Error Propagation Reduction in Direct 4D Image Reconstruction Using Time-Of-Flight PET

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Abstract— **Direct 4D image reconstruction methods have been shown to generate parametric maps of improved precision and accuracy in dynamic PET. However due to the inability to construct a common single kinetic model for the entire FOV, the interleaving between tomographic and kinetic modelling steps causes errors in erroneously modelled regions to spatial propagate. Adaptive models have be used to mitigate the problem though are complex and difficult to optimize. In this work we demonstrate a new way to minimize errors, focusing on the tomographic step rather than the kinetic modelling and limiting the actual propagation of bias by incorporating time-of-flight (TOF) within a direct 4D reconstruction framework. Using ever improving TOF resolutions (580ps, 440ps, 300ps and 160ps) we demonstrate that TOF direct 4D image reconstruction can substantially prevent error propagation from erroneous kinetic models. Errors appear to be constrained in the vicinity of erroneously modelled regions with bias reduction of up to 60% in well modelled regions compared to non-TOF direct 4D reconstruction. Combining such a TOF direct 4D image reconstruction with adaptive models, further improvements could possibly be achieved in the future.**

***Index Terms*—Time-of-flight, direct 4-D image reconstruction**

I. INTRODUCTION

Pharmacokinetic modeling of dynamic PET data allows targeted physiological parameters to be derived. Kinetic parameter maps though are particularly noisy due to limiting counting statistics leading to suboptimal parameter accuracy and precision. Direct 4D image reconstruction methods have been shown to improve parameter precision and accuracy, though so far their application to dynamic thoracic and abdominal imaging has been limited [1-5]. This is partly due to the multitude of organ structures and regions with diverse kinetics, making kinetic modelling in the body challenging and its application within a 4D framework particularly complex. Regions with differential delay and dispersion (thoracic versus abdominal organs as well as veins carrying the activity from the injection site) and activity delivery through routes other than arterial blood (such as urinary excretion, bile, as well as venous delivery in the liver), can be located within the FOV. In such cases, a common model cannot describe the kinetics within the FOV and the erroneous model fitting in certain regions will result in propagation of errors within 4D reconstruction [6-9]. This leads to biased kinetic parameters even in regions where the data are accurately modeled. One simple approach to minimize errors is to specify regions where kinetic modelling can be applied while using general models (polynomials, b-splines etc) in the rest of the regions[8]. Another approach that can alleviate the problem is the application of adaptive kinetic models [10]. Such models can minimize error in well modeled regions but can be difficult to implement, have free parameters to optimize and often reduce bias at the expense of increased variance[6].

Time-of-flight imaging has been gaining again considerable momentum the last few years owing to continuous hardware and software advancements [11, 12]. One of the benefits of TOF when used within 3D image reconstruction is the robustness under the presence of inconsistent correction data such as attenuation, scatter and normalization [13]. In an analogous way TOF-based direct 4D image reconstruction could potentially be more robust in the presence of erroneous kinetic models. The incentive behind such a hypothesis is similar to the 3D case and is based on the fact that the spatial weight derived from the TOF information could restrict propagation of kinetic model-induced errors between the tomographic steps within the 4D reconstruction and improve upon kinetic parameters in regions consistent with the TOF information.

In this work incorporating TOF information within an existing direct 4D framework we develop a direct 4D TOF image reconstruction algorithm and apply it on simulated 4D dynamic [^{15}O]H_2O TOF datasets to investigate kinetic model induced error propagation. Kinetic parameters are estimated using TOF direct 4D image reconstruction at different TOF resolutions as well as conventional non-TOF direct 4D reconstruction and 3D post-reconstruction kinetic analysis.

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978-1-4673-9862-6/15/$31.00 ©2015 IEEE

TABLE I. INPUT FUNCTION AVAILABILITY AND DELAY PARAMETERS FOR THE SIMULATED KINETICS AND KINETIC MODELLING DURING PARAMETER ESTIMATION. IN THE LIVER AND HEART VENTRICLES A MISMATCH WAS SIMULATED TO EVALUATE THE EFFECT OF ERRONEOUS MODELLING.

