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Texture in Quantitative Viscoelastic Response (QVisR) Images Differentiates Dystrophic from Control Skeletal Muscles in Boys, *In Vivo*

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***Abstract*— Quantitative Viscoelastic Response (QVisR) ultrasound is a new machine learning-based elasticity imaging method in which elastic and viscous moduli are estimated from tissue deformation in response to two consecutive acoustic radiation force (ARF) excitations. The estimated moduli are rendered into two-dimensional parametric images of elastic and viscous modulus. From QVisR images, the spatial distribution of elastic and viscous properties may be evaluated using established computational texture analysis tools. In this study, computational texture analysis by the omnidirectional gray-level run-length matrix (GLRLM) was applied to QVisR images. The images were obtained in the *vastus lateralis* (VL) muscles of 11 boys with Duchenne muscular dystrophy, aged 5-12 years, and 8 age-matched boys with no known neuromuscular disorders, who served as controls. GLRLM-derived elastic entropy in QVisR images was statistically higher (Wilcoxin, $p<0.05$) in the VL muscles of boys with DMD than control for ages between 5.5 and 7 years. This result is consistent with expected heterogeneous distribution of inflammation, necrosis, fibrosis, and fat in early stages of dystrophic degeneration. The findings suggest that texture in QVisR images may be a relevant biomarker for DMD progression and response to treatment, particularly at young ages when interventions are likely to be most impactful.**

Keywords— Viscoelasticity, Anisotropy, Muscle, Acoustic Radiation Force, Viscoelastic Response (VisR), ARFI

I. Introduction

In Duchenne Muscular Dystrophy (DMD), skeletal muscle undergoes inflammation and necrosis and is replaced by fibrous tissue and fat in an inhomogeneous manner. These compositional changes underlie viscoelastic changes that can be interrogated by a new machine learning-based approach called Quantitative Viscoelastic Response (QVisR) imaging.

QVisR ultrasound [1] is an acoustic radiation force (ARF)-based imaging method that estimates tissue elasticity and viscosity without observing shear-wave propagation. Rather, elasticity and viscosity are calculated from tissue displacements observed in the ARF region of excitation (ROE) in response to two successive ARF impulses, delivered to the same ROE but separated in time. From the observed ARF-induced displacement profiles, a trained Bagged Trees machine learning framework predicts elastic and viscous moduli. These modulus estimates are rendered into 2D parametric images of elasticity and viscosity, whereby every pixel in the 2D image is associated with an elastic and a viscous modulus value.

While directly evaluating QVisR measures of elastic and viscous moduli is relevant to monitoring dystrophic muscle degeneration, more diagnostically relevant information is available by considering the spatial distribution of elastic and viscous moduli in QVisR images. To objectively and quantitatively evaluate such spatial distributions, image texture analysis may be employed. For example, as described in [2] and more recently in [3], [4], an omnidirectional gray-level run-length matrix (GLRLM) can be used to compute 2D or 3D texture features from image data [5].

In this study, computational texture analysis is applied to 2D QVisR images of elastic and viscous modulus to evaluate compositional and structural differences in the lower limb skeletal muscles of boys with DMD versus age-matched control boys with no known neuromuscular disorders. *We hypothesize that texture in QVisR images differentiates dystrophic from control skeletal muscles in boys.*

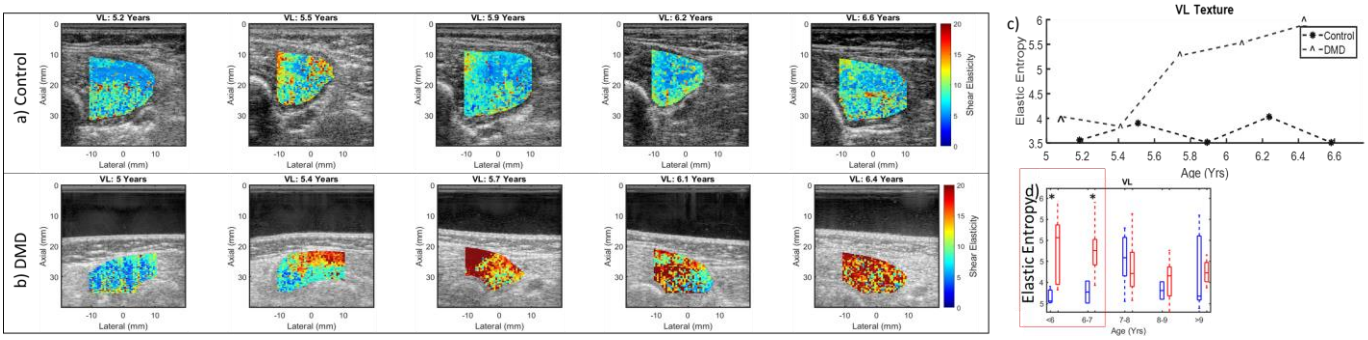

Figure 1: The top row (a) shows serial QVisR images from a representative control subject's vastus lateralis (VL) muscle, acquired approximately once every four months. The bottom row (b) shows a similar series from a subject with DMD. For panels (a-b) the age of the subject at the time of imaging is written in the title of the image. Panel (c) shows the entropy of each example image, as calculated using computational texture analysis, as a function of age. Astericks symbol represents control and arrow head represents DMD subjects. Panel (d) shows box plots of the entropy results over all examined subjects. Blue indicates control and red DMD subjects.

