Longitudinal perfusion change after intracranial stem cell implantation in chronic

Chao-Chun Lin[1,2], Wu-Chung Shen[1], Yung-Jen Ho[1], Po-Pang Tsai[1], Yu-Chien Lo[1], Chia-Wei Lin[1], Chiao-Ying Wu[1], Hing-Chiu Chang[2,3], Hsiao-Wen Chung[4], Woei-Cherng Shyu[5], and Shinn-Zong Lin[5,6]

[1]Radiology, China Medical University Hospital, Taichung, Taiwan, [2]Graduate Institute of Biomedical Engineering and Bioinformatics, National Taiwan University, Taipei, Taiwan, [3]Applied Science Laboratory, GE Healthcare, Taipei, Taiwan, [4]Electrical Engineering, National Taiwan University, Taipei, Taiwan, [5]Center for Neuropsychiatry and Graduate Institute of immunology, China Medical University Hospital, Taichung, Taiwan, [6]Neurosurgery, China Medical University Beigang Hospital, Beigang, Taiwan

Introduction

Taguchi et al. (1) have demonstrated that systemic administration of human cord blood-derived CD 34^+ cells to immunocompromised mice subjected to stroke 48 hours earlier induces neovascularization in the ischemic zone and provides a favorable environment for neuronal regeneration. Another study (2) also found that intracerebral peripheral blood stem cell (PBSC) ($CD34^+$) implantation induces neuroplasticity by angiogenesis in chronic stroke rats. Their results showed a significant increase in relative cerebral blood flow (rCBF) in the middle cerebral artery cortex of the ischemic brain in the PBSC-treated rats compared with control rats. The purpose of this study is to test the hypothesis of increased cerebral blood flow associated with stem cell implantation by MR $T2^*$ perfusion sequence.

Material and Methods

15 patients with chronic stroke were enrolled in this study; they received intracerebral stem cell implantation. Another 15 patients with chronic stroke were enrolled in the control group. 15 patients with stem cell implantation were performed with dynamic susceptibility-contrast Perfusion MR Imaging scheduled before the stem cell implantation(T1), 1 day(T2), 1 week(T3), 1 month(T4), 3 months(T5), 6 months(T6), 9 months(T7), and 12 months(T8) after stem cell implantation. Another 15 patients in the control group were followed only 3 times: first visit, 3month and 6months later. 13 sections were selected for perfusion MR imaging through the old infracted lesion based on $T2^*$-weighted images. Data processing was performed by using nICE (Nordic ICE, Nordic Imaging Lab, Norway) software. The AIF (arterial input function) deconvolution is not applied in our study. Hence both CBV and CBF are only determined in a relative sense based on the properties of the first-pass tissue response curve. We measure the region of interest (ROI) in the stem cell implanted foci. Mean perfusion values (rCBV, rCBF) of the ROI will be compared with the ROI in the contra-lateral relative normal white matter of the same patient (Fig. 1).

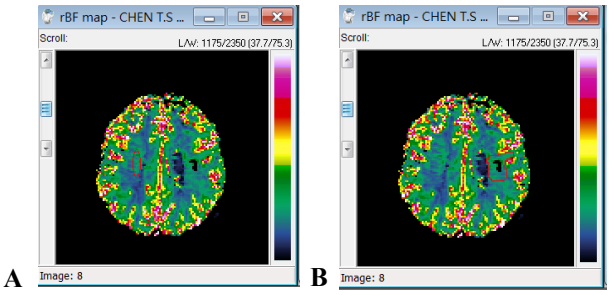


Fig 1 The perfusion ratio was calculated as the value of ROI in the stem cell implanted site (B, irregular red ROI) divided the value of ROI in the contralateral normal corona radiata (A, ovoid red circle).

Results

The perfusion in the stem cell implanted site was significant influenced by the susceptibility effect caused by the SPIO in the 1-day follow-up study (Fig 2). Therefore, the 2^{nd} point (T2) in the line chart (C, perfusion one day after implantation) suddenly dropped. The perfusion ratio of relative cerebral blood flow and volume increased in the 1-week (T3) follow-up studies.

Fig. 2

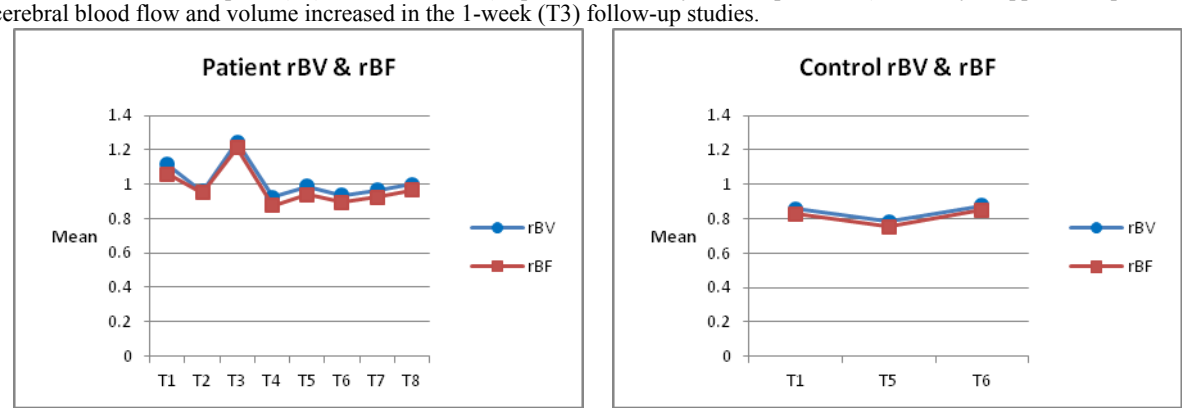
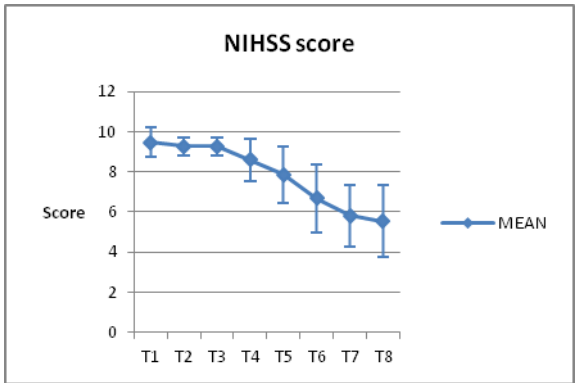


Fig. 3



Discussions

Stem cell intravenously (1) or intracerebral injection (2) induces neovascularization in the ischemic zone and provides a favorable environment for neuronal regeneration in animal study. The results of our study show temporally increase cerebral blood flow and volume which then decrease and are lower than the baselines in the long-term follow up. The perfusion change is earlier than the clinical neurologic symptoms improvement which began from the 3months (T4) after stem cell implantation.

References:

1. Taguchi A, Soma T, Tanaka H, et al. Administration of CD34+ cells after stroke enhances neurogenesis via angiogenesisin a mouse model. The Journal of Clinical Investigation. 2004;114(3):330-8.
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