Title

Specific force of the vastus lateralis in adults with Achondroplasia.

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Running Head

Reduced relative force production in disproportionately shorter individuals

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Abstract

Achondroplasia is a clinical condition defined by shorter stature and disproportionate limb length. Force production in able-bodied individuals (controls) is proportional to muscle size, but given the disproportionate nature of Achondroplasia, normalising to anatomical cross sectional area (ACSA) is inappropriate. The aim of this study was to assess specific force of the vastus lateralis (VL) in 10 adults with Achondroplasia (22 ±3 yrs) and 18 gender matched controls (22 ±2 yrs). Isometric torque (iMVCτ) of the dominant knee extensors (KE) and *in vivo* measures of VL muscle architecture, volume, activation and patella tendon moment arm were used to calculate VL physiological CSA (PCSA), fascicle force and specific force in both groups. Achondroplasia muscle volume was 53% smaller than controls (284 ±36 vs 604 ±102 cm^3, $P < 0.001$). KE iMVCτ was 63% lower in Achondroplasia compared to controls (95 ±24 vs 256 ±47 N·m, $P < 0.001$). Activation and moment arm length were similar between groups ($P > 0.05$), but coactivation of Achondroplasia bicep femoris was 70% more than controls (43 ±20 vs 13 ±5 %, $P < 0.001$). Achondroplasia had 58% less PCSA (43 ±10 vs 74.7 ±14 cm^2, $P < 0.001$), 29% lower fascicle force (702 ±235 vs 1704 ±303 N, $P < 0.001$) and 29% lower specific force than controls (17 ±6 vs 24 ±6 $N \cdot cm^{-2}$, $P = 0.012$). The smaller VL specific force in Achondroplasia may be attributed to infiltration of fat and connective tissue, rather than to any difference in myofilament function.

Keywords

Achondroplasia, specific force, vastus lateralis, physiological cross sectional area, anatomical cross sectional area

New and Note Worthy

The novel observation of this study was the measurement of normalised force production in a group of individuals with disproportionate limb length to torso ratios.

Introduction

Achondroplasia is a condition characterised by disproportionate shorter limb length, to stature, compared to age matched average sized individuals (18, 21, 39, 45). The contribution of force from the muscle in proportionally smaller groups has been investigated with force production appearing to be proportional to muscle morphology, such as muscle volume and fascicle length (23, 37). With Achondroplasia displaying disproportionate limb length and reduced whole body and segmental muscle mass, the muscle architecture and force production capacity may in turn be altered, but such observations have not been identified in Achondroplasic populations.

Muscle morphology, defined here as muscle size and architecture, is a primary determinant of muscle function and can account for some of the differences observed in proportionally smaller people (6, 23, 24, 37, 43, 44, 49). Primarily, the determinants of muscle force are: muscle shortening velocity, physiological cross sectional area (PCSA) of the muscle, fascicle length and muscle volume, respectively (38). Neural factors of the agonists and antagonists also contribute to force production as well as the biomechanical form of the joint (29, 32, 34). In numerous clinical conditions, such as the aging and cerebral palsy, the prevalence of weakness corresponds with functional impairments such as slower walking speeds and reduced performance of functional tasks (10, 22). In children with Achondroplasia isometric knee extension strength is less than age matched controls (51); there is however no comparison of force production capacity in adults with Achondroplasia, nor is there any measure of strength normalised for differences in muscle morphology or size.

The measurement of specific force integrates the measurement of muscle size, architecture, neural capacity and moment arm, providing a normalised value of force production (11, 50). While there is some variability in specific force, the values are similar across different cohorts, muscles and species (9, 11, 30, 37, 50). While specific force is similar between muscle groups, such measurement in muscles of the leg, such as vastus lateralis (VL), allow an indication of gait ability and oxygen uptake

(52). Furthermore, recently, a large cohort of adult males was measured in the VL, which can be used as a reference data set (50). To the Authors knowledge there has been no measurement of force production in Achondroplasic populations. Furthermore, to the authors knowledge, there appears to be no information on the adult Achondroplasic population in relation to force production, other than a general assumption that muscle mass is lower in this group compared to age matched average sized people, hereafter referred to as 'controls'. The measurement of specific force therefore, will allow a comparison between Achondroplasia and controls that may differ in terms of neuromuscular, biomechanical and architectural properties of the myotendinous unit

The aim of this study therefore is to assess specific force in adult males with Achondroplasia, and to identify the neural, morphological and biomechanical determinants of any difference in muscle force production between Achondroplasia and controls.

Methods

Participants

After written consent, 28 participants volunteered to participate in the study. All were free from any lower limb injury six months prior six to data collection and self-reported good health using a physical activity readiness questionnaire (mean (SD): 10 adult male Achondroplasia, age: 22 (3) yrs, mass: 61.8 (8.5) kg, stature: 1.38 (0.05) m, body fat: 29.3 (2.9) % and 18 adult males, age: 22 (2) yrs, mass: 78.3 (10.7) kg, stature: 1.79 (0.08) m, body fat: 22.4 (5.3) %). Ethical approval was attained by the local committee (Manchester Metropolitan University) and conformed to the declaration of Helsinki. Each participant attended one testing session at the laboratories of Manchester Metropolitan University where anthropometric, morphological and force measurements of the knee extensors (KE) were carried out.

Whole Body Composition

Participants were asked to fast for ~8 hrs before body composition assessment. A DEXA scanner (Hologic Discovery, Vertec Scientific Ltd, UK) was used to measure

today body fat (%). A default whole body scan (EF 8.4 lSv) was selected for all trials; scans emitted dual energy (140/100 kVp) fan-beam x-rays and lasted for ~7 minutes with each participant being exposed to ~8.4 μSv (5). The scanning region was 195 cm x 65 cm with 1.3 cm line spacing and a 0.2 cm point resolution.

