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Extramuscular Myofascial Force Transmission: Experiments and Finite Element Modeling

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Abstract

The specific purpose of the present study was to show that extramuscular myofascial force transmission exclusively has substantial effects on muscular mechanics. Muscle forces exerted at proximal and distal tendons of the rat extensor digitorium longus (EDL) were measured simultaneously, in two conditions (1) with intact extramuscular connections (2) after dissecting the muscles' extramuscular connections to a maximum extent without endangering circulation and innervation (as in most in situ muscle experiments). A finite element model of EDL including the muscles' extramuscular connections was used to assess the effects of extramuscular myofascial force transmission on muscular mechanics, primarily to test if such effects lead to distribution of length of sarcomeres within muscle fibers.

In condition (1), EDL isometric forces measured at the distal and proximal tendons were significantly different ($F_{dist} > F_{prox}$, ΔF approximates maximally 40% of the proximal force). The model results show that extramuscular myofascial force transmission causes distributions of strain in the fiber direction (shortening in the proximal, lengthening in the distal ends of fibers) at higher lengths. This indicates significant length distributions of sarcomeres arranged in series within muscle fibers. Stress distributions found are in agreement with the higher distal force measured, meaning that the muscle fiber is no longer the unit exerting equal forces at both ends. Experimental results obtained in condition (2) showed no significant changes in the length-force characteristics (i.e., proximo-distal force differences were maintained). This shows that a muscle in situ has to be distinguished from a muscle that is truly isolated in which case the force difference has to be zero.

We conclude that extramuscular myofascial force transmission has major effects on muscle functioning.

Keywords: Finite element method, extramuscular interactions, myofascial force transmission, rat extensor digitorium longus (EDL) muscle, sarcomere length distributions, neurovascular tract.

Introduction

Transmission of the force generated by the sarcomeres, from the full perimeter surface of the myofibers onto the extracellular matrix has been emphasized by some authors (e.g., Street, 1983; Danowski et al., 1992; Trotter & Purslow, 1992; Hijikata et al., 1993; Huijing et al., 1998; Huijing, 1999a; Yucesoy et al., 2002). Such transmission was referred to as myofascial force transmission (Huijing, 1999b). However, the extracellular matrix (i.e., intramuscular connective tissue) is continuous with the extramuscular connective tissue, which is comprised of neurovascular tracts that are continuous with compartmental boundaries (Huijing, 1999b; Huijing & Baan, 2001a; Huijing & Baan, 2001b; Maas et al., 2001). Such connective tissue organization allows transmission of force from muscle to surrounding non-muscular elements of a compartment (*extramuscular myofascial force transmission*) and to bone.

It should be noted that, myofascial force transmission may also occur through the direct connections between the extracellular matrices of adjacent muscles (intermuscular myofascial force transmission). In recent experiments, integrated inter- and extramuscular myofascial force transmission was

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shown to significantly affect muscle length-force characteristics, determined after proximal lengthening of the rat EDL (Huijing & Baan, 2001a; Huijing & Baan, 2001b; Maas et al., 2001). In the present study, extramuscular myofascial force transmission was studied exclusively and its effects on muscle mechanics were studied. Our first goal was to test the following hypotheses: (1) Extramuscular myofascial force transmission has sizable effects on muscle length-force characteristics. (2) Due to continuity of intra- and extramuscular connective tissues, extramuscular myofascial force transmission leads to significant alterations in distribution of length of sarcomeres arranged in series within muscle fibers. The first hypothesis was tested experimentally by measuring simultaneously the isometric EDL force exerted at proximal and distal tendons after distal lengthening. The second one was addressed by making use of a finite element model of EDL muscle including the muscles' extramuscular connections.

During the full course of a myological experiment in situ, the minimal condition is to keep blood supply and innervation of a muscle intact as much as possible. However, blood vessels and nerves are embedded in the connective tissues of the neurovascular tract. Although, a certain part of the neurovascular tract is always left intact, a muscle 'in situ' is commonly (e.g., Huijing et al., 1994; Frueh et al., 2001) considered as 'isolated' from its surroundings. It is expected that such remaining extramuscular connections also allow extramuscular myofascial force transmission. The second goal of the present work was to test this hypothesis.

Methods

I. Experimental study

Surgical procedures

Surgical and experimental procedures were in strict agreement with the guidelines and regulations concerning animal welfare and experimentation set forth by Dutch law, and approved by a Committee on Ethics of Animal Experimentation at the Vrije Universiteit, Amsterdam.

Male Wistar rats (n = 5, body mass = 304.4 ± 3.5 g) were anaesthetized by intraperitoneally injected urethane solution (initial dose: 1.2 mg 100 g^{-1} body mass, extra doses if necessary: maximally 1.5 mg). A heated water pad was used to prevent hypothermia and the ambient temperature (22 ± 0.5°C) and air humidity (80 ± 2%) were kept constant (for details see Huijing & Baan, 2001a). Muscle and tendon tissue was further prevented from dehydration by regular irrigation with isotonic saline.

The left anterior crural compartment, which consists of the tibialis anterior (TA), extensor digitorum longus (EDL) and extensor hallucis longus (EHL) muscles, was exposed by removing the skin and most of the biceps femoris muscle. Subsequently the compartment was opened and the TA, and EHL muscles were removed, leaving EDL and its extramuscular connections to the surrounding tissues intact (Fig. 1a).

With the knee joint at 90° and the ankle joint at 90° (referred to as reference position), the four distal tendons of EDL were tied together. Matching markers were placed on the distal tendons and on a fixed location on the lower leg. Subsequently, the distal tendon complex was cut as distally as possible and removed from their retinaculae near the ankle joint (after cutting the transverse crural ligament and cruciate ligament). The foot was attached to a plastic plate with tie wraps.

The femoral compartment was opened to detach the proximal tendon of EDL from the femur and to secure the femur (at a knee angle of 90°) with a metal clamp. A Kevlar thread (4% elongation at a break load of 800 N) was tied to the combined distal EDL tendons and the proximal EDL tendon with a suture. The Kevlar threads were later connected to force transducers that were aligned with the muscle line of pull (Hottinger Baldwin, maximal output error <0.1%, compliance of 0.0048 mm N^{-1}). The sciatic nerve was dissected, leaving the peroneus communis nerve branch intact. The tibial nerve and the sural branch of the sciatic nerve were cut. The sciatic nerve was cut as proximally as possible and placed on a pair of silver electrodes and covered by a saline wetted piece of tissue, which was covered by a small piece of latex.

Experimental procedures

The footplate was positioned in such a way that the ankle angle was in maximal plantar flexion. EDL was shortened proximally by 2 mm relative to the reference position (indicating a knee joint angle of >90°). This location of the proximal tendon was kept throughout the experiment.

To determine the muscle length-force characteristics, isometric EDL force was measured at various muscle-tendon complex lengths. Before each isometric contraction, these lengths were attained by moving exclusively the distal EDL force transducer with 1 mm increments starting at muscle active slack length (i.e., the length at which active force approaches zero) until approximately 2 mm over the optimum length (see Fig. 1b for a schematic representation of the experimental set up). After each tetanic contraction the muscle was allowed to recover below active slack length for 2 min.

