Supplementary Analysis

Title

Ultrasound imaging links soleus muscle neuromechanics and energetics during human walking with elastic ankle exoskeletons

Authors

Richard W. Nuckols

Taylor J.M. Dick

Owen N. Beck

Gregory S. Sawicki

Influence of increasing elastic ankle exoskeleton stiffness on the metabolic cost of soleus muscle force production

The metabolic energy utilized by leg muscles to generate ground force is a primary determinant of metabolic rate during locomotion[1-10]. In fact, the relationship between metabolic rate and the rate of muscle force production during human walking has been formalized by Griffin et al[8] and is recapitulated here in a slightly different form to focus on the soleus muscle during stance phase (Eq. S1 below); rather than *all* of the leg extensor muscles during ground contact (Eq. 3 in Griffin et al[8]). Namely, we assume that the soleus muscle consumes metabolic energy at a rate ($\dot{E}_{met}$) that is proportional to its rate ($\frac{1}{T_{act}}$) of active muscle volume (V_{act}); the volume of active muscle used to generate force per unit activation time ($\frac{V_{act}}{T_{act}}$) (Eq. S1)

$$\dot{E}_{met} = \alpha \cdot \frac{V_{act}}{T_{act}} \qquad\qquad (\text{Eq. S1})$$

The constant 'α' is the amount of soleus metabolic energy consumed per unit muscle volume (J cm^{-3}). Consistent with previous research[8], we assume that changes in the mechanical demand of the task, in this case due to changing ankle exoskeleton stiffness, does not affect α, and that soleus is active during *all* of stance phase (*i.e., $T_{act} = T_{stance}$*). This simple equation (Eq. S1) provides a framework to examine how changes in soleus muscle dynamics and activation during walking with elastic ankle exoskeletons impact soleus metabolic energy consumption by asking: How do elastic ankle exoskeletons influence the rate of active soleus muscle volume?

We start by defining active muscle volume (V_{act}) as the product of a muscle's activation (*act*), physiological cross-sectional area (*PCSA*), and fascicle optimal length (l_0) (Eq. S2).

$$V_{act} = act \cdot PCSA \cdot l_0 \qquad\qquad (\text{Eq. S2})$$

While there is some evidence that l_0 may change with muscle activation [11,12], here we assume that soleus l_0 and *PSCA* are constants that do not change with increasing elastic ankle exoskeleton stiffness. As a result, active muscle volume (V_{act}) is directly proportional to muscle activation (*act*) across all exoskeleton stiffness conditions (Eq. S2). It follows then, from Eq. S1 that changes in the rate of V_{act} ought to correlate with changes in metabolic rate of the soleus and by extension, reflect changes in whole-body metabolic rate during walking with elastic ankle exoskeletons over a range of stiffness conditions. Indeed, our electromyography measurements, which serve as proxy for muscle activation

31 (*act*), indicated a moderate correlation (R^2=0.44) between change in stance phase soleus activation rate

32 (see Methods for details on rate calculations) and changes in whole-body net metabolic rate with respect

33 to the zero exoskeleton stiffness condition (Table 2). Our finding that changes in muscle activation well-

34 explains metabolic rate during walking with exoskeletons is supported by previous work using powered

35 ankle exoskeletons (see Fig. 9, Jackson et al.[13]). Furthermore, if the correlation is causal, a linear fit to

36 the Δ net metabolic rate (W kg^{-1}) versus Δ soleus activation rate (unitless s^{-1}) data suggest that for this

37 exoskeleton a unit reduction in soleus activation rate should yield a ~1.3 W kg^{-1}reduction in whole-body

38 net metabolic rate (Fig. 5). In theory this was achieved by reducing V_{act} and/or increasing T_{stance}.

