Comparison of MRI and DXA to measure muscle size and age-related atrophy in thigh muscles

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Published version

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Original Article

Comparison of MRI and DXA to measure muscle size and age-related atrophy in thigh muscles

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Abstract

Objectives: Magnetic resonance imaging (MRI) and dual-energy x-ray absorptiometry (DXA) were used to examine the thigh lean mass in young and old men and women. **Methods:** A whole-body DXA scan was used to estimate thigh lean mass in young (20 men; 22.4±3.1y; 18 women; 22.1±2.0y) and older adults (25 men; 72.3±4.9y; 28 women; 72.0±4.5y). Thigh lean mass determined with a thigh scan on the DXA or full thigh MRI scans were compared. **Results:** Although the thigh lean mass quantified by DXA and MRI in young and older participants were correlated (R^2=0.88; p<0.001) the magnitude of the differences in thigh lean mass between young and old was smaller with DXA than MRI (old vs. young men 79.5±13.1% and 73.4±11.2%; old vs. young women 88.6±11.8% and 79.4±12.3%, respectively). Detailed analysis of MRI revealed 30% smaller quadriceps muscles in the older than young individuals, while the other thigh muscles were only 18% smaller. **Conclusions:** DXA underestimates the age-related loss of thigh muscle mass in comparison to MRI. The quadriceps muscles were more susceptible to age-related atrophy compared with other thigh muscles.

Keywords: Sarcopenia, Muscle, Quadriceps, MRI, DXA

Introduction

The age-related loss of muscle mass, often known as sarcopenia, contributes to reduced physical function and vitality in old age[1]. There is, therefore, great interest in understanding the mechanisms of muscle loss and finding ways to prevent or minimise this loss of muscle mass. However, any such research depends on accurate and reliable measurements of muscle size.

There are several imaging techniques available to measure muscle size, including magnetic resonance imaging (MRI), computer axial tomography (CT), ultrasonography, bio-electrical impedance analysis (BIA) and dual energy X-ray absorptiometry (DXA)[2-5]. Of these, sarcopenia is most often defined from measurements obtained using BIA[6] or DXA[7], both being convenient and quick methods that allow the collection of data from large cohorts. Cut-off values for diagnosis of sarcopenia are generally given as a defined deviation (usually 2SD) from the mean muscle size of a young-adult reference population. When examining a whole limb or other large body segment in a homogeneous group of subjects (of similar age) there is a good correlation between the muscle sizes estimated with DXA, Computer tomography (CT) and MRI, the latter being considered the gold standard[4,8-10]. It is not known, however, whether this correlation between muscle size determined by DXA and MRI changes with age.

A good correlation between two methods does not necessarily mean the methods show similar values because a systematic error (under- or overestimation) in one measurement would still lead to a good correlation. In a 10-week unilateral training study[11], for instance, it was found that at baseline DXA overestimated muscle mass in the thigh region by ~2 kg in comparison to CT despite a strong correlation between the measures (R=0.88, p<0.001). In this study it was also observed that DXA underestimated training-induced hypertrophy by around 25% compared with CT-derived measurements. If such an error also applies to atrophy, it could have implications in assessment of the degree of sarcopenia and muscle wasting in other clinical conditions.

Another drawback of DXA is that it does not permit a distinction to be made between individual muscles within a sin-

	YM (n=20)	OM (n=25)	YF (n=18)	OF (n=28)	Significant differences
Age (years)	22.4±3.1	72.3±4.9	22.1±2.0	72.0±4.5	Y<O
Height (m)	1.81±0.05	1.73±0.08	1.67±0.05	1.60±0.05	Y>O; M>F
Mass (kg)	72.8±9.8	77.9±13.2	61.7±9.5	64.1±11.2	M>F
BMI (kg.m^{-2})	22.2±3.3	25.8±2.7	22.0±3.2	25.0±3.9	Y<O
Lean Mass (kg)	59.2±5.8	53.0±7.5	40.1±3.4	37.4±3.8	Y>O; M>F
Total Fat Mass (kg)	12.7±6.3	22.1±8.5	19.4±8.1	23.9±8.4	Y<O; M<F

Table 1. Participant characteristics. Young Men (YM), Older Men (OM), Young Women (YF) and Older Women (OF); Significant differences between young and old, men and women; p<0.05.

gle muscle group, such as the quadriceps, or between agonists and antagonists. This may be important because various muscles may be affected differently with ageing[12,13] and after bed rest[14], although a 12-yr longitudinal follow-up of 7 elderly subjects showed no differences in atrophy between knee extensors and flexors[15].

