Combined PET-MRI: is it possible to quantify FDG perfusion based on Gd-DTPA pharmacokinetics?

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Target audience Scientists and physicians interested in combined PET-MRI and pharmacokinetic modelling.

Purpose To verify if the perfusion kinetics of FDG can be determined based on Gd-DTPA DCE-MRI in order to decouple the effects of perfusion and metabolism in PET imaging.

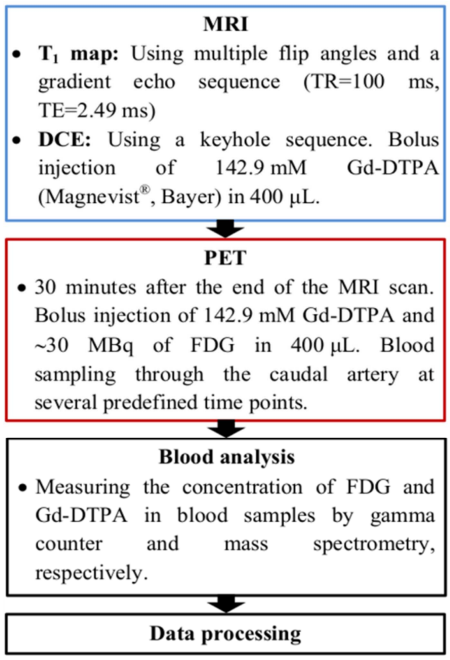

Figure 2. Outline of the PET-MRI imaging protocol.

Theory A three-compartment pharmacokinetic model (Fig. 1) is used to model perfusion (k_1 and k_2) and metabolism (k_3 and k_4) [1,2]. Passive diffusion through the capillary walls is modulated by the radius of the molecule and its chemical properties [3]. Since Gd-DTPA and FDG are both water-soluble, low-molecular-weight compounds, mathematical relations such as $k_{FDG} = f(k_{Gd-DTPA})$ for k_1 and k_2 may exist.

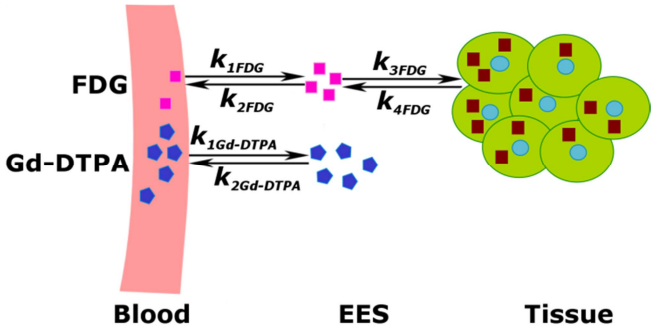

Figure 1. Compartment model showing perfusion (k_1 and k_2) and metabolism (k_3 and k_4). EES: extracellular-extravascular space.

Protocol Eight Fischer rats with F98 glioma were scanned according to a previously published protocol [4] (Fig. 2). Dynamic MRI images were acquired on a 7 T small animal system (Varian) with a 4 s temporal resolution. PET images were acquired on a LabPET4 scanner (Gamma Medica/GE Healthcare) and reconstructed with variable temporal resolution. Manual co-registration of MRI and PET images and pharmacokinetic analysis were performed using an in-house MATLAB program. Statistical analysis was performed in GraphPad Prism.

Results and discussion There is a significant linear correlation between k_{1FDG} and $k_{1Gd-DTPA}$ for different face muscles, the tongue and the tumor (Fig. 3). Note that no significant correlation was found for k_1 when various brain regions were included in the analysis (data not shown). The absence of correlation for k_1 in brain regions is to be expected because Gd-DTPA does not cross the intact blood-brain barrier and FDG is subject to facilitated diffusion by the GLUT1 transporter. No significant correlation was found for k_2 whether the brain regions were included or not, which is consistent with elimination from tissues by different mechanisms.

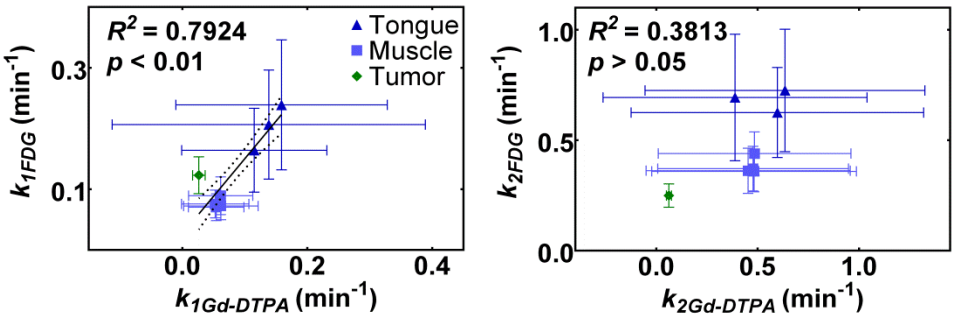

Figure 3. There is a significant linear correlation between $k_{1Gd-DTPA}$ and k_{1FDG} for muscles, the tumor and the tongue. For regions of the brain, excluding the tumor, this relation does not hold due to the blood-brain barrier.

Conclusion Gd-DTPA and FDG appear to have similar perfusion kinetics, but their elimination from tissue is unrelated. These results suggest that it would be possible to determine the k_1 parameter of FDG from the Gd-DTPA MRI data and use this information to distinguish between metabolism and perfusion.

References [1] Phelps *et al.* Ann. Neurol. 1979; 6:371-388. [2] Tofts *et al.* JMRI. 1999; 10:223-232. [3] Pandit, *Introduction to the Pharmaceutical Science,* (Baltimore: LLW, 2007), 126. [4] Poulin *et al.* Magn Reson Med. 2013; 69(3):781-792.