Diffusion Tensor Imaging of Healthy Skeletal Muscles
A Comparison Between 7 T and 3 T

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Objective: The aim of this study was to assess and compare the overall performance, reliability, variability, as well as the accuracy of diffusion tensor imaging (DTI) and fiber tracking metrics, for the muscles of the calf at 3 T and 7 T.

Materials and Methods: Ten volunteers (5 males; mean age, 29.1 ± 4.7 years), with no history of muscle disease, were examined twice at 3 T and 7 T, using a stimulated-echo acquisition mode DTI sequence. Signal-to-noise ratio (SNR) and DTI metrics (track numbers [tr_n], length [tr_l], volume [tr_v], fractional anisotropy [FA], mean [MD], axial [AD], and radial diffusivity [RD]) of the whole-calf muscles, the tibialis anterior, the gastrocnemius medialis, the gastrocnemius lateralis, and the soleus were collected. The Student *t* test was used to compare SNR and DTI metrics obtained at 3 T and 7 T. The coefficients of variation and the intraclass correlation coefficients were derived to assess the variability and the reliability of the DTI measurements at 3 T and 7 T. To further assess the accuracy of the measurements, the absolute difference was computed for each DTI metric at 3 T and 7 T and then compared (Student *t* test). The applied level of significance for all the statistical analyses was $P < 0.05$.

Results: As expected, the SNR was higher at 7 T than at 3 T (+111%; $P < 0.001$). At 7 T, the tracked fibers of the whole calf muscles, the gastrocnemii, and the soleus were more numerous (tr_n +5.5%, +3.1%, +8.5%, and +15.1%, respectively), longer (tr_l +13.1%, +18.8%, +19.3%, and +33.3%, respectively), and showed a greater volume (tr_v +12.1%, +12.2%, +14.7%, and +15.7%, respectively) than at 3 T ($P < 0.05$ each). The soleus demonstrated higher FA (+14.3%), lower MD (−1.7%), AD (−1.9%), and RD (−2%) at 7 T than at 3 T ($P < 0.05$ each), whereas the other muscles showed more heterogeneous results. The coefficients of variation were good (ie, <10%) for all DTI metrics at both 3 T and 7 T. The intraclass correlation coefficient was excellent (>0.750) at 7 T and 3 T for several DTI metrics, such as the tr_n of the gastrocnemii and the soleus, the tr_v of the gastrocnemii, the FA of the whole-calf muscles, gastrocnemius medialis, tibialis anterior, and soleus, and the RD of all investigated muscles (ie, whole-calf muscles, gastrocnemii, tibialis anterior, and soleus). There were no significant differences between the 2 consecutive measurements with each device, except for the tr_n of the whole-calf muscles and the FA of the gastrocnemius lateralis (higher mean absolute difference at 3 T and 7 T, respectively; $P < 0.05$ each).

Conclusions: Despite the numerous challenges associated with DTI of the muscles, both 3 T and 7 T demonstrated reliable and precise results.

Key Words: ultra-high field strength, high field strength, diffusion tensor imaging, muscle, STEAM sequence

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In the last decade, the application of diffusion tensor imaging (DTI) in the musculoskeletal field has increased. Diffusion tensor imaging has been applied to characterize muscle anatomy[1–3] and investigate muscle injuries[4–6] and diseases,[7,8] not only through a visual representation of the fibers using tractography, but also through a quantitative assessment of muscle biomechanical (eg, muscle fiber lengths, number and volume, and pennation angle) and diffusion parameters (eg, fractional anisotropy [FA] and mean diffusivity [MD]). It has also been demonstrated that several physiological (eg, sex, age)[9,10] and technical (eg, magnetic field strength)[11] factors may influence such DTI parameters. The technical challenges of muscle DTI include compensation for eddy current–induced distortions due to high diffusion gradient amplitudes in combination with intrinsically high off-resonance sensitivity of echo-planar imaging and poor signal-to-noise ratio (SNR) due to the small T2/T1 relaxation time ratio.[12] The optimization of acquisition parameters (eg, diffusion time, b-values, number of averages)[13] as well as the choice of sequence approaches that are more suitable for muscle DTI, such as the stimulated-echo acquisition mode (STEAM) sequence,[12,14] have demonstrated a substantial improvement for DTI of muscles. Yet, further advantages, particularly those derived from the higher SNR, may be achieved by moving to 7 T scanners.[15–18] Indeed, it has been shown that a high SNR (≥25) avoids an overestimation of the FA value[13] and an underestimation of the second and third eigenvalues (λ_2 and λ_3).[19]

In the brain, Polders et al[20] reported that the higher SNR at increased magnetic field strength decreased uncertainty in the estimation of FA and the first eigenvector.

Considering not only the high magnetic field strength, but also the reproducibility of the measurements, Fouré et al[21] recently showed that the high spatial resolution achievable at 7 T allows a reproducible assessment of DTI metrics in the muscles. Previously, only few articles had investigated the overall accuracy and reliability of DTI measurements in skeletal muscles and only at lower magnetic field strengths.[22,23] At 3 T, Froeling et al[22] demonstrated that the reproducibility of muscle DTI depends significantly on the investigated region, whereas Heemskerk et al[23] showed that measurements of the tibialis anterior, performed during the same measurement session without repositioning, have a higher reliability than those performed within the same day or on different days.

Despite the aforementioned excellent DTI results obtained in muscles at 3 T and 7 T, and the fact that a thorough knowledge of the advantages and disadvantages of DTI for muscles at different magnetic field strengths is essential to further optimize and promote clinical DTI musculoskeletal applications, to the best of our knowledge, a direct comparison between both field strengths has not yet been performed.

