

## Comparing the activity of multiple sclerosis (MS) at the minute and at 20 minutes of gadolinium application in magnetic resonance imaging (MRI) of the brain

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### Abstract

The aim was to compare active disease in patients diagnosed with multiple sclerosis, brain by MRI after gadolinium application at one minute and 20 minutes. A longitudinal, prospective, observational, analytical and comparative study was conducted in 18 patients over 18 years of age diagnosed with multiple sclerosis (MS). An analysis was made for each patient, watching for inflammatory activity in MS lesions, comparing the results to one minute and 20 minutes after the application of gadolinium. For the descriptive analysis, absolute frequencies and percentages were used, as well as means and standard deviations or medians with ranges for the inferential analysis comparing the presence or absence of enhancement in lesions at one minute and 20 minutes; the exact probability test used was Fisher. Finally, the results were analyzed, looking at the gender distribution: 14 (77.8%) were female. The average age was  $36.2 \pm 9.5$  years, with a minimum age of 18 years and a maximum of 55 years; four patients (22.2%) presented further highlight active lesions at 20 minutes, and two patients (11.1%) presented enhancement at one minute. Concluding that MRI in the diagnosis of MS is very important for the detection of activity in lesions caused by the disease, it is evident that the optimum time for evaluation of postcontrast sequences is 20 minutes. (Gac Med Mex. 2017;153:81-3)

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### Background

Multiple sclerosis (MS) is a chronic condition of the central nervous system. It is pathologically characterized by discontinuous areas of inflammation and demyelination and inflammatory activity-associated axonal lesion. One of MS key features is that lesions are disseminated in time and space. Clinically, the first symptoms occur at between 20 to 40 years of age in approximately 70% of patients,

although visible changes with magnetic resonance imaging (MRI) are more common than clinical activity and may precede it<sup>1-4</sup>.

MS average age of onset is around 30 years, and peak onset is at 23-24 years. Nearly 70% of cases originate at 20-40 years of age, with 10% occurring before and 20% after. Onset before 15 years or after 50 years of age is uncommon. However, cases have been documented of 15-month old children and sometimes it can develop in individuals at the seventh or eighth decades of life<sup>1,5</sup>.

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The most common diagnostic classification emphasizes on the growing role of MRI to demonstrate lesion dissemination in time and space<sup>8,9</sup>.

MRI is the most sensitive technique in the detection of MS lesions, since it detects lesions with demyelinating characteristics in 95% of patients with clinically defined MS<sup>2,3</sup>. As a consequence of this high sensitivity, MRI has become an essential technique not only in MS diagnosis, but also as a prognostic marker at the disease initial phase, in addition to contributing both to better understanding of its natural evolution and assessment, either as an intermediate or definitive marker of new treatments' efficacy<sup>6,11</sup>.

Gadolinium administration can substantially improve lesion identification and characterization. Contrast enhancement is produced by virtue of blood-brain barrier rupture or lesion vascularity (the latter in case of extra-axial lesions). This way, the agent's effect on surrounding water protons, which produces positive enhancement, is observed at T1. The dose commonly used in current clinical practice is 0.1 mmol/kg<sup>12</sup>.

The consideration that gadolinium enhancement on a lesion indicates inflammatory activity is based on several objective data: 1) new onset lesions, visible at T2-weighted sequences, are the ones that show enhancement; 2) enhanced lesions are more numerous during phases of clinical recurrence; 3) enhancement duration between 2 and 8 weeks, similar time to that of both clinical recurrence episodes' spontaneous clinical duration; 4) virtually any active lesion in the bone marrow is accompanied by new symptoms; and 5) the number of lesions with enhancement is correlated with the levels of basic myelin protein in cerebrospinal fluid (a marker of myelin destruction)<sup>13</sup>.

