

Identifying more economical approaches to medical imaging for the rehabilitation of traumatic military injuries

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Abstract

The cost of National Health Service care for the 265 amputee casualties of British Operations in Afghanistan between 2003 and 2014 is projected to be £288 million [1]. This cost is due to the development of secondary comorbidities such as osteoporosis, type 2 diabetes, obesity, and cardiovascular disease. An independent and physically active lifestyle can benefit health and prevent these diseases. Physical activity is restricted following lower limb amputation due to a significant loss of muscle size and strength. There is also an increased risk of developing musculoskeletal injuries such as osteoarthritis, which is a further barrier to physical activity. This research aimed to evaluate and improve the time-efficiency of methods for analysing medical images to measure muscle size with an emphasis on their use in the rehabilitation of severe military injuries. Imaging modalities considered were Magnetic Resonance Imaging (MRI) and Brightness-mode (B-mode) ultrasound. The time demand of analysing MRI images was reduced by increasing the distance between analysed slices. Further reductions were observed when using a semi-automated method. The manual time requirement of both methods was considered too long for clinical use. B-mode ultrasound provided an instant measurement and is also valuable for the assessment of patients with metallic foreign objects such as shrapnel. A limitation of B-mode ultrasound is the inability to measure individual muscle size although this does not preclude its clinical use for physiotherapists and injury rehabilitators. The method described enables clinicians to measure muscle size and monitor changes throughout rehabilitation so that appropriate and timely modifications can be made.

Keywords

Magnetic resonance imaging, ultrasound imaging, muscle size, lower limb amputation, rehabilitation, clinical application

Introduction

Following the UK Military's involvement in Afghanistan between 2003 and 2014, 265 casualties suffered 416 amputations [1]. The projected cost of care for this cohort over a 40-year period is £288 million, inclusive of trauma management, rehabilitation and prosthetic provision [1]. The true cost will be realised over time as, due to the incomparable trauma care provided, this is the largest cohort to survive previously fatal injuries. Lower limb amputation in particular is associated with a number of comorbidities such as kidney and circulatory diseases [2], osteoporosis [3], osteoarthritis [4], and obesity [5], the risk of which can be reduced by maintaining a physically and occupationally independent and active lifestyle. The current cohort of military amputees will live much longer with these risks compared to the elderly dysvascular amputees generally found in civilian populations. This increases the risk of developing overuse and degenerative injuries when performing everyday tasks with altered movement mechanics [6]–[10].

Overuse and degenerative injury limit independence and can lead to a decline in quality of life and health. Military amputee rehabilitation aims to address this by providing strength to enable prosthetic walking, while optimising individual function, and providing psychological support, pain management, and social and vocational planning [11]. This process is informed primarily and justifiably by prior research of psychosocial and perceived functional outcomes. However, little information is available to support the design of strengthening interventions in amputee rehabilitation, with only seven studies available reporting measurements of strength in a representative population [12]–[18]. Strength is important for bodyweight support during locomotion and preventing degenerative injuries such as osteoarthritis and osteoporosis. Importantly, strength is closely associated with muscle size [19]–[22] and changes in muscle size can provide an early indication of ensuing pathologies such as hip osteoarthritis [23], [24]. Changes in muscle size following the initial injury and throughout the rehabilitation process can therefore provide useful information for the design of patient-specific rehabilitation programmes. At present, only one prior study has reported muscle size following lower limb amputation in a representative population [25], likely due to the time required to obtain such measurements. Indeed, the time required to obtain bilateral measurements of muscle size in a non-amputee

population has been reported as 25.0 hours [26]. A rapid and accessible method of measuring muscle size is in need of identification to facilitate the use of this measurement in rehabilitation.