Thus, the aim of this study was to assess and compare the overall performance, reliability, variability, as well as accuracy of DTI and fiber tracking metrics, for the muscles of the calf at 3 T and 7 T.

MATERIALS AND METHODS

Subjects

Ten volunteers (5 females; mean age, 29.1 ± 4.7 years) without any history of muscle injury or disease, who gave written informed consent, were enrolled in this prospective, institutional review board–approved study.

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TABLE 1. MRI Protocol for the 2 Consecutive Scan of the Calf at 7 T and 3 T

	STEAM 3 T	STEAM 7 T	T2w-TSE 3 T	T2w-TSE 7 T
Voxel size, (mm^3)	1.875 × 1.875 × 3.5	1.875 × 1.875 × 3.5	0.7 × 0.7 × 3.5	0.7 × 0.7 × 3.5
Slice thickness, (mm)	3.5	3.5	3.5	3.5
Field of view, (mm^2)	180 × 180	180 × 180	180 × 180	180 × 180
Matrix size	96 × 96	96 × 96	256 × 256	256 × 256
Repetition time, (ms)	7400	7300	6000	10000
Echo time, (ms)	31	32.8	86	98
Diffusion time, (ms)	200	200	—	—
b value, (s/mm^2)	0, 500	0, 500	—	—
No. averages	6	6	—	—
No. directions	12	12	—	—
Fat suppression	• Frequency selective • Gradient reversal	• Frequency selective • Gradient reversal	—	—
GRAPPA factor	2	2	—	—
Acquisition time, (min)	10:01	9:46	1:54	2:22

MRI indicates magnetic resonance imaging; STEAM, stimulated-echo acquisition mode; T2w-TSE, T2-weighted turbo spin echo; GRAPPA, generalized autocalibrating partial parallel acquisition.

MR Protocol

On the same day, the right calf of each volunteer was scanned twice at rest on a clinical 3 T whole-body MR scanner (MAGNETOM Prisma) and on a research 7 T MR scanner (both Siemens Healthcare, Erlangen, Germany), using a 15- and a 28-channel knee coil, respectively.

The MR protocol included a single-shot echo-planar imaging STEAM-DTI prototype sequence and a positioning-matched, T2-weighted turbo spin echo sequence for anatomical reference (Table 1). To ensure identical positioning between test and retest sessions, as well as between scans at 3 T and 7 T, an adhesive label was put on the tibia to mark the position of the magnet isocenter.

Postprocessing

Two coregistration steps were applied to the DTI datasets: the first, designed to correct gross motion artifacts and/or misalignment, was used for images with the same contrast, whereas the second was applied for images from the same slice, but with different diffusion gradients. Before performing the second coregistration, areas of signal loss due to involuntary muscle contractions, which usually affect STEAM-based DTI images,[14,24] were corrected using a previously published method based on the weighted mean of the signal intensity of voxels (WMSI).[14]

DTI Analyses

Masking of each calf was achieved by a previously published method that multiplied MD and radial diffusivity (RD) maps.[14] Then, fourth-order Runge-Kutta tracking (DSI Studio, http://dsi-studio.labsolver.org) was used to analyze the whole-calf muscles, including the gastrocnemius medialis, the gastrocnemius lateralis, the tibialis anterior, and the soleus (Fig. 1). Fractional anisotropy and angular thresholds of 0.12 and 17 degrees were used for the whole-calf muscles, 0.15 and 20 degrees for the gastrocnemii,[10] 0.15 and 45 degrees for the tibialis anterior,[25] and 0.1 and 12 degrees for the soleus.[26]

Diffusion tensor imaging and fiber-tracking metrics (track numbers [tr_n], length [tr_l], volume [tr_v], FA, MD, axial diffusivity [AD], and RD) were collected for the whole-calf muscles, the gastrocnemii, the tibialis anterior and the soleus.

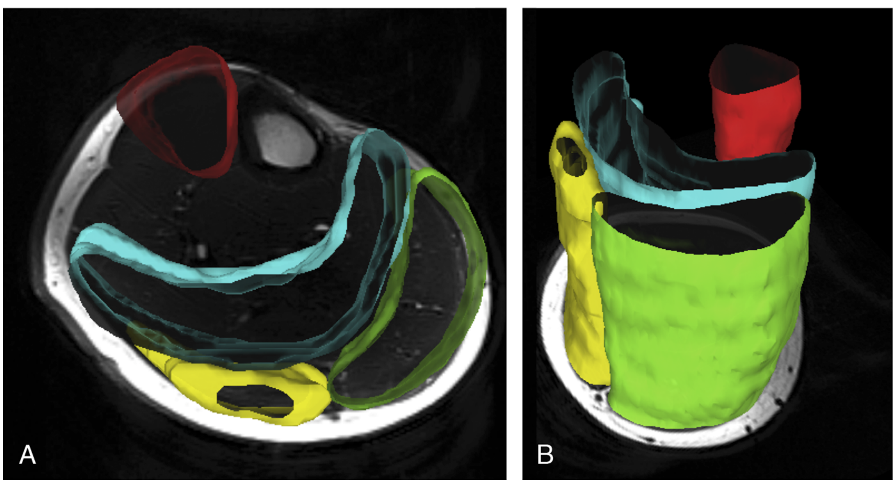

FIGURE 1. T2-weighted image of the calf muscle of 1 volunteer obtained at 7 T showing a 3-dimensional representation of the regions of interest of the 4 single investigated muscles (ie, red indicates tibialis anterior; green, gastrocnemius medialis; yellow, gastrocnemius lateralis; blue, soleus) from the axial (A) and oblique coronal (B) perspectives.

