Characterization of Skeletal Muscle Elasticity Using Magnetic Resonance Elastography

a report by

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Anatomy/Physiology/Pathology

Information on the elasticity of skeletal muscle (often called muscle stiffness) in vivo has clinical applications in several fields, including orthopaedics, sports medicine, physical medicine and rehabilitation, endocrinology, and rheumatology. Muscle stiffness can be evaluated in either the relaxed (passive) state or the contracted state; the mechanisms involved in each state are different. Muscle resistance to passive stretching comes primarily from two sources: titin and the extracellular matrix (ECM). In contrast, when muscle is actively contracted, muscle stiffness reflects the elasticity of the actin–myosin cross-bridges within the muscle fibers.

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Pathological skeletal muscle tissues often exhibit a noticeable difference in stiffness compared with normal healthy tissue. This change in muscle stiffness is thought to likely result from structural or compositional changes in either the ECM or muscle fiber. Examples of these two situations are idiopathic inflammatory myopathy (IIM) and Graves’ disease, respectively, both of which are briefly described below.

IIM is a heterogeneous group of disorders characterized by symmetrical proximal muscle weakness and elevated serum levels of enzymes derived from skeletal muscle. Types of myositis include dermatomyositis, polymyositis, and inclusion body myositis. All have in common lymphocytic infiltration of muscles, edema within the muscle, altered muscle composition, and impaired muscle function. Associated with these changes is a decrease in muscle endurance and/or strength. The following vicious cycle in IIM is hypothesized: first, the inflammation causes certain pathological degradation of the ECM in the affected muscles; next, the degradation of ECM blocks the mechanotransduction pathway; consequently, the lack of mechano-biological signaling results in decreased cellular activity of the muscle cells and the further reduced synthesis of the ECM by muscle cells.

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An additional area of interest that involves stiffness of skeletal muscle tissue is the diagnosis of myofascial pain syndrome (MPS), a painful musculoskeletal condition and a common cause of musculoskeletal pain. The main findings about myofascial pain are localized taut bands of increased tone and stiffness and even more circumscribed points of tenderness (i.e. trigger points) that when compressed produce stereotypical patterns of referred pain. Taut bands are currently thought to represent a discrete group of muscle fibers that have contracted for unknown reasons. The identification of taut bands and trigger points is important not only for diagnosis, but also for potential treatment. Despite their importance, there is still no laboratory test or imaging technique capable of objectively confirming either their nature or location, while criticisms remain in terms of repeatability and subjectivity issues of conventional manual palpation examination.

Evaluation of Skeletal Muscle Tissue Stiffness

Conventionally, in vivo skeletal muscles are clinically assessed with functional examinations, validated clinical scales, force measurements using handheld...
and isokinetic dynamometers, and surface and fine-wire electromyography (EMG). While these measurements provide information that clinicians can use to track changes in muscle function in their patients, they do not provide any quantitative information about muscle stiffness, which is an important parameter in assessing muscle properties.

Technically, Young’s modulus is the quantity delineating a material’s elasticity. In conventional in vitro evaluation of skeletal muscle stiffness in clinical settings, elasticity is often assumed, and the local slope of the non-linear stress–strain curve at a given strain is considered the ‘modulus’ at that strain level. A different approach, magnetic resonance elastography (MRE), as described in greater detail in the following section, assesses tissue stiffness in vivo by calculating the modulus from its effect on shear wave propagation.

**Magnetic Resonance Elastography**

MRE is a non-invasive phase-contrast technique that directly visualizes and quantitatively measures propagating shear waves in tissue-like materials subject to harmonic mechanical excitation. MRE uses mechanical shear vibration rather than static stress as a probe. The major advantage of this method is that it does not require estimation of the stress distribution. A phase-contrast MR imaging (MRI) technique is used to spatially map the shear wave displacement fields. Specifically, a motion-sensitizing gradient (square wave, sinusoidal wave, or triangular wave) switching in polarity at the same frequency as the mechanical shear vibration is imposed on the conventional MRI gradients of the MRI scanner. The cyclic motion of the nuclei spins in the presence of the motion-sensitizing gradient causes measurable accumulative spin-phase shifts in the received MR signal, which can be used to calculate the pixel vibratory displacement. A wave image is thus formed from the pixel vibratory displacement. Subsequently, the elastic shear modulus can be calculated locally based on analysis of the shear wave displacement pattern and its propagation, a process generally termed ‘stiffness inversion.’ The shear modulus image is termed an elastogram (see Figure 1).

Because of its ability to map material elastic modulus, MRE has been proposed for quantitative characterization of muscle tissue stiffness in vivo. Since its invention, MRE has been applied to skeletal muscles in the biceps brachii, flexor digitorum profundus, thigh muscles, and upper trapezius. Some studies have developed methods for collecting MRE data in specific muscles and reported a database of muscle stiffness, and other studies have used MRE for determination of changes in shear stiffness in pathological muscles. Specifically, examples of MRE studies on muscle stiffness in patients with IIM, Graves’ disease, and MPS are described in this article.

Compared with conventional examinations, MRE imaging of skeletal muscle offers the following advantages: visualization and quantitative measurement of tissue stiffness; high sensitivity to small motions in the order of microns; and the ability to obtain full 3D displacement information throughout a 3D volume.

**Instrumentation**

In terms of hardware realization, the motion-sensitizing gradient can be readily incorporated into gradient echo (GRE) pulse sequences, usually for 2D imaging, or, more recently, echo-planar imaging (EPI) pulse sequences, which enable the fast imaging times desirable for 3D imaging. The choice of mechanical vibration frequency for a particular application depends on a trade-off: on the one hand, increasing frequency yields higher resolution, since the propagating wavelength is small; on the other hand, increasing frequency leads to higher attenuation, as tissue viscoelasticity increases at higher frequencies. In practice, excitation frequencies in the range of 90–200 Hz are used for skeletal muscle MRE imaging.

