In Vitro Simulation of Transdermal GFR Monitoring for Diagnosis and Theragnosis in a Patient with AKI

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Background / Purpose

The MediBeacon Transdermal GFR Measurement System is in clinical studies and has been used to measure GFR from approximately 300 subjects, with renal function ranging from normal to Stage 4 CKD and for all six classes on the Fitzpatrick Skin Scale.[1,2] To date, no serious adverse events have been reported.

This system consists of a monitor, a sensor patch which is applied to the sternum (or other skin surfaces), and the proprietary fluorescent tracer agent MB-102 (Lumitrace).[3,4]

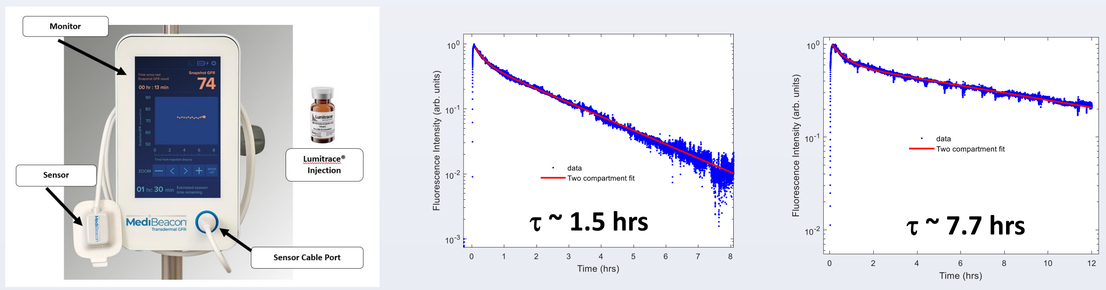

Figure 1: Left – The MediBeacon Transdermal GFR Measurement System; Middle – Data and fit from human subject with normal renal function; Right – Data and fit from human subject with Stage 3 CKD.

We previously employed the MediBeacon Transdermal GFR Measurement System with our novel fluorescent tracer agent MB-102 to assess real-time CRRT small solute clearance in nephrectomized pigs.[5] Protocolized changes to blood pump and effluent flow rates were easily reflected in real time changes of MB-102 clearance detected by the transdermal fluorescent intensity measurements with time. These data showed almost an instantaneous jump from one clearance rate to another when the blood pump and effluent flow rates were changed.

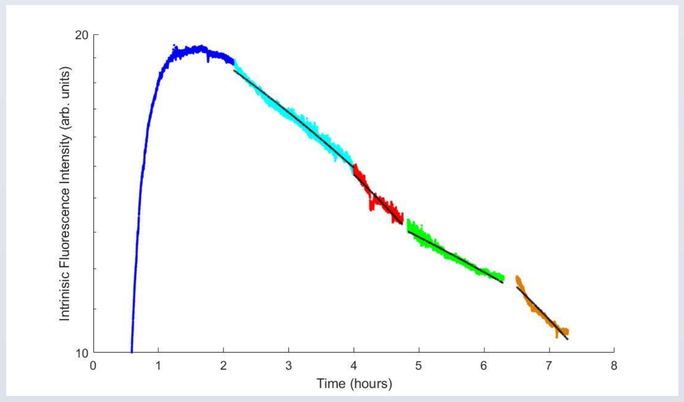

Figure 2: Decrease in transdermal fluorescence (logarithmic scale) at sternum as a function of time in a bi-lateral nephrectomized pig during CVVH for four combinations of blood and effluent flow rates.

To further explore how the MediBeacon Transdermal GFR Measurement System may perform in patients with AKI, an *in vitro* flow cell was constructed to mimic the depletion of MB-102 from the body under adjustable conditions.

Methods

The *in vitro* flow cell pumps an aqueous mixture of MB-102, intralipid, and ink through a cuvette to which the sensor portion (light source and light detector) of the transdermal system is attached. The intralipid concentration mimics tissue optical scattering properties and the ink concentration mimics optical absorption due to skin color variations in the human population. The pumps of the *in vitro* flow cell are computer controlled with programs for specific GFR. Faster pump rates (rapid depletion of MB-102) mimic normal GFR, and slower pump rates mimic impaired GFR. This enables simulation of a dynamic GFR for which the response of the transdermal fluorescence instrumentation and its data processing algorithms may be observed and measured.

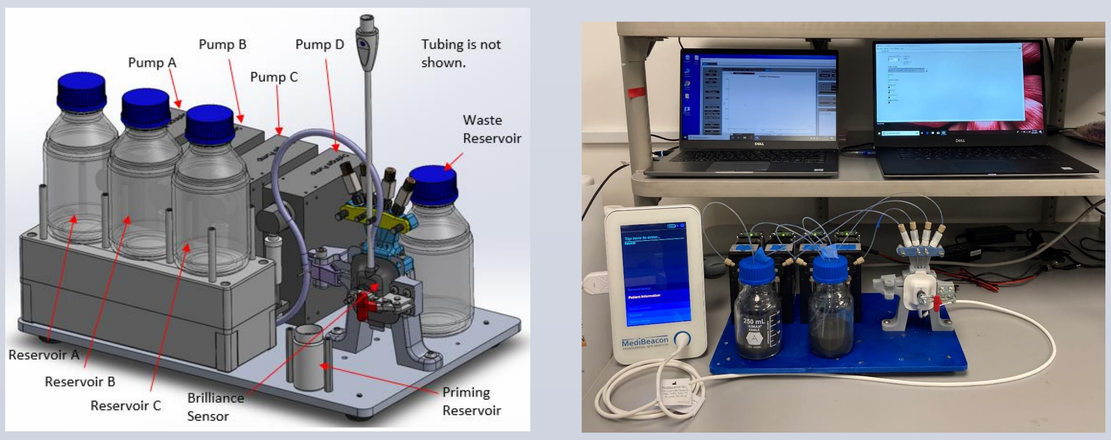

Figure 3: Left - Flow Cell Device. Note that the cuvette is hidden behind the sensor patch. For clarity, tubing is not shown; Right – entire system including the transdermal fluorescence detection instrumentation.

