Reviewer's report

Title: Longitudinal Ambulatory Measurements of Gait Abnormality in Dystrophin-Deficient Dogs

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Reviewer: Chad Markert

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Longitudinal Ambulatory Measurements of Gait Abnormality in Dystrophin-Deficient Dogs
Barthelemy I et al
Reviewed by Markert CD

This is an important and well-done communication describing results of a longitudinal 3-D gait analysis study of golden retriever muscular dystrophy (GRMD) dogs. Although maintenance of GRMD colonies is expensive, and improved mouse models have been recently described1, these dogs are widely accepted as most closely mimicking the fatal degenerative human disease, Duchenne muscular dystrophy (DMD). Likewise, the description of gait in GRMD is highly relevant as a functional outcome measure2,3.

The authors note that considerable heterogeneity exists in the GRMD model, and document gait quality heterogeneity. Heterogeneity is to be expected: similar observations are made in DMD patients. Importantly, the authors analyze several variables to simplify and bring order to this heterogeneity. Additionally, the authors offer a summary of their multivariate results with a principal component analysis (PCA). There are several other notable strengths of this study.

It was longitudinal, allowing the researchers to document changes in GRMD gait, relative to proper controls, in “clinically evolving and growing animals.”

Dogs were not pigeonholed into maintaining a certain speed, and furthermore were permitted to simply ambulate with their preferred gait. This is an important but often overlooked point. In mdx mouse models of DMD, it is becoming increasingly clear that profound differences in outcomes may occur, depending on whether exercise is forced4-6 or voluntary7-10. The authors correctly refused to impose on the dogs artificial requirements of speed and a single gait pattern.

The PCA appears to offer not only an effective means for summarizing multivariate information, but also appears to offer a dynamic framework, capable of absorbing data gathered from future studies. In other words, the authors have shown that their present dataset and their previous2 dataset can be combined, and that further addition of data is possible. It is anticipated then that the predictive ability of the variables will improve as more control and experimental data are added to the framework of the PCA method.

In conclusion this is a good descriptive study of GRMD gait in 3-D that builds
upon the authors' previous findings and promises to accommodate further evolution. The following minor concerns are suggestions to improve the readability of the manuscript.

Minor concerns (Discretionary Revisions/Minor Essential Revisions)

L35 Any reader unfamiliar with PCA will find difficulty making sense of “the Euclidean distance between healthy and GRMD dog groups also detected the early changes in gait patterns”, especially if the reader only has the time to read the abstract. Perhaps this portion of the abstract could be re-worded to make it more understandable to a wider audience.

L73-74 The key words of the title should be capitalized: Guide of the Care and the Use of Laboratory Animals

L82 Replace “to” with “in”

L99 Replace “During” with “A”

L131 The derivation of the units for force index is unclear. Please show how N/kg are derived from (W/kg)/(m/s).

L213 Replace “As for” with “Relative to”

L215 Despite L126-128, it is unclear how power of the gait from the three axes was derived in the first place. A few more sentences here or earlier (L-126-128) may preemptively prevent confusion.

L218 and L310-311 Same comment as L131

L253 Replace “others” with “other”

L297-300 Unclear; perhaps craft multiple sentences to better convey the messages.

L303 Delete “Whatever”

L399 Insert “a” between “that” and “3D-accelerometric…”

Fig1 L482 For consistency, no need to capitalize “Force”

Fig2 The difference between the empty circles and black points is not clear. The text of the legend indicates both are healthy, but it is difficult to tell which dogs were from the current study and which were from the previous study. Another matter is the sentence “94.53% of the variability is explained by the first two components.” The text would be much more reader-friendly if these two components were explicitly stated here. Alternatively, the poor labels of “Component 1” and “Component 2” on the graphs’ axes, could be replaced with something more descriptive. Finally, panel E could be reworked to better show how the variables are grouped into the components.

Supp. tables: Unclear what the open squares represent.


**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests