# Neural correlates of spatial awareness revealed by MR DTI tractography and intraoperative subcortical mapping

A. Castellano<sup>1,2</sup>, L. Bello<sup>3</sup>, E. Fava<sup>3</sup>, A. Casarotti<sup>3</sup>, C. Papagno<sup>4</sup>, G. Carrabba<sup>3</sup>, G. Scotti<sup>1</sup>, and A. Falini<sup>1</sup>

<sup>1</sup>Neuroradiology Unit and CERMAC, Scientific Institute and University Vita-Salute San Raffaele, Milan, MI, Italy, <sup>2</sup>Institute of Radiological Sciences, University of Milano, Milan, MI, Italy, <sup>3</sup>Neurosurgery, Department of Neurological Sciences, University of Milano, Milan, MI, Italy, <sup>4</sup>Neuropsychobiology of Language, Department of Psychology, University of Milano Bicocca, Milan, MI, Italy

#### Introduction

Brain mechanisms underlying spatial awareness have recently become intensely disputed: particularly, subcortical networks including prefrontal and parietal areas seems to be important for spatial attention and space-related behaviour [1-2]. Disfunction of these networks results in unilateral spatial neglect, a complex and disabling syndrome that is tipically associated with right hemisphere lesions [3]. Neglect is characterized by an impairment of awareness of contralesional left half of space, objects and mental images. Recently, damage to the superior longitudinal fascicle (SLF), a major association fiber pathway connecting parietal and frontal cortical regions, has been described in neglect patients [3]. Further evidence has come from intraoperative subcortical stimulation during brain surgery, by temporarily inactivating restricted cerebral regions to map cognitive functions in humans [4].

Aims of this study are: 1) to perform DTI preoperative tractography in patients with right cerebral gliomas by segmenting the four subdivisions of SLF; 2) to combine tractography results with identification of functional subcortical sites during intraoperative line bisection test in order to assess the contribute of this fascicle in spatial attention networks.

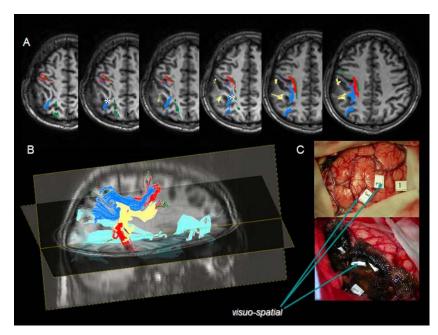
## **Materials and Methods**

MR DTI data were acquired from six patients with cerebral gliomas (4 oligodendrogliomas, 2 GBM). Imaging was performed on a 3T MR scanner (Philips Intera, Best, The Netherlands) with a 8-channel head coil. DTI data were collected using a single-shot echo planar imaging (EPI) sequence (TR/TE 8986/80 ms) with parallel imaging (SENSE factor, R = 2.5). 32 diffusion gradient directions (b=1000 s/mm²) and one image set without diffusion-weighting were obtained. A field of view of  $240 \times 240 \text{ mm}^2$  and a data matrix of  $96 \times 96$  were used and this leaded to isotropic voxel dimensions  $(2.5 \times 2.5 \times 2.5 \text{ mm}^3)$ . Acquisition coverage extended from medulla oblongata to the brain vertex (56 slices, no gap). The sequence was repeated two consecutive times and data were averaged off-line to increase signal-to-noise ratio; DTI datasets were aligned off-line to the echo-planar volume without diffusion weighting on a PC workstation using the AIR (Automatic Image Registration) software to correct artifacts due to rigid body movement during scan acquisition. 3D Fast Field Echo (FFE) T1-weighted imaging (TR/TE 8/4 ms; image resolution equal to DTI) was performed for anatomic guidance.

Preoperative tractography was performed using Dti Studio version 2.4.01 software (Jiang H, Mori S, Radiology Department, Johns Hopkins University, Baltimore, MD, USA) to reconstruct superior longitudinal fascicle and to segment its four subcomponents with a two-ROIs approach, according to the subdivision described by Makris and colleagues [5] Inferior fronto-occipital fascicle (IFO) was also reconstructed in all patients. Data were transferred to the neuronavigation system as described in [6]. Surgery was performed in asleep-awake anesthestia, allowing to correlate functional subcortical sites identified by intraoperative subcortical mapping with fiber tracts depicted by tractography.

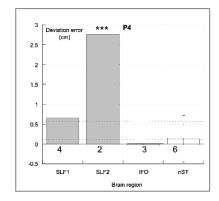
### Results

Preoperative segmentation of the four subcomponents of SLF by DTI tractography was obtained in all patients. During subcortical mapping, a rightward deviation on line bisection test indicated the stimulation of an area involved in spatial awareness, whose electrical inactivation evoked neglect. In five patients subcortical mapping demonstrated a significative correspondence between the stimulated sites corresponding to fiber tracts and the second subdivision of SLF (blue, fig.1), that extends from the angular gyrus to the caudal-lateral prefrontal regions. No significative rightward deviation was observed by stimulating the first or third subdivision of SLF (green and yellow respectively, fig.1) or inferior fronto-occipital fascicle (light blue, fig.1).



◆Fig.1. Tractography reconstruction of the four subcomponents of SLF in a patient arboring a right parietal oligodendroglioma. A, axial section (SLFI, SLFII, SLFIII, arcuate fascicle). Stimulation positive sites are indicated by (\*) B, 3D representation. C, correspondence between the intraoperative view and fiber tracts.

▼Fig.2. Mean rightward deviations (in centimeter) in the same patient at intraoperative line bisection test during stimulation of different brain region (nST, no stimulation).



## Conclusions

Combination of preoperative tractography and intraoperative mapping confirms the hypothesis that the long-range white matter pathways connecting parietal and frontal areas are involved in mechanisms of spatial awareness; particularly, disruption of the second branch of SLF seems to be critically associated with unilateral spatial neglect.

[1] Corbetta M et al. Nat Neurosci 2005; 8(11):1603-10 [2] Doricchi F et al. Cortex 2008; 44(8):983-95 [3] Bartolomeo P et al. Cereb Cortex 2007; 17(11):2479-90 [4] Thiebaut de Schotten M et al. Science 2005; 309(5744):2226-8 [5] Makris N et al. Cereb Cortex 2005; 15(6):854-69 [6] Bello L et al. Neuroimage 2008; 39(1):369-82