Traumatic lower limb amputation is a significantly debilitating injury, typically occurring during military conflicts and affecting young males who were likely at the peak of their physical fitness at the time of injury. The exceptional support service available for this population is based on readily available evidence of the psychosocial and perceived functional outcomes. Similar evidence is not currently available for muscle function, likely due to the absence of an accessible method of quantifying muscle size. This research aimed to evaluate the time-efficiency of methods for analysing medical images to quantify muscle size, with an emphasis on clinical application. Specific objectives were; 1) to quantify the time demand and measurement reliability of manually analysing magnetic resonance imaging (MRI) images to measure muscle size, 2) to evaluate a semi-automated method for reducing the time demand of measuring individual muscle size using MRI images, and 3) to explore the application of ultrasound imaging for obtaining a rapid and straightforward measurement of muscle size.

Methods

Participants

Thirty-three healthy, physically active males participated in the research (age: 28.2 \pm 5.2 years, height: 1.81 \pm 0.08 m, body mass: 80.0 \pm 11.4 kg, body mass index: 24.4 \pm 2.7 kg/m²).

MRI image acquisition

Images were acquired using 3-Tesla MRI (Discovery MR750w, GE Healthcare). In 15 participants, images were acquired bilaterally from the iliac crest to the base of the foot in three or four scanning blocks of 58 to 100 slices depending on participant height. In 18 participants, images were acquired unilaterally from the 12th thoracic

vertebrae to the base of the foot in four or five scanning blocks of 34 to 86 slices depending on participant height. Lipid reference capsules were used to identify the point of overlap between blocks in the analysis. All images were 5 mm thick, with 0 mm spacing between slices. The field of view, flip angle, axial in-plane resolution, echo time, and repetition time were varied by the radiographer to obtain the best quality image for each participant in each image block and this did not implicate the image analysis (Table 1).

Table 1
MRI image acquisition parameters

	Bi-lateral images (n = 15)	Unilateral images (n = 18)
Acquisition start	Iliac crest	12 th thoracic vertebrae
Acquisition end	Base of the foot	Base of the foot
Number of image blocks	3 to 4	4 to 5
Field of view	512 mm ²	144 mm ² to 450 mm ²
Axial in-plane resolution	0.47 mm ² to 0.92 mm ²	0.39 mm ² to 0.88 mm ²
Flip angle	111°	90 to 111°
Slice thickness	5 mm	5 mm
Inter-slice spacing	0 mm	0 mm
Echo time (TE)	7.248 to 7.968 ms	7.456 to 16.940 ms
Repetition time (TR)	506 to 850 ms	533 to 845 ms
Acquisition time (per block)	4 to 6 minutes	4 to 6 minutes

Manual analysis of MRI images

All MRI images were manually analysed in OsiriX Lite (v.8.0.1, Pixmeo) open source software by a single experienced investigator. The brightness and zoom were modified as necessary to improve tissue contrast and enable muscle boundaries to be identified clearly. The boundaries of the individual hip extensor, knee extensor and flexor, and ankle plantarflexor muscles were manually outlined on every slice (i.e. every 5 mm) and every third slice (i.e. every 15 mm) in three participants, using an online anatomical resource where required [27], to evaluate a method for reducing the time

demand of manual analysis. The analysis for all 15 participants was conducted using an inter-slice distance of 15 mm, and for two participants the analysis was repeated after seven days to evaluate between-session measurement reliability. The resulting cross-sectional area (CSA) measurements (in cm²) were used to estimate MV, using the formula:

$$\sum_{i=1}^{n-1} \left(\frac{CSA_i + CSA_{i+1}}{2} \right) \times h$$

Where CSA_i is CSA at slice i , CSA_{i+1} is CSA at slice $i + 1$, h = distance between slices, n = total number of analysed slices in the muscle.

