Susceptibility-Weighted Imaging as an alternative to contrast-enhanced T1w Images for detecting acute Multiple Sclerosis lesions

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Introduction

In patients with Multiple Sclerosis (MS), gadolinium-enhanced MRI can reveal areas of blood-brain barrier (BBB) disruption due to acute inflammation. During the course of the disease, iron accumulation within focal lesions occurs. Susceptibility-weighted imaging (SWI) is an MRI technique that allows in vivo detection of iron content in tissues due to their paramagnetic properties (deoxyhemoglobin). There is evidence that magnetic susceptibility of MS lesions tend to increase significantly as they evolve from an enhancing to a non-enhancing stage after gadolinium administration, which has been proven using quantitative MRI methods (Chen et al. Radiology 2014; Zhang et al. JMRI 2016; Zhang et al. Am J Neuroradiol 2019).

Purpose

The purpose of our study is to determine the value of visual-based qualitative analysis of signal on SWI for determining the likelihood of gadolinium enhancement of active (new) T2 MS lesions.

Methods

A retrospective review of medical records and MRI scans was made in a group of MS patients. We compared a baseline and a follow-up MRI in order to detect active T2 lesions.

Patients:. *Inclusion criteria*: relapsing MS according to 2017 McDonald criteria; age 18-65 and new T2 lesions in a follow-up MRI. *Exclusion criteria*: pregnancy and steroid therapy between the two scans *Final sample*: 54 patients (68.5% women), mean age: 34 (range 19-51), mean disease duration: 1.31 years (range 0.03-25.7). Mean expanded disability status scale (EDSS): 1.28 (range 0-3.5).

MRI Protocol: MRI scans were performed on a 3.0 T system with a 16 channel RF head coil, using SE PD/T2WI, T2-FLAIR, SWI, and SE T1WI pre and post contrast. *SWI data*: three-dimensional flow-compensated gradient-echo sequence, TR, 32 ms; TE, 24.6 ms; FOV, 187 x 250 mm; acquisition matrix size, 320 x 228 mm. Final processed images: in-plane resolution =0.65 x 0.65 mm, slice thickness =3.0 mm. *Contrast*: gadolinium-based hydrophilic and neutral macrocyclic medium (Gadobutrol, 0.1 mmol/kg). Interval from Gd administration to acquisition: 9-minutes. *Mean interval between baseline and follow-up MRI scan*: 9.4 months (range, 4.9-15.8 months).

Image analysis: New T2 lesions were visually identified. Two sets of DICOM images were stored in a local hard drive: "SWI-data" and "Gd-data". *SWI-data* was analyzed in a qualitative manner, in order to detect iron deposition within each new lesion. Four categories were considered: *a-* presence of iron rings, *b-* diffuse hypointensity, *c-* pure hyperintensity, *d-* unspecific. Findings on SWI attributable to a central vein sign were disregarded. Two different observers analyzed the *Gd-data* in a blinded manner in order to determine the presence of enhancement in each new lesion. The results were exported into a SPSS (Version 18 software) spreadsheet for statistical analysis.

