

# Diffusion Tensor Imaging of Skeletal Muscle – Correlation of Fractional Anisotropy to Muscle Power

## Diffusions-Tensor Imaging des Skelettmuskels: Korrelation von fraktioneller Anisotropie mit mechanischen Muskelleistung

### Authors

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### Key words

- MR-diffusion/perfusion
- MR-imaging
- diagnostic radiology

### Abstract

**Purpose:** Recent DTI studies demonstrated the possibility of fiber geometry visualization in skeletal muscle. We tested for an association between muscle power and standard DTI parameters, e. g. fractional anisotropy.

**Materials and Methods:** Maximal muscle power (Lmax) of the soleus muscle was determined in 11 healthy subjects. Subsequently DTI was performed and standard parameters (fractional anisotropy – FA, mean diffusivity – MD, parallel diffusivity – PD, radial diffusivity – RD) were extracted in an ROI of the soleus muscle.

**Results:** We found a significant association of Lmax with FA (neg. correlation:  $r = -0.85$ ,  $p = 0.0015$ ) and RD (pos. correlation  $r = 0.80$ ,  $p = 0.047$ ). There was no significant association of MD or PD.

**Conclusion:** Maximum muscle power is an indirect measure of fiber type distribution. The correlation between muscle power and DTI parameters can be explained by differences in fiber diameter and differences in the intracellular microstructure of type-1 and type-2 fibers. DTI should be evaluated as a tool for non-invasive quantification of fiber type distribution in skeletal muscle.

### Key Points:

- Fractional anisotropy is negatively correlated with maximum power of a muscle.
- An explanation is the association of fractional anisotropy with muscle fiber distribution.
- DTI might facilitate non-invasive assessment of fiber type distribution in skeletal muscle.

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### Zusammenfassung

**Ziel:** Studien der letzten Jahre haben gezeigt, dass mit Diffusions-Tensor Imaging die Fasergeometrie von Skelettmuskeln dargestellt werden kann. Ziel der aktuellen Studie war es zu überprüfen, ob auch zwischen funktioneller Muskelleistung und Standard DTI-Parametern, wie z.B. der Fraktionellen Anisotropie (FA) Korrelationen bestehen.

**Material und Methoden:** Bei 11 gesunden Probanden wurde zunächst die maximale mechanische Leistung (Lmax) des M. soleus bestimmt. Im Anschluss wurde bei allen Probanden DTI Messungen durchgeführt und die Standard DTI Parameter (Fraktionelle Anisotropie – FA, Mittlere Diffusivität – MD, Parallel Diffusivität – PD, Radiale Diffusivität – RD) über eine ROI Analyse im M. soleus quantifiziert.

**Ergebnisse:** Es bestand eine signifikante Assoziation zwischen Lmax und FA (negative Korrelation  $r = -0.85$ ,  $p = 0.0015$ ) bzw. RD (positive Korrelation  $r = 0.80$ ,  $p = 0.047$ ). Kein signifikanter Zusammenhang bestand zu MD oder PD.

**Schlussfolgerungen:** Die maximale mechanische Muskelleistung ist ein indirekter Parameter für die Muskelfaserzusammensetzung. Die gefundenen Korrelation zwischen Muskelleistung und DTI Parametern können durch Unterschiede im Faserdurchmesser und Unterschiede in der intrazellulären Mikrostruktur von Typ-1 und Typ-2 Fasern erklärt werden. DTI eignet sich möglicherweise als nicht-invasive Methode zur Bestimmung der Muskelfaserzusammensetzung.