Semi-automated analysis of MRI images

Semi-automated analysis was conducted in Mimics® Research 21.0 (Materialise N.V.) software. The algorithm followed is shown in Figure 1. MRI images were registered in the software, a mask was manually created using greyscale thresholding, and a gradient magnitude filtering threshold was manually identified and applied to isolate muscle tissue only. Additional manual editing was required to prepare the masks for input into the automated muscle segmentation tool. The muscle segmentation tool registered each of 10 reference atlases (five males and five females, ranging from 23 to 60 years of age, 1.60 to 1.95 m in height, and 55.5 to 91.7 kg in body mass) and two manually created reference atlases (representative of the group for: 1. body mass index, and 2. height) on the test image using non-rigid transformation. The best matching reference atlas was used to assign voxels to individual muscles. Individual muscle masks were output and used to calculate the three-dimensional shape and volume of each muscle. Manual mask preparation required 3.0 hours per leg, and the muscle segmentation tool required between 0.9 and 3.1 hours of computational processing. The time taken to create one manual reference atlas was 12.0 hours.

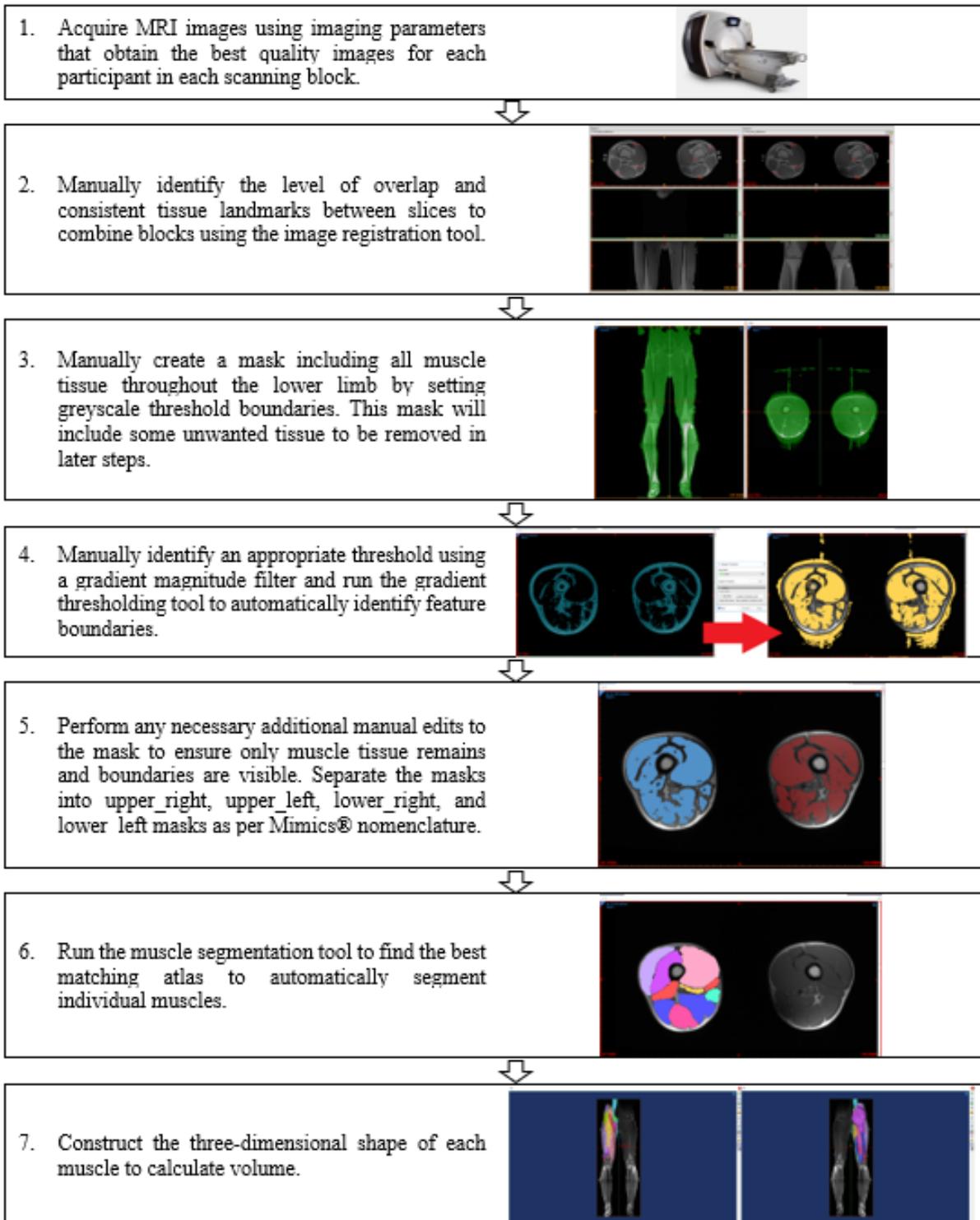


Figure 1
Semi-automated MRI image analysis algorithm.

Ultrasound image acquisition