Results

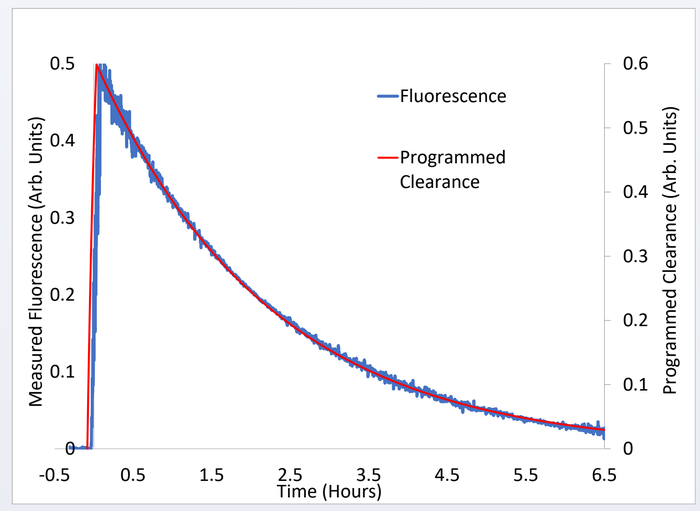

Figure 4: Red is the flow cell programming representing clearance for a subject with normal kidney function. Blue is the simultaneous acquisition of transdermal fluorescence data.

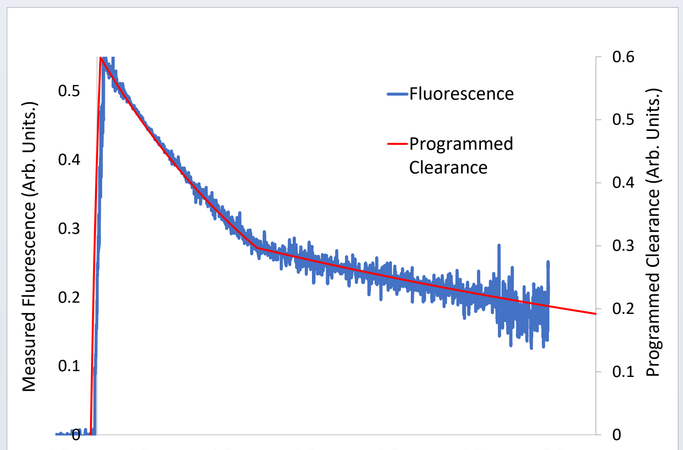

Figure 5: Red is the flow cell programming representing clearance for a subject with normal kidney function and then an abrupt decrease at 2 hours, representing a functional AKI event. Blue is the simultaneous acquisition of transdermal fluorescence data.

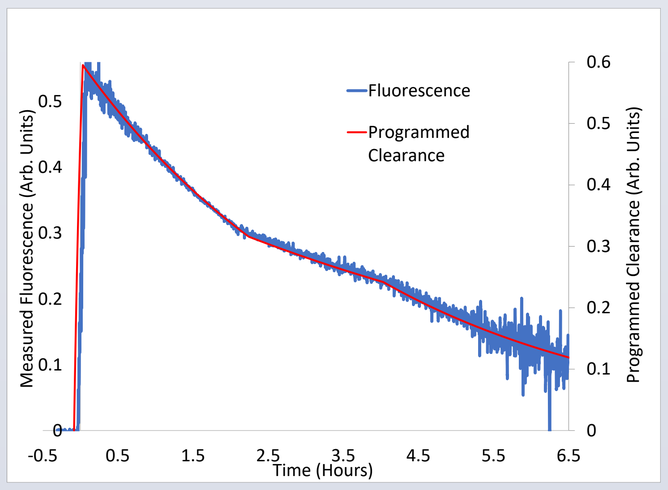

Figure 6: Red is the flow cell programming representing clearance for a subject with normal kidney function and then an abrupt change to an impaired state at 2 hours, and then an intervention at 4 hours almost returning clearance to its original state. Blue is the simultaneous acquisition of transdermal fluorescence data.

Summary

The *in vitro* flow cell was programmed to simulate a patient with a normal GFR, and a patient with a single AKI event, and a patient with an AKI event followed by a therapeutic intervention (e.g., fluid resuscitation or vasoactive medication initiation to improve renal perfusion). The transdermal fluorescence detection system precisely mimicked the flow cell program, essentially responding to the changes in programmed clearance instantaneously.

Conclusion

The dynamic capability of the MediBeacon Transdermal GFR Measurement System to monitor clearance and observe changes due to simulated kidney insult and/or intervention has been demonstrated in an *in vitro* model.

References

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