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SCIENTIFIC ARTICLE

Quantification of shoulder muscle intramuscular fatty infiltration on T1-weighted MRI: a viable alternative to the Goutallier classification system

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Abstract

Background Quantification of rotator cuff intramuscular fatty infiltration is important for clinical decision-making in patients with rotator cuff tear. The semi-quantitative Goutallier classification system is the most commonly used method, but has limited reliability. Therefore, we sought to test a freely available fuzzy C-means segmentation software program for reliability of the quantification of shoulder intramuscular fatty infiltration on T1-weighted MR images and for correlation with fat fraction by six-point Dixon MRI.

Materials and methods We performed a prospective cross-sectional study to measure visible intramuscular fat area percentage on oblique sagittal T1 MR images by fuzzy C-means segmentation and fat fraction maps by six-point Dixon MRI for 42 shoulder muscles. Intra- and inter-observer reliability were determined. Correlative analysis for fuzzy C-means and six-point Dixon intramuscular fatty infiltration measures was also performed.

Results We found that inter-observer reliability for the quantification of visible intramuscular fat area percentage by fuzzy C-means segmentation and fat fraction by six-point Dixon MRI was 0.947 and 0.951 respectively. The intra-observer reliability for the quantification of visible intramuscular fat area percentage by fuzzy C-means segmentation and fat fraction by six-point Dixon MRI was 0.871 and 0.979 respectively. We found a strong correlation between fuzzy C-means segmentation and six-point Dixon techniques; $r = 0.850$, $p < 0.001$ by individual muscle; and $r = 0.977$, $p < 0.002$ by study subject.

Conclusion Quantification of intramuscular fatty infiltration by fuzzy C-means segmentation on T1-weighted sequences demonstrates excellent reliability and strong correlation with fat fraction by six-point Dixon MRI. Quantitative fuzzy C-means segmentation is a viable alternative to the semi-quantitative Goutallier classification system.

Keywords Shoulder · Rotator cuff · Intramuscular fatty infiltration · Fuzzy C-means · Quantitative · MRI · Dixon

Introduction

Nearly 4.5 million healthcare provider visits occur every year for the evaluation of rotator cuff (RC) disease in the USA [1].

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An RC tear is a disease of aging, with 86% of surgical rotator cuff repair (RCR) taking place after the age of 44 years [2]. One out of four adults aged ≥60 years suffers from RC tear in the general population [3]. The prevalence of RC tear is expected to rise with shifting demographics, as the number of older adults in the USA continues to increase.

Shoulder imaging is important in clinical decision-making for the diagnosis of RC tear and the assessment of RC intramuscular fatty infiltration (FI). Many animal and human studies show that FI progression accelerates following RC tear, and that acquired FI does not resolve following RCR [4–8]. Assessment of FI in the setting of RC tear affects clinical decision-making, as the presence of FI of 50% or more is a relative contraindication to RCR [9]. In current clinical practice, the semi-quantitative Goutallier classification system is the most frequently used method of grading FI [9–11]. The

Goutallier classification system is graded on a five-point scale: stage 0, no fat; stage 1, streaks of fat; stage 2, muscle > fat; stage 3, muscle = fat; stage 4, muscle < fat. However, the Goutallier classification system has limitations, despite its ease of use. At best, this subjective grading scheme shows only moderate inter-observer reliability [12]. There is a strong need for reliable quantitative imaging measures of FI.

Quantitative methods offer a more accurate assessment of FI compared with semi-quantitative methods. Current validated cutting edge techniques for the quantification of FI include multi-echo Dixon MRI and proton MR spectroscopy [13–16]. The Dixon technique generates several images, including water-only, fat-only, in-phase and out-of-phase images. From these images, measurement of the fat content in each voxel allows for quantitative analysis. However, this technique is relatively new and mainly available only at large academic centers. The MR spectroscopy method takes advantage of the chemical shift difference between fat and water to provide quantitative information at the voxel level. However, this technique, although known for several years, is rarely used in daily clinical practice, as substantive technical expertise is required for its application. Given the wide use of the semi-quantitative Goutallier classification system, a reliable method for quantitative measurement of FI on T1-weighted MRI would be beneficial to aid clinical decision-making, and to stratify FI in retrospective research studies when only conventional shoulder MRI sequences are available.

