Diagnose acute gadolinium enhancing multiple sclerosis lesions using gradient echo MRI (R2* and QSM) without gadolinium injection

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TARGET AUDIENCE: All MRI researchers interested in Multiple Sclerosis (MS)

PURPOSE:

Gadolinium (Gd) enhancement of acute MS lesions only reflects breakdown of the blood-brain barrier (BBB)[1]. Gradient Echo (GRE) data provides both R2*(=1/T2*) and Quantitative Susceptibility Mapping (QSM)[2], which describe the underling microstructure integrity and total susceptibility of a voxel, respectively. During an MS lesion formation, first there is acute BBB breakdown and demyelination that reduces R2*. Then there is subacute clearance of myelin debris by microglia/macrophages (m/M)[3] that essential for stimulating remyelination, and further inflammation by m/M laden with iron, both contributing to susceptibility increase.

Our aim was to capture the different stages of early MS lesions utilizing GRE and to assess the feasibility to replace Gd injection with QSM.

METHODS:

This study analyzed all MS patients in the past 3 years in our MS center, whose MRI included multiple echo GRE, T1-weighted images (T1w), T2-weighted images (T2w). Gd-enhancement pattern on T1w were classified as either nodular (solid) or shell (ring in 2D). GRE data were processed to generate R2* and QSM[4]. MS lesion contrasts were measured on QSM.

RESULTS: 150 Gd-enhancing lesions were identified in 32 RRMS patients. Fig.1 shows example cases. On Gd-enhancement patterns, 134(89.3%) lesions were nodular, 16(10.7%) were shell. On R2*, all lesions appeared hypointense relative to adjacent normal appearing white matter (NAWM). On QSM, 131(97.8%) nodular lesions and 2(12.5%) of shell lesions appeared isointense, and 3(2.2%) nodular and 14(87.5%) shell lesions appeared hyperintense.

Only 111 lesions had identifiable NAWM on the contralateral side of the brain for estimating quantitative lesion contrast. Relative to NAWM, nodular lesions had QSM values near zero (mean =0.005ppb, p=.01), and shell lesions (including the kernel inside) had QSM values deviated from zero (mean=8.03ppb, p=.98) with QSM higher inside the kernel than at the Gd-enhancing shell (difference = 10.5ppb, p<0.01).

A total number of 617 MS lesions (hyperintense on T2w) on the same 32 patients were examined for diagnostic accuracy of identifying enhancing lesion using QSM without Gd injection. The sensitivity to identify Gd-enhancing lesions as isointense on QSM, is 89%, and the specificity is 97%.

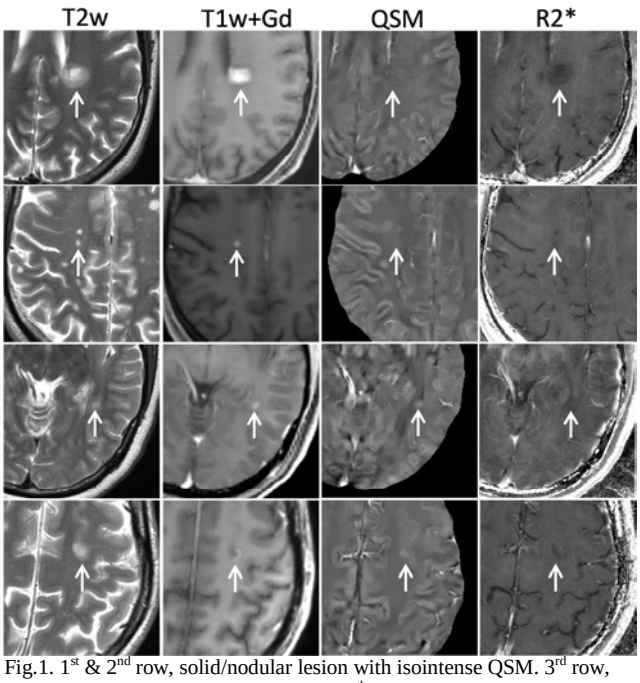

Fig.1. 1st & 2nd row, solid/nodular lesion with isointense QSM. 3rd row, nodular lesion with hyperintense QSM. 4th row, shell lesion with QSM hyperintense inside the shell.

DISCUSSION:

Our results may offer the following interpretation according to MS lesion literature[1,5-7]. Nodular Gd-enhancement may represent an earlier stage when BBB is leaking, myelin breaks down to debris (R2* decrease), however no susceptibility changes, suggesting a lack of iron deposition. The shell lesion may be at a slightly later stage or have a chronic core with high susceptibility[7]. The low percentage of QSM hyperintense nodular lesions may suggest that the time overlap between BBB leakage and significant susceptibility increase may be small (Fig.2), consistent with literature[5] that the BBB may seal rapidly within one or two weeks after opening for a few weeks. Immediately after BBB sealing, there is a significant increase in susceptibility suggesting an increase in iron, which may reflect a population of m/M containing iron and promoting continued inflammation[6]. This is consistent with the observed susceptibility increase in shell lesions (including internal kernels) and demyelinated lesions.

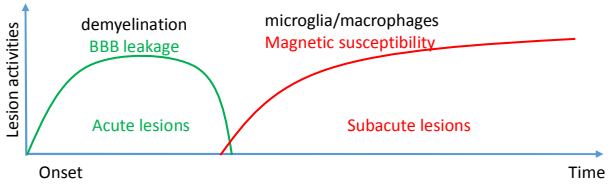

Fig.2. possible interpretation of BBB and susceptibility activities during lesion formation.

Old lesions (more than 6 years) are isointense on QSM as new nodular lesions[7], but they can be easily identified on the patients' prior MRI. In our data, most shell lesions have an older core but our MRI (approximately annually) was not frequent enough to capture the older core in the immediately prior MRI. More frequent MRI may improve the accuracy in identifying new enhancing lesion using QSM without Gd injection.

CONCLUSION:

We have analyzed Gd-enhancing lesions on GRE data (QSM and R2*). During BBB breakdown, microglia/macrophages may have not come to lesion to cause susceptibility change (measured on QSM). New enhancing lesions can be identified using QSM as opposed to Gd injection.

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