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Imaging Viscoelasticity in Control and Dystrophic Vastus Lateralis using Quantitative Viscoelastic Response (QVisR) Ultrasound

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Abstract— **Mechanical property changes associated with inflammation, necrosis, fibrosis, and fatty deposition in dystrophic muscle may be quantitatively evaluated by Quantitative Viscoelastic Response (QVisR) ultrasound. QVisR uses a machine learning (ML) framework that takes as input tissue displacement in response to two consecutive and co-located acoustic radiation force (ARF) excitations and yields as output estimates of shear elastic and shear viscous moduli. QVisR imaging was performed in the *vastus lateralis* (VL) muscles of 11 boys with Duchenne muscular dystrophy (DMD) aged 5 to 12 years and of 8 age-matched boys with no known neuromuscular disorders, who served as controls. QVisR measures of elastic moduli differed between DMD and control VL in boys aged less than six years and six-to-seven years. Similarly, QVisR measures of viscous moduli differed between DMD and control VL in boys aged six-to-seven years. These results demonstrate that QVisR measures of elastic and viscous moduli differentiate dystrophic from control muscle. The findings suggest that QVisR may be relevant to monitoring dystrophic muscle degeneration and response to intervention, particularly in early stages when interventions are most likely to be impactful.**

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

I. Introduction

In Duchenne muscular dystrophy (DMD), muscle fiber inflammation, necrosis, fatty deposition and fibrosis are expected to cause changes in muscle elasticity and viscosity. Therefore, noninvasive approaches to evaluating tissue elasticity and viscosity may be relevant to monitoring dystrophic muscle degeneration over time and in response to interventions. We have previously demonstrated that the lower limb skeletal muscles of boys with DMD were distinguishable from those of age-matched control boys in terms of elastic and viscous properties assessed by Viscoelastic Response (VisR) ultrasound.

VisR ultrasound uses two consecutive acoustic radiation force (ARF) excitations, separated in time but delivered to same region of excitation, to induce tissue displacement. The tracked displacements are fit to the mass-spring-damper model to estimate tissue elasticity and viscosity relative to the applied ARF amplitude. The amplitude of the ARF, however, is generally unknown due to the complex and varying acoustic properties of tissue. Therefore, by conventional VisR methods, elasticity and viscosity are evaluated qualitatively. Assessing elastic and viscous property qualitatively complicates comparisons of mechanical property between subjects in cross-sectional study designs and within a single subject over time in longitudinal study protocols. The purpose of this work is to make VisR assessments of elasticity and viscosity quantitative using a machine learning (ML) approach. This new approach to VisR ultrasound is referred to as 'Quantitative VisR (QVisR)' ultrasound.

II. Background

Quantitative assessment of tissue elasticity and viscosity is possible by several ultrasound methods. Some such methods calculate shear elastic moduli from observed shear wave group velocity [1]–[3]. Other approaches estimate both shear elastic and viscous moduli from observed shear wave phase velocity and dispersion [4]–[6]. Recently, Rouze et al [7] used a look-up table-based approach to estimate elastic and viscous moduli from group shear wave velocities. While these shear wave-based methods enable quantitative assessment of elasticity and viscosity in homogeneous, isotropic tissue media, the mathematical relationships that relate shear wave velocity to elastic and viscous moduli are not relevant in layered or otherwise complex tissue morphologies. Moreover, robust estimation of shear wave velocity requires spatial averaging, which limits the spatial resolution of mechanical features in heterogeneous media. Further, the requirement for measurable displacement magnitudes millimeters from the region of mechanical excitation limits penetration depth and challenges interrogation of very stiff tissues. Finally, shear wave

reflections and distortions, particularly in the elevational dimension, confound results [8].

Such complications are avoided in QVisR ultrasound because the method quantifies elastic and viscous moduli from displacements observed in only the ARF region of excitation. QVisR does not involve observation of shear wave propagation. Rather, the bagged trees machine learning framework is used to deduce elastic and viscous moduli from VisR displacement profiles.