The sciatic nerve was stimulated supra-maximally using a pair of silver electrodes connected to a constant current source (3 mA, pulse width 100 μs). Two twitches were evoked and followed by a tetanic contraction after 300 ms (pulse train 400 ms, frequency 100 Hz). Simultaneously, images of the muscle in passive and active state were recorded using a digital camera (DVC, JAI CV-M10, shutter speed 1/50 s).

To avoid possible artifacts due to differences force measurement systems (e.g., force transducers and amplifiers), prior to the experiment the two force transducers to be used

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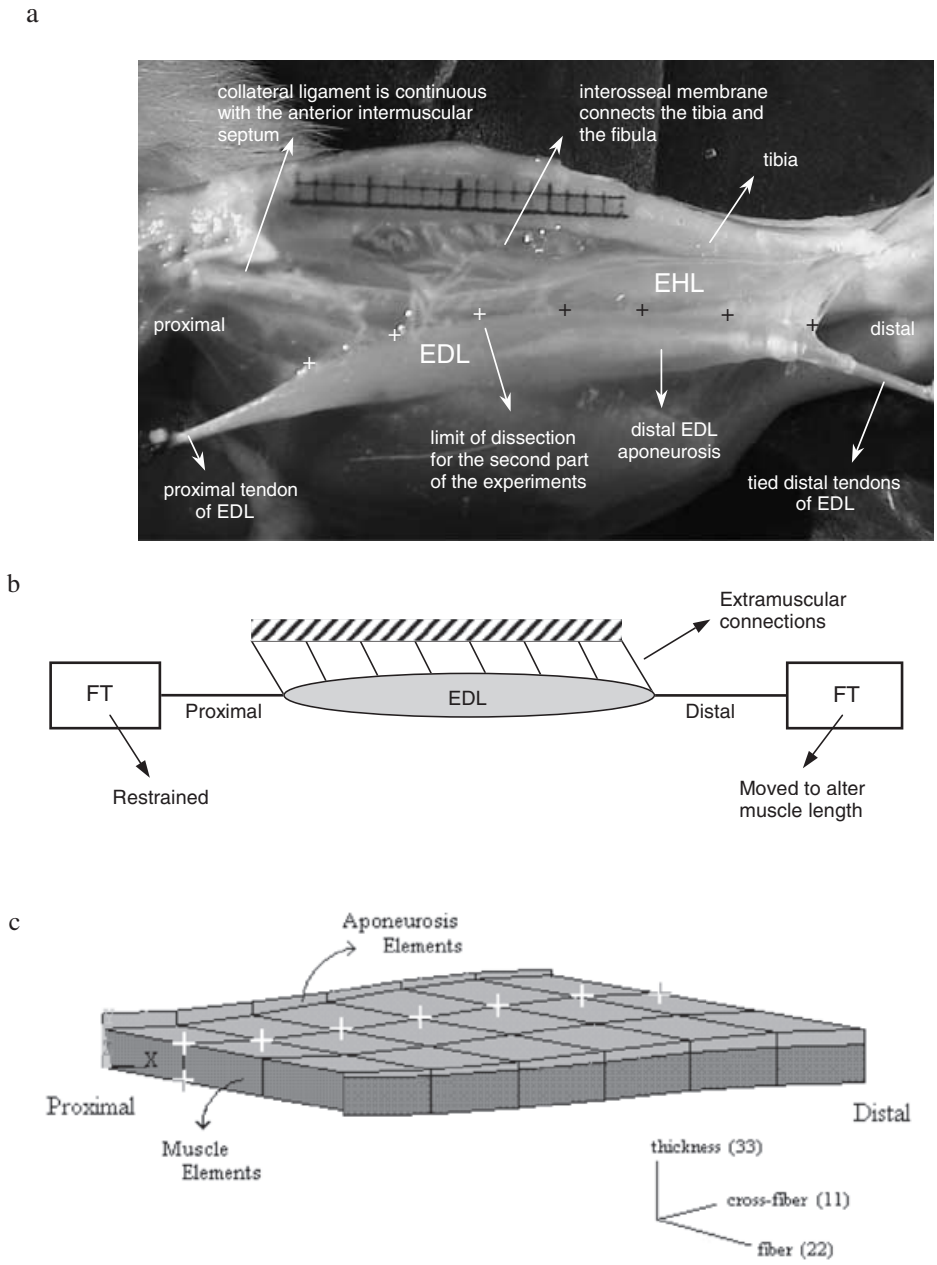


Fig. 1. Rat EDL and its extramuscular connections and the finite element muscle model. (a) Experimental EDL is shown after removal of TA, whereas the other muscle of the anterior crural compartment, EHL is not removed as yet in this image. The neurovascular tract (i.e., the connective tissue structure containing nerves and blood vessels) connects EDL all along the muscle to the tibia, part of interosseal membrane and anterior intermuscular septum (for more images see Huijing & Baan, 2001a; Maas et al., 2001). This tract (connections of which to EDL are marked by '+' signs) comprises a pathway of extramuscular myofascial force transmission. The proximal part of the tract which is shown by white '+' markers shows the extent of the tract that is left intact for the second part of the experiments. Note that in this picture, in order to show the extramuscular connective tissues clearly, a downward force is exerted on both proximal and distal tendons of EDL moving the muscle from its natural position. (b) Schematic representation of the experimental set up. The proximal EDL tendon was connected to a force transducer (FT), which was displaced by 2 mm in the distal direction with respect to its reference position. At this location it was restrained. The tied four distal EDL tendons were connected to another force transducer. The position of this distal transducer was altered during the experiment to measure isometric EDL forces at different muscle–tendon complex lengths. The links that connect the muscle to the mechanical ground represent the extramuscular connective tissue. (c) The geometry of the finite element muscle model is defined by the contour of a longitudinal slice of the rat extensor digitorum longus (EDL) muscle belly. The muscle model is composed of three muscle elements in series and six in parallel. A 3D local coordinate system is used for the analysis and presentation of the results. At the nodes indicated with a white '+' marker the extramuscular connections are made.

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for measurement of EDL forces were connected to each other using a compliant spring. The output recorded with the identical measurement system as used in the animal experiment revealed that the slope of the regression line ($r^2 = 0.999$) of the simultaneously measured forces deviated 0.6% from the expected 45°. This leads to the conclusion that any force differences between the two transducers greater than 0.6% should not be ascribed to the measurement system used. The timing of stimulation of the nerve, A/D conversion (12-bit A/D converter, sampling frequency 1000 Hz, resolution of force 0.01 N), and photography were controlled by a microcomputer.