Signal-to-Noise Ratio

The SNR was computed as the ratio of the signal amplitude of the muscles (ie, mean of the signal amplitude inside 2 regions of interest placed in the central and peripheral muscles of the calves, respectively) to the background noise measured outside the calf, corrected for 25% overestimation.[27–29]

Statistical Analysis

The paired Student *t* test was used to compare SNR and the DTI and fiber-tracking metrics obtained at 3 T and 7 T (ie, comparison of the mean values of the 2 consecutive measurements obtained with each device).

To assess the variability of the DTI measurements at 3 T and 7 T, the coefficient of variation (CV) was computed (ie, for the whole-calf muscles and each investigated muscle). To avoid biases due to the physiologic variability among subjects, the CV was calculated for each subject, and then the mean of all volunteers was obtained.

To evaluate the reliability of the 2 consecutive scans at 3 T and 7 T, the intraclass correlation coefficient (ICC) was calculated by applying a 2-way mixed model with consistency and single measures. Values above 0.750 were considered excellent.[30] To further assess the accuracy of the measurements obtained with each device, the absolute difference (ie, absolute difference between the 2 consecutive measurements with each device, for each volunteer, for the whole-calf muscles, the tibialis anterior, the gastrocnemii, and the soleus) was also assessed for each DTI and fiber tracking metric at 3 T and 7 T and then compared (paired Student *t* test).

All statistical analyses were performed with SPSS Statistics, version 23 (IBM Corp, Armonk, NY), and the level of significance was $P < 0.05$.

RESULTS

Comparison of 3 T versus 7 T

All volunteers were successfully scanned at 3 T and 7 T, and the results are summarized in Table 2.

The SNR at 7 T (SNR_{7T} mean ± SD 54 ± 6.2) was +111% higher than at 3 T (SNR_{3T} mean ± SD 25.5 ± 3.6; $P < 0.001$).

TABLE 2. Comparison Between 7 T and 3 T

		7 T	3 T	*P* (Student *t* Test)
tr_n	Whole-calf muscles	45200 ± 1400	42900 ± 2700	**0.003**
	Gastrocnemius medialis	8500 ± 1000	8200 ± 1100	**0.048**
	Gastrocnemius lateralis	4000 ± 1100	3700 ± 1000	**0.006**
	Tibialis anterior	5550 ± 460	5220 ± 400	**0.045**
	Soleus	13600 ± 2300	11800 ± 2100	**0.003**
tr_l, (mm)	Whole-calf muscles	63.1 ± 4.9	55.7 ± 3.4	**0.000**
	Gastrocnemius medialis	51.2 ± 7.1	43.1 ± 4.7	**0.001**
	Gastrocnemius lateralis	75.4 ± 11.2	63.2 ± 11	**0.017**
	Tibialis anterior	90.5 ± 3.1	89.7 ± 2.2	0.400
	Soleus	48.0 ± 8.7	36.0 ± 4.5	**0.001**
tr_v, (cm^3)	Whole-calf muscles	691 ± 52	617 ± 48	**0.000**
	Gastrocnemius medialis	144 ± 18	128 ± 18	**0.000**
	Gastrocnemius lateralis	71 ± 16	62 ± 15	**0.009**
	Tibialis anterior	93 ± 11	80 ± 74	**0.001**
	Soleus	248 ± 32	214 ± 26	**0.002**
FA	Whole-calf muscles	0.317 ± 0.021	0.323 ± 0.018	0.087
	Gastrocnemius medialis	0.288 ± 0.031	0.278 ± 0.029	0.205
	Gastrocnemius lateralis	0.323 ± 0.028	0.326 ± 0.027	0.639
	Tibialis anterior	0.395 ± 0.025	0.408 ± 0.029	**0.001**
	Soleus	0.164 ± 0.027	0.148 ± 0.021	**0.016**
MD (10^{-3} mm^2/s)	Whole-calf muscles	1.165 ± 0.029	1.149 ± 0.021	**0.027**
	Gastrocnemius medialis	1.152 ± 0.047	1.184 ± 0.039	**0.002**
	Gastrocnemius lateralis	1.149 ± 0.035	1.164 ± 0.04	0.057
	Tibialis anterior	1.186 ± 0.028	1.106 ± 0.027	**0.000**
	Soleus	1.16 ± 0.028	1.185 ± 0.027	**0.003**
AD (10^{-3} mm^2/s)	Whole-calf muscles	1.615 ± 0.028	1.613 ± 0.023	0.849
	Gastrocnemius medialis	1.57 ± 0.048	1.60 ± 0.033	**0.023**
	Gastrocnemius lateralis	1.592 ± 0.034	1.621 ± 0.054	0.066
	Tibialis anterior	1.747 ± 0.017	1.654 ± 0.018	**0.000**
	Soleus	1.565 ± 0.027	1.598 ± 0.028	**0.000**
RD (10^{-3} mm^2/s)	Whole-calf muscles	0.931 ± 0.038	0.914 ± 0.029	**0.023**
	Gastrocnemius medialis	0.943 ± 0.058	0.976 ± 0.049	**0.008**
	Gastrocnemius lateralis	0.927 ± 0.046	0.936 ± 0.044	0.313
	Tibialis anterior	0.906 ± 0.042	0.832 ± 0.042	**0.000**
	Soleus	0.957 ± 0.041	0.978 ± 0.038	**0.018**

tr_n indicates track number; tr_l, tracks length; tr_v, tracks volume; FA, fractional anisotropy; MD, mean diffusivity; AD, axial diffusivity; RD, radial diffusivity.