Specific Force Calculation

Strength measurements

The torque derived from isometric maximal voluntary contraction (iMVCτ) of the dominant KE (Achondroplasia n = 9 right leg, control n = 16 right leg) were recorded using an isokinetic dynamometer (Cybex Norm, Cybex International Inc., NY, USA). Participants were seated upright with the dynamometer and chair positioned in accordance with the calibration guidelines given by the manufacturer so the lateral epicondyle was aligned with the dynamometer's central axis of rotation. Particularly in the Achondroplasia group, the chair and dynamometer were adjusted to align the lateral epicondyle if needed; additional padding was placed behind the spine to help maintain a static knee angle throughout contractions. The participants' dominant leg was secured with Velcro straps to the chair on the distal portion of the thigh and to the dynamometer around the lower portion of the tibia (~80% tibia length), according to participant comfort. All participants warmed up by performing six continuous submaximal concentric contractions ($60^{\circ}\cdot s^{-1}$) of the KE and knee flexors (KF). Participants then completed a randomised trial of KE iMVCs at 10° degree intervals, between 60° and 100°, to anatomical zero (where 180° was anatomical zero). Due to the chair being repositioned in the Achondroplasia group, joint angles were confirmed and recorded using a manual goniometer. Each participant received ~120 seconds rest between each trial. Throughout iMVC trials, participants were verbally encouraged to exert as much force as possible. Visual feedback was also provided to all participants on a monitor. KE and KF iMVCτ values were recorded (2000 Hz) on a computer (Macintosh, iMac, Apple Computer, Cupertino, California) via an A/D converter using an acquisition system (AcqKnowledge, Biopac Systems, Santa Barbara, California). The angle that elicited peak KE iMVCτ was used for subsequent analysis.

142

143 Agonist Activation

144 Agonist activation of during KE iMVCτ production is assessed to observed maximal
145 activation of the muscle and is done so while participants are positioned in the
146 isokinetic dynamometer. Firstly, a counter weight was fixed to the dynamometer to
147 minimise the compliance of the device. To measure agonist activation, two rubber
148 stimulation pads (size ranging from 70x90 to 180x100 mm; Uni-Patch, MN, USA)
149 were placed proximally and distally along the transverse plane of the dominant
150 femur. While in a relaxed state, a percutaneous electrical doublet stimulus (DS7,
151 Digitimer stimulator, Welwyn, Garden City, UK) was passed through the KE at
152 increased increments (~50 mV) and regular intervals (~20 seconds) until a plateau of
153 twitch torque was measured. This supramaximal doublet stimulus was applied to the
154 participants KE (inter-stimulus gap 10 μs and pulse width 50 μs) during KE iMVC.
155 Doublet stimulus has been shown to improve the signal-noise ratio in the
156 assessment of central activation (4, 27). A second doublet was applied
157 approximately 5 seconds after the first stimulus when the muscles were fully
158 relaxed, termed the potentiated doublet. Agonist activation was calculated using the
159 following equation:

160

$$\text{Activation } (\%) = 100 \cdot \left(1 - \left(\frac{t - \text{iMVC}\tau}{T}\right)\right)$$

161

162 Where; t is the interpolated doublet amplitude of the twitch torque, iMVCτ is the
163 isometric maximal voluntary contraction torque and T is the potentiated doublet
164 amplitude (3).

165

166 Measurement of Coactivation

167 Co-activation of the KF was measured in all participants during a KE iMVC, and
168 subsequent KF iMVCτ produced at the angle at which peak KE iMVCτ was measured.
169 In order to determine coactivation of the KF, surface EMG was recorded over the
170 biceps femoris (BF) as it is the largest of the KF group, and is representative of the KF
171 group as a whole (26). Furthermore, surface EMG was deemed adequate despite the

adiposity levels in Achondroplasia (17, 21, 42), as no differences in EMG readings are observed between groups of differing adiposity (8). Boundaries of the BF were determined using ultrasonography (Technos MXP Biosound Esaote) to ensure consistent placement of EMG electrodes over the KF. When established two pre-gelled, unipolar, 10mm, Ag-AgCl percutaneous electromyography (EMG) electrodes (Ambu Neuroline 720, Baltorpbakken, Denmark) were placed distally at ~1/3 of muscle length, to avoid the motor unit of the BF, and ~2mm apart along the mid-sagittal plane of the muscle (NORAXON, Arizona, USA). A third electrode was placed on the lateral epicondyle of the same femur as a reference. Prior to the placement of the electrodes, areas of the skin were shaved, then cleaned using an alcoholic wipe to minimise skin impedance and hence improve the EMG signal. Raw EMG data were recorded at 2000 Hz, with a high and low band-pass filter set at 10 and 500 Hz respectively, and a notch set at 50 Hz. The integral of the root mean square was recorded 0.5 seconds either side of the KE and KF iMVCτ to quantify the level of KF muscle coactivation. Based on a linear relationship occurring between torque and EMG activity (32), KF torque during KE iMVC was derived by converting the percentage activation of KF EMG during KE iMVC to KF EMG during KF iMVC.

$$KF\tau = \left(\frac{\left((KE \div KF) \cdot 100 \right)}{100} \right) \cdot KF\ iMVC\tau$$

Where KFτ is the KF torque during KE (N·m), KE is the agonist EMG (mV) recorded of the KE during KE iMVC, KF is the antagonist EMG (mV) recorded of the KE during KE iMVC and KF iMVCτ is the torque (N·m) observed during KF iMVC.