39

40 To gain further insight into how elastic ankle exoskeletons reduce soleus V_{act} rate over the stance phase

41 of walking we took a top-down approach to examine how applying exoskeleton torque to changes in

42 underlying soleus muscle activation (*act*). We start at the joint-level by estimating the total soleus

43 fascicle force ($F_{M_{total}}$), from the force on the combined plantar flexor muscle-tendons (F_{MT}) computed

44 via inverse dynamics, accounting for the soleus's relative cross-sectional area (CSA) within the triceps

45 surae group (CSA=0.56, see Methods Eq. 2) as well as its instantaneous pennation angle (θ_p) (Eq. S3).

$$F_{M_{total}} = \left. F_{MT} \cdot CSA \middle/ \cos \theta_p \right. \tag{Eq. S3}$$

47 Elastic ankle exoskeletons directly reduce the force on the plantar flexor (F_{MT}) because they contribute

48 torque in parallel with the ankle-joint that offsets the biological moment and mechanical power required

49 to walk (Fig. 2C, D)[14,15]. In addition, our data indicate that increasing exoskeleton stiffness does not alter

50 muscle pennation angle (Supp Fig. 3D) and we assume that soleus *CSA* is constant and independent of

51 exoskeleton stiffness. Thus, according to Eq. S3, reductions in plantar flexor MT force (F_{MT}) due to

52 elastic ankle exoskeleton torque assistance should directly translate to reductions in soleus total force

53 $F_{M_{total}}$.

54

55 When linking muscle total force ($F_{M_{total}}$) and its activation (*act* ~=V_{act}), it is important to consider

56 whether all of the force is generated by active contractile machinery. For example, it is well known that

57 when a muscle is stretched beyond its optimal length (l_0) some of the total muscle force ($F_{M_{total}}$) is

58 contributed by structures in parallel with the contractile apparatus that can produce muscle force

59 passively ($F_{M_{pas}}$) (Fig. 4B, dashed curve). Thus, for relatively long muscle operating lengths, active

60 muscle force ($F_{M_{act}}$) requirements could be reduced by passive contributions (Eq. S4).

$$61 \qquad\qquad F_{M_{act}} = F_{M_{total}} - F_{M_{pas}} \qquad\qquad\qquad\text{(Eq. S4)}$$

62 Even for walking with the stiffest exoskeletons we tested (k_{exo}=250 Nm rad^{-1}), we estimate that passive

63 muscle force was likely not a factor (Fig. 4C). We note however, that for elastic ankle exoskeletons

64 stiffer than 250 Nm rad^{-1}, passive forces may contribute due to the trend toward increasing soleus

65 operating lengths (Fig. 4A). Given that in this study active and total soleus muscle force were near

66 equivalent ($F_{M_{act}} \cong F_{M_{total}}$) (Eq. S4), any reduction in $F_{M_{act}}$ due to the exoskeleton should be captured

67 by changes in $F_{M_{total}}$. Our analysis indicated a moderate correlation (R^2=0.42) between changes in

68 soleus total force rate during early stance (Fig. 3A) (see Methods for details on rate calculations) and

69 changes in whole-body net metabolic rate with respect to the zero exoskeleton stiffness condition (Table

70 2).

71

72 It is tempting to stop here and conclude that elastic ankle exoskeletons reduce metabolic rate merely by

73 reducing soleus active muscle force rate during early stance, which by itself reduces soleus activation

74 rate over stance, and ultimately reduces the volume of active muscle per unit activation time ($\frac{V_{act}}{T_{act}}$) (Eq.

75 S1). But, the Hill-type model of muscle force production[16] highlights that force is not equivalent to

76 activation and that other physiological parameters (F-L, F-V) must be considered. Using a Hill-type

77 model, we estimate a muscle's active force output as the product of maximum muscle force ($F_{M_{max}}$),

78 normalized activation (*act*) (defined as between 0 (not active) and 1 (fully active)) as well as

79 dimensionless factors due to the force-length (F-L) (Fig. 4C) and force-velocity (F-V) (Fig. 4F)

80 relationships (Eq. S5).

$$81 \qquad\qquad F_{M_{act}} = F_{M_{max}} \cdot act \cdot (F\text{-}L) \cdot (F\text{-}V) \qquad\qquad\text{(Eq. S5)}$$

