Muscular adaptations and insulin–like growth factor–I (IGF–I) responses to resistance training are stretch–mediated.
MUSCULAR ADAPTATIONS AND INSULIN-LIKE GROWTH FACTOR-1 RESPONSES TO RESISTANCE TRAINING ARE STRETCH-MEDIATED

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ABSTRACT: Introduction: Modulation of muscle characteristics was attempted through altering muscle stretch during resistance training. We hypothesized that stretch would enhance muscle responses. Methods: Participants trained for 8 weeks, loading the quadriceps in a shortened (SL, 0–50° knee flexion; n = 10) or lengthened (LL, 40–90°; n = 11) position, followed by 4 weeks of detraining. Controls (CON; n = 10) were untrained. Quadriceps strength, vastus lateralis architecture, anatomical cross-sectional area (aCSA), and serum insulin-like growth factor-1 (IGF-1) were measured at weeks 0, 8, 10, and 12. Results: Increases in fascicle length (29 ± 4% vs. 14 ± 4%), distal aCSA (53 ± 12% vs. 18 ± 8%), strength (26 ± 6% vs. 7 ± 3%), and IGF-1 (31 ± 6% vs. 7 ± 6%) were greater in LL compared with SL muscles (P < 0.05). No changes occurred in CON. Determing decrements in strength and aCSA were greater in SL than LL muscles (P < 0.05). Conclusions: Enhanced muscle in vivo (and somewhat IGF-1) adaptations to resistance training are concurrent with muscle stretch, which warrants its inclusion within training.


Skeletal muscle architectural and morphological characteristics are important due to their direct influence on functional performance (i.e., strength and power). Therefore, a key to optimizing human function is to understand the mechanical stimuli that induce alterations in muscle characteristics/properties. In relation to muscle architecture, there are reports of increases in fascicle length after resistance training.1–3 An increase in fascicle length is thought to be brought about by the addition of in-series sarcomeres. Muscle length (or passive tension/stretch) and excursion have been shown to be major regulators of serial sarcomerogenesis in animals4 and appear to be relatively independent of both muscle activation level and tension.5 However, in humans, there exists conflicting evidence from studies on the major mechanical stimuli for such an adaptation. In young adults, muscle contraction type (eccentric vs. concentric) was investigated as a possible primary candidate for fascicle length change.6 The investigators concluded that other factors (possibly excitation of muscle during resistance training) were the main mechanical stimuli for changes in fascicle length. In contrast, in older individuals, Reeves et al.1 found that eccentric contractions (through enhanced training stimulus and associated greater muscle–tendon strain) were the driving force behind greater increases in fascicle length, compared with conventional weight training. Therefore, the primary constituent in resistance training for regulating fascicle length in humans remains ambiguous.

The inextricable link between muscle cross-sectional area (CSA) and strength has been known for many years. The 2 main mechanical signals that induce muscle hypertrophy (and therefore increasing CSA) appear to be muscle force and/or stretch. In animal models, muscle stretch (i.e., lengthening) combined with force generation seems to have an additive effect on protein synthesis and muscle size over and above the effects of force generation/stretch applied separately.7,8 Furthermore, insulin-like growth factor-1 (IGF-1) mRNA has also been shown to increase to a much greater extent in response to stretch combined with electrical stimulation, as compared with stimulation or stretch alone in adult skeletal muscle.9 At the other end of the muscle-loading spectrum, the response to diminished loading, that is, detraining, is the partial or complete loss of training-induced adaptations in response to an insufficient loading stimulus. Significant decrements in strength, electromyographic (EMG) amplitude, and mean fiber CSA have been reported to occur in as little as 2 weeks of detraining,10 with similar observations in chronic detraining periods (≥4 weeks).11,12 However, in vivo changes to muscle architecture during a relatively shorter period of time (≤4 weeks, such as that found in short-term

Abbreviations: aCSA, anatomical cross-sectional area; ANOVA, analysis of variance; BF, biceps femoris; CON, control; CSA, cross-sectional area; DEXA, dual-energy X-ray absorptiometry; EMG, electromyography; FOXO, Forkhead box subgroup O; HF, half-Fourier; IGF-1, insulin-like growth factor-1; LL, longer length; MAFBx, muscle atrophy F-box; MuRF1, muscle RING finger-1; MVC, maximum voluntary contraction; PI3K/Akt/mTOR, phosphatidylinositol-3 kinase/Akt protein kinase B/mammalian target of rapamycin; RM, repetition maximum; ROM, range of motion; SL, shorter length

Key words: detraining; hypertrophy; muscle architecture; range of motion; resistance training

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injury, illness, or tapering) have not yet been described. Significant increases in fascicle length have been reported in as little as 10 days from the onset of resistance training.2 Counterintuitively, Blazevich et al.6 documented an increase in VL fascicle length during 3 months of detraining after 10 weeks of resistance training. Therefore, after resistance training, the impact of detraining/training appears to follow an unpredictable/uncharted pattern. In addition to its role in increased muscle mass, IGF-1 has been implicated in preventing expression of the Forkhead box (FOXO) class of transcription factors and the mRNA increases of muscle atrophy F-Box (MAFbx) and muscle RING finger-1 (MuRF1) seen during muscle atrophy.13 Therefore, after detraining, it would be of interest to describe the possible link between circulating IGF-1 levels and the degree of muscle mass maintenance.

