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Title: MRI Characteristics of Malignant Multiple Sclerosis

Taha Gholipour, MD, Svetlana Egorova, PhD, Velina Sevdalinova, Brian Healy, PhD, Rohit Bakshi, MD, FAAN, Charles Guttmann, MD, Samia Khoury, MD, FAAN, Howard Weiner, MD and Tanuja Chitnis, MD.

Objective: To define brain MRI characteristics of MS patients who experience a malignant course in comparison with disease duration (DD) or disability (EDSS) matched non-malignant patients.

Background: Malignant MS is defined as rapid accumulation of disability: reaching EDSS≥6 in less than five years from first symptoms. Little is known about the MRI characteristics of malignant MS.

Design/Methods: Patients meeting criteria for malignant MS who had at least one brain MRI scan after reaching malignant status were selected. Patients were from both relapsing- and progressive-onset disease categories. The first available MRI closest to attainment of EDSS≥6 was assessed. Two comparison groups were matched to the malignant group by age and gender. The first group was matched based on DD (<5 years) and the second group was matched on EDSS but had a longer DD. Brain parenchymal fraction (BPF) and T2 lesion volume were calculated using a semi-automated segmentation pipeline. Two experts also analyzed the number of gadolinium-enhancing lesions. Student's t-test was used for MRI outcomes comparison. Chi-squared test was used for categorical variables. Correlations with baseline variables were tested using linear regression.

Results: 27 malignant (16 females), 31 DD-matched and 24 EDSS-matched patients were selected. BPF in malignant MS patients (mean±SD, 0.82±0.06) was significantly lower than the DD-matched group (BPF 0.87±0.04, p<0.001) but not the EDSS-matched group (0.80±0.06, p>0.05). T2 lesion volume was significantly larger in the EDSS-matched compared to the malignant group (p<0.05), and smaller but not significantly different between the DD-matched and malignant groups. Gadolinium enhancement was infrequent and did not differ between groups. A progressive-onset MS course was not associated with MRI outcomes.

Conclusions: Malignant MS patients demonstrate increased brain atrophy compared to DD-
Conclusions: Malignant MS patients demonstrate increased brain atrophy compared to DD-matched patients, with similar brain atrophy and lower T2 lesion volumes compared to EDSS-matched patients. These results suggest more rapid cerebral neurodegeneration in malignant MS patients.

Study Supported by: Merck Serono (HLW), National MS Society-RG (TC).

Topic Preference: 121. MS and Related Diseases: Clinical Science
Presentation Type: Oral
Current Training Status: Post-Doctoral Trainee

If you indicated you are a Resident in the above question and are currently enrolled in a primary Neurology residency training program, do you wish to be considered for a resident research travel scholarship to attend the Annual Meeting? No/Not Applicable

Is this submission a case report? No
Did this study incorporate the usage of animal material in any way? No

What quality gap (limitation or problem) in the practice of neurology does this research address? Malignant MS is defined based on disability status of patients with severe disease in early years of symptoms onset. It is estimated that 9-12% of newly diagnosed MS/CIS patients will undergo this course over their first few years of disease. Despite the frequent use of MRI in MS, the MRI correlates of malignant MS is scarcely addressed in previous studies. Identification of MRI characteristics of these patients in contrast with non-malignant patients with same disease duration or same disability level over longer duration may give us some insight on disease course-specific MRI changes. Some characteristics might be used to help predict this course and tailor treatment plan according to disease severity.