At 7 T, the tracked fibers of the whole-calf muscles, the gastrocnemii, and the soleus were more numerous (tr_n +5.5%, +3.1%, +8.5%, and +15.1%, respectively), longer (tr_l +13.1%, +18.8%, +19.3%, and +33.3%, respectively), and showed a greater volume (tr_v +12.1%, +12.2%, +14.7%, and +15.7%, respectively) than at 3 T ($P < 0.05$ each), whereas the tibialis anterior demonstrated only greater tr_n and tr_v (+6.3% and +16.4%; $P < 0.05$ each) (Fig. 2).

For the other DTI metrics, the whole-calf muscles showed higher MD (+0.9%) and RD (+2.2%) at 7 T ($P < 0.05$). The soleus demonstrated higher FA (+14.3%), lower MD (−1.7%), AD (−1.9%), and RD (−2%) at 7 T than at 3 T ($P < 0.05$ each). Lower FA (−2.5%) and a higher MD (+7.3%), AD (+5.4%), and RD (+8.4%) were found in the tibialis anterior at 7 T ($P < 0.05$ each). The analysis of the gastrocnemius medialis revealed lower MD (−2.5%), AD (−1.9%), and RD (−3.1%) ($P < 0.05$ each).

The gastrocnemius lateralis did not show any statistically significant difference between 3 T and 7 T for FA, MD, RD, and AD ($P > 0.05$ each).

Variability, Reliability, and Accuracy

The CV was good (ie, <10%) for all DTI metrics at both 3 T and 7 T (Table 3).

The ICC was excellent (>0.750) at 7 T and 3 T for several DTI metrics, such as the tr_n of the gastrocnemii and the soleus, the tr_v of the gastrocnemii, the FA of the whole-calf muscles, the gastrocnemius medialis, the tibialis anterior, and the soleus, and the RD of all investigated muscles (ie, whole-calf muscles, gastrocnemii, tibialis anterior, and soleus) (Fig. 3). The gastrocnemius medialis and the soleus also showed an excellent reliability with both techniques, respectively, for MD and tr_l.

At 7 T only, the tr_l of the gastrocnemius medialis and the tr_v of the tibialis anterior and the soleus showed excellent reliability, whereas such high ICC values occurred at 3 T only for the MD of the gastrocnemius lateralis and the soleus, for the FA of the gastrocnemius lateralis, and for the AD of each investigated muscle, except the tibialis anterior.

No significant differences emerged when comparing the absolute differences of the 2 consecutive measurements obtained with each device ($P > 0.05$ each), except for the tr_n of the whole-calf muscles (mean absolute difference at 7 T was 900 ± 1100 and mean absolute difference at 3 T was 2300 ± 2100; $P = 0.034$) and the FA of the gastrocnemius lateralis (mean absolute difference at 7 T was 0.019 ± 0.011 and mean absolute difference at 3 T was 0.007 ± 0.107; $P = 0.01$) (Table 3).

DISCUSSION

The results of our study have demonstrated that both 7 T and 3 T guarantee very robust DTI analyses and that data acquisition at 7 T may provide specific advantages.

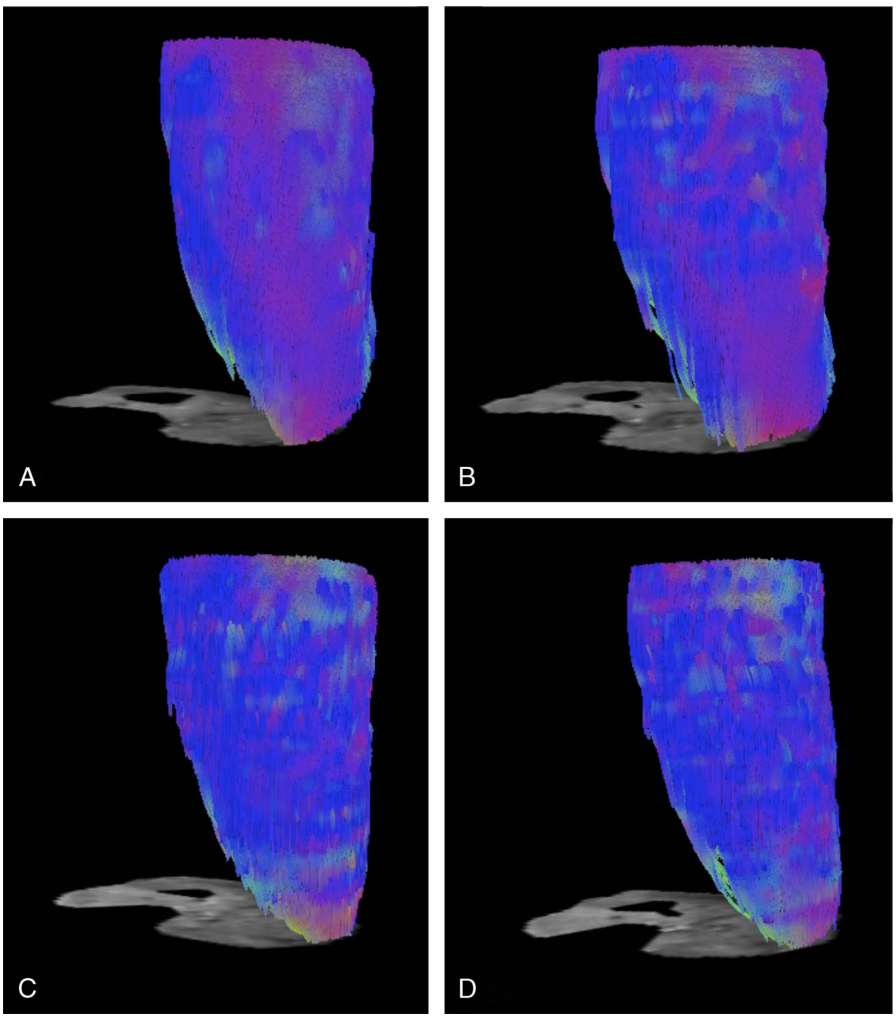

FIGURE 2. Fiber tracking of the medial gastrocnemius of 1 volunteer, demonstrating longer and more numerous fibers on both consecutive measurements at 7 T (A and B) than at 3 T (C and D).

