Correlation of breath biomarkers with current gold standards for modelling acute renal failure in rats

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Current measurements of renal function rely on daily measurements of plasma creatinine. When most glomerular filtration function is lost, the diagnosis of kidney failure is delayed by up to 3 - 5 days in clinical situations, and may be overestimated by traditional creatinine methods. This results in unacceptable delays in instituting treatment. Consequently, there have been no improvements in mortality in the management of Acute Renal Failure (ARF) for over 50 years, despite the availability of many useful experimentally effective treatments.

Selected Ion Flow Tube-Mass Spectrometry (SIFT-MS) is an analytical technique for Volatile Organic Compound (VOC) quantification which can offer non-invasive diagnosis of disease state in real-time. In this study, ARF is induced via a 60-minute bilateral renal artery clamp in 8 Sprague-Dawley rats, and renal function is monitored via Glomerular Filtration Rate (GFR) estimation for 1 week following surgery. A two-compartment model was developed for estimating renal function via a bolus injection of a radio-labelled inulin tracer, and was compared with the current gold standard plasma creatinine measurement, modified using the Cockcroft-Gault equation for rats. These two methods were compared with SIFT-MS monitoring of breath analytes.

Although the relative decrease in function is of most significance, a population model for absolute GFR estimation was able to be generated for rats, whereby plasma creatinine and breath ammonia concentrations are inversely proportional to GFR. A typical result is shown in Figure 1, where breath ammonia, plasma creatinine and inulin clearance are monitored following ARF induction at 120 hours.

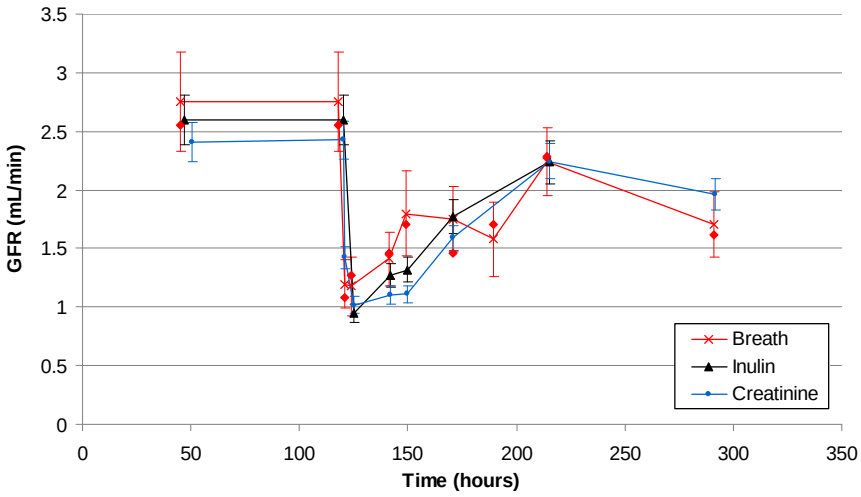

Figure One: GFR monitored during recovery from ARF

Relative decreases in GFR show excellent correlation between methods, and indicate good promise for fast, non-invasive determination of renal function via breath testing.

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