These experimental procedures were applied in two conditions:

(1) First the extramuscular connective tissue associated with EDL was left intact as much as possible.
(2) Subsequently, the extramuscular connective tissues were dissected to a maximum possible extent, without endangering circulation and innervation. The remaining connective tissue structure supports major blood vessels and nerves and it is crucial for maintaining a physiological situation for the muscle. Therefore, this is a common condition in muscle experiments in situ, after dissection from other muscles and connective tissues. Note that the remaining part of the neurovascular tract is located proximally and it comprises less than half of the complete extramuscular connections (Fig. 1a).

Processing of experimental data and statistics

Data for total muscle force (F_{mt}) in relation to muscle tendon complex length (l_{oi}) were fitted by a polynomial function

$$y = b_0 + b_1x + b_2x^2 + b_3x^3 + b_4x^4 + \ldots + b_nx^n, \qquad (1)$$

where y represents F_{mt} and x represents l_{oi}. b_0, $b_1 \ldots b_n$ are coefficients determined in the fitting process. Polynomials that best described the experimental data were selected (see below). These polynomials were used for averaging of data and calculation of standard errors.

In the fitting procedure one-way analysis of variance (ANOVA) (Neter et al., 1996) was used to select the lowest order of the polynomials that still added a significant improvement of the description of changes of muscle tendon complex length and muscle force data for EDL. Two-way analysis of variance (ANOVA) was performed to test for length effects and for differences between the EDL force measured at the proximal and distal tendons. Bonferroni post-hoc tests were carried out to identify the significance of proximo-distal force difference at each l_{oi} (Neter et al., 1996). Differences were considered significant at $p < 0.05$.

II. Modeling study

A 3D-finite element muscle model (linked fiber-matrix mesh model: lfmm model) with a two-domain approach was developed (Yucesoy et al., 2002). In summary, this model consists of two meshes occupying the same space that are linked elastically representing the extracellular matrix domain (matrix mesh) and intracellular domain (fiber mesh). The two meshes are built using the self-programmed 'myofiber' or 'extracellular matrix' elements that are introduced as user defined elements into the finite element program ANSYS 5.7.1. The elements have eight nodes, linear interpolation functions and a large deformation analysis formulation. A 3D local coordinate system representing the fiber, cross-fiber (normal to the fiber direction), and thickness directions is used. For the myofiber element, the total stress that acts only in the local fiber direction is the sum of the active stress of the contractile elements and the stress due to intracellular passive tension (Yucesoy et al., 2002). It is assumed that, at initial muscle length and passive state, the sarcomeres arranged in series within muscle fibers have identical lengths and material properties. The extracellular matrix element incorporates a strain energy density function that accounts for the non-linear and anisotropic material properties and the constancy of muscle volume (Yucesoy et al., 2002).

Within the biological context, one muscle element is defined to represent a segment of a bundle of muscle fibers with identical material properties, its connective tissues and the links between them. This is realized as a linked system of extracellular matrix and myofiber elements. Both matrix and fiber meshes are rigidly connected to single layers of elements forming the muscles' proximal and distal aponeurosis. To represent the aponeuroses, a standard 3D, 8-node element HYPER58, from the element library of ANSYS 5.7.1 was used. This element has a hyperelastic mechanical formulation for which the strain energy density function is defined using the Mooney-Rivlin material law. For the elastic links between the two meshes, which represent the transmembranous attachments of the cytoskeleton and extracellular matrix, another standard element COMBIN39 was used. This is a 2-node spring element, which is set to be uniaxial and have linear stiffness characteristics.

The geometry of the model (Fig. 1c) is defined by the contour of a longitudinal slice at the middle of the isolated rat EDL muscle belly. Three muscle elements in series and six in parallel fill this slice. Therefore any collection of three muscle elements arranged in series represents a big muscle fascicle. All aponeurosis elements have identical mechanical properties but using a variable thickness in the fiber-cross fiber plane, the increasing cross-sectional area of the aponeurosis toward the tendon (Zuurbier et al., 1994) is accounted for.

Local strain, as a measure of change of length, reflects the lengthening (positive strain) or shortening (negative strain) of sarcomeres. Note that zero strain in the model represents the undeformed state of sarcomeres (i.e., sarcomere length $\cong 2.5\,\mu m$) in the passive condition at initial muscle length (28.7 mm). Fiber direction strain within the fiber mesh of the lfmm model was used to assess the non-uniformity of

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sarcomere lengths arranged in-series within muscle fibers (referred to as *serial distribution*).

(1) Model of EDL with extramuscular connections

For the present application, the lfmm model was extended to include extramuscular connections of EDL muscle to the tibia via surrounding connective tissues. Using spring elements, these connections were realized by linking a set of nodes of the matrix mesh (Fig. 1c) to a set of fixed points, representing the 'mechanical ground'. In the experiments of the present study, the locations of the extramuscular connections of EDL muscle were determined to be at one-third of the fascicle length from the most proximal side of each muscle fascicle. For the extramuscular linking elements the spring element COMBIN39 was used with longitudinal force-deflection capability and linear stiffness characteristics. A suitable stiffness (k) was determined for these elements that provides a sufficiently good agreement between the experimental and modeled muscle forces. This model is referred to as model of EDL with extramuscular connections.

The corresponding fixed points of the mechanical ground and the nodes of the model were at identical locations initially (i.e., muscle length = 28.7 mm, and before moving any of the tendon ends). Mimicking the experimental conditions, first the modeled EDL was shortened proximally by 2 mm. This end was then fixed at that position. Note that the proximal shortening introduced a stretch of the modeled extramuscular linking elements. The isometric analysis was carried out after displacing the distal end of the modeled EDL.

(2) Model of EDL with minimal extramuscular connections

To investigate the functional significance of the remaining extramuscular connective tissue considered in the second part of the experimental study, most of the extramuscular linking elements were removed from the model. Only the first three proximal linking elements were remained. For these elements, a suitable stiffness value was determined that maintains the agreement between the experimental and modeled muscle forces after the second part of the experimental study. This model is referred to as model of EDL with minimal extramuscular connections. In addition, an isolated EDL model (i.e., a model of EDL muscle, from which all extramuscular linking spring elements were removed) was used. The results of the model with minimal extramuscular connections are compared to those of the isolated model.

Results

EDL with extramuscular connections

The length-total force characteristics for EDL muscle with intact extramuscular connections, as determined experimentally, as well as calculated using the lfmm model are compared in Figure 2. The experimental data show significant differences between EDL forces measured at the distal and proximal tendons (Fig. 2a). After distal lengthening of EDL, distal isometric force is higher than proximal forces throughout almost all of the muscle length range studied. This proximo-distal EDL force difference increases as a function of the muscle length to a maximum value of almost 0.8 N (i.e., approximately 40% of the proximal force). The experimental and modeled forces agree quite well (Fig. 2b), as long as a suitable stiffness (k) is selected for extramuscular links from the range of values given in Table 1. The model indicates that the extramuscular connections cause the proximo-distal force differences. Table 1, also provides estimates of goodness of fit between modeled and experimental data: RMSD represents the root mean squared deviation of model data from experimental data. The shaded cells indicate the linking stiffness selected for the results presented. Cells above and below the shaded ones show values for stiffer and for more compliant links, respectively. Figure 2b includes a comparison of the experimental and modeled passive forces.

