posturografia do *balance rehabilitation unit (BRUTM)* na esclerose múltipla recorrente-remitente

Resumo- Objetivo: Avaliar o equilíbrio corporal à posturografia do *Balance Rehabilitation Unit (BRUTM)* em pacientes com esclerose múltipla (EM). **Método:** Estudo transversal controlado em 39 pacientes com esclerose múltipla do tipo recorrente-remitente, com pontuação menor ou igual a 4 na escala de incapacidade funcional expandida, e por um grupo controle homogêneo, constituído por 65 indivíduos hígidos, homogêneo em relação à idade e gênero. O grupo experimental foi distribuído, de acordo com a pontuação da EDSS, em 0-2.5 e 3-4. Para avaliar a função do sistema vestibular, os pacientes foram submetidos a uma avaliação otoneurológica, incluindo a posturografia do *Balance Rehabilitation Unit (BRUTM)*. **Resultados:** Foram observadas diferenças significantes na comparação dos valores da velocidade de oscilação e da área de elipse do grupo EM 0-2.5 com o controle e do grupo EM 3-4 com o controle; diferença significativa foi verificada entre os grupos EM 0-2.5 e EM 3-4 nos valores da área de elipse na condição três. **Conclusão:** A avaliação do equilíbrio corporal por meio da posturografia do *Balance Rehabilitation Unit (BRUTM)* possibilita a identificação de anormalidades da velocidade de oscilação e da área de elipse em pacientes com esclerose múltipla.

Palavras-Chave: esclerose múltipla, tontura, testes de função vestibular.

Multiple sclerosis (MS) is an autoimmune demyelinating disease of the central nervous system. It is considered the commonest cause of neurological disability in young adults and can be classified in two major clinical forms: relapsing-remitting and primary progressive¹.

The relapsing-remitting MS occurs in approximate 85% of the cases; the most common initial clinical manifestations are pyramidal, sensitive and cerebellar disorders². The MS preferentially affects caucasians, young adults and females³. The clinical feature of the disease in the Brazilians is similar to the one described in other countries⁴.

Progressive demyelination of vestibulo-spinal pathways fibers may cause balance disturbances⁵. In 5% of the cases, dizziness is the first manifestation of the disease⁶. Posturography may be useful not only to assess the damages of the vestibular system but also to monitor the course of the MS⁵.

The Balance Rehabilitation Unit (BRUTM) posturography developed by Medicaa[®] provides information about the position of the patients' center of pressure in ten sensorial conditions through quantitative indicators, limit of stability, ellipse area and sway velocity. Moreover, this equipment enables to select adequate balance rehabilitation exercises according to the found disorder and follows the performance of the patients⁷.

References about Balance Rehabilitation Unit (BRUTM) posturography to evaluate balance control in patients with multiple sclerosis were not found. That is the reason this research was performed.

The purpose of this research is to evaluate the balance control with the posturography of the Balance Rehabilitation Unit (BRUTM) in patients with relapsing-remitting multiple sclerosis.

METHOD

This was a cross controlled study performed in the Otolaryngology and Neurotology Discipline of the Department of Otolaryngology, Head and Neck Surgery of the Federal University of São Paulo - Paulista School of Medicine. The project was submitted to the Ethic Committee of the Institution and approved under the number 01723/07. Written consent was obtained from all the patients before enrollment.

One hundred and four patients were evaluated. Thirty-nine of them were clinically and/or laboratorially diagnosed with relapsing-remitting MS according to McDonald⁸, with scores less than or equal to 4.0 in the Expanded Disability Status Scale (EDSS)⁹, in the Neuromuscular and Autoimmune Diseases Clinic of the Neurology Discipline of the Federal University of São Paulo. Sixty-five healthy homogeneous individuals, insofar as age and gender are concerned, constituted the control group. The experimental group was distributed according to the EDSS scale score in 0-2.5 (mild disability) and 3-4 (moderate). Patients that presented outbreaks of the disease during the evaluation, with musculoskeletal or visual disorders, dementia, and neuropathy, or were incapable of understanding simple verbal instructions were excluded from this study.

Patients underwent a neurotological assessment: clinical history, ENT examination, audiological and vestibular evaluation, including posturography of the Balance Rehabilitation Unit (BRUTM). If the patient had dizziness complaint, they answered the Dizziness Handicap Inventory¹⁰, adapted to the Portuguese of Brazil¹¹ and the dizziness analogical scale¹².

