Bootstrap methods for estimating uncertainty in Constrained Spherical Deconvolution fiber orientations

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Introduction

Diffusion-weighted (DW) MR images contain information about the orientation of brain white matter fibers that can be used to study brain connectivity using tractography techniques. Currently, the diffusion tensor model is widely used to extract fiber directions from DW MRI data, but fails in regions containing multiple fiber orientations. The constrained spherical deconvolution (CSD) technique has recently been proposed to address this limitation [1]. CSD estimates fiber orientations within each voxel directly from the DW data, using the concept of spherical deconvolution. However, since the fiber orientations are estimated from noisy DW images, they are subject to errors, which propagate in tractography [2]. It has already been shown that the bootstrap method is a very powerful method for characterizing uncertainty in estimates of DTI fiber orientation [3-4] and it has been successfully used to perform probabilistic DTI tractography [5]. However, this technique has not yet been assessed for CSD. In this work, we used Monte Carlo methods to investigate how the bootstrap method performs in terms of accuracy and precision, when estimating confidence intervals (CI) of the CSD fiber orientations. We also investigate the performance of an alternative bootstrap method, called bootknife [6-7].

Methods

<u>Gold standard</u>: The noiseless DW signal of a two fiber population was simulated by combining two diffusion tensor profiles at angles ranging from 90 to 60° (fractional anisotropy (FA): 0.8; mean apparent diffusion constant (ADC): 600 ×10^{-6} mm²/s**;** number of gradient directions: 60; b-value: 3000 s/mm²). Gaussian noise was added in quadrature to give SNR (in the b=0 images) of 25. This procedure was repeated 10,000 times. Fiber orientation distribution function (FOD) was calculated for every DW signal, using CSD with harmonic order 8 [1]. From these FOD's, peaks were extracted using a quasi Newton optimization method. The average peak directions were calculated as the first eigenvector of the mean dyadic tensor of all 10,000 peak directions [3]. Finally, the 95% CI of the angular deviation between the individual and average peak orientations was calculated, representing the "cone of uncertainty" [4] around the average peak orientation. <u>Bootstrap</u>: Five bootstrap designs [4] were considered, with the number of repeated acquisitions, *N*, ranging from 2 to 10. For each bootstrap design, we derived 1000 bootstrap realizations of the FOD. Fiber orientations were extracted as above. To determine the effect of the number of bootstrap realizations on the estimated fiber orientations, the number of realizations was incremented from 100 to 1000 in steps of 100. The entire procedure was repeated 50 times to determine the precision of a particular bootstrap experiment. Mean and standard deviation of the 95% CI (across the 50 repeats) was computed. <u>Bootknife</u>: The bootknife is a combination of the jackknife and bootstrap, aiming to reduce the downward bias of the bootstrap estimates [6]. Prior to selecting one of the *N* available samples for each direction, one of the 60 gradient directions is randomly omitted (jackknife), and bootstrapping is performed on the 59 remaining directions. The simulations for the bootknife were performed in the same way as for the bootstrap.

Results

Fig. 1

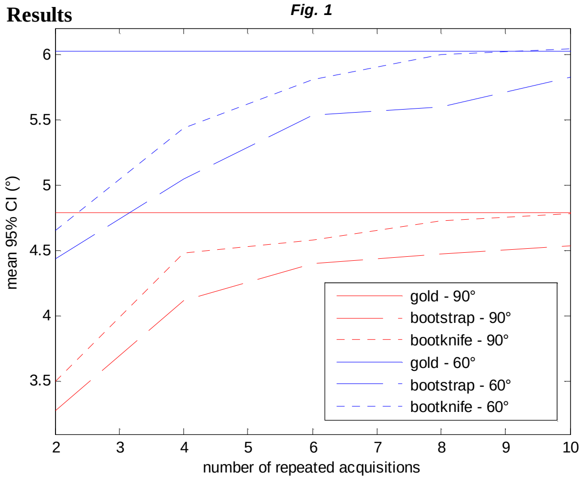

Fig. 2

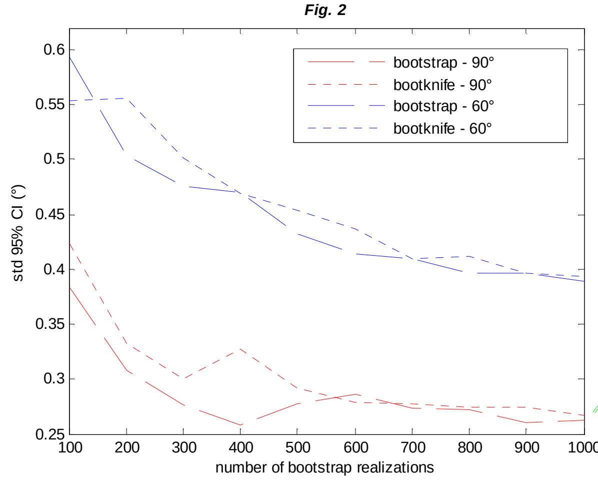

Fig. 3

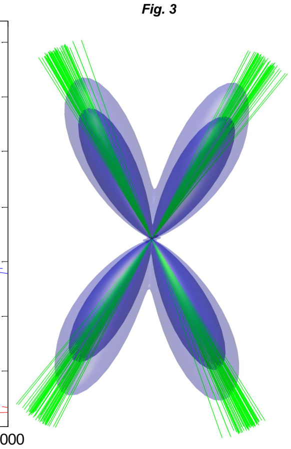

Fig. 1 and 2 were calculated for inter-fiber angles of 90° (red curves) and 60° (blue curves) at SNR 25. Other inter-fiber angles and single fiber population showed similar results, but were left out for clarity. ***Fig. 1*** shows the mean 95% CI as a function of *N*. The number of bootstrap realizations was fixed to 1000. The solid curve indicates the gold standard CI. The dashed curves indicate the mean over 50 bootstrap estimations. The dotted curves indicate the mean over 50 bootknife estimations. ***Fig. 2*** shows the standard deviation of the 95% CI as a function of number of bootstrap realizations. *N* was fixed to 8. The dashed curves indicate the standard deviation over 50 bootstrap estimations. The dotted curves indicate the standard deviation over 50 bootknife estimations. ***Fig.3*** shows the effect of the bootknife procedure on a two fiber population with inter-fiber angle of 60°. *N* was set to 8 and SNR to 25. The dark blue surface corresponds to the mean FOD over 60 bootknife realizations, whereas the light blue surface corresponds to the mean + 2 standard deviations. The green lines are the peak orientations extracted from the 60 bootknife realizations.

Discussion

As expected from earlier bootstrap studies on DTI [7-8], the CI's are significantly underestimated by the bootstrap when the number of repeated acquisitions *N* (***Fig. 1***). Although the difference between the 'gold standard' and the bootstrap estimates decreases as *N* increases, there still remains a negative bias even at *N*=10. The consequences when using the bootstrap for probabilistic tractography are considerable, since the error introduced by this bias accumulates during tracking. The bootknife estimates however tend to be much closer to the gold standard over the entire range of *N* and at different inter-fiber angles. Similar results were obtained for DTI in [8]. These results demonstrate that using the bootknife approach for CSD is preferred especially when *N* is small. In addition, ***Fig. 2*** suggests an improvement in precision by increasing the number of bootstrap realizations for both the bootstrap and bootknife estimates. However, increasing this number is only beneficial up to approximately 700. Finally, the small difference in precision between the standard bootstrap and bootknife becomes negligible as the number of bootstrap realizations goes up.

References

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