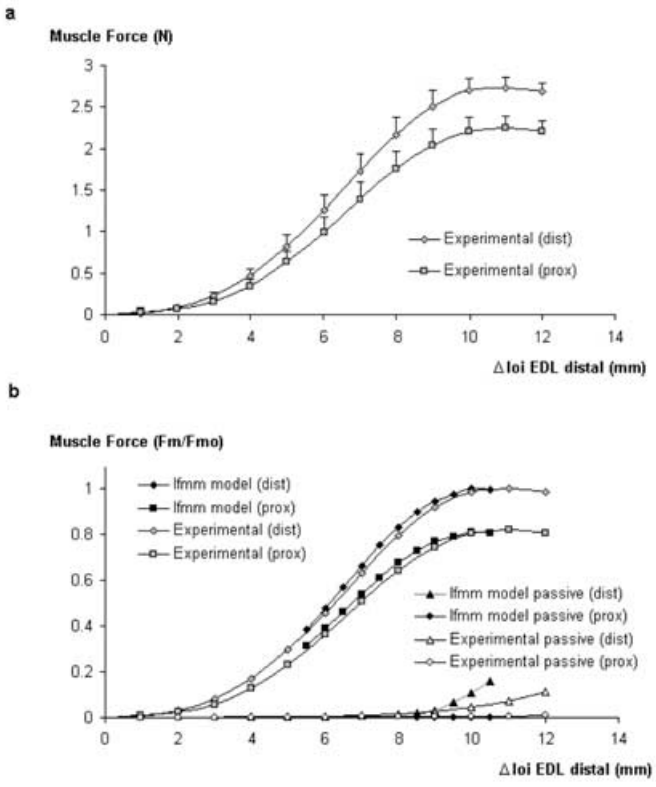


Fig. 2. The isometric muscle length-total force curve for rat EDL muscle with extramuscular connections. (a) Absolute values of the experimental total muscle force at the proximal and distal tendons of the EDL muscle tendon complex expressed as a function of deviation (Δloi) from the active slack length. Mean results and standard errors of the mean (n = 5) are shown. (b) Comparison of the experimental data and model data for muscle force (Fm) normalized for optimal force (Fmo).

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The distal passive forces of the model are over-estimated. A remarkable result is build up of passive forces well before optimum muscle length is reached. Both experimental and modeled passive proximal forces indicate that the proximal tendon of the muscle remains slack even at high muscle lengths.

Table 1. Goodness of fit of model results to experimental data for EDL with intact extramuscular connections.

	Distal length-force characteristics	Proximal length-force characteristics
k	RMSD	RMSD
0.267	0.0429	0.0606
0.133	0.0365	0.0252
0.067	0.0279	0.0279
0.033	0.0272	0.0432
0.017	0.0256	0.0513

For selected muscle lengths, fiber direction strain and stress distributions in the fiber mesh are shown in Figure 3. Figure 3a, b and c shows that as muscle length increases (1) the range of the serial distribution increases that is, the difference between the largest and smallest values of sarcomere lengths is higher and (2) more sarcomeres arranged in series within muscle fibers are at different lengths. A remarkable model result is that even at high muscle lengths, the proximal ends of muscle fibers remained shortened (by maximally 24%) while the most distally located sarcomeres are lengthened by up to 30% (Fig. 3c). Figure 7 shows a comparison of the nodal strains plotted in parallel rows, to illustrate clearly that the serial distribution becomes more pronounced as a function of muscle length. At low muscle length the strains plotted at nodal positions for different rows are highly similar (Fig. 7a). This shows that the serial distribution is minimal. However, at high lengths, the strain plots for different rows are substantially heterogeneous (Fig. 7b and c). This shows the enhanced distribution of sarcomere