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### Bibliography

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## Introduction

Diffusions-Tensor-Imaging (DTI) is an MRI method facilitating microstructural examination of biological tissues. The most commonly known clinical application of DTI would certainly be the imaging of brain fibre tracts for optimizing the planning of radiation therapy or surgery, for example. However, DTI also enables very early detection of potential changes associated with neurodegenerative diseases (e.g., Alzheimer's, dementia, amyotrophic lateral sclerosis) [1–3]. What is less known is that DTI can also be used to examine the microarchitecture of organs other than those of the central nervous system. For example, one of the first biological tissues demonstrated using DTI was not cerebral white matter, but rather the skeletal muscle of a porcine loin [4]. It thus comes as no surprise that DTI has also been used for examining muscle tissue for the past several years. A series of studies has shown that DTI can be used to visualize the fibre geometry of the muscles of the extremities or the pelvic floor [5–7]. Furthermore, DTI has been used in diagnosing various muscle pathologies, e.g., denervation or muscle ischemia [8–10]. For a summary of the significance of MRI and DTI examination in analysing muscle tissue, those interested are advised to refer to the appropriate survey articles [11–14].

The human skeletal muscle is divided into two basic types of fibres having key differences in terms of function and microstructure. Type-1 fibres contract slowly and are endowed with major endurance owing to their mitochondria, myoglobin, capillaries and, above all, oxidative metabolism. Type-2 fibres, in contrast, contract rapidly, exhibit higher maximum muscle performance and, having less myoglobin and fewer capillaries, rely on anaerobic metabolism, which leads more quickly to exhaustion. Because both fibre types differ in both average fibre diameter and microstructural intracellular makeup, it can be assumed that these differences result in different diffusion coefficients that are great enough to be measured by DTI.

The quantity of type-1 and type-2 fibres in a muscle influence the functional performance parameters thereof, such as maximum mechanical muscle power [15]. Type-2 muscle fibres exhibit a maximum mechanical power up to three times greater than that of their counterparts [16].

Our study thus hypothesized that there would have to be an association between DTI parameters and muscle performance. The aim of the study was to test whether there are correlations between the standard DTI parameters of the soleus muscle and the maximum mechanical power thereof in healthy test subjects.

## Material and methods

### Test subjects

Following approval by the local ethics committee, 11 male subjects were recruited for the study (BMI =  $23.5 \pm 3.1$ ; age =  $27.2 \pm 10.7$  – all test subjects were involved in sports as a leisure activity). The maximum mechanical power of the soleus muscle was initially ascertained in all test subjects. DTI-measurement was then performed in intervals not exceeding 10 day (see below for details).

## Ascertaining maximum mechanical power

To ascertain the maximum mechanical power ( $L_{\max}$ ) of the soleus muscle, isokinetic maximum plantarflexion strength was measured on a dynamometer (Biodex System 3, Biodex Medical Systems, New York, USA) using a sharply bent knee angle of approximately  $40^\circ$  (► Fig. 1). In this position, the muscle length of the gastrocnemii muscles is in a functional range in which no significant contraction can be produced [17]. The measured torque is thus generated almost exclusively by the soleus muscle. A total of seven different angular velocities (60, 90, 120, 150, 180, 210 und  $240^\circ/\text{s}$ ) was measured, since maximum mechanical power is achieved in this range. Following a warm-up period, the test subjects performed isokinetic contractions at various angular velocities in randomized order. Prior to each contraction, the rotational axis of the dynamometer and the ankle were aligned. During the maximal isokinetic contractions, however, the rotational axes shifted despite the foot being fixed into position. The measured torques therefore do not equal the resulting torques of the ankle [18]. Ankle angle and ankle angular velocity were thus additionally recorded using a movement analysis system (Vicon Motion Systems, Los Angeles, USA), and the corrected resulting ankle torque was computed by means of inverse dynamics [17, 18].

## MRI measurement and evaluation

All measurements were performed on a 1.5 T Avanto (gradient system with a maximal amplitude =  $45 \text{ mT/m}$  and a maximal slew rate =  $200 \text{ Tm}^{-1}\text{s}^{-1}$  – Siemens, Erlangen) with a flexible extremities coil (4-channel flex coil). The ankle was fixed at  $90^\circ$ , while cushioning beneath the heel and knee ensured comfort and prevented the compression of the muscles of the lower leg.