We herein describe the application of QVisR ultrasound to differentiating dystrophic muscle degeneration in boys with DMD. *We hypothesize that QVisR elasticity and viscosity measures in the vastus lateralis (VL) muscles of boys with DMD statistically differ from those in control boys aged less than 10 years.*

III. Methods

A. Development of the machine learning model

Finite element method (FEM) simulations of 100 viscoelastic materials (1.66 kPa to 33.3 kPa in steps of 3.52 kPa, 0.003 Pa.s to 2.34 Pa.s in steps of 0.26 Pa.s) were performed in LS-DYNA (Livermore Software Technology Corp., Livermore, CA) to simulate displacement in response to VisR ARF excitations generated by a linear array with an F/3.0 focal configuration and a 300 µs pulse length. Ultrasonic tracking of the induced displacements was simulated using Field II according to the methods described in [9], [10]. The resulting simulated VisR data sets from 80 viscoelastic materials were used to train a bagged trees ML model [11], and the simulated data sets from the remaining 20 viscoelastic materials were used to test the accuracy of the trained ML model.

B. In vivo data acquisition in boys

All procedures were approved by the Institutional Review Board at the University of North Carolina at Chapel Hill. *In vivo* QVisR imaging was performed on the VL muscles of 11 boys (aged 5-12 years) with DMD and 8 age-matched boys with no known neuromuscular disorders, who served as controls.

QVisR imaging was performed using a custom beam sequence implemented on a Siemens Acuson Antares imaging system equipped for research purposes and a VF 7-3 linear array transducer (Siemens Healthcare, Ultrasound Business Unit, Issaquah, WA, USA). The two ARF excitations were centered at 4.21 MHz with an F/3.0 focal configuration. They were each 70 µs in duration and separated in time by 0.3 ms. Tracking pulses were centered at 6.15 MHz with an F/3.0 focal configuration and collected in ensembles of length 3.7 ms. The focal depth for each data acquisition was set to the bottom of the examined muscle at the center of the lateral field of view. A trained sonographer manually positioned the imaging transducer using B-mode guidance to evaluate the muscle at approximate its length-wise middle in a cross-sectional view.

The acquired raw RF data were transferred to a computational work station for off-line QVisR processing. Displacements were tracked using one-dimensional axial cross-correlation. The resulting displacement profiles were inputs to the trained bagged trees ML model, which estimated elastic and viscous shear moduli. These moduli values were rendered into 2D parametric images.

Wilcoxon rank-sum statistical tests were performed to evaluate the null hypothesis of equal medians between QVisR derived moduli in DMD and control VL muscles. P-values of < 0.05 were considered significant in this work.

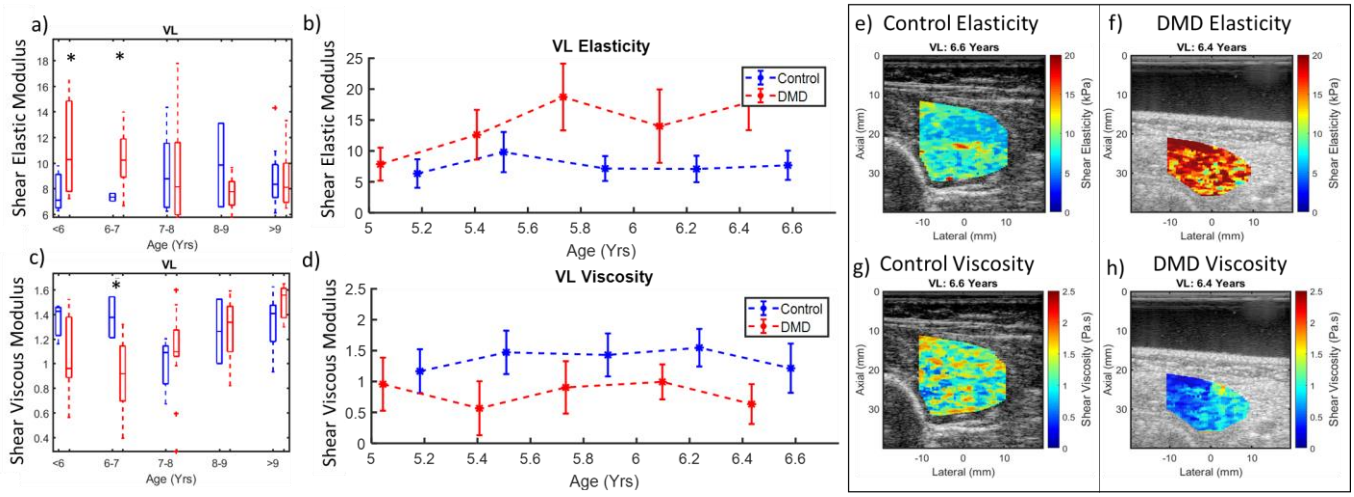

Figure 1: a) boxplots of control (blue) and DMD (red) QVisR shear elastic modulus as a function of age. Statistical significance is indicated by asterisks. b) In a representative boy with DMD and control boy, QVisR shear elastic modulus (median ± 1 MAD) over the 2D muscle region in the QVisR image versus age. c) Box plots of shear viscous modulus and d) representative examples of shear viscous modulus versus age, organized as described for (a) and (b). (e-h) QVisR images