The best way of assessing muscle-specific atrophy is by examination of multiple axial-plane MR images along the length of the limb. Consequently, the purpose of the present study was two-fold; first, to examine the level of agreement between MRI and DXA in estimating thigh muscle size in young and older men and women and, secondly, to examine age and sex differences in size of individual thigh muscles.

Methods

Participants and ethical approval

The study was carried out on a sub-group of 91 volunteers participating in a larger study designed to understand age-related muscle weakness (www.myoage.eu)[16]. The study was approved by the ethics committee of Manchester Metropolitan University and conformed to the Declaration of Helsinki. Written informed consent was obtained from each participant prior to participating in the study. Young-adult participants (20 men, 18 women) were recruited from amongst the university student population and older participants (25 men, 28 women) from the local community. Participant characteristics are presented in Table 1. All participants were healthy, not known to suffer from any musculoskeletal or cardiovascular disease, nor had suffered any limb fractures within the last 5 years. Other exclusion criteria were; not being able to walk 250 m unassisted, institutionalisation, co-morbidities such as neurological disorders (e.g. Parkinson's Disease), heart failure, chronic obstructive pulmonary disease, chronic pain syndrome or metabolic disease. In addition participants were excluded if they had undergone hip or knee replacement in the previous 2 years, or had a period of immobilisation greater than 1 week in the 3 months prior to testing. Older participants were all socially active and community dwelling and their medical doctor (General Practitioner) confirmed there was no medical reason why they should not participate.

Anthropometrics

Body mass was recorded on a digital scale with participants in light indoor clothing. Standing height was measured with a portable Stadiometer to the nearest 0.1 cm. Body mass index (BMI) was calculated by dividing the participant's body mass in kilograms by their height-squared in metres.

Magnetic Resonance Imaging (MRI)

A 0.25 T MRI scanner (G-Scan, Esaote, Genova, Italy) was used to measure thigh muscle volume. The participant was positioned supine in the scanner. A turbo 3D-T1-weighted protocol was used (matrix 256 x 256, TR 40 ms, TE 16 ms) and multiple 3.1-mm thick serial transverse sections were obtained every 25 mm from the distal to the proximal heads of the femur. Computing imaging software (OsiriX medical imaging software, OsiriX, Atlanta, USA) was used to determine the cross-sectional area of each of the four muscles of the quadriceps group and other thigh muscles (adductors, hamstrings and abductors) in each slice (Figure 1A).

The total thigh volume was estimated by summation of the cross-sectional area of each head of the individual quadriceps muscles and other muscles in each slice multiplied by the distance between slices, as previously described[17,18]. To aid comparison between the two measures, MRI volumes were converted to mass by multiplying by 1.04 g.cm^{-3} (the density of muscle tissue)[19].

To examine changes in muscle cross-sectional area along the length of the femur, scan locations were normalised to % Femur Length to allow comparisons between participants of different height. The length of the femur was defined as the distance between the greater trochanter and the distal lateral condyle at the knee. The locations of the slices along the femur length were rounded to the nearest 5% Femur Length. The muscle cross-sectional areas at a given % femur length were used for comparison between individuals.

Dual Energy X-ray Absorptiometry (DXA)

A total body DXA (Lunar Prodigy Advance, GE Healthcare) scan was performed to measure total body composition and bone mineral density. Participants lay supine on the scanning bed. Computer software (Prodigy, Encore 2006 v 10.50.086, GE healthcare) was used to provide estimations of total body
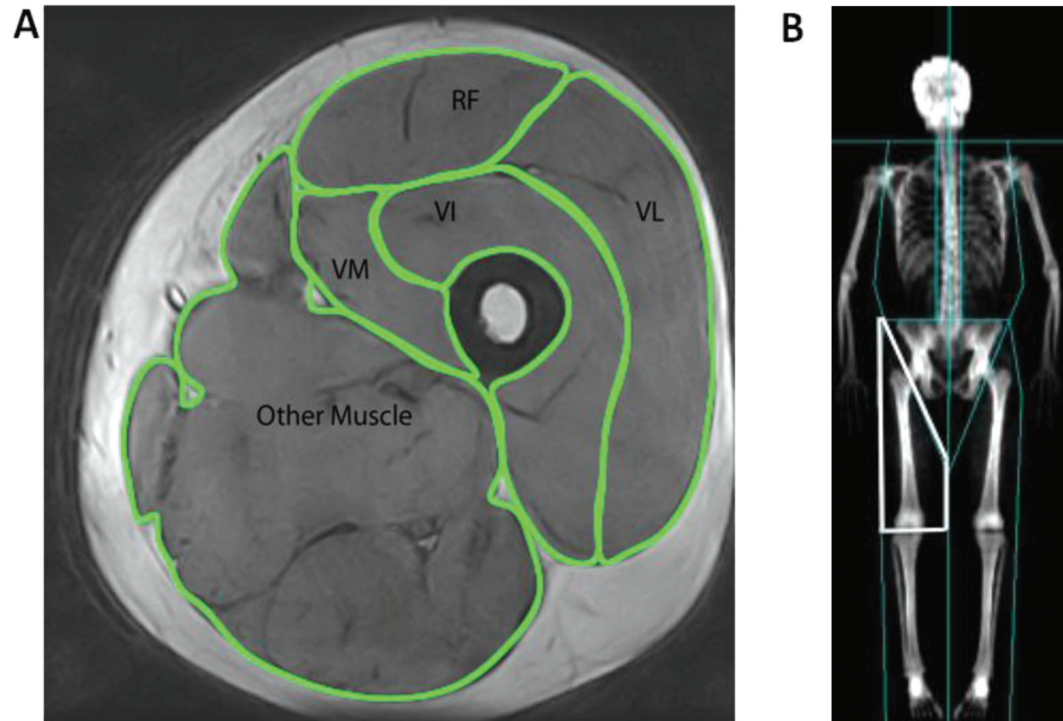
Figure 1. (**A**) Representative magnetic resonance image of the thigh with *rectus femoris (RF), vastus lateralis (VL), vastus intermedius (VI)* and *vastus medialis (VM)* labelled and highlighted. (**B**) Diagram showing the region of interest in DXA scans highlighted.

