Stretched Sarcomeres May Contribute to Contracture in Cerebral Palsy

Margie Mathewson1, Samuel Ward1,2,3, Henry Chambers4, and Richard Lieber1,3
Departments of 1Bioengineering, 2Radiology, and 3Orthopaedic Surgery, University of California San Diego, CA
4Division of Orthopaedics, Rady Children’s Hospital, San Diego, CA

INTRODUCTION

Children with cerebral palsy (CP) can develop muscle-shortening contractures, leading to the assumption that muscle fascicles in children with CP are shorter than in typically developing (TD) children. Ultrasound data, however, are conflicting. We believe this conflict occurs because muscle sarcomere length (Ls), which ultrasound cannot measure, has not been correlated with ultrasound data. Adaptations in architectural properties, specifically in vivo Ls, can have a significant impact on the passive mechanical environment of muscle. We therefore set out to quantify fascicle length, Ls, and serial sarcomere number in CP and TD muscles, as well as to characterize passive mechanical muscle environment.

METHODS

Patients:
• CP: n=20, age=12.1±5.3 years
• TD: n=21, age=12.4±3.4 years

Experimental Procedure:
• Obtained soleus ultrasound images
• Ankle angles recorded for CP patients, TD measurements taken at CP average

• Measured distance between fascial planes (d) and angle of muscle fascicles (θ) as previously described:
  \[ L_f = d / \sin(\theta) \]

• Collected muscle biopsy at angle corresponding to clamps
• Measured sarcomere length using laser diffraction
• TD values taken from literature and adjusted for ankle angle
• Calculated serial sarcomere number: \( N_s = L_f / L_s \)

• Passive mechanical properties tested by stretching muscle fibers and fiber bundles incrementally
  • 3 min relaxation between stretches
• Measured force and sarcomere length for each stretch
• Calculated stress and tangent stiffness with respect to sarcomere length

RESULTS

Figure 2. There was no difference (p=0.6) in average soleus fascicle length between CP (3.6±1.2 cm) and TD (3.5±0.9 cm). Results are shown as mean±SD.

Figure 3. Sarcomere lengths in patients with CP (4.07±0.45 µm) were significantly longer (p<0.0001) than previously reported sarcomere lengths in TD patients (2.17±0.24 µm).

Figure 4. Serial sarcomere number was significantly smaller (p<0.0001) in patients with CP (9,190±3,810) compared to TD individuals (16,040±4,160).

Figure 5A. When calculated using muscle architecture, at the in vivo sarcomere length, an average patient with CP has a predicted muscle force production of only 13% of maximum.

Figure 5B. After a hypothetical muscle-tendon unit lengthening of 2.5 cm in the average patient, sarcomere length decreases to 3.8 µm and maximal theoretical force production increases to 31% of maximum.

Figure 6. At measured in vivo sarcomere lengths for CP and TD, CP fibers (CP=21.0±15.1 kPa/µm vs TD=2.5±4.6 kPa/µm) and bundles (CP=24.9±16.5 kPa/µm vs TD=0.3±7.3 kPa/µm) are significantly stiffer (p<0.0001).

DISCUSSION

• Muscle fascicles in patients with CP have the same fascicle length as TD patients because their sarcomeres are highly stretched.
• At their in vivo sarcomere lengths, both fibers and bundles from patients with CP are significantly stiffer than those of TD patients.
• These data suggest that, along with connective tissue dysfunction, contractures in CP may be related to highly stretched sarcomeres, which create high passive muscle stiffness and reduced joint range of motion.
• Information regarding these long sarcomere lengths and high in vivo passive stiffness may help to advise clinical practices such as stretching regimes and surgical interventions.

References:

* This work was supported by NIH grant AR057393 and an NSF Graduate Research Fellowship (MAM).