Automatic Segmentation of Thigh Muscle in Longitudinal 3D T1-Weighted Magnetic Resonance (MR) Images

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Abstract. The quantification of muscle mass is important in clinical populations with chronic paralysis, cachexia, and sarcopenia. This is especially true when testing interventions which are designed to maintain or improve muscle mass. The purpose of this paper is to report on an automated method of MRI-based thigh muscle segmentation framework that minimizes longitudinal deviation by using femur segmentation as a reference in a two-phase registration. Imaging data from seven patients with severe multiple sclerosis who had undergone MRI scans at multiple time points were used to develop and validate our method. The proposed framework results in robust, automated co-registration between baseline and follow up scans, and generates a reliable thigh muscle mask that excludes intramuscular fat.

1 Introduction

Multiple sclerosis (MS) is an inflammatory disease of the central nervous system that can affect electrical conduction in axons in the brain, spinal cord, and optic nerves [3]. The clinical manifestations are partly driven by the location of focal inflammatory lesions and include paralysis/paresis, spasticity, fatigue, cognitive impairment, and sphincter dysfunction.

Regular exercise may benefit patients with MS, primarily by ameliorating deconditioning associated with disability. However, disability associated with advanced disease (Expanded Disability Status Scale (EDSS) of 7.0 or more) impedes regular exercise in this patient cohort [11,12]. Previous exercise interventions in patients with advanced MS have been short-term and largely limited

to arm exercise. Recently, studies have begun to investigate the potential of electrical stimulation and other treatments to maintain leg muscle mass. To assess the efficacy of these treatments in MS, a precise and accurate quantification of limb muscle mass change is critical.

In this study, we assessed the change in longitudinal thigh muscle volume in patients with advanced MS undergoing an exercise regime based on a modified version of NMES (Neuromuscular Electrical Stimulation) cycling [5,6]. This work describes an automated segmentation pipeline to rapidly quantitate lean thigh muscle volume, and accurately estimate change over time.

Previously described methods for segmenting thigh muscle volume from MR images have utilised semi-automated approaches, including threshold algorithms and model matching techniques [2,9]. More recently, semantic segmentation has become a popular approach for solving computer vision problems; and attempts have been made to segment muscle masks from MR images with deep learning based algorithms [1]. However, these models normally do not take the intramuscular fat of subject into account. Additionally, longitudinal changes in thigh muscle ROIs (regions of interest) have been seldom studied, and most published methods [4,10,13] employ cross-sectional segmentation without indicating the method of alignment of ROIs between baseline and follow-up images.

Hence, we propose an automated segmentation framework to rapidly and accurately quantitate longitudinal change in thigh muscle volume from MR images. The framework uses a novel two-phase registration method to strictly align the relevant ROIs between baseline and follow-up; and has been evaluated in 7 subjects. Our results indicate that the proposed method achieves a consistent geometric alignment in longitudinal MR thigh images in terms of Complex Wavelet Structural Similarity Image Metric (CW-SSIM).

2   Method

The proposed automated longitudinal thigh muscle segmentation framework is shown in Fig. 1. Any number of 3D T1-weighted MR images of both left and right thighs are used as the input to generate the corresponding muscle segmentation masks. To facilitate comparative analysis, region of interest (ROI) is defined by the analyst based on the anatomical landmarks and extends from the axial slice immediately superior to the patella to the inferior border of the gluteus maximus muscle. The pipeline only requires the analyst to select these two ROI endpoints on the baseline scan.

To maintain longitudinal coherence, the femur, which remains morphologically stable over time, is segmented at each time point. A two-phase process is used to co-register follow-up to baseline images and derive follow up ROIs in the baseline space. Inhomogeneity correction, thresholding and morphological processing are then applied to generate the final thigh muscle masks. The details is described as follow.
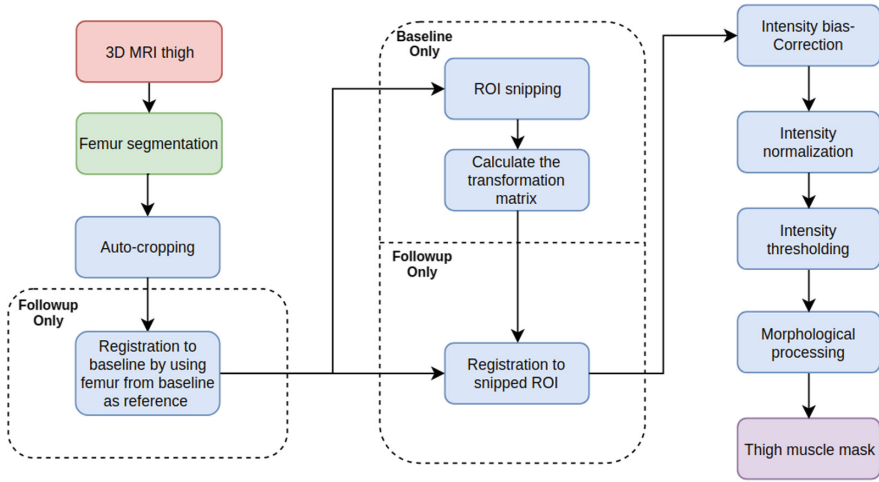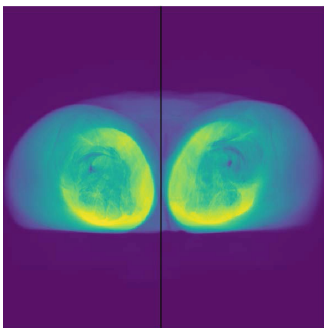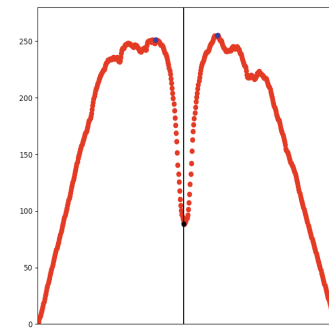
Fig. 1. Overall workflow for longitudinal thigh muscle segmentation. The raw input comprises 3D T1-weighted MR images of bilateral thighs; the pipeline outputs corresponding thigh muscle masks.

