In Vivo Quantification of Inflammation in Experimental Autoimmune Encephalomyelitis Rats Using Fluorine-19 Magnetic Resonance Imaging Reveals Immune Cell Recruitment outside the Nervous System.

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Public Summary:
Progress in identifying new therapies for multiple sclerosis (MS) can be accelerated by using imaging biomarkers of disease progression or abatement in model systems. In this study, we evaluate the ability to noninvasively image and quantitate disease pathology using emerging "hot-spot" 19F MRI methods in an experimental autoimmune encephalomyelitis (EAE) rat, a model of MS. Rats with clinical symptoms of EAE were compared to control rats without EAE, as well as to EAE rats that received daily prophylactic treatments with cyclophosphamide. Perfluorocarbon (PFC) nanoemulsion was injected intravenously, which labels predominately monocytes and macrophages in situ. Analysis of the spin-density weighted 19F MRI data enabled quantification of the apparent macrophage burden in the central nervous system and other tissues. The in vivo MRI results were confirmed by extremely high-resolution 19F/1H magnetic resonance microscopy in excised tissue samples and histopathologic analyses. Additionally, 19F nuclear magnetic resonance spectroscopy of intact tissue samples was used to assay the PFC biodistribution in EAE and control rats. In vivo hot-spot 19F signals were detected predominantly in the EAE spinal cord, consistent with the presence of inflammatory infiltrates. Surprising, prominent 19F hot-spots were observed in bone-marrow cavities adjacent to spinal cord lesions; these were not observed in control animals. Quantitative evaluation of cohorts receiving cyclophosphamide treatment displayed significant reduction in 19F signal within the spinal cord and bone marrow of EAE rats. Overall, 19F MRI can be used to quantitatively monitored EAE disease burden, discover unexpected sites of inflammatory activity, and may serve as a sensitive biomarker for the discovery and preclinical assessment of novel MS therapeutic interventions.

Scientific Abstract:
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