

Purpose: To non-invasively quantify the interstitial volume fraction (IVF), vascular volume fraction (VVF), and interstitial fluid pressure (IFP) in solid tumours. These properties have been shown to influence the delivery of micro- and macro-molecular weight drugs and predict for radiation therapy outcome.

Method and Materials: A macro-molecular weight (MW) CT Liposome contrast agent was injected into orthotopic cervix tumour bearing mice (N=4) followed by the injection of a micro-MW iohexol agent. In-vivo kinetics of the two agents were measured using micro computed tomography (CT). The VVF was quantified by taking the ratio of the tumour to arterial enhancement 2 minutes post liposome injection. The VVF was used to subtract the plasma signal from the tumour enhancement curves obtained from the micro-MW agent. The ratio of tumour to arterial enhancement 2 minutes post administration of iohexol gave an estimate of the IVF. The VVF and IVF were incorporated into a biophysical model of macro-MW agent transport to predict IFP. The transport model was fit the liposome CT measurements and a prediction of IFP obtained. Predicted IFP was compared with the wick in needle technique.

Results: The estimated average VVF and IVF were $(0.036 \pm 0.004)\%$ and $(0.19 \pm 0.05)\%$ respectively. These values are within the accepted range reported in the literature. The predicted tumour IFP was 5.5 ± 2.4 mmHg and was in the range of wick in needle measurements (4-21 mmHg).

Conclusions: This work indicates the potential of simultaneously detecting macro- and micro-MW CT contrast agents to non-invasively quantify tumour transport properties; Specifically IFP which has been shown to be a predictor of radiotherapy outcome in cervix cancer patients. Future work will be to use the estimates of VVF and IVF to improve DCE compartmental modeling. The long term goal is to offer a quantitative, image-based approach to non-invasively estimate transport properties in the clinical environment.