How well does the residual bootstrap predict scan-rescan repeatability of spherical deconvolution diffusion MRI?

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Introduction: An appealing approach to quantifying uncertainty in diffusion MRI is the residual bootstrap technique, since it permits estimation of the probability density function (pdf) for the fibre orientation(s) from a single measurement. The technique assumes a certain degree of smoothness of the diffusion weighted signal profile by, for example, fitting it to a spherical harmonic (SH) series of a specific order, and then exploits the residuals of the fit to generate a large number of synthetic datasets that are used to estimate the pdf. The purpose of this study was to determine how well the residual bootstrap statistical technique predicts the variability in scan-rescan estimates of fibre orientation, using spherical deconvolution diffusion MRI. We evaluated how well the fibre orientations obtained from different, coregistered datasets in the same subject fit the fibre pdf obtained from the residual bootstrap technique.

Methods: Four separate diffusion weighted datasets were acquired for a single healthy subject on a Siemens 3T Trio MR scanner (Siemens Medical Systems, Erlangen, Germany) using an 8-channel phased-array head coil. Diffusion encoding was achieved using a single-shot spin-echo echo planar sequence with twice-refocused balanced diffusion gradients. A dataset designed for high angular resolution reconstruction was acquired with 99 diffusion encoding directions, 2 mm isotropic voxel size, 63 slices, b=3000 s/mm^2, TE=121 ms, TR=11.1 s, and GRAPPA parallel reconstruction with acceleration factor 2. Ten images with b=0 s/mm^2 were also acquired for each dataset. The scans were acquired without repositioning, and were corrected for subject motion using a mutual information based registration algorithm[1] applied to the b=0 s/mm^2 images only. For each of the four datasets, the diffusion weighted signal profiles were fit to a SH basis of order eight. A residual bootstrap spherical deconvolution algorithm[2,3] was run using 1000 iterations. Additionally, each of the four datasets was processed using spherical deconvolution of the original diffusion weighted signal profile, without bootstrapping. A tensor fit was also performed to generate fractional anisotropy (FA) maps.

In order to perform a voxelwise comparison between the fibre pdf obtained from bootstrapping and that obtained from multiple acquisitions, many more than four registered datasets would have to be acquired. However, with O(10^5) voxels, the degree to which the observed data match the bootstrap prediction for variability can be assessed on average for all voxels, despite the pdf being different at each voxel. FA ranges from 0.1 up were used to create brain masks in which to investigate repeatability. The threshold of FA>0.1 is expected to include many voxels with little or no white matter, but is often used for fibre tractography in pathways that go through, e.g., the thalamus, and other regions of partial volume averaging of fibres with other fibres or grey matter[4]. For each dataset, the fibre orientation distribution function (ODF) maxima obtained from spherical deconvolution of each of the other three datasets were compared to the pdf for the fibre ODF maxima obtained from bootstrapping. The number of voxels in which the fibre ODF maxima lay within the 68% and 95% confidence intervals obtained from the bootstrap analysis, assuming Gaussianity, was counted.

Results: Fig. 1 (a-c) shows the fibre ODFs from deconvolution in a small ROI at the decussation of the cortical spinal tract and corpus callosum. Fig. 1 (d) shows the bootstrap-predicted pdf for the maximum of the fibre ODF. Fig. 2 shows the percentage of the observed ODF maxima that lay within the bootstrap predicted confidence intervals for the different FA ranges.

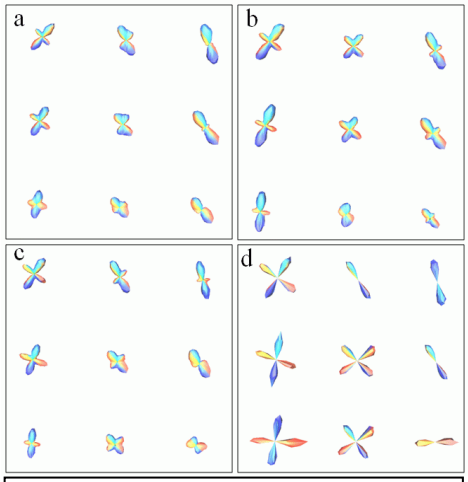

Fig. 1: (a-c) Fibre ODF obtained from spherical deconvolution for three separate, coregistered datasets. (d) pdf for the maximum of the fibre ODF, obtained from bootstrap processing of a separate dataset, coregistered with those shown in (a-c). The pdf is shown for the most likely fibre geometry in each voxel.

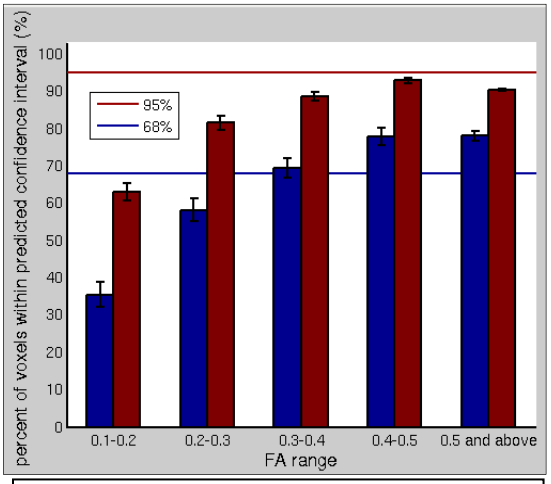

Fig. 2: Correspondence between observed and predicted confidence intervals. Bars show percent of voxels with ODF maxima within predicted confidence intervals.

Discussion: For major fibre tracts (i.e., FA>0.3), the correspondence between the observed variability in the fibre ODF maxima and the variability predicted by the bootstrap was very good. For low FA, the residual bootstrap underestimates the scan-rescan repeatability. This could be due in part to the order 8 SH expansion overfitting the noise at low FA values. The underestimation of the variability could also be attributed to slight misregistration between the acquired datasets, despite automated registration. The bootstrap predicts the variability due to noise, but cannot be expected to predict the variability due to subject positioning. Misregistration, even at the subvoxel level, would be expected to affect the cores of major fibre pathways, which span multiple voxels, less than the edges (i.e., low FA), where there is significant partial volume averaging. The goal of the residual bootstrap processing is to predict the uncertainty in the fibre orientation(s) in order to propagate this uncertainty into fibre tractography results. Hence, variability of scan-rescan tractography results may be greater than predicted by residual bootstrap tractography, in tracking experiments using a low FA threshold.

Conclusion: We evaluated the residual bootstrap spherical deconvolution technique for estimating the pdf for the fibre orientation by comparing with scan-rescan data, and determined it performs very well in major tracts (FA>0.3) but underestimates variability in lower FA regions.

References 1. Maes *et al*. IEEE TMI 1997. 2. Jeurissen *et al*. HBM 2010. 3. MamayyezSiahkal *et al*. MICCAI 2009. 4. Parker *et al*. TMI 2002.