In vivo quantification of pulmonary β_2-adrenergic receptors with ^{18}F-Fluorethyl-Fenoterol (^{18}F-FEFE) in a small animal model.

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Objectives: I*n vivo* quantification of pulmonary β_2-adrenergic receptors with PET would allow for the assessment of specific changes in this system relevant for the understanding of pathogenesis, therapy and prognosis of various lung disorders, especially obstructive lung diseases. We present first results of the *in vivo* evaluation of the new β_2-receptor ligand ^{18}F-Fluorethyl-Fenoterol [1]. This study was conducted in a guinea pig model, where density and affinity of pulmonary β_2-receptors are closely resembling the human situation.

Methods: Dynamic PET studies over 60 min with ^{18}F-FEFE were performed in 9 female Hartley-guinea pigs where either a baseline study (group 1, n=3), a predose study (group 2, n=3; 2 mg Fenoterol 10 min prior injection of ^{18}F-FEFE) or a displacement study (group 3, n=3; 2 mg Fenoterol 10 min post injection of ^{18}F-FEFE) was done. We used the PET camera ECAT EXACT with a resolution of 4.5 mm in the central field of view in 2D-mode with partial volume correction [2] and iterative reconstruction with OSEM. The administered activity was 12-18 MBq i.v., 60 min p.i. the animals were sacrificed, their lungs rapidly explanted, weighted and homogenized. ^{18}F organ activity (lung, heart, liver, kidney) was measured *ex vivo*, decay corrected and compared with the mean lung SUV of the PET. For the modeling of the β_2-receptor binding potentials we used a ROI-based reference tissue model [3].

Results: Despite the limited spatial resolution of the used PET scanner, all guinea pig lungs could be visualized and quantified separately. 60 min p.i. the pulmonary binding potentials of group 1, 2 and 3 were 3.5, 0.1 and 1.7, respectively. These results correlated well with *ex vivo* measurements of the explanted lungs (r=0.81).

Conclusions: ^{18}F-FEFE is suitable for the *in vivo* quantification of the pulmonary β_2-receptors in this animal model. Our results demonstrate that this tracer exhibits specific, displaceable binding to the pulmonary β_2-receptor in accordance with *ex vivo* measurements. The great structural similarity between the pulmonary β_2-receptors of this animal model and humans makes it likely that this tracer can be used in patients as well.

References:

[1] E. Schirrmacher et al., Biomed Chem Lett 2003, submitted
[2] A. Helisch et al., Eur J Nucl Med 2002, 29: 138
[3] R.N. Gunn et al., J Cereb Blood Flow Metab 2001, 21: 635-52

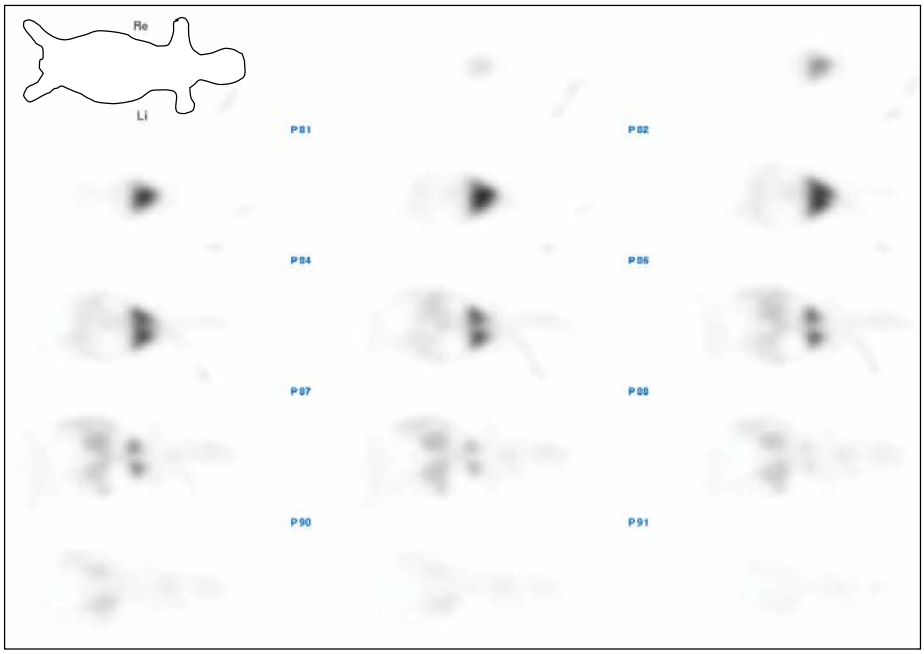

Figure 1

^{18}F-FEFE PET of a guinea-pig (baseline study, 0-5 min p.i., coronary slices)