(a) Input 3D MRI thigh image

(b) Projection of input 3D MRI thigh image to axial plane

(c) Mean intensity values along sagittal plane

Fig. 2. Automated division of left and right thighs in the sagittal plane.

2.1   Cropping

The input data for each patient/scan contains both thighs, and their relative position is slightly different at each time point. Direct co-registration between baseline and follow-up will lead to an inaccurate rigid alignment result. In our pipeline, thigh muscle analysis is performed separately for left and right thighs. To achieve this, as shown in Fig. 2(b), each 3D image is firstly projected to the axial plane by averaging the voxels along the superior-inferior direction, and then further averaged to L-R line to obtain the mean intensity profile as shown in Fig. 2(c). The 3D MR thigh image is divided into left and right thigh (black line, Fig. 2(c)) in the sagittal plane, located automatically by the interpeak nadir in the associated intensity plot.

2.2   Two-Phase Registration

External deformation of muscle during scanning, or longitudinal change in muscle morphology hampers geometric alignment and accurate co-registration of baseline and follow up 3D thigh images. This is a critical step when calculating volumetric change of a ROI over time. We use a modified form of FLIRT [7] for the registration in our framework. FLIRT was originally designed for longitudinal brain registration, and is based on determining the transformation (T^*) that minimizes the intensity-based cost function:

$$T^* = arg \min_{T \in S_T} C(BL, T(FU)), \tag{1}$$

where BL and FU represent for baseline (reference) and follow-up respectively, $T(FU)$ represents for the transformed FU, S_T is the set of all affine transformations and $C(X, Y)$ is the cost function. Here we use the correlation ratio (CR) [8] as the cost function:

$$C(BL, T(FU)) = \frac{1}{Var(BL)} \sum_k \frac{n_k}{N} Var(BL_k). \tag{2}$$

When applied in this study, the default registration uses the whole thigh as the reference target. Unlike soft tissues, changes in bone morphology are negligible over the observation period; we therefore elect to define the femur as the reference target and propose a two-phase registration process: in the first phase, the transformation T_{femur}, is derived and "BL" and "FU" in Eqs. (1) and (2) are replaced with "BL_{femur}" and "FU_{femur}" respectively. T_{femur} is then applied to FU to obtain the FU_{reg}. Since we snip the ROI of the thigh along inferior-superior direction on the baseline image, the same measurement area along the thigh at follow-up is obtained by aligning the BL_{ROI} to FU_{reg}.

Figure 3 demonstrates scenarios where the use of the whole thigh as the registration reference fails to align the follow-ups with the baseline due to: (1) morphological change of muscle and fat (Fig. 3(a)); and (2) absence of distal thigh in the image (Fig. 3(b)).
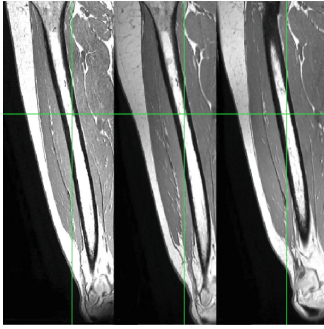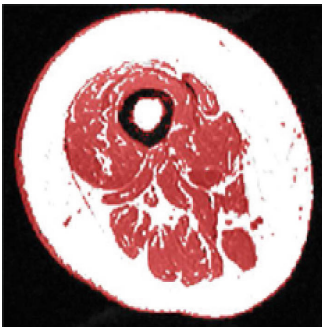
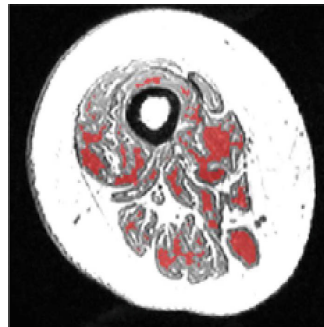(a) A subject with massive increase of muscle volume
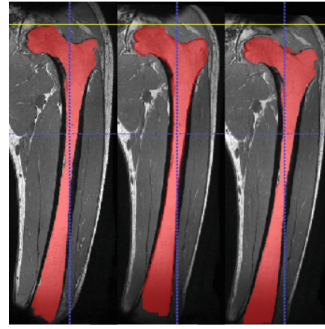
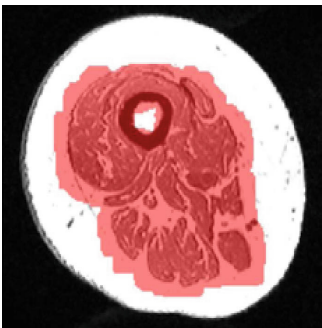(b) A subject with the bottom end of femur missing

Fig. 3. Comparison of registration results in different scenarios (from left to right): baseline, registration using femur as reference and registration without using femur as reference.
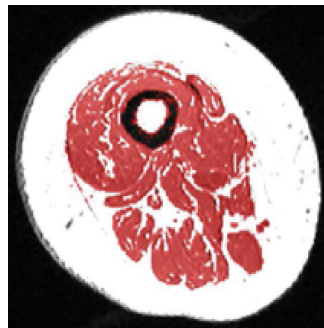

(a) Threshold mask

(b) Erosion

(c) Dilation

(d) Final mask

Fig. 4. The intermediate steps of morphological processing.

2.3   Inhomogeneity Correction and Normalization

Inherent intensity inhomogeneity in MR images requires correction before a fixed threshold is applied for the segmentation of muscle from ROIs. In our pipeline, N4 [16], an improved version of the N3 framework [15], was used. N4 achieves the result by feeding the input image iteratively into a smoothing operator which contains a B-spline approximator.

2.4   Morphological Processing

After intensity inhomogeneity-correction and normalization, a fixed intensity threshold is used to segment the thigh muscle from surrounding tissues and differentiate the muscle from the intramuscular fat. To eliminate the noisy "ring" between the outer boundary of thigh and the background, and also the border between the femur and the thigh muscle, we perform following morphological process: first performing an opening of the threshold mask then take its intersection with the original mask. The demonstration of intermediate steps is shown in Fig. 4.

3   Experimental Results

Seven participants (five females and two males) with progressive MS (median age: 55 ± 6 years old, EDSS: 7.3 ± 0.6, patients with this level of EDSS lose majority of their mobility functions) were recruited for this study from a multidisciplinary MS clinic. Participants were asked to maintain with their usual activity and exercise routines in the first 12 weeks (control period) of the study; they undertook NMES leg cycling exercises three times per week during the second 12 week study epoch. In order to obtain consistent and reliable femur imaging, patients with following scenarios were not included in the analysis: (a) inability to lie in a standard position, (b) hip replacement and (c) severe spasticity.

MRI scans (both thighs) were acquired at the time of enrolment (baseline; week 0), following the 12 week control period, and post 12 weeks of NMES training (week 24). Additionally, long-term data was acquired from two patients. In summary, 21 MRI exams (7 baseline, 7 mid-study and 7 post-NMES) were acquired on a GE Discovery MR750 Scanner with 32-channel torso coil. All subjects were scanned with a 3DT1 sequence (IRFSPGR, TE = 2.7 ms, TR = 6.5 ms, acquisition metrix = 480×480, Slice thickness = 1 mm).

For qualitative evaluation of the co-registration between baseline and followups, Complex Wavelet Structural Similarity Image Metric (CW-SSIM) was computed as previously described [14]. Based on CW-SSIM score, our method yielded a higher similarity between baseline femur and femur on the co-registered followups as shown in Table 1.

Table 1. Similarities between the baseline femur and femur on the co-registered follow-ups.

Subject	FLIRT	Proposed
Subject1	0.2073 ± 0.0227	0.2109 ± 0.0218
Subject2	0.2265 ± 0.0373	0.2315 ± 0.0374
Subject3	0.2303 ± 0.0392	0.2577 ± 0.0330
Subject4	0.2133 ± 0.0210	0.2165 ± 0.0201
Subject5	0.2693 ± 0.0027	0.3338 ± 0.0089
Subject6	0.2002 ± 0.0199	0.2451 ± 0.0165
Subject7	0.1145 ± 0.0497	0.1503 ± 0.0466

4   Conclusion

In this paper, we propose an automated longitudinal thigh muscle segmentation framework to calculate muscle volume change over time to assess the treatment effect. The technique can be potentially modified to sample upper arm musculature, and is ideally suited to applications requiring calculation of longitudinal changes in lean muscle mass. Femur-based co-registration minimised registration error and resulted in improved baseline to follow up image alignment, as measured by CW-SSIM. Low longitudinal measurement error and automation suggest that our technique will be suited to future inclusion in large clinical trials, both in the physical therapy and pharmacotherapy domains.

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