A registration strategy to characterize DTI-observed changes in skeletal muscle architecture due to passive shortening

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23   **Short title:** Image registration strategy to assess changes in muscle architecture

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Abstract (250 words)

Skeletal muscle architecture is a key determinant of muscle function. Architectural properties such as fascicle length, pennation angle, and curvature can be characterized using Diffusion Tensor Imaging (DTI), but acquiring these data during a contraction is not currently feasible. However, an image registration-based strategy may be able to convert muscle architectural properties observed at rest to their contracted state. As an initial step toward this long-term objective, the aim of this study was to determine if an image registration strategy could be used to convert the whole-muscle average architectural properties observed in the extended joint position to those of a flexed position, following passive rotation. DTI and high-resolution fat/water scans were acquired in the lower leg of seven healthy participants on a 3T MR system in +20° (plantarflexion) and -10° (dorsiflexion) foot positions. The diffusion and anatomical images from the two positions were used to propagate DTI fiber-tracts from seed points along a mesh representation of the aponeurosis of fiber insertion. The -10° and +20° anatomical images were registered and the displacement fields were used to transform the mesh and fiber-tracts from the +20° to the -10° position. Student's paired t-tests were used to compare the mean architectural parameters between the original and transformed fiber-tracts. The whole-muscle average fiber-tract length, pennation angle, curvature, and physiological cross-sectional areas estimates did not differ significantly. DTI fiber-tracts in plantarflexion can be transformed to dorsiflexion position without significantly affecting the average architectural characteristics of the fiber-tracts. In the future, a similar approach could be used to evaluate muscle architecture in a contracted state.

Introduction

The diversity of human motion, including movements that vary in velocity, degree of precision, force, and duration, requires a broad range of outputs from the musculoskeletal system. The mechanisms for these varied outputs include neural control strategies (the activation patterns of multiple muscles; the motor unit recruitment and rate coding strategies within a muscle) and the activated muscles' metabolic, structural, and mechanical properties (1, 2). Several determinants of a muscle's mechanical properties include its gross morphology; its internal structure (or architecture, as represented by the pennation angle, length, and curvature of its fibers); and the structural and mechanical properties of the collagen-rich structures (such as tendons and aponeuroses) with which it interacts (3). Skeletal muscle architecture can be non-invasively characterized using Diffusion Tensor Imaging (DTI), a magnetic resonance imaging (MRI) technique that measures the reduced and anisotropic diffusion of water molecules (4, 5). By measuring the anisotropic movement of water molecules, it is possible to derive information about the micro-structure and architecture of healthy and diseased muscle (6-23).

To date, DTI has primarily been applied in non-contracting, healthy muscle tissue. From such measurements, the microstructural and architectural properties of resting muscle have been characterized, including following passive joint motions (14, 16, 24). Furthermore, these microstructural and architectural properties have been used as inputs to musculoskeletal models to predict changes in muscle function in healthy, diseased, and injured muscle (25-30). DTI has intrinsic three-dimensional sensitivity, whole-muscle coverage, and the potential to be integrated with other forms of functionally relevant MRI contrast. With this approach, it may be possible to answer previously unrealizable questions in the study of muscle structure-function relationships.

To realize such possibilities, DTI data would ideally be acquired during a muscle contraction; but this is challenging due to long scan times required for muscle DTI, the potential for motion artefacts, and signal voids that may occur when diffusion-weighted images are acquired during contraction (31-33). This challenge is amplified by the fact that whole muscle DTI is required to provide a complete understanding

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73 of the architectural changes during contraction, which typically requires multi-stack acquisitions thereby

74 increasing the total acquisition time in direct proportion to the number of stacks acquired. Hence, to be

75 able to obtain information about architectural properties in a whole muscle, during a contraction, a

76 different approach is required.

77 Planar ultrasonography has been used in dynamic settings to characterize changes in architectural

78 properties with a high temporal resolution, but lacks the coverage required to visualize the whole muscle

79 (34-37) and limited soft tissue contrast. Recent work showed that high resolution displacement fields

80 derived from MR image registration were able to accurately quantify tissue displacement and strain in

81 skeletal muscle during isometric contractions (38, 39). Based on these findings, we hypothesize that we

82 can use displacement fields derived from registration of high-resolution anatomical images in different

83 ankle positions to transform muscle fiber-tracts from a plantarflexed to a dorsiflexed ankle position,

84 without significant differences in the observed mean architectural properties from those directly observed

85 in the dorsiflexed position. If so, this would provide critical proof of the concept that a registration-based

86 approach could be similarly used to transform the DTI-observed skeletal muscle architecture patterns due

87 to contraction. The accuracy of the displacement fields, and thus the transformation of muscle fiber-tracts,

88 depends highly on the quality of the registration. Therefore, we first optimized the registration parameters

89 of the anatomical images; thereafter used interpolation to transform fiber-tracts from a plantarflexed to a

90 dorsi-flexed ankle position; and finally determined whether the original tracts' mean architectural

91 properties differed from those of the transformed tracts.

92

93 **Materials and methods**

94 *Study participants*

95 Seven healthy volunteers (5 men; age: 25.1 ± 2.7 yrs. with range $23 - 31$ yrs.) provided written informed

96 consent to participate in this IRB-approved study. The written consent was obtained between 01-09-2019

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97   and 01-11-2019. The inclusion criteria were healthy men and woman in the age range of 18 - 40 years.

98   Exclusion criteria included the inability to provide informed consent, MRI contraindications,

99   claustrophobia, physician-diagnosed muscle disease or other disease affecting muscle function, an

100   inability to exercise safely, drug and alcohol use to the point of intoxication more than twice a week, and

101   smoking tobacco. All participants were asked to abstain from alcohol (24 hours prior to the examination),

102   caffeine (6 hours prior to the examination), and moderate or intense exercise (24 hours prior to the

103   examination).

104   *MR examination*

105   MR datasets were acquired in the right lower leg on a 3 Tesla MR System (Philips Elition; Best, the

106   Netherlands) using a 16-element receiver coil (anterior) and the 10-element receiver coil built into the

107   patient table (posterior). The participants were positioned supine, feet-first in the MR scanner with the

108   right leg as close as possible to the centre of the bore. The foot was placed in an MR compatible exercise

109   device which could be fixed in ankle angles ranging from +25° degrees plantarflexion to -15° degrees

110   dorsiflexion. The anterior coil was placed on top of the legs and supported with foam pillows and fixation

111   bands to ensure that the coil covered the full lower leg, did not compress the muscle, and did not move

112   during the change of foot position from plantarflexion (+20°) to dorsiflexion (-10°). MRI data were first

113   acquired with the foot passively held at +20° and again after the foot was passively rotated to -10°. The

114   MR examination consisted of:

115   I.   Chemical shift-based water-fat separation scan for anatomical reference and muscle and

116   aponeurosis segmentation. (3D FFE; mDixon-Quant; TR/TE/ΔTE/FA, 210ms/1.01ms/0.96ms/3°;

117   voxel size, 1×1×1.75mm^3; number of excitations (N_{EX}), 1; acquired matrix, 192×192; number of

118   slices, 176; no slice gap; SENSE, 2; and scan duration, 36.2 seconds)

119   II. Two diffusion-weighted acquisition to assess muscle fascicle architecture (SE-EPI; TR/TE,

120   4800ms/53ms; 24 directions; b-values, 0 and 450 s/mm^2; recon voxel size, 1×1×7mm^3; N_{EX}, 6;

6

121   acquired/reconstructed matrices, 96×96/192×192; number of slices, 24; no slice gap, SENSE, 1.7;

122   combination of three fat suppression techniques: SPectral Adiabatic Inversion Recovery (SPAIR)

123   and Slice Selected Gradient Reversal (SSGR) for the aliphatic lipid peaks and a SPIR pulse for

124   the olefinic peak (40); scan duration, 725 seconds). The DTI data were acquired in two transverse

125   stacks with 28 mm overlap, fully covering 308 mm in the superior-inferior direction with a field

126   of view (FOV) of 192×192 mm^2.

127   For each type of sequence, the superior end of the slice stack was positioned at the level of the tibia plateau

128   and the image stacks were rotated to align their midpoint with the tibia bone.

129   **Data-analysis**

130   All data-analyses were performed in MATLAB R2019 (Mathworks) using the publicly available

131   MuscleDTI_Toolbox (41) and additional custom written scripts. The full workflow of the study is shown

132   in Figure 1.

133

134   **Figure 1. *Overview of the analysis workflow.***

135   MR data were acquired in two ankle positions, +20° (blue outline) and -10° (green outline). Anatomical

136   images were manually segmented to derive masks for the TA aponeurosis and TA muscle (binarized

137   images). After the tensor calculation, fiber tracking was performed. A quality check was used to exclude

138   obviously erroneous results (resulting in the selected fibers). Displacement fields were used to transform

139   fiber-tracts and the aponeurosis mesh from +20° to -10° ankle position (orange arrows). The transformed

140   aponeurosis is used to initiate tracking in the -10° position to allow direct comparison between

141   transformed (orange dotted outline) and original fiber-tracts (green dotted outline).

142

143   *VOIs and aponeurosis mesh*

144 For each foot position, masks of the Tibialis Anterior (TA) boundaries and aponeurosis were manually

145 drawn in ITK-snap (version 3.8.0; www.itksnap.org) (42) on the high resolution mDixon-Quant water

146 image. The manually segmented aponeurosis masks were converted to a low-resolution seed-point mesh

147 (mesh size: 30×20) using *define_roi( )*. An additional high-resolution seed-point mesh (size 100×50) was

148 also defined for visualizing the outcomes of the optimized method.

149 *Optimization of anatomical image registration*

150 The high-resolution anatomical scans from the +20° ankle position were registered to the anatomical scan

151 from the -10° position using MATLAB's *imregdemons( )* function (2000 iterations, 4 pyramid levels and

152 AccumulatedFieldSmoothing of 1.0; Fig. 1). This function uses a 3D registration based on a Demons

153 algorithm (43, 44), resulting in displacement fields for the X, Y and Z directions. A variety of registration

154 inputs were explored, including various contrasts (*2 settings; water image and out-of-phase images*); slice

155 thickness (*3 settings; 7 mm, 3.5 mm and 1.75 mm*); normalization (*2 settings; normalized images and non-*

156 *normalized images*); and masking options (*2 settings; full mask lower leg; mask for the TA muscle).* Image

157 normalization was performed by dividing the signal intensities in the original water or out-of-phase image

158 by the maximal signal intensity in the image slice. Masking of the full lower leg was based on an empirically

159 determined signal intensity threshold. For the TA-only mask, the manually segmented boundary mask was

160 used.

