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Diffusion Tensor Imaging of the Anterior Cruciate Ligament Graft

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Running Title: DTI of the ACL Graft: a Feasibility Study

Diffusion Tensor Imaging of the Anterior Cruciate Ligament Graft

ABSTRACT

Purpose:

A great need exists for objective biomarkers to assess graft healing following anterior cruciate ligament (ACL) reconstruction to guide the time of return to sports. The purpose of this study was to evaluate the feasibility and reliability of diffusion tensor imaging (DTI) to delineate the ACL graft and to investigate its diffusion properties using a clinical 3T scanner.

Materials and Methods:

DTI of the knee (b=0, 400 and 800 s/mm², 10 diffusion directions, repeated 16 times for a total of 336 diffusion weighted volumes) was performed at 3T in 17 patients between 3 and 7 months (mean, 4 months) following ACL reconstruction. Tractography was performed by 2 independent observers to delineate the ACL graft. Fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) were calculated within the graft. Interrater reliability was assessed using the intraclass correlation coefficient (ICC) and the scan-rescan reproducibility was evaluated based on the percentage coefficient of variance (%CV) across 20 repetition bootknife samples.

Results:

In all subjects, tractography of the ACL graft was feasible. Quantitative evaluation of the diffusion properties of the ACL graft yielded the following mean \pm SD values: FA=0.23 \pm 0.04; MD=1.30 \pm 0.11 x 10⁻³ mm²/s; AD=1.61 \pm 0.12 x 10⁻³ mm²/s and RD=1.15 \pm 0.11 x 10⁻³ mm²/s. Interrater

reliability for the DTI parameters was excellent (ICC= 0.91-0.98). Mean %CVs for FA, MD, AD and RD were 4.6%, 3.5%, 3.7% and 4.4%, respectively.

Conclusion:

We demonstrated the feasibility and reliability of DTI for the visualization and quantitative evaluation of the ACL graft at 3T.

Keywords:

Diffusion Tensor Imaging – Anterior Cruciate Ligament Graft – Fiber Tractography - Reproducibility

INTRODUCTION

Surgical anterior cruciate ligament (ACL) reconstruction using a tendon graft remains the standard of care for ACL injuries, especially for young and active patients who aim to return to sports (1). Postoperatively, the tendon graft undergoes a biologic transition from tendinous to ligamentous in appearance. This 'ligamentization' process includes an acute inflammatory phase characterized by resynovialization, revascularization and cell proliferation, followed by a more chronic stage in which collagen remodeling and restructuring towards the properties of the native ACL occurs (2). Despite substantial research, this process is still poorly understood in the human knee. For example, the time needed by the graft to reach ligamentous maturity is a matter of debate, reported to occur between 12 and 24 months postoperatively (2,3).

Successful and timely maturation of the ACL graft is crucial as it provides mechanical strength to the tissue, and thus, is related to the safe return to full activity and sports (4). In general, evaluation of return to sports is performed before the first postoperative year, with many surgeons allowing return to pivoting sports at 6 months after ACL reconstruction (5). However, objective guidelines permitting safe return to sport following ACL reconstruction are lacking (4,5).

Traditional criteria for evaluating the success of ACL surgery include clinical assessment of knee laxity and patient-oriented outcome questionnaires (5).

These, however, are only an indirect measure of graft health and integrity, and may lack objectivity to measure subtle changes in tendon status, which is needed to evaluate and monitor progression of graft healing. Previous human biopsy studies have examined the remodeling process of the ACL graft (2,3,6). However, biopsy is invasive, may suffer from sampling error, and is not suitable for follow-up of subjects in clinical trials (6). Thus, an objective non-invasive method is needed to longitudinally assess ACL graft maturation in vivo to guide the time of return to sports.

MRI has been widely used to gain insight into the biology of tendon graft maturation (7). Conventional MRI using a qualitative measure such as signal intensity to assess the ACL graft is not reliable and does not predict clinical or functional outcomes of ACL reconstruction (8). There are very few MR approaches to quantify the structural and functional integrity of the ACL graft. Biercevicz et al. (9) found that both MR graft volume (a measure of tissue quantity) and its corresponding T_2^* value (a measure of tissue organization) are associated with the structural integrity of the healing ACL. According to a previous animal study by Fleming et al. (10), the T_2 value alone cannot predict the structural properties of the graft.

