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A comprehensive study on automated muscle segmentation for assessing fat infiltration in neuromuscular diseases

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ABSTRACT

Severity and progression of degenerative neuromuscular diseases can be sensitively captured by evaluating the fat infiltration of muscle tissue in T1-weighted MRI scans of human limbs. For computing the fat fraction, the original muscle needs to be first separated from other tissue.

Five conceptionally different approaches were investigated and evaluated with respect to the segmentation of muscles of human thighs. Besides a rather basic thresholding approach, local (level set) as well as global (graph cut) energy-minimizing segmentation approaches with and without a shape prior energy term were examined. For experimental evaluations, a dataset containing 37 subjects was divided into four classes according to the degree of fat infiltration.

Results show that the choice of the best method depends on the severity of fat infiltration. In severe cases, the best results were obtained with shape prior based graph cuts, whereas in marginal cases thresholding was sufficient. With the best approach, the worst-case error in fat fraction computation was always below 11% and on average between 2% for tissue showing no fat infiltrations and 6% for heavily infiltrated tissue. The obtained Dice similarity coefficients, measuring the segmentation quality, were on average between 0.85 and 0.92.

Although segmentation of heavily infiltrated muscle tissue is extremely difficult, an approach for reasonably segmenting these image data was identified. Especially the negative impact on the calculated fat fraction can be reduced significantly.

1. Introduction

Neuromuscular disease is a collective term that describes disorders in the motor function unit, such as hereditary or inflammatory myopathies and neuropathies, motor neuron disorders and neuromuscular junction diseases.

For assessment of neuromuscular diseases, established approaches exist, such as the Medical Research Council (MRC) sum score [9] and the Neuropathy Impairment Score [14], relying on judgement by an expert or by patient's impressions. A further commonly used method relies on hand-held or fixed myometry by force measurements, which is quite objective but becomes difficult and loses sensitivity in later stages of different neuromuscular diseases [29].

Though very important for clinical practice and study outcomes, functional testing cannot reveal the underlying anatomical and morphological changes in muscles, which can routinely be visualized by muscle MRI.

Driven by the demand for more objective disease markers, MRI has been increasingly utilized for the assessment of neuromuscular diseases. Recently, numerous methods have been proposed to extract markers from MRI scans for assessment of certain myopathies based on different visual scores [1,10,11,15,20,25,26,28,34,35].

Although relying on image data, most approaches still contain processing steps which are conducted manually. Lareau-Trudel et al. [25] for example performed manual segmentation of muscle tissue in case of severely affected subjects while in most other literature, segmentation was performed fully manually [10,15,20,28]. The grading system proposed by Mercuri et al. [26] is completely based on visual inspection of MRI scans.

This visual semi-quantitative analysis, however, is still subjective and time consuming which thereby provides a strong incentive for the development of fully-automated observer-independent methods for processing the MRI data [10].

This work focuses on the so-called fat fraction [28] computed on thigh MRIs, which proved to provide a high sensitivity for assessing disease progression of neuromuscular diseases. This measure is defined

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as the ratio between fat-infiltrated muscle tissue and overall muscle tissue and exhibits a single metric extracted from 3D MRI data for assessment, diagnosis and research. The fat-fraction in muscle tissue is not only relevant for assessing neuromuscular diseases, but is also used for investigations of other diseases such as low back pain [19,23,36] and traumatic neck pain [1,15,20]. It was suggested that the fat fraction should be calculated on the complete 3D muscle tissue instead of single 2D slices to gain additional information [28,38] providing a further incentive for developing automated methods.

The first essential step in computing the fat fraction is to segment the original muscle tissue to primarily separate it from bone and subcutaneous fat tissue. However, a manual segmentation, especially if the complete 3D image is considered, is highly time consuming and is furthermore subject to significant interobserver variability [10,27] providing motivation for the development of automated segmentation methods.

1.1. Related work

There is comparatively little literature on muscle segmentation of MRI scans of thighs showing pathological muscle tissue. Lareau-Trudel et al. [25] applied a rather basic segmentation method, originally developed for the assessment of persons classified as obese [31], to patients with facioscapulohumeral muscular dystrophy. In a first step, k-means clustering was utilized to discriminate between three tissue classes. Subsequently, the boundaries were determined by applying the active contours (snakes) approach [22]. The proposed method failed in 20% of the slices. Especially when the fat fraction is high, snakes are unable to reliably determine the muscle's boundary as the border between fat-infiltrated muscle and fat tissue cannot be effectively detected by edge-based active contours without relying on a shape model. Although a manual correction of 20% of the cases saves time (compared to a completely manual segmentation), the approach is still subject to interobserver variability which is supposed to be particularly distinct for highly-affected subjects [27].

