



## Original paper

# Robustness of post-reconstruction and direct kinetic parameter estimates under rigid head motion in dynamic brain PET imaging

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## ABSTRACT

**Objective:** Dynamic PET imaging is extensively used in brain imaging to estimate parametric maps. Inter-frame motion can substantially disrupt the voxel-wise time-activity curves (TACs), leading to erroneous maps during kinetic modelling. Therefore, it is important to characterize the robustness of kinetic parameters under various motion and kinetic model related factors.

**Methods:** Fully 4D brain simulations ( $[^{15}\text{O}]\text{H}_2\text{O}$  and  $[^{18}\text{F}]\text{FDG}$  dynamic datasets) were performed using a variety of clinically observed motion patterns. Increasing levels of head motion were investigated as well as varying temporal frames of motion initiation. Kinetic parameter estimation was performed using both post-reconstruction kinetic analysis and direct 4D image reconstruction to assess bias from inter-frame emission blurring and emission/attenuation mismatch.

**Results:** Kinetic parameter bias heavily depends on the time point of motion initiation. Motion initiated towards the end of the scan results in the most biased parameters. For the  $[^{18}\text{F}]\text{FDG}$  data,  $k_4$  is the more sensitive parameter to positional changes, while  $K_1$  and blood volume were proven to be relatively robust to motion. Direct 4D image reconstruction appeared more sensitive to changes in TACs due to motion, with parameter bias spatially propagating and depending on the level of motion.

**Conclusion:** Kinetic parameter bias highly depends upon the time frame at which motion occurred, with late frame motion-induced TAC discontinuities resulting in the least accurate parameters. This is of importance during prolonged data acquisition as is often the case in neuro-receptor imaging studies. In the absence of a motion correction, use of TOF information within 4D image reconstruction could limit the error propagation.

## 1. Introduction

Dynamic positron emission tomography (PET) is extensively used in neuro-receptor and brain imaging to probe a number of functional aspects of the living brain. Following data acquisition, the time course of the activity distribution can be modelled to derive pharmacokinetic parameters related to metabolism, blood flow, oxygen utilization and different aspects of neurotransmission amongst others. Due to the long data acquisition lasting frequently over 1.5 h, voluntary and involuntary, inter- as well as intra- frame head motion can significantly affect and distort the regional and voxel-wise time activity curves (TACs). Voluntary motion occurs as a result of the patient taking a new posture to alleviate aches and pressure points from prolonged

positioning to an uncomfortable posture (mostly young children in paediatric PET and elderly people), interacting with scanning personnel (during injection, moving feet to new position or positioning of a feet or other rest, talking) or in response to a verbal or other activation paradigm (speech tasks or movement of extremities). On the other hand, involuntary movements involve slow as well as rapid changes in the head posture. Slow changes are often caused by the subject gradually relaxing as the scan progresses, or even falling asleep and can account for translations in excess of 15 mm due to the head slowly drifting. Rapid involuntary changes in the head posture can be caused by sneezing, coughing or instinctively responding to unexpected external stimuli. On top of that, such rapid movements can be originating from the pathology of the subject, such as in patients with Tourette

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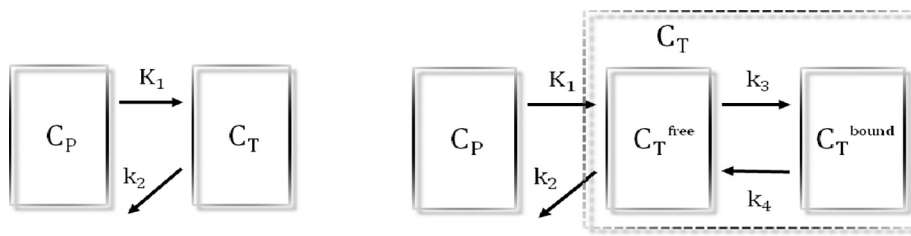


Fig. 1. Schematic diagram of a single-tissue and a two-tissue kinetic model showing the different compartments as well as the constant rate controlling the rate of change in activity concentration for each compartment.

Table 1  
Simulated motion patterns for the dynamic [<sup>15</sup>O]H<sub>2</sub>O study.