What type of research relates to your abstract? Clinical Research
Would you like to have your abstract considered for the Clinical Trials session? No
Does this abstract relate to patient safety in any way? No

INS/FNC Preference: Do Not Consider my Abstract for an INS Program

Keyword 1: Multiple Sclerosis
Keyword 2: Magnetic Resonance Imaging
Keyword 3: Atrophy
Keyword 4: Disease Progression

Author Acknowledgement: Yes
Has the work described in this abstract been previously published? No
Aspects of the work described in this abstract were published in: Question not answered yet

Has the work described in this abstract been previously presented? No
Aspects of the work described in this abstract were presented at: Question not answered yet

Will your presentation include information on unlabeled use of products? No

Please explain the scientific relevance of this abstract: This study compared the brain MRI of patients with malignant MS to two appropriate non-malignant groups. It is interesting to understand if patients with a rapid increase in disability levels, often scored on exam as EDSS, have distinct brain imaging characteristics compared to non-malignant patients with similar disease duration. In other words, we asked if this contrast in disability matches the MRI findings, specifically brain atrophy and lesion load. On the other hand, we would like to see if achieving severe disability in short term differs from having the same level of disability over longer period, sometime decades. These two comparisons can give us clues for finding a predictive factor in simple brain MRIs or even different disease mechanisms (neuroinflammation vs neurodegeneration). We think that this study and abstract scientifically approached these questions.

Taha Gholipour, MD

Disclosure Information:
1. Within the past year, did you receive personal compensation from any commercial entity (for-profit business) as an employee, for consulting, serving on a scientific advisory board, speaking, or other activities? If yes, please describe the relationship(s), including the name of the commercial entity and the type of relationship No.
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7. Within the past year, did you receive research support from any commercial entity? If yes, please list the name of the sponsor(s) and the type of project supported: (This excludes investments in mutual funds held by you or your dependents.) Yes. Dr. Gholipour received financial support for research activities from Merck Serono.

Svetlana Egorova, PhD

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**Velina Sevdalinova**

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**Brian Healy, PhD**

**Disclosure Information:**

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Dr. Healy has received research support from Merck Serono.

Rohit Bakshi, MD, FAAN

Disclosure Information:

1. Within the past year, did you receive personal compensation from any commercial entity (for-profit business) as an employee, for consulting, serving on a scientific advisory board, speaking, or other activities? If yes, please describe the relationship(s), including the name of the commercial entity and the type of relationship Yes.

Consulting fees from Biogen Idec, Novartis, Questcor, and Teva Neuroscience.

2. Within the past year, did you receive personal compensation for serving as a journal editor, associate editor, or member of an editorial advisory board? This may include a journal published by your national medical/scientific organization. If yes please describe the relationship(s), including the name of the commercial entity and type of relationship Yes.

Serve as a Associate Editor for the journal Neurotherapeutics.

3. Within the past year, did you receive any type of compensation, including stock, stock options or expense compensation for serving on a board of directors for a commercial entity (for-profit business)? If yes, please describe the relationship(s), including the name of the commercial entity and the type of relationship No.

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Research support from Biogen Idec, EMD Serono, and Teva Neuroscience.

Charles Guttmann, MD

Disclosure Information:

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Samia Khoury has received personal compensation for consulting with EpiVax, Argos, LifeCycle, TcLand, Wyeth

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Samia Khoury, MD, FAAN

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Howard Weiner, MD

Disclosure Information:

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entity (for-profit business) as an employee, for consulting, serving on a scientific advisory board, speaking, or other activities? If yes, please describe the relationship(s), including the name of the commercial entity and the type of relationship Yes.

Dr. Weiner has received personal compensation for consulting, speaking activities and has served on the scientific advisory board of companies including Biogen Idec, Novartis, EMD Serono, Teva Neurosciences, GSK, Nasvax, Xenoprot and Genzyme.

2. Within the past year, did you receive personal compensation for serving as a journal editor, associate editor, or member of an editorial advisory board? This may include a journal published by your national medical/scientific organization. If yes please describe the relationship(s), including the name of the commercial entity and type of relationship No.

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Tanuja Chitnis, MD

Disclosure Information:

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Dr. Chitnis received personal compensation from Teva Neurosciences, Biogen Idec, Sanofi-Aventis, and Novartis for consulting services.

2. Within the past year, did you receive personal compensation for serving as a journal editor, associate editor, or member of an editorial advisory board? This may include a journal published by your national medical/scientific organization. If yes please describe the relationship(s), including the name of the commercial entity and type of relationship No.

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