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Model equations for myocardial perfusion studies with [^{15}O]H_2O PET: right ventricular region

The myocardial blood flow (MBF) model for [^{15}O]H_2O PET studies presented here is mainly developed and validated by Hidehiro Iida (Iida et al., 1991, 1992; Araujo et al., 1991;Hermansen 1998; Watabe et al., 2005).

Table 1. Definition of symbols:

$C_i(t)$	True myocardial tissue radioactivity concentration at time *t*; radioactivity of perfusable myocardium [kBq ml^{-1}]
$a(t)$	True input function; radioactivity concentration in (coronary) arterial blood [kBq ml^{-1}]
$ROI(t)$	Time-activity curve of radioactivity of region-of-interest (ROI) which is drawn on the left ventricular (LV) myocardial region [kBq ml^{-1}]
$LV(t)$	Time-activity curve of radioactivity of ROI which is drawn on the LV cavity [kBq ml^{-1}]
f	Regional MBF; the blood flow of perfusable tissue [ml min^{-1} ml^{-1}]
p	Myocardium-to-blood partition coefficient of water [ml ml^{-1}]
α	Tissue fraction; volume of perfusable tissue in ROI [ml ml^{-1}]
V_a	Arterial blood volume; volume of arterial vascular space (including the spill-over from the chamber) in ROI [ml ml^{-1}]
β	Recovery coefficient of left-ventricular ROI ($0<\beta\leq1$)
λ	Physical decay constant of ^{15}O [s^{-1}]
$RV(t)$	Time-activity curve of radioactivity of ROI which is drawn on the RV cavity [kBq ml^{-1}]
V_{a_RV}	RV arterial blood volume; volume of RV arterial vascular space (including the spill-over from the chamber) in ROI [ml ml^{-1}]

In contrary to the original model publications, in this report all masses are converted to volumes and radioactivity concentrations are given in units [kBq/ml]. In the original articles, p=0.91 ml/g was assumed; in this presentation this is multiplied by the density of myocardium, ρ=1.04 g/ml, giving p=0.9464 ml/ml. The spill-over fraction of tissue radioactivity into LV ROI, γ, is replaced in the equations with $1-\beta$; this is an assumption in the original model ($\beta+\gamma=1$). The spill-over fraction of blood activity in right ventricular cavity is also considered in this model. The radioactivity from RV cavity ROI assumes to be equal to the RV blood activity

The perfusion calculations are based on three equations:

$$C_i(T) = f\int_0^T a(t)dt - \frac{f}{p}\int_0^T C_i(t)dt \qquad (1)$$

$$ROI(T) = \alpha C_i(T) + V_a a(T) + V_{a\_RV} RV(T) \qquad (2)$$

$$LV(T) = \beta a(T) + (1-\beta)C_i(T) \qquad (3)$$

To estimate the model parameters, f, α, V_a, and V_{a_RV}, the **model is at first fitted only to the data from a large ROI, covering the whole LV myocardium**. With those parameters and the curves of large ROI and LV cavity, the arterial blood curve, $a(t)$, is calculated, and it is then used to estimate the parameters of other smaller myocardial ROIs.

From Eqs. (2) and (3), the myocardial tissue activity and its integral can be solved:

$$C_i(T) = \left(ROI(T) - \frac{V_a}{\beta} LV(T) - V_{a\_RV} RV(T) \right) \Big/ \left(\alpha - \frac{V_a(1-\beta)}{\beta} \right) \qquad (4)$$

$$\int_0^T C_i(t)dt = \left(\int_0^T ROI(t)dt - \frac{V_a}{\beta} \int_0^T LV(t)dt - V_{a\_RV} \int_0^T RV(T) \right) \Big/ \left(\alpha - \frac{V_a(1-\beta)}{\beta} \right) \qquad (5)$$

The coronary arterial radioactivity can be solved from Eq. (3) and integrated to form Eq. (6):

$$\int_0^T a(T)dt = \frac{1}{\beta} \int_0^T LV(T)dt - \frac{1-\beta}{\beta} \int_0^T C_i(T)dt \qquad (6)$$

Thereafter, the Eqs. (6), (4) and (5) can be substituted into Eq. (1) to solve the radioactivity concentration in the large myocardial ROI as a function of measured quantities only:

$$ROI(t) = \frac{V_a}{\beta} LV(t) + \frac{f}{\beta}\left(\alpha + \frac{V_a}{p} \right) \int_0^T LV(t)dt - f\left(\frac{1}{p} + \frac{1-\beta}{\beta} \right) \int_0^T ROI(t) + V_{a\_RV} RV(t)$$
$$- f\left(\frac{1}{p} + \frac{1-\beta}{\beta} \right) \int_0^T RV(t) \qquad (7)$$