Diffusion tensor imaging (DTI) is a potential candidate to assess ACL graft maturation. It allows for noninvasive *in vivo* quantification of the diffusion of water in biological tissues and assessment of its directional anisotropy, thereby providing a proxy measure of microstructural integrity (11). The most common DTI parameters include 1) fractional anisotropy (FA), a scalar

metric that describes the degree of anisotropy of a diffusion process and ranges between 0 (isotropic) and 1 (anisotropic); 2) mean diffusivity (MD), an estimate of the overall free diffusion of water; 3) axial diffusivity (AD), representing diffusion of water along the long axes of the fibers; 4) radial diffusivity (RD), representing diffusion perpendicular to the long axes of the fibers. The principal diffusion directions of neighboring voxels can be integrated to form long range connections using fiber tractography, enabling three-dimensional (3D) visualization of tissue fiber architecture. This can provide important information about the tissue's architectural organization that cannot be obtained from conventional MR imaging (12). Track-based methods can then be used to evaluate the quantitative DTI parameters of the entire tract volume (12). The vast majority of DTI studies have investigated the brain (11), peripheral nerves (13) and muscles (14). More recently, DTI of articular cartilage has been described (15).

The highly-organized anisotropic structure of tendons and ligaments is likely well suited for DTI evaluation. However, little data is available in the literature regarding the use of DTI for these tissues, mainly because of the technical challenges, including short T₂ relaxation time and small size of the tissues being studied, and the presence of susceptibility artifacts induced by the complex joint anatomy (14,15).

Two previous studies (16,17) have reported on the feasibility of DTI of the ACL graft. Their results, however, have not yet been confirmed by other authors. In these studies, the time interval between surgery and DTI varied

widely between 3 months and 10 years postoperatively. The ideal time to evaluate the healing process is between 4 to 8 months following ACL reconstruction, as this is the time of most intensive graft remodeling (2,3). In addition, the evaluation of return to sports is performed at around 6 months postoperatively (5). DTI measures obtained at this time period can serve as a baseline for future longitudinal follow-up. The purpose of the present study was to evaluate the feasibility and reliability of DTI to delineate the ACL graft and to investigate its diffusion properties in vivo using a clinical 3T scanner, including patients at an early postoperative time.

MATERIALS AND METHODS

Subjects

Our institutional review board approved this prospective study. Written informed consent was obtained from all participants. Between March and June 2016, 17 patients who had undergone ACL reconstruction using autograft hamstrings (1) were enrolled in this study. The time since surgery ranged between 3 and 7 months (3 months, n=11; 4 months, n=2; 6 months, n=1; and 7 months, n=3).). Postoperatively, all patients followed a standardized rehabilitation program and were scheduled for planned follow-up visits in order to assess knee stability. Exclusion criteria for participating were a clinically unstable knee, and the presence of (relative) contraindications for the use of MRI, claustrophobia and pregnancy.

Imaging was performed using a 3T scanner (Magnetom PrismaFit, Siemens Medical Solutions, Erlangen, Germany) with a maximum gradient amplitude of 80 mT/m and maximum slew rate 200 T/m/s. A 15-channel knee coil was used, with subjects placed in the supine position with their knee in a slightly flexed position within the coil. Standard automatic B₀ shimming was applied to reduce field inhomogeneities.

Diffusion weighted (DW) volumes were acquired using a multislice single-shot spin-echo echo planar imaging (SE-EPI) sequence. Diffusion weightings of b=0, 400 and 800 s/mm² were applied using 10 diffusion gradient directions distributed uniformly on the unit sphere. Spectral Adiabatic Inversion Recovery (SPAIR) was used for fat suppression. The full sequence was repeated 16 times, resulting in a total of 336 DW volumes and scan time of 7min 25s. Multiplanar turbo spin-echo (TSE) images were acquired to serve as an anatomical reference for fiber tracking. Imaging parameters are summarized in Table 1. Signal-to-noise ratio (SNR) was calculated in the ACL graft using random matrix theory (18).