From the evidence of the current literature, the aim of this study was to determine whether performing resistance training at a longer muscle length (high muscle stretch condition) compared with a shorter muscle length (low muscle stretch condition), with identical load magnitude, would differentially modulate specific in vivo muscle responses such as size, architecture, and circulating IGF-1. In addition, we questioned whether the magnitude of the preceding training responses would also influence the change in muscle parameters during detraining. It was hypothesized that a group training at longer (LL) muscle lengths (40–90° excursion) would undergo greater skeletal muscle hypertrophy and fascicle lengthening compared with a group training at 0–50° excursion (SL). Second, it was also hypothesized that the LL group would still have a larger muscle mass after detraining, probably due to greater initial gains and/or IGF-1-mediated effects on protein degradation rate. Strength- and fascicle angle-related parameters were expected to follow a similar response to those associated with hypertrophy.

METHODS

Subjects. Thirty-one volunteers were recruited from the local university and gave written informed consent to participate in the study. All procedures and experimental protocols were approved by the local ethics committee. Exclusion criteria included the presence of any known musculoskeletal, neurological, inflammatory, or metabolic disorders or injury. Participants took part in recreational activities such as team sports and had either never taken part in lower limb resistance training or had not done so within the previous 12 months. Team sports included rugby union and league, soccer, hockey, and netball. Where several participants had the same sporting background, they were divided evenly and randomly allocated to a training group. All participants took part habitually in up to 5–5 hours of non–resistance-based activity per week. Twenty-one activity-matched participants were allocated to a training group, either SL (shorter muscle length; 6 men and 4 women; aged 19 ± 2.2 years, 1.76 ± 0.15 m, 75.7 ± 13.2 kg) or LL (longer muscle length; 5 men and 6 women; 21 ± 3.4 years, 1.75 ± 0.14 m, 74.9 ± 14.7 kg). Ten participants (6 men and 4 women; 23 ± 2.4 years, 1.76 ± 0.09 m, 77.9 ± 13.1 kg) were assigned to the non-training control group (CON), and continued their normal habitual activity throughout the study period. Inclusion of both genders would allow a general response to the training regime to be identified regardless of gender and was possible due to very similar numbers of men and women. A 1-way analysis of variance (ANOVA) revealed that the population was homogeneous at baseline for all parameters of interest (P > 0.05).

Study Design. The study design was convenience sampling, with random allocation to 1 of 3 groups. After familiarization with the testing procedures at least 1 week prior to testing proper, participants were tested for muscle size, architecture, strength, and serum IGF-1 at baseline (week 0). The measurements were repeated after 8 weeks of resistance training (week 8), after 2 weeks of detraining (week 10), and after a further 2 weeks of detraining (week 12). Blood sampling was always at the same time of day, whereas the in vivo tests were completed within 2 hours of the time of day of these tests when carried out at week 0 to minimize any impact of diurnal variability in muscle function. It should be noted that all sonographs (and other muscle parameters) were taken/measured ~3–4 days posttraining to avoid osmotic fluid shifts that may confound architectural or morphological measurements.14

Muscle Excursion. Total muscle excursion was set at that which occurred during 50° range of motion (ROM) carried out at different portions of the knee angle–muscle length spectrum, depending on the training group (Fig. 1). With 0° being full knee extension, SL followed an excursion from 0–50° of knee flexion (i.e., shorter muscle lengths), and LL followed an excursion from 40–90° (muscle loaded at a longer length). Therefore, the work done, because external loads were also made comparable [force (see Muscle Force Modeling subsection below) × distance], was also matched closely. These joint angles were chosen, as both 50° and 90° have been used frequently to determine physiological responses to various stimuli and
are usually referred to as being “longer” or “shorter” muscle lengths. In addition, placing the muscle at these discrete angles also allowed the investigators to compare the effect of muscle length change within a common ROM for this particular muscle group, that is, 0–90°.