161 The registration displacement fields were smoothed using a Savitzky-Golay filter with a polynomial order

162 of 2 and frame length of 2, as implemented in the MATLAB function *sgolay( )*. This registration field was

163 used to transform the muscle boundary mask and the seed-point mesh from +20° foot position to the -10°

164 position by 3D interpolation (MATLAB's function *interp3*) to the -10° foot position; see Fig. 1. For each

165 set of registration inputs, the outcomes were assessed by calculating the Sorensen Dice Similarity

166 Coefficient (DSC) for the muscle mask (DSC_{mask}) and aponeurosis (DSC_{apo}) mask and the average

167 Hausdorff distance (D_H) and Euclidean distance (D_E) between corresponding points on the aponeurosis

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168   mesh. The optimal registration approach was defined as the method with the best ordinal ranking across all

169   outcome assessments.

170   *Pre-processing of diffusion images*

171   The diffusion images were registered to the scanner-reconstructed water images of the Dixon series using

172   the *imregdemons( )* function. Then the diffusion data were denoised using an anisotropic smoothing

173   algorithm (45, 46) using a noise level of 5% (47) The diffusion tensor was estimated in each voxel from

174   the denoised diffusion data using weighted least squares fitting(41).

175   *Fiber-tracking*

176   The diffusion tensor field, seed-point mesh, and muscle boundary mask were used as inputs for fiber-

177   tracking. Fiber-tracts were initiated from points along the seed-point mesh and propagated using 4th-order

178   Runge-Kutta integration of the principal eigenvector at a step size of 1.0 pixel-width. Stopping criteria

179   included either 1) reaching the muscle mask boundary or 2) if two consecutive data points had a

180   Fractional Anisotropy value <0.1 or >0.4 or a trajectory angle between consecutive tracking steps of

181   >30°. Three sets of fiber-tracts were generated:

182   1. Fiber-tracts were generated for the +20° foot position after initiation from the seed-point mesh

183   originally defined for this position (Original +20°).

184   2. The seed-point mesh was transformed from the +20° position to the -10° position. Fiber-tracts for

185   the -10° position were then generated from the transformed mesh (Original -10°). The

186   transformed mesh was used to enable direct comparison between the transformed and original

187   datasets.

188   3. The fiber-tracts from the +20° position were transformed to their predicted locations at a foot

189   angle of -10° (Transformed -10°). Transformation was performed as described above.

190   *Architectural quantification and goodness filtering*

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191   Prior to architectural quantification of the fiber-tracts, the row, column and slice positions were smoothed

192   using 3rd order polynomial fitting (48, 49). Architectural tract properties, including pennation angle (θ;

193   (7)), fiber-tract length (L_{FT}), and curvature (κ; (48)), were quantified for each tract in all subjects using the

194   *fiber_quantifier( )* function. Pennation angle was defined as the complement to the angle formed by the

195   normal vector to the aponeurosis at the seed point and the position vectors. The tract length was

196   calculated by summing the inter-point distances, and the curvature was calculated using a discrete

197   implementation of the Frenet-Serret equations. The *fiber_goodness( )* function was used to exclude fiber-

198   tracts if their Z-positions did not increase monotonically; if their mean curvature was >40 m^{-1}, their mean

199   pennation angle was >40°, and/or their length was <10 mm or > 98 mm; or if there were local outliers in

200   any of these architectural properties. The maximum length was based on the average fascicle length plus

201   two times the standard deviation reported in an ultrasonography study (54) In addition, the muscle

202   volume (V_M), mean (L_{FT}), and θ were used to calculate the Physiological Cross-sectional Area (PCSA) as

203   (50): PCSA = V_M * cos (θ) / L_{FT}, using L_{FT} as a proxy for fascicle length.

204   *Fiber Similarity Measures*

205   To compare the original and transformed -10° fiber-tract outcomes, we determined the differences in the

206   mean pennation angle ($\Delta\theta$), fiber-tract length (ΔL_{FT}) and curvature ($\Delta\underline{\kappa}$) for the deep compartment,

207   superficial compartment, and whole muscle. Additionally, the similarity (S_i) was calculated between the

208   transformed and its corresponding original fiber (similar mesh starting point) using: $S_i = R_{CS} \cdot e^{(-D_E/C)}$ (8,

209   51), where R_{CS} is the corresponding segment ratio, D_E is the mean Euclidean distance between

210   corresponding points, and C is a weighting factor (here set to 1.50 mm). We used the median S_i to

211   characterize this property on a whole-muscle level. As exploratory analyses, we also compared the

212   differences in architectural properties and S_i at the individual fiber-tract level.

213   *Statistical Analysis*

214   All statistical analysis were performed using SPSS (IBM SPSS Statistics 28.01.1.1, Armonk, NY: IBM

215   Corp). Data were checked for normality using a Shapiro – Wilk test. Paired *t*-tests or the non-parametric

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216 version of the *t*-test were used to evaluate the difference in mean architectural properties (θ, L_{FT}, κ, and

217 PCSA) between the original and transformed fiber-tracts in the deep compartment, superficial

218 compartment, and whole muscle. Pearson correlation and Bland-Altman analyses were used to

219 exploratory evaluate architectural properties on the fiber-tract level. Furthermore, Spearman correlations

220 were used to explore the relation between the registration outcome measures (DSC_{mask}, DSC_{apo}, D_H and

221 D_E) and the similarity measures ($\Delta\theta$, ΔL_{FT}, $\Delta\underline{\kappa}$ and S_i).

Results

222 **Results**

223 *Data quality*

224 All MR datasets were complete and without observable fat and/or motion artefacts.

225 *Registration approaches*

226 The DSC, D_H and D_E for the muscle mask, aponeurosis mask and aponeurosis mesh using the different

227 registration approaches are shown in Table 1. Overall, the non-normalized out-of-phase (TE= 1.01ms)

228 images with a slice thickness of 3.5 mm resulted in the lowest ordinal scale and were selected to

229 transform the aponeurosis mesh and fiber-tracts. One of the datasets did not register correctly, as assessed

230 by visual inspection by MH and low DSC values for the muscle and the aponeurosis masks. Thus, for the

231 comparison of architectural properties and correlation analysis we excluded this dataset.

232

Output	Water Image (7 mm)	OP Image (7 mm)	OP Image (3.5 mm)	OP Image (1.75 mm)	Image Mask	TA mask
DSC_{mask}	0.91±0.005	0.91±0.001	**0.92±0.002**	0.91±0.004	0.90±0.002	**0.92±0.002**
DSC_{apo}	0.76±0.05	0.78±0.05	0.74±0.05	0.76±0.05	0.77±0.05	**0.78±0.02**
D_H mesh	41.4±8.5	20.3±6.9	**17.2±4.1**	17.5±3.5	40.8±7.3	40.4±7.1

D_E mesh	3.6±1.4	2.8±1.1	**2.3±0.9**	2.3±0.9	3.5±1.3	2.9±0.8
Ordinal output	5	4	**1**	3	6	2

Table 1. Evaluation of the registration approaches

Table legend 1: Data table showing the average and standard deviation of the DSC, Hausdorff distance (D_H), Euclidean distance (D_E) and overall ordinal grading for the muscle mask, aponeurosis mask and aponeurosis mesh using a selection of the different registration strategies. In bold text is shown the best approach per category. Note the overall best strategy: Non-normalized Out-of-phase images with a slice thickness of 3.5mm.

Architectural properties

Representative original and transformed datasets, using the high-resolution seed-point mesh definition and the optimized registration criteria from Table 1, are shown in Figure 2. Data were normally distributed and analysed using a paired t-test. No significant differences were detected between the original and transformed fiber-tracts for the mean values of θ, L_{FT}, and κ in the deep compartment (*p*-value θ: 0.64, L_{FT}: 0.74, and κ: 0.39), superficial compartment (*p*-value θ: 0.10, L_{FT}: 0.44, and κ: 0.92), and whole TA muscle (*p*-value θ: 0.13, L_{FT}: 0.72, and κ: 0.52)) (Figure 3). No significant differences were detected in PCSA between the original and transformed fiber-tracts in the whole TA muscle (*p*-value: 0.454). On an individual fiber-tract level variations were observed in the agreement in pennation angle and fiber-tract length between the original and transformed fiber's for both a high and a low similarity dataset (Supplemental Figure 1). A significantly higher pennation angle (*p* = 0.004) was found in -10° ankle position compared to +20°, while no differences were detected in fiber-tract length and curvature between the two ankle positions (*p* = 0.54) (Figure 4).

255   **Figure 2.** *Original and transformed fiber-tracts*.

256   The original fiber-tracts (green) and aponeurosis mesh are shown on the left side and the corresponding

257   transformed fiber-tracts (orange) and aponeurosis mesh on the right side for a representative dataset. For

258   visualization purposes we used a high-density mesh (size 100×50).

259

260   **Figure 3.** *Architectural properties of the original and transformed fibers.*

261   Line plots showing the pennation angle (left), fascicle length (middle) and fascicle curvature for the

262   original and transformed fiber-tracts in the full TA muscle (top row), the deep compartment of the TA

263   muscle (middle row) and the superficial compartment of the TA muscle (bottom row). In black the mean

264   and standard deviation for all the subjects and in light grey the individual subjects. Significant differences

265   are indicated with an asterisk.

266

267   **Figure 4.** *Pennation angle and fascicle lengths of the original fibers in the two foot positions*

268   Line plots showing the pennation angle (left) and fascicle length (middle) and the curvature (right) for the

269   original fiber-tracts in -10° and +20° ankle position in the full TA muscle. In black symbols are shown

270   the mean and standard deviation for all the subjects and in light grey symbols are shown the individual

271   subjects' data. Significant differences are indicated with an asterisk.

272   **Table 2.** *Architectural properties of the original fascicles in the -10° and +20° ankle position and the*

273   *transformed fascicles*

Outcome measure	Ankle position	Full TA muscle	Deep compartment	Superficial compartment
Angle (°)	**Original +20⁰**	6.3±1.0°	6.4 ±1.5°	6.5 ±1.2°
	Original -10⁰	9.1±1.4°	10.7 ±3.3	10.0 ±3.5°
	Transformed -10⁰	7.3 ±1.7°	5.9 ±1.2	7.8 ±1.4°

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Length (mm)	Original +20⁰	51.5 +4.51	56.4 ±13	59.2± 8.8
	Original -10⁰	49.9 ±4.25	52.3 ±8.6	47.7 ±7.6
	Transformed -10⁰	48.3 ±10.8	50.7 ±13.7	43.9 ±9.8
Curvature (m⁻¹)	Original +20⁰	7.2 ±0.7	7.2 ±1.6	6.9 ±0.6
	Original -10⁰	8.7 ±1.4	7.5 ±3.0	9.8 ±2.1
	Transformed -10⁰	9.8 ±3.2	9.8 ±4.5	9.8 ±2.1

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Table legend 2:

Data table showing the average and standard deviation pennation angle, fiber-tract length and curvature

values for the original fiber-tracts in the dorsiflexed -10° ankle position, plantarflexed +20° ankle position

and the transformed fiber-tracts.

