Q-ball MR imaging of longitudinal brain rewiring during functional recovery after ischemic stroke

C. Granziera[1], T. Benner[2], D. Tuch[2], A. Singhal[3], W. Koroshetz[3], G. Krueger[4], and G. A. Sorensen[2]

[1]Neurology, CHUV, Lausanne, VD, Switzerland, [2]Radiology, Martinos Center-MGH-Harvard medical school, Charlestown, MA, United States, [3]Neurology, MGH, Boston, MA, United States, [4]Neurology, Advanced Clinical Imaging Technology, Siemens Medical Solutions-CIBM, Boston, MA

Background: Investigating connectivity changes underlying post-stroke recovery is a challenging but attractive research's field, seen the potential applications in treatment options and rehabilitation. *Ex-vivo* experimental studies showed that functional improvement after cerebral ischemia is characterised by complex white matter remodelling in terms of dendritic arborisation, synaptic modulation, wallerian degeneration and axonal sprouting [1,2]. Recent technical developments, like Diffusion Spectrum Imaging[3] and q-ball methods[4] made it feasible to accurately visualize in *vivo* complex brain connectivity through disentangling intra-voxel orientational heterogeneity. **Objectives:** Monitoring connectivity changes in patients recovering from small MCA strokes using a clinical protocol of q-ball MRI. **Methods:** Five patients with small ischemic MCA strokes were studied and followed-up longitudinally up to six months after stroke. MR q-ball imaging was performed within one week of symptoms onset and at 1 and 6 months (m) after the acute event on 1.5-T scanner (Magneton Avanto, Siemens, Erlangen, Germany) using an in-house 23 channel head coil. (Single-shot spin-echo EPI, 2.8 mm isotropic resolution, b=3000 s/mm^2, q=0.35 m-1, TR=8s, TE=110ms, and 30 slices). AutoAlign was used to ensure closely matching slice prescription over all time points [5]. NIHSS scores were recorded at every time point. Four age and gender matched controls were subjected twice to the same MR protocol within 1 month time interval (± 15 days). Q-ball tractography was performed using an in-house tool, based on a streamline algorithm [6]. A 3D ROI was placed in the periphery of the infarct area (figure 1 A, yellow arrow) to track the functional tract sub-serving the injured region and involved in the main symptoms (cortico-spinal tract for 2 patients, arcuate fascicle for 2 patients and insulo-somatosensory area I connections for 1 patient). Quantitative analysis of each 3D ROI was performed calculating the percentage of: number of fibers solutions tracked by the ROI/ number of whole brain tracks. **Results:** All patients had complete functional recovery (final NIHSS=0). Qualitative and quantitative analysis showed a decrease in the number of fiber trajectories tracked from the ROI at 1 month compared to the acute phase and a relative increase at 6 months compared to 1 month, in all the patients but #1 (Figure 1 A and 2 A, acute vs 1 m, $p < 0.005$; 1 m vs 6 m, $p \leq 0.5$; acute vs 6m $p \leq 0.5$). This phenomenon could be due to masking/unmasking of the dominant ODF (oedema, cellular/connectivity necrosis or damage) or to initial axonal degeneration followed by regenerative phenomena. In patient #1 we observed a decrease in fiber trajectories at 1 month persisting at 6m. It is probable that, in this case, different mechanisms contributing to stroke recovery are taking place. Such additional plasticity mechanisms are also possible for the rest of the cohort. Control patients did not show any qualitative or significant quantitative changes (figure 1 B and 2 B, p=0.1).

Conclusion: This is the first study applying Q-ball MRI to monitor connectivity plasticity after stroke. Q-ball MRI gave a new insight in the mechanisms of connectivity remodelling after brain ischemia showing a decrease in fiber trajectories at 1 month after stroke followed by an increase at 6 months in functional tracts involved in patients' symptoms. Our results indicate that q-ball MRI is a valuable non-invasive method to clarify potential therapeutic targets in stroke rehabilitation. Larger cohort studies are needed to confirm these preliminary findings.