After measuring body mass, height, and thigh and shank length, participants (n = 18) lay at rest while images were acquired by a single investigator at the mid-hip, 25%, 50%, and 75% of thigh length, and 25% of shank length using a Logiq E9 ultrasound scanner (GE Healthcare) with a 44 mm, 2 to 8 MHz 9L linear-array transducer. The transducer was coated in water-soluble transmission gel, enabling acoustic contact without depression of the underlying tissue. Images were reviewed on the ultrasound machine visual display and repeated when necessary to ensure measurements could be made in post-processing. Image acquisition required under 60 seconds per measurement site.

Analysis of ultrasound images

Using OsiriX Lite software, muscle thickness (MT) measurements were taken at each of the measurement sites, and for individual muscles where possible, by manually drawing two parallel lines perpendicular to a straight line on the superficial aponeurosis of each muscle, extending to the deep aponeurosis (Figure 2). The mean value of the length of the two perpendicular lines was taken as MT (in cm). Each MT measurement was acquired in under 30 seconds. The images acquired at 25% of shank length had sufficient resolution for CSA measurements (cm²) to be made for the medial and lateral gastrocnemii. Regression models were developed (described below) to estimate the volume of the hip extensor, knee extensor and flexor, and ankle plantarflexor muscle groups from MT, CSA, and anthropometric measurements.