The purpose of our study is to test for correlation between a fat fraction estimated using the six-point Dixon MRI technique and visible intramuscular fat area percentage by fuzzy C-means segmentation on T1-weighted MRI. We hypothesize that quantitative estimation of FI by fuzzy C-means segmentation on T1-weighted images might have a strong correlation with the fat fraction by Dixon MRI, and also that both methods might demonstrate strong reliability.

Materials and methods

Study population

The study was approved by an institutional review board and complied with Health Insurance Portability and Accountability Act guidelines. During our prospective cross-sectional study, informed consent was obtained. The study population consisted of adults aged ≥18 years. Inclusion criteria were asymptomatic shoulder (volunteer subjects) or painful shoulder with full-thickness RC tear (subjects referred by an orthopedic surgeon). Exclusion criteria were a history of joint replacement for the ipsilateral shoulder; contraindication to MRI; and ipsilateral chronic upper extremity paralysis. Subjects were recruited consecutively from January 2016 to February 2017. Three shoulders from asymptomatic volunteers (mean age, 28.3 years ±3.2; age range, 26–32 years) and four shoulders from subjects (mean age, 59.7 years ±12.7; age range 45–68 years) with painful full-thickness RC tear confirmed by an orthopedic surgeon were included in the study, allowing for inclusion of 42 shoulder muscles in the analysis.

Magnetic resonance imaging

All imaging examinations were performed at 3.0 T (Magnetom Trio; Siemens Healthcare, Erlangen, Germany) using a four-channel flexible coil. All shoulders with known painful full-thickness RC tear were imaged before RCR. The imaging protocol included a standard two-dimensional (2D) turbo spin-echo (TSE) oblique sagittal T1-weighted sequence (matrix, 448 × 448; repetition time ms (TR)/echo time[s] (TE) ms, 600/22; field of view (FOV), 160 mm; number of acquisitions, 3; slice thickness, 4 mm; and axial, oblique sagittal, and oblique coronal 2D short tau inversion recovery sequences (matrix, 448 × 448; TR/TE ms, 4,420/50; inversion time 180 ms; FOV, 160, number of acquisitions, 1; slice thickness, 4 mm). A three-dimensional six-point Dixon volumetric sequence was also obtained in the sagittal orientation (matrix, 320 × 320; TR, 9 ms, TE,1.35, 2.65, 3.95, 5.25, 6.55, 7.85 ms; flip angle, 9; FOV 312 × 400 mm; number of acquisitions, 1; slice thickness, 4 mm). From the six-point Dixon sequence, fat- and water-only images, in addition to fat fraction and water fraction maps, were reconstructed. The fat fraction maps were reformatted in the oblique sagittal plane to match the orientation of the T1-weighted MRI.

MRI evaluation of rotator cuff tendons

A board-certified musculoskeletal radiologist with 8 years of experience determined the presence or absence of a full-thickness RC tear for each shoulder. RC evaluation included the supraspinatus, infraspinatus, subscapularis, and teres minor tendons. Each RC tendon was defined as either intact or with full-thickness RC tear.

Quantitative MRI evaluation of intramuscular fatty infiltration

A research coordinator created DICOM image modules for each shoulder included in the study ($N = 7$). Each module contained a T1-weighted MRI and six-point Dixon MR fat fraction map image corresponding to the Y-shaped view in the oblique sagittal plane [16–18]. A blinded radiology resident evaluated six muscles (Fig. 1) on MR images in each module using Medical Image Processing, Analysis and Visualization software (MIPAV, version 7, National Institutes of Health, Bethesda, Maryland, USA). MIPAV software is

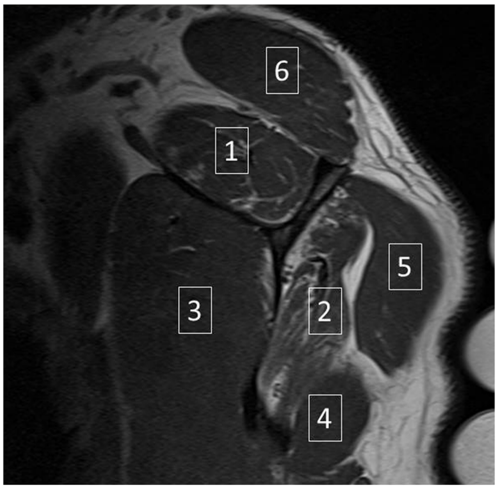

Fig. 1 Example oblique sagittal T1-weighted MRI of the shoulder. Six skeletal muscles were evaluated: *1* supraspinatus; *2* infraspinatus; *3* subscapularis; *4* teres minor; *5* deltoid; *6* trapezius