IV. Results and Discussion

Figure 1(a) shows that, in general, dystrophic VL had significantly higher elastic moduli than control in boys aged 5-7 years. Panel (b) shows, in one representative boy with DMD and one without, shear elastic moduli increased over the ages of 5-7 years in dystrophic VL, while elastic moduli generally remained constant in control VL. Figure 1(c) illustrates that shear viscous moduli were lower in dystrophic versus control VL in boys aged 5-7 years, significantly so in boys aged 6-7 years. In panel (d), QVisR-derived shear viscous moduli were generally lower the VL muscle of one representative boy with DMD versus one representative control boy between the ages of 5.4 and 6.4 years. QVisR images corresponding to the last time points in (b) and (d) are shown in (e-h).

V. Conclusion

These results demonstrate that *in vivo* QVisR measures of shear elastic and viscous moduli differentiate dystrophic from control VL muscle in age-matched boys. Importantly, the observed differences in elastic moduli were statistically significant in boys aged less than six and six-to-seven years. Similarly, the observed differences in viscous moduli were statistically significant in boys ages six-to-seven years. These results suggest that QVisR is relevant for monitoring dystrophic muscle degeneration, particularly in its early stages when interventions are most likely to be impactful.

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References

[1] A. P. Sarvazyan, O. V Rudenko, S. D. Swanson, J. B. Fowlkes, and S. Y. Emelianov, "Shear wave elasticity imaging: a new ultrasonic technology of medical diagnostics.," *Ultrasound Med. Biol.*, vol. 24, no. 9, pp. 1419–35, Nov. 1998.

[2] K. Nightingale, S. McAleavey, and G. Trahey, "Shear-wave generation using acoustic radiation force: in vivo and ex vivo results.," *Ultrasound Med. Biol.*, vol. 29, no. 12, pp. 1715–23, Dec. 2003.

[3] J. Bercoff, M. Tanter, and M. Fink, "Supersonic shear imaging: A new technique for soft tissue elasticity mapping," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 51, no. 4, pp. 396–409, 2004.

[4] S. G. Chen *et al.*, "Shearwave Dispersion Ultrasound Vibrometry (SDUV) for Measuring Tissue Elasticity and Viscosity," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 56, no. 1, pp. 55–62, 2009.

[5] M. W. Urban, S. Chen, and M. Fatemi, "A Review of Shearwave Dispersion Ultrasound Vibrometry (SDUV) and its Applications," *Curr. Med. Imaging Rev.*, vol. 8, no. 1, pp. 27–36, 2012.

[6] T. Deffieux, G. Montaldo, M. Tanter, and M. Fink, "Shear wave spectroscopy for in vivo quantification of human soft tissues visco-elasticity," *IEEE Trans. Med. Imaging*, vol. 28, no. 3, pp. 313–322, 2009.

[7] N. C. Rouze, Y. Deng, C. A. Trutna, M. L. Palmeri, and K. R. Nightingale, "Characterization of Viscoelastic Materials Using Group Shear Wave Speeds," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 65, no. 5, pp. 780–794, 2018.

[8] A. Sarvazyan, T. T. J. Hall, M. M. W. Urban, M. Fatemi, S. R. Aglyamov, and B. S. Garra, "an Overview of Elastography - an Emerging Branch of Medical Imaging.," *Curr. Med. Imaging Rev.*, vol. 7, no. 4, pp. 255–282, 2011.

[9] J. Jensen, "SImulation of advanced ultrasound systems using Field II," *Proc. IEEE Int. Symp. Biomed. Imaging Nano to macro, 2004.*, vol. 1, pp. 636–639, 2004.

[10] M. L. Palmeri, A. C. Sharma, R. R. Bouchard, R. W. Nightingale, and K. R. Nightingale, "A finite-element method model of soft tissue response to impulsive acoustic radiation force," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 52, no. 10, pp. 1699–1712, 2005.

[11] T. G. Dietterich, "Ensemble methods in machine learning," *Int. Work. Mult. Classif. Syst.*, pp. 1–15, 2000.