



**Ruprecht-Karls-Universität Heidelberg**  
**Medizinische Fakultät Mannheim**  
**Dissertations-Kurzfassung**

**Long Term Dynamics of Brain Atrophy Development in Multiple Sclerosis – A 10 Year Follow Up Magnetic Resonance Imaging Study**

Autor: Philipp Eisele  
Institut / Klinik: Neurologische Universitätsklinik  
Doktorvater: Prof. Dr. A. Gass

Brain atrophy is a known feature in multiple sclerosis (MS). Current studies suggest that atrophy may reflect the neurodegenerative and destructive components of the disease. There are indications that atrophy correlates with neurological impairment and disability. Yet there is little data about the long term development of atrophy. We investigated brain atrophy development over 10 years in 3 active MS patients who underwent relatively frequent MRI. We analyzed clinical and MRI data over a period from 1996 to 2008 on 3 patients with MS (mean observation period 10.3 years/per subject). Patients were examined with 2 MR systems (1.5T Siemens MAGNETOM Sonata and Vision). Brain atrophy between each 2 timepoints was determined with SIENA (Structural Image Evaluation, using Normalization, of Atrophy). Additionally we examined brain atrophy with a subjective method by comparing 23 regions between baseline and follow up using a point scale ranging from zero to three. A higher score indicates an increasing severity of atrophy. 0 = No indications for brain atrophy, 1 = Minimal Indications, 2 = Mild signs for brain atrophy, 3 = Marked signs.

Patient 1 (Relapsing Remitting MS): MRI observation 0 – 134 months, 6 time points.

Expanded Disability Status Scale (EDSS) constantly between 0 and 1.

Patient 2 (Relapsing Remitting MS): MRI observation 0 – 109 months, 8 time points.

EDSS increase from 2.5 to 5.5 during follow up.

Patient 3 (Initially Relapsing Remitting MS to Secondary Progressive MS): MRI observation 0 – 117, 7 time points. EDSS increase from 2 to 7 during follow up.

Results:

Patient 1: Brain atrophy after 54 months: 0.908%, after 57 months: 1.454%, after 94 months: 7.951%, after 120 months: 10.381% and after 134 months: 12.014%

Average value: 0.089% per month

Brain atrophy examined with the subjective method between 1996 and 2001: 9/69 points, between 2001 and 2008: 14/69 points and between 1996 and 2008: 20/69 points.

Patient 2: Brain atrophy after 11 months: 3.922%, after 25 months: 4.744%, after 38 months: 6.578%, after 64 months: 6.923%, after 73 months: 6.928, after 90 months: 10.088% and after 109 months: 19.044%

Average value: 0.171% per month

Brain atrophy examined with the subjective method between 1997 and 2002: 31/69 points, between 2002 and 2006: 23/69 points and between 1997 and 2006: 37/69 points.

Patient 3: Brain atrophy after 12 months: 5.815%, after 22 months: 6.431% after 31 months: 14.076%, after 71 months: 16.536%, after 102 months: 22.502% and after 117 months: 26.557%

Average value: 0.226% per month

Brain atrophy examined with the subjective method between 1996 and 2002: 49/69 points, between 2002 and 2006: 16/69 points and between 1996 and 2006: 53/69 points.

Brain atrophy is a well known phenomenon to occur in MS. In this study we could demonstrate that brain atrophy is not a linear process, but clearly has stepwise non-linear dynamics over time. In this long term follow-up we have shown greater annual atrophy rates in 3 MS patients than commonly reported in short term follow-up studies. Brain atrophy was observed throughout the observation periods in all patients and did not follow a definite pattern in terms of timing of brain atrophy development or location. It rather developed at different time points of the progressing MS and could occur even after periods with small annual brain atrophy rates.