**Muscle Force Modeling.** Due to the changing moment arm length of the patella tendon at discrete knee-joint angles, differences in muscle force produced between the groups were accounted for. Thus, quadriceps forces at the patella tendon were calculated as follows:

\[
\text{Quad Force} = \left( \frac{\text{Quad MaxTorque} + \text{Ham CoTorque}}{\text{Moment Arm PT}} \right)
\]

(1)

where:

\[
\text{Ham CoTorque} = \left( \frac{\text{Co-Con EMG} \times \text{Flex MaxTorque}}{\text{Max BF EMG}} \right)
\]

(2)

where Co-ConEMG is co-contraction of the antagonist muscle group (using the biceps femoris as representative of the hamstrings), and Max BFEMG is the maximum antagonist EMG. FlexMaxTorque is maximum flexion torque, and Moment Arm PT is the moment arm of the patellar tendon [values obtained from dual-energy X-ray absorptiometry (DEXA) scans]. Based on previous training data from our laboratory at end ROM, where a short isometric hold would take place, tendon forces produced at 90° were, on average, ~32% greater than those produced at 50° [to quantify the training load to apply, the torque of the external resistance (in Nm) is added to the left-hand side of Equation (1)]. Thus, it was calculated that, whereas SL would exercise at a high intensity of 80% 1 repetition maximum (RM) (for a more detailed description see Resistance Training Program subsection), the LL group would train at a lower intensity of 55% 1 RM to equate the absolute load seen by the tendon (i.e., at the joint center of rotation) in the 2 groups.

**Patella Tendon Moment Arm Measurement.** The patella moment arm was estimated from sagittal scans of the right leg of each participant using single-energy DEXA scanning (Hologic QDR; Vertec, Reading, UK), with the knee placed at 90° of knee flexion. The patella tendon moment arm was defined as the perpendicular distance between the tibiofemoral contact point and the mid-portion of the patella tendon. DEXA imaging has been used to estimate moment arm previously in other anatomical sites with good reliability. The single-energy scanning method has also been compared with magnetic resonance imaging (0.2-Tesla MRI

![Diagram of training excursions and testing joint angle.](image-url)
scanner; E-scan; Esaote Biomedica, Genoa, Italy) images [taken in the sagittal plane using a spin-echo TI half-Fourier (HF) sequence with a slice thickness of 8 mm, interslice gap of 0.6 mm, and parameters of time to repetition/echo time/number of excitations (TR/TE/NEX) 420/18/1; field of view 160 × 160 mm; matrix 256 × 256 pixels] in our laboratory and provides externally valid measurements. We have measured systematically the knee moment arms of 4 participants (2 men and 2 women) using both pieces of equipment. This revealed a non-significant (Wilcoxon signed-rank test: Zscore = −1.826, 2-tailed \( P > 0.05 \)) trend for the moment arm values using the DEXA to be 7.5 ± 1.5% (or 3.2 ± 0.6 mm) greater than those obtained using an MRI scan.

Estimation of Co-Contraction from EMG Activity. A pair of self-adhesive Ag–AgCl electrodes, 15 mm in diameter (Neurolite 720; Ambu, Ballerup, Denmark), were placed on clean, shaved, and previously abraded skin in a bipolar configuration with an interelectrode distance of 20 mm at 50% of femur length in the mid-sagittal plane of the biceps femoris muscle (BF). The reference electrode (Blue Sensor L; Ambu) was placed on the lateral tibial condyle. The raw EMG signal was pre-amplified (MP100; Biopac Systems, Inc., Goleta, California), amplified (MP100; Biopac), bandpass filtered between 10 and 500 Hz (Biopac), and sampled at 2000 Hz. All EMG and torque signals were displayed in real time using AcqKnowledge software (Biopac) on a personal computer (iMac, Apple, Inc., Cupertino, California). Two maximal flexion contractions were carried out to obtain the EMG at maximal flexion torque. The root-mean-square (RMS) EMG activity was averaged for a 500-ms period which coincided with the plateau of peak torque.

As mentioned above, the EMG of the long head of the biceps femoris muscle was measured to ascertain the level of antagonist muscle co-contraction during the required isometric knee-extension performances. Biceps femoris torque during a knee-flexion contraction was calculated by the biceps femoris EMG activity during knee extension divided by the biceps femoris peak flexor EMG at 70° knee flexion; the maximal flexor torque was then multiplied by this value to determine co-contraction torque. The co-contraction torque values are used to correct the voluntary knee-extension torques (and hence the forces during the ramped contractions) using the following formula:

\[
CT = OT + CcT
\]

where CT represents corrected knee-extensor torque, OT is the observed knee-extensor torque, and \( CcT \) is the calculated hamstring torque during knee extension (i.e., antagonist co-contraction torque).

