Microvascular Density Quantitative Changes after rat Embolic Stroke Using MRI

A. Bosomtwi[1,2], Q. Jiang[2,3], G. Ding[2], L. Zhang[2], Z. G. Zhang[2,3], M. Lu[4], J. R. Ewing[2,3], and M. Chopp[2,3]

[1]Yerkes Imaging Center, Emory University, Atlanta, Georgia, United States, [2]Neurology, Henry Ford Hospital, Detroit, Michigan, United States, [3]Physics, Oakland University, Rochester, Michigan, United States, [4]Biostatistics and Research Epidemiology, Henry Ford Hospital, Detroit, Michigan, United States

Introduction: Neurorestorative therapy improves functional recovery in experimental stroke (1), which may be related to therapy induced angiogenesis (1). Microvessel density (MVD) is one of the most important parameters in the study of angiogenesis after recovery from stroke. However, MRI measurement of MVD has not been applied to stroke recovery study yet. We believe our data demonstrate for the first time that MRI measurement of MVD can be used to dynamically monitor vascular remodeling after stroke and correlates highly with the gold standard, histological evaluation.

Methods: Eight Male Wistar rats were subjected to embolic MCA occlusion. MRI measurements of T_2 and T_2* were obtained before and after intravascular injection of Feridex (Berlex, Wayne, NJ) from 1 day to 5 weeks after stroke. The index $Q \equiv \Delta R_2/(\Delta R_2^*)^{2/3}$, where ΔR_2 and ΔR_2* are changes in spin-echo and gradient-echo relaxation rates, respectively, caused by intravascular injection of a contrast agent (2). MVD was calculated based on Q values using the equation $MVD \sim Q^3 \times 329$ s/mm^2 (3). von Willebrand factor (vWF) staining was applied 5 weeks after stroke to assess vascular reorganization. Morphologically intact vessels in vWF immunostained sections were counted in the center of the recovery region and normal tissue in the contralateral hemisphere. Ischemic areas were determined using the threshold T_2 value of mean + 2 standard deviations from the T_2 value measured in the contralateral hemisphere on T_2 maps after stroke. Regions of ischemic recovery were identified by subtracting the ischemic core areas obtained 5 weeks after stroke from the ischemic area on the T_2 maps obtained 1 day after stroke. A 5 x 5 pixel region of interest (ROI) was selected from the center of each area.

Fig. 1 T2 maps at 1 day (A) and 5 weeks (B) after stroke show the evolution of the ischemic area. The corresponding Q map (C), which is proportional to MVD, shows the relative values in the contralateral normal tissue (1), ischemic recovery (2) and ischemic core (3).

Results: Fig. 1 shows T_2 maps at 1 day (A) and 5 weeks after stroke (B) and the corresponding Q map (C) at 5 weeks after stroke. The MVD values measured in the contralateral normal tissue (ROI 1), ischemic recovery (ROI 2), and ischemic core (ROI 3) were 285, 169, and 11/mm^2, respectively. Fig. 2 shows the agreement between MVDs measured by MRI and histopathology with intracorrelation coefficient (ICC) = 0.85 in the area of ischemic recovery (triangles) and contralateral normal tissue (circles). The MVD measured by MRI correlated highly with histological measures of MVD (R^2 = 0.82) after adjusting for correlated region factors (the generalized estimation equation or GEE approach).

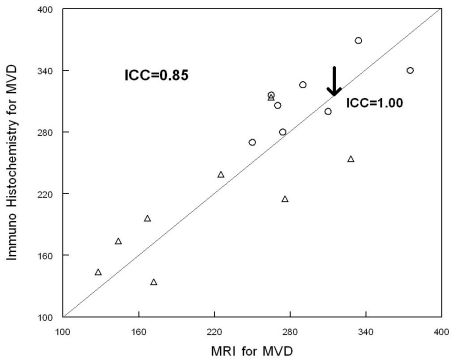

Fig. 2 MVD correlation between MRI and histopathology.

Discussion and Conclusion: The MVD value in the contralateral normal ROI we obtained in this study is in reasonable agreement with the histologically determined values for the rat brain of 277 ± 118/mm^2 by Weiss et al. (4), 430 ± 183/mm^2 by Klein et al. (5), and 370 ± 94/mm^2 by Pathak et al. (6). The MVD values in the ischemic boundary were also reasonable. Our data demonstrate that the Q index can quantitatively evaluate the status of vascular remodeling after neurorestorative treatment of stroke These data demonstrate that MRI MVD measurement can quantitatively evaluate microvascular density after stroke.

References:

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