The measurement protocol consisted of a high-resolution T1-weighted turbo spin-echo-sequence (TR/TE =  $626/11 \text{ ms}$ , FOV =  $180 \text{ mm}$ , resolution =  $0.7 \times 0.7 \text{ mm}$ , slice thickness =  $6 \text{ mm}$ , measurement time =  $2:54 \text{ min}$ ) and a single-shot-EPI-DTI-sequence (TR/TE =  $3400/79 \text{ ms}$ , FOV =  $192 \text{ mm}$ , resolution =  $3.0 \times 3.0 \text{ mm}$ , slice thickness =  $3 \text{ mm}$ , measurement time =  $4:37 \text{ min}$ , acceleration by means of parallel imaging



**Fig. 1** Setup for maximal mechanical power measurement during plantar flexion. Measurements were performed with knees bent to minimise the effect of gastrocnemius muscle and selectively determine the power of the soleus muscle.

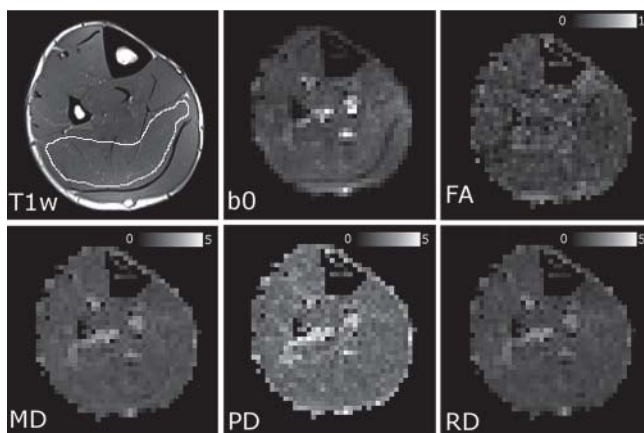
GRAPPA factor=2). In this process, b-values of 0 and 600 s/mm<sup>2</sup> were used in 12 directions. A study conducted by Saupe et al. found a b-value of 600 s/mm<sup>2</sup> to be the optimal b-value for muscle DTI at 1.5 T. [19]. To increase the SNR (signal-to-noise ratio) the DTI sequence was repeated a total of 6 times and averaged over the further course of the analyses. Using a test subject as example, Fig. 2 shows the T1-weighting, the image with a b-value of 0 s/mm<sup>2</sup> of the DTI sequence (b0-image) and the DTI parameter cards (FA, MD, PD, RD).

Analysis of DTI data was performed using the software FSL (FMRIB Software Library, Oxford, UK) and involved a pre-processing of the data with corrections being made for movement and eddy current distortions. The tensor-computation was then performed by means of a Linear-Least-Square-Fit using the averaged raw data, and the corresponding standard DTI parameter maps were computed. The most commonly known of these are mean diffusivity (MD – mean of the eigenvalues of the diffusion ellipsoid) and fractional anisotropy (FA). FA describes the diffusion-anisotropy, i.e., the degree to which the diffusion profile is aligned, and can range from 0 (isotropic – equally strong diffusion in all direction) to 1 (maximal anisotropic – diffusion only in one direction) [20]. Additional DTI parameters that were computed include parallel diffusivity (PD – equals the longest ellipsoid eigenvalue) and radial diffusivity (RD – average of the medium and shortest ellipsoid).

Using the high-resolution T1, a region of interest (ROI) was manually plotted for the soleus muscle (Fig. 2) and co-registered on the DTI data (ROI-size = 990 ± 303 mm<sup>2</sup> – mean ± standard deviation). From this ROI, means were computed for the respective parameters for each test subject and used for further correlation analyses.

### Statistical analysis

An association was performed between maximal mechanical power and the various DTI parameters using a non-parametric Spearman correlation analysis (Software Prism 5, GraphPad). Because of the relatively small number of cases, a non-parametric test was selected. A p-value < 0.05 was regarded as statistically significant.



**Fig. 2** Example images for T1w (including outline of M. soleus ROI), DW-Image with b-value = 0 s/mm<sup>2</sup> and the DTI parameter maps (FA – fractional anisotropy, MD – mean diffusivity, PD – parallel diffusivity, RD – radial diffusivity). MD, PD and RD in µm<sup>2</sup>/s.