Resistive Training Program. Resistance training was performed 3 times per week (2 supervised and 1 home-based session) by both SL and LL training groups for 8 weeks, using a combination of free, machine (Technogym, UK), and body weights exercises. Exercises for knee extensors included bilateral barbell squat, seated leg press, seated knee extension, Bulgarian split squat, and the Sampson chair. Throughout the training period, participants performed 3 or 4 sets of 8–10 repetitions (depending on stage of program and exercise) at 80% (SL) or 55% (LL) 1 RM, defined by the maximum load that could be lifted throughout the designated ROM (i.e., for the LL group, the maximum amount of weight that could be lifted from 90° to 40° in a controlled manner). The 1 RMs were reassessed every 2 weeks for each of the exercises and training loads adjusted accordingly.

A generalized warm-up was completed at 70–75% age-predicted maximum heart rate on a treadmill for 5 minutes, after which a goniometer was attached (using double-sided sticky tape) to the center of rotation of the knee. As the participant performed squat exercises, the goniometer rotated. The investigator/training partner confirmed from the scale that 50° or 90° of knee flexion was reached (depending on the training group) during the eccentric phase and therefore could hold the load steady over 2 seconds, before beginning the concentric phase of movement and return to the starting joint angle (i.e., either 0° or 40°).

As participants performed the leg-press and knee-extension exercises, the concentric movement was performed first, followed by a hold, and then the eccentric phase was performed back to the starting joint angle, which again was confirmed and timed by the investigator/training partner. The short isometric hold over 2 seconds was to emphasize the stretch at the end of the excursion. Therefore, the majority of quadriceps time-under-tension in SL was spent at shorter muscle lengths close to and including 50°, whereas the LL group quadriceps was predominantly at longer muscle lengths close to and including 90° (note: the load was removed in LL prior to the subject straightening up at between 40° to 0° at the end of each set). All exercises involved eccentric and concentric contractions, except for the Sampson chair, which was isometric loading, with LL holding the position with the knee at 90° and the knee at 50° angle. The timing of contractions was controlled using a metronome (1-second eccentric, 2-second isometric hold, 1-second concentric). The subjects
completed 2 familiarization sessions at 70% (SL) and 40% (LL) of 1 RM prior to commencing the resistance training program.

**Muscle Architecture and Muscle Length.** Architecture was measured at rest with each participant seated in an upright position on an isokinetic dynamometer (Cybex, Phoenix Healthcare Products, UK). After equipment calibration, each participant was positioned with a hip angle of 80° (straight back 90°) and kneecap at 90° knee flexion (straight leg 0°). All muscle architectural measurements were determined at rest using real-time ultrasonography (7.5-MHZ, 40-mm linear array, B-mode ultrasound probe; AU5; Esaote Biomedica, Italy) at rest. Images were captured using a digital video recorder (Tevion, UK). The vastus lateralis fascicle pennation angle (θ) was measured as the angle of fascicle insertion into the deep aponeurosis. Images were obtained perpendicular to the dermal surface of the VL and oriented along the plane of the muscle fascicles. Images were taken at 25% (proximal), 50% (central), and 75% (distal) of total femur length (as described below) and 50% of muscle width at each point (where 50% muscle width is defined as the midpoint between the fascia separating the VL and rectus femoris, and fascia separating the VL and biceps femoris muscles). Fascicle length was defined as the length of the fascicular path between the deep aponeurosis and superficial aponeurosis of the VL. The majority of fascicles extended off the acquired image, and the missing portion was estimated by linear extrapolation. This was achieved by measuring the linear distance from the identifiable end of a fascicle to the intersection of a line drawn from the fascicle and a line drawn from the superficial aponeurosis. This method has been shown to produce reliable results. All images were analyzed and measured using Image J (Wayne Rasband, National Institutes of Health, Bethesda, Maryland).

VL muscle lengths were also determined using ultrasound in the mid-sagittal plane. This measurement was taken as the length from the myotendinous junction of the VL and patellar tendon to the point where VL adjoins the tensor fascia latae and rectus femoris muscle. These points were marked on the skin and measured with standard anthropometric measuring tape.

**Muscle aCSA.** VL muscle anatomical cross-sectional area (aCSA) was measured using real-time ultrasonography at rest. aCSA was measured with the ultrasound probe in the transverse plane at 3 sites: 25%, 50%, and 75% of total femur length. Femur length was defined as the line passing from the greater trochanter to the central palpable point of the space between the femoral and tibial condyles when the knee was flexed at 90°.

Echo-absorptive tape was placed at regular intervals (≈3 cm) along the muscle width at each site so that, when the probe was placed on the leg, 2 distinct shadows were cast on the ultrasound image. Therefore, each ultrasound image provided a section of VL within the boundaries set by the 2 shadows and fascia surrounding the muscle. Individual images were reconstructed using the femur and superficial markers as reference points, and the total aCSA was measured using Image J software. The validity and reliability of this technique has been shown previously.