Organs	Simulated kinetics		Kinetic modelling		Match
	Input	Delay	Input	Delay	
Liver	**Dual**	**No**	**Single**	**No**	**No**
Myocardium	Single	No	Single	No	Yes
Liver Tumors	Single	No	Single	No	Yes
Lungs	Single	No	Single	No	Yes
Lung Tumors	Single	No	Single	No	Yes
Soft tissue	Single	No	Single	No	Yes
Bones	Single	No	Single	No	Yes
Heart ventricles	**Single**	**Yes**	**Single**	**No**	**No**

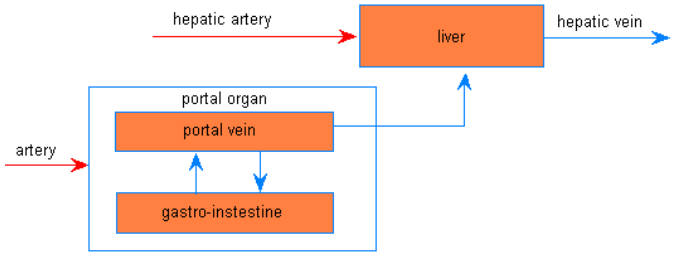

Fig.1 Schematic diagram showing the dual input model with both the hepatic artery and portal vein supplying blood to the liver. The venous blood in the portal vein is drained from the gastro-intestine organs.

II. METHODS

The TOF 4D reconstruction is based on a previously derived 4D algorithm for direct parameter estimation [14] in which the tomographic EM step has been extended to incorporate TOF information. To evaluate the effect of TOF on kinetic model- induced error propagation, a realistic body phantom was used to simulate [^{15}O]H_2O kinetics (6-minute scan, 28-frames). Diverse kinetics were simulated to be present in the FOV: an input function with a differential delay and dispersion was used in the heart ventricles but with no delay and dispersion in the other regions (Table 1). Furthermore a dual input model was used in the liver (hepatic artery + portal vein) with a single input model for the rest of the organs (Fig. 1) [15]. A virtual TOF scanner corresponding to the geometry of the mCT PET, was used to generate the dynamic TOF datasets [16]. Dynamic TOF data were simulated using 580ps, 440ps, 300ps and 160ps TOF resolutions (FWHM). To isolate the impact of TOF on kinetic model-induced bias propagation, only noiseless data were considered as TOF influences the SNR and as such would be difficult to decompose the kinetic model induced from the noise induced bias. Kinetic modeling was performed using a common 1-tissue model with no delay and dispersion in the input function and a single arterial input. As such the model is accurate for all regions apart from the heart ventricles and liver where no correspondence exists. The model was linearized using the generalized linear least squares method [17] and parametric images of perfusion (K_1), clearance rate (k_2), fractional blood volume (bv) and volume of distribution (Vd) were derived using traditional 3D reconstruction followed by kinetic analysis, non-TOF direct 4D image reconstruction and the new TOF direct 4D image reconstruction.

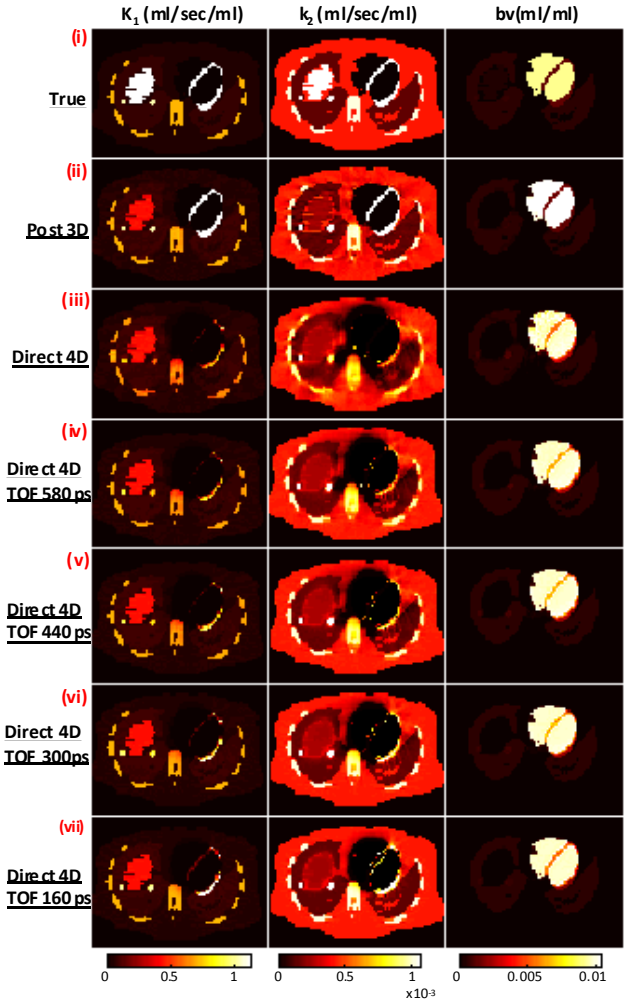

Fig.2 True(i) and estimated kinetics parameter maps using post-reconstruction (ii), non-TOF direct 4D (iii) and TOF direct 4D (iv-vii) (580ps, 440ps, 300ps, 160ps), parameter estimation methods .