freely available for download at: https://mipav.cit.nih.gov/. The resident independently measured the visible intramuscular fat area percentage of the supraspinatus, infraspinatus, subscapularis, teres minor, deltoid, and trapezius muscles in each module on the T1-weighted images with fuzzy C-means by manual segmentation (Fig. 2a). Fuzzy-C means is a pattern recognition clustering mathematical algorithm that allocates each voxel to a pre-defined category based on signal intensity through a process of iterative optimization [19]. Fuzzy-C means is widely used for segmentation in medical imaging and has been applied in clinical scenarios such as separating fat from fibroglandular tissue on breast MRI [19, 20]. The cross-sectional area (CSA) of visually perceptible fat within a muscle was determined by fuzzy C-means segmentation, which parcellated the muscle into two classes using the following parameters: number of desired classes, 2; desired exponent value, 2; end tolerance, 0.01; maximum number of iterations, 200; signal threshold, −1,024.0; region, VOI region; segmentation, hard and fuzzy both. The percentage of FI in each ROI was estimated by taking the CSA of visible intramuscular fat segmented by fuzzy C-means segmentation divided by the CSA of the entire ROI. The resident also independently performed a separate analysis, where the mean fat fraction for each muscle on the corresponding Dixon fat fraction map was determined, by taking the average signal from each ROI (Fig. 2b). For both T1-weighted and Dixon MRI analysis, a region of interest was placed at the border of each muscle by manual segmentation, with one exception. A line perpendicular to the inferior scapular border marked the inferior extent of the subscapularis muscle included in the ROI [16]. To determine intra-observer reliability for the six-point Dixon and T1-weighted MRI FI measures, each measurement was repeated 4 weeks later by the same resident. To allow for determination of inter-observer reliability for the six-point Dixon and T1-weighted MRI FI measures, each measurement was also performed once by a blinded board-certified musculoskeletal radiologist. Twenty weeks after the quantitative analyses, the same radiology resident and board-certified musculoskeletal radiologist determined a Goutallier grade for each individual muscle by consensus.

Statistical analysis

Statistical analysis was performed using Stata statistical software version 14 (StataCorp LP, College Station, TS, USA). The visible intramuscular fat area percentage on T1-weighted MR images and the fat faction on Dixon MRI for each of the muscle groups were obtained for each individual shoulder by the resident. Asymptomatic shoulder group and painful full-thickness RC tear group means were compared by use of the unpaired *t* test. The mean age of each group was compared using the unpaired *t* test. Intra-observer and inter-observer reliability were assessed by calculating the intra-class correlation coefficient (ICC), according to the technique proposed by Landis and Koch [21]. The Pearson correlation coefficient (*r*)

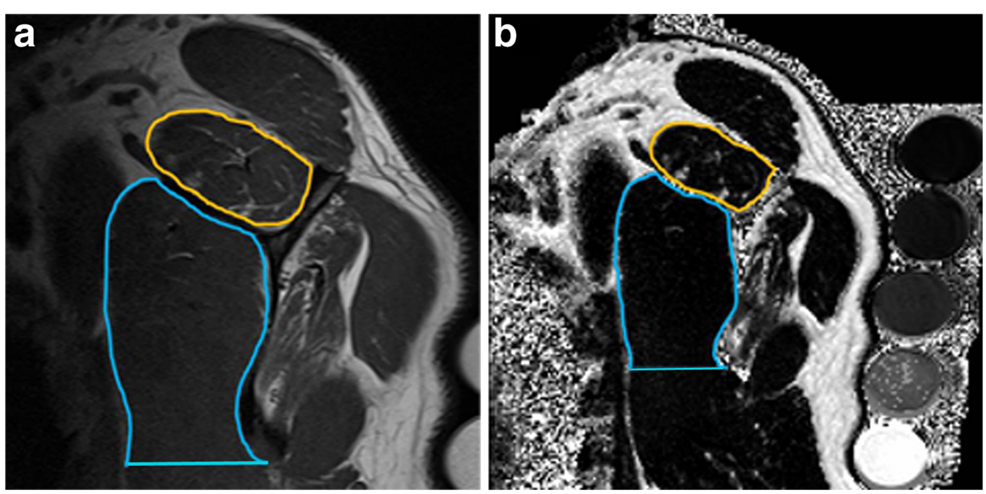

Fig. 2 Method for the calculation of visualized intramuscular fat area percentage and muscle fat fraction on **a** oblique sagittal T1-weighted and **b** corresponding Dixon MRI. A region of interest (ROI) was drawn around the border of every individual muscle (as depicted by the gold ROI on both images for the supraspinatus muscles) in the study with one exception. A line perpendicular to the inferior scapular border marked the inferior extent of the subscapularis muscle included in the ROI (*blue ROI*)