## Results



The maximum mechanical power  $L_{\max}$  of the soleus muscle was 139 ± 40 Watts (mean ± standard deviation). Table 1 and Fig. 3 present the descriptive statistics and the correlations of the various DTI parameters. There was a significant negative correlation between  $L_{\max}$  and FA ( $r = -0.85$ ,  $p = 0.0015$ ). In contrast, there was positive correlation between  $L_{\max}$  and RD ( $r = 0.80$ ,  $p = 0.0047$ ). PD and MD showed no significant correlations.

## Discussion



The present study demonstrated a significant connection between maximal mechanical power  $L_{\max}$  and DTI-parameters FA and RD in the soleus muscle. The MD and PD exhibited no significant connection with muscle power.

In principle, a higher mechanical power would suggest a higher portion of type-2 fibres. Compared to their type-1 counterparts, these fibres have on average a greater diameter and lower mitochondrial density [21]. These two facts could account for the elevated RD we observed, which would in turn also explain the lower FA values.

However, DTI parameters are influenced by a series of other factors. In particular the b-value of a DTI measurement, which is directly related to diffusion time, has a decisive influence on structural sensitivity, i.e., which particular cellular structures could be influenced by the measured diffusion. Diffusion times in typical DTI sequences range from 20 to 40 ms. This means an average diffusion distance ranging between 20 and 27 µm. In this context, it becomes clear that in addition to fibre diameter, in other words restriction of diffusion through the cell membrane, intracellular barriers would also have to decisively influence the measured diffusion rates. This has already been demonstrated in an in-vitro study performed on skeletal muscle fibres [22].

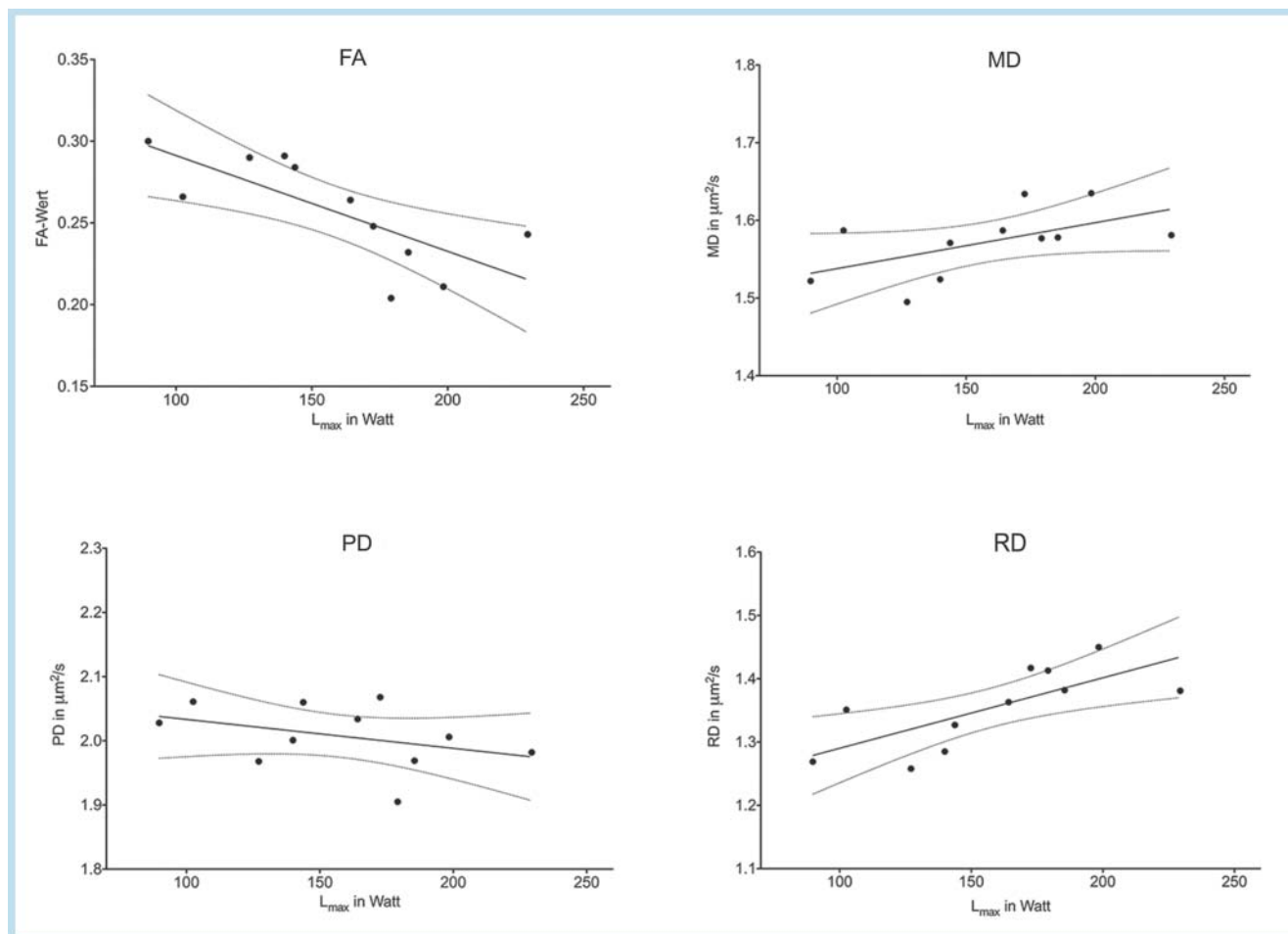
Developing a non-invasive way of quantifying fibre types in a muscle would be interesting not only for monitoring physical training in competitive sports, but also for diagnosing and evaluating the course of muscle diseases. The gold standard for determining muscle fibre composition is a combination of muscle biopsy and histological study. Due to the invasive nature of these methods, this procedure is very rarely performed, being employed only under special circumstances, and should naturally be avoided particularly in the case of healthy athletes.