lean mass and fat mass. The thigh was identified as a region of interest using previously reported borders from the femoral neck[10] to the knee joint (Figure 1B). In the thigh of the dominant leg lean mass, fat mass and bone mineral content were estimated. All DXA analyses were performed by the same experienced investigator (TMW). In estimating "lean mass" the typical DXA machine (including the Lunar Prodigy used in this study) includes not just muscle mass but also connective tissue and the non-mineral components of bone. Bone mineral content accounts for approximately 55% of total bone mass with the rest being made up by protein and water. For this reason, an adjusted lean mass was calculated as follows[2]:

Lean mass = total mass - fat mass - (1.82 * BMC)

DXA also includes non-adipose components of fat tissue, such as protein, in the lean mass but the contribution this makes is unclear, so no further adjustments were applied.

Statistics

Data were analysed using SPSS v18 (IBM, 2011). A univariate two-way ANOVA with "as between factors" Age and Gender, was used to examine differences between groups. Significant interactions indicate that the effects of age differed between men and women. Pearson's product moment correlation was used to determine the relationships between variables. Repeated-measures ANOVA, with distance as "within" factor and Age and Gender as "between" factors, was used to determine differences along the femur and also sex-related differences in

the atrophy in individual muscles. One-way ANOVA with Bonferroni post-hoc analysis was used to determine age-related differences in individual muscle atrophy. Data were expressed as mean ± standard deviation unless stated otherwise. Statistical significance was accepted as $p<0.05$.

Results

Participant characteristics

It can be seen from Table 1 that the older subjects were shorter than the young ($p<0.001$), but had a similar body mass ($p=0.114$) and thus a higher BMI ($p<0.001$). The older participants had higher total-body fat mass ($p<0.001$) and a lower total-body lean mass ($p<0.001$).

Relationship between MRI and DXA to determine thigh muscle size

Total thigh muscle size measured by MRI and by DXA was significantly greater in young participants than old ($p<0.001$) and in men than in women ($p<0.001$). The age x gender interaction ($p=0.006$) is reflected by a larger age-related decrease in muscle mass in men than women (Table 2). Women had a higher thigh fat mass than men ($p<0.0005$), but there was no significant difference between young and old in thigh fat mass ($p=0.144$).

Figure 2 shows a strong relationship between thigh muscle size measured by MRI and DXA. In young adults the correla-

	YM (n=20)	OM (n=25)	YF (n=18)	OF (n=28)	Significant differences
MRI thigh muscle volume (cm^3)	4546±740	3328±509	2911±4.11	2312±359	Y>O; M>F
MRI Quad Volume (cm^3)	2237±351	1523±301	1374±207	991±180	Y>O; M>F
MRI Other Muscle volume (cm^3)	2309±431	1805±276	1537±238	1321±212	Y>O; M>F
DXA Thigh Fat Free Mass (kg)	6.33±0.74	5.03±0.85	4.01±0.5	3.55±0.45	Y>O; M>F
DXA Thigh Lean Mass (kg)	5.81±0.68	4.56±0.76	3.61±0.47	3.21±0.43	Y>O; M>F
DXA Thigh Fat Mass (kg)	2.06±1.02	2.43±1.04	2.91±1.09	3.10±0.98	M<F

