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Skeletal muscle blood flow determination using gold standard invasive arterial input function and non-invasive image-based input function by positron emission tomography (PET)

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Objective Skeletal muscle is unique among organs in that its blood flow, thus oxygen supply that is critical for muscular function, can change over a remarkably large range. Compared to the rest, muscle blood flow can increase over 20-fold during intense exercise. Positron emission tomography (PET) and [15O]-H2O tracer provide a unique tool for the direct measurement of muscle blood flow in specific muscle regions. Quantification of PET blood flow requires knowledge of the arterial input function, which is usually provided by arterial blood sampling. However, arterial sampling is an invasive approach requiring arterial cannulation. In the current study, we aimed to explore the analysis and error estimation based on non-invasive, PET image-based input function for skeletal muscle blood flow in PET [15O]-labeled radiowater study.
Methods Thirty healthy untrained men volunteered to participate in this study. [15O]-labeled radio water PET perfusion scans were performed at rest and right after cycling exercise. GE Discovery PET-CT scanner was used for image acquisition. The 15O isotope was produced with a Cyclone 3 cyclotron (IBA Molecular, Belgium). After 455 MBq of 15O-H2O was injected intravenously and after 20 seconds, dynamic scanning images were performed in following frames: 6x5 seconds, 12x10 seconds, 7x30 seconds and 12x10 seconds. Arterial blood was sampled continuously from radial artery during imaging for radioactivity with a detector during PET scanning. All the data analysis was performed using all in-house developed programs. Arterial input function was preprocessed with delay correction. Image-based input function was defined based on sum image of dynamic images. Blood flow was calculated using the 1-tissue compartment model, k1 is considered as blood flow without any further correction. All data analysis was performed by Carimas software (http://www.turkupetcentre.fi/carimas).
Data analysis was performed in five parts: 1) Modelling data using input function from artery. 2) By defining femoral artery Volume Of Interest (VOI) on PET images. 3) Modelling data using image-based input function. 4) Calculating the correlation for blood flow between artery (blood) input function and image-based input function. 5) Predicted true blood flow was calculated based on correlation based on the initial linear relationship between blood and image-based input functions.
Results Skeletal muscle blood flow had a good linear relationship calculated by femoral artery VOI and by arterial (blood) input function ($y = 2{,}9587x - 0{,}096$, $R^2 = 0{,}8852$, $p<0.0001$).
Further, by using the prediction equation obtained by the linear relationship between VOI-determined (femoral) artery blood flow and direct gold standard (radial) artery input function determined blood

flow, image-based input function determined blood flow was well predicted using this non-invasive approach ($y = 1{,}1812x + 0{,}1219$, $R^2 = 0{,}9259$, $p<0.0001$).
Conclusions It is concluded that there is a strong linear correlation between gold standard invasive approach and non-invasive image-based approach to measure skeletal muscle blood flow by PET, but if no further corrections are made, image-based approach overestimates correct blood flow. However, this can be corrected by linear prediction equation, suggesting that invasive arterial input function may not always be needed in the future when measuring skeletal muscle blood flow by PET. This will be of benefit particularly for exercise studies.