	Early frames	Middle frames	Late frames
High frequency movement – permanent new position	1°, 2° and 4° around x-axis at the 7th frame [30 sec]	No motion	No motion
High frequency movement – permanent new position	No motion	1°, 2° and 4° around x-axis at the 16th frame [80 sec]	No motion
High frequency movement – permanent new position	No motion	No motion	1°, 2° and 4° at the 25th frame [ 240 sec]
High frequency movement – return to original position	2° around the x-axis at the 7th frame [30 sec], –2° around the x-axis at the 13th frame [60 sec]	No motion	No motion
High frequency movement – return to original position	No motion	2° around the x-axis at the 16th frame [80 sec], –2° around the x-axis at the 18th frame [100 sec]	No motion
High frequency movement – return to original position	No motion	No motion	2° around the x-axis at the 25th frame [240 sec], –2° around the x-axis at the 27th frame [300 sec]
Continuous drift	1° around the x-axis at the 7th frame [30 sec] and at the 13th frame [60 sec]	1° around the x-axis at the 18th frame [100 sec] and at the 24th frame [210 sec]	1° around the x-axis at the 27th frame [300 sec]
Simulated clinical case 1	Multiple frames with maximum rotations and translations of up to 6.2° and 19 mm		
Simulated clinical case 2	Multiple frames with maximum rotations and translations of up to 4° and 4.1 mm		

syndrome, Parkinson or epilepsy [1–6].

Methods to minimize potential head motion include the use of head immobilization and restraining equipment (thermoplastic masks, forehead and chin velcro restrains, stereotactic head fixation). However, such equipment, depending on the rigidity of the fixation, could also contribute to additional movement as the subject could try to alleviate pressure points and aches. Furthermore, some fixations cannot always be tolerated, especially by elderly patients and often those presenting neurological/psychiatric disorders. Therefore, a number of approaches were proposed to continuously track and subsequently correct for head motion if needed [7]. These can be divided into projection-based techniques [4,8–12] and post-reconstruction or image-based techniques [13–17]. However, image-based techniques for frame-by-frame transformations are usually tracer/activity dependent and susceptible to noise (especially in early frames). They also suffer from problems related to rigid marker fixation when optical devices are used. Alternatively, projection-based approaches can be more computationally intensive and slow to converge, have difficulties to handle out-of-field-of-view (FOV) events and are limited by the optical tracking device accuracy. Therefore, in cases where no motion correction is used or residual errors remain due to the shortcomings of the selected motion correction scheme, the errors introduced by either emission/attenuation mismatch, intra- and inter-frame motion blurring, or both, could lead to kinetic parameter errors. Motion-induced errors can substantially reduce the spatial resolution in parametric images. This is particularly of importance given that parametric maps are preferred over regional kinetic analysis when probing information from small brain structures, since they can provide kinetic parameters at the voxel level. However, even more important is that sudden changes between temporal frames can generate severe discontinuities in time-activity curves (TACs), therefore resulting in highly biased kinetic parameters

especially at the boundaries of regions with high activity and attenuation gradients [8,18,19]. The impact of head rotations and translations on kinetic parameters has been previously investigated for specific tracers and for varying levels of motion [19,20]. However, given the fact that certain parameters are derived from certain parts of the TACs, some are expected to be more robust to a given motion pattern than others. This would depend not only on the magnitude of motion but also on the time when it occurs relative to the beginning of the scan and the kinetic model order (number of compartments and kinetic parameters) used. Furthermore, motion-induced errors might be different amongst kinetic parameter estimation methods. Direct parameter estimation methods have been shown to generate parametric images of improved accuracy and precision when used in brain imaging applications [21–23]. However, it has also been shown that when used in body imaging, motion-induced kinetic parameter errors tend to spatially propagate in the FOV during parameter estimation [24]. Therefore, it is of importance to investigate their behaviour in dynamic brain imaging given the different nature and magnitude of motion compared to abdominal imaging, as such algorithms have been consistently shown to supersede traditional post-reconstruction kinetic modelling approaches.

In this work, we systematically investigate the robustness of kinetic parameters against head motion in dynamic brain imaging using motion rotations and translations of varying amplitude and at different time points.

Both 1-tissue and 2-tissue kinetic models are used based on [<sup>18</sup>F] FDG and [<sup>15</sup>O]H<sub>2</sub>O kinetics. In addition, we performed realistic simulations based on externally tracked motion data recorded during patient dynamic scans. Kinetic parameter estimation was performed using both post-reconstruction kinetic analysis as well as direct 4D image reconstruction.

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