Table 2. Fat free mass (DXA) was adjusted for bone mineral content[2]. Quadriceps Volume represented the sum of muscle volume for the four Quadriceps muscles including other muscle volumes of the hamstring, adductors and abductors in the region of interest. Significant differences between young and old, men and women; p<0.05.

tion was very strong (R^2=0.90, p<0.001), with a positive y-axis (DXA) intercept of 0.37 kg (Figure 2A). In older subjects, the correlation was also very strong (R^2=0.83, p<0.001), again, with a positive intercept on the y-axis (0.40 kg)(Figure 2B). This intercept is also evident in the Bland-Altman plot which illustrates that DXA overestimated muscle size in all conditions (Figure 3). The positive intercept on the y-axis (DXA) contributes a relatively larger proportion of the older muscle compared with young and as a consequence, DXA underestimates the difference of thigh muscle size between young and older participants in comparison to differences detected with MRI. In men, the MRI showed older thigh muscles to be 73.4%±11.2, while the DXA scan showed thigh lean mass of older men to be 79.5%±13.1 of young men (Figure 4). In women, the thigh muscle volume of older women measured using MRI was 79.4%±12.3 of young women, while the DXA-derived measurement showed older women to have thigh lean mass that was 88.6%±11.8 of younger women (Figure 4). The discrepancy between the MRI and DXA in determining the extent of the difference between young and old in muscle size was significant (p<0.001). There was no significant discrepancy between the MRI and DXA in determining muscle size differences between men and women (p=0.718, interaction p=0.268).

Quadriceps in relation to other muscles of the thigh

Quadriceps volume, determined from MRI serial axial-plane scans, showed the difference in volume between old and young men to be 1218 cm^3 and between young and old women to be 599 cm^3 (Table 2; p<0.001). When expressed as percentage of the young values the differences were 68% for older men and 72% for older women (Table 2). The other thigh muscles (knee flexors, hip abductors and adductors) were also smaller in old compared with young, although the extent of the difference was not as great as seen for the quadriceps. In older men, the "non-quadriceps" muscles of the thigh were 78% of young men while those of the older women were 86% of young women (Table 2). Thus, the proportion of the quadriceps to the total thigh muscle volume was significantly lower in old than young individuals (p<0.001).
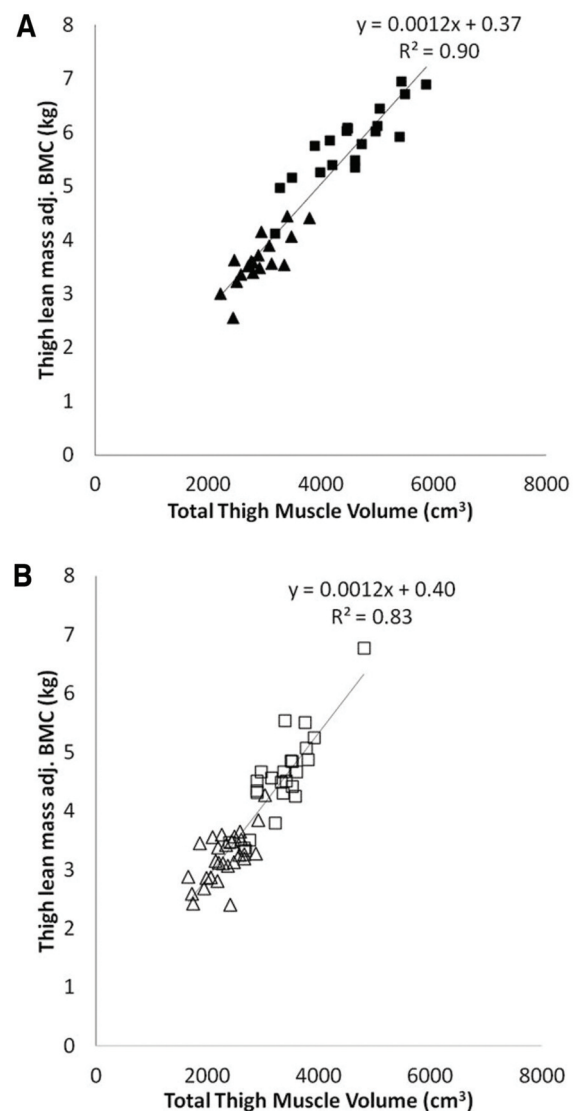