By replacing the coefficients with V_{fit}, K_1 and k_2, the equation can be represented in the form of traditional two-compartmental model:

$$\begin{cases} V_{fit} = \dfrac{V_a}{\beta} \\ V_{fit\_RV} = V_{a\_RV} \\ K_1 = \dfrac{f}{\beta}\left(\alpha + \dfrac{V_a}{p} \right) \\ k_2 = f\left(\dfrac{1}{p} + \dfrac{1-\beta}{\beta} \right) \end{cases} \qquad (8)$$

$$ROI(T) = V_{fit} LV(T) + K_1 \int_0^T LV(t)dt - k_2 \int_0^T ROI(t)dt + V_{fit\_RV} RV(T) + V_{fit\_RV} k_2 \int_0^T RV(t)dt \qquad (9)$$

The parameters of Eq. (9) could be solved with multilinear regression analysis, which idea was first proposed by Blomqvist (1984). By applying linear interpolation and Kuwabara's approach for partial solution of the differential equations (Kuwabara et al., 1993), the integral of regional radioactivity can be presented as in Eq. (10), and substituted in Eq. (9) to give Eq. (11):

$$\int_0^T ROI(t)dt = \int_0^{T-\Delta t} ROI(t)dt + \frac{\Delta t}{2} ROI(T-\Delta t) + \frac{\Delta t}{2} ROI(T) \qquad (10)$$

$$ROI(T) = \frac{V_{fit} LV(T) + K_1 \int_t^T LV(t)dt + V_{fit\_RV} RV(T) + V_{fit\_RV} k_2 \int_0^T RV(t)dt - k_2 \left[\int_0^{T-\Delta t} ROI(t) + \frac{\Delta t}{2} ROI(T-\Delta t) \right]}{1 + \frac{\Delta t}{2} k_2} \qquad (11)$$

To calculate the arterial blood curve, the $C_i(t)$ is first solved from Eq. (2) and substituted into Eq. (3). **Thereafter, *a(t)* can be solved** based on the curves of LV cavity and whole myocardium ROIs:

$$a(T) = \frac{\alpha LV(T) - (1-\beta) ROI(T) + (1-\beta) V_{a\_RV} RV(T)}{\alpha\beta - V_a (1-\beta)} \qquad (12)$$

To derive equations for **the smaller LV myocardial ROIs**, the tissue activity is as a first step solved from Eq. (2), and then integrated to give Eqs. (13) and (14):

$$C_i(T) = \left(ROI(T) - V_a a(T) - V_{a\_RV} RV(T) \right) / \alpha \qquad (13)$$

$$\int_0^T C_i(t)dt = \left(\int_0^T ROI(t)dt - V_a \int_0^T a(t)dt - V_{a\_RV} \int_0^T RV(t)dt \right) \Big/ \alpha \qquad (14)$$

These can be substituted into Eq. (1) to give the regional myocardium radioactivity as a function of arterial blood radioactivity:

$$ROI(T) = V_a a(T) + f\left(\alpha + \frac{V_a}{p} \right) \int_0^T a(t)dt + V_{a\_RV} RV(T) - \frac{f}{p} \int_0^T ROI(t)dt + V_{a\_RV} \frac{f}{p} \int_0^T RV(t)dt \qquad (15)$$

Again, this can be represented in a form of two-compartmental model after the coefficients are replaced with V_{fit}, K_1 and k_2:

$$\begin{cases} V_{fit} = V_a \\ V_{fit\_RV} = V_{a\_RV} \\ K_1 = f\left(\alpha + \dfrac{V_a}{p}\right) \\ k_2 = \dfrac{f}{p} \end{cases} \quad (16)$$

$$ROI(T) = V_{fit}a(T) + K_1\int_0^T a(t)dt + V_{fit\_RV}RV(T) + V_{fit\_RV}k_2\int_0^T RV(t)dt - k_2\int_0^T ROI(t)dt \quad (17)$$

The parameters of Eq. (17) could be solved with multilinear regression analysis. By applying linear interpolation, the integral of regional radioactivity from Eq. (10) can be substituted into Eq. (17) to give Eq. (18) for smaller myocardial ROIs. Note that the parameters V_{fit}, K_1 and k_2 are different than in Eq. (11).

$$ROI(T) = \frac{V_{fit}a(T) + K_1\int_t^T a(t)dt + V_{fit\_RV}RV(T) - K_2\int_t^T RV(t)dt - k_2\left[\int_0^{T-\Delta t} ROI(t) + \dfrac{\Delta t}{2}ROI(T-\Delta t)\right]}{1 + \dfrac{\Delta t}{2}k_2} \quad (18)$$

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