Measuring Skeletal Muscle Elasticity in Patients with Hypogonadism by MR Elastography

C. J. Galban[1], S. Maderwald[1], B. L. Herrmann[1], K. Brauck[1], W. Grote[1], A. de Greiff[1], K. Uffmann[1], M. E. Ladd[1]

[1]University Hospital of Essen, Essen, Germany

Abstract:
Men afflicted with hypogonadism have reduced fat-free mass and in some cases a loss in muscle strength. We hypothesize that muscle elasticity of the lower extremities differs between patients with hypogonadism and healthy 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 applied force.

Introduction:
The reduction of testosterone concentrations in men with hypogonadism has been shown to reduce bone density, prostate volume and fat-free mass. Many of these patients, once diagnosed, undergo testosterone replacement therapy, where the patient is provided with a controlled dosage of testosterone over a period of time. Over approximately six months, many of these patients recover to near normal levels. To determine the state of the patient, a multitude of tests, some invasive, must be performed. MRE provides a novel approach for monitoring patient response to testosterone therapy 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 hypogonadism could be measured by MRE.

Methods and Materials
Subjects: Men over 18 years of age who were diagnosed with unequivocal hypogonadism (n=6), defined as a serum testosterone concentration less than 300 mg/dL (10.4 nmol/L), and age-related healthy controls (n=8) 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%, and 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[1] 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°, a TR of 120 ms and a TE of 33.3 ms were used for the acquisition of phase images with a 180 x 80 matrix. A total of 8 phase offsets were acquired.
Data Analyses: All phase images were phase unwrapped and reconstructed into shear modulus elastograms using the local frequency estimation (LFE) technique[2]. 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 normalized 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)[3], which has been shown to be proportional to the maximum force, was determined assuming a muscle fiber length in the soleus of 3 cm[4]. 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:
Phase images of the soleus muscle at 0%, 10% and 20% of the MVC are presented in Figure 1. No mean statistical difference was seen between healthy subjects and patients with hypogonadism for the absolute shear modulus versus MVC, whereas an interactive effect ($p<0.05$) was present. Statistical differences were seen for the normalized values of the shear modulus, with mean and interactive effects (Figure 2). PCSA and maximum force were similar between the two groups.

Discussion:
The present study clearly demonstrates that differences in muscle stiffness exist between healthy age-related controls and patients with hypogonadism. Although there was no statistical difference in the absolute shear modulus between the groups, in general the controls produced stiffer muscle when applying a force. The differences in muscle stiffness, while there was no difference in PCSA and maximum force, might be attributable to a reduction in fat-free mass and an increase in fat mass, which is a common response in men to testosterone deficiency. Further investigation of hypogonadism patients over time is required to determine if the muscle stiffness response returns to normal under testosterone therapy.

References:
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[4] Maganaris C.N., Acta Physiol Scand 2001;172:279-85.

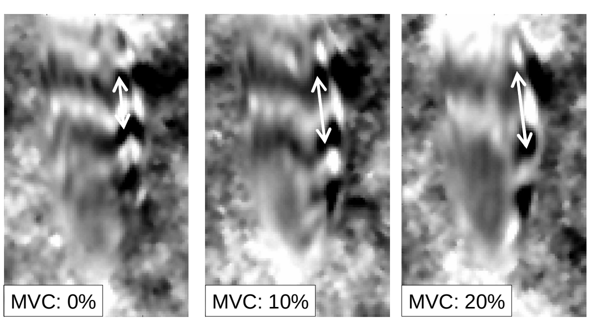

Figure 1: Phase images of the soleus muscle at 0%, 10%, and 20% MVC (maximum voluntary contraction).

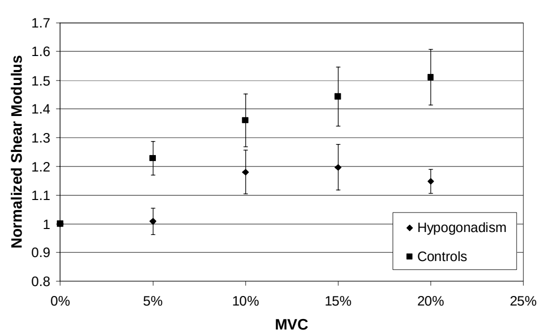

Figure 2: Normalized shear modulus, μ/μ(0% MVC), versus MVC of controls and patients with hypogonadism.