## Material and methods

Brain MRIs with gadolinium administration were performed to assess lesions at one and 20 minutes post-contrast in 18 MS-diagnosed patients older than 18 years. A 1.5-Tesla Siemens Magnetom Symphony equipment with series number 23439 (numaris/4 software, version syngo MR A35) was used. The gadolinium dose was 0.1 mg/kg of weight. To optimize time in our unit, owing to the high volume of patients managed by the MRI department, a brain MRI protocol was used, which establishes the performance of: 1) three-plane scout for study planning; 2) T1-weighted images with axial and coronal slices; 3) T1-weighted images with axial slices after gadolinium administration at minute 1; 4) FLAIR sequence images with axial and sagittal slices;

**Table 1. General characteristics and enhancement at 1 minute and 20 minutes in brain MRI with gadolinium in 18 MS patients**

Age (years)	36.2 ± 9.5
Gender	
Male	4 (22.2%)
Female	14 (77.8%)
Lesion enhancement*	
At 1 minute	2 (11.1%)
At 20 minutes	4 (22.2%)

Values presented as the mean ± standard deviation or absolute frequency (percentage).

\*p = 0.329 for the proportion of patients with lesion enhancement at 1 and 20 minutes.

5) T2-weighted images with axial slices; and 6) T1-weighted images with axial and sagittal slices at 20 minutes of gadolinium administration. The results were interpreted by the study's main investigator, who classified them as positive or negative for active demyelinating plaque differentiation at minute 1 and subsequently at 20 minutes, with the findings being compared.

## Results

Eighteen patients who underwent brain MRI with gadolinium under the diagnosis of MS were included. In the distribution by gender, 14 (77.8%) were from the female gender. Mean age was 36.2 ± 9.5 years, with minimum age of 18 years and maximum of 55 years (Table 1).

Two patients (11.1%) had MS lesions enhancement at 1 minute of gadolinium administration: one 31-year old female and one 28-year old male. Conversely, 4 patients (22.2%) had MS-caused lesions enhancement at 20 minutes of gadolinium administration; two of them had MS lesions enhancement at one minute of gadolinium application. Of these, the female gender was predominant (n = 3, 75%) (Table 1).

## Discussion

MRI is the most sensitive technique for the detection of MS lesions, as it detects lesions with demyelinating characteristics in 95% of patients with clinically defined MS. As a consequence of this high sensitivity, MRI has become an essential technique not only in MS diagnosis, but also as a prognostic marker at disease initial phase, in addition to contributing both to better understanding

its natural evolution and assessment, either as an intermediate or definitive marker of new treatments' efficacy<sup>13</sup>.

The use of T1-weighted sequences in combination with paramagnetic contrast (gadolinium) injection allows to selectively identifying lesions with inflammatory activity<sup>13</sup>.

Standardizing the acquisition protocol in all centers offers advantages in MS diagnosis. The MRI department has a high volume of patients, and a standard protocol was therefore followed where post-contrast sequences were carried out immediately after gadolinium administration in order decrease the time of study and not to prolong the waiting time for other patients. Since there was failure to observe activity in a large percentage of patients, we were interested in establishing a protocol that was adequate to this institution in order to attain an adequate study and optimize the time of the procedures. The aforementioned protocol was compared and a protocol adequate to our needs was adopted<sup>17</sup>.

Eighteen patients were assessed in the study, in which we observed higher visualization of MS lesions with inflammatory activity contrast-enhancement 20 minutes after gadolinium administration, with 4 cases (22.2%) resulting positive, and out of them only 2 (11.1%) showed enhancement at 1 minute of contrast administration, with contrast being more evident at 20 minutes in these patients.

All patients were administered the same gadolinium weight-based dose (0.1 ml/kg, equivalent to 1 mmol/ml). In comparison with other studies in the literature, greater lesion enhancement has been observed by administering a dose of 1 mol/l, unlike to applying half the dose (0.5 mol/l), as well as delaying post-contrast image acquisition, with lesions being assessed at 5 and 10 minutes, and being more evident at minute 10 post-contrast<sup>18</sup>.

Fourteen of the assessed patients did not exhibit inflammatory activity in MS lesions, accounting for

77.78% of assessed patients; this might be due owing to the treatment they receive prior to the study. Lovblad et al.<sup>17</sup> mention that treatment with high-dose intravenous steroids produces a resolution or marked reduction of all active lesions, although this effect is transitory, since in consecutive examinations, reappearance of active lesions has been observed several weeks after treatment completion<sup>17</sup>.

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