II. Methods

A. QVisR Methods

The measured displacement profiles were inputs to a trained Bagged Trees machine learning framework. The framework was trained using 100 simulated viscoelastic materials with varying elasticities (1.66 kPa to 33.3 kPa in steps of 3.52 kPa) and viscosities (0.003 Pa.s to 2.34 Pa.s in steps of 0.26 Pa.s). For each material, displacement in response to QVisR ARF excitations was simulated in LS-DYNA (Livermore Software Technology Corp., Livermore, CA). Then, ultrasonic tracking of the predicted displacements was performed using Field II. The material simulation methods were adapted from those previously described in [6]. Displacement tracking was applied to the simulated ultrasound data, and the simulated displacement profiles were used to train the Bagged Trees machine learning framework with the modeled elastic and viscous moduli as ground truth. Among the 100 simulated materials, displacements profiles from 80, randomly selected, were used for training, while the remaining 20 materials served as test sets (data not shown for brevity).

B. Data Acquisition

All procedures were approved by the Institutional Review Board at the University of North Carolina at Chapel Hill. QVisR imaging was performed using a Siemens VF7-3 linear array transducer and Acuson Antares imaging system equipped for research purposes (Siemens Healthineers, Ultrasound Division, Issaquah, WA, USA). VisR beam sequences consisted of two ARF excitations co-located and separated in time by 0.4 ms. Each ARF impulse was 70 μs in duration and centered at 4.2 MHz with an F/3.0 focal configuration. Conventional B-Mode style tracking pulses centered at 6.15 MHz were acquired before, between, and after the ARF excitations for a 4 ms ensemble length. The focal depth for each acquisition was set to the bottom of the examined muscle at the center of the lateral imaging field of view. A trained sonographer positioned the transducer such that data were acquired with the muscle in cross-sectional view at the approximate middle length-wise.

QVisR data were acquired *in vivo* in the rectus femoris (RF), vastus lateralis (VL), sartorius (ST), and gastrocnemius (GM) medial head muscles of 11 boys with DMD and 8 age-matched control boys. The acquired QVisR raw RF data were transferred to a computational workstation for off-line processing. One-dimensional axial displacement tracking by normalized cross-correlation generated displacement profiles corresponding to every pixel in the two-dimensional (axial x lateral) QVisR imaging field of view.

The QVisR images from each muscle were analyzed using the University of North Carolina at Chapel Hill Neuro Imaging Research and Analysis Laboratories (NIRAL) gray-level-run-length-matrix (GLRLM) tool, which is an open source computational texture analysis package for medical images [2]–[5]. Entropy, as well as run-length non-uniformity, gray level non-uniformity, short run emphasis, and long run emphasis, were computed. For brevity, only results of elastic entropy in the vastus lateralis (VL) muscle are shown. Statistical comparisons were performed using Wilcoxon rank sum with $p<0.05$ suggesting statistical significance.

III. Results and Discussion

Fig. 1 shows serial QVisR images in a representative control (a, top row) and dystrophic (b, bottom row) VL muscle in boys aged 5.2-6.6 years. Note that by visual inspection he DMD images become more heterogeneous with age, while the control images do not. The corresponding plots of entropy versus time (c) show that after 5.5 years of age, entropy in the dystrophic VL increases to levels that are statistically higher than those in the control VL. Across all examined subjects (d), entropy is statistically higher in dystrophic versus control VL for ages less than 7 years (boxed). After 7 years, entropy in

dystrophic VL becomes more like that of control, suggesting that the muscle is then more homogenously replaced by fatty and fibrous tissue.

IV. Conclusion

In this study, computation texture analysis was applied to parametric QVisR images of elastic and viscous moduli in the lower limb skeletal muscles of boys with DMD and age-matched controls. The results shown for the VL muscle demonstrate that elastic entropy in dystrophic muscle is statistically significant higher than in control at ages 5.5 to 7 years. This result is consistent expectations for heterogeneously distributed, recurring cycles of inflammation, necrosis, fibrosis, and fatty deposition with dystrophic muscle degeneration. Notable, entropy differences between dystrophic and control VL were most pronounced at young ages, when intervention is most likely to be impactful. Overall, these results suggest that texture in QVisR ultrasound images is a relevant biomarker for dystrophic muscle degeneration, which could help to elucidate the complex and poorly understood pathophysiology of DMD and serve as an outcome measure for interventions.

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