

Cancer Therapy & Oncology International Journal

Research Article Volume 1 Issue 2 - April 2016 Canc Therapy & Oncol Int J Copyright © All rights are reserved by Somya Aggarwal

Thigh Muscle Bundle Volume by Magnetic Resonance Muscle Quantification (MRMQ) in Skeletal Muscle Wasting and Relevance of Supine Rest

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Submission: March 22, 2016; Published: April 05, 2016

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Abstract

MRI is beginning to be extensively used in clinical trials in the quantitative analysis of muscle volume in muscle wasting pathologies with the help of magnetic resonance muscle quantification (MRMQ). Muscle wasting occurs in various kinds of diseases, such as, muscular dystrophies, cachexia, sports injuries or ageing. This can results in progressive disability and eventually a possible deformity. Clinical trials are increasingly done to target an increase in the muscle volume by new drugs. The variability in measurement of the change in muscle volume needs standardization with accurately delineated measurement methods such as mid -thigh muscle bundle volume changes. Imaging of patients after a defined supine rest period, rather than taking them directly to MRI gantry on arrival, is also important to accurately assess muscle volume changes. Measurements in a clinical setting may not always be possible as the methods to quantify changes by measurement in muscle bundle volume may not exist.

Keywords: MRI; MRMQ; Clinical trials; Muscle wasting; Standardization; Mid-thigh muscle; Bundle volume; Supine rest period; Muscular dystrophies

Abbreviations: MRMQ: Magnetic Resonance Muscle Quantification; MRI: Magnetic Resonance Imaging

Introduction

Diseases causing muscle wasting can increasingly cause loss of muscle strength and atrophy. This could cause critical recovery issues. More and more clinical trials are using MRMQ as the way forward to quantify changes in muscle volume. New drugs target about 2-10% mean percentage change in the thigh muscle volume in such patients. This needs very appropriate and standardized measurement biomarkers [1] and a well-defined protocol that involves a definite supine rest period before getting the patient to MR scanner [2-5].

Muscular dystrophies are a group of diseases involving progressive muscle weakness and atrophy. There are many kinds of muscular dystrophies and some may even be debilitating resulting in deprived quality of life. Progressive decrease in muscle mass as seen in cancer patients can cause decreased survival rate and poor functioning [6]. Muscle mass volume changes is, therefore, known to be an important indicator of functional status in clinical trial studies of sarcopenia and cachexia [7].

Technique of Segmentation in MRMQ

MRMQ is an MRI technique that involves thigh segmentation and quantification of muscle bundle volume. Segmentation can be performed in a semi-automated or manual representation detailing most external as subcutaneous adipose tissue, muscle bundle and the innermost bone (Figure 1 & 2). A trained technologist may be used or the segmentation. Reader involved with the trial has to make sure that maximum accuracy is achieved with the segmentation of these regions so as to get the most accurate biomarker measurement. Role of supine rest of 15 minutes before scanning must be made a protocol for accurate results [1,2].



Figure 1: Segmentation of muscle bundle volume outlined in green, bone in yellow and subcutaneous fat in red.



Figure 2: Representation of muscle bundle volume painted in green and subcutaneous adipose tissue in red.

MRMQ Imaging Protocols

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Non-invasive magnetic resonance imaging is the widely used assessment method in various clinical trials of muscle wasting and use of appropriate MR imaging protocols is fundamental. Magnet of 1.5 Tesla Axial T1-w images, T2 mapping or gadolinium contrast enhanced images are some of them. Accurate delineation of mid- thigh muscle volume, before and after drug introduction, is the critical factor. Some clinical trials use dedicated software for automated assessment while others do it manually by use of appropriate segmentation. An imaging guideline is required that allows patients to rest supine and not change postures, that may be from supine to prone or supine to standing, as the posture change can cause the fluid content in muscles to decrease [1,4].

Role of Posture Changes in Final Outcome

It has been seen that a posture change from supine to prone or standing to supine can alter the fluid content in the muscles. An axial T-1w image taken immediately after the patient walks in to scanning center has physiological muscle volume difference than a patient that takes supine rest before shifted to a scanner [2,3]. The set of imaging guidelines for the clinical trial sites should be in place so that there is a standardization done for image acquisition.

Clinical Measurements vs MRMQ

In critically ill patients, muscle wasting can occur early and rapidly and more pronounced in those with multi-organ failure. Muscle volume measurements are not routinely performed in clinics as they cannot be substantiated by reproducible valid qualitative measurements. Segmentation of thigh muscles by muscle quantification by MRI is, in contrast, more standardized to obtain a valid data when used with an imaging guideline and an imaging protocol.MRI substantiated measures can assess muscle volume changes and yield maximum response to accurate measurements with reliability and validity, and detect changes in muscle water content [5,8].

Conclusion

Muscle volume changes are not practically done in a clinical setting and MRMQ is increasingly gaining importance with the use of manual, semi-automated of fully automated quantitative measurements. An approach to get the accurate measurements would need a dedicated imaging guideline and a skilled imaging protocol. TMBV measurement is one approach towards gaining more insight into various clinical trials done across the globe with different set of population and software used in segmentation. More extensive clinical information by various quantitative trials in skeletal muscle and mid- thigh muscle bundle volume measurements can help to increase the knowledge and substantiate results.

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