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Measurement of *In Vitro* Responses of Skeletal Muscle Mechanics: Improved Prediction of *In Vivo* Systems

Kazi M. Tasneem, Kristen L. Pirozzi, Chris J. Long, Chris W. McAleer, Alec S. T. Smith, Balaji Srinivasan and **James J. Hickman**
University of Central Florida, USA

In vitro systems capable of measuring contractile peak force of skeletal muscle that mimic organ functionality have become increasingly important in drug development. A multiplexed atomic force microscopy based silicon cantilever system amenable to measuring myotube deflection would be invaluable in this discovery process. Human skeletal muscle was grown on silicon based cantilever arrays that deflect in response to myotube contraction. Conversion of force measurements using a modified version of Stoney's equation closely correlates with data acquired by the more rigorous method of finite element analysis (FEA) which requires the measurement of cross-sectional area (CSA) of the myotubes. From a physiological perspective, the conclusion that myotube force generation scales with CSA validates that the *in vitro* data collected from the cantilever bioMEMS system matches *in vivo* data trends. While the best normative predictor of *in vivo / in vitro* correlation is CSA utilizing FEA analysis, Stoney's equation approach is suitable for calculating the myotube force, but with only a very small increase in variation versus the FEA approach. The normalizing of functional output data to biophysical attributes facilitates closer comparisons between experimental groups, and improves the power of the statistical differences observed. These improved predictions of *in vivo* responses from *in vitro* data are likely to accelerate future drug development and toxicology studies.

ktasneem@knights.ucf.edu

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