Figure 2. The relationship between total thigh muscle volume as assessed by magnetic resonance imaging and thigh lean mass as quantified by DXA. (**A**) Young men are depicted with filled squares, young women are represented by filled triangles. (**B**) Older men are depicted with open squares, older women are represented by open triangles.
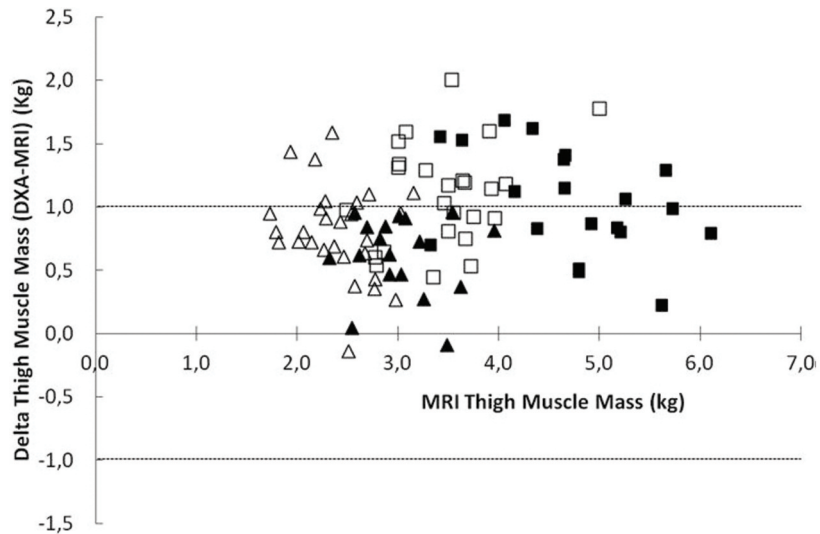
Figure 3. A Bland-Altman plot of thigh muscle mass determined with MRI on the x-axis and the difference between DXA-estimated muscle mass with MRI. Horizontal dotted lines represent one standard deviation above and below the average of MRI. Young men are depicted with filled squares, young women are represented by filled triangles. Older men are depicted with open squares, older women are represented by open triangles.
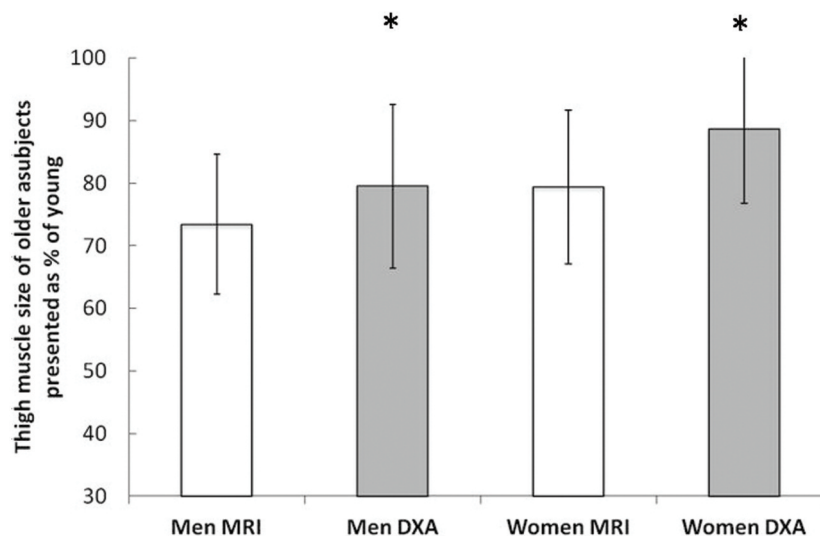

Figure 4. Muscle mass of older individuals expressed as % of young. * indicates significant difference between the DXA- and MRI-determined measurements of muscle size p<0.001.

Component muscles of the quadriceps

In Figures 5 & 6 it can be seen that each of the individual quadriceps muscles were smaller in old compared with young and for women compared with men (both p<0.001). The atrophy of the older muscle was evident across the entire muscle length, with the exception of the most proximal and distal muscle-tendon insertions.

In older women, the *rectus femoris* was more atrophied, at 37%, than the other three muscles (*medialis*, 23.5%; *intermedius*, 25.5%; *lateralis*, 29.6%) with the differences between

rectus femoris and *vastus intermedius* as well as between *rectus femoris* and *vastus medialis* being significant (p=0.01). In older men, there were no significant differences in the degree of atrophy between the individual Quadriceps muscles.