The measurement of agonist and antagonist muscle activation are required for the accurate quantification of net KE iMVCτ production, both of which are used in the calculation of specific force (30, 50). Therefore, net KE iMVCτ was given as the sum of KE iMVCτ and KFτ while a ratio of KF iMVCτ and KE iMVCτ was calculated to describe a balance of quadriceps to hamstring strength.

Measurement of Muscle volume

To measure VL ACSA, B-mode ultrasonography (Technos MXP Biosound Esaote) was used to obtain a 50 % muscle length transverse plane image of the VL (48). The origin and insertion of the dominant VL were marked, along with regular intervals of the medial and lateral edges. Muscle length (cm) was determined by the distance between the origin and insertion points with the 50 % percentile marked on the skin. A wire mesh was secured to the skin using non-allergic tape along the transverse plane. The wires were separated ~3 cm apart and ran sagittal to the muscle to act as echo absorbing markers that projected a shadow on the ultrasound image to act as reference points for analysis (48). The 5cm 7.5 MHz linear array probe was placed transversely to the VL with ultrasound transmission gel across the skin. While the probe moved from the medial to the lateral border of the VL, an audio video interleave (AVI) recording with a sampling frequency of 25 Hz (Adobe Premiere Elements version 10, Adobe Systems) was taken. The field of view was set so that anatomical references (femur and aponeurosis between VL and vastus intermedius) were visible at all times. Measurements were taken while the participant was supine and at rest. Individual images (between 5-9), with at least two wire references, were extracted from the recording and used to re-construct the muscle by overlapping the wire and aforementioned anatomical references, on photo editing software (Gimp, Version 2.8.8, GNU Image Manipulation Program). Digitising software (NIH Image J, Version 1.44o, National Institutes of Health, Bethesda, Maryland) was used to measure the ACSA of the VL. The volume of the VL was calculated using previously reported constants of MRI regression (35), where:

$$\text{VL Volume} = \left(\frac{-2.9244}{4} + \frac{0.74}{3} + \frac{2.2178}{2} + 0.0244\right) \cdot \text{VL length} \cdot 50\%\ \text{ACSA}$$

Muscle architecture

In vivo muscle architecture of the VL was conducted using B-mode ultrasonography (Technos MXP Biosound Esaote) during KE iMVC to observe fascicle length (cm) and pennation angle (θ). The 5cm, 7.5 MHz linear array probe was held on the mid-sagittal plane on a previously established mid-point of the VL; measured equidistant from the origin-insertion and medial-lateral muscular borders. With water-soluble

transmission gel the probe was held against, and at a perpendicular angle to, the skin with minimal pressure. The depth of view was set to ensure a number of fasciculi insertion points and deep aponeurosis were in view (30). Ultrasound imaging and torque production were synchronised using an external square wave voltage trigger enabling the accurate attainment of iMVC-to-ultrasound. Image recordings were AVI format at a sample frequency of 25 Hz; single images were selected using capture software (Adobe Premiere Elements version 10, Adobe Systems). Images of the VL at rest and iMVC were analysed using digitising software (NIH ImageJ, Version 1.44o, National Institutes of Health, Bethesda, Maryland) whereby fascicle length was determined as the length between the superficial and deep aponeuroses (38) and pennation angle was defined as the insertion angle of the fascicle into the deep aponeurosis (30). With the VL being one of the larger muscles in the body, invariably the dimensions of the probe was not large enough to capture a full fascicle, for these cases linear extrapolation was used to determine fascicle length as little error (2-7%) is observed at the midpoint of the muscle (14, 15), again using digitising software described above.

Physiological Cross Sectional Area

The PCSA (cm^2) was estimated as the ratio of VL muscle volume to fascicle length (30), assuming the model used to calculate muscle volume is cylindrical and that the muscle fibres are constant length (48).

Moment arm length

A dual-energy X-ray absorptiometry (DEXA) scanning (Hologic Discovery, Vertec Scientific Ltd, UK), in single energy mode (100 kVp), was used to obtain moment arm length of the patella tendon (PT_{MA}) (12). Participants were asked to lie on their side in a relaxed state. The dominant knee was positioned at the angle acquired from optimal peak force production using a manual goniometer. A single array sagittal plane scan was taken of the knee using a 22.3 x 13.7 cm field of view. Obtained scans were exported to and analysed on a Dicom viewer (OsiriZ 5.0.2, Pixmeo Sarl, Geneva, Switzerland). Moment arm length (m) was determined as the perpendicular distance

between the estimated tibiofemoral contact point and the posterior aspect of the patella tendon (57).

Fascicle Force and Specific Force

To estimate VL fascicle force and in turn specific force the following steps were used: Patella tendon force (N) was calculated using the following equation (41):

$$F_{PT} = \frac{\text{Net KE iMVC}\tau}{\text{MA}}$$

Where F_{PT} is the force at the patella tendon (N) during KE iMVC, net KE iMVCτ is calculated above, and MA is the length of the moment arm (m).

Previously reported data shows the relative contribution of the VL to the patella tendon to be around 22% (38). This calculation was then used to calculate VL fascicle force by expressing the VL fascicle force as a ratio of the VL contribution to the cosine of the pennation angle (radians) at KE iMVC.

$$\text{Fascicle Force} = \frac{VL_{con}}{\cos\theta}$$

Where VL_{Con} is the VL contribution (N) and cosθ is the cosine of pennation at iMVC (radians).

Specific force was represented as the ratio between VL fascicle force and VL PCSA.