Preprocessing and Parameter Estimation

Combined eddy-current induced distortion and motion correction (19) was performed using FSL 5.0.9. This correction included the required B-matrix

adjustments (20) and appropriate modulation of the DW images with the Jacobian of the transformation matrix (21).

After correction of the DW scans, diffusion tensors were obtained for each imaging voxel using the weighted linear least square estimator (22). From the diffusion tensors, the following scalar metrics were obtained using MRtrix 0.3.15. (23): fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD) and radial diffusivity (RD).

To account for subject motion between the DW and structural scans, a six-degrees-of-freedom rigid-body registration between the structural images and the DW scans was performed using the tools provided in the Statistical Parametric Mapping (SPM) toolbox, with the b=0 s/mm² image as the target image, and the structural images as the sources. Normalized mutual information was used as a similarity metric for registration as the contrasts of the two images differ. The resulting structural data sets are aligned spatially to the corresponding DW images (apart from susceptibility-induced distortions, which we did not correct).

Fiber Tracking and Diffusion Quantification of the ACL Graft

Deterministic diffusion tensor tractography was performed, using the following parameters: step size: 0.15mm; maximum angle: 2°; and FA threshold: 0.1. To isolate the ACL graft, a spherical region-of-interest (ROI) of 1cm diameter was placed at the aperture of the femoral (Fig. 1a) and the tibial (Fig. 1b) bone tunnel on anatomical images. These ROIs were used as

both seed and target regions for the diffusion tensor tractography algorithm. The resulting fiber tractogram was converted to a track density image (24), which was automatically thresholded to obtain a binary mask of the ACL graft (25). Within this mask, the average FA, MD, AD and RD were extracted to obtain quantitative diffusion indices specifically for the ACL graft. All fiber tracking operations were performed using MRtrix 0.3.15. (23).

Assessment of Interrater Reliability

ROI placement and subsequent fiber tracking was repeated by 2 independent radiologists (PVD, with 13 years of experience in musculoskeletal radiology, and MT, research fellow in musculoskeletal radiology) to assess interrater reliability using the intra-class correlation coefficient (ICC) with ICC<0.40 indicating poor reliability, ICC=0.4-0.75 indicating fair-to-good reliability, and ICC>0.75 indicating excellent reliability.

Assessment of Scan-Rescan Reproducibility

To measure the scan-rescan reproducibility of our experiments we used the repetition bootstrap technique (26). The bootstrap is an empirical, nonparametric, statistical technique based on data resampling. The bootstrap method requires the acquisition of N repeats of a complete DW data set, so that N samples are available for each gradient direction (in this work N=16 as the entire DW sequence was repeated 16 times). A new

realization of the DW data set can then be produced by randomly selecting N=16 samples with replacement for each direction. In this way, a new, 'virtual' data set is produced from a random combination of the images in the N=16 repeats of the original data set, which can then be processed using the method under investigation (27,28). By repeating this procedure, one can then obtain metrics on the reproducibility of the results. In this work, we calculated the coefficient of variation (CV), also known as the relative standard deviation, based on 20 bootstrap realizations. Note that prior to selecting N samples with replacement, we randomly eliminated one measurement, a procedure known as the repetition bootknife, as this is shown to avoid a downward bias in the uncertainty measures (27-29).

RESULTS

Image Acquisition and Fiber Tracking of the ACL Graft

Twelve males and 5 females (mean age, 32 years; range, 18-51 years) were included in this study. All patients had a clinically stable knee at the time of the study. For the raw (unprocessed) data, mean SNR (±SD) in the ACL graft was 13.6 (±2.0, range 10-17.9), 7.4 (±0.9, range 6-9.2), and 4.6 (±0.5, range 4-5.3) for the b0, b400, and b800 images, respectively. There were no major susceptibility distortions at the intercondylar notch (Fig. 2). 3D fiber tractography of the ACL graft was feasible in all patients. The fibers of the graft could be followed from the femur to the tibia with normal course of the

graft within the intercondylar notch as perceptible on corresponding anatomical sequences (Figs. 3-5).

