Studies reveal evolution of paramagnetic rim lesions in MS

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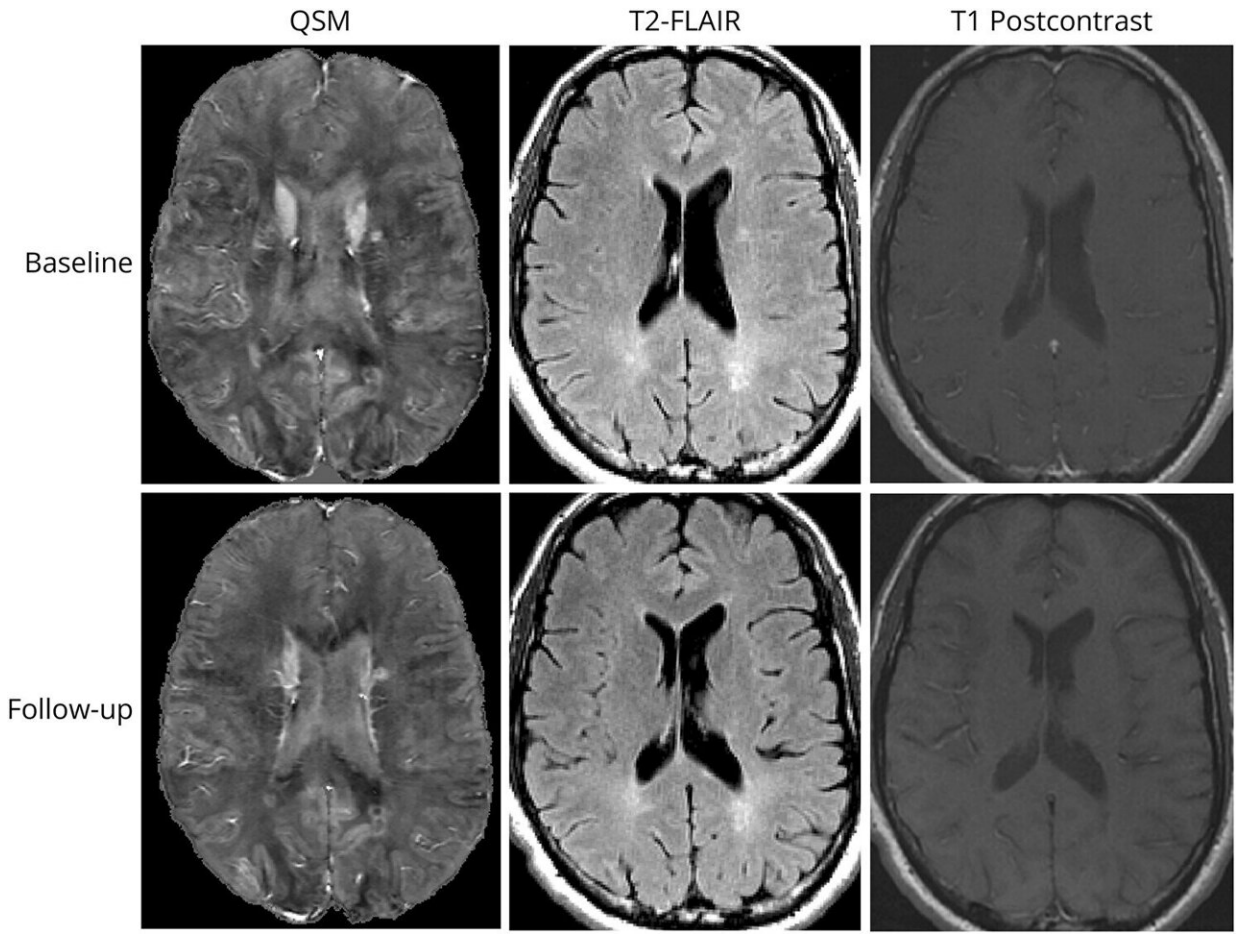

Example QSM, T2-FLAIR, and Postcontrast T1 Images at Baseline and Follow-Up. Credit: *Neurology* (2024). DOI: 10.1212/WNL.0000000000210004

In recent years, researchers studying multiple sclerosis have concluded that white matter lesion volume in the brain, long considered the best way to monitor MS disease progression, may not be the most accurate predictor of how an individual's disease will progress.