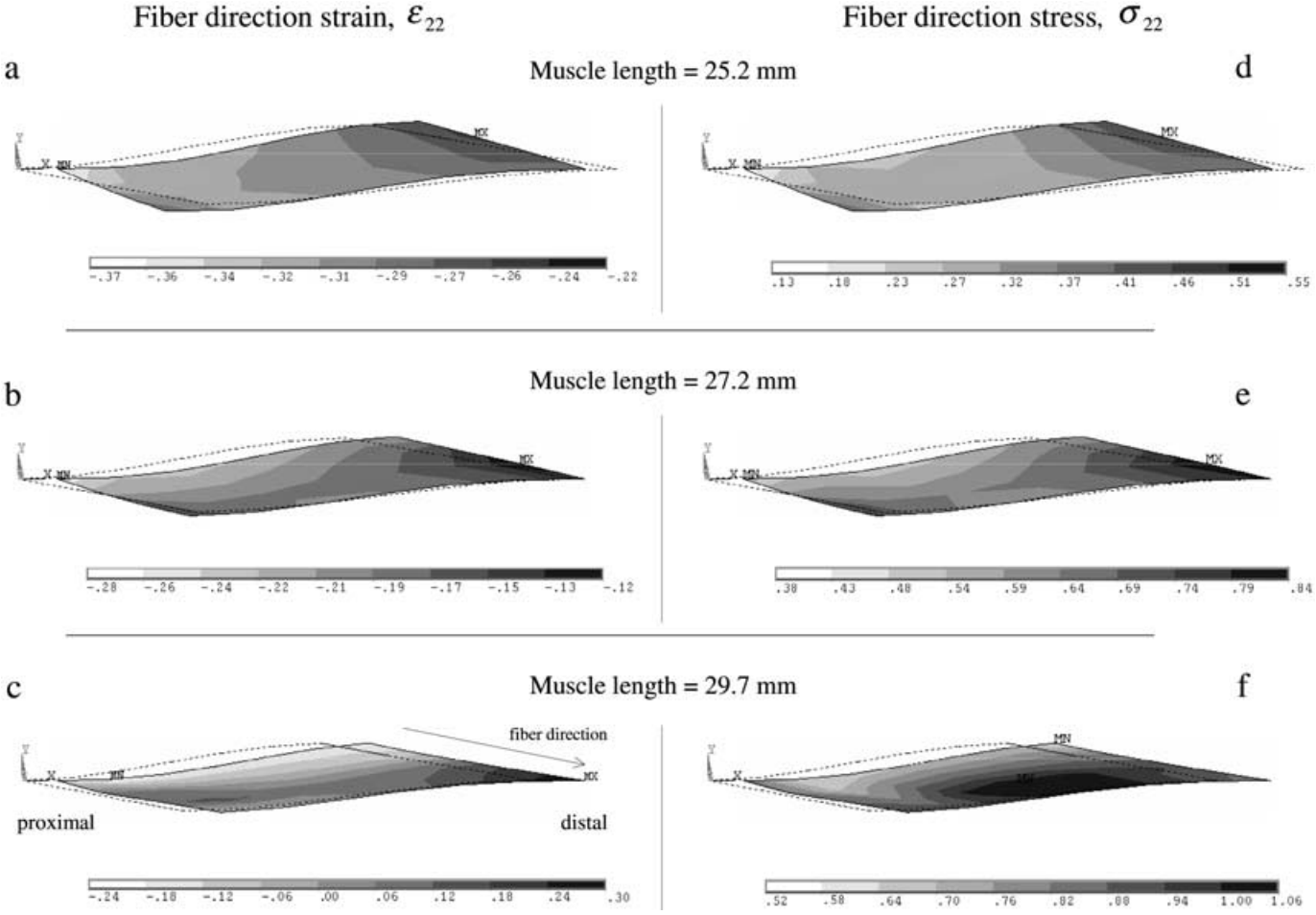


Fig. 3. Stress and strain distributions for the fiber mesh of the EDL model with extramuscular connections at selected muscle lengths. (a) (b) and (c) Strain distributions of the fiber mesh for the fiber (22) direction. (d) (e) and (f) Stress distributions of the fiber mesh for the fiber (22) direction. The distributions are shown for the muscle lengths 25.2 mm, 27.2 mm and 29.7 mm (i.e., Δloi = 6 mm, Δloi = 8 mm and Δloi = 10.5 mm respectively). The dotted line contour indicates muscle geometry at the initial length. The fiber direction as well as the proximal and distal ends of the muscle is shown in part (c).

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lengths as a function of increased extramuscular myofascial force transmission. Accordingly, distribution of stress along the fiber direction increases as a function of muscle length (Fig. 3d, e and f). At high length (Fig. 3f) the stress at the proximal side of the muscle fibers is approximately 50% lower than the stress at their distal side. These results show that the extramuscular connections of the muscle lead to substantial local strain and stress distributions, not only for the whole muscle, but also for the sarcomeres arranged in series within muscle fibers, without affecting mechanical stability.

The forces acting in the direction of line of pull of the muscle include the distal and proximal muscle forces, as well as the component of total force exerted on the extramuscular links in that direction. The deformed shapes of the extramuscular linking elements, indicating the magnitude and direction of the extramuscular force, are shown in Figure 4. Distal lengthening of the muscle leads to stretching of the extramuscular links (Fig. 4a and b). Distally located links are stretched more than proximal links and rotated more in distal direction. Each spring element applies a certain force on the muscle in proximal direction. Therefore total extramuscular link force is directed towards the proximal side. For the force equilibrium in the present conditions, the sum of the proximal force and the total extramuscular link force must be equal to the distal force (i.e., the proximo-distal force difference is equal to the total extramuscular link force). Note that this total link force increases, as the muscle is distally lengthened. Such increase explains the increasing proximo-distal force difference in favor of the distal force as a function of the distal muscle lengthening.

EDL with minimal extramuscular connections

Figure 5 shows the experimental and modeled length-total force characteristics of EDL muscle with minimal extramuscular connections. Significant proximo-distal force differences ($F_{dist} > F_{prox}$) remain maintained (Figure 5a) also in this experimental condition. Moreover, statistical analysis shows that the differences between experimental length-force data of EDL with full and minimal intact extramuscular connections are not significant. This indicates that the dominant role is played by the proximal neurovascular tract in extramuscular myofascial force transmission. Figure 5b shows that after making the remaining extramuscular linking elements stiffer, the modeled and experimental forces agreed well (k = 0.286 unit force/mm is used for minimal extramuscular connections case whereas, k = 0.067 unit force/mm was the selected value for the previous case).

In Figure 6 the local fiber direction strain and stress distributions within the fiber mesh of EDL with minimal extramuscular connections are shown. Distributions of the isolated EDL model are presented in smaller size contours. For this muscle no significant strain or stress variation within muscle fibers is found. Also for EDL with minimal extramuscular connections, in the distal half of the muscle belly, both strain and stress distributions are rather uniform. However, the proximal half shows significant distributions:

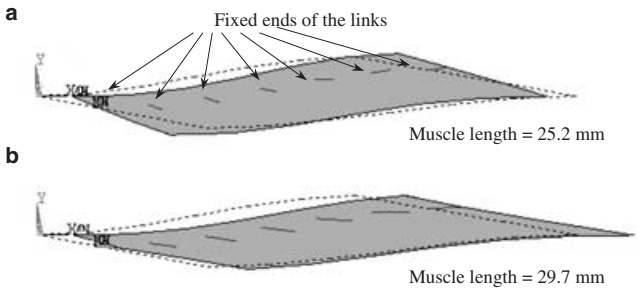


Fig. 4. Comparison of length and orientation of the spring elements representing the modeled muscles' extramuscular connections. (a) At the lowest length studied. (b) At the highest length studied. The locations of the fixed ends of the links are indicated by arrows in (a). The dotted line contour indicates muscle geometry at the initial length.

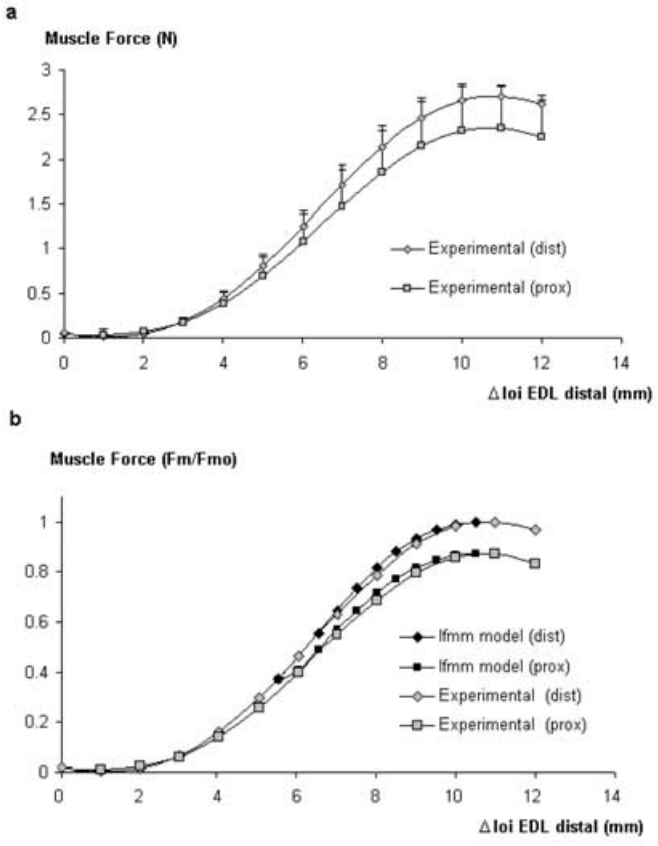


Fig. 5. The isometric muscle length-total force curve for rat EDL muscle with minimal extramuscular connections. (a) Absolute values of the experimental total muscle force at the proximal and distal tendons of the EDL muscle tendon complex expressed as a function of deviation (Δloi) from the active slack length. Mean results and standard errors of the mean (n = 5) are shown. (b) Comparison of the experimental data to the model predictions for which the muscle force (Fm) is normalized for optimum force (Fmo).