279

Registration quality measures in relation to fiber similarity measures

On a whole muscle basis, no significant correlations were observed between the similarity (S_i) or

registration quality measures (D_H (r=-0.41; p=0.42), D_E (r=0.08; p=0.91), DSC_{apo} (r=0.64; p=0.18) and

DSC_{mask} (r=-0.65; p=0.18) and $\Delta\theta$ (r=-0.42 ;p=0.42), ΔL_{FT} (r=-0.26; p=0.66) (Figure 5.) or $\Delta\kappa$. Similarly,

no clear pattern was evident between $\Delta\theta$ and ΔL_{FT} and the registration quality measures (Spearman R

absolute range = 0.03-0.67; $p > 0.18$) (Supplemental Figures 2 and 3). Within subjects, the similarity

values ranged widely (between 0.03-0.77). Typical example fiber-tracts for a low and high similarity

cases are shown in Figure 6. The average per-subject similarity value ranged between 0.14 and 0.31

across the sample. We did not find a clear pattern for the comparison of S_i and $\Delta\theta$, ΔL_{FT} on a fiber-tract

basis for both the highest and lowest averaged similarity score (Supplemental Figure 4).

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291 **Figure 5.** *Correlation analysis between the Similarity index, similarity measures and registration*

292 *measures.*

293 Dot plots showing the correlation between the tract similarity measure and registration quality measures.

294 The black dots represent the individual participants. D_H : Hausdorf Distance, D_E: Euclidean Distance; $\Delta\theta$:

295 the difference in pennation angle between the original and transformed fiber-tracts, ΔL_{FT}: the difference

296 in length between the original and transformed fiber-tracts.

297

298 **Figure 6.** *Visualization of the transformation of high and low similarity fiber-tracts.*

299 Visualization of variations in the quality of transforming muscle architecture by highlighting two

300 individual fiber-tracts (one with a more proximal aponeurosis attachment and one with a more distal

301 aponeurosis attachment). In green the original fiber-tracts and in orange the corresponding transformed

302 fiber-tracts for one representative subject. The image on the left shows original and transformed fiber-

303 tracts with high similarity (S_i =0.53 & 0.55) and the image on the right displays original and transformed

304 fiber-tracts with low similarity(S_i =0.03 & 0.07).

Discussion

305

306   We showed that DTI-determined muscle fiber-tracts can be transformed from a plantarflexed ankle

307   position to the dorsiflexed ankle position using registration of high-resolution anatomical images. On the

308   whole-muscle and whole-compartment scales, the original and transformed fiber-tracts did not differ in

309   architectural characteristics, i.e. mean length, pennation angle, curvature, and PCSA. This finding

310   emphasizes the potential of this approach for analysing compartmental or whole-muscle variations in

311   architectural properties during passive movements about a joint. However, there was variability in the

312   quality of the outcomes across participants and across fiber-tracts within a participant. The applicability

313   of this method therefore depends on the intended application of the data.

314   To our knowledge, this is the first study exploring the use of high-resolution displacement fields to

315   transform DTI-determined muscle fiber-tracts between joint angles. The original and the corresponding

316   transformed fiber-tracts showed similar mean architectural properties at the whole-muscle and

317   compartmental scales. These properties were also in the same range as pennation angles and fascicle

318   lengths previously reported in the TA muscle using DTI (7, 15, 16, 52-54), ultrasonography (55-58), and

319   cadaver (59, 60) studies. When comparing the original and transformed tracts from the -10° position, we

320   did observe compartment-specific variations in the fiber-tract lengths, but these did not rise to the level of

321   statistical significance.

322   Besides non-invasively reflecting anatomy, muscle fiber-tract architecture is also used to predict function

323   (3, 61) and to detect changes in architectural properties between conditions. Indeed, the PCSA (62) is

324   considered one of the key predictors of muscle force production; therefore, not finding changes in PCSA

325   between the transformed and original fiber-tracts is very relevant with respect to the use of this method in

326   musculoskeletal modelling (25-30). Additionally, we observed a smaller pennation angle in the full TA in

327   the plantarflexed (+20°) compared to dorsiflexed (-10°) ankle position, which is consistent with

328   physiological predictions based on the relative compliance of resting muscle vs. tendinous structures and

329   previous observations (55, 63, 64). Interestingly, we did not observe a clear pattern for fiber-tract length

330   on a group-level basis, and both longer and shorter fiber-tracts were seen across participants. This was

331   contrary to both physiologically based predictions and prior work on the full TA muscle that showed a

332   reduced fascicle length in dorsiflexed position (-15°) compared to plantarflexed (+30°) ankle position (24,

333   65). Possible causes for the shorter fiber-tracts are muscle tendon complex lengthening, or some

334   inconsistency or error in fiber-tracking due to a small mismatch in registration between the DTI and

335   anatomical data.

336   The quality of the transformation of fiber-tracts highly depends on the performance of the registration, in

337   this case using the Demons algorithm. Previously, the Demons algorithm has been used and validated to

338   accurately quantify displacement and deformations in skeletal muscle tissue (38, 66), pelvic floor, lung

339   and cortical bone tissue (67, 68). In addition, the reliability of this algorithm has been tested by imposing

340   known deformations to an image set (38) with the measured strains being conservative estimators of the

341   local deformations. To establish the quality of fiber-tract transformations, we evaluated a variety of

342   registration inputs to optimize displacement fields derived from the Demons algorithm and showed that

343   the out–of–phase (OP) images with an intermediate slice thickness led to the best registration result. This

344   may be due to the higher internal contrast between anatomic structures in these images compared to the

345   water-only images, the lower leg mask, and muscle mask. The difference in registration quality between

346   the three slice thicknesses was minimal, which may indicate that these slice thicknesses are sufficient to

347   sample any foot-head variations in structure, at least in the case of this muscle in healthy adults. The in-

348   plane resolution of the anatomical images used for registration was similar to the resolution of the DTI

349   data. Future work could explore if higher in-plane resolution could benefit the registration further.

350   In addition to comparing the compartmental and whole-muscle architectural properties of the entire

351   dataset, similarity and architectural measures were evaluated at the fiber-tract level. The Bland-Altman

352   analysis clearly visualized variations in similarity in architectural properties on an individual fiber-tract

353   level, independent of a high or low similarity analysis. This finding is consistent with the correlation

354   analysis which displayed clearly that tracts with both high and low similarities could have very similar

17

355   architectural properties and that tract pairs with low similarity values could exhibit either high or low

356   levels agreement among their architectural properties (Supplemental Figure 4). This suggests that the

357   similarity index used here does not adequately assess fiber-tract likeness. This may be because the

358   similarity measure accounts for both the amount of length overlap of two tracts and the distance between

359   their corresponding points, allowing both adjacent fiber-tracts and fiber-tracts that lay further apart to

360   have the same similarity scores (8, 51, 69). Also, our registration quality measures did not show

361   convincing correlations with our fiber similarity measures. This was contrary to our expectations, since

362   we optimized according to these measures; however, this evaluation may have been impacted by the low

363   number of datasets, the imperfect nature of this similarity index as an outcome measure, and the small

364   dynamic range of some of the registration outcome parameters. The problem of low dynamic range is

365   exacerbated by excluding the dataset that did not register properly. In the next development phase of the

366   registration-based approach to transforming fiber-tracts, it may be useful to expand the calculation of the

367   similarity measure to also include differences in architecture between the tracts or include other structural

368   features as terms in the similarity calculation.

369   The end goal of this approach is to explore muscle architecture during dynamic contractions. To address

370   that goal, DTI data would be acquired in relaxed position and then transformed to its contracted state

371   using anatomical images acquired at rest and during contraction. This approach necessarily rules out the

372   possibility to compare fiber-tracts according to the similarity measure or the observed architectural

373   properties, making validation less straightforward. From pilot data, we know that smaller displacements

374   occur from relaxed to contracted state in a fixed ankle angle isometric contraction, suggesting that

375   registration of these type of datasets should be less challenging. Furthermore, the displacement fields

376   derived from the registration have also been used to quantify strain values in muscle tissue; which showed

377   to correspond well with values measured with other techniques (MR-tagging and PC-MRI). The amount

378   of correspondence between strain values derived from displacement fields and measured with other MR

379   techniques during active contractions could possibly function as justification in active situations. All

380 combined, this study emphasizes the potential of a registration-based approach for observing whole-

381 muscle or compartment changes in architectural properties during isometric muscle contractions.

382 Our study has several limitations. First, it is a proof-of-concept study, in a limited number of young,

383 healthy participants, which makes detecting meaningful differences challenging. Consequently, no

384 difference between the original and transformed fiber-tracts does not automatically indicate the accuracy

385 of this registration-based approach; rather, this work primarily showcases its potential. Further, the

386 translatability to other populations (such as aging and neuromuscular diseases) should be explored further.

387 However, some of the pathological features known to characterize aging and diseased muscle, i.e. the

388 replacement of muscle tissue by fat, result in more contrast in the images, potentially benefitting the

389 registration and the transformation of muscle fiber-tracts. Additionally, how well the fiber-tracts can be

390 transformed depends highly on the performance of the registration. Here we only evaluated a narrow band

391 of data for which the registration worked well and therefore may have overestimated the performance of

392 the approach. Despite the relatively high DSC indices and low D_H and D_E we found using our registration

393 approach, alternative or novel registration strategies or approaches could improve the outcomes from this

394 study even further. We also note that the method did not perform as well at the fiber-tract level as it did at

395 the compartmental and whole-muscle levels, which again motivates exploration of alternative or novel

396 registration strategies. Lastly, we used the fiber-tracts generated in -10° ankle position with the

397 transformed mesh as ground truth. However, noise and other image quality issues will affect the

398 performance of DTI tractography (65, 70, 71), perhaps leading to an underestimation of the performance

399 of our approach.

400 In summary, we showed that muscle fiber-tract architecture from one ankle position can be transformed in

401 the other ankle position using registration derived displacement fields. Whole-muscle architectural

402 characteristics, i.e. fiber-tract length, pennation angle, curvature, and physiological cross-sectional area of

403 the original and transformed fiber-tracts did not differ significantly on a group-level basis. Consequently,

404   this approach to transform muscle architecture is very promising, and our next step will be to evaluate if

405   muscle architecture can be reconstructed in a contracted state using a similar approach.

406

411   **Competing Interest Statement**

412   The authors have declared that no competing interests exist.

413

414   **Data Availability Statement**

415   The fat/water MRI and unprocessed DTI data are available to any qualified investigator at an academic

416   institution or private research organization who has current human subjects research ethics training

417   certification and can describe a scientific use for the data. Interested parties can contact the corresponding

418   author to establish a Data Use Agreement.

419

References

1. Huijing PA. Architecture of the Human Gastrocnemius-Muscle and Some Functional Consequences. Acta Anat. 1985;123(2):101-7.

2. Sopher RS, Amis AA, Davies DC, Jeffers JR. The influence of muscle pennation angle and cross-sectional area on contact forces in the ankle joint. J Strain Anal Eng Des. 2017;52(1):12-23.