Figure 1 *– Diffuse hypointensity on SWI in two non-enhancing lesions*

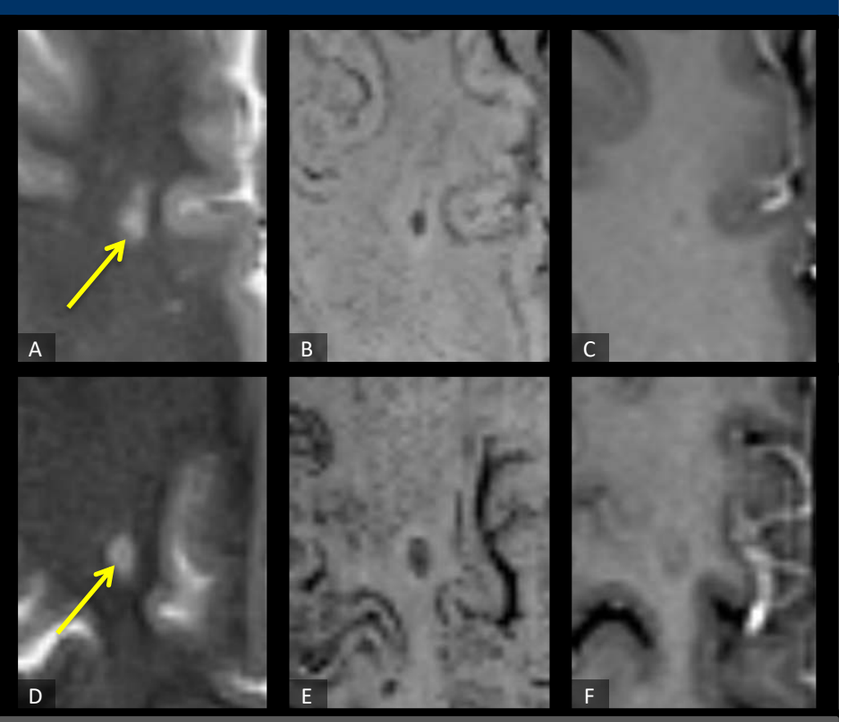

Figure 1 *- Two new demyelinating lesions are seen on T2WI, located in the subcortical right frontal (**A**) and right fronto-parietal white matter (**D**), both of which show a diffuse hypointensity on SWI (**B, E**). On post-contrast T1WI (**C, F**), no enhancement is detected.*

Results

Sample: 54 patients.
Total amount new T2 lesions: **173**.
•43 (**24.8%**) showed **enhancement**.
•130 (**75.2%**) showed **no enhancement**.
SWI signal:
•*Iron rings*: 49 (28.3%). Only 2 enhanced.
•*Diffuse hypointensity*: 93 (53.7%). Only two showed enhancement.
•*Pure hyperintensity*: 39 (22.5%). 97.4% enhanced.

Figure 2 *– Iron rings and central vein sign in two non-enhancing lesions and in one ring-enhancing lesion*