TABLE 3. Variability, Reliability and Accuracy of Consecutive DTI Measurements at 7 T and 3 T MRI

		7 T MRI					3 T MRI				
		Scan 1	Scan 2	ab.d.	CV	ICC	Scan 1	Scan 2	ab.d.	CV	ICC
tr_n	Whole-calf muscles	45300 ± 1400	45200 ± 1700	900*	1.3	0.622	43200 ± 3300	42500 ± 2900	2300*	3.9	0.509
	Gastrocnemius medialis	8500 ± 1000	8400 ± 1000	400	1.8	**0.821**	8200 ± 1300	8200 ± 1100	600	5	**0.840**
	Gastrocnemius lateralis	4000 ± 1200	4000 ± 1000	200	3.7	**0.963**	3600 ± 1000	3700 ± 1100	300	5.2	**0.958**
	Tibialis anterior	5600 ± 600	5500 ± 400	300	3.5	0.722	5200 ± 400	5300 ± 500	300	4.4	0.564
	Soleus	13900 ± 2500	13400 ± 2200	800	4	**0.872**	11500 ± 1700	12100 ± 2700	1000	5.2	**0.778**
tr_l, (mm)	Whole-calf muscles	62.9 ± 6.1	63.3 ± 4.5	3.6	4.1	0.685	56.4 ± 4.1	54.9 ± 3.8	3.5	4.4	0.464
	Gastrocnemius medialis	50.3 ± 7.6	52 ± 7.2	3.4	4.9	**0.806**	44.5 ± 5.8	43.4 ± 5.5	5.1	7.9	0.411
	Gastrocnemius lateralis	74.9 ± 15.1	75.8 ± 11.1	9	9.1	0.636	64.3 ± 13.7	62.1 ± 9.6	6.9	7.8	0.743
	Tibialis anterior	89.7 ± 3.5	91.2 ± 3.4	3.1	2.4	0.557	90.2 ± 2.6	89.2 ± 3.6	3.5	2.7	0.000†
	Soleus	48.7 ± 8.9	47.4 ± 8.9	3.4	5.3	**0.892**	36.78 ± 4.9	35.3 ± 4.6	2.8	5.4	**0.783**
tr_v (cm^3)	Whole-calf muscles	689 ± 59	694 ± 58	42.6	4.4	0.618	630 ± 71	604 ± 49	62.7	7.2	0.234
	Gastrocnemius medialis	145 ± 21	143 ± 19	10.9	5.4	**0.767**	128 ± 22	128 ± 17	10.2	5.5	**0.769**
	Gastrocnemius lateralis	71 ± 19	71 ± 13	6.4	6.3	**0.891**	61 ± 14	62 ± 17	5.3	6.1	**0.910**
	Tibialis anterior	93 ± 12	93 ± 11	5.4	4.3	**0.865**	81 ± 8	80 ± 8	6.0	5.3	0.563
	Soleus	252 ± 34	245 ± 32	9.8	2.8	**0.928**	215 ± 22	214 ± 35	17.5	5.4	0.625
FA	Whole-calf muscles	0.312 ± 0.021	0.321 ± 0.022	0.01	2.2	**0.878**	0.320 ± 0.017	0.325 ± 0.019	0.01	1.3	**0.915**
	Gastrocnemius medialis	0.283 ± 0.031	0.293 ± 0.035	0.01	3.8	**0.810**	0.275 ± 0.029	0.281 ± 0.030	0.01	2.2	**0.926**
	Gastrocnemius lateralis	0.316 ± 0.029	0.329 ± 0.030	0.02*	4.3	0.742	0.323 ± 0.027	0.330 ± 0.029	0.01*	1.7	**0.898**
	Tibialis anterior	0.392 ± 0.025	0.398 ± 0.026	0.01	1.2	**0.948**	0.405 ± 0.029	0.410 ± 0.029	0.01	0.9	**0.975**
	Soleus	0.162 ± 0.026	0.166 ± 0.028	0.01	4.4	**0.910**	0.146 ± 0.022	0.150 ± 0.023	0.01	0.8	**0.843**
MD (10^{-3} mm^2/s)	Whole-calf muscles	1.176 ± 0.035	1.153 ± 0.028	0.02	1.4	0.610	1.157 ± 0.023	1.142 ± 0.021	0.02	1.0	0.741
	Gastrocnemius medialis	1.163 ± 0.052	1.141 ± 0.047	0.02	1.5	**0.774**	1.192 ± 0.040	1.177 ± 0.040	0.02	1.1	**0.867**
	Gastrocnemius lateralis	1.159 ± 0.042	1.139 ± 0.032	0.02	1.4	0.677	1.169 ± 0.038	1.160 ± 0.043	0.01	0.9	**0.895**
	Tibialis anterior	1.199 ± 0.031	1.174 ± 0.027	0.02	1.5	0.616	1.115 ± 0.028	1.096 ± 0.026	0.02	1.2	0.734
	Soleus	1.168 ± 0.034	1.151 ± 0.027	0.02	1.3	0.673	1.190 ± 0.030	1.179 ± 0.025	0.01	0.8	**0.932**
AD (10^{-3} mm^2/s)	Whole-calf muscles	1.624 ± 0.038	1.606 ± 0.021	0.02	0.9	0.576	1.619 ± 0.023	1.608 ± 0.025	0.01	0.6	**0.768**
	Gastrocnemius medialis	1.581 ± 0.062	1.558 ± 0.039	0.03	1.2	0.677	1.608 ± 0.033	1.596 ± 0.036	0.02	0.8	**0.810**
	Gastrocnemius lateralis	1.596 ± 0.048	1.588 ± 0.031	0.03	1.4	0.457	1.622 ± 0.027	1.621 ± 0.054	0.02	1.0	**0.861**
	Tibialis anterior	1.761 ± 0.023	1.733 ± 0.015	0.03	1.1	0.267	1.664 ± 0.013	1.643 ± 0.023	0.02	1.0	0.481
	Soleus	1.571 ± 0.031	1.558 ± 0.027	0.02	0.9	**0.737**	1.602 ± 0.026	1.594 ± 0.031	0.01	0.5	**0.913**
RD (10^{-3} mm^2/s)	Whole-calf muscles	0.942 ± 0.040	0.919 ± 0.039	0.02	1.8	**0.763**	0.921 ± 0.029	0.907 ± 0.029	0.01	1.1	**0.862**
	Gastrocnemius medialis	0.953 ± 0.058	0.932 ± 0.060	0.02	1.9	**0.857**	0.984 ± 0.050	0.967 ± 0.050	0.02	1.4	**0.904**
	Gastrocnemius lateralis	0.940 ± 0.050	0.914 ± 0.046	0.03	2.3	**0.755**	0.942 ± 0.040	0.929 ± 0.048	0.02	1.3	**0.909**
	Tibialis anterior	0.919 ± 0.043	0.894 ± 0.041	0.02	1.8	**0.802**	0.841 ± 0.043	0.823 ± 0.040	0.02	1.5	**0.883**
	Soleus	0.967 ± 0.045	0.947 ± 0.042	0.02	1.8	**0.775**	0.985 ± 0.041	0.971 ± 0.036	0.01	1.1	**0.951**