82

83 Solving Equation S5 for muscle activation, *act* yields:

$$84 \qquad\qquad act \cong \frac{F_{M_{act}}}{F_{M_{max}}} \cdot \frac{1}{(F\text{-}L) \cdot (F\text{-}V)} \qquad\qquad\text{(Eq. S6)}$$

85 Since muscle force does not always reflect muscle activation (Eqs. S4-S6)[17], in addition to reducing

86 soleus force rate, elastic ankle exoskeletons may also act to reduce activation by improving the economy

87 of muscle force production. Combining Eq. 4 and 6, we see that, independent of the muscle force

88 required, exoskeletons could shift soleus' operating point on the F-L and/or F-V curve to a point with

89 greater force capacity (*e.g.,* up to or beyond the optimal length, *lo* or closer to isometric) yielding

improved economy by increasing the muscle force per unit muscle activation (Eq. S7) (*i.e.,* by decreasing the activation and thus metabolic energy consumed per unit force [18-21]).

$$\frac{F_{M_{tot}}}{act} = F_{M_{max}} \cdot (FL) \cdot (FV) \cdot (1 + \frac{F_{M_{pas}}}{F_{M_{act}}})$$ (Eq. S7)

Indeed, our data indicate that during early stance, increasing exoskeleton stiffness increased soleus operating length, pushing it toward its optimal length, l_0 (Fig. 4C), and increasing its force per activation (Fig. 4B). However, increasing exoskeleton stiffness also increased soleus shortening velocity in late stance pushing it toward v_{max} (Fig. 4F) and decreasing its force per activation (Fig. 4E).

It is difficult to disentangle the effects of increasing ankle exoskeleton stiffness on soleus F-L and F-V effects as they relate to metabolic rate, because they tend to counteract each other's effects. This trade-off is perhaps reflected in the lack of correlation between changes in force per activation during stance and changes in whole-body net metabolic rate (Table 2). Nevertheless, our data suggest that the F-V driven decrease in soleus force per activation in late stance (Fig. 4E,F) outweighed the F-L driven increase in soleus force per activation in early stance (Fig. 4B,C) and contributed to the observed increase in both stance phase soleus muscle activation rate (Fig. 3B) and whole-body net metabolic rate (Fig. 2A) for the stiffest ankle exoskeletons. This notion is supported by a moderate negative correlation (R^2=0.53) between changes in soleus force rate in late stance (Fig. 3A) and changes in whole-body net metabolic rate (Fig. 2A) with respect to the zero exoskeleton stiffness condition (Table 2). That is, the stiffest exoskeletons, which also yielded the highest whole-body net metabolic rates were associated with reduced soleus muscle force rates in late stance (Fig. 3A); a consequence that is likely derived from poor F-V contractile conditions (Fig. 4F). As a result, in late stance, markedly reduced soleus force rate (Fig. 3A) did not translate to reductions in soleus muscle activation rate (Fig. 3B). This suggests that for the stiffest exoskeletons, reduced force capacity (*i.e.,* force per activation) (Eq. S7) (Figs. 4B,E) outweighed reduced force demand (Eqs. S3-S4) (Fig. 3A) and increased whole-body net metabolic rate (Fig. 2A). Taken together, these data support our hypothesis that a trade-off between reduced soleus force demand and a shift to soleus fascicle contractile conditions that are less economical for force production (*i.e.,* reduced force capacity) , both contribute to an intermediate stiffness 'sweet-spot' where users can use elastic ankle exoskeletons to reduce their metabolic rate during walking.

References

1   Taylor, C. R. Relating mechanics and energetics during exercise. *Advances in veterinary science and comparative medicine* **38A**, 181-215 (1994).

123   2   Roberts, T. J., Kram, R., Weyand, P. G. & Taylor, C. R. Energetics of bipedal running. I. Metabolic cost of
124   generating force. *The Journal of experimental biology* **201**, 2745-2751 (1998).

125   3   Roberts, T. J., Chen, M. S. & Taylor, C. R. Energetics of bipedal running. II. Limb design and running mechanics.
126   *The Journal of experimental biology* **201**, 2753-2762 (1998).