Statistical Analysis

All data was collated onto a personal computer (Macintosh, MacBook Pro, Apple Computer, Cupertino, California) and analysed using SPSS (v22.0, IBM). Data was assumed parametric following Shapiro-Wilk and Levene's tests. Independent t-tests were carried out on most measured variables. In addition, Pearson's correlations were performed between related dependent variables. For variables that violated parametric assumptions, a Levene's adjusted P value or a Mann-Whitney U (denoted

by * and †, respectively, in Tables 1 and 2) was performed. Study power was assessed using G*Power and was found to be above 0.8 and alpha was set at ≤ 0.05. All results are reported as means (SD).

Results

Achondroplasia were 23% smaller in stature ($P < 0.001$) and 19% lighter in body mass ($P < 0.001$). There was no difference in age between groups ($P = 0.487$).

KE and KF iMVCτ

Adult males with Achondroplasia produced 63% less KE iMVCτ than controls (Table 1). KF iMVCτ was also significantly different (Table 1), again with Achondroplasia producing 82% less KE iMVCτ than controls. When expressed as a ratio between absolute KE iMVCτ and KF iMVCτ, Achondroplasia produced 49% more iMVCτ from the KE compared to KF than controls (Table 2).

Activation and Coactivation

There was no difference in maximal activation between Achondroplasia and control participants, however Achondroplasia had a 70% greater coactivation of the BF during KE iMVC compared to controls (Table 1).

Net KE iMVCτ

Paired samples t-test revealed that both groups significantly increased KE iMVC when corrected for BF coactivation, with Achondroplasia increasing by 7% and controls by 5% respectively (Table 1). The net KE iMVCτ produced by the VL was 63% less in Achondroplasia compared to controls (Table 1). There was no significant correlation between body fat percentage and net KE iMVCτ in Achondroplasia ($r = 0.110$, $P = 0.763$) or controls ($r = 0.411$, $P = 0.090$).

Morphology and Architecture

Achondroplasia had 41% smaller VL length than control (Table 1). VL morphology differed between groups with Achondroplasia having a 20% smaller ACSA than

control (Table 1, Figure 2) and in turn a 53% smaller muscle volume than controls (Table 1). Achondroplasia exhibited a 17% greater pennation angle (Table 1) but 17% smaller fascicle length (Table 1) during KE iMVC. PCSA was found to be 42% smaller in Achondroplasia than controls (Table 1). Correlations revealed no significant relationship between VL muscle volume and net KE iMVCτ production in Achondroplasia (R^2 = 0.056, P = 0.508, Figure 1), whereas for the same variables in controls, a significant relationship did exist (R^2 = 0.286, P = 0.022, Figure 1). Despite the diverging regression lines, a Z-transformation showed the slopes were similar (P = 0.442).

Presenting KE iMVCτ as a ratio to ACSA, Achondroplasia produce 53% less force per unit area compared to controls (Table 2). When net KE iMVCτ is expressed as a ratio with total body mass, Achondroplasia again display a 43% reduction to controls (Table 2). Achondroplasia displayed a 67%, reduction in net KE iMVCτ when presented as a ratio to LBM (Table 2). There was no relationship between ACSA and PCSA (R^2 = 0.016, P > 0.05) for Achondroplasia, whereas a significant relationship for the same variables was observed for controls (R^2 = 0.254, P = 0.032).

Force Measurements

The length of the PT_{MA} were similar between Achondroplasia and controls (Table 1). All force measurements were statistically lower in Achondroplasia compared to controls with patella tendon force, fascicle force and specific force being 60, 59 and 29% lower, respectively (Table 1).

Discussion

Here we aimed to assess the *in vivo* muscle morphology, KE iMVCτ production and specific force of the VL in adults with Achondroplasia and age and gender-matched healthy adults. The main findings were 1) net KE iMVCτ, VL ACSA, volume and PCSA were smaller in Achondroplasia than controls, 2) differences in net KE iMVCτ were not accounted for by the differences in muscle size 3) KF coactivation was higher in Achondroplasia than controls, 4) when morphological, architectural, neurological

and biomechanical differences were accounted for, a 29% smaller specific force was observed in Achondroplasia.

A large portion of neuromuscular function research describes the relationship between muscle size and force production, suggesting that muscle size is the predetermining factor for muscle strength (7, 33, 50, 54). Groups of shorter statures consistently present with smaller muscle size and lower MVC strength than their taller counterparts (6, 23, 37, 43, 49); when iMVCτ is normalised to muscle size, differences between control and short stature groups are nullified (6, 23, 49). The data from the present study is partially consistent with these previous findings. Achondroplasia were 82% weaker than controls in terms of KE iMVCτ, however this was not entirely accounted for by ACSA which was only 20% smaller. It is likely therefore that architectural and neurological factors contribute to weakness in Achondroplasia. It should be noted however that despite accounting for these factors, a deficit in Achondroplasic specific force remains, which could be subsequently attributed to physiological factors between groups or methodological measures of specific force, as discussed below.

Muscle Morphology in Achondroplasia

The extent of group differences in muscle size between Achondroplasia and controls was not consistent for each variable. For example, a 20% smaller VL ACSA in Achondroplasia underestimated the difference in PCSA which was 42% smaller than controls. This was due to the smaller muscle length and hence smaller VL volume in Achondroplasia compared to controls. ACSA must therefore be considered an inaccurate method of assessing contractile area between groups of heterogeneous muscle length such as presented here.