was calculated between the visible intramuscular fat area percentage on T1-weighted MRI and the fat faction on Dixon MRI for each muscle ($n = 42$). To correct for any potential clustering, we determined the average mean visible intramuscular fat area percentage on T1-weighted MRI and the mean fat faction on Dixon MRI of the supraspinatus, subscapularis, infraspinatus, teres minor, deltoid, and trapezius muscles for each individual study subject; and then calculated the r between the study subject's mean visible intramuscular fat area percentage on T1-weighted MRI and the mean fat faction on Dixon MRI ($n = 7$). A p value <0.05 was considered to indicate a significant difference.

Results

The shoulder MRIs of the asymptomatic volunteers ($n = 3$) all showed intact RC tendons. The shoulder MRIs of subjects with painful shoulders ($n = 4$) all demonstrated the presence of a full-thickness supraspinatus tendon tear, and 2 also had full-thickness infraspinatus tendon tears. The mean age of the asymptomatic shoulders was lower than those with painful full-thickness RC tear ($p = 0.014$). As expected, subjects with painful full-thickness RC tear showed a significant difference compared with asymptomatic subjects for supraspinatus muscle visible intramuscular fat area percentage on T1-weighted MRI and fat fraction on Dixon MRI (Tables 1 and 2). Overall, differences detected in the quantification of FI between shoulders with full-thickness RC tear and asymptomatic shoulders were similar for the T1-weighted MRI fuzzy C-means segmentation and Dixon MRI methods for all muscles. The mean Goutallier grades for asymptomatic volunteer muscles were: supraspinatus, 1.0 ± 0.0; subscapularis, 0.7 ± 0.6; infraspinatus, 1.0 ± 0.0; teres minor, 0.0 ± 0.0; deltoid, 0.7 ± 0.6; and trapezius, 0.0 ± 0.0. The mean Goutallier grades for muscles with painful full-thickness RC tear were: supraspinatus, 2.0 ± 0.0; subscapularis, 1.3 ± 0.5; infraspinatus, 1.8 ± 0.5; teres minor 1.3 ± 1.0; deltoid, 1.5 ± 0.6; and trapezius, 2.0 ± 0.0.

Table 1 Comparison of mean visible intramuscular fat area percentage on T1-weighted MRI in shoulders with painful full-thickness supraspinatus tendon tears and asymptomatic volunteers with intact rotator cuffs

Muscle	Full-thickness tear mean ± SD ($n = 4$)	Intact mean ± SD ($n = 3$)	p value
Supraspinatus	16.4 ± 0.7	4.6 ± 1.1	<0.001
Infraspinatus	12.0 ± 6.2	4.4 ± 3.2	0.116
Subscapularis	8.4 ± 5.6	5.1 ± 0.9	0.370
Teres minor	8.4 ± 1.8	4.8 ± 2.4	0.070
Deltoid	12.6 ± 3.4	7.1 ± 2.3	0.064
Trapezius	13.8 ± 4.5	6.6 ± 1.8	0.050

Table 2 Comparison of mean fat fraction on Dixon MRI in shoulders with painful full-thickness supraspinatus tendon tears and asymptomatic volunteers with intact rotator cuffs

Muscle	Full-thickness tear mean[a] ± SD ($n = 4$)	Intact mean ± SD ($n = 3$)	p value
Supraspinatus	13.2 ± 3.6	5.5 ± 2.3	0.025
Infraspinatus	17.2 ± 8.7	4.4 ± 1.1	0.056
Subscapularis	8.0 ± 5.0	5.2 ± 1.5	0.402
Teres minor	10.3 ± 4.3	4.0 ± 0.6	0.059
Deltoid	10.7 ± 3.5	4.3 ± 0.8	0.029
Trapezius	14.8 ± 6.8	8.1 ± 1.8	0.159

[a] Fat fraction expressed as a percentage

Both intra-observer and inter-observer intra-class correlation was strong for both the T1-weighted MRI fuzzy C-means segmentation and the Dixon MRI methods (Table 3). The ICC for intra-observer reliability was 0.871 and 0.979 for fuzzy C-means segmentation and Dixon measures of FI respectively. The ICC for inter-observer reliability for was 0.947 and 0.951 for fuzzy C-means segmentation and Dixon measures of FI respectively. Strong correlation was found between the T1-weighted MRI fuzzy C-means and the six-point Dixon MRI measures of FI for all muscles; $r = 0.850$, $p < 0.001$ (Fig. 3). Strong correlation was also found between shoulder muscle mean T1-weighted MRI fuzzy C-means and the mean six-point Dixon MRI by study subject; $r = 0.977$, $p < 0.002$ (Fig. 4).

