Monitoring the Effects of Chronic Obstructive Pulmonary Disease on Muscle Elasticity by MR Elastography

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Abstract:
Men afflicted with chronic obstructive pulmonary disease (COPD) show signs of muscle dysfunction, such as increased muscle fatigue and acidosis during exercise. We hypothesize that muscle elasticity of the lower extremities differs between patients with COPD and age-related controls. The shear modulus of the soleus muscle was measured non-invasively using MR elastography (MRE) at 0%, 5%, 10%, 15%, and 20% of the subject's maximum applied force. The results from this study showed statistical differences between the patients and controls, even though there were no statistical differences in the maximum applied force.

Introduction:
COPD afflicts a large number of the population, which has been attributed to the worldwide prevalence of cigarette smoking. Aside from the primary symptoms, such as excessive coughing and dyspnea, this disease has been shown to have secondary effects on muscle function[1]. Most of the changes that occur in the skeletal muscle have been attributed to deconditioning, which has led many to suggest the addition of physical therapy and reconditioning for combating this disease. MRE provides a novel approach for monitoring muscle health by measuring muscle stiffness under various loads. In this study, preliminary work was performed to determine if differences in muscle elasticity between healthy age-related controls and patients with COPD could be measured by MRE.

Methods and Materials
Subjects: Men diagnosed with COPD (n=6), based on pulmonary function tests, and age-related healthy controls (n=6) were recruited for this study.
MRI Experiment: All MRI experiments were performed on a 1.5T full-body Siemens Sonata. The subjects lay supine on the MR table with their feet securely fastened to a home-built foot-plate. The foot-plate, used for measuring applied force via a strain gauge, was fixed at a 90° angle. Localization and volumetric scans (T_1 FLASH sequence TR/TE 165ms/4.46ms, slice thickness 8, and 36 contiguous slices) were initially performed followed by 5 MRE scans. During the individual MRE scans, the subjects were required to maintain a force on the foot-plate of 0%, 5%, 10%, 15% or 20% of their maximum voluntary contraction (MVC). All force measurements were recorded on a PC and were later analyzed to determine if the target force was maintained during the MRE scans.
MR Elastography: MRE was performed by mechanically exciting the muscle tissue with a custom designed piezoelectric actuator[2] and using a modified gradient echo sequence.. For the mechanical excitation of the muscle tissue, the actuator lever was placed on the anterior surface of the calf approximately 5 cm below the knee. An excitation frequency of 100 Hz was used for imaging the soleus muscles. The actuator displacement was set at 700 µm. With a bandwidth of 260 Hz/Pixel and a flip angle of 15°, the TR was 120 ms and TE was 33.3 ms for the acquisition of phase images with a 180 x 80 matrix. A total of 8 phase offsets were acquired. Presented in Figure 1 is an axial slice of the human calf. The highlighted region, narrow rectangle, and arrow designate the soleus muscle, slice position, and approximate position of the actuator, respectively.
Data Analyses: All phase images were phase unwrapped and reconstructed into shear modulus elastograms using the local frequency estimation (LFE) technique[3]. The resultant elastograms were then averaged over all 8 phase offsets, where regions-of-interest were used to calculate the shear modulus of the soleus muscle. The data was presented as the absolute shear modulus and the ratio of the shear modulus over shear modulus at 0% MVC. From the volumetrics, the physiological cross-sectional area (PCSA=muscle volume/muscle fiber length)[4], which has been shown to be proportional to the maximum force, was determined assuming a muscle fiber length for the soleus of 3 cm[5]. Two-way repeated-measures ANOVA (Statview 5.0; SAS Institute Inc. Cary, NC) was used to determine statistical differences in absolute and normalized shear moduli for various MVC between the two groups. Age, PCSA, and maximum force were analyzed using an ANOVA. Statistical significance was assessed at $P<0.05$. Data are shown as mean ± SEM.

Results:
Statistically there were no differences between the groups for PCSA, age, or maximum force. No mean statistical difference was seen between healthy subjects and patients with COPD for the absolute shear modulus versus MVC, whereas an interactive effect ($p<0.05$) was present (Figure 2). Statistical differences were seen for the normalized values of the shear modulus, with mean and interactive effects.

Discussion:
The present study clearly demonstrates that differences in muscle stiffness exist between healthy age-related controls and patients with COPD. Although there was no statistical difference in the absolute shear modulus between the groups, in general the controls produced stiffer muscle than COPD patients for a given applied force. Patients with COPD, due to difficulty in breathing, are generally less active than healthy age-related subjects. This deconditioning of the muscles may contribute to the differences in muscle stiffness seen in this study.

References:
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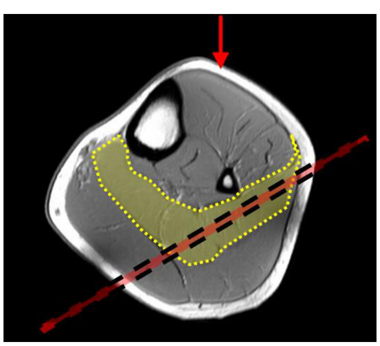

Figure 1: Anatomical image of the soleus (irregular region) showing the acquired slice and point of mechanical excitation.

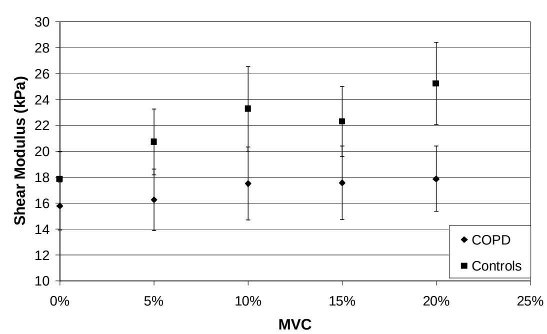

Figure 2: Shear modulus (kPa) versus MVC of controls and patients with COPD.