We were excited to read the article by Rakhilin et al., titled “Electrical Impedance as a Novel Biomarker of Myotube Atrophy and Hypertrophy.” The work was a well-executed study demonstrating, in part, how impedance changes can be used to detect alterations in myotube size with growth and the effects of drug therapy, including insulin-like growth factor 1. To our knowledge, this is the first use of electrical impedance methods in vitro to detect alterations in muscle progenitor tissue. However, we did wish to make the authors aware of a substantial body of work (including over two dozen peer-reviewed studies) using electrical impedance methods in vivo, in both humans and in animals, to assess muscle health and the effects of disease. The basic approach, which we have termed electrical impedance myography (EIM), is a noninvasive procedure in which electrical current is applied and the resulting voltages measured across a region of muscle tissue via the use of surface electrodes. EIM is based on the basic premise that changes in the microscopic structure of the tissue, including hypertrophy or atrophy of muscle fibers, the presence of increasing muscle fibrosis and fatty infiltration (common occurrences in longstanding nerve and muscle disease), and the presence of increased free water (common in acute or subacute nerve and muscle injury), will alter the obtained impedance data. The technique promises to be useful as a means of monitoring muscle status and as a biomarker in a variety of neuromuscular diseases, ranging from amyotrophic lateral sclerosis to inflammatory myositis. In addition, EIM may also be of use in categorizing the type of muscle injury present (e.g., primary muscle disease vs. primary nerve disease vs. disuse) because different types of injury may produce different characteristics to the measured impedance values.

The system the authors used, to our knowledge, only applies a single frequency of electrical current, which is certainly sufficient to identify changes over time. However, we have identified that using multiple frequencies can provide a richer and more sensitive measure of change than that obtained with just a single frequency. In addition, EIM studies assessing the electrical anisotropy, or directional dependence to current flow, have also suggested the potential power of assessing muscle tissue in different directions relative to the main muscle fiber orientation. Although certainly not easily applicable to work with myotubes, the anisotropic characteristics of the tissue may also provide useful measures of the disease status in vivo.

In parallel to the authors’ findings, we have also identified impedance changes that correlate with muscle fiber size in animals that have undergone sciatic nerve crush. We are also currently investigating the relationship between microscopic structure and impedance data in a variety of other applications, including disuse, neurodegeneration (amyotrophic lateral sclerosis), and primary muscle disease, including muscular dystrophy and inflammatory myositis.

Extracting the muscle postmortem also allows us to obtain the material properties (the inherent electrical conductivity and permittivity) of the tissue, which alters in different disease states. With these data in hand, we are able to use mathematical modeling to evaluate how these inherent electrical properties of the tissue relate to the surface-obtained data. Identifying the material properties of these myotubes may also be of interest for future study. Finally, we are also working on dedicated technology to assist with the rapid acquisition of electrical impedance data in human subjects such that EIM can be more easily applied.

In conclusion, it is a pleasure to read of the authors’ carefully performed work using electrical impedance to assess myotube size. To our knowledge, this is the first work published in this area outside of that of our own research group or immediate associates. Our wealth of clinical and preclinical work in vivo using electrical impedance to assess muscle strongly supports the potential value of their discovery for the assessment of muscle tissue in vitro.

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REFERENCES