Essafi et al. [16,17] investigated the problem of segmenting the medial gastocnemius muscle (of the calf) in T1-MRI images for healthy and diseased subjects is tackled. This problem definition is more difficult compared to Lareau-Trudel et al. [25] where muscle is considered as one single class. The goal of the proposed algorithm is to find landmark positions based on local texture features combined with shape knowledge. Geometrical information was inserted by means of diffusion wavelets. By applying a hierarchical diffusion operator, wavelet coefficients were gained for each individual training shape. Subsequently, the dimensionality of these coefficients was reduced by principle component analysis [16] or by means of the orthomax method [17]. Unfortunately, in both studies [16,17], the results were not separately assessed for healthy and pathological cases. Therefore, the performance of the approach for pathological cases is difficult to assess. A mean landmark error of approximately 12 voxels [17] and a Dice similarity coefficient (DSC) of 0.55 [16] indicate that the method is not robust enough to process data showing highly affected muscle tissue. In further approaches, focus was on detecting the fascia lata [24,39] (tissue inside the fascia lata was labelled as muscle) which allows a rough localization of muscle tissue, but not a completely accurate segmentation.

Further segmentation approaches were developed and evaluated for healthy muscle tissue, or for tissue showing at least no distinct fat infiltration, leading to a completely different segmentation task. Orgiu et al. and Positano et al. [30,31] proposed a method based on active contours for segmenting MRI scans of human thighs. Baudin et al. [3,4] developed approaches for segmenting healthy muscle tissue in the thighs by means of random walks. A further approach relying on a PCA-based shape prior for separately segmenting single thigh muscles was proposed by Andrews et al. [2]. The considered data set contains both healthy and pathological cases, however only muscle deformation and no fat infiltration occurs. Gilles and Pai [18] proposed an atlas-based approach for segmenting muscles in healthy thighs. Karlsson et al. [21] evaluated whole-body muscle segmentation method by applying a multi-atlas approach.

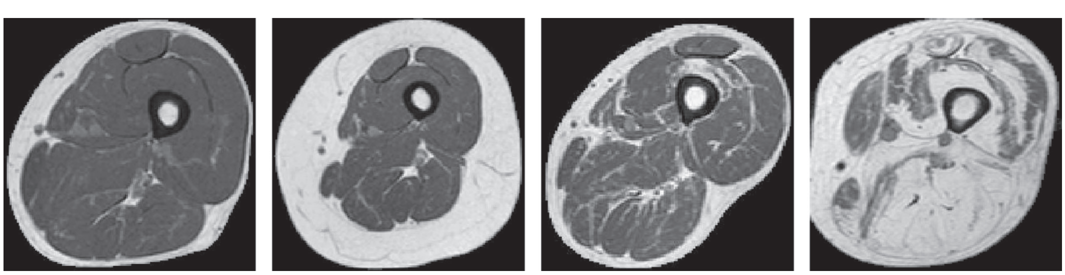
In summary, we identified a lack of a quantitative evaluation of segmentation approaches with respect to subjects showing fat infiltrations. Literature on segmenting thighs focus either on healthy subjects only or on subjects showing no distinct fat infiltration, or the evaluation is not performed separately.

Considering the proposed methodologies, most approaches are either atlas-based [18,21] or incorporate a shape model [2-4,16,17]. One method only [25] performs segmentation by applying a level set approach without incorporating prior knowledge of the shape.

The utilization of state-of-the-art deep neural networks [33] is currently inhibited by the small amount of available training data, especially considering severely affected patients.

1.2. Contribution

In this study, we systematically implemented, extended and evaluated several conceptionally different segmentation approaches which were inspired by methods in literature [17,25]. Evaluation was performed in combination with variably affected (fat-infiltrated) T1-MRI scans (Fig. 1) which were partitioned into four categories reaching from healthy to severely affected muscle tissue. For segmentation, we compared a basic clustering-based technique with a statistical level set (featuring a local optimization method) and a graph cut approach (featuring a global optimization method). To introduce knowledge of the shape, which was supposed to be important especially in severe cases [2-4,16,17], we added statistical shape models into the energy formulation. We focused on segmentation approaches in combination with implicitly parametrized shape models because especially in the case of severely affected patient's data, a reliable manual annotation based on anatomic keypoints [16,17] for training would be extremely difficult. Level set (also motivated by the work of Lareau-Trudel et al. [25]) and graph cut approaches were compared in order to assess



(a) 'healthy' (b) 'easy' (c) 'moderate' (d) 'hard'

Fig. 1. For evaluation purposes, the data set was partitioned into four categories according to the prevalent fat infiltration. Whereas the 'healthy' (a) and the 'easy' (b) samples do not show any fat infiltration, samples of the 'moderate' category (c) show moderate, local and the 'hard' category (d) exhibits infiltrations in significant muscle areas.