*Statistically significant difference ($P < 0.05$).

†Value due to the small population (n = 10).

MRI indicates magnetic resonance imaging; tr_n, track number; tr_l, tracks length; tr_v, tracks volume; FA, fractional anisotropy; MD, mean diffusivity; AD, axial diffusivity; RD, radial diffusivity; ab.d., absolute difference between the 2 consecutive measurements; CV, coefficient of variation; ICC, intraclass correlation coefficient.

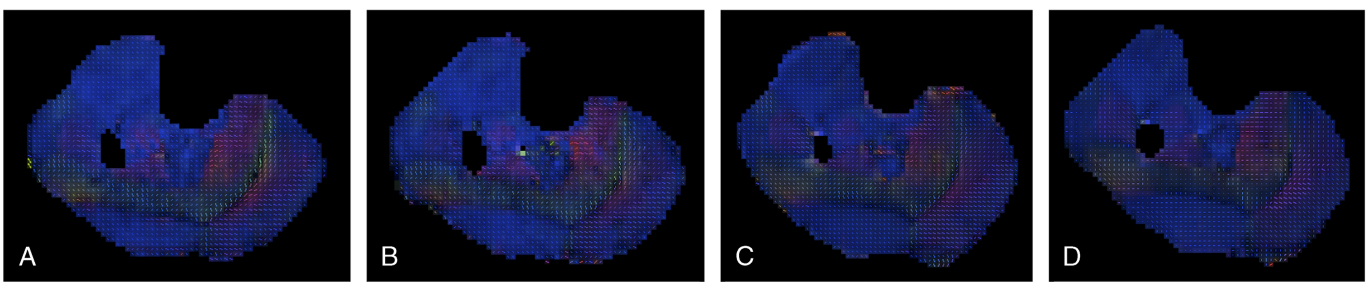

FIGURE 3. Color-coded maps of the calf muscles of 1 volunteer obtained with the 2 consecutive measurements at 3 T (A and B) and 7 T (C and D): excellent intraclass correlation coefficients were obtained with both devices with regard to fractional anisotropy of the whole-calf muscles.

As expected, a higher SNR was obtained at 7 T and led to a significant improvement of fiber tracking (ie, increased number, length, and volume of the tracked fibers) compared with 3 T.[13,31] At 7 T, the average FAs were higher, whereas the MD values were lower in the soleus. In the other muscles, the results were less straightforward, especially in the tibialis anterior (ie, lower FA and higher MD). This heterogeneity can be considered consistent with the findings of Polders et al,[20] who found a higher uncertainty in peripheral areas of the brain, such as the temporal lobe at 7 T. This evidence suggests that imaging at 7 T might be beneficial only in certain regions. However, it should be noted that Saupe et al,[11] using 1.5 T and 3 T for muscle analysis, and Choi et al,[32] comparing 3 T and 7 T in the brain, did not find any significant differences in DTI metrics. This may be explained, at least partially, by stronger field inhomogeneities at 7 T.

