Generating Color-Coded Anatomic Muscle Maps for Correlation of Quantitative MRI Analysis with Clinical Examination in Neuromuscular Disorders

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ABSTRACT:

Introduction: Fatty infiltration of muscles may be seen in many neuromuscular disorders, including glycogen storage diseases (GSD), muscular dystrophies, and amyotrophic lateral sclerosis. Recording pathologic involvement of musculature in these patients is cumbersome, given marked disease heterogeneity within each individual. We describe a novel method for simplifying this process and present its application in a patient with GSD type IIIa. Methods: A color-coded visual mapping tool was developed based on a commonly used spreadsheet platform. Results: This tool depicts individual muscle groups as shapes linked to data cells corresponding to quantitative MRI-based measures of fatty infiltration and weakness assessed by physical examination. It allows for rapid evaluation and chronological comparison of all mapped muscle groups on a single graphical sheet, as well as assessment of response to therapy. Discussion: This can be applied in any neuromuscular disorder where muscle function is assessed by clinical or imaging scores.

KEYWORDS:
Neuromuscular disorders, glycogen storage disease, whole-body MRI, muscle fat fraction, color-coded maps
INTRODUCTION

Neuromuscular disorders encompass a wide variety of disease processes and cause substantial morbidity and mortality. Monitoring disease progression and assessing effectiveness of treatment are essential in routine care of affected patients, as well as in clinical trials [1]. Tracking muscle involvement is often tedious and inefficient, due to the numerous muscles examined, heterogeneity of disease involvement, and the need to perform and compare multiple examinations longitudinally [2]. In addition, assessments are often multi-modal, including physical examination, electromyography, measures of muscle strength and function, and muscle biopsy, which creates large amounts of data to summarize efficiently [1].

Use of imaging techniques such as whole-body MRI, have recently gained increasing use in neuromuscular disorders [3-5]. They can provide an exceptionally large amount of additional data by capturing most or all peripheral musculature in a single acquisition [5]. The availability of this additional information and its potential impact on patient care underscores the need for a method to clearly and efficiently display large amounts of data for treating clinicians. Additionally, in clinical trials which include repeated measures of clinical and imaging data [6],[7], change over time in multiple muscle groups may be difficult to display or assess efficiently. Furthermore, given the limitations of currently available measures of response to therapy in clinical trials, the need for a robust method is evident.
In order to address these challenges, we describe a tool for visual representation of complex disease involvement in the musculature. This tool simplifies display of data and can be used to compare results of different types of testing and follow disease longitudinally. We illustrate the utility of the technique by applying it to a patient with Glycogen storage disease type IIIa (GSD-IIIa) who underwent both clinical strength testing and whole-body MRI.

METHODS

A “muscle mapping” tool was developed using BeGraphic (Aldecis; Paris, France), a third-party graphical data visualization plug-in for Microsoft Excel (Microsoft Corporation; Redmond, WA, USA) [8]. Initial diagrams of the human body from anterior and posterior views were drawn, delineating individual major muscle groups based on function and distribution. Color scales were associated with disease severity, and each data cell was linked to its corresponding shape in the muscle maps. The end result was a graphical display tool which would automatically be updated with each data entry.

To demonstrate the use of the mapping tool, data were analyzed from a 38-year-old woman with GSD-IIIa, under an institutional review board-approved protocol. Data regarding muscle weakness, and muscle fatty infiltration measured by MRI using a T2*-corrected Dixon method, were input into the display tool, generating “muscle maps”.

RESULTS
Output images from the visual display tool are shown in the Figure. The tool allowed rapid assessment of disease involvement and comparison between quantitative MRI-based scores and quantitative clinical scores. Asymmetry of involvement and imbalance in upper/lower extremity disease reflects the heterogeneity of this disease.

In this patient, gluteal musculature/hip extensors were the most severely involved muscle group on the combined clinical/imaging assessment, consistent with previously reported descriptions of clinical phenotype. The viewer’s attention is effectively drawn to this group by the its coloring on the images. The tool also highlights additional abnormal muscle groups, which had not previously undergone clinical testing, in particular the tongue and right forearm extensors.

**DISCUSSION**

Complete muscle examinations with whole-body MRI can produce large amounts of data, which allow detailed comparison of clinical and imaging scores. Previous clinical reports and literature publications of MRI-based muscle fatty infiltration characterization generally have been limited to data reports in serial table format [3],[5]. The data visualization tool we describe reduces large amounts of tabular data into a simple, color-coded map system. The color scale used in the presented example is not absolute and can be adjusted according to the needs of the user to more closely correlate clinical scores with imaging-based scores.
In addition, though not presented here, the visualization tool may facilitate longitudinal assessment of disease and can serve as an important tool in both clinical care of patients and in the design of clinical trials that investigate the benefits of therapeutic interventions [6],[7]. Color-coded maps from follow-up examinations can be displayed side-by-side; alternatively, data could be combined in the form of subtraction maps, where interval change in muscle weakness score or muscle fat fraction (FF) is displayed, allowing for targeted physical therapy and exercise planning.

MRI-based FF quantification techniques have been extensively and successfully explored and implemented in liver imaging [9-11]. In order to validate the use of these techniques in muscle tissue, Gaeta et al demonstrated excellent agreement between estimations of muscle FF measured by MRI and muscle biopsy histopathologic findings [12]. These methods have recently proven promising in studies of Duchenne muscular dystrophy, Charcot-Marie-Tooth disease, and GSD [3-5],[13],[14]. In patients with GSD-IIIa, excessive glycogen deposition in muscle tissue leads to skeletal muscle fatty infiltration and eventual atrophy [15]. Genetic and molecular analyses as well as single-muscle biopsy do not consistently reflect the clinical severity, variability in disease progression, or phenotypic heterogeneity in whole-body muscle group involvement [16]. Clinical measures of strength and function alone may lack sensitivity as markers of muscle involvement in the presence of subtle or profound weakness, with limitations due to dependence on effort and the effects of fatigue, pain, and contextual variables [17-19]. Muscle damage may be evident on imaging prior to the emergence of measurable clinical change in strength, with potentially greater isolation of location of damage within muscle.
Whole-body MRI, therefore, may allow for efficient, objective, and reproducible measurements of disease, which can be obtained noninvasively and complement and precede clinical data. Subtle changes over time can be seen, and other organs, such as the liver can be assessed. These examinations, however, result in an immense amount of data, for which the clinician should ideally have an efficient evaluation method.

Obtaining measurements from those image data sets may be time consuming, however the described display tool facilitates data summarization, as inputting the numerical data into the tool requires only a few minutes, and the color-coded display is generated nearly instantaneously.

In this report, we have described the application of a muscle mapping technique, which allows rapid visual evaluation of clinical and imaging-based disease scores for patients with neuromuscular disorders. This may be particularly useful for tracking disease progression in routine clinical care as well as in the setting of clinical trials.
Figure - Image created by the visualization tool, in a patient with GSD-IIIa. Note that the viewer’s attention is immediately drawn to the sites of greatest disease involvement, in particular the gluteal musculature. This image also provides side-by-side comparison of the results of clinical strength testing (left) and MRI fat quantification (right). The color scale at the bottom demonstrates increasing severity of involvement from left to right.
ABBREVIATIONS:

MRI: Magnetic Resonance Imaging
GSD: Glycogen Storage Diseases
FF: Fat Fraction
REFERENCES


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