Although PCSA is the closest approximation to sarcomeres in parallel and therefore contractile area (28), it is possible that PCSA may be overestimated in the Achondroplasic group. The over estimation of PCSA in Achondroplasia is likely due to the differences in architectural properties at iMVC between groups. In controls, increased tendon compliance (i.e. more strain when under a relative force) alters

muscle architecture at iMVC, with increased pennation angle, fibre shortening and a leftward shift in the length tension relationship observed (30, 46, 47). Here, only increased pennation angle between groups was observed as resting fibre length not measured. Assuming the Achondroplasic patella tendon is more compliant than controls, given the observations made here, Achondroplasic fibre length is likely to be shorter at iMVC than it would be were patella tendon compliance the same between groups. PCSA is therefore overestimated as PCSA = ACSA/fibre length. Given that PCSA is the denominator when calculating specific force, a large PCSA (with the same fascicle force) equates to a lower specific force. For example, in the present study, Achondroplasia fibre length was 17% shorter and were 17% more pennate at iMVC than controls. Were the fibre angle to remain the same between groups at KE iMVC, fibre length of Achondroplasia would be 9% longer than the presented values and result in a 47% smaller PCSA compared to controls, 5% more than the measured values. This consequently leads to a 15% smaller Achondroplasic specific force compared to controls. The differences in muscle architecture at iMVC between groups therefore appears to contribute to the difference in specific force and could be partly due to a more compliant Achondroplasia patella tendon. However, there appears to be no measure of Achondroplasic tendon compliance within the literature to confirm this. Furthermore, this theory may only explain some of the 23% difference in specific force between groups.

Specific Force

Specific force provides an accurate representation of the *in vivo* contractile properties of the whole muscle and has been used to described the force characteristics of numerous different cohorts and muscle groups (9, 11, 15, 30, 36-38, 43, 50). Recently it has been shown that inter-individual variability in the measurements of specific force eludes to the fact that population variance in specific force may be due to a lower fibre specific force (i.e. myofilament differences), or an overestimation of muscle area through the inclusion of non-contractile material in the measurement of muscle mass (50). Several research groups have investigated specific force production at the myofilament level to identify intramuscular differences (55, 56, 58). In the present study, specific force was measured at the

fascicle level, with no apparent measure of force production made at the myofilament level in Achondroplasia. It could be suggested though, that as Achondroplasia is determined by a collagenous defect during development (19, 20), the protein structures at the myofilament level may be different to controls, which may contribute to the presented lower Achondroplasic specific force.

It is possible that the presentation of a lower specific force could be due, in part, to an overestimation of muscle size owing to the use of ultrasound to measure ACSA. Ultrasound, as with MRI, requires the measurement of the area encapsulated by aponeuroses to determine ACSA. The area within these limits includes muscle, connective tissue and fat infiltration. Previous reports (16, 17, 42) and here, show that Achondroplasic individuals have increased body fat percentage. The fibroblast mutation that causes Achondroplasia may also play some part in connective tissue distribution within the muscle, although this is at present unreported. Therefore, the measured Achondroplasic ACSA may reflect a “pseudo-hypertrophy” due to the probable increase of intramuscular fat infiltration, as observed in people with increased body fat (53). This pseudo-hypertrophy would increase muscle volume and PCSA measurement, with no change in contractile mass and in turn reduce the calculation of Achondroplasic specific force; it is important to note here that this methodological limitation is not only present in Achondroplasia. Regardless of these methodological discrepancies, when scaling strength and muscle size, a lower specific force persists in the present Achondroplasia participants which could be attributed to either an infiltration of non-contractile material, differences in single fibre properties or differences in tendon properties.

Coactivation and Moment Arm Length

In this study, the use of DEXA to measure PT_{MA} led to two important observations of the Achondroplasic knee. Firstly, there appears to be a lower joint congruency between femur and tibia in the Achondroplasic knee (Figure 3), agreeing with observations by Aykol et al. (1). The apparent reduced tibiofemoral joint congruency in Achondroplasia would likely reduce tibiofemoral joint stability. In clinical, injured and juvenile populations, where joint congruency is reduced, increased coactivation

of the BF is observed during KE (13, 25, 26). In the present study, Achondroplasia had a 70% increased coactivation of the BF during KE iMVC compared to controls. Therefore, the increased coactivation of Achondroplasic BF during KE iMVC is likely due to the reduced tibiofemoral joint congruency. Furthermore, the increased coactivation of the Achondroplasic BF may act as an injury prevention mechanism. In this case, Achondroplasic hamstrings are activating during KE to reduce the anterior movement of the tibia in relation to the femur. This would protect ligamentous structures in the knee, such as the anterior cruciate ligament. It is probable that this mechanism exists in other Achondroplasic muscle groups and joints as well as the knee. The increased coactivation of hamstrings, and other muscles, may also influence activities of daily living, such as walking economy. There is however, a lack of comparative data expressing the activation profiles of Achondroplasic muscle during contraction to expand on the theories presented. Therefore, the suggestions made from the current findings warrant further work.

The second observation from DEXA scanning of the Achondroplasic knee was that absolute PT_{MA} between groups was the same, meaning that Achondroplasia have a longer PT_{MA} relative to the femur (here measured as VL length). This finding is different to other shorter statured groups who show a proportionally smaller moment arms compared to taller statured individuals (37). The relatively larger PT_{MA} in Achondroplasia is likely to aid KE torque production, despite the 63% lower net KE iMVCτ compared to controls. For example, were the PT_{MA} of the current Achondroplasic population to be proportionally smaller to their femur length (i.e. 37% shorter), Achondroplasia would have produced 76% less net KE iMVCτ than controls. Whilst PT_{MA} appears to aid Achondroplasic torque production, PT_{MA} changes during KE (2, 31, 32) which leads to differences in force production (57). In the present study, we measured PT_{MA} at rest and did not account for changes of PT_{MA} during contraction. We assumed that the changes in PT_{MA} during KE iMVC would be similar between groups as it is unreported if Achondroplasic PT_{MA} changes in a similar fashion to control's PT_{MA} during KE. Any change in Achondroplasic PT_{MA} during contraction may further aid or hinder Achondroplasic torque production, but

this is yet to be observed. The presented data from this study appears to be the only data that accounts for Achondroplasic moment arm during contraction in any joint.

Clinical Implications

The present observations of a lower specific force, higher body fat, shorter stature and lower muscle volume in Achondroplasia, could contribute to those with Achondroplasia requiring a greater relative force production to complete activities of daily living compared to controls, such as walking. During walking, the lower muscle volume and higher body mass of Achondroplasic individuals would likely increase the required force production per step to maintain locomotion. This increased force production may in turn increase Achondroplasic walking economy. Furthermore, the decrease in Achondroplasic KE and KF iMVCτ, higher hamstring coactivation and lower specific force would suggest Achondroplasia may be at greater risk of falls and reduced postural stability compared to controls, as observed in control groups (40). Therefore, addressing interventions which aim to increase the absolute force production of Achondroplasic muscle would likely increase their quality of life by aiding walking economy, reducing the risk of falling and reducing injury risk.

Conclusion

This is the first study, to the authors knowledge, that has systematically accounted for various physiological and biomechanical modulators of force production in muscles of Achondroplasia. The main finding is that Achondroplasia produce 23% less specific force than controls. These results may only explain the variance in muscle morphology as further work into methodological, and myofilament differences within Achondroplasic specific force is needed to increase the validity of these data.

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Figure and table titles

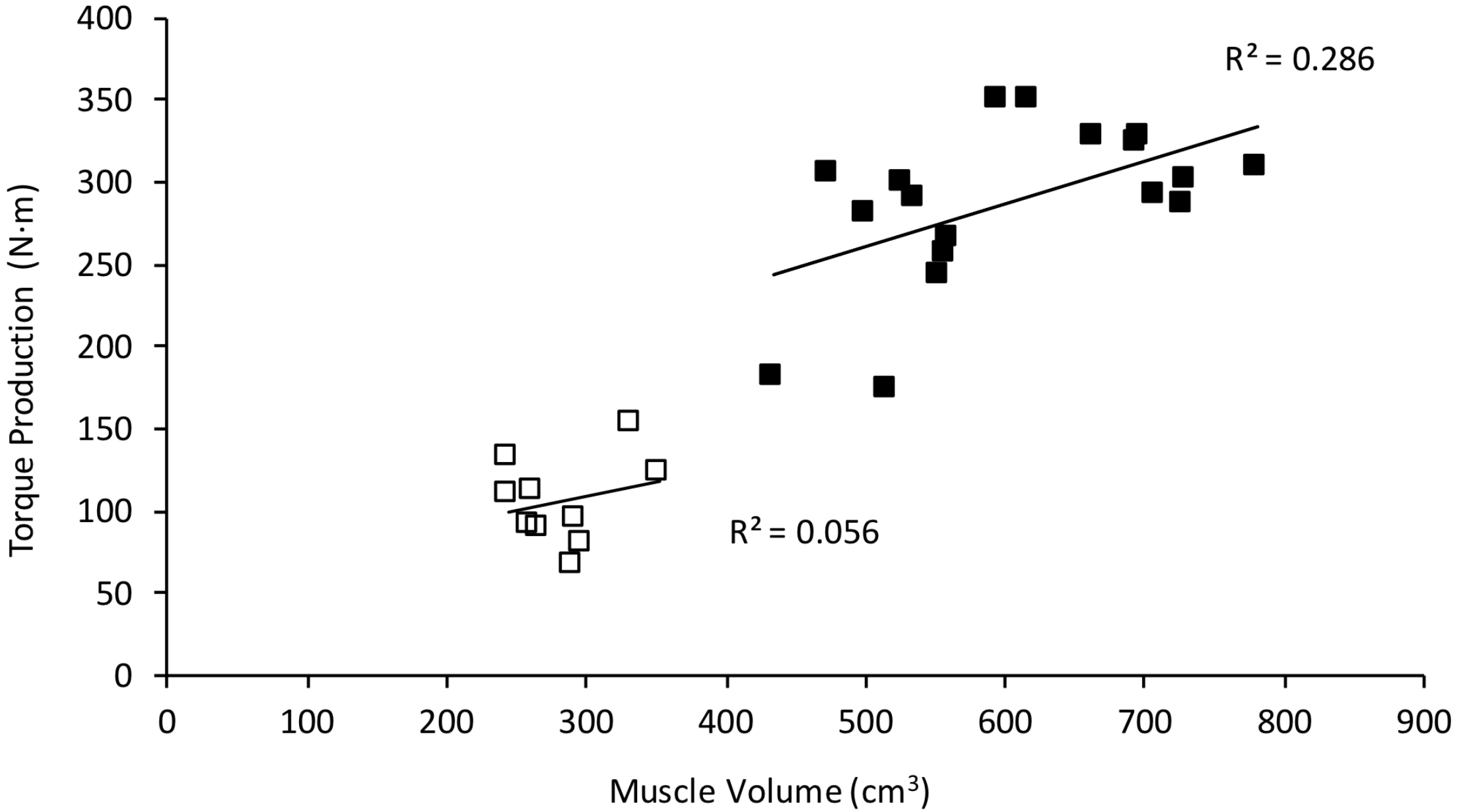
Figure 1: Scatter plot showing the relationship between VL muscle volume (cm^3) and torque production (N·m) for Achondroplasia (open) and controls (closed). Trend lines including R^2 are also given for each group respectively.