In our study, heterogeneous results also occurred with regard to the reliability of the DTI metrics with both scanners. Indeed, even if both devices showed excellent values (ie, ICC > 0.750) for most of the variables in all the examined muscles, some differences emerged for specific metrics and muscles. For instance, fiber tracking (ie, track volume and length) showed higher ICCs when the magnetic field strength was increased, whereas other DTI metrics (ie, especially MD and AD) were more robust at 3 T. Considering each investigated muscle, at 7 T, the gastrocnemius medialis demonstrated excellent ICCs for all DTI metrics except AD. The tibialis anterior showed low reliability for several metrics (ie, tr_n, tr_l, MD, and AD) at both 3 T and 7 T. In agreement with our results, Froeling et al[22] demonstrated a variation in reliability for the analyzed muscles of the forearm using a 3 T scanner (ie, higher ICC of FA and MD in the whole muscle volume and in the flexor digitorum profundus than in the extensor digitorum). These results further support the aforementioned beneficial application of 7 T for the investigation of specific areas.

Even if some variables, such as the AD, showed lower reliability at 7 T, all DTI metrics demonstrated a good CV (ie, less than 10%)[33] with both scanners. Considering that the CV is, in contrast to the ICC, not affected by between-subject variability, it provides a better insight into the robustness of DTI for muscles. The low variability of DTI is a core finding, especially for implementing the application of DTI analyses of muscle injuries or lesions. Indeed, if DTI metrics show a low variability in healthy subjects, even very small changes may then reflect alteration due to injuries.

In agreement with the findings of Froeling et al[22] and Damon,[19] the variability of FA, albeit low (ie, below 10%),[33] was higher than that of MD, AD, and RD. Somewhat in contrast to the simulations of Damon, which demonstrated an increase in the CV of MD and FA with decreasing SNR,[19] in our population, despite the overall higher SNR at 7 T, the CV of these metrics was slightly lower at 3 T. Future studies should evaluate the impact of magnetic susceptibility, field inhomogeneity, and chemical shift at 7 T to provide a complete overview of these findings.

Supporting the evidence that the investigation of the peripheral regions is more critical at 7 T, both the CV and ICC of the gastrocnemius lateralis were slightly lower using the 7 T scanner than at 3 T, which was also the case for the length and volume of the tracked fibers.

Finally, regarding not only the variability, but also the accuracy of the measurements, our 7 T results are in accordance with those of Fouré et al (ie, CV and absolute differences lower than 10%).[21] The comparisons of the absolute differences at 3 T and 7 T demonstrate an overall equivalence of the 2 scanners except for a superior performance of 7 T for the number of tracked fibers in the entire calf and the higher FA of the gastrocnemius lateralis at 3 T.

Despite our promising results, this study has several limitations. The examined population was quite small (ie, 10 volunteers), and this might have affected the evaluation of the reliability (ie, ICC). Nevertheless, a very low variability and high accuracy were obtained, demonstrating the robustness of DTI for muscles.

Moreover, it should be noted that a single rater performed all the analyses, and thus, the interrater reliability was not assessed. To provide a complete overview of the applicability of DTI for muscles in clinical practice, in the future, it might be useful to perform a dedicated study with different raters with the same and different levels of experience.

It has also to be considered that, even if DTI of muscles is still mainly applied for research purposes, the quite long acquisition time (~10 minutes at 3 T and 7 T) may limit its application in the clinical routine. Therefore, future studies investigating accelerating methods should be further promoted.[34]

Finally, field inhomogeneities in the RF field that likely lowered the performance of 7 T DTI can be overcome by using parallel-transmit coils,[35,36] which were not available for this study.

In conclusion, despite the numerous challenges associated with DTI for muscles, both 3 T and 7 T demonstrated reliable and precise results.

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REFERENCES

1. Sinha S, Sinha U, Edgerton VR. In vivo diffusion tensor imaging of the human calf muscle. *J Magn Reson Imaging*. 2006;24:182–190.
2. Kermarrec E, Budzik JF, Khalil C, et al. In vivo diffusion tensor imaging and tractography of human thigh muscles in healthy subjects. *AJR Am J Roentgenol*. 2010;195:352–356.
3. Froeling M, Nederveen AJ, Heijtel DF, et al. Diffusion-tensor MRI reveals the complex muscle architecture of the human forearm. *J Magn Reson Imaging*. 2012;36:237–248.
4. Zaraiskaya T, Kumbhare D, Noseworthy M. Diffusion tensor imaging in evaluation of human skeletal muscle injury. *J Magn Reson Imaging*. 2006;24:402–408.
5. McMillan A, Shi D, Pratt S, et al. Diffusion tensor MRI to assess damage in healthy and dystrophic skeletal muscle after lengthening contractions. *J Biomed Biotechnol*. 2011;2011:970726.
6. Giraudo C, Motyka S, Weber M, et al. Normalized STEAM-based diffusion tensor imaging provides a robust assessment of muscle tears in football players: preliminary results of a new approach to evaluate muscle injuries. *Eur Radiol*. 2018; 28:2882–2889.
7. Ponrartana S, Ramos-Platt L, Wren TA, et al. Effectiveness of diffusion tensor imaging in assessing disease severity in Duchenne muscular dystrophy: preliminary study. *Pediatr Radiol*. 2015;45:582–589.
8. Sigmund EE, Sui D, Ukpebor O, et al. Stimulated echo diffusion tensor imaging and SPAIR T2-weighted imaging in chronic exertional compartment syndrome of the lower leg muscles. *J Magn Reson Imaging*. 2013;38:1073–1082.
9. Okamoto Y, Kunimatsu A, Kono T, et al. Gender differences in MR muscle tractography. *Magn Reson Med Sci*. 2010;9:111–118.
10. Sinha U, Csapo R, Malis V, et al. Age-related differences in diffusion tensor indices and fiber architecture in the medial and lateral gastrocnemius. *J Magn Reson Imaging*. 2015;41:941–953.
11. Saupe N, White LM, Sussman MS, et al. Diffusion tensor magnetic resonance imaging of the human calf: comparison between 1.5 T and 3.0 T—preliminary results. *Invest Radiol*. 2008;43:612–618.
12. Noehren B, Andersen A, Feiweier T, et al. Comparison of twice refocused spin echo versus stimulated echo diffusion tensor imaging for tracking muscle fibers. *J Magn Reson Imaging*. 2015;41:624–632.
13. Froeling M, Nederveen AJ, Nicolay K, et al. DTI of human skeletal muscle: the effects of diffusion encoding parameters, signal-to-noise ratio and T2 on tensor indices and fiber tracts. *NMR Biomed*. 2013;26:1339–1352.
14. Giraudo C, Motyka S, Weber M, et al. Weighted mean of signal intensity for unbiased fiber tracking of skeletal muscles: development of a new method and comparison with other correction techniques. *Invest Radiol*. 2017;52:488–497.
15. Trattnig S, Bogner W, Gruber S, et al. Clinical applications at ultrahigh field (7 T). Where does it make the difference? *NMR Biomed*. 2016;29:1316–1334.
16. Umutlu L, Ladd ME, Forsting M, et al. 7 Tesla MR imaging: opportunities and challenges. *Rofo*. 2014;186:121–129.
17. Regatte RR, Schweitzer ME. Ultra-high-field MRI of the musculoskeletal system at 7.0T. *J Magn Reson Imaging*. 2007;25:262–269.

