

NEWS UPDATE

Renal Business Today “Renal Function Monitoring”

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(ST. LOUIS, November 2013) – Renal Business Today published in the November 2013 edition an article entitled “Kidney Function Monitoring: Pathway to the Future” authored by Dr. Richard B. Dorshow, Ph.D., President, Chief Scientific Officer and Founder of MediBeacon.

Renal Business
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Richard B. Dorshow, PhD

Kidney Function Monitoring: Pathway to the Future

Kidney injury and disease worldwide is a major healthcare concern as well as a major healthcare economics concern. Acute kidney injury (commonly referred to as AKI) affects upwards of 20% of hospitalized patients and upwards of 70% of patients in the intensive care units (ICU), with ~5% of those in the ICU requiring renal replacement therapy (such as dialysis).¹

Chronic kidney disease (commonly referred to as CKD) affects 26 million Americans with ~44% of new cases each year caused by diabetes. The World Health Organization estimates ~200 million people worldwide have diabetes and 10-20% of those will die of kidney failure.² Furthermore, there are 93,000 patients in the United States on the waiting list for a kidney transplant, with a typical 5 to 10 year wait.³

The assessment of kidney function is a critical part of patient care. Real-time measurement is essential for detecting and monitoring AKI. Accurate measurement is essential for monitoring and choice of therapeutic pathway for CKD. Glomerular filtration rate (GFR), which is the volume of plasma filtered by the glomeruli of the kidney per unit time, is now accepted as the best index of kidney function.⁴ Current clinical guidelines of the National Kidney Foundation advocate the staging of kidney disease by GFR.⁵

The optimum measure of GFR is the plasma clearance of exogenous filtration agents such as inulin, iothalamate, iohexol, and ^{99m}Tc-DTPA.⁶ However the measurement process for all these agents is complex, involving laborious sample collection and analysis with laboratory based instrumentation. Thus these measured GFR techniques are most often employed in a research setting and infrequently in the clinical setting.

Clinicians routinely use a serum creatinine assay and one of several empirically constructed equations to estimate GFR in patients.⁷ Creatinine is endogenously produced by muscle and mainly eliminated by the kidney. The concentration of creatinine in the serum can easily and cheaply be measured from a blood draw and a laboratory analysis. Thus for a normally functioning kidney, the serum creatinine concentration is stable with a low “normal” value. For an impaired functioning kidney, this value may be much higher since the kidney no longer excretes as much as is being produced by the muscle mass. However, the serum creatinine concentration change from a normal value to an abnormal value following a kidney insult or injury may take 24 hours or longer. Furthermore the serum creatinine value is affected by variables other than renal clearance. Age, gender, hydration, muscle mass, dietary intake, and more affect the creatinine concentration in the blood. In addition, the empirical equations for conversion of the serum creatinine concentration to an estimated GFR have their own limitations.⁸ Thus the current clinical methodology is not a real-time measurement and also is often not an accurate measure of GFR.^{9,1}

Melding a measured GFR technique using an exogenous filtration agent (real-time and accurate) with a point-of-care technique useful for routine measurements in the clinic has been an on-going effort since the early 1990's. Rabito et al developed an arm-band radioactivity detector to measure plasma clearance of $^{99m}\text{Tc-DTPA}$.¹¹ Refinements to this instrumentation and technique exist to date. However, translation to clinical use, such as in the ICU, never occurred due to the necessity of processing and handling radioactivity as a routine part of this methodology.

The logical next step taken by researchers in this field was development of an exogenous optical GFR agent. Such an agent would be easily measurable with simple detectors, similar to the Rabito arm band device, but without the associated complications of radioactivity.

The rational design of an ideal fluorescent GFR tracer agent would require characteristics of extreme hydrophilicity, little to no protein plasma binding, no in vivo metabolism, clearance exclusively by glomerular filtration in a timeframe appropriate for the clinic, inherent fluorescence that is easily detectable through the skin, and extreme non-toxicity. In addition, secondary attributes such as photo and chemical stability as well as ease and low cost of synthesis are important. Most known dyes are either lipophilic, non-biocompatible, excrete mainly via the hepatobiliary system, and thus do not have the required properties for a fluorescent GFR tracer agent.

One approach to development of such, from research at Covidien/Mallinckrodt over the last ten years, resulted in the invention of many fluorescent GFR tracer agent compounds.^{12,13} This technology is now being commercialized by MediBeacon, LLC.¹⁴ A combination product is being developed which employs a novel fluorescent tracer agent and a noninvasive fluorescence detection system (somewhat similar to a pulse oximeter detection system). The agent is administered by IV, excitation light is delivered to the skin and emission light is collected. The emission light intensity is correlated to the tracer agent concentration in the body. GFR is calculated from the time dependence of this emission light as the fluorescent agent is cleared from the body by the renal system.

Successful results employing this combination product system in two animal models have been obtained. Translational research now on-going should yield a robust real-time accurate GFR measurement that could be done at the bedside and/or point-of-care in the hospital and clinic.

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About Renal Business Today:

Renal Business Today is the kidney care community's go-to resource for the latest industry news and information on practice management trends and business advice for dialysis care. Since 2006, Renal Business Today has been serving the needs of the chain and independent freestanding dialysis centers, hospital based dialysis centers and private practices.

About MediBeacon, LLC:

MediBeacon LLC is a Medical Device company focused initially on kidney function monitoring in real-time. MediBeacon is housed within the Helix Center Biotech Incubator. Information regarding MediBeacon can be found at www.medibeacon.com.

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