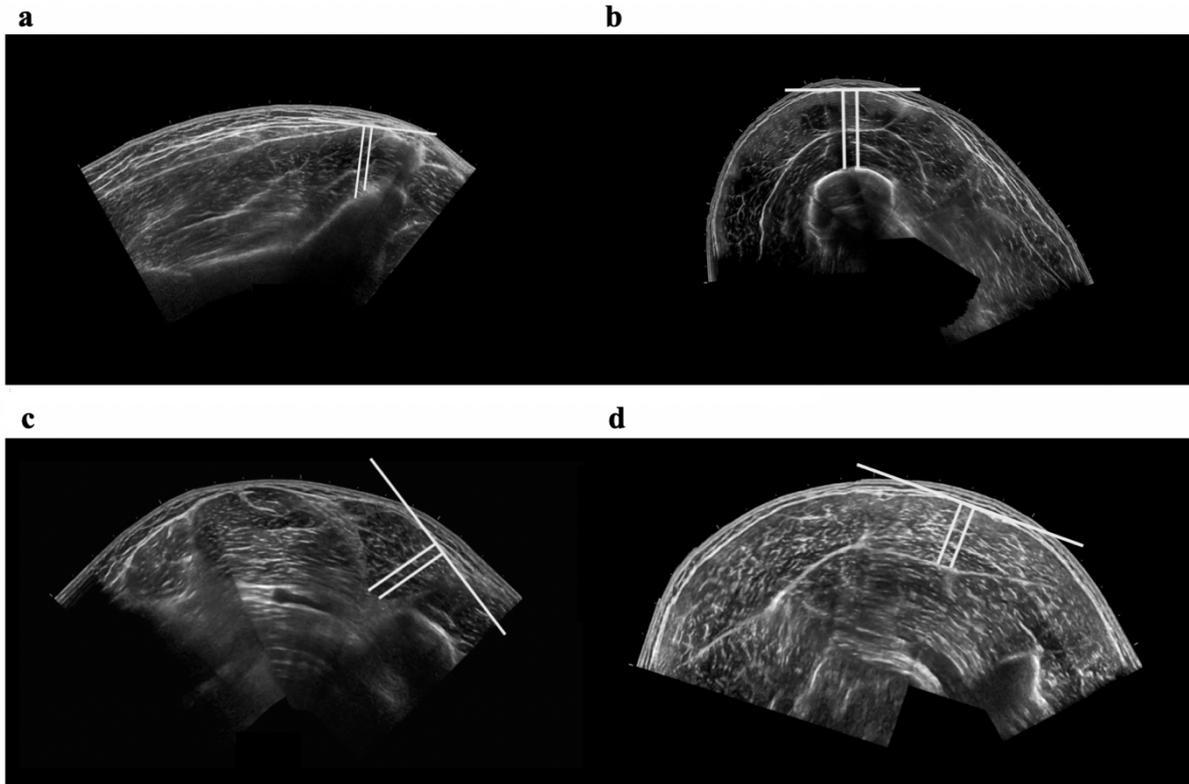


Figure 2
 Ultrasound muscle thickness measurements of; a) the gluteals, b) 50% anterior thigh, c) 75% posterior thigh, and d) 25% posterior shank.

Statistical analysis

The reliability of manual MRI image analysis was evaluated using absolute percentage differences, typical error of measurement (TEM), and two-way mixed measures single intra-class correlation coefficients (ICC). The absolute percentage difference was calculated for the difference between manual and semi-automated MRI muscle volume estimation methods.

The regression analysis was conducted in SPSS Statistics 23 (IBM Corporation) using MT, CSA, and anthropometric measurements. Semi-partial and bivariate correlation analyses were used to identify redundant variables which were excluded. A *k*-fold leave one out cross-validation regression analysis was conducted using an 80% subsample to estimate the MRI criterion muscle volume of the hip extensor, knee extensor and flexor, and ankle plantarflexor groups. Independent variables that were present in

all of the k -fold analyses were used in a forced entry regression analysis of all participants in the 80% sub-sample to identify the final model. The final model was cross validated using the remaining 20% sub-sample. Standard error of the estimate (SEE) was used to determine the accuracy of the models developed. Systematic error was evaluated by plotting the mean against the residuals [28].

Results

Manual MRI time demand and measurement reliability

The time demand of manually analysing MRI images was 24.0 hours when every slice was included, and 8.0 hours when every third slice was used, with minimal differences observed between methods (mean difference = $0.7 \pm 0.7\%$). Good between-session reliability was observed with high ICC, and low TEM and percentage differences (ICC > 0.99, TEM = 14.3 cm^3 , 1.0%, mean absolute difference = $5.1 \pm 5.6\%$).

Manual versus semi-automated MRI analysis

The mean difference between manual and semi-automated methods was 11.1%, requiring 4.2 hours analysis time (3.0 hours manual and 1.2 hours computational processing).

Ultrasound prediction models

The model developed for the hip extensors did not use a MT measurement and included body mass and thigh length only (Table 2). MT measurements were included in the models developed for the knee extensors and flexors, and CSA was included in the ankle plantarflexor model (Table 2). Body mass was included in the knee extensor and ankle plantarflexor models and thigh length was included in the knee flexor model. Statistically significant positive trends were observed for the plot of residuals versus mean for the knee flexors and ankle plantarflexors (Figure 3).

Table 2
Ultrasound prediction models [29].

