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# Noninvasive quantification of elastic anisotropy factor by steered ultrasound pushing beams: Towards a novel imaging biomarker of muscle health

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## INTRODUCTION

Muscular diseases such as Duchenne muscular dystrophy (DMD) lack reliable biomarkers for disease progression and response to therapies<sup>1</sup>. Tissue mechanical and structural properties are vital for the function of human physiological systems, and often reflect pathophysiological conditions<sup>2</sup>.

Ultrasound shear wave elastography (SWE) uses focused acoustic pushing beams to generate shear waves and ultrafast ultrasound imaging to visualize and quantify the shear wave propagation velocity in biological soft tissues<sup>3</sup>. Shear wave propagation is governed by tissue elasticity such that wave velocity provides an accurate estimate of the shear modulus (µ). However, muscles exhibit complex tissue architecture and marked mechanical directional dependence (i.e., elastic anisotropy), both affecting the shear wave velocity and rendering the clinical applicability of ultrasound elastography challenging.



Here we propose a new elastography sequence, based on steered pushing beams (SPB), for real-time assessment of the apparent muscle shear modulus  $(\mu_{I})$  and two elastic anisotropy factors ( $X_E$  and  $X_E$ ,  $\mu_{\perp}$ ), promising indicators of muscle mechanical and structural integrity, respectively. The sensitivity of the new SPB sequence is demonstrated on phantoms and ex-vivo muscles. Mechanical validation was conducted in ex-vivo pig muscles. The feasibility of the technique was then demonstrated on human muscles in-vivo: healthy adults and a patient with DMD.



Push beam simulation Ultrasound steered pushing beam

Ultrasound ultrafast imaging with compounding

**Commercial ultrasound scanner** 

Data acquisition, fitting the shear wave propagation, and calculation of anisotropy parameters

Fig. 1. Schematic of ultrasound shear wave elastography using a novel steered pushing beam is electronically programmed by using focus delays law to generate a steered acoustic radiation force that acts as a shear wave source. Several pushing beams are programmed between -20° and 20°. (B) Example of simulated steered pushing beams at 0°, +10° and +20° in Field II software. (C) Ultrafast acquisition of the propagating shear waves with different ultrafast ultrasound plane waves tilted around the axis of the pushing beam. (D) The new sequence was implemented in a Mach 30 ultrasound scanner (Hologic Supersonic Imagine, Aix-en-Provence, France). For comparison, the traditional elastography sequences implemented in commercially available scanners use a single pushing beam angle (corresponds to angle = 0° of the SPB). (E) Group wave velocity of an ex-vivo muscle obtained for each push angle is modelled by shear vertical (SV) propagation mode  $(\mu_{SV}(\psi) = \rho v_{SV}^2(\psi) = \mu_{//} + 4(\chi_{E,}\mu_T - \mu_{//}) \sin(\psi)^2 \cos(\psi)^2)$ , making it possible to calculate the apparent shear modulus  $(\mu_{//})$  and two elastic anisotropy factors  $(\chi_{E,}\mu_T - \mu_{//}) \sin(\psi)^2 \cos(\psi)^2)$ , making it possible to calculate the apparent shear modulus  $(\mu_{//})$  and two elastic anisotropy factors  $(\chi_{E,}\mu_T - \mu_{//}) \sin(\psi)^2 \cos(\psi)^2)$ , making it possible to calculate the apparent shear modulus  $(\mu_{//})$  and two elastic anisotropy factors  $(\chi_{E,}\mu_T - \mu_{//}) \sin(\psi)^2 \cos(\psi)^2$ .

### RESULTS



Fig. 2. Shear wave propagation using SPB sequence and its sensitivity to detect tensile anisotropy. (A) Snapshots showing the shear wave propagation in an isotropic Polyvinyl Alcohol (PVA) phantom. The solid red line corresponds to the head of the ultrasonic array. (B) Averaged shear wave velocity  $(V_{sv})$  as a function of the steered push angle in the isotropic phantom showing similar shear wave velocity across push angles  $(8.09 \pm 0.17 \text{ m/s})$ . (C). Shear wave velocity maps for three different push angles showing different velocities depending on the push beam (i.e., anisotropy effect). (D) Ultrasound shear wave elastography parallel (longitudinal) and perpendicular (transverse) to the muscle fibers. (E) Averaged shear wave velocity  $(V_{sv})$  as a function of the steered push angle in the anisotropic beef muscle, showing different shear wave velocity across push angles.

and parallel to the main fiber axis. The Young's moduli (E) were calculated by fitting the stress/strain curve from 2 to 8%. Tensile anisotropy is then calculated as follows:  $X_E = \frac{E_{II}}{E_{\perp}}$ . (C) Elastography scans were performed parallel and perpendicular to the muscle fibers to quantify  $X_E$ . (D) Comparison of anisotropy  $X_E$  obtained from tensile testing and ultrasound SPB. Wilcoxon Mann-Whitney test shows no significant differences between methods (p-value=0.8).





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Fig. 5. Comparison of the novel SPB markers between a patient with DMD and age-matched controls

<b>CONCLUSIONS AND FUTURE WORK</b>	REFERENCES
This study shows a translational proof of concept for a novel ultrasound imaging approach, offering real-time quantification of noninvasive mechanical parameters with potential for monitoring neuromuscular diseases	<sup>1</sup> Szigyarto, C. A. & Spitali, P. Biomarkers of Duchenne muscular dystrophy: current findings. Degener. Neurol. Neuromuscul. Dis. 8, 1–13 (2018); <sup>2</sup> Puttini, S. et al. Gene-mediated restoration of
affecting skeletal muscle biomechanics and structure. Further research is required to investigate the clinical value of these biophysical parameters.	19-25 (2009); <sup>3</sup> Gennisson, JL. et al. Ultrasound elastoraphy: Principles and techniques. Doagno. Interv. Imaging. 94, 487-495 (2013).