Discussion

Sarcopenia is associated with muscle weakness and mobility problems in old age. With the global rise in life expectancy
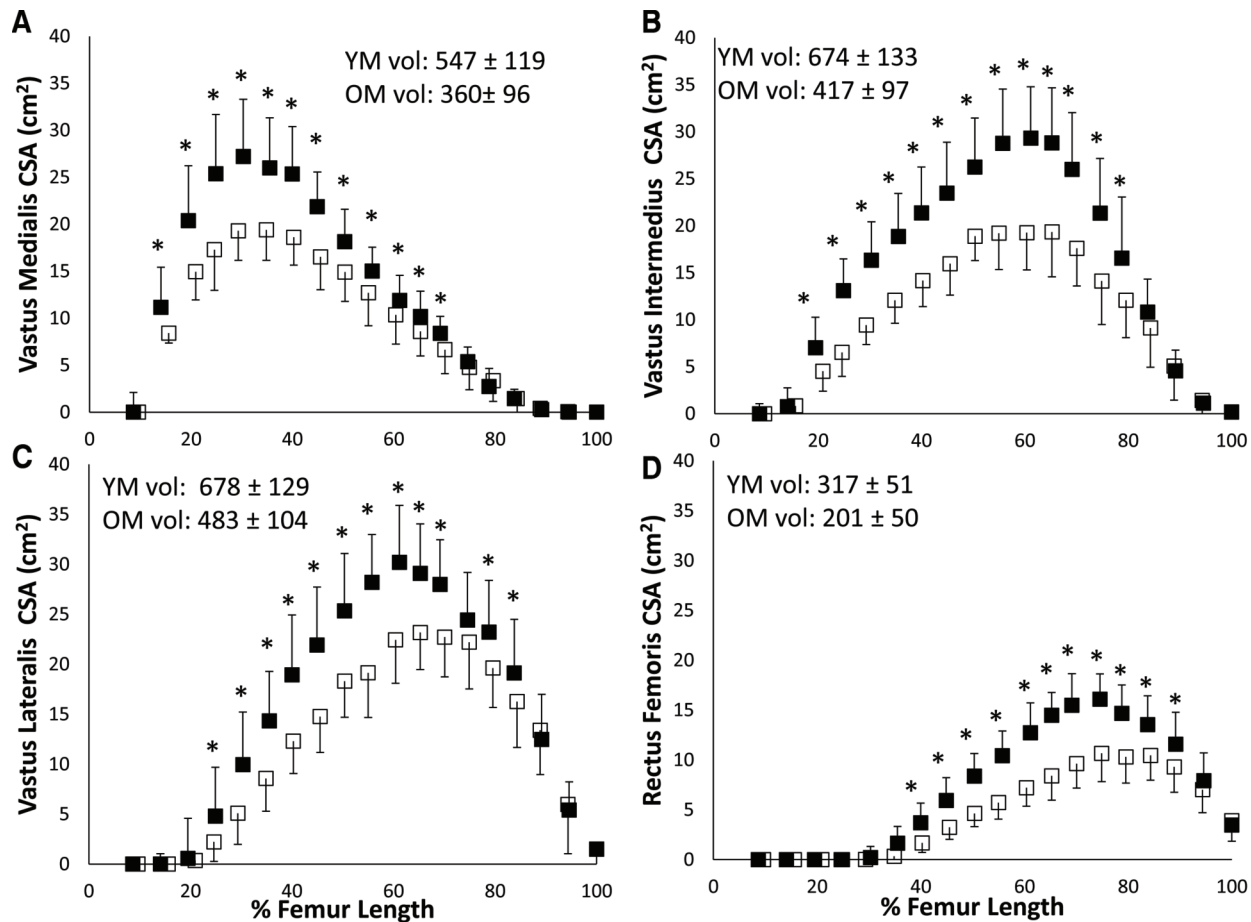
Figure 5. Cross sectional areas of the constituent muscles of the quadriceps along the length of the femur in men. Filled symbols represent young men, open symbols are older men. (**A**) *vastus medialis* (**B**) *vastus intermedius* (**C**) *vastus lateralis* (**D**) *rectus femoris*. *indicates a significant difference between young and old (p<0.05). The volume (cm³) is given for each muscle.

the need to understand the progression and causes of sarcopenia becomes more pressing. Dual-energy x-ray absorptiometry is often used in large clinical and epidemiological studies of sarcopenia. However, the results of the present study show that DXA underestimates the incidence of sarcopenia in thigh muscles compared with more detailed measurements derived from MRI. The major advantage of MRI over DXA is that it enables a distinction to be made between individual muscles. The detailed analysis of thigh muscle sizes in MRI revealed that the knee extensors are particularly susceptible to age-related atrophy (Table 2). The other muscles of the thigh (flexors, adductors and abductors) also experience loss of muscle mass with ageing, but to a significantly lesser extent than the quadriceps, especially in women. Our results also suggest that men are more affected by age-related muscle wasting than women.