III. RESULTS

Fig 2 illustrates k1, k2 and blood volume parameters generated from post reconstruction analysis, direct 4D and TOF direct 4D reconstruction (all reconstructions are shown to the point of convergence, so little if any bias is due to convergence). Traditional post-reconstruction analysis suffers from bias in the liver and heart ventricles being regions where the model is erroneous. However, as demonstrated previously, in non-TOF direct 4D reconstruction these errors spatially propagate between tomographic steps, with substantial bias in

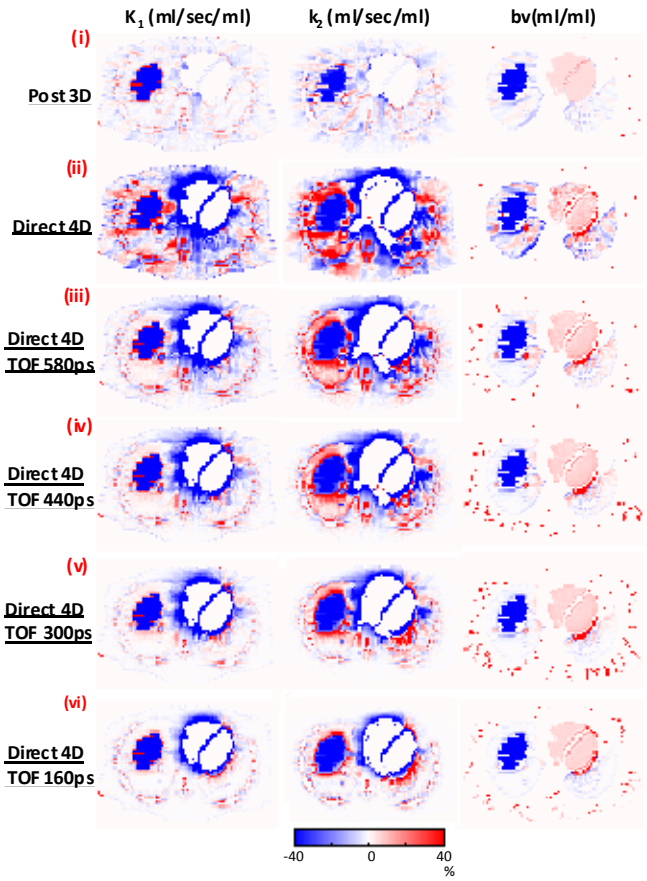

Fig.3 Kinetic parameter bias maps using post-reconstruction (i), non-TOF direct 4D (ii) and TOF direct 4D (iii-vi) (580ps, 440ps, 300ps, 160ps), parameter estimation methods .

other well modelled regions. Incorporating TOF information within the 4D reconstruction gradual improvements are visible looking at the bias maps in Fig 3, which become substantial as the TOF resolution is improved. At 160 ps the errors due to propagation appear very similar to the post-reconstruction case with bias reduction up to 60% in well modelled regions. However due to the finite TOF resolution they still persist around the heart ventricles, mainly in the myocardium, though minimal compared to the non-TOF 4D case. The reduction in bias appears to be spatially related with improvements at the beginning appearing away from the badly modelled regions and becoming more substantial closer to these regions at increasing TOF resolutions. This is consistent with the fact that at increasing TOF resolutions due to the ever decreasing overlap between neighbouring TOF bins, potential errors are becoming more localizing and less likely to propagate.

IV. DISCUSSION - CONCLUSION

Initial results suggest that TOF information can substantially limit kinetic model-induced error propagation when used within direct 4D reconstruction. This is of importance for application of direct 4D methods in the body since due to the multitude of kinetics in the FOV, errors from the application of a single common model will spatially propagate. Limiting such propagation is directly dependent on TOF resolution. Further improvements could be obtained by combining TOF direct 4D reconstruction with adaptive kinetic models.

V. ACKNOWLEDGMENTS

This work was supported by the Swiss National Science Foundation under Grant SNSF 31003A-149957

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