Diffusion Quantification of the ACL Graft

Quantitative evaluation of the obtained fiber tracks yielded the following mean ± SD values across the population (averaged across raters): FA=0.23±0.04; MD=1.30±0.11 x 10⁻³ mm²/s; AD=1.61±0.12 x 10⁻³ mm²/s and RD=1.15±0.11 x 10⁻³ mm²/s (Table 2). Interrater reliability for the diffusion parameters was excellent (ICC for FA, MD, AD and RD of 0.98, 0.91, 0.91 and 0.92, respectively). Mean number of voxels from which DTI parameters were measured was 174±141 (ICC 0.89).

Scan-Rescan Reproducibility

The scan-rescan reproducibility of the DTI measures for rater 1 are summarized in Table 3. Mean CVs (%) across all subjects for FA, MD, AD and RD were 4.6% (range 1.8%-8.7%), 3.5% (range 0.9%-11.1%), 3.7% (range 1.0%-10.4%) and 4.4% (range 1.2%-11.8%), respectively.

DISCUSSION

Our study demonstrates that DTI with fiber tractography of the ACL graft is feasible at 3T and that it is possible to obtain reliable estimation of DTI indices of the ACL graft in a scan time adequate for routine clinical practice (7min25sec).

DTI of ligament and tendon is technically challenging because of the small size and short T₂ relaxation times of these tissues (14). Additionally, the knee joint has a complex anatomy that causes changes in the magnetic field (B₀) that can lead to susceptibility artifacts, especially at the intercondylar notch and ACL insertion sites (15,16). We performed DTI of the ACL graft using new state-of-the-art 3T technology equipped with powerful gradients (maximum amplitude=80 mT/m; slew rate 200 T/m/s) permitting DWIs to be acquired at a shorter TE (45ms), which improves SNR and reduces susceptibility artifacts (14). In our study, there were no major influencing susceptibility distortions at the intercondylar notch. It appears that the effects of susceptibility and off-resonance artifacts on DTI have largely been reduced using acceleration with parallel imaging (12). Recently, the use of reversed phase encoding scans was proposed to further reduce EPI distortions (30).

According to Jones DK et al. (21), the SNR should be above 3:1 in order to avoid problems associated with the rectified noise floor. With an SNR of 13.6, 7.4, and 4.6 for the b0, b400, and b800 images, respectively, we are well above this lower limit. In this SNR regime, our tensor fitting routine (the weighted linear least squares estimator) is nearly unbiased (22). Moreover, we obtained 16 averages to boost SNR, resulting in an effective SNR of 54.4, 29.6 and 18.4 for the average b0, b400, and b800 images, respectively, which should be more than sufficient for robust diffusion tensor estimation and fiber tractography (31).

The fact that we studied ACL grafts instead of native ACLs had several advantages: first, we avoided gross magnetic field inhomogeneity at the apertures of the bone tunnels, thereby facilitating the delineation of the intra-articular tendon graft; second, the ACL graft has larger cross-sectional dimensions compared with the native ACL (32), which offers advantages in terms of SNR; third, at 4 to 8 months after surgery, remodeling reaches a peak resulting in increased signal intensity of the graft on MRI (3,32). The use of a multichannel knee coil with parallel transmit capabilities further enabled to increase the number of averages per image (16 repetitions) resulting in a clinically feasible scan time (12).

At 4 to 8 months after ACL reconstruction, thick synovial tissue envelops the graft, providing its vascular supply (3). This leads to extra-cellular matrix changes and increased water content, loss of regular collagen orientation and decrease in collagen fibril density (2,3,6). Building on previous DTI studies in muscle (33) and articular cartilage (15), we hypothesize that, as remodeling continues and the graft restructures towards the properties of the native ACL with decrease of water content and collagen fibers regaining their organization and attaining a more densely packed, parallel alignment, FA will increase and MD will decrease over time. This warrants further exploration in a longitudinal DTI follow-up study.

Mean FA value of the ACL graft found in our study was much lower and MD value was higher compared to that found in the study by Yang et al. (17) (0.23 vs 0.55 and 1.30 vs 1.17, respectively). These authors examined ACL grafts at a later maturation stage, whereas the mean age of the ACL grafts in

our study was 4 months. Although the different values found in both studies may reflect genuine differences in the graft maturation stage, and thus confirm our hypothesis, other factors may be more likely to account for these variations. First, MR imaging scanner types and acquisition protocols were different in both studies. In a simulation study of skeletal muscle DTI (31), it was shown that FA is overestimated and MD is underestimated at low SNR. Second, fiber tracking in the study by Yang was performed on a commercial workstation, whereas we used specialized software (23) for all fiber tracking operations. As AD and RD, which have not been reported previously, provide more subtle insight into the changes in FA and MD, we believe they may be useful for complete evaluation of the healing process of the graft (34).