The Balance Rehabilitation Unit (BRUTM) posturography assessed the postural control by measuring the limit of stability, the confidence ellipse of the body's center of pressure distribution area and the sway velocity. The confidence ellipse and the sway velocity were measured in ten different sensorial conditions on the platform: 1) standing position, eyes open; 2) standing position, eyes closed; 3) standing position on foam, eyes closed; 4) standing position, eyes open with surrounding saccadic stimulation 5) standing position, eyes open with surrounding optokinetic stimulation to the right, 6) standing position, eyes open with surrounding optokinetic stimulation to the left, 7) standing position, eyes open with surrounding optokinetic stimulation downwards, 8) standing position, eyes open with surrounding optokinetic stimulation upwards, 9) standing position, visuovestibular interaction - horizontal stimulation, 10) standing position, visuovestibular interaction - vertical stimulation. The virtual reality helmet was used on sensorial condition from four to ten. To determine the limit of stability, the patient received the instruction to sway forwards, backwards and laterally along the ankles, without neither losing balance nor using trunk strategies. Statistical analyses were performed using a Chi-Squared (χ^2) test, T-Student test, Mann-Whitney test, *Kolmogorov-Smirnov* test, Anova test e Bonferroni test. Statistical analyses were performed using SPSS 10.0 for Windows (Statistical

Package for Social Sciences, version 10.0, 1999). The significance level was set at 5% ($\alpha=0.05$).

RESULTS

Sixty-five individuals of the control group and thirty-nine patients with relapsing-remitting MS were evaluated. The control group consisted of 5 males (7.7%) and 60 females (92.3%). The MS group consisted of 4 males (10.3%) and 35 females (89.7%). There was no significant difference between the groups in relation to the gender ($p=0.653$). The control group showed an average age of 34.91 ± 13.97 years old and the experimental group showed an average age of 39.72 ± 11.78 years old. There was no significant difference between the groups in relation to the age group average ($p=0.075$). In relation to the EDSS score, the experimental group showed the minimum value of zero and the maximum of four scores (average = 1.77; standard-deviation = 1.12). According to the EDSS scale score, 29 patients (74.4%) were included in the 0-2.5 MS group and 10 (25.6%), in the 3-4 MS group.

As for vestibular system evaluation, 30 MS patients (76.9%) reported dizziness. The average total score obtained at the Dizziness Handicap Inventory was 31.60 points (standard-deviation = 21.33 points). The average score obtained at the dizziness analogical scale was 4.18 (standard-deviation = 2.69). Unterberger-Fukuda test was abnormal in 34 patients (87.2%). Nystagmography showed 22 (56.4%) patients with normal results, 15 (38.5%) with peripheral vestibular disorders and 2 (5.1%) with central signs.

As for the posturography evaluation, there was no significant difference ($p=0.144$) between the values of the limit of stability (cm^2) of the control group (average = 185.43; standard-deviation = 51.94; median = 180.00; variation = 77-298) and the values of the MS 0-2.5 group (average = 165.17, standard-deviation = 57.38, variation = 67-286) and the MS 3-4 group (average = 157.80, standard-deviation = 75.04, variation = 92-287). Table 1 displays the descriptive values and comparative analysis of the sway velocity in the ten stimulation conditions for the 0-2.5 and 3-4 multiple sclerosis groups according to the EDSS scale score, and for the control group. Table 2 displays the descriptive values and comparative analysis of the ellipse area in the ten stimulation conditions for the 0-2.5 and 3-4 multiple sclerosis groups according to the EDSS scale score, and for the control group. Statistically

significant differences were observed when comparing the values of the sway velocity and the ellipse area of the MS 0-2.5 group with the control and of the MS 3-4 group with the control. A statistically significant difference was verified between the MS 0-2.5 and the MS 3-4 groups in the condition 3 ellipse area values.

DISCUSSION

The majority of the patients with relapsing-remitting MS in our study complained about vertigo and other kinds of dizziness, probably related to vestibular system disorders, which moderately affected their quality of life. They also showed dynamic balance disorder, and vestibular disorder signals were found in approximately fifty percent (50%) of the patients. The majority of them presented peripheral vestibular disturbances and only two showed central signs.

In our study, the values of the limit of stability of the control group were similar to the values of the MS groups, indicating that there are no abnormalities in motor coordination while patients do the maximum oscillation of their body pressure center on the platform.

