Title: Personalized dosing of renally cleared drugs based on measured kidney function

Trainee Name: Fiona Li

Supervisor(s): Dr. Ting-Yim Lee and Dr. James Koropatnick

Structured Abstract:

Introduction: Kidney is the main excretory organ for many cancer drugs like carboplatin. Renal insufficiencies can lead to high drug concentration in blood and hence increased drug toxicity. Therefore, it is imperative to measure kidney function in order to optimize drug dosing while minimizing toxicity and complications. Existing methods of measuring kidney function is to determine the kidney clearance rate of a substance which is filtered from blood as it passes through the glomeruli of the kidneys or glomerular filtration rate (GFR). Measurement of GFR requires collecting either blood or urine for extended periods of time, from a couple up to 24 hours. In addition, determining the concentration or amount of the glomerular filtered substance in the collected samples can be time consuming leading to delay in reporting the measured GFR. The goal of my project is to develop a point-of-care GFR measurement method without blood sampling or urine collection, can be performed at physicians’ offices within 30 minutes and the measurement result is available immediately without delay.

Methods: The method is based on transcutaneous near infrared (NIR) pulse dye densitometry (TPDD). Light transmission at two wavelengths through an extremity is measured. One wavelength is tuned to the absorption maximum of the NIR dye Cy7.5-inulin, a GFR agent, and is synthesized in the lab of our collaborator (Dr. Len Luyt). The other wavelength is in the red region of the visible spectrum where the absorption by Cy7.5-inulin is minimal. With every heartbeat, blood vessels in the extremity pulsate changing their thickness and hence attenuation of light. The recorded intensity of the transmitted light, thus, exhibit peaks and troughs. The ratio of the ratio of the peak and trough transmitted light at the two wavelengths can then be used to calculate the arterial Cy7.5-inulin concentration. The ratio of the ratio (RoR) method ignores scattering of light, we have extended TPDD theory to include scattering based on the theoretical model of Schuster.

Result: Using data acquired with our in-house developed TPDD, the measured Cy7.5-inulin concentration curves based on the RoR method without and with consideration of scatter were almost the same. Furthermore, these curves were comparable to that measured by the commercially available Nihon Kohden (NK) TPDD.

Discussion: NK-TPDD cannot be used for measuring clearance of Cy7.5-inulin because it is optimized for measuring ICG which is excreted by the liver with a much faster clearance time. As such, the measurement time of the NK unit is limited to 15 minutes. On the other hand, the plasma half-life of Cy7.5-inulin is at least 60 minutes which necessitates a much longer acquisition time than 15 minutes. Our in-house developed TPDD will overcome this limitation to allow point of care monitoring of kidney function with the optical dye Cy7.5-inulin which will lead to accurate dosing of renal excreted cancer drugs for better therapeutic efficacy without excessive drug related toxicities.