3. Lieber RL, Friden J. Functional and clinical significance of skeletal muscle architecture. Muscle Nerve. 2000;23(11):1647-66.

4. Basser PJ, Mattiello J, LeBihan D. MR diffusion tensor spectroscopy and imaging. Biophys J. 1994;66(1):259-67.

5. Basser PJ, Pierpaoli C. Microstructural and physiological features of tissues elucidated by quantitative-diffusion-tensor MRI. J Magn Reson B. 1996;111(3):209-19.

6. Noseworthy MD, Davis AD, Elzibak AH. Advanced MR imaging techniques for skeletal muscle evaluation. Semin Musculoskelet Radiol. 2010;14(2):257-68.

7. Lansdown DA, Ding Z, Wadington M, Hornberger JL, Damon BM. Quantitative diffusion tensor MRI-based fiber tracking of human skeletal muscle. J Appl Physiol (1985). 2007;103(2):673-81.

8. Damon BM, Ding Z, Anderson AW, Freyer AS, Gore JC. Validation of diffusion tensor MRI-based muscle fiber tracking. Magn Reson Med. 2002;48(1):97-104.

9. Heemskerk AM, Drost MR, van Bochove GS, van Oosterhout MF, Nicolay K, Strijkers GJ. DTI-based assessment of ischemia-reperfusion in mouse skeletal muscle. Magn Reson Med. 2006;56(2):272-81.

10. Galban CJ, Maderwald S, Uffmann K, de Greiff A, Ladd ME. Diffusive sensitivity to muscle architecture: a magnetic resonance diffusion tensor imaging study of the human calf. Eur J Appl Physiol. 2004;93(3):253-62.

11. Froeling M, Oudeman J, Strijkers GJ, Maas M, Drost MR, Nicolay K, Nederveen AJ. Muscle changes detected with diffusion-tensor imaging after long-distance running. Radiology. 2015;274(2):548-62.

12. Hooijmans MT, Damon BM, Froeling M, Versluis MJ, Burakiewicz J, Verschuuren JJ, et al. Evaluation of skeletal muscle DTI in patients with duchenne muscular dystrophy. NMR Biomed. 2015;28(11):1589-97.

13. Zaraiskaya T, Kumbhare D, Noseworthy MD. Diffusion tensor imaging in evaluation of human skeletal muscle injury. J Magn Reson Imaging. 2006;24(2):402-8.

14. Bolsterlee B, Finni T, D'Souza A, Eguchi J, Clarke EC, Herbert RD. Three-dimensional architecture of the whole human soleus muscle in vivo. PeerJ. 2018;6:e4610.

15. Foure A, Ogier AC, Le Troter A, Vilmen C, Feiweier T, Guye M, et al. Diffusion Properties and 3D Architecture of Human Lower Leg Muscles Assessed with Ultra-High-Field-Strength Diffusion-Tensor MR Imaging and Tractography: Reproducibility and Sensitivity to Sex Difference and Intramuscular Variability. Radiology. 2018;287(2):592-607.

16. Oudeman J, Mazzoli V, Marra MA, Nicolay K, Maas M, Verdonschot N, et al. A novel diffusion-tensor MRI approach for skeletal muscle fascicle length measurements. Physiol Rep. 2016;4(24).

17. Sinha S, Sinha U, Edgerton VR. In vivo diffusion tensor imaging of the human calf muscle. J Magn Reson Imaging. 2006;24(1):182-90.

18. Qi J, Olsen NJ, Price RR, Winston JA, Park JH. Diffusion-weighted imaging of inflammatory myopathies: polymyositis and dermatomyositis. J Magn Reson Imaging. 2008;27(1):212-7.

19. Sinha U, Yao L. In vivo diffusion tensor imaging of human calf muscle. J Magn Reson Imaging. 2002;15(1):87-95.

20.   Van Donkelaar CC, Kretzers LJ, Bovendeerd PH, Lataster LM, Nicolay K, Janssen JD, Drost MR. Diffusion tensor imaging in biomechanical studies of skeletal muscle function. J Anat. 1999;194 (Pt 1)(Pt 1):79-88.

21.   Guttsches AK, Rehmann R, Schreiner A, Rohm M, Forsting J, Froeling M, et al. Quantitative Muscle-MRI Correlates with Histopathology in Skeletal Muscle Biopsies. J Neuromuscul Dis. 2021;8(4):669-78.

22.   Berry DB, Englund EK, Galinsky V, Frank LR, Ward SR. Varying diffusion time to discriminate between simulated skeletal muscle injury models using stimulated echo diffusion tensor imaging. Magn Reson Med. 2021;85(5):2524-36.

23.   Sigmund EE, Novikov DS, Sui D, Ukpebor O, Baete S, Babb JS, et al. Time-dependent diffusion in skeletal muscle with the random permeable barrier model (RPBM): application to normal controls and chronic exertional compartment syndrome patients. NMR Biomed. 2014;27(5):519-28.

24.   Mazzoli V, Oudeman J, Nicolay K, Maas M, Verdonschot N, Sprengers AM, et al. Assessment of passive muscle elongation using Diffusion Tensor MRI: Correlation between fiber length and diffusion coefficients. NMR Biomed. 2016;29(12):1813-24.

25.   Yucesoy CA, Koopman BH, Baan GC, Grootenboer HJ, Huijing PA. Extramuscular myofascial force transmission: experiments and finite element modeling. Arch Physiol Biochem. 2003;111(4):377-88.

26.   Charles JP, Moon CH, Anderst WJ. Determining Subject-Specific Lower-Limb Muscle Architecture Data for Musculoskeletal Models Using Diffusion Tensor Imaging. J Biomech Eng. 2019;141(6).

27.   Arnold EM, Ward SR, Lieber RL, Delp SL. A model of the lower limb for analysis of human movement. Ann Biomed Eng. 2010;38(2):269-79.

28.   Rajagopal A, Dembia CL, DeMers MS, Delp DD, Hicks JL, Delp SL. Full-Body Musculoskeletal Model for Muscle-Driven Simulation of Human Gait. IEEE Trans Biomed Eng. 2016;63(10):2068-79.

29.   Delp SL, Anderson FC, Arnold AS, Loan P, Habib A, John CT, et al. OpenSim: open-source software to create and analyze dynamic simulations of movement. IEEE Trans Biomed Eng. 2007;54(11):1940-50.

30.   Chen Z, Franklin DW. Musculotendon Parameters in Lower Limb Models: Simplifications, Uncertainties, and Muscle Force Estimation Sensitivity. Ann Biomed Eng. 2023;51(6):1147-64.

31.   Okamoto Y, Kunimatsu A, Kono T, Nasu K, Sonobe J, Minami M. Changes in MR diffusion properties during active muscle contraction in the calf. Magn Reson Med Sci. 2010;9(1):1-8.

32.   Damon BM, Froeling M, Buck AK, Oudeman J, Ding Z, Nederveen AJ, et al. Skeletal muscle diffusion tensor-MRI fiber tracking: rationale, data acquisition and analysis methods, applications and future directions. NMR Biomed. 2017;30(3).

33.   Mazzoli V, Moulin K, Kogan F, Hargreaves BA, Gold GE. Diffusion Tensor Imaging of Skeletal Muscle Contraction Using Oscillating Gradient Spin Echo. Front Neurol. 2021;12:608549.

34.   Deffieux T, Gennisson JL, Tanter M, Fink M. Assessment of the mechanical properties of the musculoskeletal system using 2-D and 3-D very high frame rate ultrasound. IEEE Trans Ultrason Ferroelectr Freq Control. 2008;55(10):2177-90.

35.   Gijsbertse K, Goselink R, Lassche S, Nillesen M, Sprengers A, Verdonschot N, et al. Ultrasound Imaging of Muscle Contraction of the Tibialis Anterior in Patients with Facioscapulohumeral Dystrophy. Ultrasound Med Biol. 2017;43(11):2537-45.

36.   Gijsbertse K, Sprengers AM, Nillesen MM, Hansen HH, Lopata RG, Verdonschot N, de Korte CL. Three-dimensional ultrasound strain imaging of skeletal muscles. Phys Med Biol. 2017;62(2):596-611.

37.   Raiteri BJ, Cresswell AG, Lichtwark GA. Three-dimensional geometrical changes of the human tibialis anterior muscle and its central aponeurosis measured with three-dimensional ultrasound during isometric contractions. PeerJ. 2016;4:e2260.

38.   Yaman A, Ozturk C, Huijing PA, Yucesoy CA. Magnetic resonance imaging assessment of mechanical interactions between human lower leg muscles in vivo. J Biomech Eng. 2013;135(9):91003.

513   39.   Pamuk U, Karakuzu A, Ozturk C, Acar B, Yucesoy CA. Combined magnetic resonance and
514   diffusion tensor imaging analyses provide a powerful tool for in vivo assessment of deformation along
515   human muscle fibers. J Mech Behav Biomed Mater. 2016;63:207-19.
516   40.   Williams SE, Heemskerk AM, Welch EB, Li K, Damon BM, Park JH. Quantitative effects of
517   inclusion of fat on muscle diffusion tensor MRI measurements. J Magn Reson Imaging. 2013;38(5):1292-
518   7.
519   41.   Damon BM, Ding Z, Hooijmans MT, Anderson AW, Zhou X, Coolbaugh CL, et al. A MATLAB
520   toolbox for muscle diffusion-tensor MRI tractography. J Biomech. 2021;124:110540.
521   42.   Yushkevich PA, Piven J, Hazlett HC, Smith RG, Ho S, Gee JC, Gerig G. User-guided 3D active
522   contour segmentation of anatomical structures: significantly improved efficiency and reliability.
523   Neuroimage. 2006;31(3):1116-28.
524   43.   Thirion JP. Image matching as a diffusion process: an analogy with Maxwell's demons. Med
525   Image Anal. 1998;2(3):243-60.
526   44.   Vercauteren T, Pennec X, Perchant A, Ayache N. Diffeomorphic demons: efficient non-
527   parametric image registration. Neuroimage. 2009;45(1 Suppl):S61-72.
528   45.   Xu Q, Anderson AW, Gore JC, Ding Z. Efficient anisotropic filtering of diffusion tensor images.
529   Magn Reson Imaging. 2010;28(2):200-11.
530   46.   Ding Z, Gore JC, Anderson AW. Reduction of noise in diffusion tensor images using anisotropic
531   smoothing. Magn Reson Med. 2005;53(2):485-90.
532   47.   Buck AK, Ding Z, Elder CP, Towse TF, Damon BM. Anisotropic Smoothing Improves DT-MRI-Based
533   Muscle Fiber Tractography. PLoS One. 2015;10(5):e0126953.
534   48.   Damon BM, Heemskerk AM, Ding Z. Polynomial fitting of DT-MRI fiber tracts allows accurate
535   estimation of muscle architectural parameters. Magn Reson Imaging. 2012;30(5):589-600.
536   49.   Lockard C. Impact of tract propogation stop criteria on skeletal muscle diffusion-tensor-imaging
537   fiber completeness and characteristics. In: Hooijmans MT, editor. Proceedings International Society of
538   Magnetic Resonance Imaging 2022.
539   50.   Sacks RD, Roy RR. Architecture of the hind limb muscles of cats: functional significance. J
540   Morphol. 1982;173(2):185-95.
541   51.   Ding Z. Case study: reconstruction, visualization and quantification of neuronal fiber pathways.
542   In: Gore JC, editor. Proceedings Visualization: VIS'01., 2001•ieeexplore.ieee.org; 2001.
543   52.   Heemskerk AM, Damon BM. Diffusion Tensor MRI Assessment of Skeletal Muscle Architecture.
544   Curr Med Imaging Rev. 2007;3(3):152-60.
545   53.   Bolsterlee B, D'Souza A, Herbert RD. Reliability and robustness of muscle architecture
546   measurements obtained using diffusion tensor imaging with anatomically constrained tractography. J
547   Biomech. 2019;86:71-8.
548   54.   Charles JP, Suntaxi F, Anderst WJ. In vivo human lower limb muscle architecture dataset
549   obtained using diffusion tensor imaging. PLoS One. 2019;14(10):e0223531.
550   55.   Maganaris CN, Baltzopoulos V. Predictability of in vivo changes in pennation angle of human
551   tibialis anterior muscle from rest to maximum isometric dorsiflexion. Eur J Appl Physiol Occup Physiol.
552   1999;79(3):294-7.
553   56.   Chleboun GS, Busic AB, Graham KK, Stuckey HA. Fascicle length change of the human tibialis
554   anterior and vastus lateralis during walking. J Orthop Sports Phys Ther. 2007;37(7):372-9.
555   57.   Klimstra M, Dowling J, Durkin JL, MacDonald M. The effect of ultrasound probe orientation on
556   muscle architecture measurement. J Electromyogr Kinesiol. 2007;17(4):504-14.
557   58.   de Boer MD, Seynnes OR, di Prampero PE, Pisot R, Mekjavic IB, Biolo G, Narici MV. Effect of 5
558   weeks horizontal bed rest on human muscle thickness and architecture of weight bearing and non-
559   weight bearing muscles. Eur J Appl Physiol. 2008;104(2):401-7.