The values of the sway velocity and the confidence ellipse of the body's center of pressure distribution area in the ten evaluated conditions on the posturography of the Balance Rehabilitation Unit (BRUTM), in the relapsing-remitting MS groups, showed statistically significant differences ($p < 0.001$) when compared to the ones of the control group. It was observed that patients with MS showed a worse performance on steady surface with their eyes closed, foam surface with their eyes closed, and visual-vestibular interaction conditions. Patients with MS 3-4 showed worse performance on foam surface with their eyes closed when compared to the MS 0-2.5 group. These data show the involvement of static balance when there is visual deprivation and somatosensory conflict. We can compare our results with others¹³⁻¹⁵ which also demonstrated balance control disturbances in patients with MS, especially in conditions of high sensorial conflict.

It was also verified in our study that the Balance Rehabilitation Unit (BRUTM) was able to detect disturbances when it was performed on patients in the orthostatic position with their eyes closed and open. However, one study showed that the average displacement of anterior-posterior sway was not able to detect disorders in patients when the test was performed with eyes open, suggesting that the test was

more sensitive to detect balance control disturbances in patients with MS when it was performed in the orthostatic position with their eyes closed ¹⁶.

Our findings in patients with MS evaluated by Balance Rehabilitation Unit (BRU™) posturography are difficult to be compared with others from different posturography tests, because of differences between evaluation parameters and procedures. Besides the different parameters of the posturographies and different classification criteria, it is also important to consider differences among the studies as for the duration of the disease, neurological capability, and physical and sensorial conditions at the moment of the evaluation.

An exclusive routine neurological assessment might not be sufficient to analyze the balance in patients with relapsing-remitting MS without any disability or minimal neurological incapacity, according to the EDSS evaluation. Our results showed that posturography is a method that provides relevant data about the MS patients' body balance. Abnormal findings on posturography, as to the sway velocity and the confidence ellipse of the body's center of pressure distribution, might be useful not only to the diagnoses and characterization of the body balance disturbances in the MS, but also to follow the evolution of the disease under treatment. Therefore, posturography was sensitive to identify abnormalities in the balance of patients with no obvious equilibrium disturbances.

In conclusion, the evaluation of balance control with the posturography of the Balance Rehabilitation Unit (BRU™) enables the identification of abnormalities of the sway velocity and confidence ellipse of the body's center of pressure distribution area in patients with relapsing-remitting multiple sclerosis.

References

1. Bar-Or A, Oliveira EML, Anderson DE, Hafler DA. Molecular pathogenesis of multiple sclerosis. *J Neuroimmunol* 1999;100:252-259.
2. Lublin FD, Reingold SC. Defining the clinical course of multiple sclerosis. *Neurology* 1996;46:907-911.
3. Kurtzke JF. Epidemiologic contributions to multiple sclerosis: an overview. *Neurology* 1980;30:61-79.

4. Oliveira EML, Annes M, Oliveira ASB, Gabbai AA. Esclerose múltipla: estudo clínico de 50 pacientes acompanhados no Ambulatório de Neurologia UNIFESP-EPM. *Arq Neuropsiquiatr* 1999;57:51-55.
5. Shimizu K, Murofushi T, Sakurai M, Halmagyi M. Vestibular evoked myogenic potentials in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2000;69:276-277.
6. Mangabeira Albernaz PL, Ganança MM, et al. Aspectos otoneurológicos da esclerose múltipla: caso clínico. *Acta AWHO* 1983;2:35-48.
7. BRUTM. Unidade de Reabilitação do Equilíbrio. Manual do usuário. Versão 1.0.7. Versão do Software: 1.3.5.0. Uruguai: Medicaa, 2006.
8. McDonald WI, Compston A, Edan G, Goodkin D, Hartung HP, Lublin FD et al. Recommended diagnostic criteria for multiple sclerosis: guidelines from the international panel on the diagnosis of multiple sclerosis. *Ann Neurol* 2001;50:121-127.
9. Kurtzke JF. Rating neurological impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* 1983;33:1444-1452.
10. Jacobson GP, Newman CW. The development of the dizziness handicap inventory. *Otolaryngol Head Neck Surg* 1990;116:424-427.
11. Castro ASO, Natour J, Gazzola JM, Ganança FF. Dizziness Handicap Inventory: adaptação cultural para o português brasileiro. *Pró-Fono Rev Atualiz Científ* 2007;19:97-104.
12. Whitney SL, Herdman SJ. Physical therapy assessment of vestibular hypofunction. In: Herdman SJ, (Ed). *Vestibular rehabilitation*. Philadelphia: FA. Davis; 2000. p. 336.
13. Williams NP, Roland PS, Yelli W. Vestibular evaluation in patients with early multiple sclerosis. *Am J Otol* 1997;18:93-100.
14. Nelson SR, Di Fabio RP, Anderson JH. Vestibular and sensory interaction deficits assessed by dynamic platform posturography in patients with multiple sclerosis. *Ann Otol Rhinol Laryngol* 1995;104:62-68.
15. Jackson RT, Epstein CM, De l'Aune WR. Abnormalities in posturography and estimations of visual vertical and horizontal in multiple sclerosis. *Am J Otol* 1995;16:88-93.
16. Daley ML, Swank RL. Quantitative posturography: use in multiple sclerosis. *IEEE Trans Eng* 1981;28:668-671.