Muscle group	Equation	Standard error of the estimate (SEE, cm ³ , %)
Hip extensors	1087.037 + (64.946 * body mass.thigh length)	283.01 (8.92%)
Knee extensors	996.168 + (4.664 * anterior thigh MT at 50% of thigh length.body mass)	121.10 (5.24%)
Knee flexors	1199.444 + (318.147 * biceps femoris short head MT at 75% of thigh length.thigh length)	125.37 (7.89%)
Ankle plantarflexors	878.606 + (0.553 * lateral gastrocnemius CSA at 25% of shank length.body mass)	134.91 (10.78%)

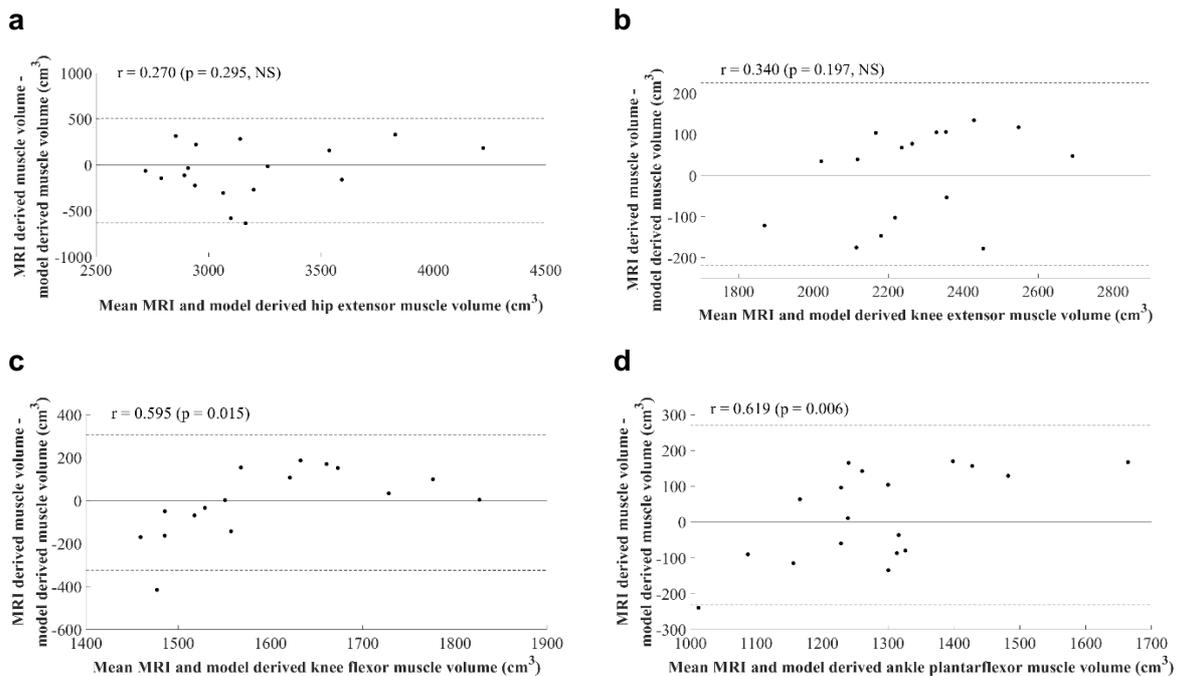


Figure 3
Plots of residuals versus mean for the ultrasound models; a) hip extensors, b) knee extensors, c) knee flexors, d) ankle plantarflexors. Images from [29].

Discussion

This research evaluated the time-efficiency of methods for analysing medical images to quantify muscle size, with an emphasis on clinical application. The time demand of manually analysing MRI images was reduced by three-fold when increasing the distance between slices from 5 mm to 15 mm, without impacting on measurement accuracy, and showing good between-session reliability. Semi-automated software reduced the time demand to approximately half although the 3.0 hours manual analysis time necessary for preparing the input masks remained a limitation to clinical application. The ultrasound prediction models developed were rapid (i.e. almost instantaneous) and straightforward to acquire and could be used in a clinical environment to monitor changes in muscle size.

