ePoster at the European Academy of Neurology (EAN) 2023, July 1–4, 2023

EPV-508

Quantitative MRI in the routine clinical care of MS patients: Final results from MAGNON

Olaf Hoffmann[1], Manda Jankovic[2], Verena Isabell Leussink[3], Lothar Spies[4], Cordula Weiss[5]

1 Alexianer St. Josefs-Krankenhaus Potsdam-Sanssouci, Potsdam, Germany; Medizinische Hochschule Brandenburg Theodor Fontane, Neuruppin, Germany
2 Sauerlandklinik Hachen, Sundern, Germany
3 Praxis Neurologie in Meerbusch, Meerbusch, Germany
4 jung diagnostics GmbH, Hamburg, Germany
5 Novartis Pharma GmbH, Clinical Research Neuroscience, Nuremberg, Germany

CONCLUSIONS

1. **In diagnosing transition to SPMS, physicians rely primarily on disability progression confirmed at 6 and 3 months, cognition, and new MRI findings with or without clinical disease activity.**
2. **The highest number and volume of white matter lesions were observed in patients with SPMS, followed by RRMS patients with suspected SPMS, while patients with RRMS diagnosed less than 3 years ago had the lowest values.**
3. **Normalized thalamic volume showed considerable variance particularly in RRMS patients with suspected SPMS. Of these, almost half had an abnormally reduced z-score.**
4. **According to the physicians, the quantitative MRI reports at baseline and at follow-up provided additional information about the transition from RRMS to SPMS in almost half of the patients.**
5. **In more than one quarter of all cases across all three subgroups, the additional information from quantitative MRI analysis had an impact on the physicians' assessment of the current patient phenotype.**

Visit the web at: https://bit.ly/ean2023

Presenter email address: o.hoffmann@alexianer.de

INTRODUCTION

- In clinical routine, there are no standardized and well-established approaches for classification of disease activity and early detection of disease progression.
- Revised Lublin criteria[1] provide a definition of relapsing and progressive Multiple Sclerosis to classify disease activity of patients with Relapsing Remitting (RRMS) and Secondary Progressive Multiple Sclerosis (SPMS). However, Lublin criteria are only rarely applied in clinical practice.
- Similarly, quantitative and standardized magnetic resonance imaging (MRI) analyses are not regularly used in clinical routine yet.

OBJECTIVE

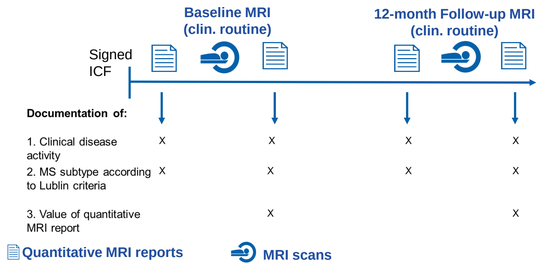
- **MAGNON aims to evaluate if standardized quantification of MRI data and assessment of MS patients based on the Lublin criteria provide benefits to neurologists in day-to-day management of MS patients.**
- The following results focus on the quantification of MRI data and the utility of quantitative MRI reports as perceived by treating neurologists.

METHODS

Project Scope

- 629 Multiple Sclerosis (MS) patients at 55 sites in Germany were enrolled in this prospective data collection project.
- Patients with early RRMS (max. 3 years since diagnosis), RRMS with suspected SPMS, or SPMS according to the treating physicians' evaluation were eligible to participate. Phenotyping or description of multiple sclerosis progression was performed by the treating physicians (neurologists) for each patient, using the current Lublin criteria.
- Project setup (**Fig. 1**):
  - Per patient, two MRI scans (baseline and 12-month follow-up) were performed as part of clinical routine.
  - MRI scans were analyzed using a centralized automatic processing pipeline (Biometrica MS®, jung diagnostics GmbH), and quantitative reports were provided to neurologists including information on a) new/enlarging T2 lesions, b) brain and thalamic volume and c) brain and thalamic volume loss per year.
  - Neurologists completed questionnaires before and after receiving quantitative MRI reports.
- To compare individual brain volume loss rates against brain volume loss rates of healthy subjects by age z-score were calculated.