Discussion

To assess the feasibility and reliability of quantifying shoulder muscle FI on conventional T1-weighted MRI, we compared the freely available MIPAV software fuzzy C-means segmentation with the six-point Dixon method. Our study shows that quantification of the visible intramuscular fat area percentage by T1-weighted MRI fuzzy C-means segmentation correlates strongly with fat fraction by six-point Dixon MRI for shoulder muscles. The fuzzy C-means segmentation and Dixon fat fraction are fundamentally two different methods of estimating FI. The fuzzy C-means technique in our study estimates the

Table 3 Intra-observer and inter-observer agreement for all muscles ($N = 42$) for visible intramuscular fat area percentage on T1-weighted MRI and mean fat fraction on Dixon MRI

Sequence	Intra-observer ICC	Inter-observer ICC
T1-weighted	0.871	0.947
Dixon	0.979	0.951

*ICC*intra-class correlation coefficient

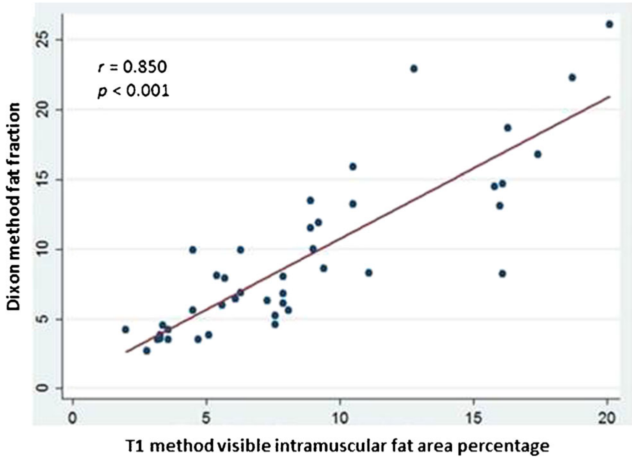

Fig. 3 Correlation of fat fraction by the Dixon MRI method and visible intramuscular fat area percentage by the T1-weighted fuzzy C-means segmentation MRI method for all muscles included in the study (N= 42). Dixon fat fraction is expressed as a percentage

percentage of visible intramuscular fat present within an ROI, by classifying each voxel as either a fat voxel or a nonfat voxel. The six-point Dixon method is different in that it computes the fat fraction within each voxel and a map of this information is provided as either a fat image or a water image. The fat fraction map estimates the fraction of fat within each voxel. The Dixon method fat fraction estimates FI as an average of all voxels within an ROI.

Reliable quantitative methods for the measurement of RC FI are necessary tools for future research studies and clinical decision-making in current practice. Fuzzy C-means segmentation for the quantification of FI is a viable alternative to the semi-quantitative Goutallier classification system for the measurement of intramuscular fat when only standard imaging sequences are available. Continuous variable grading schemes offer a more reliable and accurate measure of FI than five-point ordinal scales for RC tear imaging research [22].

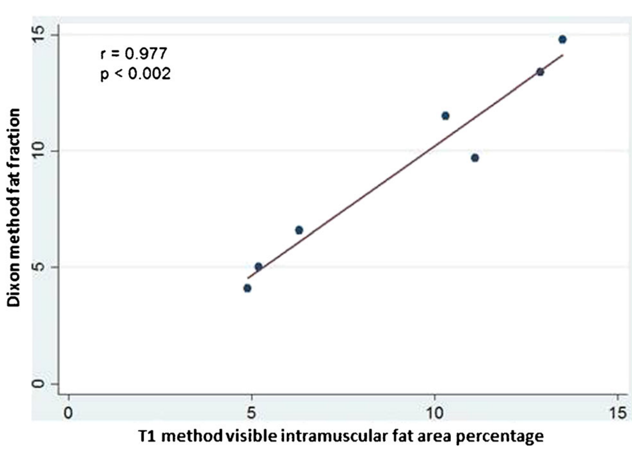

Fig. 4 Correlation of study subject shoulder muscle mean fat fraction by the Dixon MRI method and mean visible intramuscular fat area percentage by the T1-weighted fuzzy C-means segmentation MRI method. Dixon fat fraction is expressed as a percentage

Quantitative imaging also offers greater certainty in challenging cases, when there is uncertainty as to whether a RC muscle is Goutallier grade 2 (muscle > fat) or Goutallier grade 3 (muscle = fat). The fuzzy C-means segmentation algorithm is one of several freely available tools designed to meet the goal of applying quantitative imaging techniques in biomedical research.