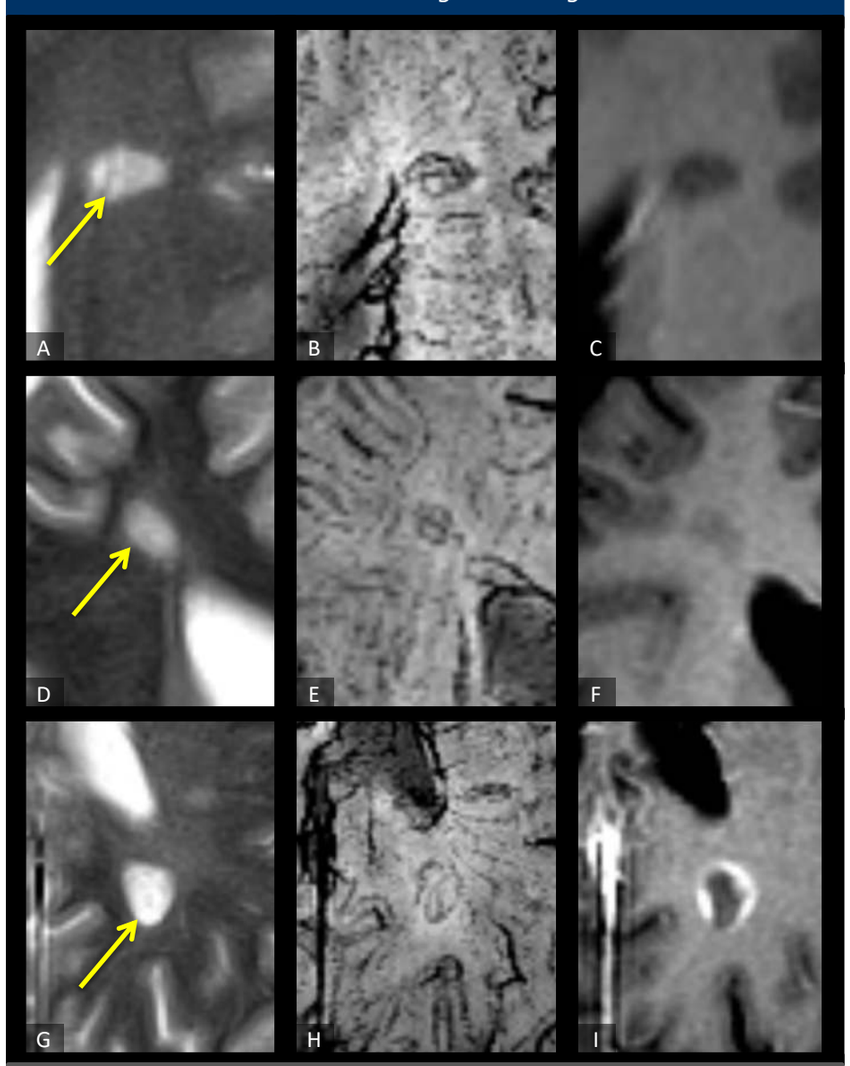

Figure 2 *- Three new subcortical lesions on T2WI in the left corona radiata (**A**), right frontal lobe (**D**) and left parietal lobe (**G**). On SWI (**B, E, H**), a hypointense peripheral rim is seen, suggesting iron deposition (iron rings). Also, central vein signs are seen on SWI. A lack of gadolinium enhancement is seen on the first two lesions (**C, F**), and a ring-enhancement in seen in the third one (**I**). This could be explained by a superposition of a late enhancing stage and an initial iron deposition stage.*

Figure 3 *– Pure hyperintensity on SWI, without evidence of iron deposition in three nodular-enhancing lesions*