127   4   Pontzer, H. A unified theory for the energy cost of legged locomotion. *Biology letters* **12**, 20150935,
128   https://doi.org/10.1098/rsbl.2015.0935 (2016).

129   5   Pontzer, H. A new model predicting locomotor cost from limb length via force production. *The Journal of
130   experimental biology* **208**, 1513-1524, https://doi.org/10.1242/jeb.01549 (2005).

131   6   Kram, R. & Taylor, C. R. Energetics of running: a new perspective. *Nature* **346**, 265-267,
132   https://doi.org/10.1038/346265a0 (1990).

133   7   Kram, R. Muscular force or work: what determines the metabolic energy cost of running? *Exercise and sport
134   sciences reviews* **28**, 138-143 (2000).

135   8   Griffin, T. M., Roberts, T. J. & Kram, R. Metabolic cost of generating muscular force in human walking: insights
136   from load-carrying and speed experiments. *J Appl Physiol (1985)* **95**, 172-183,
137   https://doi.org/10.1152/japplphysiol.00944.2002 (2003).

138   9   Biewener, A. A., Farley, C. T., Roberts, T. J. & Temaner, M. Muscle mechanical advantage of human walking and
139   running: implications for energy cost. *J Appl Physiol (1985)* **97**, 2266-2274,
140   https://doi.org/10.1152/japplphysiol.00003.2004 (2004).

141   10   Kipp, S., Grabowski, A. M. & Kram, R. What determines the metabolic cost of human running across a wide range
142   of velocities? *The Journal of experimental biology* **221**, https://doi.org/10.1242/jeb.184218 (2018).

143   11   Holt, N. C. & Azizi, E. What drives activation-dependent shifts in the force-length curve? *Biology letters* **10**,
144   https://doi.org/10.1098/rsbl.2014.0651 (2014).

145   12   Holt, N. C. & Azizi, E. The effect of activation level on muscle function during locomotion: are optimal lengths and
146   velocities always used? *Proceedings. Biological sciences* **283**, https://doi.org/10.1098/rspb.2015.2832 (2016).

147   13   Jackson, R. W. & Collins, S. H. An experimental comparison of the relative benefits of work and torque assistance
148   in ankle exoskeletons. *J Appl Physiol (1985)* **119**, 541-557, https://doi.org/10.1152/japplphysiol.01133.2014 (2015).

149   14   Collins, S. H., Wiggin, M. B. & Sawicki, G. S. Reducing the energy cost of human walking using an unpowered
150   exoskeleton. *Nature* **522**, 212-215, https://doi.org/10.1038/nature14288 (2015).

151   15   Nuckols, R. W. & Sawicki, G. S. Impact of elastic ankle exoskeleton stiffness on neuromechanics and energetics of
152   human walking across multiple speeds. *Science Robotics* (2019 (in review)).

153   16   Zajac, F. E. Muscle and tendon: properties, models, scaling, and application to biomechanics and motor control. *Crit
154   Rev Biomed Eng* **17**, 359-411 (1989).

155   17   Enoka, R. M. *Neuromechanics of human movement*. (Human kinetics, 2008).

156   18   Hilber, K., Sun, Y. B. & Irving, M. Effects of sarcomere length and temperature on the rate of ATP utilisation by
157   rabbit psoas muscle fibres. *The Journal of physiology* **531**, 771-780, https://doi.org/10.1111/j.1469-
158   7793.2001.0771h.x (2001).

159   19   Alexander, R. M. Optimum muscle design for oscillatory movements. *Journal of theoretical Biology* **184**, 253-259
160   (1997).

161   20   Ma, S. P. & Zahalak, G. I. A distribution-moment model of energetics in skeletal muscle. *Journal of biomechanics*
162   **24**, 21-35, https://doi.org/10.1016/0021-9290(91)90323-f (1991).

163   21   Umberger, B. R., Gerritsen, K. G. & Martin, P. E. A model of human muscle energy expenditure. *Computer
164   methods in biomechanics and biomedical engineering* **6**, 99-111, https://doi.org/10.1080/1025584031000091678
165   (2003).

166