Evaluation of kidney function for personalized dosing of renally excreted cancer drugs

Fiona Li

Supervisors: Dr. Ting-Yim Lee and Dr. James Koropatnick

Over-dosing of cancer drugs can lead to complications ranging from fatigue to death. The therapeutic effectiveness and complications of these drugs are related to their plasma concentration. The optimal dose can be determined using Calvert’s formula as long as the glomerular filtration rate (GFR) is known. Accurate measurement of GFR is therefore required for personalized drug dosing. GFR is a measure of kidney function. Clinically it is assessed by measuring creatinine content in a blood sample or in urine collected over 24-hr. However, the assessment is inaccurate in persons with either high or low muscle mass, as creatinine is also produced by muscle turn-over. Therefore, the goal of the project is to develop an optical method for accurate GFR measurement without the requirement of blood sampling or urine collections.

To accomplish this, first, in collaboration with chemistry department, an optical dye, Cy7.5, was conjugated to a GFR reference agent, inulin. Transcutaneous pulse dye densitometry (TPDD) was used to measure the plasma clearance of Cy7.5-inulin following intravenous injection. An open 2-compartment model was developed to estimate GFR from the measured plasma clearance curve. TPDD measurements were validated against CT contrast agent (CTCA), also a GFR agent, on farm pigs. Simulation studies estimated the reproducibility and accuracy of GFR estimation for 30, 20 and 15 min data acquisition as 0.13±0.56, -0.05±2.0 and -0.97±4.62 respectively. This suggests that the difference in the GFR of 2.2, 7.9 and 18.1 mL/min can be measured with 95% confidence interval when the plasma clearance curve is acquired over 30, 20 and 15 min respectively. In conclusion, TPDD can be used to non-invasively measure GFR of an optical agent without the need for blood sampling or urine collection. Personalized drug dosing based on GFR can lead to more efficient treatment without the risk of drug toxicity.