Of course, the measurement of muscle strength is only an indirect parameter for the portion of muscle fibre types

**Table 1** Correlation between DTI parameters (fractional anisotropy – FA, mean diffusivity – MD, parallel diffusivity – PD, radial diffusivity – RD) and maximal power  $L_{\max}$ .

	mean ± standard deviation	Spearman correlation coefficient	p-value
FA	0.26 ± 0.03	–0.85	0.0015 <sup>1</sup>
MD in µm <sup>2</sup> /s	1.57 ± 0.04	0.55	0.0876
PD in µm <sup>2</sup> /s	2.01 ± 0.05	–0.31	0.3560
RD in µm <sup>2</sup> /s	1.35 ± 0.06	0.80	0.0047

<sup>1</sup> significance at  $p < 0.01$



**Fig. 3** Correlation of maximal mechanical power in watt with fractional anisotropy (FA), mean diffusivity (MD), parallel diffusivity (PD) and radial diffusivity (RD). MD, PD und RD in  $\mu\text{m}^2/\text{s}$ .

and cannot replace the gold standard of an invasive muscle biopsy. Nevertheless, this study was able to show that there is a connection between the mechanical power of a muscle and diffusivity. Further research shall be required to determine whether or not it will be possible in the future for DTI measurements to predict the strength or training status of a muscle. Our cohort consisted exclusively of healthy, young men, and we conducted strength measurements in only in one muscle. Future studies shall demonstrate to what extent our results can be generalized to other muscle groups and test subjects. It has also been reported that DTI parameters vary depending on muscle examined [23–26], sex and age [27, 28]. DTI parameters also vary with passive and active changes in muscle length [29, 30]. The intra-individual reliability of DTI parameters of skeletal muscle also warrant further examination. Nonetheless, the initial studies in this area have been highly promising [31].

To what extent DTI is effective as a non-invasive method for determining muscle fibre composition shall be the subject of future studies. It shall also be interesting to see what type of advantages and disadvantages DTI examination of muscle tissue poses relative to other advanced MRI (e.g. MR-spectroscopy) and to what extent the newly available combination of MRI and PET shall change the diagnosing of muscle diseases [32, 33]. In summary, our study has shown

that DTI parameters of the soleus muscle have significant correlations with muscle-specific performance.

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