Table 1. Average values, standard deviations and p-values of sway velocity in the ten stimulation conditions for the 0-2.5 and 3-4 multiple sclerosis groups according to the EDSS scale score and control group.

| Sway velocity (cm/s) | | | | |
|--|----------|---------|--------------------|--|
| Sensory conditions in BRU | Group | Average | Standard deviation | p Value |
| 1. SS/ EO/ non stimulus | MS 0-2.5 | 0.95 | 0.36 | <0.001 ^a MS 0-2.5 x MS 3-4 =1.000 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C =0.001 ^b |
| | MS 3-4 | 1.08 | 0.50 | |
| | control | 0.69 | 0.18 | |
| 2. SS/ EC | MS 0-2.5 | 1.49 | 0.77 | <0.001 ^a MS 0-2.5 x MS 3-4 =0.257 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C <0.001 ^b |
| | MS 3-4 | 2.03 | 1.30 | |
| | control | 0.86 | 0.27 | |
| 3. Foam / EC | MS 0-2.5 | 3.71 | 1.90 | <0.001 ^a MS 0-2.5 x MS 3-4 =0.516 ^b MS 0-2.5 x C =0.001 ^b MS 3-4 x C =0.001 ^b |
| | MS 3-4 | 4.06 | 0.94 | |
| | control | 2.59 | 0.79 | |
| 4. SS / Saccadic | MS 0-2.5 | 1.28 | 0.55 | <0.001 ^a MS 0-2.5 x MS 3-4 =1.000 ^b MS 0-2.5 x C =0.001 ^b MS 3-4 x C =0.016 ^b |
| | MS 3-4 | 1.34 | 0.59 | |
| | control | 0.90 | 0.29 | |
| 5. SS / Bars / optokinetic to the right | MS 0-2.5 | 1.23 | 0.59 | <0.001 ^a MS 0-2.5 x MS 3-4 =0.917 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C =0.001 ^b |
| | MS 3-4 | 1.44 | 0.72 | |
| | control | 0.85 | 0.25 | |
| 6. SS / Bars / optokinetic to the left | MS 0-2.5 | 1.23 | 0.63 | <0.001 ^a MS 0-2.5 x MS 3-4 =1.000 ^b MS 0-2.5 x C =0.001 ^b MS 3-4 x C =0.009 ^b |
| | MS 3-4 | 1.37 | 0.75 | |
| | control | 0.86 | 0.28 | |
| 7. SS / Bars / optokinetic downward | MS 0-2.5 | 1.29 | 0.70 | <0.001 ^a MS 0-2.5 x MS 3-4 =1.000 ^b MS 0-2.5 x C =0.001 ^b MS 3-4 x C =0.007 ^b |
| | MS 3-4 | 1.47 | 0.92 | |
| | control | 0.88 | 0.28 | |
| 8. SS / Bars optokinetic upward | MS 0-2.5 | 1.33 | 0.62 | <0.001 ^a MS 0-2.5 x MS 3-4 =1.000 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C =0.005 ^b |
| | MS 3-4 | 1.49 | 0.91 | |
| | control | 0.88 | 0.30 | |
| 9. SS/ Bars visual – vestibular interaction / horizontal | MS 0-2.5 | 1.52 | 0.71 | <0.001 ^a MS 0-2.5 x MS 3-4 =0.496 ^b MS 0-2.5 x C =0.002 ^b MS 3-4 x C =0.001 ^b |
| | MS 3-4 | 2.00 | 1.37 | |
| | control | 1.08 | 0.38 | |
| 10. SS/ Bars Visual – vestibular interaction / vertical | MS 0-2.5 | 1.72 | 0.75 | <0.001 ^a MS 0-2.5 x MS 3-4 =1.000 ^b MS 0-2.5 x C =0.001 ^b MS 3-4 x C =0.011 ^b |
| | MS 3-4 | 1.91 | 1.15 | |
| | control | 1.24 | 0.38 | |