The time taken to estimate the volume of the individual hip extensor, knee extensor and flexor, and ankle plantarflexor muscles was 8.0 hours when analysing every third slice (i.e. every 15 mm), compared to 24.0 hours when analysing every slice (i.e. every 5 mm). The difference between methods was small (mean difference = $0.7 \pm 0.7\%$), supporting this approach. The time taken to analyse these key muscle groups may be suitable in a research environment, allowing one participant to be analysed per day, but is not clinically useful. The inter-slice distance could potentially be increased further to elicit a reduction in the analysis time. However, based on the current findings, to achieve a clinically reasonable time demand of 1.0 hour, an inter-slice distance of 120 mm would be required. This may be an effective approach for muscles with relatively consistent shape throughout length, such as the quadriceps and hamstrings, but would implicate the measurement of smaller muscles such as the gastrocnemii, popliteus, and gluteus minimus and medius. These muscles would be measured by no more than three slices with a 120 mm inter-slice distance, disregarding changes in muscle geometry throughout length, and leading to an inaccurate measurement. This would also be the case for smaller individuals, and lower limb amputees where muscles are unstructured and shortened as a result of the injury and subsequent surgical interventions.

A significant reduction in the time taken to measure individual muscle volumes was achieved with the semi-automated method. The same measurements previously requiring 8.0 hours of manual analysis were obtained with 3.0 hours of manual analysis, plus 1.2 hours of computational processing. This time requirement remains excessive for clinical application but can more than double the number of analyses possible per day in a research environment. The main limitation to the semi-automated method is the manual time demand, and further improvement is required to facilitate a fully automated analysis, with methods such as feature extraction for identifying boundaries [30], and machine learning to classify voxels being worthy of exploration. In addition, the application of this method, and the time required to do so, should be evaluated in an amputee population where additional manual work will be necessary to quantify muscle size in the significantly altered residual limb. The large difference observed between semi-automated and manual methods (mean difference = 11.1%) precludes the interchangeability of the two, although the measurement reliability of the semi-automated method should be evaluated to determine its use as a clinical tool.

The size of four key lower limb muscle groups was obtained using ultrasound imaging in under five minutes, making this a clinically useful tool. The regression models developed showed sufficient accuracy to identify changes in muscle size of the hip extensors in unilateral transfemoral amputees compared to the intact limb [25], the knee extensors and flexors in Type 2 diabetes patients compared to controls [31], and the ankle plantarflexors in chronic ankle instability patients compared to controls [19]. The inclusion of body mass in the hip and knee extensor and ankle plantarflexor models highlights the role that these muscle groups play in supporting body mass during weight bearing activities. On the other hand, the knee flexors originate on the pelvis and attach to the tibia and are thus closely associated with thigh length, which was included in the model developed. One limitation of ultrasound imaging is the inability to measure individual muscle sizes, which is of clinical importance for populations such as lower limb amputees. This requires significant improvements in ultrasound imaging technology to improve image resolution. In addition, the method established in this research should be evaluated in a clinical population to determine its utility, and the residual limb is likely to be a challenge to establishing a method with high external validity.

Conclusion

This research evaluated the time-efficiency of methods for measuring muscle size from medical images and considered their clinical application. Semi-automated analysis of MRI images is much faster than manual analysis, although large differences exist between methods (mean difference = 11.1%). The semi-automated method is the most time-efficient for estimating individual muscle volumes and measurement reliability is currently being evaluated to determine its clinical utility. Ultrasound imaging provided the most rapid measurement of muscle size, although this is presently limited to muscle groups and further technological improvements are required to obtain individual muscle volume measurements. At present, a clinically applicable method of measuring and monitoring changes in muscle size can be achieved in under five minutes using B-mode ultrasound imaging. Future work is planned and a MoDREC application is currently under SAC review to evaluate this and the semi-automated MRI image analysis method in a population of young, military, lower limb amputees.

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