**Circulating IGF-1 Levels.** At each of the designated testing intervals (i.e., baseline and weeks 8, 10, and 12) and after an overnight fasting period (≈10 hours for all participants), participants reported to the laboratory. A 21-gauge, 1-inch ultrathin wall needle (Terumo Medical Corp., Somerset, New Jersey) was inserted into the antecubital vein of the forearm. Using a vacutainer assembly and serum separator tubes (Monovette; Sarstedt, Numbrecht, Germany), 5-ml blood samples were collected. After being kept on an ice bed for up to 2 hours (or a minimum of 30 minutes as per the recommendations of the manufacturer of the enzyme-linked immunoassay), the sample was then centrifuged at 4°C for 10 minutes at 4800 rpm, with the supernatant being removed and stored in Eppendorf tubes at −20°C for later analysis. IGF-1 (R&D Systems, Europe, Abington, UK), with a sensitivity of 0.026 ng/ml and intraassay variability of 4.0% (manufacturer’s data), was analyzed using standard enzyme-linked immunoassortant assay (ELISA) procedures.

**Strength Measurement.** Maximal isometric knee extension torque was measured with the right knee at 70° knee flexion (full knee extension = 0°) for all participants. The testing angle of 70° was chosen, as this is often the optimum angle or very close to that reported for maximal isometric strength of knee extensors. After a series of warm-up trials consisting of 10 isokinetic contractions at 60°/s at 50–85% maximal effort, participants were instructed to rapidly exert maximal isometric force against the dynamometer (Cybex, Phoenix Healthcare, UK) lever arm. Participants were given both verbal and visual encouragement/feedback throughout their effort. Joint torque data were displayed on the screen of a MacBook Air computer (Apple, Inc.), which was interfaced with an A/D system (AcqKnowledge, Biopac) with a sampling frequency of 2000 Hz. Isometric contractions were held for ≈2 seconds at the plateau with a 60-second rest period between contractions. Peak torque was expressed as the average of data points over a 200-ms period at the plateau phase (i.e.,
100 ms either side of the instantaneous peak torque. The greatest value of peak torque from 3 extensions was used as the measure of strength in each participant. Measurements were made on the right leg only due to time and ethical constraints, the fact that morphological and architectural measures were only determined on the right limb, and to reduce the impact of fatigue due to prolonged testing.

**Statistics.** Data were analyzed using IBM SPSS, version 19 (IBM, Inc., Armonk, New York). The Shapiro–Wilk and Levene’s tests revealed the data sets to be parametric, and they were therefore analyzed using a mixed-design repeated-measures 3 × 4 ANOVA. The within-group factor was the phase of training (i.e., weeks 0, 8, 10, and 12) and the between-group factor was training group (i.e., SL, LL, or CON). Post hoc contrast analyses with Bonferroni corrections were used to compare data with baseline (“within factor”) and with control group (“between factor”). All data are presented as mean ± standard error of the mean (SEM). Statistical significance was set at $p \leq 0.05$. The average statistical power of the measured muscle parameters (CSA, pennation angle, fascicle length, and strength) was statistically adequate at $\beta \geq 0.86$.

**RESULTS**

**Measurement Precision.** A pilot study was conducted at the onset of an investigation performed with a similar population (i.e., age and physical characteristics). Repeated measures of VL muscle anatomical CSA, architecture, and strength on a group of 5 individuals (2 men, 3 women) were collected on 3 separate occasions (spanning 7 consecutive days). Within-day coefficients of variation (CVs, in percent) of 1.5%, 1.9%, 3.3%, 2.2%, and 0.8%, and between-day CVs of 2.6%, 2.1%, 3.6%, and 1.8% were found for aCSA, fascicle length, fascicle pennation angle, DEXA moment arm (within-day only—measurements all performed on same day), and strength, respectively. Thus, the repeatability of the measurements was considered acceptable.

**Quantification of Muscle–Tendon Complex Stretch.** To measure the extent of lengthening (or passive stretch) at each training joint angle compared with full extension, VL muscle length was measured as the distance between the 2 myotendinous junctions of the muscle (Table 1). At 90° knee flexion, the VL was significantly ($P = 0.03$) lengthened compared with full extension, but not at either 40° or 50°.

**Architecture: Fascicle Length.** There were significant relative increases in VL fascicle lengths as a result of the training protocol in both groups for posttraining and detraining when compared with baseline, at all 3 measurement sites (see Fig. 2; $P < 0.001$). For posttraining, fascicles increased in length to a greater extent at all sites in LL compared with SL ($\Delta27 \pm 3$ mm, $\Delta21 \pm 3$ mm, $\Delta24 \pm 3$ mm, as compared with $\Delta18 \pm 4$ mm, $\Delta9 \pm 6$ mm, $\Delta12 \pm 5$ mm; $P = 0.02$ proximal, $P < 0.01$ central and distal, respectively). This significant main effect of group was retained throughout the entire detraining period at all sites ($P < 0.01$). The control group did not display any significant changes in fascicle length during the training and detraining periods (averaged over 3 sites, $\Delta3 \pm 4$ mm; $P > 0.05$).