We found a high reproducibility of the DTI measures of the ACL graft in our study. Although this was only measured for the most experienced rater, the reproducibility of the other rater is not expected to be significantly different given the very high agreement between both raters.

Our DTI protocol used 10 diffusion directions with 16 averages. Although more diffusion directions are generally applied in DTI studies (12), previous work found that 10 unique sampling directions distributed uniformly on the unit sphere provide comparable values of FA and MD and similar tracking, and thus, can be used for reliable diffusion tensor estimation (35-37). We hypothesized that it would be possible to reduce the number of diffusion directions in ACL graft DTI because tendons are typically linear with fibers aligned parallel to each other and not expected to cross, diverge or kiss (as is common in the brain, inviting more complex diffusion models) (12).

Our study had several limitations. First, imaging was performed with thick slices (6mm) for SNR purposes. Partial volume averaging within imaging slices may have contributed to the low FA measures and variability of the measurements (14). Second, only the intra-articular segment of the ACL graft was assessed in this study. Assessment of the bone tunnels using DTI is technically challenging because of the susceptibility-artifacts related to the presence of bone and metal screw in the tunnels. Third, the present study did not specifically assess the optimal b-value for ligament and tendon DTI, nor the optimal number of diffusion-encoding directions. It was not, however, the purpose of this study to optimize the DTI protocol for imaging ligament and tendon, but rather to demonstrate the feasibility of DTI to evaluate the ACL graft. Based on the MD value of the ACL graft found in our study, the optimal b-value would be close to 800 s/mm² (38). Fourth, a powerful gradient strength (80 mT/m) was used in our study for DTI of the ACL graft. Thus, our results may not be applicable to MRI systems using lower gradient strength which will result in lower SNR and larger susceptibility-induced distortions. Fifth, the feasibility of the proposed DTI technique needs further evaluation in fully matured grafts (>1 to 2y). However, as patients with such grafts have a stable knee, this may not be a priority from a clinical point of view. Other limitations of this feasibility study include its small sample size and the lack of arthroscopic correlation.

In conclusion, we demonstrated the feasibility and reliability of DTI for the visualization and quantitative evaluation of the ACL graft using a clinical 3T system. Future studies should perform longitudinal follow-up of DTI

parameters of the healing graft and seek to assess whether these measures can predict traditional clinical and functional outcomes after ACL reconstruction. The role of DTI as a potential biomarker of ACL graft healing warrants further exploration to help determine the appropriate time to return to sports.

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Table 1 MRI Acquisition Parameters for Knee Examinations

| | Sagittal PD | Axial IW | Coronal T1 | Axial DTI |
|----------------------------|-------------|-------------|-------------|-------------|
| TR (ms) | 2510 | 4310 | 450 | 1300 |
| TE (ms) | 20 | 50 | 10 | 45 |
| FOV read (mm) | 140 | 140 | 140 | 192 |
| ETL | 60 | 33 | 124 | 32 |
| Phase encoding dir. | H>>F | R>>L | R>>L | A>>P |
| FOV phase (%) | 100 | 100 | 100 | 100 |
| Slice thickness (mm) | 2.5 | 3 | 3 | 6 |
| Effective resolution (mm³) | 0.3x0.3x2.5 | 0.4x0.4x3.0 | 0.3x0.3x3.0 | 1.5x1.5x6.0 |
| Bandwidth (Hz/px) | 257 | 181 | 192 | 1860 |
| Fat suppression | - | fs | - | SPAIR |
| b-value (s/mm²) | - | - | - | 0/400/800 |
| Turbo factor | 5 | 7 | 2 | - |
| No. of signals acquired | 1 | 1 | 1 | 16 |
| PAT* | 2 | 2 | 2 | 3 |
| Partial Fourier | off | off | off | 6/8 |
| Interslice gap (%) | 10 | 10 | 10 | 0 |
| No. of slices | 35 | 38 | 29 | 10 |
| Time of acquisition | 2:35 min. | 2:27 min. | 1:42 min. | 7:25min |

