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Real-time point-of-care measurement of impaired renal function in a rat acute injury model employing exogenous fluorescent tracer agents

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Abstract

Renal function assessment is needed for the detection of acute kidney injury and chronic kidney disease. Glomerular filtration rate (GFR) is now widely accepted as the best indicator of renal function, and current clinical guidelines advocate its use in the staging of kidney disease. The optimum measure of GFR is by the use of exogenous tracer agents. However current clinically employed agents lack sensitivity or are cumbersome to use. An exogenous GFR fluorescent tracer agent, whose elimination rate could be monitored noninvasively through skin would provide a substantial improvement over currently available methods. We developed a series of novel aminopyrazine analogs for use as exogenous fluorescent GFR tracer agents that emit light in the visible region for monitoring GFR noninvasively over skin. In rats, these compounds are eliminated by the kidney with urine recovery greater than 90% of injected dose, are not broken down or metabolized in vivo, are not secreted by the renal tubules, and have clearance values similar to a GFR reference compound, iothalamate. In addition, biological half-life of these compounds measured in rats by noninvasive optical methods correlated with plasma derived methods. In this study, we show that this noninvasive methodology with our novel fluorescent tracer agents can detect impaired renal function. A 5/6th nephrectomy rat model is employed.