**Fascicle Pennation Angle.** Both training groups had significant increases in fascicle pennation angle posttraining at proximal [SL: 9.9 ± 0.4° to 10.7 ± 0.4° ($\Delta9 \pm 4$%); LL: 9.0 ± 0.4° to 10.3 ± 0.3° ($\Delta14 \pm 7$%); $P = 0.034$], central [SL: 16.2 ± 0.5° to 17.2 ± 0.4° ($\Delta7 \pm 2$%); LL: 15.3 ± 0.4° to 16.2 ± 0.5° ($\Delta6 \pm 3$%); $P = 0.041$], and distal [SL: 16.5 ± 1.2° to 18.1 ± 1.0° ($\Delta11 \pm 4$%); LL: 18.1 ± 0.9° to 19.2 ± 0.8° ($\Delta7 \pm 3$%); $P = 0.003$] sites. Fascicle pennation angle remained elevated compared with baseline ($P < 0.05$) at week 10 at all 3 sites, but not at week 12 in both training groups at any measurement site. There was no difference ($P > 0.05$) between SL and LL groups in fascicle angle at any stage. The control group displayed no changes in fascicle angle over the 12-week period [averaged over 3 sites—15.9 ± 0.5° to 15.7 ± 0.5° ($\Delta1 \pm 1$%); $P > 0.05$].

**Anatomical Cross-Sectional Area.** Changes in aCSA are shown in Figure 3. VL aCSA increased significantly ($P < 0.0001$) relative to baseline after training at all sites in both training groups, which was still evident at the conclusion of the detraining period in both training groups at proximal, central, and distal sites ($P < 0.01$). There was also a trend for LL to exhibit greater relative gains in aCSA compared with SL at all sites at week 8 ($P < 0.06$), but only significantly so distally. Here there was a main group effect ($P = 0.030$); LL exhibited a

<table>
<thead>
<tr>
<th>Knee-joint angle (° knee flexion)</th>
<th>VL muscle length (cm)</th>
<th>Muscle length to femur length ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0° (full extension)</td>
<td>32.8 ± 1.1</td>
<td>0.74:1</td>
</tr>
<tr>
<td>40°</td>
<td>34.7 ± 0.9</td>
<td>0.78:1</td>
</tr>
<tr>
<td>50°</td>
<td>35.3 ± 0.9</td>
<td>0.80:1</td>
</tr>
<tr>
<td>90°</td>
<td>37.0 ± 1.1</td>
<td>0.83:1</td>
</tr>
</tbody>
</table>

In this population, the average femur length was 44.6 ± 1.0 cm (n = 6). *Significantly different from full extension ($P < 0.05$).
53 ± 12% increase compared with SL, showing an 18 ± 8% increment in VL aCSA. The superior adaptations were retained distally at both week 10 (LL: 45 ± 13%; SL: 11 ± 10%; \( P = 0.043 \)) and week 12 (LL: 32 ± 9%; SL: 2 ± 7%; \( P = 0.022 \)). There was no notable VL aCSA change over the 12-week period for controls (0 ± 2%, 4 ± 6%, and 3 ± 4% for proximal, central, and distal, respectively; \( P > 0.05 \)).

**Insulin-Like Growth Factor-1.** Changes in IGF-1 are shown in Figure 4. IGF-1 levels increased significantly as a result of training in the LL group, but not in the SL group at week 8 [SL: 407 ± 25 ng/ml to 429 ± 30 ng/ml (7 ± 6%); \( P = 0.438 \); LL: 375 ± 18 ng/ml to 489 ± 29 ng/ml (31 ± 6%); \( P = 0.033 \)], with a significant between-group effect (\( P < 0.001 \)). The LL group maintained greater IGF-1 levels compared with baseline (\( P = 0.006 \)) and SL group (\( P = 0.013 \)) at week 10, but had returned to baseline levels by week 12, and no main group effect was evident at the conclusion of detraining (\( P > 0.05 \)). The control group showed no significant change in the circulating levels of this hormone at any stage of the study period (\( P > 0.05 \)).
Muscle Strength. Both SL and LL groups had increased strength at 70° knee flexion as a result of the training protocols ($P<0.001$), with LL showing a significantly ($P=0.015$) greater increase from $223 \pm 30 \text{Nm}$ to $268 \pm 28 \text{Nm}$ ($26 \pm 6\%$) compared with SL, which reached $273 \pm 37 \text{Nm}$ from a pretraining torque of $253 \pm 32 \text{Nm}$ ($7 \pm 3\%$). The strength improvements in LL were retained to a greater extent throughout the detraining phase (week 10: $P=0.008$; week 12: $P=0.011$) compared with SL, although by week 12 SL had returned to baseline strength measures, whereas LL remained elevated relative to week 0 ($P<0.05$). The control group strength did not change significantly during the 12-week training and detraining period ($P>0.05$).

