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Last Word on Viewpoint: Principles, Insights and Potential Pitfalls of the Non-Invasive Determination of Muscle Oxidative Capacity by Near-Infrared Spectroscopy

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TO THE EDITOR: We thank the authors for their insightful contributions to the discussion on use of the NIRS muscle oxidative capacity test. Several good points were raised: here we develop three general themes that emerged.

There is ongoing concern about the potential influence of skin blood flow (BF) on the measurement and the ability of NIRS to assess skeletal muscle in obese individuals. Naturally, the NIRS muscle oxidative capacity test relies on sufficient diffusion of light to reach muscle tissue. Skin BF, melanin content and adipose thickness may each affect the validity of this assumption (1). However, the method is effective in isolating the muscle compartment, because it relies upon oxygen consumption ($m\dot{V}O_2$) recovery kinetics that is induced by brief, low intensity, muscle contractions. Thus, if these conditions are met, they obviate the potential influence of skin BF on the $m\dot{V}O_2$ recovery rate constant (*k*) estimation. High-power time-resolved (TRS) NIRS (4) is a developing method that increases the depth sensitivity of NIRS. This technique may overcome difficulty in assessing $m\dot{V}O_2$ in muscles where light absorption or the covering adiposity is large. In addition, as deeper muscles have greater type I fiber expression (3), high-power TRS NIRS provides the opportunity to assess *k* in wider range of muscles and fiber compositions compared to other NIRS systems.

The influence of muscle BF on *k* remains another concern. The NIRS muscle oxidative capacity test requires that BF is occluded, such that measurement validity depends on: a) ceasing convective O_2 delivery and; b) a PO_2 that does not limit $m\dot{V}O_2$ (1). We, as others, believe that the method benefits from its simplicity, especially in the clinical setting. The addition of, for example, Doppler ultrasound to verify BF occlusion is unlikely to bring significant improvement. The question remains open, however, of what is the necessary PO_2 (or tissue saturation) to ensure that the method effectively 'isolates' the intramuscular compartment, and that it is not influenced by capillary-myocyte O_2 diffusion. It is typically recommended to maintain tissue saturation >50% of the physiologic normalization range (1,5). On the other hand, the method could be effectively adapted to investigate the integrated muscle O_2 transport and utilization response, providing additional

information in disease states or interventional studies beyond muscle oxidative capacity alone.

Muscle oxidative capacity is one property of muscle that has heretofore been complex to assess. The ability to quantify *k* using a simple, potentially automated, system provides an advance in our ability to investigate the strong associations among muscle mitochondrial function, health and longevity. Oxidative capacity is, however, a single piece in the puzzle that drives this association, together with phosphorylative capacity, coupling (P/O ratio) and reactive oxygen species production, among other mitochondrial functions. These latter currently require more complex methods, including biopsy or combined optical and magnetic resonance spectroscopy approaches (e.g. 2). Nevertheless, the relatively simple, validated and reproducible, NIRS-based assessment outlined in the Viewpoint offers a first step towards a widely-applicable analysis of muscle mitochondrial function in health, aging and disease.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by authors.

AUTHORS CONTRIBUTIONS

A.A. drafted manuscript; A.A. and H.B.R. edited and revised manuscript; A.A. and H.B.R. approved final version of the manuscript.

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