A longitudinal MTR study in mild to severe Alzheimer's disease

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Introduction:

The magnetization transfer ratio (MTR) is widely used as a sensitive measure to probe structural changes of the brain tissue. Recent MTR analyses in patients suffering from Alzheimer's disease (AD) suggest that pathology in AD is global. This is supported by MTR reductions in grey and white matter and by the notion of an overall rather than regional impact of these changes on cognitive impairment (1-3). In this context whole brain MTR histogram analysis allows to obtain composite metrics (1,2,4) which might serve as surrogate markers for the evolution of brain damage in AD. However, no longitudinal MTR data are available so far. Therefore the goal of this study was to investigate the temporal evolution of global MTR parameters in AD patients and their association with changes in neuropsychological performance.

Material and Methods:

21 patients (age 61-87 years) diagnosed with AD underwent serial MRI and cognitive testing. MRI was performed on a 1.5T whole body scanner (Philips Intera, Philips Medical Systems, Best) and included conventional imaging and MT imaging. The MT sequence was based on a spoiled 2D gradient echo sequence (TR = 480ms, TE = 10ms, FA = 50°, number of slices = 24) that was performed with and without a binomial MT saturation pulse (90-180-90). A follow-up MRI was performed after 6 months and 11 patients had an additional MRI after 12 months. Neuropsychological testing at each time point included the Mini-Mental State Examination (MMSE), clinical dementia rating (CDR), and the ADAS-COG test.
Using a brain extraction tool, brain masks were produced for the baseline scans to identify those pixels that were included in the histogram analysis. These masks were then used for all follow-up MTR maps after they had been registered to the baseline examination. The following parameters were derived from the histograms: mean MTR value, relative peak height, and peak position.

Results

All histogram parameters showed a significant decrease over time. The most marked changes were found for the mean MTR ($p<0.01$) and the peak position ($p<0.001$) (Figure 1 and Figure 2). The correlation between changes of specific histogram parameters and in neuropsychological performance was poor or absent. However, regression analysis revealed that the peak position was a predictor for subsequent changes of the neuropsychological performance. We found significant correlations between the MTR peak position and MMSE change (R=0.55, $p=0.001$) and ADAS change (R=-0.5, $p=0.003$) 6 months later (Figure 3).

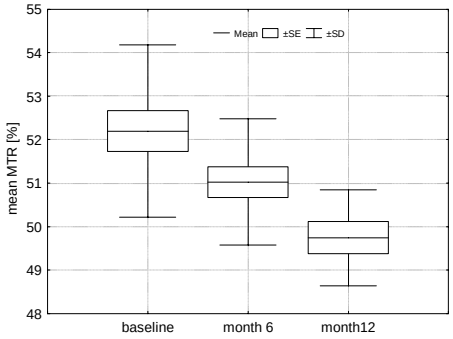

Fig.1

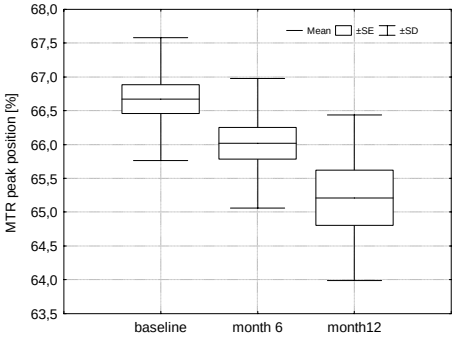

Fig.2

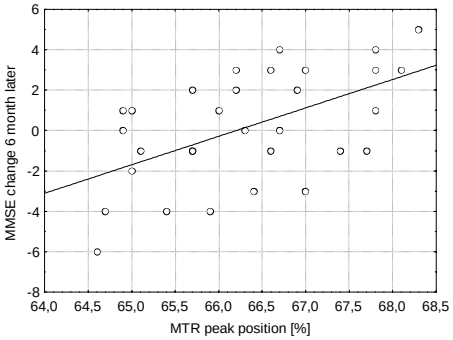

Fig.3

Discussion:

The high MTR values observed in this study are due to the choice of the MT pulse and the very short inter pulse delay and may also have contributed to the high sensitivity of the analysis. In contrast to conventional off resonant MT pulses, binominal pulses are T2 selective which means that they may be more sensitive for structural changes usually associated with AD such as amyloid plaques, vascular lesions or iron deposition. As we also observed a change in peak position towards a lower MTR over time, which reflects the tissue component with the highest MTR, this is likely to suggest that the myelin density or integrity are also significantly affected in AD.

Conclusion:

The results of this study indicates a very high sensitivity of MTR histogram metrics for ongoing tissue changes in AD as we observed a significant decline of all MTR histogram metrics already within 6 months with a relatively small sample of AD patients. The fact that MTR metrics were predictive of cognitive deterioration rather than changed in parallel with neuropsychologic performance needs further exploration.

References:

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