Legend:

BRU: Balance Rehabilitation Unit; SS: Steady Surface; EO: Eyes Open; EC: Eyes Closed; MS: Multiple Sclerosis; C: Control

^a p – Value / Anova Test ; ^b p – Value / Bonferroni Test; Significance level $\alpha = 0.05$

Table 2. Average values, standard deviations and p-values of ellipse area in the ten stimulation conditions for the 0-2.5 and 3-4 multiple sclerosis groups according to the EDSS scale score and control group.

| Ellipse area cm ² | | | | |
|--|----------|---------|--------------------|--|
| Sensory conditions in BRU | Group | Average | Standard deviation | p Value |
| 1. SS/ EO/ non stimulus | MS 0-2.5 | 4.91 | 4.77 | <0.001 ^a MS 0-2.5 x MS 3-4 =1.000 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C =0.003 ^b |
| | MS 3-4 | 4.43 | 3.50 | |
| | control | 1.71 | 0.89 | |
| 2. SS/ EC | MS 0-2.5 | 7.86 | 11.55 | <0.001 ^a MS 0-2.5 x MS 3-4 =0.236 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C <0.001 ^b |
| | MS 3-4 | 19.57 | 41.87 | |
| | control | 1.80 | 1.29 | |
| 3. Foam / EC | MS 0-2.5 | 19.57 | 13.78 | <0.001 ^a MS 0-2.5 x MS 3-4 =0.037 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C <0.001 ^b |
| | MS 3-4 | 32.60 | 25.41 | |
| | control | 8.55 | 5.48 | |
| 4. SS / Saccadic | MS 0-2.5 | 4.42 | 5.40 | <0.001 ^a MS 0-2.5 x MS 3-4 =1.000 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C <0.001 ^b |
| | MS 3-4 | 4.17 | 3.56 | |
| | control | 1.38 | 1.06 | |
| 5. SS / Bars / optokinetic to the right | MS 0-2.5 | 4.72 | 4.42 | <0.001 ^a MS 0-2.5 x MS 3-4 =1.000 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C =0.001 ^b |
| | MS 3-4 | 5.85 | 6.54 | |
| | control | 1.61 | 1.06 | |
| 6. SS / Bars / optokinetic to the left | MS 0-2.5 | 6.28 | 10.69 | <0.001 ^a MS 0-2.5 x MS 3-4 =1.000 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C =0.004 ^b |
| | MS 3-4 | 4.03 | 3.58 | |
| | control | 1.53 | 1.06 | |
| 7. SS / Bars / optokinetic downward | MS 0-2.5 | 5.28 | 5.57 | <0.001 ^a MS 0-2.5 x MS 3-4 =1.000 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C =0.004 ^b |
| | MS 3-4 | 4.27 | 3.41 | |
| | control | 1.65 | 1.42 | |
| 8. SS / Bars optokinetic upward | MS 0-2.5 | 5.59 | 5.72 | <0.001 ^a MS 0-2.5 x MS 3-4 =1.000 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C =0.002 ^b |
| | MS 3-4 | 4.31 | 2.98 | |
| | control | 1.72 | 1.45 | |
| 9. SS/ Bars Visual – Vestibular Interaction / horizontal | MS 0-2.5 | 6.05 | 5.66 | <0.001 ^a MS 0-2.5 x MS 3-4 =0.198 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C <0.001 ^b |
| | MS 3-4 | 10.77 | 11.11 | |
| | control | 2.28 | 1.79 | |
| 10. SS/ Bars Visual – Vestibular Interaction / vertical | MS 0-2.5 | 6.44 | 6.27 | <0.001 ^a MS 0-2.5 x MS 3-4 =0.329 ^b MS 0-2.5 x C <0.001 ^b MS 3-4 x C <0.001 ^b |
| | MS 3-4 | 8.67 | 6.10 | |
| | control | 2.32 | 1.66 | |

Legend:

BRU: Balance Rehabilitation Unit; SS: Steady Surface; EO: Eyes Open; EC: Eyes Closed; MS: Multiple Sclerosis; C: Control

^a p value / Anova Test

^b p value / Bonferroni Test

Significance level $\alpha = 0.05$