560 59. Ward SR, Eng CM, Smallwood LH, Lieber RL. Are current measurements of lower extremity
561 muscle architecture accurate? Clin Orthop Relat Res. 2009;467(4):1074-82.
562 60. Wickiewicz TL, Roy RR, Powell PL, Edgerton VR. Muscle architecture of the human lower limb.
563 Clin Orthop Relat Res. 1983(179):275-83.
564 61. Lieber RL, Friden J. Clinical significance of skeletal muscle architecture. Clin Orthop Relat Res.
565 2001(383):140-51.
566 62. Powell PL, Roy RR, Kanim P, Bello MA, Edgerton VR. Predictability of skeletal muscle tension
567 from architectural determinations in guinea pig hindlimbs. J Appl Physiol Respir Environ Exerc Physiol.
568 1984;57(6):1715-21.
569 63. Secondulfo L, Hooijmans MT, Suskens JJ, Mazzoli V, Maas M, Tol JL, et al. A diffusion tensor-
570 based method facilitating volumetric assessment of fiber orientations in skeletal muscle. PLoS One.
571 2022;17(1):e0261777.
572 64. Deux JF, Malzy P, Paragios N, Bassez G, Luciani A, Zerbib P, et al. Assessment of calf muscle
573 contraction by diffusion tensor imaging. Eur Radiol. 2008;18(10):2303-10.
574 65. Oudeman J, Nederveen AJ, Strijkers GJ, Maas M, Luijten PR, Froeling M. Techniques and
575 applications of skeletal muscle diffusion tensor imaging: A review. J Magn Reson Imaging.
576 2016;43(4):773-88.
577 66. Huijing PA, Yaman A, Ozturk C, Yucesoy CA. Effects of knee joint angle on global and local strains
578 within human triceps surae muscle: MRI analysis indicating in vivo myofascial force transmission
579 between synergistic muscles. Surg Radiol Anat. 2011;33(10):869-79.
580 67. Wang H, Dong L, O'Daniel J, Mohan R, Garden AS, Ang KK, et al. Validation of an accelerated
581 'demons' algorithm for deformable image registration in radiation therapy. Phys Med Biol.
582 2005;50(12):2887-905.
583 68. Latifi K, Zhang G, Stawicki M, van Elmpt W, Dekker A, Forster K. Validation of three deformable
584 image registration algorithms for the thorax. J Appl Clin Med Phys. 2013;14(1):3834.
585 69. Zhou X. Predicted effects of Image Acquisition and Analysis Conditions on muscle DTMRI
586 Tractography-Based Architectural Estimates. In: Lockard C, editor. Proceedings International Society of
587 Magnetic Resonance Imaging in Medicine2023.
588 70. Damon BM. Effects of image noise in muscle diffusion tensor (DT)-MRI assessed using numerical
589 simulations. Magn Reson Med. 2008;60(4):934-44.
590 71. Froeling M, Nederveen AJ, Nicolay K, Strijkers GJ. DTI of human skeletal muscle: the effects of
591 diffusion encoding parameters, signal-to-noise ratio and T2 on tensor indices and fiber tracts. NMR
592 Biomed. 2013;26(11):1339-52.

593

594

595 **Supplemental Figures**

596

597 **Supplemental Figure legend 1.**

598 Bland-Altman Plots showing the similarity between the original and transformed fiber-tracts for

599 pennation angle ($\Delta\theta$) and fiber-tract length (ΔL_{FT}), on a fiber tract level, for high similarity (left) and low

600 similarity (right) dataset. Note differences in Y-axis scales between the left and right panels.

601

602 **Supplemental figure 2.**

603 Dot plots displaying the correlation between the registration quality measures and the difference in

604 pennation angle ($\Delta\theta$) between the original and transformed fiber-tracts for each of the participants (black

605 dots).

606

607 **Supplemental figure 3.**

608 Dot plots displaying the correlation between registration quality measures and the difference in fiber-tract

609 length (ΔL_{FT}) between the original and transformed fiber-tracts for each of the participants (black dots).

610

611 **Supplemental Figure legend 4.**

612 Scatterplots showing the relation between the similarity (S_i) and the difference in pennation angle ($\Delta\theta$)

613 and fiber-tract length (ΔL_{FT}) between the original and transformed fiber-tracts for each of the individual

614 fiber-tracts for the dataset with the highest and lowest averaged similarity value.