**DISCUSSION**

The aim of this study was to identify the *in vivo* effects of dynamic resistance training at 2 distinct average muscle–tendon unit lengths (shorter vs. longer) and to determine the time-course of any reversibility during detraining on morphological, architectural, and functional properties of VL and IGF-1 levels. It was hypothesized that, due to greater internal physiological stress (i.e., higher activation and metabolic demands of producing force at longer muscle lengths compared to shorter muscle lengths even when forces are normalized$^{15,17}$) and stretch on the VL muscle when training at longer muscle lengths compared with shorter muscle lengths, the LL group would have
superior adaptations to training compared with SL in terms of size and function. The results show that both the SL and LL groups displayed marked increases in muscle structural and mechanical characteristics compared with a control group. In general, the effect of training at longer muscle lengths showed greater adaptation in many of the parameters measured, thus partially confirming our hypotheses. In addition, we theorized that adaptations would be retained by the group training at a longer muscle length (due to the greater adaptations of the preceding training) during a subsequent period of detraining, and this was also confirmed in our observations.

In vivo changes in muscle architecture after a length-restricted resistance training protocol have, to our knowledge, have not been previously reported. Therefore, we contend that this is the first study to demonstrate superior increases in VL fascicle length after an extended period of loading at longer muscle lengths. The relative increases in fascicle length were greater in the LL group than in the SL posttraining group at each of the 3 measured sites. Earlier observations from animal models have demonstrated the importance of stretch in modulation of sarcomere number, which is also associated with an increase in protein synthesis. Table 1 shows that, by placing the leg at 90° of knee flexion, the VL muscle was stretched to a greater extent than at any other training knee-joint angle. By performing load-bearing exercise with the muscle–tendon complex in a relatively lengthened position (i.e., 40–90° in the LL group), an enhanced mechanical stimulus is experienced (i.e., greater stretch), thereby augmenting fascicle length increase by an increase in the number of in-series sarcomeres to allow each sarcomere to work at optimal length in line with the length–tension relationship of this unit. It should be pointed out here that, although fascicle length was measured at 90° of knee flexion and the SL group did not encounter this joint angle during training specifically, the SL group would still have experienced this joint angle during their normal daily routine, which includes sit-to-stand transitions. Therefore, when measuring fascicle length in the laboratory, the in-series and parallel elastic components should not be sufficiently “stiffer” in this group to justify the large between-group changes we have described.

Excursion range has been suggested to be important for regulating sarcomere number in the rabbit, although our results suggest that an excursion with the muscle in a predominantly lengthened position is the major regulator of fascicle length in vivo. This is due to the fact that both groups performed the same degree of excursion of 50°, yet they had different levels of adaptation. In addition, in support of the excursion offset hypothesis is that muscle forces at the tendon were also matched during resistance training. Therefore, no additional mechanical stimulus for fascicle length change (i.e., greater force) was present in the LL group, which coincides with previous work.
The relationship between muscle aCSA and strength is well established. The LL group had greater relative increases in aCSAs at all 3 measured sites along the VL after the training period, but they were only statistically so distally. A heterogeneous hypertrophic response after knee-extensor resistance training has been reported previously in the VL muscle. A lack of intramuscular homogeneity in stress in knee extensors may be due to 1 or a combination of several factors to provide “mechanical stability” (here the latter refers to the ability to efficiently use the combined properties of muscle strength, architecture, proprioception, and tendon characteristics to effect movement about a joint), force generation, and/or force transfer.

It has been shown that muscle undergoes both serial and parallel force distribution, and that, depending on muscle length, it can exhibit a proximal-distal difference in force transmission. The difference in the VL distribution of force due to alteration in its length may be a reason for the observed distal hypertrophy in the LL group compared with the SL group. The increase in strength after the training period, as measured by isometric MVC, was greater in the LL group than the SL group and may be reflective of the changes in aCSA and not in changes in fascicle pennation angle (Fig. 3). Nevertheless, we acknowledge that aCSA may not be as strongly correlated with force as physiological cross-sectional area (pCSA), because aCSA taken at right angles will therefore not pass through all the fibers of a highly pennate muscle. Nonetheless, Bamman et al. found aCSA to be as effective as pCSA for estimating strength.

