Quantification of pulmonary inflammation in experimental ARDS using static vs. dynamic positron emission tomography

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Background

Positron Emission Tomography (PET) imaging using ¹⁸F-FDG followed by mathematical modelling of the pulmonary uptake rate of ¹⁸F-FDG (K_i) has been used for the assessment of pulmonary inflammation in experimental studies of the acute respiratory distress syndrome (ARDS). However, dynamic PET covers only a 15 cm cranio-caudal field of view and requires 60-75min (**Figure 1**). It has been shown in patients with liver metastasis that K_i values are highly correlated with tumor-to-blood standard uptake ratios (SUR), derived from one frame of a 60min dynamic ¹⁸F-FDG-PET scan [van den Hoff et al., EJNMMI Research 2013;3(1):77]. We investigated whether K_i values derived from dynamic ¹⁸F-FDG-PET correlate with SUR derived from static ¹⁸F-FDG-PET in experimental ARDS.

Methods

- 12 pigs
- Induction of lung injury (**lung lavage + injurious ventilation**)
- Imaging sequences after injury (day1) and after 24h of mechanical ventilation (day2) including (**Figure 2**):
 - Computed tomography
 - Dynamic PET scan after injection of ¹⁸F-FDG,
 - Static PET scan (77-80min after ¹⁸F-FDG injection)
- Analysis of imaging data:
 - Dynamic PET scans: Patlak graphical analysis; voxelwise calculation of ¹⁸F-FDG uptake rates (K_i); mean K_i values for 5 ventro-dorsal ROIs
 - Static PET scans: voxelwise calculation of standard uptake ratios (SUR) for field of view of static PET scan using interpolated plasma activities:
$$SUR(T) = \frac{C_{PET}(t=T)}{C_{Plasma}(t=T)} = \frac{\text{Lungen-SUV}}{\text{Plasma-SUV}}$$
 calculation of mean SUR values for the same 5 ventro-dorsal ROIs as used for K_i analyses
- Linear regression of K_i and SUR of all regions and animals (n=60) on day1 and day2; comparison of coefficients of determination (r^2)
- Analysis of ¹⁸F-FDG-activity in blood plasma (C_{Plasma})
 - Sampling at mean frame timepoints of dyn. PET
 - Time-averaging of C_{Plasma} for each animal and day (n=24)
- Comparison of $\frac{\int_{t=0}^T C_{Plasma}(t) \cdot dt}{C_{Plasma}(T)}$ at timepoint of static PET scan

Results

- Linear correlation of SUR and K_i within all ROIs: day1 ($r^2=0.83$); day2 ($r^2=0.96$); (**Figure 3**)
- The time-averaged plasma ¹⁸F-FDG-activities exhibited an essentially invariant shape across all animals and timepoints (**Figure 4**), as indicated by very little deviation from the group-averaged curve ($r^2=0.99$)

→ Similar $\frac{\int_{t=0}^T C_{Plasma}(t) \cdot dt}{C_{Plasma}(T)}$ at timepoint of static PET: 154 ± 14 min

Conclusion

For quantification of pulmonary inflammation in experimental ARDS, SUR determined with static PET scanning is a valuable and faster alternative to dynamic PET scanning and Patlak analysis. The relatively high correlation between SUR and K_i is likely explained by low inter-study variability of the plasma input function among animals and timepoints.

Figure 1: Superimposed image of computed tomography and ¹⁸F-FDG-PET data derived by dynamic PET (left) and static PET scanning (right), respectively. Dynamic PET imaging only allows the assessment of a 15cm cranial-caudal field of view, whereas static PET imaging allows the assessment of the whole lung.

Figure 2: Time course of imaging and analysis of imaging data.

Patlak Equation

$$\frac{C_{PET}(t)}{C_{Plasma}(t)} = K_i \cdot \frac{\int_{t=0}^t C_{Plasma}(t) \cdot dt}{C_{Plasma}(t)} + V_{dist}$$

$SUR \sim K_i$

V_{dist} ... initial distribution volume
 C ... ¹⁸F-FDG tracer concentration
 t ... time
 K_i ... ¹⁸F-FDG uptake rate
 SUR ... standard uptake ratios

Figure 3: Linear correlation of tissue-to-plasma-SUV (SUR), assessed by static PET scanning, and of the metabolic ¹⁸F-FDG uptake rate according to Patlak (K_i), assessed by dynamic PET scanning, on the 1. experimental day (left) and on the 2. experimental day (right).

Figure 4: Time course of the ¹⁸F-FDG activity in blood plasma (C_{Plasma}) normalized to the respective mean value shown for all 12 animals and both experimental days. Red: Interpolation for samples taken during the period of the dynamic PET scan.