Figure 1. Project design



RESULTS

Demographics and baseline information

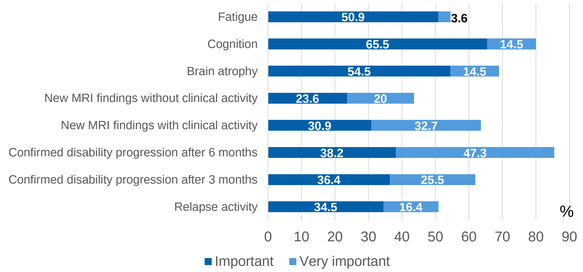
- 629 Multiple Sclerosis (MS) patients classified as early RRMS, RRMS with suspected SPMS or SPMS were enrolled in this prospective data collection project (**Tab. 1**).
- The majority of participants were categorized as RRMS patients with suspected SPMS
- Within this subgroup of RRMS with suspected SPMS, time since first suspecting SPMS ranged between 0 and 10 years with a mean of 1.5 years.
- On average, enrolled RRMS patients with suspected SPMS were about 10 years older compared to patients with early RRMS (35.2 years vs. 47.6 years) and younger than patients diagnosed as SPMS (55.9 years).

Table 1. Demographics and baseline characteristics

Variable*	Early RRMS**	RRMS with suspected SPMS	SPMS
N (%)	51 (8.1)	386 (61.4)	192 (30.5)
Age, years	35.2 [19; 67]	47.6 [20; 75]	55.9 [33; 77]
Sex, female, n (%)	39 (76.5)	268 (69.4)	135 (70.3)
Time since diagnosis, years	1.5 [0; 3]	13.3 [1; 68]	17.0 [1; 39]
Time since suspected SPMS, years	N/A	1.5 [0; 10]	N/A
EDSS	1.4 [0; 5.0]	3.0 [0; 8.0]	5 [1.0; 8.5]
Time since last relapse, years	1.25 [0; 3]	3.5 [0; 19]	5.1 [0; 40]

* if not indicated otherwise, data are presented as mean [min; max]
** defined as max. 3 years since diagnosis
EDSS= Expanded Disability Status Scale

Figure 2. Rating of factors used to evaluate phenotype



- According to the physicians, the most important parameters (rated as 'very important') in the decision to diagnose transition to SPMS are confirmed disability progression at 6 months, cognition, new MRI findings with clinical activity, confirmed disability progression at 3 months, and new MRI findings without clinical activity (**Fig. 2**). Relapse activity, brain atrophy, cognition, and fatigue were rated as 'important' by treating physicians (**Fig. 2**).

Quantitative MRI Results

- The highest lesion number and volume were observed in patients with SPMS whereas patients with RRMS diagnosed less than 3 years ago had the lowest values (**Fig. 3**).
- Quantitative MRI analyses at baseline MR revealed a median of 28 hyperintense lesions per patient with RRMS with suspected SPMS (mean: 31.5±19.9) and a median volume of T2 hyperintense lesions of 7.0 ml (mean: 12.3±14.2 ml) (**Fig. 3A, B**).
- At follow-up, the number of hyperintense lesions per patient with RRMS with suspected SPMS had increased to 30 (mean: 34.5±20.8) while the median volume of T2 hyperintense lesions was 7.4 ml (mean: 11.9±13.4 ml) (**Fig. 3C, D**).
- In all patient groups, mean normalized thalamic volumes (adjusted for head size and age) were lower than the mean of a reference population of healthy subjects (**Fig. 4A, B**).
- SPMS patients had lower z-scores than RRMS patients with suspected SPMS.

Figure 3. T2 lesion number and volume
Number (A,C) and volume (B,D) of T2-hyperintense lesions per subgroup. (A,B) MRI at baseline; (C,D) MRI at 12 months of follow-up

