DCE-MRI K^{trans} Mapping of MS Lesion Evolution in Individuals

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Introduction

Transient focal disruption of the blood-brain barrier (BBB) is the most pronounced cerebrovascular abnormality in multiple sclerosis (MS) brain tissue.[1,2] Serial MRI studies involving monomeric Gd(III) chelate contrast reagents (CRs) have provided evidence that BBB permeability compromise is among the earliest expressions of MS pathology detectable by imaging techniques.[3,4] However, quantitative BBB permeability changes throughout the course of lesion evolution have not be examined. With the advent of BBB permeability pharmacokinetic mapping *via* dynamic-contrast-enhanced (DCE) MRI,[3,5] such monitoring of lesion development is possible. The ability to observe heterogeneous BBB permeability changes during MS lesion evolution (spanning pre- and post-acute lesion phases) would provide much insight into the evaluation of appropriate treatment strategies,[6] as well as disease pathology progression. To our knowledge, this is the first study designed to investigate quantitative BBB permeability heterogeneity changes in relapsing-remitting MS (RRMS) brain tissue throughout the different phases of lesion development.

Methods

Sixteen RRMS subjects provided informed consent before participating in this study. All MR data were obtained using a 4T Varian INOVA instrument. The experimental details pertaining to ^1H_2O data collection and quantitative R_1 [$\equiv T_1^{-1}$] mapping are as reported elsewhere.[5,7] R_1 map data were acquired prior to, and at five time (measured at acquisition mid-points) after CR (Gadoteridol, ProHance; Bracco) was administered using a power injector. Each subject was examined every two months over the course of about one year. CR BBB permeability was determined from K^{trans} values (i.e. the volume CR transfer constant of across the BBB)[8] *via* a two-compartmental model (for CR and for water) that accounts for equilibrium transendothelial[9,10] and/or transcytolemmal[11,12] water exchanges. The serial R_1 maps (s^{-1}) of each subject were co-registered to that for a particular time (i.e. visit) using a rigid-body transformation technique; via PMOD 2.75 (PMOD Technologies, Adliswil, Switzerland). MATLAB 7.0 (MathWorks Inc., Natick, MA, USA) was used to obtain the K^{trans} maps via multi-parameter fittings.[9-12]

Results

Figure 1 displays pre- and post-CR (7 min. post-CR; the first post-CR time point) R_1 maps and parametric K^{trans} maps obtained from four consecutive scans (separated by 2-month intervals) of two RRMS subjects [A) a 21 y woman, , and B) a 49 y man]. The vertical direction represents the four consecutive visits: the top row shows R_1 maps containing pre-acute lesion areas in normal appearing white matter (NAWM), the second row shows maps containing acute lesions, and the third and fourth (bottom two rows) show maps containing 2-month and 4-month post acute lesions, respectively. The pre-lesion NAWM (retrospectively), acute lesion, and post-acute lesion areas are outlined by square regions-of-interest (ROIs); overlaid on both the pre- and post-CR R_1 maps. Zoomed K^{trans} maps (with two different color scales to better accommodate the large K^{trans} dynamic range) of these ROIs are shown to the right of the R_1 maps.

Discussion

While the pre-acute lesion NAWM K^{trans} maps may indicate disease activity prior to the presentation of the acute lesion, the post-acute lesion K^{trans} maps clearly demonstrate significant and heterogeneous BBB permeability compromise. **Figure 1A** indicates that disease progression starts in the lesion center, then progresses towards the edge; creating a ring-like pattern of increased BBB permeability in this white matter lesion. **Figure 1B** suggests that disease progression of this (periventricular) lesion progresses from the center towards the *choroid plexus* and a white matter tract adjacent to the ventricle. These parametric maps demonstrate spatial disease progression in MS brain tissue.

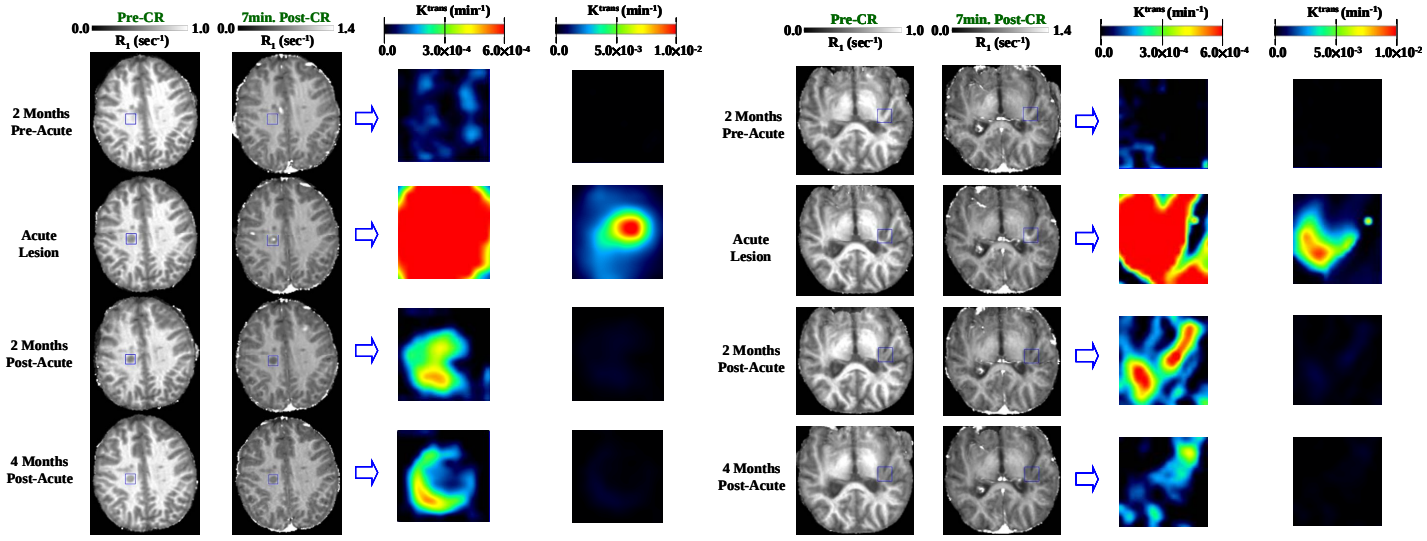

Figure 1. **A)** From top to bottom (four rows): pre- and post-CR R_1 maps (s^{-1}) of four consecutive visits by a 21 yr. old female RRMS subject; the gray scales of the pre- and post-CR R_1 maps are displayed above the R_1 maps (i.e. above the first two columns). Next to the R_1 maps are zoomed K^{trans} (min^{-1}) color maps of the pre-acute, acute, and post-acute ROIs; shown with two different color scales (located above the third and fourth columns). **B**) R_1 and K^{trans} maps from four consecutive visits by a 49 yr. old male RRMS subject.

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