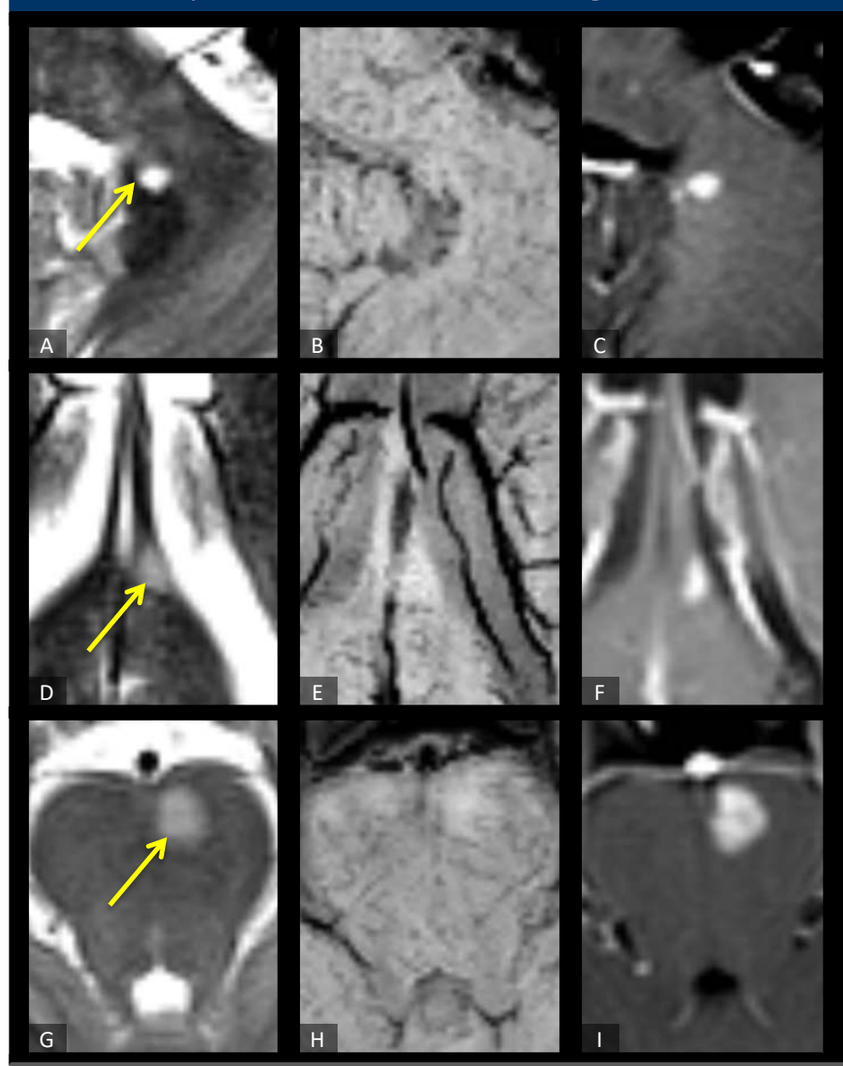

Figure 3 *- Three new demyelinating lesions are seen on T2WI, located between the left middle cerebellar peduncle and the nucleus dentatus (**A**), in the left parasagital callososeptal interface (**D**) and in the left parasagital pontine white matter (**G**). On SWI (**B, E, H**) there is no evidence of iron deposition; on the contrary, a diffuse subtle hyperintensity is seen. After gadolinium administration (**C, F, I**), a nodular enhancement is seen in the three lesions, denoting blood-brain barrier disruption.*

SWI for detecting non-enhancing/enhancing new T2 lesions

	Iron Rings	Diffuse Hypoint.	Iron Rings OR Diffuse Hypoint.	Pure Hyperint.
Sensitivity	36.15%	70.00%	97.69%	88.37%
Specificity	95.35%	95.35%	90.70%	99.23%
Positive predictive value	95.92%	97.85%	96.95%	97.44%
Negative predictive value	33.06%	51.25%	92.86%	96.27%
Positive likelihood ratio	7.77	15.05	10.50	114.88
Negative likelihood ratio	0.67	0.31	0.03	0.12
Accuracy	50.87%	76.30%	95.95%	96.53%

Note 1: *A diffuse hypointense pattern on SWI does not allow to identify iron deposition in the periphery of the lesion. Given that both situations (diffuse pattern and iron rings) correspond to the same physiopathology, an additional category was included considering the presence of either a diffuse pattern or iron rings on SWI. When considered this way, **sensitivity** inceases up to **97.69%**.*

Note 2*: The interobserver agreement was almost perfect, with percents of overall agreement ranging from 93.4% to 98.35%, and free-marginal kappa values ranging from 0.87 to 0.97.*

Conclusions

Based on the results of our study, we suggest that the qualitative analysis of the signal on post-processed SWI of new MS lesions, allows to determine the likelihood of enhancement after gadolinium administration. In particular, we draw attention to the fact that lesions with a pure hyperintense signal on SWI without any evidence of iron deposition, are more likely to enhance after gadolinium administration. On the other hand, lesions showing peripheral iron rings or a diffuse hypointensity on SWI are more likely to show no enhancement.
This phenomenon could have its theoretical basis in the pathobiology of demyelinating lesions over time, characterized by an acute stage without iron deposition (gadolinium enhancement), and a late (subacute-chronic) stage with iron deposition (marker of chronic inflammatory activity).

Disclosure of conflict of interest

Dr. Rovira serves on scientific advisory boards for Novartis, Sanofi-Genzyme, Icometrix, SyntheticMR, Bayer, Biogen and OLEA Medical, and has received speaker honoraria from Bayer, Sanofi-Genzyme, Bracco, Merck-Serono, Teva Pharmaceutical Industries Ltd, Novartis, Roche and Biogen. Dr. Pessini Ferreira, Dr. Barros and Dr. Salerno have nothing to disclose.
Dr. Auger has received speaking honoraria from Novartis, Stendhal and Biogen.