The wide accessibility of DXA, with its low radiation dose, ease of use and better accuracy compared with most other common measurements, such as bioelectrical impedance, has enabled its use in large cohort studies of sarcopenia and body composition[7,21-25]. We observed a strong correlation between DXA and MRI measurements of thigh muscle size (Figure 2), similar to that reported in previous studies[4,8,9,13], suggesting that DXA can detect differences in muscle size between people. However the results from DXA showed a lesser degree of sarcopenia of the thigh muscles than when using MRI, with older muscle being 21% and 11% smaller than young in men and women, respectively, while MRI measurements were 27% and 21% smaller for older men and women, respectively (Figure 4). The reason for this disparity is evident from the data shown in Figure 2 where the regression line has an intercept of approximately 0.4 kg on the DXA axis. It is not clear why the positive intercept exists, but it is also evident in other similar studies[4,9,26]. The positive intercept makes up an increasingly large proportion of the total thigh mass of smaller muscles such as in the older people. Consequently, the tendency will be for DXA to underestimate the extent of sarcopenia. One possibility is that the algorithms used by the computer software (Prodigy, Encore 2006 v 10.50.086, GE healthcare) to obtain lean mass may need some adjustment, taking better account of the protein content of bone and fat tissue and the age-related changes in proportions of these non-muscle tissues.
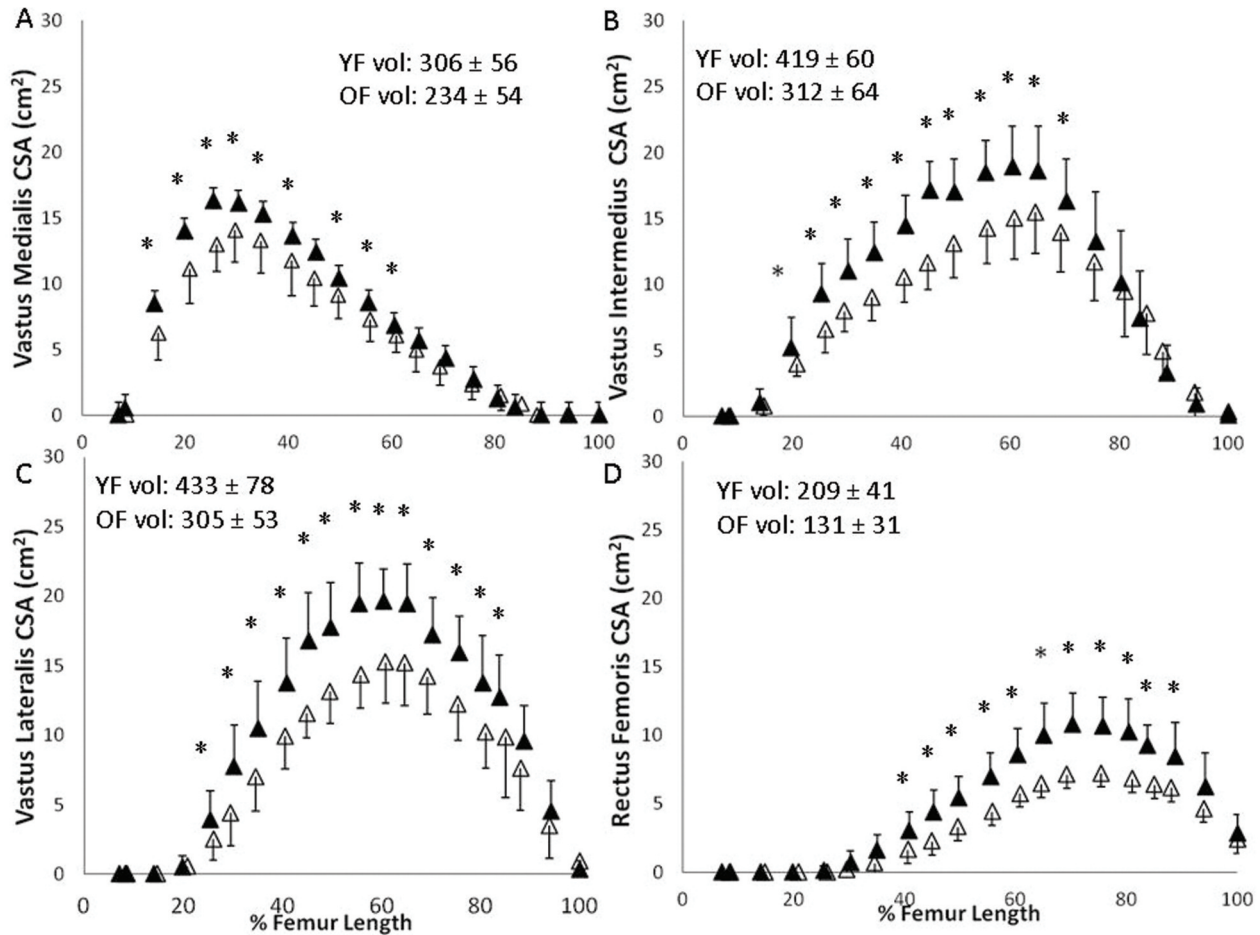
Figure 6. Cross sectional areas of the constituent muscles of the quadriceps along the length of the femur in women. Filled symbols represent young women and open symbols are older women. (**A**) *vastus medialis* (**B**) *vastus intermedius* (**C**) *vastus lateralis* (**D**) *rectus femoris*. *indicates a significant difference between young and old (p<0.05). The volume (cm³) is given for each muscle.

