Robust assessment of the sensitivity of DCE-MRI parameterisation to breathing motion

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Introduction Microvascular characteristics of tumours can be assessed by fitting models such as the extended Kety model[1] to contrast agent concentration time course data derived from dynamic contrast-enhanced (DCE-) MRI time series. The estimated model parameters, such as K^{trans}, can be estimated on a per voxel basis and summary parameters such as the median value for the tumour region used to monitor the efficacy of anti-angiogenic drugs[2]. If the tumour is located in the liver it will be subject to respiratory motion during a typical DCE-MR acquisition (typically between 5-10 minutes). The resulting disruption of the tissue-to-voxel mapping could affect the accuracy and precision of estimated K^{trans} values. Buonaccorsi et al[3] assessed a model-driven registration algorithm for re-aligning the time series images. Using synthetic data which had a geometry and motion pattern much simplified from that seen in acquired data sets they demonstrated improved accuracy of K^{trans}. However, a change in the reproducibility of median K^{trans} was not seen when the registration was applied to repeated patient data acquisitions. In this work, we present a synthetic data set with an anatomy and respiratory motion based on a multi-organ biomechanical model[4] of an acquired data set. We use this data set to assess the sensitivity of K^{trans} to breathing motion and the possible benefit of using the model driven registration algorithm.

Synthetic data We have developed a flexible software phantom generator[5] that can be used to generate liver tumour DCE-MRI time series from known ground truth model values based on known tissue physiology. Contrast agent time courses (75 time-points, temporal resolution of 4.97 s) were generated using the extended Kety model for the tumour core and rim and the dual-input Materne model[6] for the liver. A population arterial input function[7] (AIF) was used as input to both models with a portal input function estimated from the AIF[8]. Dynamic T_1 values were generated using the known relationship with contrast agent concentration and relaxivity. Signal intensity time courses were then simulated using the spoiled gradient echo pulse sequence equation (TR = 4 ms, TE = 0.82 ms, flip angle = 20°). The ground truth values for the tracer kinetic model parameters were based on 6 patient liver metastases data sets where the modelling had been applied, giving tumour core and rim K^{trans} values of 0.18 min^{-1} and 0.36 min^{-1} respectively. The anatomy was generated from masks defined on an end-exhale high resolution contrast-enhanced CT data set from a single individual. Motion was emulated by applying displacement maps to the end-exhale image. The displacement maps were generated by aligning the end-inhale to end-exhale image using a multi-organ deformable registration procedure based on finite element modelling[4]. A breathing trace, acquired using respiratory bellows during a dynamic MR acquisition, was used to determine the percentage of displacement to apply at each time point. The median (interquartile range) of displacements within the tumour region between end-exhale and inhale positions during free breathing are 0.7 (0.6) mm for lateral displacements, 0.2 (0.7) mm for anterior-posterior displacements and 11.7 (0.3) mm for cranio-caudal displacements. The generated images were downsampled to a resolution of 2.9 x 2.9 x 4 mm^3, which produced partial volume effects, and zero mean Gaussian noise with an SNR of 10 was added to the signal. Two synthetic data sets were produced: motion-free and motion-corrupted (see Fig. 1).

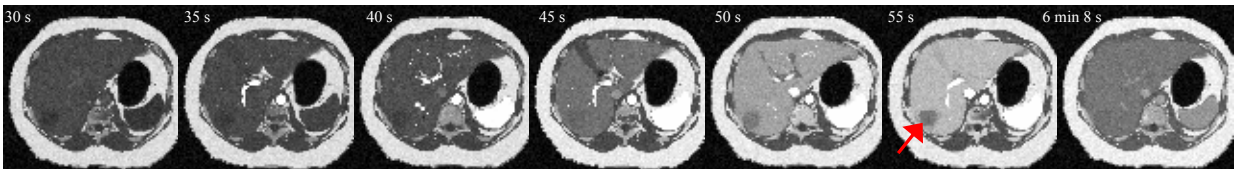

Figure 1. Time-points 7 to 12 and 75 from the synthetic data set with motion emulation. The tumour core is indicated by the arrow on the 12th time-point.

Data analysis Model driven registration was applied to the motion-corrupted data set using translation only followed by affine deformations. The extended Kety model was then fitted to motion-free, motion-corrupted, translation-registered and affine-registered data sets on a per voxel basis. The AIF and portal input function as described above were used as input to the model fitting process.

Results Median K^{trans} for the tumour region is 0.32 min^{-1} for motion-free, 0.30 min^{-1} for motion-corrupted, 0.32 min^{-1} for translation-registered and 0.27 min^{-1} for affine-registered data sets, see Fig. 2. Only the affine-registered median value is found to be significantly different to the motion corrupted data set using the Mann-Whitney U test. K^{trans} histograms for the tumour region are shown in Fig. 3. A bi-modal distribution is seen in the motion-free and both registered data sets but not the motion-corrupted data set.

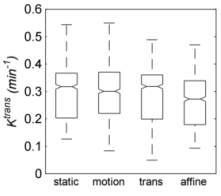

Figure 2. K^{trans} box plots for the tumour region. The central line is the median value.

Conclusion We have generated a DCE-MR liver tumour synthetic data set with non-rigid deformations that mimic those produced by respiratory motion. We have used this data set to test the robustness of DCE model-fitting analysis to breathing motion and the benefit of applying a model driven registration algorithm. The results indicate that median tumour K^{trans} values are robust to motion. However, if measures relying on tumour heterogeneity are required, the recovery of the bi-modal distribution indicates that applying translation-only registration is beneficial. This supports previous work[9] which showed that the model driven registration improved tumour sub-segmentation in acquired data. Increasing the level of registration complexity to affine deformations resulted in a median value which is significantly different from the motion-free data, probably due to failed optimisation. We conclude that more complex registration algorithms should be used with caution and that synthetic data provides a good test set for assessing their suitability. Importantly, our results indicate that median parameterisations of DCE-MRI data are largely insensitive to motion.

References [**1]** Tofts, Mag Res Im 7:91 1997. [**2]** O'Connor, Br J Cancer 96:189 2007. [**3]** Buonaccorsi, Mag Res Med 58:1010 2007. [**4**] Brock, Int J Oncol Biol Phys 64:1245 2006. [**5]** Banerji, Proc ISMRM 16:493 2008. [**6]** Materne, Clin Sci (Lond) 99:517 2000. **[7]** Parker, Mag Res Med 56:993 2006. [**8]** Banerji A, Mag Res Im, on-line 2011. **[9]** Buonaccorsi, Proc ISMRM 19:1091 2011.

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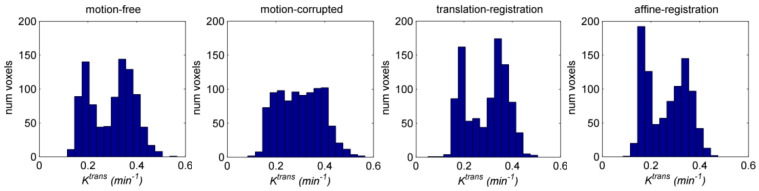

Figure 3. K^{trans} histograms for the tumour region for the motion-free, motion-corrupted, rigid-registered and affine-registered data sets.