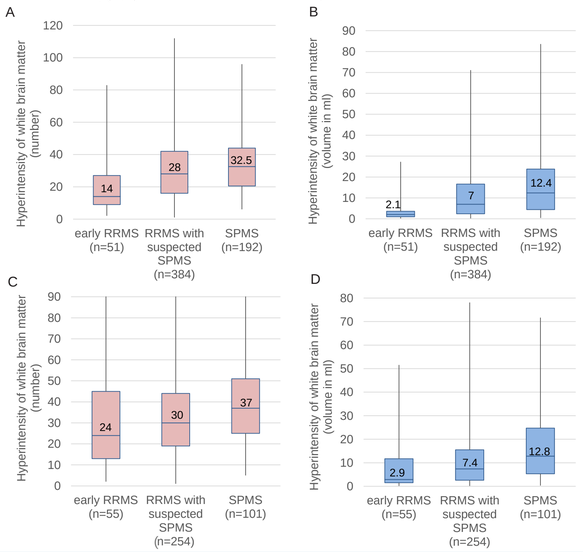
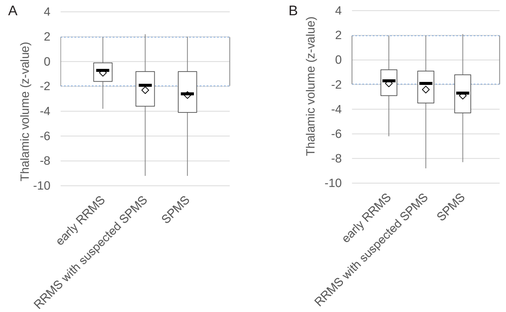


Figure 4. Normalized thalamic volume (z-value) according to MRI reports at A) baseline and B) follow-up.



Normalized thalamic volumes (z-scores) show the deviation from the mean of a reference population of healthy individuals in units of the standard deviation. Dashed areas represent 95% of all healthy individuals (mean ± 1.96 standard deviations). Values below the cut-off of -1.96 represent an abnormal thalamic volume reduction with a maximal error probability of 2.5%.

Impact of MRI results from the physicians' perspective

- For 48.7% (baseline MRI) and for 43.8% (follow-up MRI) of patients with RRMS with suspected SPMS the quantitative report provided additional information that the patient was in transition from RRMS to SPMS (**Tab. 2**).
- In more than one quarter of cases (31.8% after baseline MRI and 27.6% after follow up MRI), the additional information from quantitative MRI analysis at follow up had an impact on the physicians' assessment of the current patient phenotype. For Baseline MRI: RRMS [N=51]: 12 patients (23.5%); RRMS with suspected SPMS [N=386]: 146 patients (37.8%); SPMS [N=192]: 42 patients (21.9%) (**Tab. 3**).

Table 2. Impact on the classification of patients with suspected SPMS
The report provides additional information that the patient is in the transition phase between RRMS and SPMS

	after 1st MRI		after 2nd MRI	
RRMS with suspected SPMS	**N**	**%**	**N**	**%**
Total	386	100.0	260	100.0
Yes	188	48.7	114	43.8
No	198	51.3	146	56.2

Table 3. Physicians' assessment of current patient phenotype after MRI

After baseline MRI	Total		Yes		No	
	N	%	N	%	N	%
Total	629	(100.0)	200	(31.8)	429	(68.2)
Early RRMS	51	(100.0)	12	(23.5)	39	(76.5)
RRMS with suspected SPMS	386	(100.0)	146	(37.8)	240	(62.2)
SPMS	192	(100.0)	42	(21.9)	150	(78.1)

After follow up MRI	Total		Yes		No	
	N	%	N	%	N	%
Total	420	(100.0)	116	(27.6)	304	(72.4)
Early RRMS	59	(100.0)	13	(22.0)	46	(78.0)
RRMS with suspected SPMS	260	(100.0)	81	(31.2)	179	(68.8)
SPMS	101	(100.0)	22	(21.8)	79	(78.2)

REFERENCES: 1. Lublin FD et al., Defining the clinical course of multiple sclerosis: the 2013 revisions. Neurology. 2014 Jul 15;83(3):278-86. doi: 10.1212/WNL.0000000000000560. Epub 2014 May 28. PMID: 24871874; PMCID: PMC4117366.

Disclosures: Olaf Hoffmann served on scientific advisory boards and/or received speaker honoraria from Bayer Healthcare, Biogen, Bristol Myers Squibb/Celgene, Merck, Novartis, Roche, Sandoz, Sanofi, Teva; received financial support for research activities from Biogen, Novartis, and Sanofi. Manda Jankovic has received research support and/or consulting fee and honoraria for lectures from Bristol Myers Squibb and Novartis (2021-2022). Verena Isabell Leussink has received research support, consulting fee and honoraria for lectures from Biogen, Novartis, Roche, and Teva. Lothar Spies is an employee of jung diagnostics GmbH. Cordula Weiss is an employee of Novartis Pharma GmbH.

Funding source: This study is supported by Novartis Pharma Vertriebs GmbH, Germany.