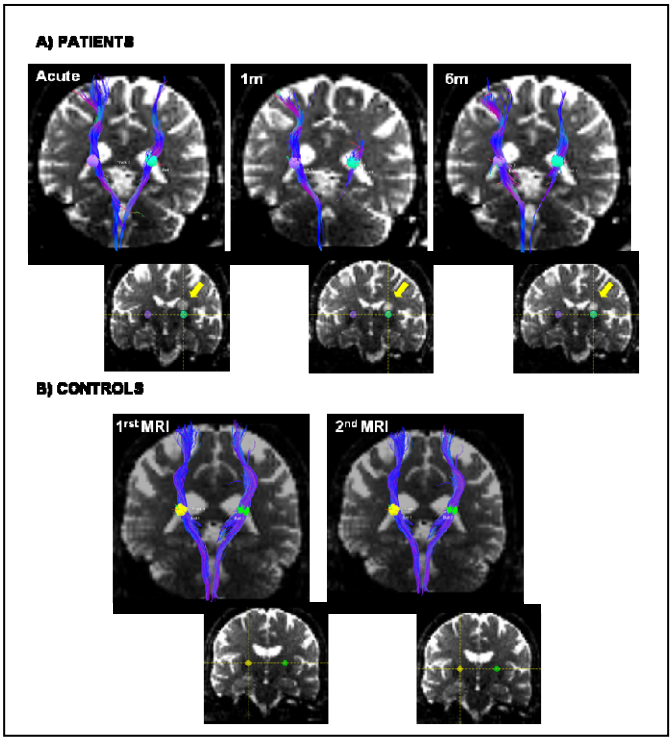

Figure 1: Coronal B0 images showing the cortico-spinal tract (CST) on the stroke side (right) and on the contra-lateral hemisphere (left) on the top; the ROIS used on the bottom. A) One patient, B) Age and gender matched control.

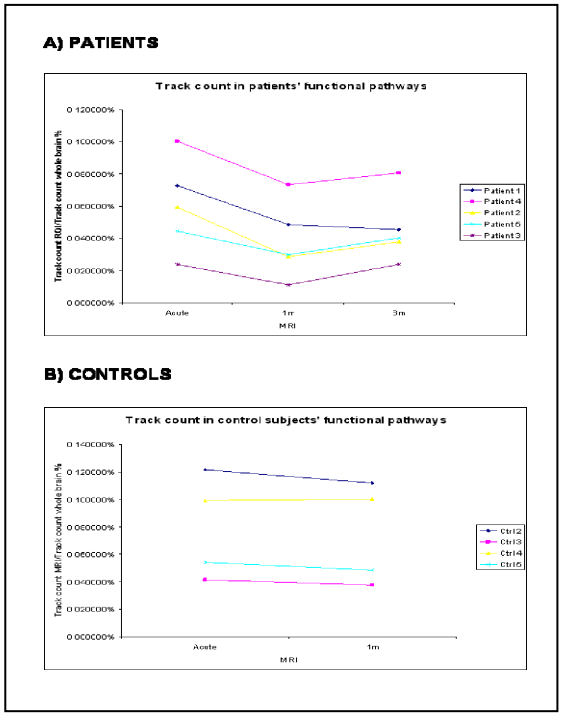

Figure 2: Quantitative tractography for patients A) and controls B) ROI Tracks' count is express as % of the whole brain

References: 1.Carmichael ST. *Neuroscientist*. 2003;; 2.Nudo RJ.*Stroke*. 2007; 3.Wedeen VJ et al. *Magn Reson Med.*2005; 4.Tuch DS. *Magn ResonMed*. 2004; ; 5.Benner T et al. *Radiology*. 2006; ; 6.Wang RW and Wedeen V. *ISMRM*. 2007.