## Multiple fibre orientations estimated by spherical deconvolution: assessment of precision using the 'bootstrap' method

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Introduction: A key issue for MRI-based tractography techniques is the accuracy and precision of the estimated fibre orientations. The bootstrap method has recently been proposed to assess the precision of the fibre orientations estimated using the diffusion tensor model [1]. We have recently proposed a novel method to estimate the fibre orientation distribution (FOD) directly from high angular resolution diffusion-weighted data, using the concept of spherical deconvolution [2]. This technique was shown to estimate the FOD adequately even in regions containing multiple fibre populations, where diffusion tensor based techniques are known to be deficient. In this study, we apply the bootstrap concept to the spherical deconvolution method to assess the precision of the various estimated fibre orientations, and hence the reproducibility of the technique.

**Methods:** The bootstrap method is used to produce samples from a larger distribution, so that statistical analyses can be performed on these samples. To apply this technique to diffusion-weighted MRI, the acquisition of the data set needs to be repeated *N* times, so that *N* samples are available for each diffusion-weighted direction. A sample diffusion-weighted data set can then be produced: for each direction, one of the *N* available samples is picked. In this way, a full diffusion-weighted data set is produced from a random combination of the images in the *N* repeats of the original data set.

We acquired three consecutive repeat diffusion-weighted data sets from a healthy 26-year old volunteer on a 1.5T Siemens Vision system using a twice-refocused EPI sequence [3] (b = 2971 s/mm<sup>2</sup>, TE = 140 ms, FOV = 384 × 384 mm, matrix size 128 × 128 zero-filled to 256 × 256, slice thickness 3 mm, 40 contiguous slices, 60 directions, 6 b=0 images). The spherical deconvolution technique estimates the FOD by assuming a *response function* (the diffusion profile for a typical fibre bundle) and deconvolving it from the diffusion-weighted signal profile over spherical coordinates [2]. The response function and filter parameters used for the spherical deconvolution were estimated from the data themselves using a minimum entropy principle.

For each voxel, the following steps were performed. First, the full diffusion-weighted data set (including all three repeats) was used to produce a reference FOD using the spherical deconvolution technique [2]. The orientations of the three largest peaks of this FOD were then estimated using a modified Newton-Raphson gradient descent algorithm [4]. These are referred to as the 'reference peaks'. The bootstrap method was then used to produce 100 sample diffusion-weighted data sets, from which the corresponding FODs were estimated using spherical deconvolution. For each FOD, the peaks nearest to the reference peaks were estimated, and the deviation angle between the orientation of the reference peak and the orientation of the corresponding peak in the sample FOD was stored. Finally, the mean, median and 95% confidence interval for the deviation angle of each peak were computed. For comparison, the same procedure was applied to the diffusion tensor model.

**Results & Discussion:** Figure 1 shows results obtained from a region in the centrum semiovale, where three major pathways intersect: the ascending fibres from the corona radiata, the comissural fibres from the corpus callosum, and the superior longitudinal fasciculus (SLF). By comparing figures 1A & 1B in regions containing a single fibre population, it can be seen that the diffusion tensor model is more precise than the spherical deconvolution technique. This is expected, since the diffusion tensor model only needs to fit 7 parameters, as opposed to the 45 needed for the 8th order spherical harmonic series used in the spherical deconvolution technique. However, the 95% confidence intervals obtained using the spherical deconvolution technique for the fibre orientations in these regions is still relatively tight: 2.3° in the corpus callosum, 4.0° in the upper corona radiata, 4.9° in the SLF, and 10.5° in the lower part of the corona radiata (the large deviation in the latter reflects the 'fanning' observed in this region).

However, the orientation of the major eigenvector of the diffusion tensor is unreliable in crossing fibre regions [6]. In the region highlighted in figure 1, the spherical deconvolution technique does identify the three main orientations, each with good precision (see table 1). Although the precision of the diffusion tensor model is even higher in this region (for the reasons mentioned above), this is misleading in that the tensor model is unable to reliably identify any of the underlying orientations.

**Conclusion:** Although an assessment of the accuracy of the technique *in vivo* is not currently feasible due to the lack of a 'gold standard', previous simulations have shown that the bias in the orientations estimated using spherical deconvolution is negligible [2]. In this study, we have shown that the precision of the spherical deconvolution method is good, and this precision would be expected to improve with the higher quality of data that can be obtained using modern hardware.

**References:** [1] Jones DK, MRM 49:7 (2003). [2] Tournier JD *et al.* NeuroImage 23:1176 (2004). [3] Reese TG *et al.* MRM 49:177 (2003). [4] Press WH *et al.* Numerical Recipes (2nd ed.) Cambridge University Press (1992). [6] Tuch *et al.* MRM 48: 577 (2002).

		Mean	Median	95% conf.
Diffusion tensor	major eigenvector	2.0°	1.9°	3.8°
Spherical deconvolution	1st peak	2.9°	2.6°	5.6°
	2nd peak	3.8°	3.4°	7.9°
	3rd peak	6.2°	5.4°	13.8°

**Table 1:** mean, median and 95% confidence intervals of the deviation angle for the various estimated fibre orientations, averaged over the voxels highlighted in figure 1.



**Figure 1:** right: a coronal colourcoded major eigenvector map, showing the region of interest. (A) the 95% confidence cones around the three largest peaks in the FOD calculated using the spherical deconvolution technique. (B) the 95% confidence cones around the major eigenvector of the diffusion tensor. The region highlighted in (A) refers to the data shown in table 1.