With the advent of new, iron-sensitive neuroimaging techniques, studies over the past decade have revealed that a different indicator of brain inflammation in MS, paramagnetic rim lesions (PRLs), may be a better predictor of disease progression. But how these brain structures evolve over time and how they may be impacted by disease-modifying treatments, that is, drugs designed to slow or reverse disease progression in MS, has not been well-understood.

Now, researchers from the University at Buffalo's Buffalo Neuroimaging Analysis Center (BNAC) have published the first longitudinal studies of PRLs: when they appear, disappear or persist. Jack Reeves, an MD/Ph.D. candidate in the Jacobs School of Medicine and Biomedical Sciences at UB, was first author on both papers, which were published last month.

Conducted in MS patients over 5- and 10-year periods, the results indicate that these lesions, which are associated with activation of brain immune cells called microglia, may be a more accurate indicator of disease progression in MS.

"Our group is among the first to study the factors that influence how PRLs evolve over time, and the first to study how this evolution is related to multiple sclerosis disease progression," says Robert Zivadinov, MD, Ph.D., senior author on both papers and professor of neurology and director of BNAC in the Jacobs School.

"We were motivated to study them because existing multiple sclerosis imaging markers, such as overall white matter lesion volume, poorly

predict future MS disease progression," he continues. "However, much is still unknown regarding the long-term evolution of PRLs and their relationship with disease progression."

In "Determinants of long-term paramagnetic rim lesion evolution in people with multiple sclerosis," published in the *Annals of Clinical and Translational Neurology*, the researchers report that in a study of 152 people with MS, the use of disease-modifying treatments was associated with lower odds of PRL appearance but not with complete disappearance. Patients who are current smokers, a risk factor for disease progression, had a higher prevalence of PRLs.

Reeves cautioned: "Based on our findings, the utility of PRL disappearance or new PRL appearance as outcome measures in clinical trials is to some extent limited. A clinical trial with significantly more participants will be needed in order to more precisely determine how moderate efficacy drugs affect PRLs."

In "Associations Between Paramagnetic Rim Lesion Evolution and Clinical and Radiologic Disease Progression in Persons With Multiple Sclerosis," published in *Neurology*, the researchers report that greater PRL disappearance rates were associated with reduced rates of confirmed disability progression. The study involved 160 people with MS and 27 healthy controls.

The results discussed in both studies show that both the resolution of existing PRLs and the absence of new PRLs are associated with improved clinical outcomes.

"These findings further motivate the need for novel therapies targeting microglia-mediated brain inflammation and adoption of clinical strategies to prevent appearance of new PRLs," says Zivadinov.

The studies show that high-efficacy disease-modifying treatments, which are effective at reducing relapses, slowing disease progression and minimizing disability, were associated with reduced appearance of PRLs. These results, he says, indicate that PRLs can be used to separate people with multiple sclerosis into high-risk and low-risk groups for disease progression, which may guide selection of disease-modifying therapies.

"These papers looked at how PRLs evolve over long time periods, five to 10 years," Zivadinov says, "but it would be valuable to look at PRL evolution at more regular intervals, such as annually, to better understand the exact trajectory of how PRLs evolve in serial imaging studies.

"Since we at BNAC have one of the largest longitudinal databases of PRLs in the world, we are currently working on additional studies looking into this," he says.

More information: Jack A. Reeves et al, Determinants of long-term paramagnetic rim lesion evolution in people with multiple sclerosis, *Annals of Clinical and Translational Neurology* (2024). DOI: 10.1002/acn3.52253

Jack A. Reeves et al, Associations Between Paramagnetic Rim Lesion Evolution and Clinical and Radiologic Disease Progression in Persons With Multiple Sclerosis, *Neurology* (2024). DOI: 10.1212/WNL.0000000000210004

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