Changes in elastic modulus of muscles from multi-parametric MRI and agglomerative hierarchical clustering

Delphine Perie[1,2] and Daniel Curnier[3,4]
[1]*Mechanical Engineering, Ecole Polytechnique de Montreal, Montreal, QC, Canada,* [2]*Research center, CHU Sainte Justine, Montreal, Quebec, Canada,* [3]*Kinesiology, Université de Montréal, Montreal, QC, Canada,* [4]*Research center, CHU Sainte Justine, Montreal, QC, Canada*

INTRODUCTION: The passive tension of muscles is affected by several pathologies and need to be characterized in vivo for diagnostic and treatment purposes [1, 2]. Despite an incremental utilization of multi-parametric magnetic resonance imaging (MRI) for soft tissue characteristics and function [3, 4], the link between multi-parametric MRI and the mechanical properties of muscle has not been established yet. We sought to determine the parametric relationship between different muscle mechanical properties and the MR parameters. We hypothesized that multi-parametric MRI could characterize muscles with large mechanical differences. The specific aim was to develop a reproducible evaluative quantitative tool of the mechanical properties of muscle tissue using multi-parametric MRI associated to principal component analysis and agglomerative hierarchical clustering.

METHODS: Leg and arm muscles of adult rabbits (n=24) were dissected, and tested 12 hours post mortem, in a state of rigor mortis, or 72 hours post mortem, in a state of post-rigor mortis. Porcine hearts (n=12) were obtained from a local slaughterhouse within 2 hours of death and placed in a chamber filled with a tyrode saline solution. All samples were submitted to a multi-parametric MRI acquisition (3T whole-body system, Philips Achieva X-Series) followed by a uniaxial tensile test at a constant speed of 1mm/s (Mach-1, Biomomentum Inc.). Images for the quantification of T1 and T2 were acquired using a multiple inversion recovery TSE sequence for T1 and a multi-echo TSE sequence for T2. The MT ratio (MTR) was obtained using two GE sequences, one with an off-resonance pulse applied at 1100Hz down to the free water proton resonance frequency and the other one without it. The last sequence measured the ADC and the fractional anisotropy (FA) using a multi-shot SE EPI diffusion-weighted sequence with 15 non-collinear diffusion and a b value of 1000s/mm^2. The Young's modulus E was calculated from the slope of the force-displacement curve in the linear part. A principal component analysis (XLSTATS, Addinsoft, New York, United States) was used to convert the set of possibly correlated variables into a set of linearly uncorrelated variables (F1, F2, …Fn). Agglomerative Hierarchical Clustering was performed on the 3 first principal components (F1, F2 and F3). Each observation was a cluster and the process successively merged clusters into larger clusters until it reached one big cluster containing all the samples using the Ward's distance between clusters. These successive clustering operations produced a binary clustering tree (dendrogram), whose roots contained all the observations.

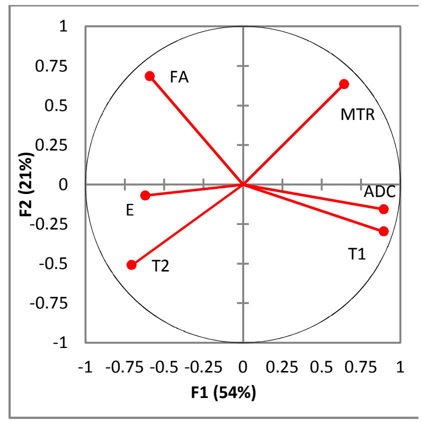

Figure 1: Principal component analysis

RESULTS: The principal component analysis reduced our six variables (E, T1, T2, MTR, ADC and FA) to two principal components F1 and F2 with a cumulative variability of 75%, which increased to 88% when considering the third principal component F3. The representation of the six variables in the (F1, F2) plane (Figure 1) showed a positive correlation between T1 and ADC as they were located near the circle and near to each other and a negative correlation between T2 and MTR as they were located near the circle and symmetric relatively to the circle origin. The position of T1, ADC, MTR, FA and T2 near the X-axis suggested that F1 expressed mainly these parameters. The position of E far away from the circle suggested that this parameter is not only expressed by F1 or F2, but also by F3, as shown by the eigenvectors of the covariance matrix. One way to determine the natural cluster division in a dataset is to compare the height of each link in the dendogram. A link, whose height differs noticeably from the height of the links below, indicates that the objects joined at this level are much farther apart from each other than their components were when they were joined. The dendograms obtained from the 3 first principal components showed a natural division into two clusters (Figure 2). The first cluster contained samples from skeletal muscles while the second cluster contains samples from the heart muscles.

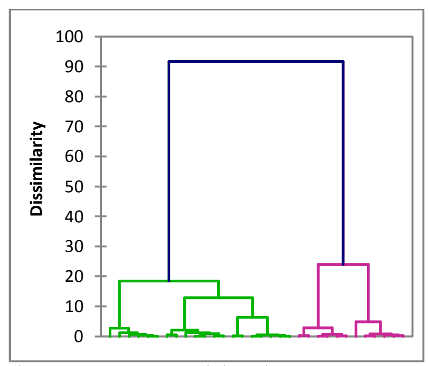

Figure 2: Dendogram divided into 2 clusters corresponding to cardiac or skeletal muscle

DISCUSSION

We confirmed our hypothesis that a relationship exists between the Young's modulus and the MRI parameters of different type of muscle, and that this relationship may be in part non linear. The natural division into two clusters on the dendrograms reflected the different tissues. The principle components were able to classify the different muscle tissues. The proposed multi-parametric MRI protocol associated to principal component analysis is a promising tool for the evaluation of mechanical properties within the muscle. Our in vitro experiments will now allow us focused in vivo testing on different type of healthy and disable muscles in order to determine useful quantitative MR-based biomarkers. Based on our data it is also possible now to perform longitudinal in vivo testing on disable muscle at different pathological states. Future directions of our laboratory aim to better understand and to implement novel multi-parametric MRI parameters as biomarkers of myocardial viability and potential prognostic scoring of myocardial relaxation and contraction.

REFERENCES

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