TR=repetition time; TE=time to echo; FOV=field of view; ETL=echo train length; PAT=parallel acquisition technique; PD=proton-density; IW=intermediate-weighted; fs=fat saturation; DTI=diffusion tensor imaging; SPAIR=spectral adiabatic inversion recovery

 $\textbf{Table 2} \ \, \textbf{DTI} \ \, \textbf{values of the ACL graft}$

| | F | 'A | MD (x10- | ³ mm ² /s) | AD (x10- | 3 mm ² /s) | RD (x10- | ³ mm ² /s) | Co | unt |
|------|-----------|-----------|-----------|----------------------------------|-----------|-----------------------|-----------|----------------------------------|------|------|
| N° | R1 | R2 | R1 | R2 | R1 | R2 | R1 | R2 | R1 | R2 |
| 1 | 0.25±0.07 | 0.25±0.07 | 1.29±0.34 | 1.26±0.32 | 1.62±0.39 | 1.60±0.38 | 1.13±0.31 | 1.09±0,30 | 157 | 143 |
| 2 | 0.19±0.05 | 0.19±0.06 | 1.37±0.24 | 1.35±0.26 | 1.65±0.26 | 1.62±0.27 | 1.24±0.24 | 1.22±0.26 | 71 | 100 |
| 3 | 0.19±0.05 | 0.18±0.05 | 1.32±0.23 | 1.33±0.23 | 1.58±0.23 | 1.59±0.24 | 1.19±0.23 | 1.20±0.24 | 94 | 101 |
| 4 | 0.21±0.05 | 0.21±0.04 | 1.36±0.24 | 1.35±0.20 | 1.64±0.26 | 1.66±0.22 | 1.21±0.24 | 1.20±0.20 | 163 | 70 |
| 5 | 0.31±0.12 | 0.33±0.13 | 0.93±0.41 | 1.02±0.44 | 1.23±0.50 | 1.35±0.50 | 0.79±0.37 | 0.86±0.41 | 104 | 90 |
| 6 | 0.27±0.07 | 0.25±0.07 | 1.26±0.24 | 1.26±0.24 | 1.62±0.27 | 1.61±0.29 | 1.07±0.24 | 1.08±0.24 | 102 | 102 |
| 7 | 0.23±0.08 | 0.22±0.08 | 1.31±0.31 | 1.31±0.33 | 1.63±0.34 | 1.62±0.37 | 1.15±0.30 | 1.16±0.31 | 468 | 519 |
| 8 | 0.19±0.06 | 0.20±0.06 | 1.35±0.27 | 1.33±0.28 | 1.62±0.27 | 1.60±0.28 | 1.21±0.28 | 1.19±0.28 | 155 | 125 |
| 9 | 0.22±0.05 | 0.22±0.05 | 1.49±0.27 | 1.49±0.28 | 1.83±0.29 | 1.82±0.30 | 1.33±0.27 | 1.32±0.27 | 179 | 169 |
| 10 | 0.23±0.05 | 0.23±0.06 | 1.31±0.25 | 1.30±0.25 | 1.63±0.29 | 1.63±0.31 | 1.14±0.24 | 1.13±0.23 | 506 | 188 |
| 11 | 0.20±0.06 | 0.20±0.05 | 1.33±0.29 | 1.31±0.29 | 1.62±0.34 | 1.59±0.35 | 1.18±0.27 | 1.17±0.27 | 143 | 127 |
| 12 | 0.17±0.03 | 0.17±0.03 | 1.38±0.22 | 1.18±0.21 | 1.61±0.24 | 1.38±0.25 | 1.26±0.21 | 1.08±0.19 | 66 | 32 |
| 13 | 0.31±0.08 | 0.31±0.09 | 1.25±0.23 | 1.24±0.22 | 1.68±0.29 | 1.67±0.29 | 1.04±0.23 | 1.02±0.21 | 601 | 502 |
| 14 | 0.24±0.07 | 0.26±0.10 | 1.46±0.36 | 1.37±0.47 | 1.85±0.36 | 1.73±0.52 | 1.27±0.37 | 1.18±0.45 | 82 | 101 |
| 15 | 0.25±0.07 | 0.23±0.06 | 1.32±0.25 | 1.28±0.25 | 1.67±0.28 | 1.60±0.30 | 1.14±0.24 | 1.12±0.23 | 102 | 71 |
| 16 | 0.22±0.05 | 0.23±0.05 | 1.22±0.34 | 1.19±0.36 | 1.51±0.41 | 1.48±0.44 | 1.07±0.31 | 1.04±0.33 | 246 | 153 |
| 17 | 0.16±0.04 | 0.17±0.05 | 1.33±0.45 | 1.41±0.45 | 1.55±0.52 | 1.66±0.52 | 1.22±0.41 | 1.29±0.42 | 57 | 41 |
| Mean | 0.23 | ±0.04 | 1.30 | ±0.11 | 1.61: | ±0.12 | 1.15: | ±0.11 | 174: | ±141 |