The changes in strength for the LL group are similar to those reported in other training studies but those of the SL group are lower (we propose that the seemingly low training responsiveness of SL is due to a combination of lower training duration, volume, and chronic muscle activation compared with that described by Jones and Rutherford). In addition, not only was the range of motion similar between the training groups, but the isometric strength test angle was 20° from the end range of motion in each group (i.e., 50° and 90°), thereby conferring a high degree of equity to the assessment of strength. Further, in a similar study, we recently showed that the muscle increased IGF-1 mRNA 12-fold with a concomitant increase in fractional (138%) and total (191%) protein synthesis rates. Furthermore, stretch combined with electrical stimulation increased IGF-1 mRNA concentration 40-fold, with fractional and total protein synthesis rates increasing by 345% and 450%, respectively, in this condition. This evidence suggests that by training at longer muscle lengths (i.e., the LL group), muscle is activated to a greater degree and undergoes greater metabolic and mechanical stress. In response, there is coordinated activation of probably several signaling cascades, which may be mediated, at least in part, by the activity of IGF-1. A combination of these factors may explain the larger hypertrophic response in the LL group compared with the SL group.

The temporal response of in vivo changes to architecture during a short period of detraining has not been reported previously. In an earlier study, during a 3-month period of detraining, fascicle length was found to increase after removal of the training protocol. In our study, the results show that, in both SL and LL groups, fascicle lengths decreased in the detraining period, and these decreases were fairly linear in each group. For example, there were decreases of 6% (14% to 8%) and 5% (29% to 24%), when averaged across the 3 sites, when compared with baseline in the SL and LL groups, respectively, at week 10, with

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almost identical reductions at week 12 (SL: −5%, 8% to 3%; LL: −6%, 24% to 18%). These data indicate that, although there appears to be no difference in the rate of loss of adaptation between groups, the LL group’s greater initial increases in fascicle length during training resulted in retention of increased fascicle lengths after 4 weeks detraining.

From the results of the effect of detraining on VL aCSA, there were similar magnitudes of relative losses in aCSA and fascicle length (parallel and serial sarcomere number) in the SL group (week 10: −4%, week 12: −5%, relative to baseline averaged over 3 sites). In the LL group, the magnitudes of decrement in aCSA were more pronounced compared with fascicle length, especially in the later stages (week 10: −6%, week 12: −13%); however, the LL group retained higher overall aCSA values relative to baseline at week 12 (+21 ± 6%) compared with SL group (+11 ± 4%). Another study demonstrated that IGF-1 was implicated in preventing expression of the FOXO class of transcription factors and the mRNA increases of MAFbx and MuRF1 seen during muscle atrophy. The LL group continued to have significantly greater IGF-1 levels than SL at both week 8 and week 10. Although a chronic increase in IGF-1 level was not observed, the LL group’s responses clearly lasted longer than the transient increase in IGF-1 observed with acute bouts of resistance exercise. Therefore, there may have been a protective role played by IGF-1 to allow greater retention in LL group muscle mass. In support of this notion is the observation that LL group IGF-1 levels at week 12 had returned to baseline, and that this period also coincided with the relatively larger magnitude of neural drive is likely to be retained, thereby sustaining muscle strength gains during at least the first 4 weeks of detraining.

In conclusion, previous evidence in young humans demonstrated that eccentric training was not the major determinant for fascicle length adaptations. However, in the current study, greater increases in fascicle length of the VL were present after longer muscle length training, despite identical overall degrees of excursion and muscle forces at the tendon. We have shown that, in humans, muscle length–controlled excursion is the major mechanical stimulus for changes in fascicle length, although the exact mechanisms underpinning such adaptations are complex and have yet to be elucidated. A previous study of isometric training at longer and shorter muscle lengths indicated no differences between training groups in muscle morphology. Here we have presented evidence that prolonged dynamic resistance training at predominantly longer compared with shorter muscle lengths resulted in more marked improvements in strength and regional muscle hypertrophy, and these adaptations may be in part mediated by a greater hormonal response being elicited. Furthermore, with muscle architecture and strength being major influences on the determinants of functional performance from athletes to the elderly, our findings suggest that length-specific training should be implemented. In addition, because adaptations are retained more successfully over 4 weeks of detraining with the muscle lengthened, such training could also be used to offset deleterious effects of detraining or hypoactivity.

Future work should consider the fact that the hip angle, although standardized for most exercises, was not strictly controlled during the squats. Arguably, here, 4 of 5 exercises standardized hip angles (hence the impact of 1 exercise with no such control would be minimal), for a protocol with more “squat-like” exercises, it would be advisable to monitor the activity of the rectus femoris. Indeed, this is the only knee extensor (out of a possible 4) that crosses the hip joint, and it is possible that its contribution to hip flexion may impact overall quadriceps muscle shortening within a resistance training program.

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