Figure 2: 50% ACSA of Achondroplasia (A) and a healthy adult (B). VL: Vastus Lateralis; VI: Vastus Intermedius; F: Femur.

Figure 3: Sagittal knee scans of 1 Achondroplasia (A) and 1 control (B) showing the reduced femoral contact point with the tibia in Achondroplasia.

Table 1: Morphological and functional characteristics of the vastus lateralis in controls and Achondroplasic adults. Values presented as mean (SD).

Table 2: Morphological and functional characteristics of the vastus lateralis normalised anatomical structures in controls and Achondroplasic adults. Values presented as mean (SD).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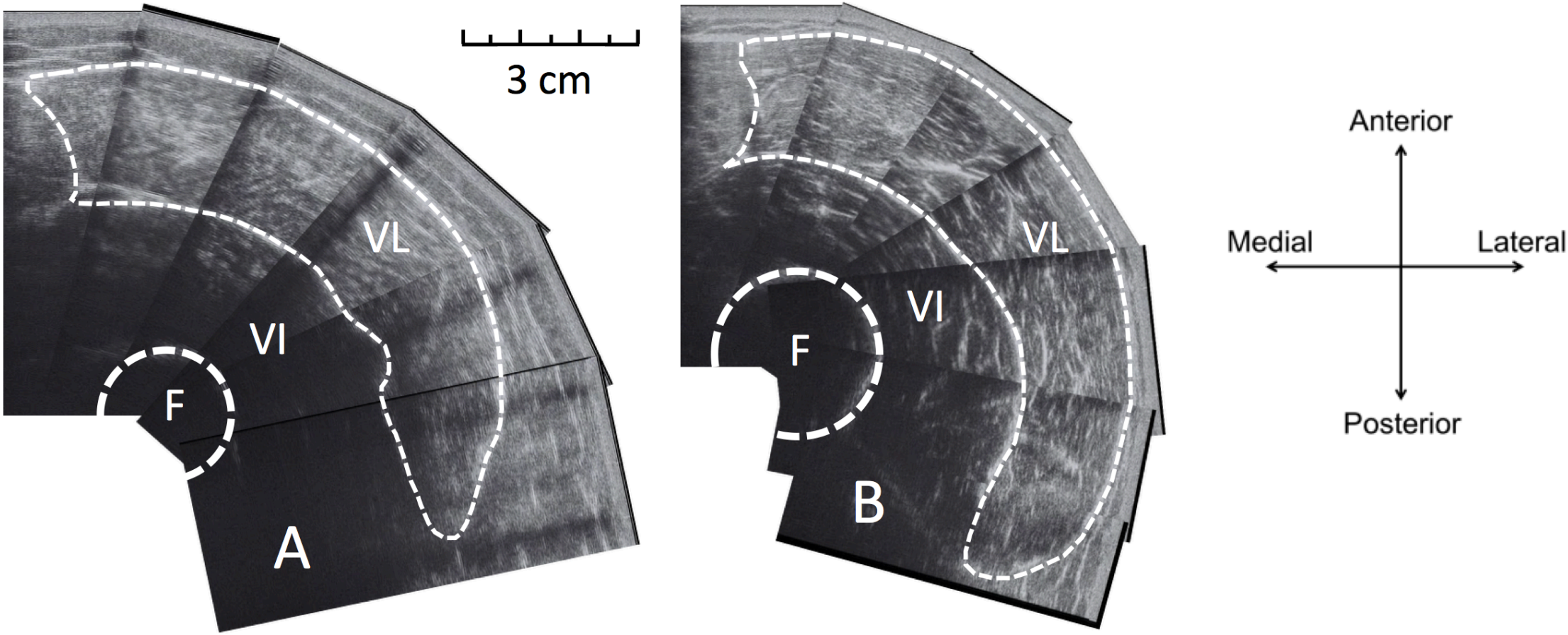
Torque Production (N·m)
Muscle Volume (cm³)
R² = 0.286
R² = 0.056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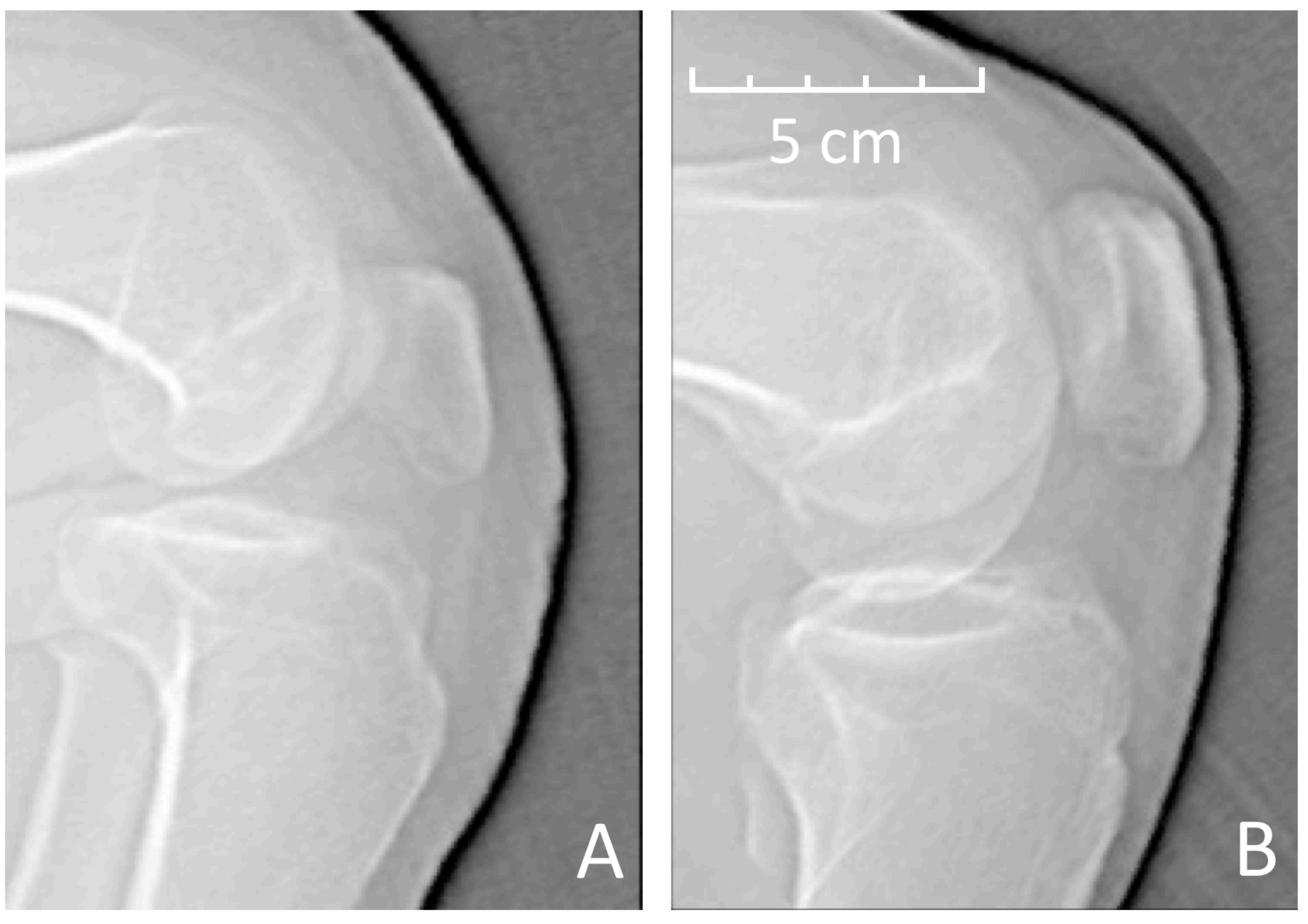
5 cm
A
B