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(1) substantial serial sarcomere length distributions are found especially at higher muscle lengths (Fig. 6a, b and c). At low muscle length, the similarity of the strains plotted at nodal positions for different rows (Fig. 7d) indicates a minimal serial distribution. In contrast, the increased heterogeneity between strain plots for different rows shows the enhanced distribution of sarcomere lengths at higher muscle lengths (Fig. 7e and d). (2) Also the distribution of stress in the fiber direction becomes more pronounced as a function of muscle length (Fig. 6d, e and f). At high length, the stress at the distal end of the most proximal fibers is nearly twice as high as the stress at their proximal end (Fig. 6f).

In summary, the present experimental results confirmed that extramuscular myofascial force transmission has a major effect on the length-force characteristics of a muscle leading to significant force differences between the proximal and distal ends. The model results showed that as the muscle is lengthened distally, it is increasingly loaded in proximal direction by its extramuscular connections, which causes significant distributions of length of sarcomeres arranged in series within muscle fibers. As a result, stress distributions occur leading to the exertion of proximal and distal muscle forces, which ensure the mechanical equilibrium. The different stress at the proximal and distal ends of muscle fibers indicate that the muscle fiber is no longer a unit exerting equal forces at both ends. Furthermore, the minimal extramuscular connections necessary to keep a muscle within physiological ranges causes highly similar effects on muscle

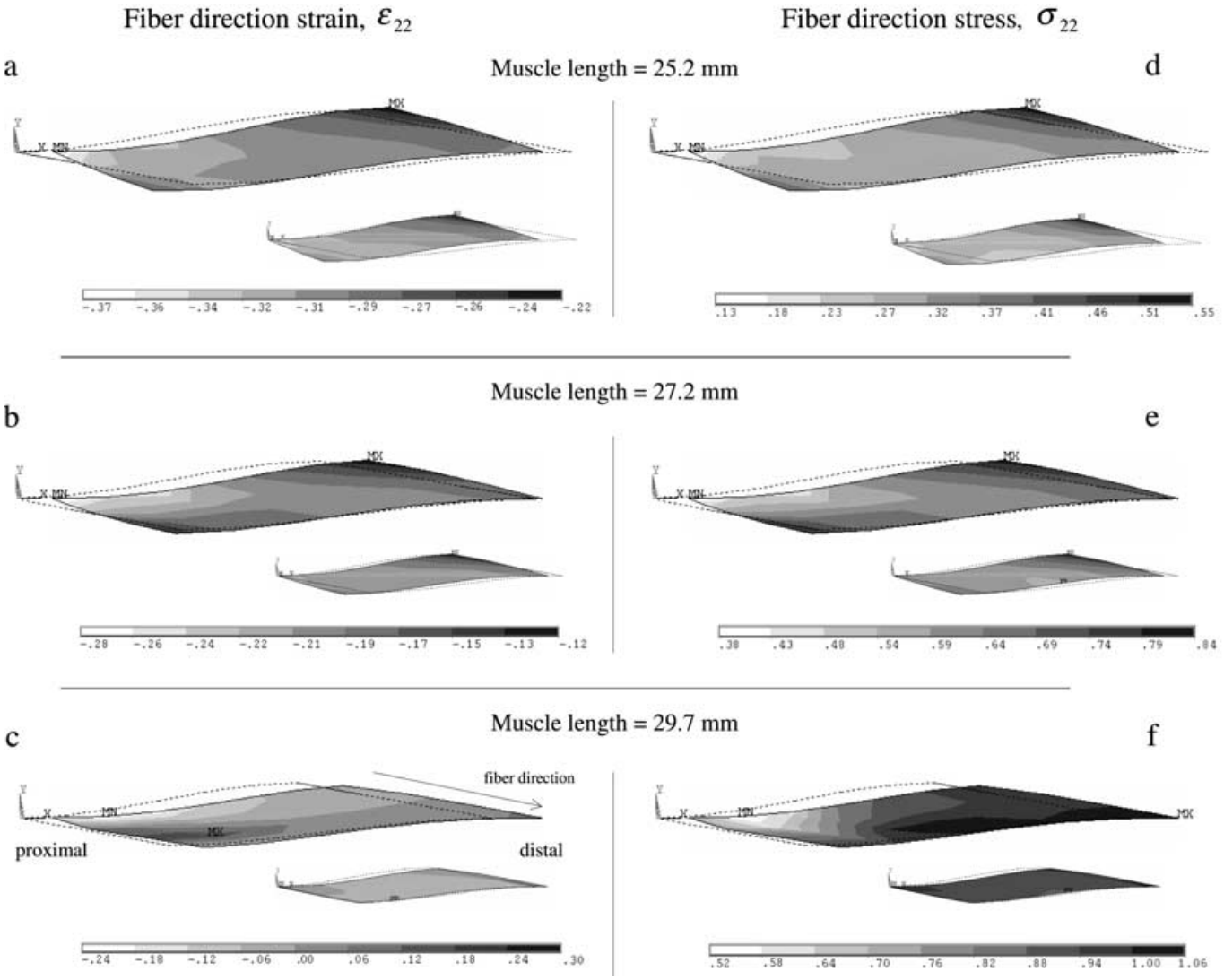


Fig. 6. Stress and strain distributions for the fiber mesh of the model of EDL with minimal extramuscular connections (bigger contours) compared to the distributions of isolated EDL model (smaller contours) at selected muscle lengths. (a) (b) and (c) Strain distributions of the fiber mesh for the fiber (22) direction. (d) (e) and (f) Stress distributions of the fiber mesh for the fiber (22) direction. The distributions are shown for the muscle lengths 25.2 mm, 27.2 mm and 29.7 mm (i.e., $\Delta loi = 6$ mm, $\Delta loi = 8$ mm and $\Delta loi = 10.5$ mm, respectively). The dotted line contour indicates muscle geometry at the initial length. The fiber direction as well as the proximal and distal ends of the muscle is shown in part (c) in the upper panel.

