

# Reply to correspondence: “Near Infra-Red Spectroscopy dynamic assessment as an important tool to explore pulmonary arterial hypertension pathophysiology”

Panagiotou, Marios; Vogiatzis, Ioannis; Louvaris, Zafeiris; Jayasekera, Geeshath; McKenzie, Alison; Mcglinchey, Neil; Baker, Julien; Church, Alistair; Peacock, Andrew; K. Johnson, Martin

*Published in:*
European Respiratory Journal

*DOI:*
10.1183/13993003.02161-2016

E-pub ahead of print: 04/01/2017

*Document Version*
Peer reviewed version

Reply to correspondence: "**Near Infra-Red Spectroscopy dynamic assessment as an important tool to explore pulmonary arterial hypertension pathophysiology**"

**Authors:**

Marios Panagiotou[1], Ioannis Vogiatzis[2], Zafeiris Louvaris[2], Geeshath Jayasekera[1], Alison McKenzie[1], Neil Mcglinchey[1], Julien S. Baker[3], Alistair C. Church[1], Andrew J. Peacock[1], Martin K. Johnson[1].

**Affiliations:**

[1]Scottish Pulmonary Vascular Unit, Golden Jubilee National Hospital, Glasgow, UK; [2]National and Kapodistrian University of Athens, Faculty of Physical Education and Sports Sciences, Athens, Greece; [3]Institute of Clinical Exercise and Health Science, University of the West of Scotland, Hamilton, UK.

**Corresponding author:**

Marios Panagiotou: Scottish Pulmonary Vascular Unit, Golden Jubilee National Hospital, Agamemnon Street, Glasgow, G81 4DY, UK; mariopanag@gmail.com; (+44) 141 951 5497.

**Grants:**

Dr. Marios Panagiotou is the recipient of an ERS PAH Long-Term Research fellowship n° LTRF 2014-3106 supported by an unrestricted grant by GSK.

**"Take Home" message:** Near infrared spectroscopy offers a qualitative, noninvasive indication of mixed venous oxygen saturation in PAH.

***From the authors:***

We thank Dimopoulos et al. for their particular interest in our study (1) and their contributions to this issue.

The peripheral muscle hypothesis in pulmonary arterial hypertension (PAH) (2) is certainly of great and growing interest due to the potential of muscle function as a target for meaningful interventions. Accordingly, our study explored the value of quadriceps muscle oxygenation profiles in patients with PAH by means of near infrared spectroscopy (NIRS) (1). The satisfactory correlations between vastus lateralis muscle tissue oxygenation index ($StO_2$) and mixed venous oxygen saturation ($SvO_2$) at both rest and exercise support the use of NIRS in the noninvasive investigation of patients with PAH. Importantly, they suggest that skeletal muscle oxygenation profiles reflect the pathophysiology of PAH.

We know that factors determining local muscle oxygenation are modulated by the rate of oxygen delivery and oxygen extraction (3). Exploration of the relative contribution of oxygen delivery and oxygen extraction in peripheral muscle $StO_2$ in PAH would be of paramount significance as it would help clarify whether muscle dysfunction in PAH is a mere consequence of the impaired central haemodynamics or due to a primary, intrinsic myopathy (4). To this end, application of NIRS technology during exercise and/or in combination with other methods such as the occlusion technique (5), indocyanine green dye technique (6) and histological examination offers a very promising opportunity. Indocyanine green dye, which has long been used for the assessment of cardiac output and plasma volume is detectable by NIRS and has been used in this way to measure regional blood flow in respiratory and locomotor muscles (7-9).

Prompted by Dimopoulos et al. and despite the fact that our study was limited by design (including the use of supplementary oxygen and submaximal exercise protocol and, the absence of a control group) in the investigation of muscle function as such, we proceeded to further interrogation of our data. Calculations in the exercising patient group (n=10) was unfortunately not feasible due to missing data. However, interrogation of complete patient resting data sets (n=25) revealed some interesting results.

