

# A "kissing lesion"

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## Case Report

# A “kissing lesion”: In-vivo 7T evidence of meningeal inflammation in early multiple sclerosis

Pierre Kolber, Amgad Droby, Alard Roebroek, Rainer Goebel, Vinzenz Fleischer, Sergiu Groppa and Frauke Zipp

## Abstract

**Background:** The role of cortical lesions (CLs) in disease progression and clinical deficits is increasingly recognized in multiple sclerosis (MS); however the origin of CLs in MS still remains unclear.

**Objective:** Here, we report a para-sulcal CL detected two years after diagnosis in a relapsing-remitting MS (RRMS) patient without manifestation of clinical deficit.

**Methods:** Ultra-high field (7T) MR imaging using magnetization-prepared 2 rapid acquisition gradient echoes (MP2RAGE) sequence was performed.

**Results:** A para-sulcal CL was detected which showed hypointense rim and iso- to hyperintense core. This was detected in the proximity of the leptomeninges in the left precentral gyrus extending to the adjacent postcentral gyrus.

**Conclusion:** This finding indicates that inflammatory infiltration into the cortex through the meninges underlies cortical pathology already in the early stage of disease and in mild disease course.

**Keywords:** Multiple sclerosis, 7T, atypical cortical lesions, magnetic resonance imaging

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## Introduction

The role of cortical lesions (CLs) in the clinical outcome of multiple sclerosis (MS) patients is being increasingly acknowledged and has been associated with disease progression and clinical deficits.<sup>1</sup> Nevertheless, the origins of CLs in MS remain unclear.<sup>2</sup> Post-mortem studies have confirmed that widespread cortical demyelination is accompanied by the presence of immune cell infiltrates in the advanced stages of MS.<sup>3</sup> However, histopathological findings from cortical tissue biopsies obtained from MS patients shortly after disease onset reported that meningeal inflammation may lead to subpial cortical demyelination in the early stages of the disease.<sup>4</sup>

The use of advanced magnetic resonance imaging (MRI) sequences as well as the implementation of ultra-high field MRI techniques has resulted in an increased detection rate of gray matter (GM) lesions in MS.<sup>5</sup> For example, magnetization-prepared two rapid acquisition gradient echoes (MP2RAGE) has been developed as a method to acquire MR images

corrected for B1 bias fields, leading to enhanced contrast between the brain tissues.<sup>6</sup> In 3T, MP2RAGE was found to outperform conventional MR sequences such as T1-magnetization-prepared rapid acquired gradient echoes (MPRAGE) and double inversion recovery (DIR) and was found to be more sensitive to both lesion count and volume.<sup>7</sup> Furthermore, due to its decreased false-positive detection rate, MP2RAGE was found superior to DIR in detecting CLs.<sup>7</sup>

## Case report

A 53-year-old female with relapsing–remitting multiple sclerosis (RRMS) underwent a routine follow-up (FU) 2 years post-diagnosis (Expanded Disability Status Scale (EDSS)=0). Subcutaneous interferon-beta-1a treatment was discontinued 6 months prior to FU due to side effects. No new focal clinical deficits were manifested; however, the patient reported occasional paresthesia in the right hand. Routine 3T MRI showed a new T2-hyperintense and gadolinium-enhancing elongated CL in the left

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Correspondence to:

**F Zipp**

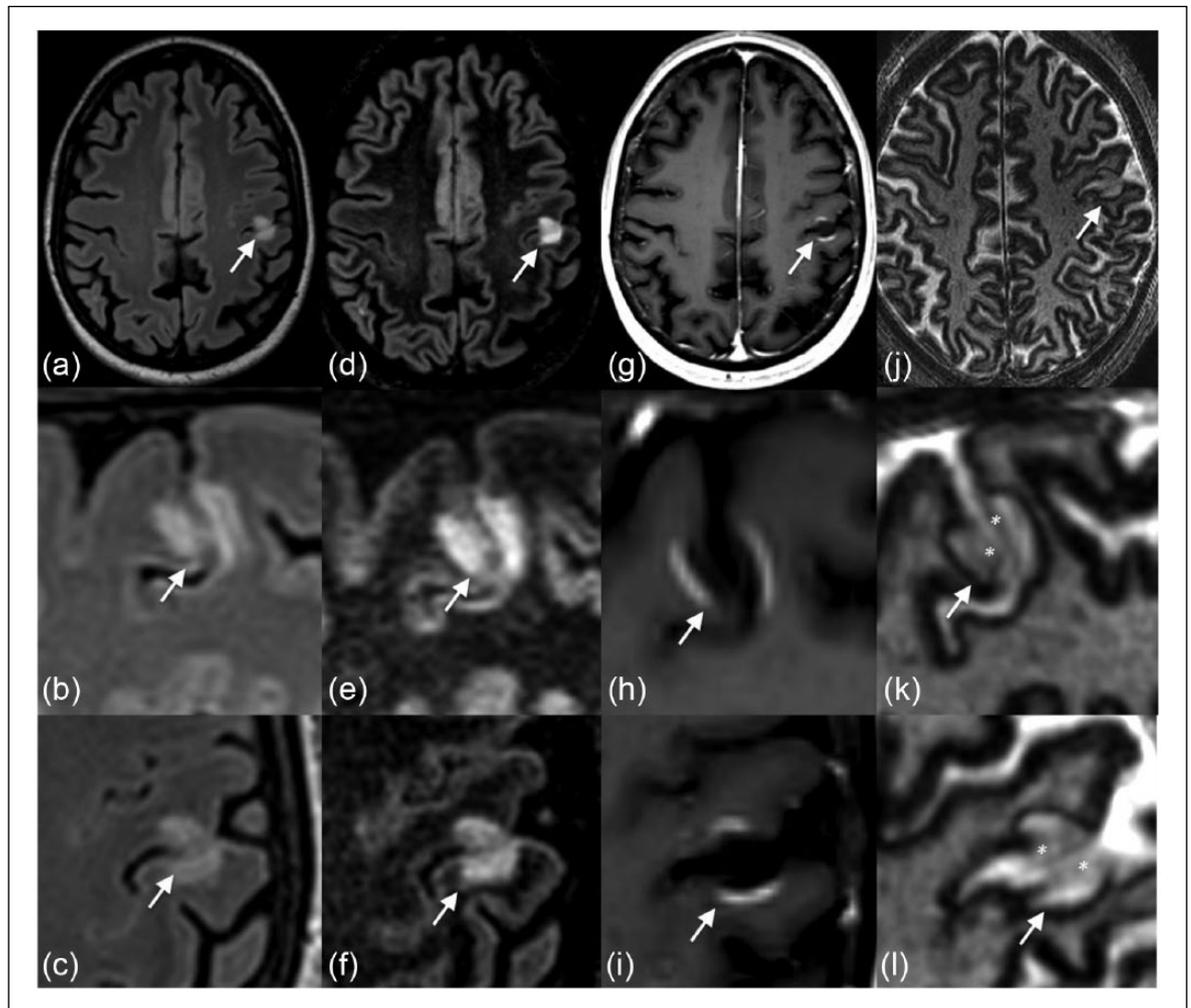
Department of Neurology,  
Focus Program Translational  
Neuroscience (FTN), Rhine  
Main Neuroscience Network  
(rnn<sup>2</sup>), University Medical  
Center of the Johannes  
Gutenberg University Mainz,  
55131 Mainz, Germany.  
[frauke.zipp@unimedizin-  
mainz.de](mailto:frauke.zipp@unimedizin-mainz.de)

**Pierre Kolber**  
**Amgad Droby**  
**Vinzenz Fleischer**  
**Sergiu Groppa**  
**Frauke Zipp**

Focus Program Translational  
Neurosciences (FTN),  
Rhine Main Neuroscience  
Network (rnn<sup>2</sup>), Department  
of Neurology, University  
Medical Center of the  
Johannes Gutenberg  
University Mainz, Mainz,  
Germany

**Alard Roebroek**

**Rainer Goebel**  
Maastricht Brain Imaging  
Center, Department of  
Cognitive Neuroscience,  
Faculty of Psychology and  
Neuroscience, Maastricht  
University, Maastricht, The  
Netherlands



**Figure 1.** MR image depicting the “kissing lesion” (arrows): (a, d, g, j) whole-brain transversal sections, magnified sagittal (b, e, h, k), and transversal (c, f, i, l) sequences of the CL. (a–c): 3T 3D fluid-attenuated inversion recovery (FLAIR). (d–f): 3T 3D double inversion recovery (DIR). (g–i): 3T 3D T1 MPRAGE upon gadolinium injection. (j–l): 7T 3D MP2RAGE showing a hypointense rim-like border corresponding to the gadolinium-enhanced meningeal thickening shown in (g–i) and edematous meninges (\*).

precentral gyrus extending to the adjacent postcentral gyrus (Figure 1(a)–(i)). Subsequently, ultra-high field 7T MRI was performed for further investigation. In MP2RAGE, this acute CL was characterized by a hypointense rim and iso- to hyperintense core (Figure 1(j)–(l)). Thickening of the leptomeninges in the proximity of the lesion was observed (Figure 1(k)–(l)) but did not exhibit contrast enhancement (Figure 1(g)–(i)). Both the 3T and 7T measurements were performed on the same day and compared to measurements of another RRMS patient and a healthy individual as control cases in order to exclude possible MRI artifacts (Supplementary Figure S1). In an FU MRI 1 year later at 3T, the lesion had regressed considerably (Supplementary Figure S2).

### Discussion

We present evidence for an acute CL across both sides of the central sulcus in the proximity of the leptomeninges in an early RRMS patient confirmed using 7T MP2RAGE, where acute lesions are viewed with a thin hypointense phase rim.<sup>8</sup> MP2RAGE has been suggested as a means to obtain bias field free  $T_1$ -weighted images and estimating  $T_1$  maps at ultra-high fields, permitting an enhanced delineation of anatomical structures.<sup>6</sup> Previous findings observed meningeal B-cell follicles mainly in secondary progressive MS<sup>9</sup> and more aggressive disease course and led to the hypothesis that soluble factors from these sites induce demyelination of the outer cortical layers.<sup>3,10</sup> Our observations go beyond existing reports and suggest

that inflammatory infiltration into the cortex through the meninges can also give rise to subpial cortical MS lesions in the early stages of the disease and in mild disease course. In conclusion, we present *in vivo* evidence for a lesion with cortical inflammation across a sulcus spreading from the meninges in early MS.

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### Author Contribution

PK and AD equally contributing first authors; SG and FZ equally contributing senior authors.

### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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## In-vivo imaging of meningeal inflammation in multiple sclerosis: Presence of evidence or evidence of presence?

Iris D Kilsdonk, Menno Schoonheim and Mike P Wattjes

**Keywords:** Multiple sclerosis, high-field magnetic resonance imaging, cortical lesions, meningeal inflammation

Recent histopathology studies suggest the presence of meningeal inflammation in patients with multiple sclerosis (MS) that might be associated with subpial cortical demyelination and a rather worse disease course.<sup>1</sup> Although a radiologist is not a pathologist, diagnostic neuroradiology aims to visualize and to detect almost every (subtle) pathological feature of a disease to its full extent. To be able to translate histopathological

results into radiological images will create an opportunity to visualize them in an *in-vivo* setting.

A good example of this in terms of MS pathology is the *in-vivo* detection of (subpial) cortical damage. It has been conclusively demonstrated that dedicated pulse sequences and the acquisition at higher magnetic field strengths can improve the detection rate of

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Correspondence to:  
**MP Wattjes**  
Department of Radiology  
and Nuclear Medicine,  
Amsterdam Neuroscience,  
MS Center Amsterdam,  
VU University Medical  
Center, De Boelelaan 1117,  
1081 HV Amsterdam, The  
Netherlands.  
[m.wattjes@vumc.nl](mailto:m.wattjes@vumc.nl)