18. Trattnig S, Zbyn S, Schmitt B, et al. Advanced MR methods at ultra-high field (7 Tesla) for clinical musculoskeletal applications. *Eur Radiol*. 2012;22: 2338–2346.

19. Damon B. Effects of image noise in Muscle DT-MRI assessed using numerical simulations. *Magn Reson Med*. 2008;60:934–944.

20. Polders DL, Leemans A, Hendrikse J, et al. Signal to noise ratio and uncertainty in diffusion tensor imaging at 1.5, 3.0, and 7.0 Tesla. *J Magn Reson Imaging*. 2011; 33:1456–1463.

21. Fouré A, Ogier AC, Le Troter A, et al. Diffusion properties and 3D architecture of human lower leg muscles assessed with UHF strength diffusion-tensor MR imaging and tractography: reproducibility and sensitivity to sex difference and intramuscular variability. *Radiology.* 2018;287:592–607.

22. Froeling M, Oudeman J, van den Berg S, et al. Reproducibility of diffusion tensor imaging in human forearm muscles at 3.0 T in a clinical setting. *Magn Reson Med*. 2010;64:1182–1190.

23. Heemskerk AM, Sinha TK, Wilson KJ, et al. Repeatability of DTI-based skeletal muscle fiber tracking. *NMR Biomed*. 2010;23:294–303.

24. Karampinos DC, Banerjee S, King FK, et al. Considerations in high-resolution skeletal muscle diffusion tensor imaging using single-shot echo planar imaging with stimulated-echo preparation and sensitivity encoding. *NMR Biomed*. 2012; 25:766–778.

25. Heemskerk A, Sinha TK, Wilson KJ, et al. Quantitative assessment of DTI-based muscle fiber tracking and optimal tracking parameters. *Magn Res Medic*. 2009; 61:467–472.

26. Sinha U, Sinha S, Hodgson JA, et al. Human soleus muscle architecture at different ankle joint angles from magnetic resonance diffusion tensor imaging. *J Appl Physiol (1985)*. 2011;110:807–819.

27. Kaufman L, Kramer DM, Crooks LE, et al. Measuring signal-to-noise ratios in MR imaging. *Radiology.* 1989;173:265–267.

28. Bogner W, Gruber S, Pinker K, et al. Diffusion-weighted MR for differentiation of breast lesions at 3.0 T: how does selection of diffusion protocols affect diagnosis? *Radiology.* 2009;253:341–351.

29. Bogner W, Pinker K, Zaric O, et al. Bilateral diffusion-weighted MR imaging of breast tumors with submillimeter resolution using readout-segmented echo-planar imaging at 7 T. *Radiology.* 2015;274:74–84.

30. Cicchetti DV. Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology. *Psychol Assess*. 1994;6: 284–290.

31. Yao X, Yu T, Liang B, et al. Effect of increasing diffusion gradient direction number on diffusion tensor imaging fiber tracking in the human brain. *Korean J Radiol*. 2015;16:410–418.

32. Choi S, Cunningham DT, Aguila F, et al. DTI at 7 and 3 T: systematic comparison of SNR and its influence on quantitative metrics. *Magn Reson Imaging*. 2011;29: 739–751.

33. Sigmund EE, Vivier PH, Sui D, et al. Intra-voxel incoherent motion and diffusion-tensor imaging in renal tissue under hydration and furosemide flow challenges. *Radiology.* 2012;263:758–769.

34. Filli L, Piccirelli M, Kenkel D, et al. Simultaneous multislice echo planar imaging with blipped controlled aliasing in parallel imaging results in higher acceleration: a promising technique for accelerated diffusion tensor imaging of skeletal muscle. *Invest Radiol*. 2015;50:456–463.

35. Kraff O, Quick HH. 7T: physics, safety, and potential clinical applications. *J Magn Reson Imaging*. 2017;46:1573–1589.

36. Padormo F, Beqiri A, Hajnal JV, et al. Parallel transmission for ultrahigh-field imaging. *NMR Biomed*. 2016;29:1145–1161.