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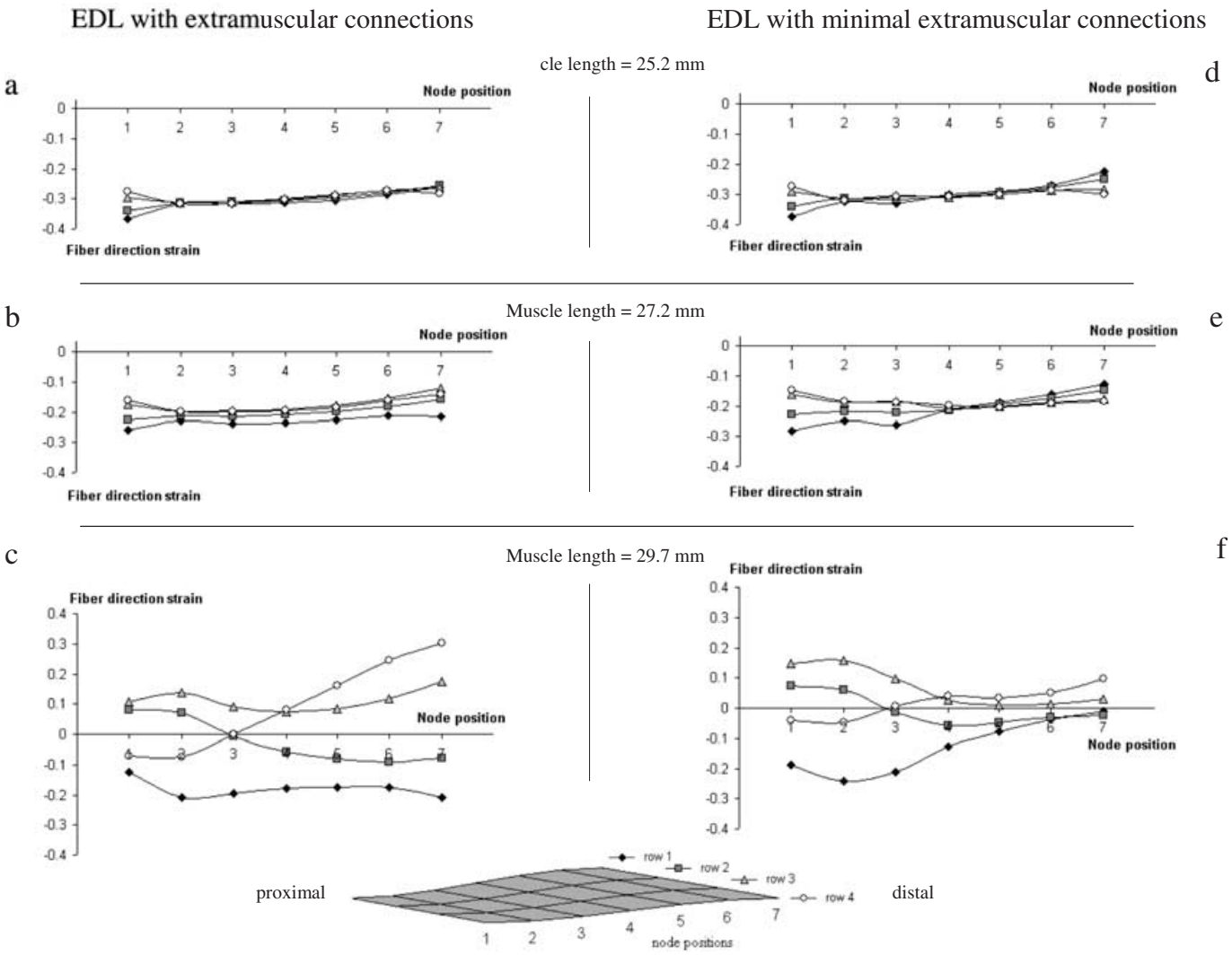


Fig. 7. Comparison of the nodal strains plotted in parallel rows.
The fiber direction strains within the fiber mesh are plotted in four parallel rows of nodes numbered from 1 to 7 (i.e., from proximal to distal side, lower panel). The differences between the strain plots provide a measure of distribution of length of sarcomeres arranged in series within muscle fibers. (a) (b) and (c) Strain plots for EDL with extramuscular connections, shown for the muscle lengths 25.2 mm, 27.2 mm and 29.7 mm (i.e., for Δloi = 6 mm, Δloi = 8 mm and Δloi = 10.5 mm), respectively. (d) (e) and (f) Strain plots for EDL with minimal extramuscular connections, shown for the muscle lengths 25.2 mm, 27.2 mm and 29.7 mm (i.e., for Δloi = 6 mm, Δloi = 8 mm and Δloi = 10.5 mm), respectively. Note that the strain values for the lower and upper surfaces of the model are identical as both faces have identical extramuscular connections. Strain is defined as the ratio of the change in length to the original length. Zero strain in the model is assumed to represent the undeformed state of sarcomeres (i.e., sarcomere length ≅ 2.5 μm) in the passive condition, at initial muscle length (28.7 mm). Positive strain shows lengthening and negative strain shows shortening of the sarcomeres with respect to this undeformed state.

mechanics to the effects caused by the full extramuscular connections.

Discussion

Intermuscular and extramuscular myofascial force transmission

Specific recent studies focussing on myofascial force transmission showed that such transmission has major effects on muscle mechanics, on muscle length-force characteristics in particular. Such effects include significant differences of isometric muscle force measured simultaneously at both proximal and distal tendons of EDL muscle within the intact anterior tibial compartment (Huijing, 1999b; Huijing, 2000). Completely altered muscle length-force characteristics were found after blunt dissection and compartmental fasciotomy that is, due to a systematic manipulation of the extra and inter-muscular connective tissue structures (Huijing & Baan, 2001b). Huijing and Baan (2001a) measured isometric EDL

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force after proximal EDL lengthening while TA, EHL as well as EDL were simultaneously and maximally activated. They found significant proximo-distal differences of active and passive EDL force, which they ascribed to extramuscular myofascial force transmission. Experiments focused on integrated effects of extra- and intermuscular myofascial force transmission also showed unequal proximal and distal EDL forces (Maas et al., 2001). In the present study on EDL with extramuscular connections exclusively, we studied the simplest level of interaction of a muscle with its surroundings. This study presents an important step in identifying the specific effects of myofascial force transmission in different levels.

Distribution of length of sarcomeres arranged in series within muscle fibers

The intramuscular connective tissues interact mechanically with the myofibers (e.g., Danowski et al., 1992; Huijing, 1999b) through the multimolecular trans-sarcolemmal systems (e.g., for a review see Berthier & Blaineau, 1997). This allows transmission of force, generated within myofibers, onto the extracellular matrix. Such transmission is an important determinant of the distribution of sarcomere lengths in series within muscle fibers. Results of a finite element modeling study on isolated muscle (Yucesoy et al., 2002) support this conclusion. In that work it was demonstrated that if there is an inadequate linking of sarcomeres to the extracellular matrix (as occurs in muscular dystrophies), at high muscle lengths the myofibers may be deformed beyond physiological limits. A major goal of the present work was to test the hypothesis that, coupled with intramuscular myofascial force transmission, extramuscular myofascial force transmission can alter distribution of lengths of sarcomeres. Our modeling results show sizeable distributions of fiber direction strain, indicating distributions of lengths sarcomeres arranged in series within muscle fibers and confirm this hypothesis. Intermuscular myofascial force transmission is also conceived to affect sarcomere length distributions (for an explorative modeling work see Yucesoy et al., 2001). However, such distributions have not been validated experimentally. It should be noted that doing this for a whole muscle surrounded by compartmental connective tissues and other muscles is very difficult due to the obscured view. A possibility could be using ultrasound or MRI imaging techniques to show length distributions within muscle fascicles.