25

+20° ankle position

DTI Water Image

Registration

-10° ankle position

Water Image DTI

Displacement Fields

D_X D_Y D_Z

Tensor

Tensor
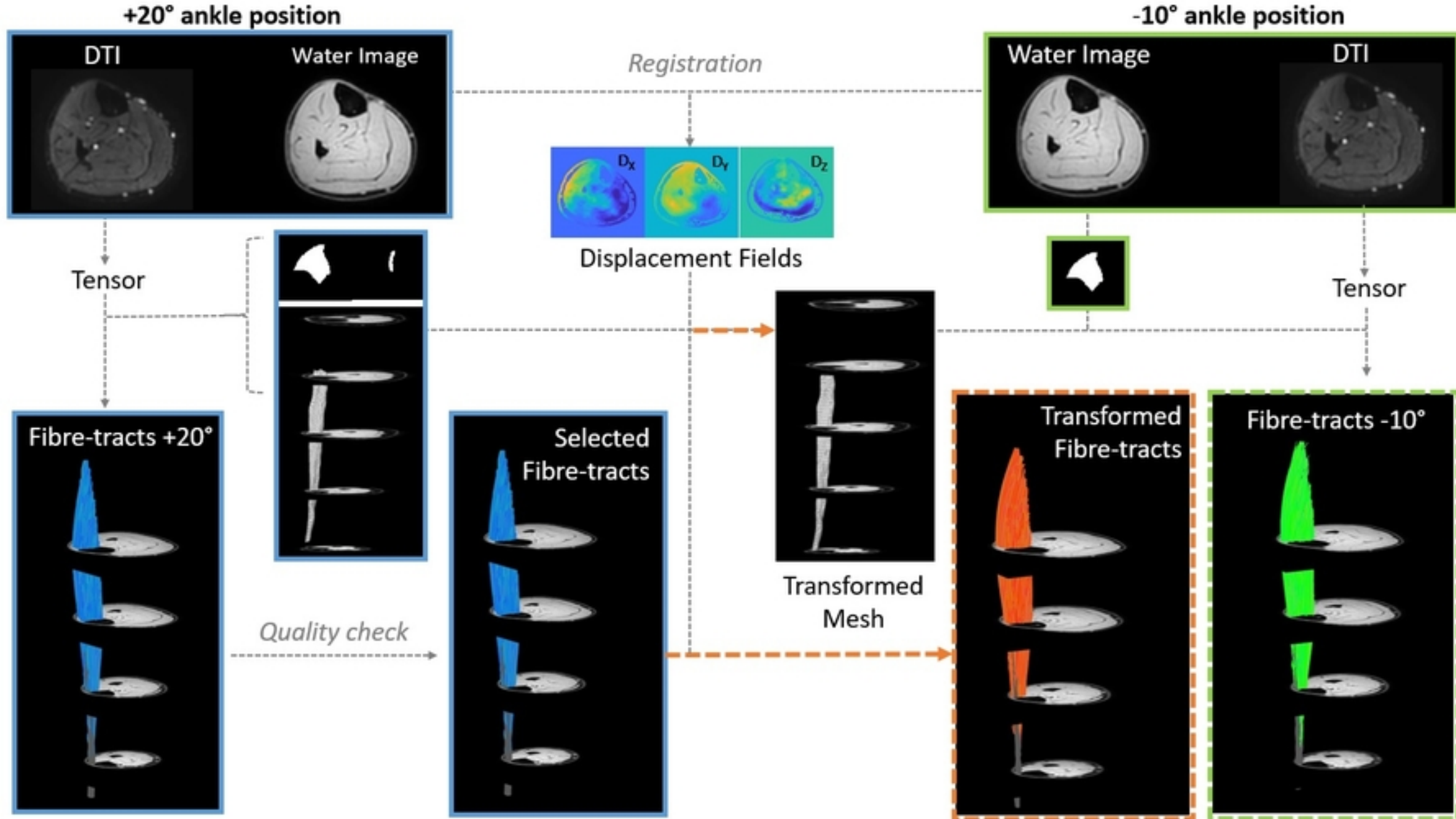
Fibre-tracts +20°

Selected Fibre-tracts
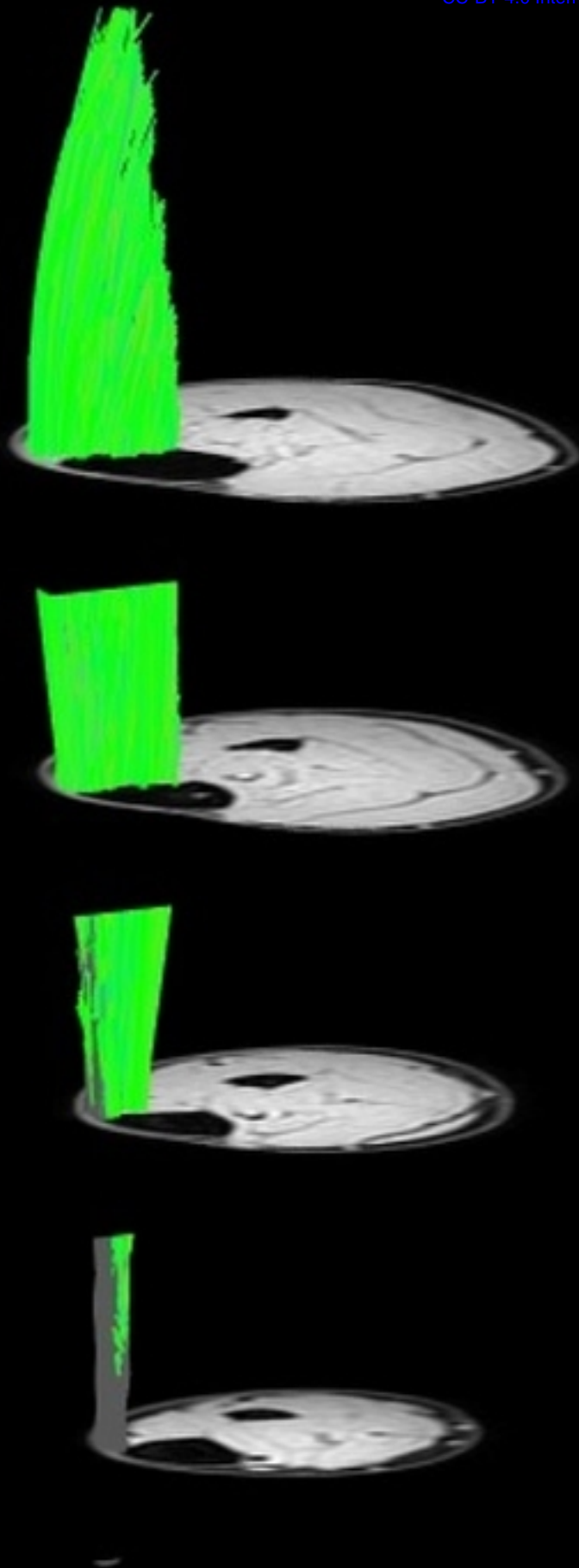
Transformed Mesh

Transformed Fibre-tracts

Fibre-tracts -10°

Quality check
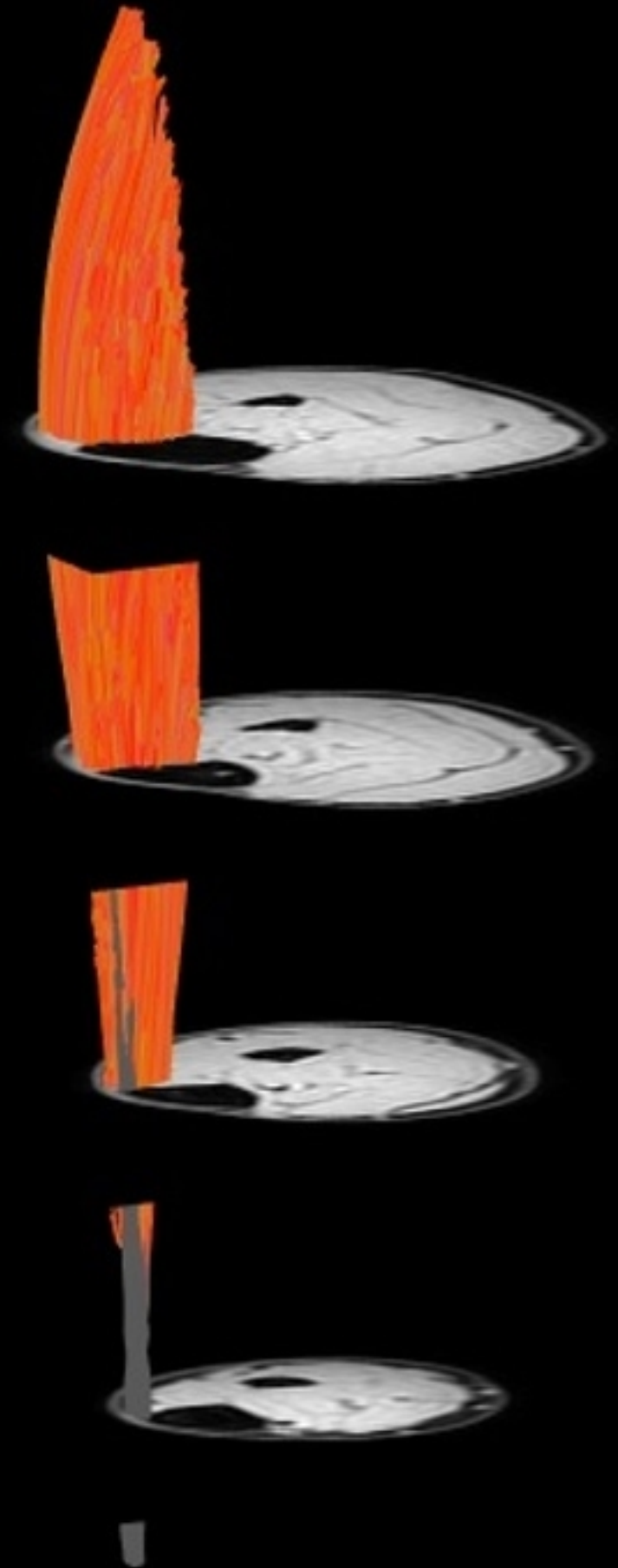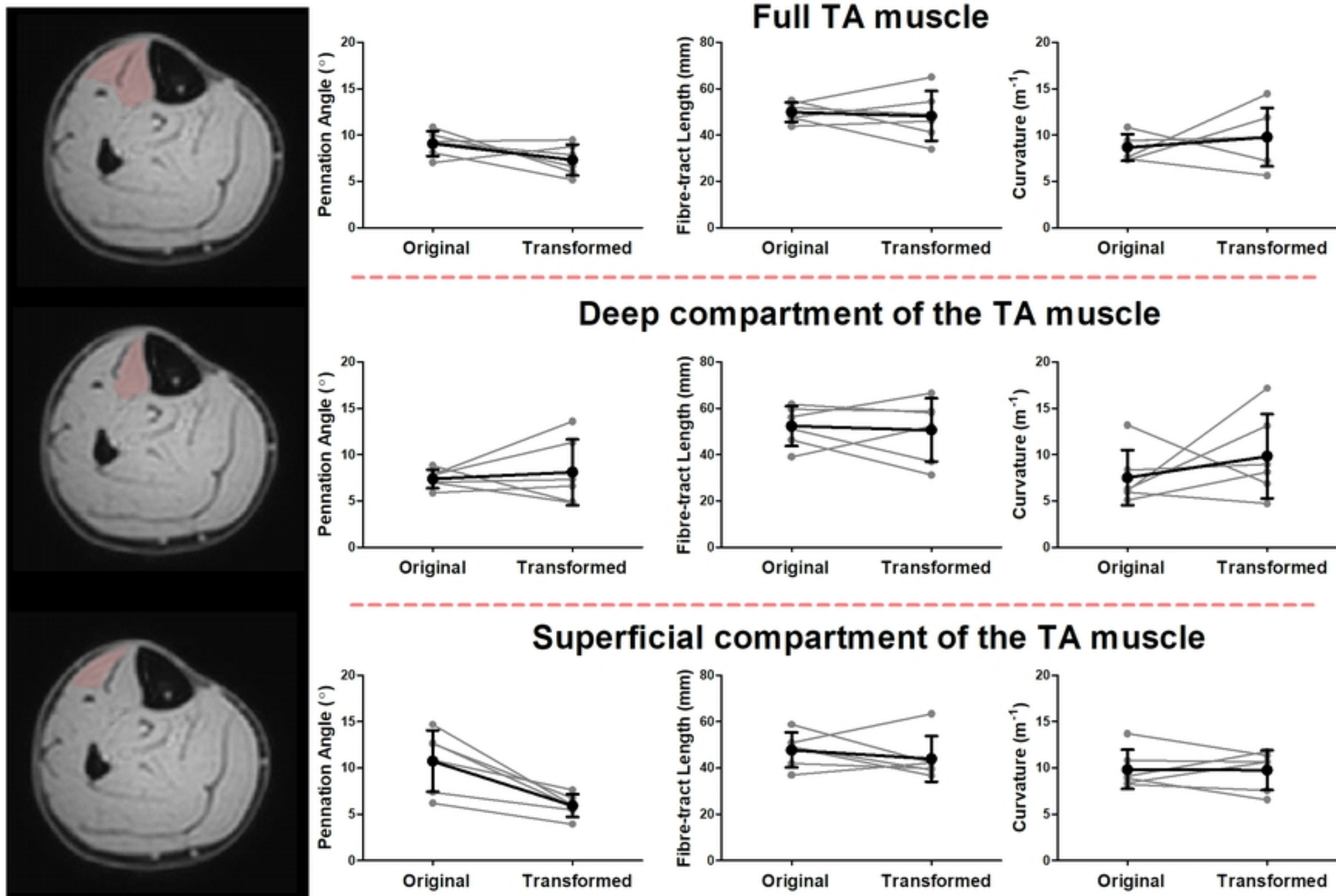
Figure 1
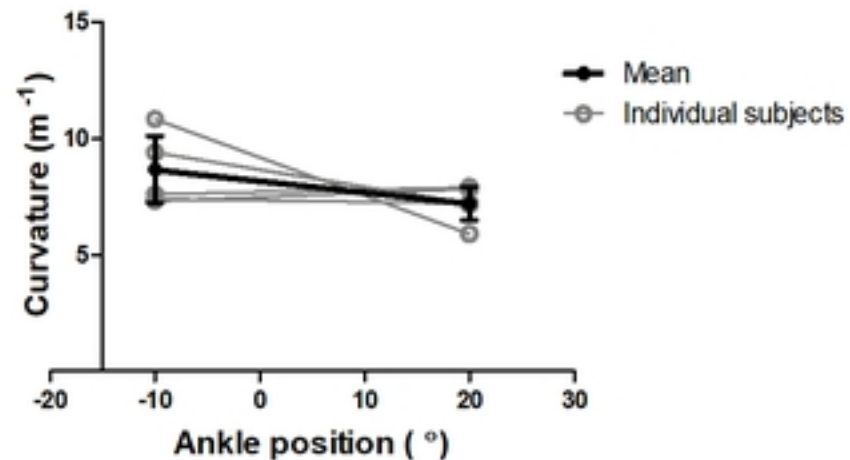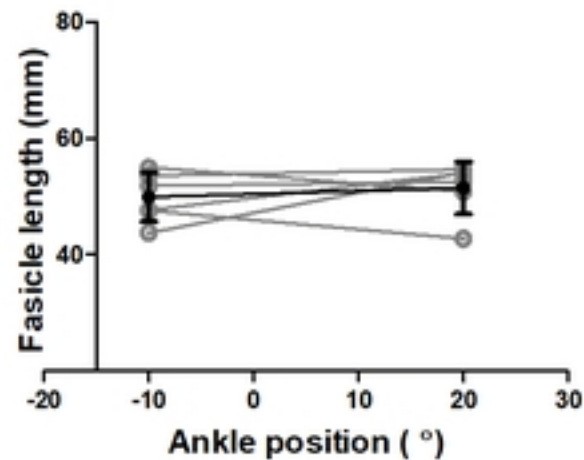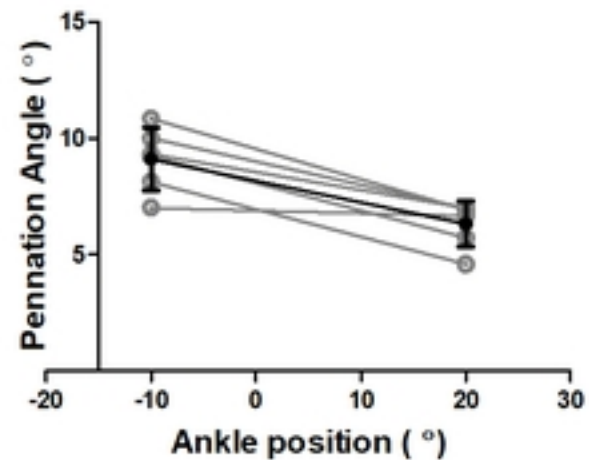
Figure 2