There are reports that the extent of muscle ageing may be greater in men than women[27,28], although others suggest women are affected more than men[29]. The discrepancy is most likely due to differences in the definition of sarcopenia, with some defining sarcopenia only as loss of muscle mass[30], others normalising lean mass to total body mass[6] or using muscle mass and function[31] (e.g. walking speed or strength). Our own results are not conclusive, but tend towards a greater loss of muscle in men (Figures 4 and 5). Changes to habitual physical activity levels as well as altered hormonal status will affect both men and women and contribute to loss of muscle size, but it is possible that the reduced testosterone experienced by older men removes the anabolic "advantage" seen in younger men and leads to relatively greater loss of muscle size[32].

In the MRI analysis, around 20 equidistant axial-plane cross-sectional slices from the most proximal insertion of *vastus medialis* through to the proximal origin of the *rectus femoris* on the anterior inferior iliac spine were analysed per subject. For every slice, the four individual quadriceps muscles were identified while all the other thigh muscles (knee flexors,

and hip adductors and abductors) were grouped together. The cost of MRI as well as the time needed to analyse images can restrict its use. If access is limited, our comprehensive analysis suggests that a single scan taken at 60% femur length (the distal lateral condyle being 0% and the proximal end at the greater trochanter being 100%) provides the optimal location to examine differences between groups. At 55-60% femur length the quadriceps cross-sectional area is largest. Of the thigh muscle groups, the quadriceps were affected most by age-related atrophy; in older men they were 32% smaller than those of young men and in older women they were 28% smaller than younger women. This difference of around 30% between young and old is similar to those reported in other studies that used MRI to measure muscle volume in young and elderly[33,34]. It is notable, however, that the other muscles of the thigh showed less of a difference between young and old. These muscles were 22% and 14% smaller for older men and women, respectively, compared to the younger subjects. It remains to be determined why the knee extensors should be more affected by ageing than other muscles of the thigh.

The quadriceps muscles have a complex anatomical arrangement; not only does the whole group consist of four muscles, but the *vastus lateralis* muscle, for instance, can be subdivided into 4 compartments, with each being innervated by individual nerve branches and having different fascicular arrangement[35]. The *rectus femoris* is bipennate and biarticular and the *vastus medialis* muscle belly is located more distally along the thigh length. The different portions of the quadriceps probably have slightly different functions and might thus be subjected to different metabolic or mechanical stimuli that affect muscle ageing. While each of the four quadriceps muscles was smaller in old than young participants, in older women the degree of atrophy in the *rectus femoris* was larger than that of the *vastus medialis* and *vastus intermedius*. However, in men, no differences were observed in the extent of age-related atrophy between different portions of the quadriceps.

Limitations

In some subjects it was difficult to distinguish between the *vastus medialis* and the *vastus lateralis* muscles in the MRI images of the proximal thigh, possibly due to fusion of these muscles, as seen in cadaveric specimens[35]. Furthermore, we were not able to clearly distinguish between hip abductor and adductor muscles and the knee flexors, so these muscles were grouped and labelled "other muscles". Therefore, we could not determine age or sex differences in these other muscles individually.

To enable a direct comparison between MRI-measured muscle volume (cm^3) and DXA-derived estimations of mass (kg), the MRI data was converted to mass using a previously reported conversion of 1.04 g.cm^{-3} [19]. A further correction was used to adjust DXA values to account for the non-mineral component of bone[2]. However, the bones of older people may have a higher non-mineral content than those from young people and this correction may thus result in an overestimation of muscle density in older age and hence underestimate the connective tissue and fat infiltration[36]. This, however, is not a major factor as conclusions remained even when the data were not adjusted for the non-mineral component of bone.

In conclusion, there was a good overall correlation between DXA and MRI-derived measurements of thigh lean mass. However, there was a discrepancy between the two methods when estimating the extent of age-related loss of muscle mass. Compared with MRI, the DXA underestimates the difference between young and old in thigh lean mass, which could lead to an underestimate of the loss of muscle mass with age. The MRI data indicate that the age-related decrease in muscle size was greater for the quadriceps than the other muscles of the thigh.

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