Our results also show distribution of mean sarcomere length of different fibers. The principle effects of such distributions were discussed previously (e.g., Edman et al., 1993; Huijing, 1998). An increased heterogeneity of mean sarcomere length of different fibers was shown to enhance the muscle length range of force exertion (Willems & Huijing, 1994). It is expected that contributing to such heterogeneity, myofascial force transmission functions as a major determinant of the variables of muscle length-force characteristics.

Passive forces

Both experimental and modeling parts of the present study show interesting results regarding passive force. For an isolated muscle, passive force is due to the tensile resistance of the muscle tissue only. The present results show that the distal passive forces start building up already at lengths lower than optimum muscle length. This happens because the extramuscular connections cause a certain passive resistance at those lengths. It is also interesting that while the distal EDL passive force increases the proximal force remains near zero. This shows that any tensile loading of the proximal part of the passive muscle is prevented by the extramuscular connections.

Relative position of a muscle with respect to its surroundings

The present study involves changes in EDL muscle length. However, changes in muscle length also involve changes in relative position of (parts of) the muscle with respect to neighboring tissues. Manipulating the position of EDL relative to intact extramuscular connective tissues of the anterior crural compartment without changing its muscle-tendon complex length yielded significant effects on EDL forces measured at the muscles' proximal and distal tendons (Maas et al., 2003). This suggests that in addition to muscle length, relative position of a muscle is a co-determinant of isometric muscle force.

A recent study, focused on the effects of relative position of EDL muscle, showed that effects of combined inter- and extramuscular myofascial force transmission on muscle force are not identical after equal distal or proximal lengthening (Huijing & Baan, 2003). Our present results show that mechanical properties of the extramuscular connections are not homogeneous but the tissues of the proximal part of the neurovascular tract are stiffer due to the collagen-reinforced structure (for anatomical details see Huijing, 1999a; Huijing & Baan, 2001a). It is likely that this is one of the reasons of the asymmetric effects reported by Huijing and Baan (2003).

Truly isolated muscle and muscle in situ

Despite the large body of earlier experimental work on muscle, only a few studies show evidence for extramuscular myofascial effects. One reason for that may be that in the majority of the earlier work, muscle tissues were investigated in experimental conditions, which eliminate structures possibly involved in mechanisms of intermuscular or extramuscular force transmission (e.g., Faulkner et al., 1982; Street, 1983; Huijing et al., 1994; Jaspers et al., 1999). Such conditions were referred to as either 'isolated' or 'in situ'. However, it is necessary to clearly distinguish these conditions. If a muscle is isolated, the extramuscular connective tissues are completely dissected, whereas for a muscle in situ, the tissues of the major neurovascular tract are always left

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intact. Isolation of a muscle leads to identical proximal and distal forces. Besides, sarcomere length distribution remains limited as determined by intramuscular myofascial force transmission only. In contrast, for muscle in situ, our present results show that proximal and distal forces are unequal and a significant distribution of sarcomere length takes place. The majority of the earlier experimental work was performed on muscles in situ, with measurement of muscle force only at one of the tendons. This approach was based on the implicit assumption that the conditions for an in situ muscle are not different than that of an isolated muscle. Our results show that due to the highly stiff extramuscular connections provided by the major neurovascular tract, such an assumption is not tenable. Therefore it seems likely that, the earlier experiments were affected also by extramuscular myofascial force transmission.

Limitations and implications of this study

The results of the present study show significant effects of extramuscular myofascial force transmission on muscle functional characteristics. Nevertheless, it should be noted that, the conditions experimentally imposed are not completely physiological: (1) Experiments were performed with maximal activation of the muscle, whereas this is hardly the case vivo. The level of activation will change the stiffness of the muscular tissues and is expected to effect extramuscular mechanical interaction. This needs to be studied in the future. (2) In the course of distal lengthening, the surrounding connective tissues of EDL muscle were kept in their original positions. Our results suggest that a major determinant of the myofascial effects is the relative position of a muscle with respect to its surroundings. However, in vivo, not only the muscle studied, but also some of the surrounding connective tissues (particularly joint related connective tissues) and muscles may change position with joint motion. Therefore, studies aimed at identification of the in vivo relative positions of muscles with respect to each other and their surroundings for given tasks, are indicated.

Using spring elements with linear stiffness and identical properties representing the intact extramuscular connections must be considered as a significant simplification. However, this approach indicated that the remaining links for the minimally connected condition should be stiffer in order to show the experimental effects of the intact connections on length-force characteristics. In future modeling, the mechanical properties of the linking elements should be defined accordingly and possible nonlinear behavior should be accounted for.

The effects of myofascial force transmission on muscle mechanics suggest that new approaches to studies of the musculo-skeletal system may be necessary in several fields. In such approaches, the concept of mechanical interaction of muscle fibers and connective tissue has to be placed central. Examples of such fields could be genetic muscle diseases such as the muscular dystrophies (as the pathology is associated with inadequate linking of muscle fibers to the extracellular matrix) or diseases associated with over-use such as repetitive strain injury (as the pathology of the connective tissue is likely to be caused by the mechanical interaction of adjacent muscles or parts of muscles). Another example is surgery such as tendon transfer. In such operations improved movement is aimed at by altering the action of a muscle (i.e., detaching the tendon and reattaching it to an antagonistic muscle in order to convert the muscle from an extensor of a joint to a flexor or vice versa). However, postoperative success is not observed in all patients (e.g., Asakawa et al., 2002). The proposed explanations for this result include formation of scar tissue that would restrict muscle motion and limit the exertion of the desired force (Asakawa et al., 2002) and an imperfect choice of muscle length for tendon reattachment (Lieber & Friden, 1997). The latter study describes sarcomere length as the variable to determine the best muscle length and suggests intraoperative measurement of that. However, these authors make use of a single sample of sarcomere length as being representative of the entire muscle. In contrast, our present results indicate that a substantial inhomogeneity in lengths of sarcomeres is to be expected. Moreover, myofascial force transmission is likely to lead to an ehanced number of sarcomeres to attain different lengths at several muscle lengths. We believe that the system that is handled in tendon transfer operations includes the mechanism of myofascial force transmission and is incomplete without it. Therefore, we suggest that in designing of surgical procedures with reconstructive purposes, myofascial force transmission has to be accounted for.

In conclusion, the exclusive effects of extramuscular myofascial force transmission are substantial. Unequal muscle forces measured at the proximal and distal tendons provide evidence for myofascial pathways for transmission of force as additional sites of transmission in addition to myotendinous junctions. Sarcomere length distributions indicated by finite element modeling require experimental verification. However, both model and experimental results indicate that muscle length-force characteristics are not unique properties of a muscle. Instead, muscle length-force characteristics can be variable as a function of muscle relative position and its associated altered sarcomere lengths. Moreover, the hypothesis that extramuscular myofascial force transmission occurs even via the connective tissues of the major neurovascular tract is confirmed. This shows that a dissected muscle in situ should be distinguished from a fully isolated muscle.

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