MRI characterization of individual muscles in patients with sporadic inclusion body myositis (sIBM) using a semi-automatic segmentation approach

Didier Laurent[1], Attila Nagy[2], Steve Pieper[2], Harlem Gongxeka[1], Celeste Pretorius[1], and Stefan Baumann[1]
[1]Biomarker Department, Novartis, Basel, Switzerland, [2]Isomics, Inc, Cambridge, Ma, United States

Target audience: Physicians, pharmacologists and expert scientists in automated segmentation processes interested in muscle diseases and studies on muscle wasting

Introduction: Muscle atrophy leading to profound disability is a clinical finding common to many congenital and acquired conditions, such as sarcopenia and cachexia. While quadriceps and hamstring muscles form part of the frequently affected muscle groups, sporadic inclusion body myositis (sIBM) is known to cause atrophy in a non-uniform distribution across leg muscles (1). As the disease relentlessly progresses, patients may experience signs of imbalance in the legs. Consequently, falls may start to happen in these patients, as this may be due to changes in contractile apparatus and/or neuronal activation of specific muscles in the leg. Comprehensive measures of the muscle volume may help to examine more precisely the relative contribution of each muscle and the overall function of these patients. So that effective drug treatments be developed, it is also crucial that the anabolic response to new therapies be monitored at the individual muscle level.

High spatial resolution and unparalleled soft tissue contrast make MRI the ideal tool to measure muscle volume with high precision. However, manual segmentation of individual muscles from MR image series can be challenging and time consuming. The main difficulty resides in the correct delineation of muscle boundaries with respect to subcutaneous adipose tissue (SAT) or intermuscular adipose tissue (IMAT, or "marbled" fat), which is defined as the visible adipose tissue beneath the muscle fascia, between muscles, and even within the muscle, but outside the actual muscle cell. Decreased muscle performance and physical function have been associated with high levels of IMAT (2).

Here we show results obtained from the open source and freely downloadable 3D Slicer-based algorithm (3) that was developed for semi-automated segmentation and measuring of all individual muscle volumes within the thigh of both healthy volunteers and sIBM patients. We also report validation data including both comparison with manual segmentation and reproducibility measurements, as well as data on the degree of fattiness measured in each of the thigh muscles as a potential marker of muscle fitness.

Methods: The image segmentation was performed on images series obtained from the thigh of 11 healthy volunteers (HV) and 14 sIBM patients using a 1.5T MRI scanner, a Q-body coil and a proton density-weighted spin echo pulse sequence (TR 3s, TE 13ms, FOV 24cm, NEX 2, ~100 consecutive slices). Individual thigh muscles were segmented through the combined use of a signal thresholding and fuzzy pixel clustering approach as well as active contours. For muscle contours, the 3D Slicer semi-automated segmentation tool, which is based on the hermite spline interpolation technique, consisted of user selection of seed points on a set of slices from the MR dataset to define a closed curve 1) in the acquisition plane and 2) for any slice that does not contain user-supplied seed points. Resulting segmented regions, which were then divided into individual lean muscle and IMAT volumes, were reviewed by the rater and, if necessary, corrected using manual editing tools. For instance, additional control points may be added after visual check to incrementally refine the results of the segmentation.

Results: Results showed that determination of individual muscle volumes (such as *vastus lateralis intermedialis*-VLI, *rectis femoris*-RF and *semi-membranosus*-SM) was highly reproducible between two readers both using manual segmentation (R^2=0.99) and the semi-automated technique (R^2= 0.99). Comparison between both approaches showed that individual muscle volumes were nearly identical (y=0.98 x-18911, R^2=0.99, P<0.0001). However, it took ~3 to 4x less time to segment out these volumes using 3D Slicer (~45 min/thigh) compared to the manual segmentation approach (~3 hours/thigh). Based on such data, 15-20, ~30 and 35-40 patients would be needed to observe with 80% power a 2% increase in SM, REC and VLI muscle, respectively. Interestingly, the degree of fat infiltration ("fattiness"), as measured from IMAT% of muscle volumes in healthy subjects, varies from 3% to 7% and 16% (p<0.05) in RF, VLI and SM muscles, respectively. As expected, the degree of muscle fattiness in sIBM patients was much greater in average (~35-40%), with values varying from 10% in posterior muscles such as the BFL muscle to 58% in anterior muscles of the thigh such as the VM. Along with fat infiltration, sIBM also caused atrophy of thigh muscles, more so in the anterior (A) (e.g. RF: sIBM 143±56 cm^3 *vs* HV 235±73 cm^3; VLI: sIBM 143±56 cm^3 *vs* HV 235±73 cm^3, p<0.05) than in the posterior (P) compartment (e.g. SM: sIBM 216±85 cm^3 *vs* HV 255±80 cm^3, NS) (Fig. 1).

Discussion: 3D Slicer is an open source multi-platform software that was developed for visualization of medical images. For this study, its embedded semi-automated segmentation tool to assess individual thigh muscle volumes was successfully validated, both based on the high reproducibility and high correlation observed *vs* manual segmentation. This method, which combines the perceptual recognition of a human expert and the reliability of a computer, appears as an excellent alternative to the time-consuming process of manually outlining each muscle at a time. The successful implementation for image analysis of sIBM patients allowed to measure all 10 muscles in the thigh in less than 2 hours/patient scan. Results have shown that each of these muscles may not be affected to the same degree in sIBM patients, both in terms of atrophy and degree of fat infiltration.

Conclusion: Such analysis may prove particularly useful when assessing effects of new muscle therapies on restoration of muscle structure and function in relation to the overall patient balance.

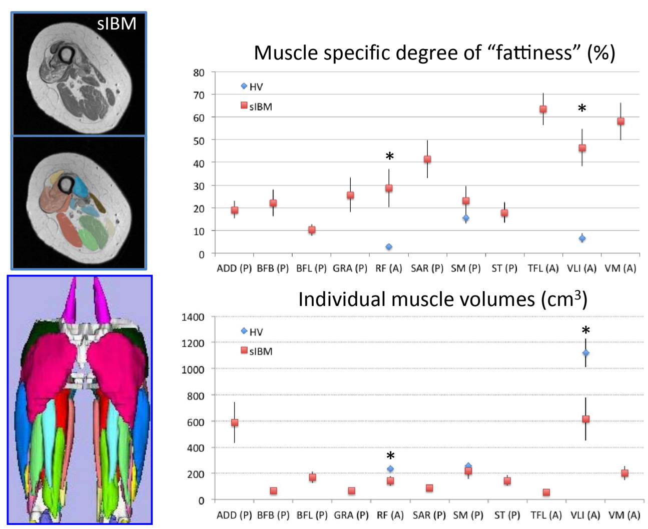

Fig.1 Differences in individual thigh muscle volumes and fat infiltration levels between healthy volunteers and sIBM patients

References

1. MC Dalakas. Sporadic inclusion body myositis—diagnosis, pathogenesis and therapeutic strategies. Nature Clinical Practice Neurology. 2006;2:437-447
2. Hilton TN, Tuttle LJ, et al. Excessive adipose tissue infiltration in skeletal muscle in individuals with obesity, diabetes mellitus, and peripheral neuropathy: association with performance and function. Phys Ther. 2008;88:1336–1344.
3. S Pieper, B Lorensen, et al. The NA-MIC Kit: ITK, VTK, Pipelines, Grids and 3D Slicer as an Open Platform for the Medical Image Computing Community. Proceedings of the 3rd IEEE International Symposium on Biomedical Imaging: From Nano to Macro. 2006; 698-701.