Imaging evaluation of RC muscle fat content is critical for clinical decision-making in RC tears, since ≥50% FI is a relative contraindication to RCR. There is mounting evidence that FI is predictive of postoperative healing and shoulder function for patients treated with RCR [4, 6, 7, 23]. Therefore, surgeons increasingly advocate early surgical intervention for the treatment of active patients with acute traumatic RC tears. Several animal and human studies show that RC muscle FI accumulation rapidly progresses following acute RC tear, and that early RCR does not reverse FI, but instead helps to mitigate the greater accumulation of FI associated with delayed RCR [4, 5, 7, 24–26].

Fuzzy C-means segmentation is appropriate for shoulder muscle FI quantification analysis on T1-weighted MRI, using a similar assumption of the Goutallier classification system that muscle signal is either “fat” or “muscle” signal. Raters assign one of five subjective Goutallier grades to report the perceived degree of FI for a muscle. Our method of fuzzy C-means segmentation operates on a similar premise. The cross-sectional area (CSA) within the region of interest (ROI; Fig. 1a) is dichotomized into two predominant signals, producing a CSA corresponding to an area of fat and a CSA corresponding to an area of muscle. This process allows for the calculation of percentage fat signal within the ROI. Fuzzy C-means segmentation on MIPAV provides accurate quantification of T1-weighted signal on MRI. Previous studies have utilized varied methods for the segmentation of skeletal muscle signal on T1-weighted images in the spine, pelvis, and lower limb [27–29].

Fatty infiltration has two components on the cellular level: intramyocellular lipid (IMCL) and extramyocellular lipid (EMCL). IMCL is in a dynamic equilibrium and is adjacent to the mitochondria within a myofibril for use during active metabolism, whereas EMCL is deposited between myofibrils for longer-term storage [13, 30]. Multi-echo Dixon MRI techniques are a validated method for the quantification of FI in animal and human studies [14–16, 22]. The calculation of fat fraction measured by Dixon MRI includes both IMCL and EMCL. Proton MRI spectroscopy techniques are capable of measuring EMCL and IMCL separately, but are not widely available and require specialized expertise for analysis [13, 14, 30].

There were some limitations to our study. Fuzzy C-means segmentation of T1-weighted MRI provides only quantification of image signal and does not measure fat directly. However, our technique for the calculation of the visible intramuscular fat area percentage correlates strongly with Dixon fat fraction. Additionally, our method mirrors the assumption underlying the Goutallier classification system, where a human rater assigns a grade based on subjective visible perception of fat and muscle content. During our study, we identified a specific pitfall limiting the use of fuzzy C-means segmentation on T1-weighted images. Fuzzy C-means segmentation may not be appropriate for the evaluation of Goutallier grade 0 (all muscle, with no visible fat). In this circumstance, neither of the two dichotomized signals represent fat content. We would advocate placement of the ROI abutting the entire border edge of a muscle, and avoid placement of the ROI entirely within the muscle away from the border edge. Additionally, T1-weighted MRI should be correlated with other standard shoulder imaging sequences to exclude an unexpected pathological condition in a muscle. Potential mimickers of fat signal on T1-weighted images include melanin, protein, blood products, and gadolinium.

Conclusion

Quantification of shoulder muscle intramuscular fatty infiltration by fuzzy C-means segmentation on T1-weighted MRI correlates strongly with fat fraction by the six-point Dixon technique. Fuzzy C-means segmentation for the quantitative measurement of visible intramuscular fat area percentage in RC muscles is a viable alternative to the semi-quantitative Goutallier classification system for future research studies.

Compliance with ethical standards

Conflicts of interest Dr. Derik L. Davis receives partial salary support from the University of Maryland Claude D. Pepper Older Americans Independence Center (NIA P30 2P30AG028747). He also received a research seed grant in 2016 from the Radiological Society of North America Research & Education Foundation & Hitachi Medical Systems.

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