Figure 3

Figure 4

Registration quality measures
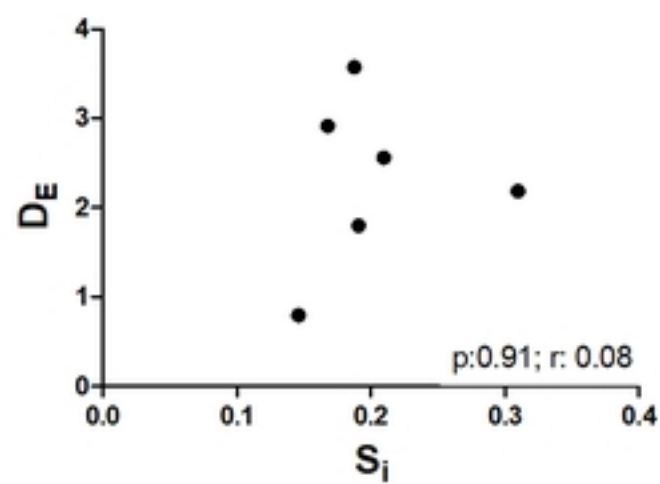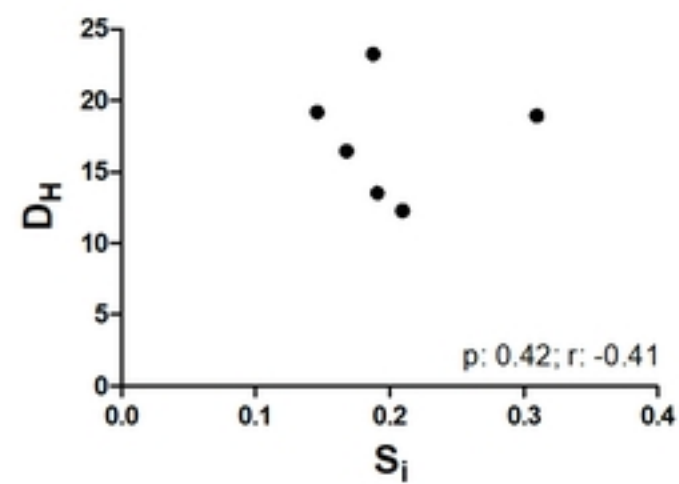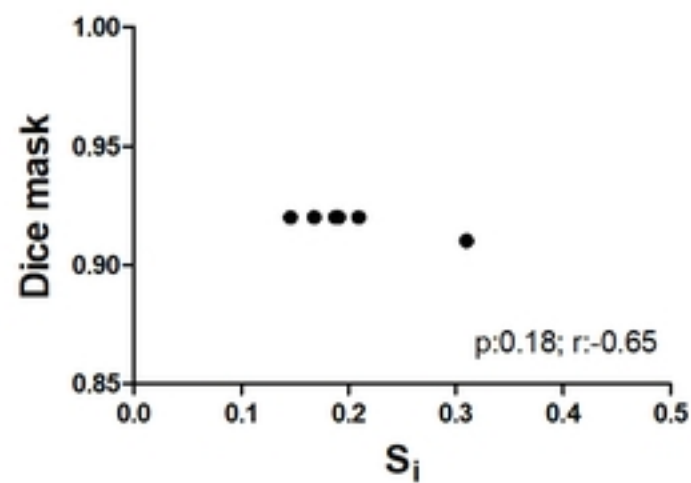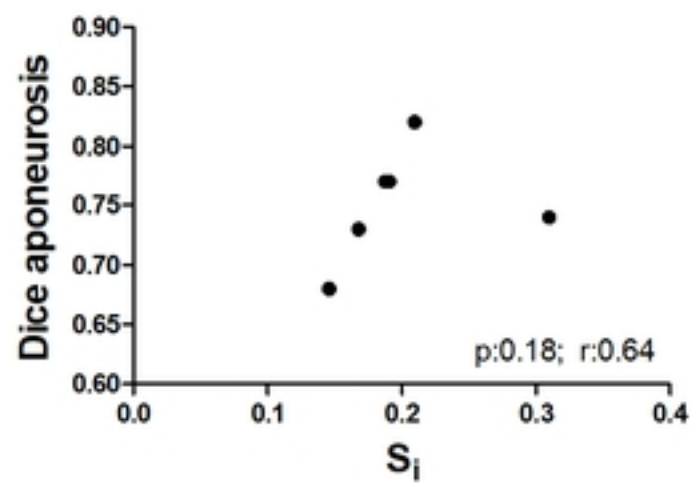
Similarity measures

Figure 5

High Similarity fibre-tracts

Low Similarity fibre-tracts

Figure 6

High S_i dataset

Bland-Altman: pennation angle

Bland-Altman: fibre-tract length

Low S_i dataset

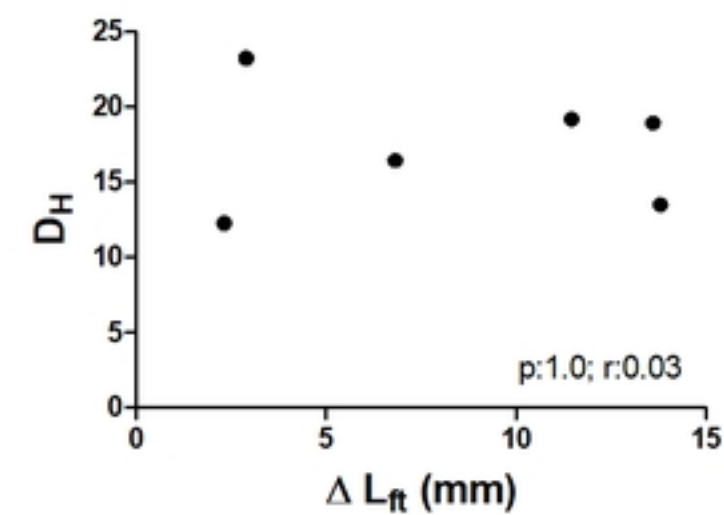Bland-Altman: pennation angle

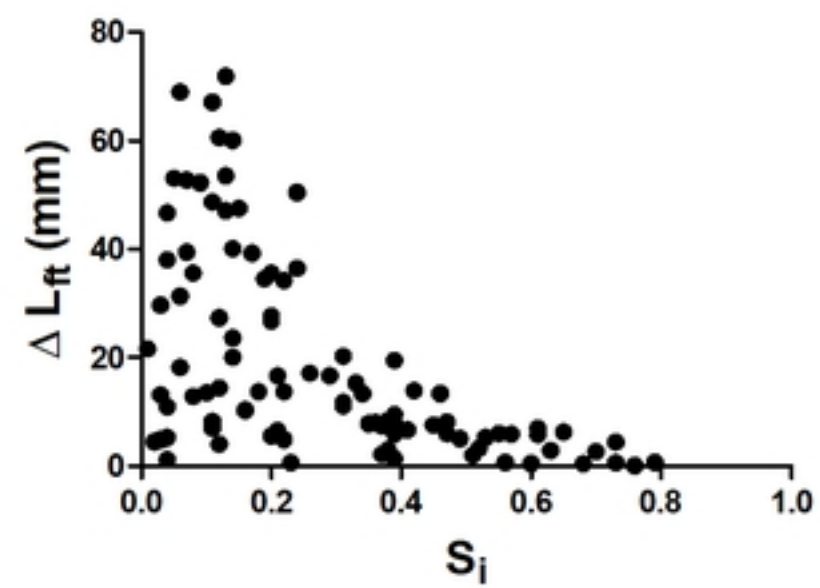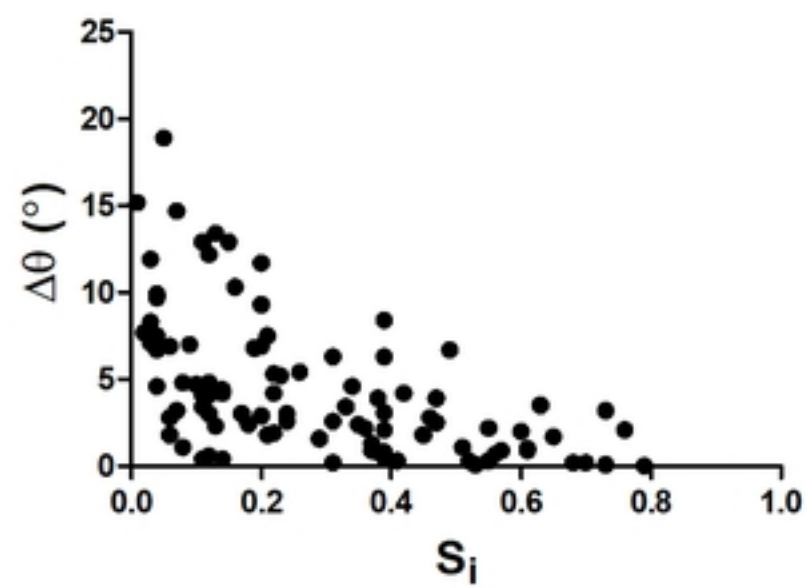Bland-Altman: fibre-tract length

