

Editorial

Does eccentric exercise stimulate sarcomerogenesis?

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Eccentric exercise has been associated with an increase in serial sarcomere number in some studies,¹ but not in others.² Similarly, increasing excursion of muscles resulted in sarcomerogenesis in some studies using growing animals,³ but not in others using skeletally mature animals.⁴ However, chronic elongation and chronic shortening appears to be a strong regulator of sarcomere number increase^{5,6} and decrease,^{5,7} respectively, in animal models. Despite an abundance of research on the regulation of sarcomerogenesis under a variety of conditions, the mechanisms underlying in series sarcomere number adaptations in skeletal muscles remain a puzzle, especially in non-invasive human studies where measurements of sarcomerogenesis following interventions have not been possible to date.

In this issue of the *Journal of Sport and Health Science*, Pincheira et al.⁸ combined state-of-the-art ultrasound imaging for fascicle length and second harmonic generation micro-endoscopy for sarcomere length measurements to estimate sarcomere number before and after a 3-week Nordic hamstring eccentric exercise protocol. The combination of these techniques provides an exciting avenue for studying basic muscle mechanics in human subjects, resulting in unique data and novel insight into *in vivo* muscle adaptation and function. Specifically, Pincheira et al.⁸ confirmed that the Nordic hamstring eccentric exercise intervention resulted in increased fascicle length⁹ in some parts of the long head of the biceps femoris, but added the novel information that this was not accompanied by a corresponding increase in serial sarcomere number, as one might have expected, but was caused by a corresponding increase in the average sarcomere length. Not surprisingly, they also found that strength (measured using the Nordic hamstring apparatus) increased with training and assuming (as the authors did) that the hip angle remained constant during the exercise, peak force would occur at a more extended knee angle (and thus greater biceps femoris length) after compared to before the exercise intervention.

Whether the sarcomere length at which peak force occurred changed with intervention is not known, but an increase in sarcomere length at rest (prone position and passive muscle) from an average of 2.9 μm to 3.4 μm occurred, suggesting a shift

within the descending limb of the force–length relationship.¹⁰ This is somewhat surprising as human knee flexor strength curves show that the hamstring muscles typically operate on the ascending part of the force–length relationship, that is below average sarcomere length of 2.6 μm ,¹¹ reaching their greatest strength near the longest muscle length (fully extended knee angle). Combined, these results infer a substantial shortening of fascicle length in maximally contracting compared to passive muscle, resulting in a sarcomere shortening of around 1.0 μm upon muscle activation. Another possibility is that the timeline assessed in the study was not sufficient to observe sarcomerogenesis and that the increase in sarcomere length precedes the addition of sarcomeres in series¹² with sarcomeres later returning to their baseline length and to excursions that encompass the ascending limb of the force–length relationship.

One of the missed opportunities in the study by Pincheira et al.⁸ was that they did not attempt to measure/estimate sarcomere length in the active muscle. Although obtaining dynamic sarcomere lengths during an exercise is probably impossible using micro-endoscopy, measuring dynamic fascicle length using ultrasound imaging is relatively straight forward. By knowing the number of serial sarcomeres (as they do from the static measurements), the average sarcomere lengths for the dynamic Nordic hamstring exercise could have been estimated by dividing the instantaneous fascicle length by the serial sarcomere number.^{13,14} By doing so, the average sarcomere length at which peak forces were obtained could have been estimated, and it would have been of great interest to see if indeed peak forces following training occurred at a longer sarcomere length than prior to training, or if peak forces, despite occurring at different joint angles, occurred at about the same sarcomere lengths, as found previously for maximal and sub-maximal muscle activation.¹⁵ Such an analysis would have revealed if changes in passive properties (tendon length, tendon stiffness, collagen matrix, and titin stiffness) were affected by the Nordic hamstring exercise intervention, thereby allowing for different amounts of fascicle/sarcomere shortening with activation prior to and post-exercise intervention.

Sarcomere lengths non-uniformities within subjects and at a given location were great and covered a range of 1.0 μm and more for most subjects in this study (Pincheira et al.,⁸

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Fig. 5), corresponding to about 37% of human optimal sarcomere length.¹⁰ These results agree with the great sarcomere length non-uniformities found in frog,¹⁶ mouse,¹⁷ rabbit,¹⁸ and human skeletal muscles,¹⁹ but are in stark contrast to the essentially uniform sarcomere lengths found, for example, in insect indirect flight muscles (personal observation). Although it has been argued that vertebrate skeletal muscles have inherently uniform sarcomere lengths in passive or isometrically contracting muscles, and sarcomere length non-uniformities only occur following active muscle stretching on the descending limb of the force–length relationship,^{20,21} this study, like many others, suggests that this is not the case. Sarcomere length non-uniformities appear to be a natural occurrence in vertebrate skeletal muscles at all levels and all contractile conditions, including isometric contractions. The “perfectly” uniform sarcomere lengths of insect indirect flight muscle are likely a by-product of a stiff muscle containing structural proteins that allow for very small sarcomere excursions and produce extremely high passive forces at short sarcomere lengths.²² Such a structural arrangement may be of great advantage for muscles that rely heavily on their passive components during normal locomotion (insect flight), but would not work well for human skeletal muscles where a large range of sarcomere lengths needs to be accommodated with (preferably) little passive resistance from the muscles.

Aside from the long sarcomere lengths found by Pincheira et al.⁸ compared to others²³ for the biceps femoris in the prone, passive position, they also found great variations in the median sarcomere lengths across subjects (Pincheira et al.,⁸ Fig. 3B). Median sarcomere lengths for the distal portion of the biceps femoris ranged from about 2.5 μm (before training) to 4.0 μm (after training), and disregarding training effects ranged by about 1.0 μm for both, the before and after training conditions. Force–angle properties in humans and animals tend to be remarkably similar, suggesting that sarcomere lengths are similar as well for given levels of activation (passive in this case) and joint angles. Also, sarcomere length measurements on cadaveric specimens indicated great similarity in average sarcomere length across human lower limb muscles in the anatomical configuration.²³ Therefore, the great variability in median sarcomere length observed by Pincheira et al.⁸ is surprising and implies that the knee flexor strength curves for these subjects would have varied substantially. Measuring the force–angle properties for the knee flexors, even with all the difficulties in interpretation, might have provided important clues as to the functional effects of these substantial differences in median sarcomere lengths across subjects.

Interestingly, the variation in estimated serial sarcomere number across subjects was reduced substantially after training (Pincheira et al.,⁸ Fig. 3C) for the distal portion of the biceps femoris long head where changes in fascicle lengths and sarcomere lengths were observed, suggesting that the variability in sarcomere lengths across subjects may have influenced how

the muscle responded to the Nordic hamstring eccentric exercise intervention.

The study by Pincheira et al.⁸ provides an exciting glimpse at *in vivo* muscle function across structural levels and opens unimagined possibilities for future research on the properties and function of *in vivo* human skeletal muscles. Despite centuries of recognition of the striation/sarcomere pattern in skeletal muscles, the complex interaction between serial sarcomere adaptation, sarcomere length non-uniformity, and muscle properties remains a puzzle yet to be resolved satisfactorily.

Competing interests

Both authors declare that they have no competing interests.

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