The choice of drivers that create the mechanical excitation on skeletal muscles in vivo include electromagnetic coil drivers, piezoelectric drivers, pneumatic drivers, and focused ultrasound. An electromagnetic coil driver applies alternating currents to an annular coil to generate motion. It is easy to construct and relatively low-cost, and can be customized easily for special in vivo applications such as muscle, breast, or brain MRE. However, artifacts may be produced due to the magnetic interference of the driver coil. A piezoelectric driver has the advantage of arbitrary orientation with respect to the main magnetic field, but its fabrication is elaborate and time-consuming, and it has a limited maximum
displacement. A pneumatic driver is easy to construct, free of artifacts, and low-cost, and has good frequency response. In focused ultrasound, the ultrasound beam is temporally modulated to create cyclic variation in acoustic radiation pressure at the focus of the ultrasound source, which can be localized deep within an object. Regardless of the type of driver chosen, trigger pulses are always provided by the sequencing computer of the MR scanner, and are fed to a function generator to generate a coupled-motion waveform that is amplified and applied to the driver.

Positioning and loading devices are often used to acquire MRE image data on skeletal muscles in relaxed, passively loaded, and isometrically contracted conditions. These devices usually run at 5–20% of maximal voluntary contracture (MVC). For instance, to test the biceps under load, a pulley system consisting of a hand grip at one end and weights at the other end was used.38 The muscles in the lower limb were tested in the relaxed configuration as well as in an actively contracted state using three types of positioning and loading devices:

- a positioning and loading device capable of adjusting the position of the ankle joint where weights connected to a cable and pulley system applied plantarflexion and dorsiflexion moments, thus investigating an isotonic contraction;33
- a foot plate with a strain gauge incorporated to measure isometric force with the ankle fixed in a neutral position;37 or
- a positioning and loading device with an MR-compatible torque cell to measure isometric moments and allowing for passive joint positioning.29,36

Examples of the positioning, loading, and force measurement devices and drivers are shown in Figure 2.

An increase in shear stiffness was observed when the muscles were isometrically contracting. For example, when the volunteers extended their proximal legs at 10% of MVC, there was a significant increase (p<0.05) in the shear stiffness of the vastus lateralis. At 20% of MVC, there was a significant increase in the shear stiffness of the vastus medialis.36

Repeatability of Magnetic Resonance Elastography Imaging on Skeletal Muscles

The repeatability of muscle MRE acquisition was assessed in the biceps brachii and lateral gastrocnemius. Repeat data were collected in the relaxed biceps brachii of two volunteers over seven days. The mean and standard deviations of the stiffness values of the repeat trials were calculated. Repeat data were collected from nine volunteers in the relaxed lateral gastrocnemius. The coefficient of variation was 15.7%, which was comparable to the standard deviations reported in the biceps brachii. When the lateral gastrocnemius was contracted, the coefficient of variation increased to 19.4%.37

Assessing Pathological Muscle with Magnetic Resonance Elastography

In vivo MRE examinations on the stiffness of the proximal lower limb muscle (vastus medialis) have been shown to be capable of detecting differences in stiffness between healthy and hyperthyroid subjects. Mechanical vibration was applied to the proximal lower limb via a pneumatic tube driver, and muscle contracture was monitored by the MR-compatible torque cell assembled to the foot plate.34 MRE scans on the patients with hyperthyroid myopathy showed a lower shear stiffness in the relaxed condition (2.11±0.61kPa) compared with the shear stiffness following treatment of hyperthyroidism (5.52±1.52kPa). Pre-treatment muscle stiffness was also significantly lower than that of the age-matched healthy volunteers (4.56±0.40kPa)26 (see Figure 3).
Because of its ability to differentiate tissue stiffness, MRE has been proposed as an imaging method to objectively detect the location and quantify the stiffness of myofascial taut band, thereby facilitating the diagnosis of myofascial pain. First, the myofascial pain patients underwent manual palpatory examination by an experienced physician, and the location of the myofascial taut band detected by palpation was marked. An MRE scan was then performed on the patients. Mechanical vibration (planar wave) was applied on the muscle–tendon junction at spin of scapula, allowing a shear wave to propagate through the upper trapezius, one of the most frequent locations of myofascial taut band and trigger point.

MRE phase images showed a chevron-shaped wave front in the vicinity of myofascial taut band detected by manual palpation. Stiffness images showed a statistically significant 50–100% (p=0.01) increase of shear stiffness (8.4kPa) in the taut band regions of the involved subjects (see Figure 4) relative to that of the controls (4.2kPa) or in nearby uninvolved muscle (4.8kPa).

Conclusions
MRE has gained popularity in biomechanical imaging of skeletal muscles. Combining in vivo MRE stiffness measurements and commonly used clinical measures such as muscle biopsy and subjective scales would facilitate the understanding of how changes in the skeletal muscle tissues by pathology alter their function. In vitro MRE imaging of appropriate models of ECM damaging and/or changes would help us to gain further insight into the role of ECM in the mechanical properties of muscles. MRE can also be used to objectively evaluate the efficacy of treatments for muscles altered by pathologies and injury. Primary technical challenges for MRE imaging on skeletal muscles include: further development of MRE pulse sequences to allow fast or realtime image data acquisition; improvement of stiffness inversion to be more robust and to handle material anisotropy; and more advanced design and instrumentation of drivers that more efficiently deliver mechanical vibrations to the tissue. Meanwhile, 1D MRE acquisitions can also be examined in different muscles and can be investigated as a method to monitor realtime changes during active contractions.