Supplemental Figure 1

Supplemental Figure 2
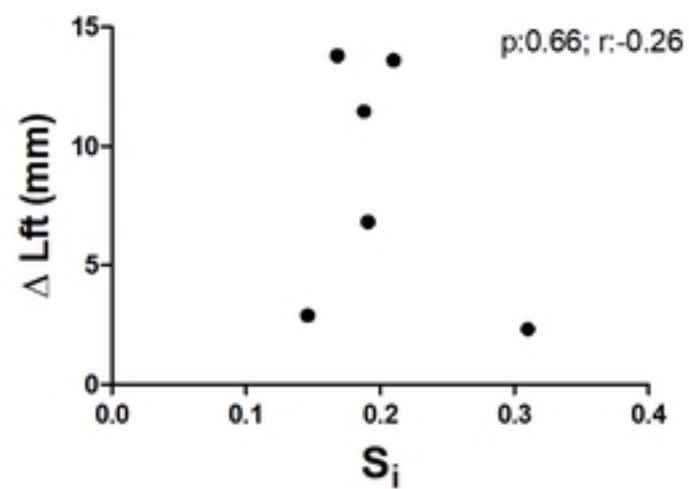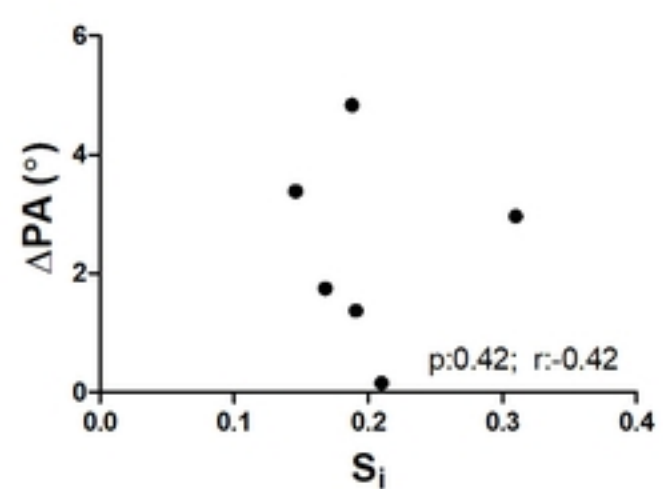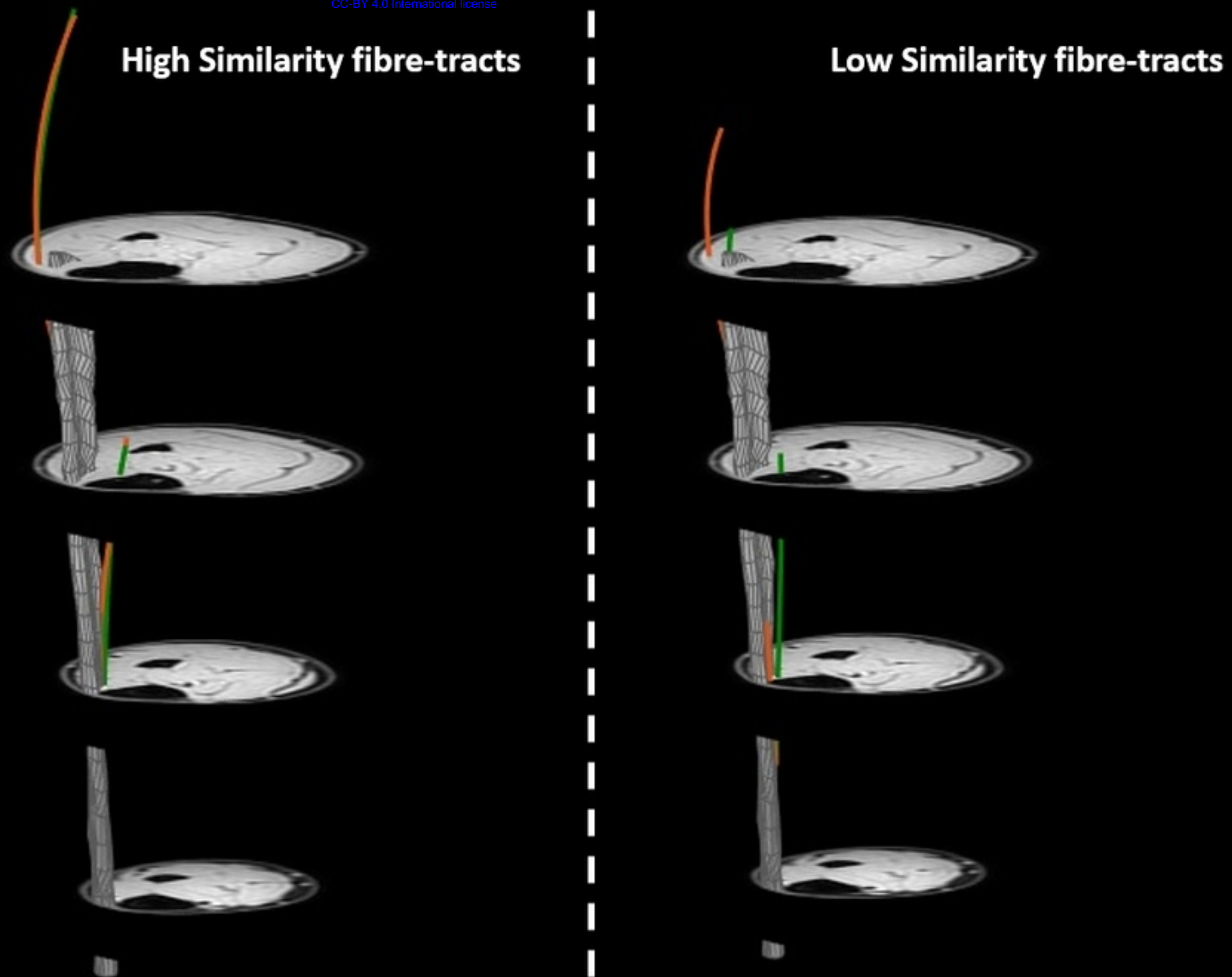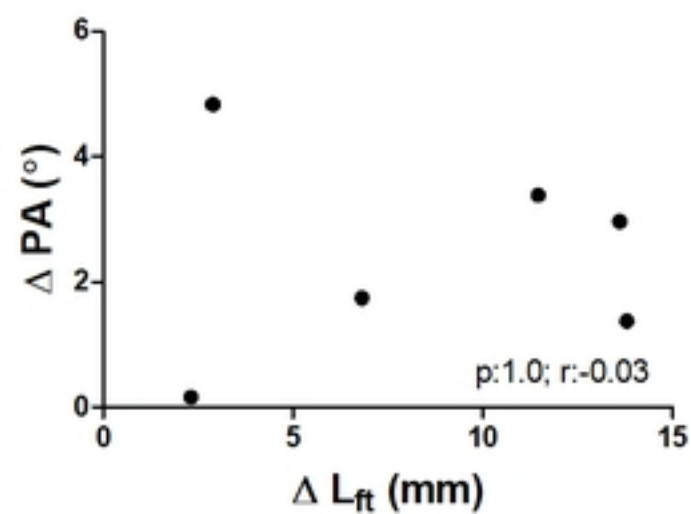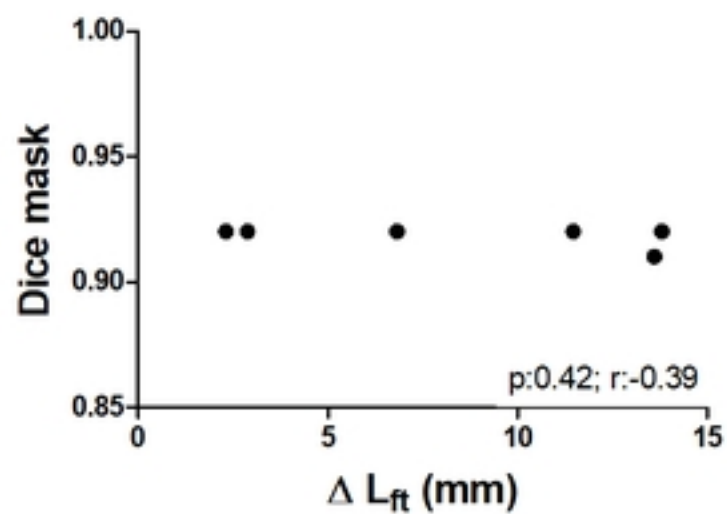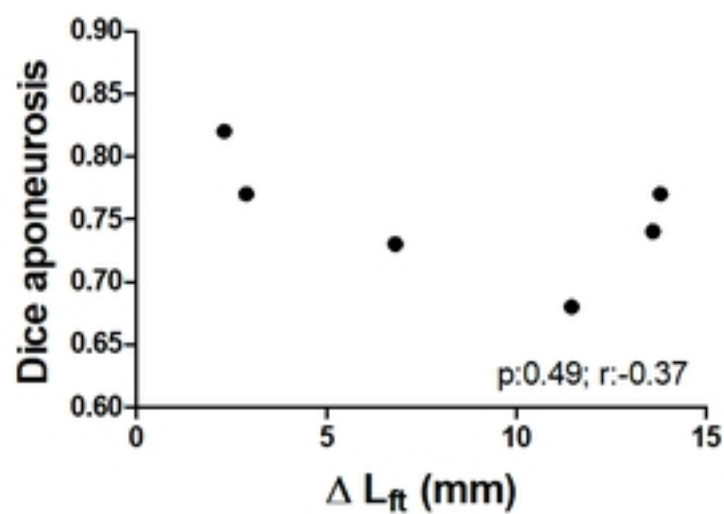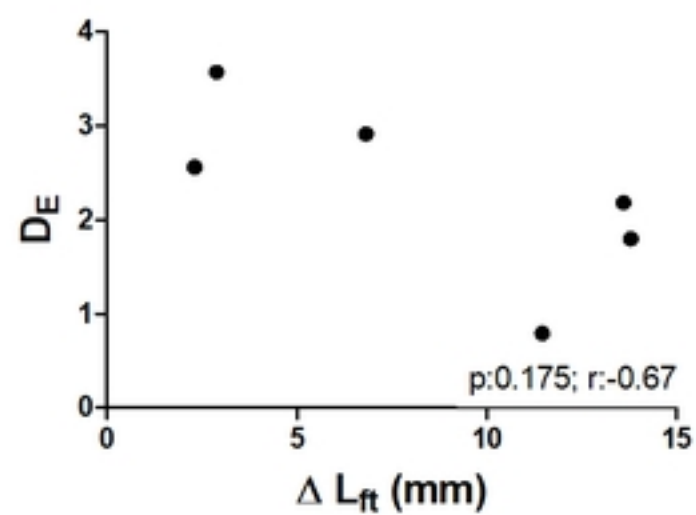
Supplemental Figure 3

High S_i dataset

Low S_i dataset

Supplemental Figure 4