We calculated the estimated systemic oxygen delivery ($DO_2$) the product of cardiac output and arterial oxygen content; the latter was calculated as the product of 1.34 × hemoglobin

concentration × %$SpO_2$. The systemic arteriovenous oxygen content difference (a-$vO_2$ difference) was calculated by dividing oxygen uptake by cardiac output (Fick principle) whereas the systemic oxygen extraction rate was calculated as the ratio of the a-$vO_2$ difference to arterial oxygen content (10).

Resting oxygen content (ml/dl) was 17.2±2.9, $DO_2$ (ml/min) 794±317, a-$vO_2$ difference ($mlO_2$/dl) 5.7±2.2 and oxygen extraction rate (%) at 34±13. These results do not diverge significantly from normality and do not suggest an overt skeletal muscle dysfunction at rest. However, they cannot exclude an underlying muscle impairment that may become clinically significant during exercise.

Importantly, resting $StO_2$ correlated positively with $DO_2$ ($r=0.556$, $p=0.004$) and inversely with oxygen extraction rate ($r=-0.695$, $p<0.001$). In a similar fashion, resting $SvO_2$ also correlated positively with $DO_2$ ($r=0.761$, $p<0.001$) and inversely with oxygen extraction rate ($r=-0.980$, $p<0.001$). These novel findings are important because a) they confirm a positive correlation of peripheral muscle $StO_2$ in PAH with systemic oxygen delivery and an inverse correlation with systemic oxygen extraction rate and, b) they strengthen further the value of $StO_2$ as a qualitative, noninvasive marker of $SvO_2$ thus laying the foundation for further use of NIRS in the investigation of the pathophysiology of PAH. The absence of exercise data of course does not allow for complete extension of these results. However, our findings are still sufficient to support the use of NIRS in PAH, where the routine patient assessment with right heart catheterisation and $SvO_2$ sampling is most often undertaken in resting conditions, nevertheless.

**References**


1. Panagiotou M, Vogiatzis I, Louvaris Z, et al. Near infrared spectroscopy for the assessment of peripheral tissue oxygenation in pulmonary arterial hypertension. Eur Respir J 2016; 48: 1224-1227.
2. Naeije R. Breathing more with weaker respiratory muscles in pulmonary arterial hypertension. Eur Respir J 2005; 25: 6–8.
3. DeLorey DS, Kowalchuk JM, Paterson DH. Relationship between pulmonary O2 uptake kinetics and muscle deoxygenation during moderate-intensity exercise. J Appl Physiol (1985) 2003; 95: 113-20.
4. Panagiotou M, Peacock AJ, Johnson MK. Respiratory and limb muscle dysfunction in pulmonary arterial hypertension: a role for exercise training? Pulm Circ 2015; 5: 424-34.
5. Dimopoulos S, Tzanis G, Manetos C, et al. Peripheral muscle microcirculatory alterations in patients with pulmonary arterial hypertension: a pilot study. Respir Care 2013; 58: 2134-214.
6. Bradley EC, Barr JW. Determination of blood volume using indocyanine green (cardio-green) dye. Life Sci 1968; 7: 1001–1007.
7. Vogiatzis I, Habazettl H, Louvaris Z, et al. A method for assessing heterogeneity of blood flow and metabolism in exercising normal human muscle by near-infrared spectroscopy. J Appl Physiol (1985) 2015; 118: 783-79.
8. Habazettl H, Athanasopoulos D, Kuebler WM, et al. Near-infrared spectroscopy and indocyanine green derived blood flow index for noninvasive measurement of muscle perfusion during exercise. J Appl Physiol (1985) 2010; 108: 962-7.
9. Guenette JA, Vogiatzis I, Zakynthinos S, et al. Human respiratory muscle blood flow measured by near-infrared spectroscopy and indocyanine green. J Appl Physiol (1985) 2008; 104: 1202-10.
10. Louvaris Z, Kortianou EA, Spetsioti S, et al. Intensity of daily physical activity is associated with central hemodynamic and leg muscle oxygen availability in COPD. J Appl Physiol (1985) 2013; 115: 794-802.