QUANTIFICATION OF OXYGEN CONSUMPTION IN SKELETAL MUSCLE WITH PET AND OXYGEN-15 BOLUS

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BACKGROUND

High myoglobin content and low blood flow in skeletal muscle invalidates the results of the steady-state and bolus $[^{15}O]O_2$ inhalation models developed for brain and myocardium.

THEORY

We developed a new compartmental model for muscle oxygen studies (fig. 1). Myoglobin bound $[^{15}O]O_2$, and both arterial and venous radioactivity concentrations are included in this model. The extraction of oxygen and water is assumed to be 1. Oxygen consumption i.e. muscle metabolic rate of oxygen ($MMRO_2$) is calculated as blood flow*OER*$[O_2]$ in arterial blood.

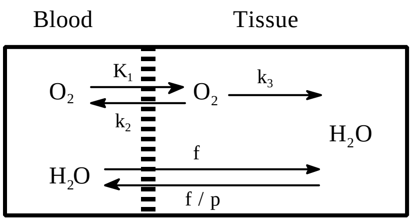

Fig.1. Compartmental model for muscle $[^{15}O]O_2$ studies. K_1 is assumed to be equal to blood flow (f). The partition coefficient of water (p) is assumed to be 0.99. In this model oxygen extraction factor OER is calculated as $k_3/(k_2+k_3)$. The compartments for free and myoglobin bound O_2 are combined.

METHODS

Femoral $MMRO_2$s were estimated from 5-min bolus $[^{15}O]O_2$ inhalation PET studies of seven healthy persons. For comparison, whole leg $MMRO_2$ was estimated also from blood flow and OER measured with bolus of $[^{15}O]H_2O$ and arteriovenous oxygen difference. Four of the subjects performed constant light exercise with the knee extensors of one leg through both PET studies.

PET examinations were made with ECAT 931/08-12. Images (fig. 2) were reconstructed with a new iterative MRP method, which effectively reduces noise in the images (Ref. 1).

Parameters for model (K_1=flow, k_2, k_3 and V_B) were estimated with a non-linear least-squares method utilizing a new global minimization algorithm (Ref. 2). $[^{15}O]H_2O$ studies were analyzed as described before (Ref. 3).

RESULTS

Example radioactivity concentration curves of resting and exercising muscle from a $[^{15}O]O_2$ study are in fig. 3 and 4. Especially in resting muscle the contribution of myoglobin bound and venous $[^{15}O]O_2$ is considerable.

The results of $[^{15}O]O_2$ bolus studies from resting (left leg, n=7) and exercising (right leg, n=4) rectus femoris (Table 1) were in good agreement with the values found in literature.

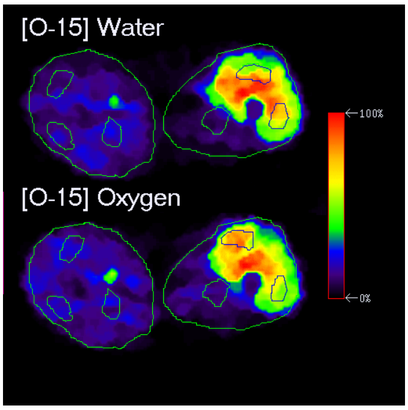

Fig.2. PET images of femoral region after $[^{15}O]H_2O$ (integrated over 250 sec) and $[^{15}O]O_2$ bolus (integrated over 300 sec), including the muscle and whole leg ROIs in resting (left) and working leg (right).

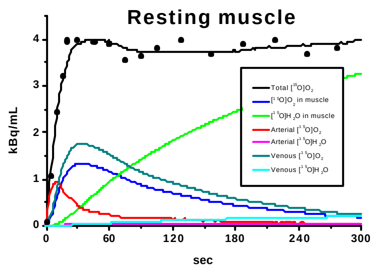

Fig.3. Measured and fitted time-activity curves from a resting muscle (left rectus femoris). Note the high contribution to overall radioactivity from venous blood.

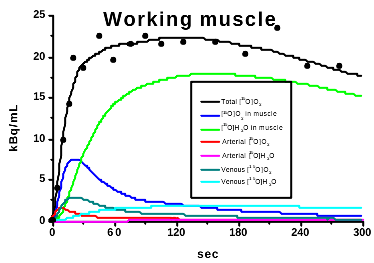

Fig.4. Measured and fitted time-activity curves from a exercising muscle (right rectus femoris). Note that the radioactivity concentration is five times higher than in resting muscle.

Table 1. Results of $[^{15}O]O_2$ studies in rectus femoris

	Rest±SD	Work±SD
Flow (mL/min/dL)	3.8±1.3	29±10
OER	0.35±0.18	0.70±0.15
V_B (%)	2.4±3.2	4.8±4.4
$MMRO_2$ (ml O_2/min/dL)	0.24±0.10	3.6±0.9

$MMRO_2$s in whole leg ROIs correlated well (r=0.96, p=0.0005) with the values calculated using A-V oxygen differences (fig. 5). Also the correlation (r=0.97, p=0.0002) between blood flow values from $[^{15}O]O_2$ and $[^{15}O]H_2O$ bolus studies was very good (fig. 6).

Monte Carlo simulations, done with realistic noise levels, showed that in resting muscle fitting gives very variable results for OER (SD=45 %), but performs better with $MMRO_2$ (SD=25 %). In working muscle the results were more reliable: SD for both OER and $MMRO_2$ was 10 %.

Simulations showed also that $[^{15}O]O_2$ bolus model is very sensitive to tissue heterogeneity; blood flow, and especially OER and $MMRO_2$ can be severely underestimated. This may explain the lower than expected parameter values, that were obtained for correlations from exercised whole leg ROIs.

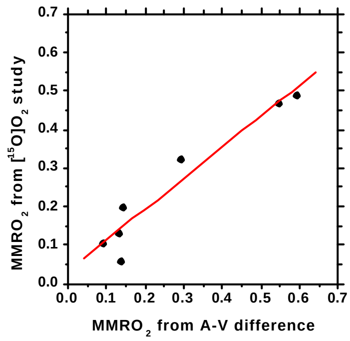

Fig. 5. Correlation of $MMRO_2$ from $[^{15}O]O_2$ bolus method and from A-V oxygen differences and $[^{15}O]H_2O$ measurements.

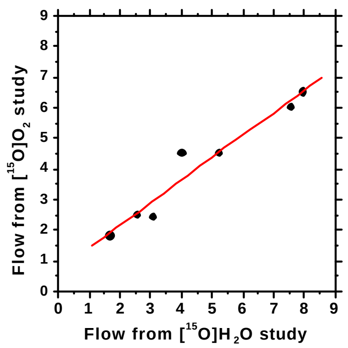

Fig. 6. Correlation of blood flow from $[^{15}O]O_2$ bolus method and from $[^{15}O]H_2O$ measurements.

CONCLUSIONS

Oxygen consumption of skeletal muscle can be quantified with a single PET study after $[^{15}O]O_2$ bolus inhalation.

Prerequisites of successful parameter estimation are: 1) good quality PET images even with very low radioactivity concentrations, 2) the homogeneity of muscle regions of interest, and 3) a global minimization procedure, which does not fall into local minima.

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