Data represent DTI values ±SD; R1=rater 1; R2=rater 2; FA=fractional anisotropy; MD=mean diffusivity; AD=axial diffusivity; RD=radial diffusivity; Count refers to number of voxels from which DTI parameters were measured

Table 3 Scan-rescan reproducibility for the DTI measures

| | FA | MD | AD | RD |
|------------|-----|------|------|------|
| Patient n° | | | | |
| 1 | 7.3 | 5.7 | 4.8 | 6.4 |
| 2 | 7.9 | 5.9 | 5.2 | 6.5 |
| 3 | 3.4 | 2.9 | 2.7 | 3.1 |
| 4 | 5.8 | 4.6 | 3.6 | 5.4 |
| 5 | 6.3 | 11.1 | 10.4 | 11.8 |
| 6 | 4.0 | 2.8 | 2.3 | 3.3 |
| 7 | 1.9 | 1.5 | 1.4 | 1.7 |
| 8 | 4.5 | 2.7 | 2.6 | 2.8 |
| 9 | 2.7 | 2.5 | 2.1 | 2.9 |
| 10 | 1.9 | 1.2 | 1.1 | 1.3 |
| 11 | 4.3 | 2.2 | 2.2 | 2.4 |
| 12 | 7.6 | 9.2 | 8.9 | 9.5 |
| 13 | 1.8 | 0.9 | 1.0 | 1.2 |
| 14 | 4.1 | 3.0 | 2.7 | 3.3 |
| 15 | 3.3 | 1.4 | 1.5 | 1.6 |
| 16 | 2.7 | 2.2 | 2.0 | 2.4 |
| 17 | 8.7 | 8.5 | 8.0 | 8.8 |
| Mean | 4.6 | 3.5 | 3.7 | 4.4 |

Data are the percentage coefficient of variation (%CV) for rater 1; FA=fractional anisotropy; MD=mean diffusivity; AD=axial diffusivity; RD=radial diffusivity

FIGURE LEGEND

- Fig. 1. A 36-year-old male patient 3 months after ACL reconstruction using autologous hamstring tendon graft of the right knee. (a) Coronal T1-weighted and (b) sagittal proton density-weighted TSE images. To isolate the ACL graft, a spherical region-of-interest (ROI) of 1cm diameter was placed at the apertures of the femoral (a) and tibial (b) bone tunnels on anatomical sequences. These ROIs were used as both seed and target regions for the diffusion tensor tractography algorithm.
- Fig. 2. A 25-year-old male patient 3 months after ACL reconstruction of the right knee. Diffusion weighted images show no major distortions due to susceptibility artifacts at the intercondylar notch. The SNR in the ACL graft (arrow) was 15.3, 8.5, and 5.2 for the b0 (a), b400 (b), and b800 (c) images, respectively.
- Fig. 3. A 27-year-old female patient 4 months after ACL reconstruction of the right knee. Tractography images of the ACL graft are superimposed on sagittal proton density-weighted TSE images.
- Fig. 4. Same patient as Fig. 3. Tractography images of the ACL graft are superimposed on axial fat-suppressed intermediate-weighted TSE images.
- Fig. 5. Same patient as Figs. 3 and 4. Three-dimensional fiber tractography of the ACL graft from a medial view. Fiber tracks are demonstrated from the

femoral to the tibial tunnel matching the global appearance of the ACL graft within the intercondylar notch.