	Control	Achondroplasia	P value
iMVCτ KE (N·m)	256 (47)	95 (24)	< 0.001
iMVCτ KF (N·m) *	105 (19)	19 (7)	< 0.01
Activation (%) *	92.0 (5.9)	83.9 (13.9)	0.105
Coactivation (%) *	12.6 (5.3)	42.6 (20)	0.001
Net iMVCτ (N·m) †	287 (49)	106 (26)	< 0.001
Volume (cm^3) *	604 (102)	284 (36)	< 0.001
Fascicle Length (cm) *	8.2 (1.5)	6.8 (1.5)	0.027
ACSA (cm^2) *	27.7 (4.4)	22.2 (2.6)	< 0.001
Pennation Angle (°) †	17.4 (2.4)	20.9 (4.6)	0.027
Muscle Thickness (cm)	28.4 (7.6)	20.6 (8.3)	0.550
PCSA (cm^2)	74.7 (13.7)	43.2 (9.9)	< 0.001
Moment Arm (m) †	0.040 (0.002)	0.037 (0.005)	0.309
Patella Tendon Force (N)	7296 (1319)	2930 (974)	< 0.001
VL Fascicle Force (N)	1704 (303)	702 (235)	< 0.001
Specific Force ($N \cdot cm^{-2}$) †	23.6 (6.4)	16.7 (6.0)	0.014

iMVCτ, isometric maximal voluntary contraction torque; ACSA, anatomical cross-sectional area; PCSA, physiological cross-sectional area. * adjusted P value following Levene's; † Mann Whitney-U.

	Control	Achondroplasia	P Value
iMVCτ KE:KF (%)	41.1 (9.2)	20.2 (6.7)	< 0.001
VL Length:Stature (%) †	18.8 (0.8)	14.3 (0.7)	< 0.001
TBM:Volume ($kg \cdot cm^{-3}$)	7.76 (1.17)	4.65 (0.69)	< 0.001
Net iMVCτ:ASCA ($N \cdot m \cdot cm^{-2}$)	2.14 (0.37)	2.81 (0.73)	0.003
Net iMVCτ:TBM ($N \cdot m \cdot kg^{-1}$)	3.72 (0.71)	1.71 (0.28)	< 0.001
Net iMVCτ:LBM ($N \cdot m \cdot kg^{-1}$) †	4.99 (0.78)	2.54 (0.43)	< 0.001
Net iMVCτ:Volume ($N \cdot m \cdot cm^{-3}$)	0.48 (0.08)	0.38 (0.10)	0.006
PT Moment arm:VL Length (cm) †	11.78 (0.96)	19.07 (3.25)	< 0.001
Net iMVCτ:PSCA ($N \cdot m \cdot cm^{-2}$)	3.96 (0.99)	2.55 (0.80)	0.001

VL, vastus lateralis; TBM, Total Body Mass, iMVCτ, isometric maximal voluntary contraction torque; ACSA, anatomical cross-sectional area; PCSA, physiological cross-sectional area; PT, patella tendon. † Mann Whitney-U.