

C L O S E R L O O K

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Hospital Technology

Thomas Peyser, PhD (GluMetrics, Irvine, CA) discussed findings from the first human clinical study of the Glucath device, an intravascular continuous glucose monitoring system.

The Glucath is an investigational device being developed by GluMetrics, a venture funded start-up with 36 employees. Dr. Peyser noted that there remain several unmet clinical needs for glucose monitoring devices in the ICU including an accurate continuous measurement, especially in the hypoglycemic range. In addition, there is a need to minimize the work for ICU nurses. He stressed the necessity for the device to be compatible within the workflow of the ICU.

Despite all the publicity, he noted several limitations to the NICE-SUGAR study: the study design excluded post-surgical cardiac patients, there was a limited duration of tight glycemic control, a failure to meet treatment targets, a 14-fold increase in severe hypoglycemia, the treatment algorithm led to high glycemic variability and the study mixed ICU sub-groups that benefit from tight glycemic control with those do not (Falciglia et al., *Crit Care Med* 2009). Dr. Peyser noted that in a July 2009 article in the NY Times on FDA interest in tighter standards for blood glucose meters in general, a prominent FDA official expressed his concern that the inappropriate use of home blood glucose meters in the ICU may have been a contributing factor to the poor result of the NICE-SUGAR study.

The GluCath is intended to provide doctors and nurses with a better tool to monitor glucose in the ICU. The GluCath is based on the principle of quenched fluorescence. In the presence of glucose, it gives off greater amounts of green light. For example, there is a two-fold increase in the brightness of the green light at 100 mg/dl of glucose compared with 0 mg/dL. The GluMetrics system consists of three components: the receptor, the quencher, and the fluorophore. The receptor is highly selective for glucose compared to other saccharides. The fluorophore (or dye) emits green fluorescent light when excited by blue light. The glucose detection is based on a non-consuming reversible covalent bond between glucose and the boronic-acid based receptor - a different chemical mechanism than currently available enzymatic CGM devices. The sensor response to glucose is nonlinear: for 150 mg/dl (from 250 mg/dl to 400 mg/dl), there is a 6% increase in signal intensity; however, from 50 to 200 mg/dl, there is a 37% increase in signal intensity. The key strength for this device is its accuracy in the hypoglycemic range.

The GluCath sensor is a small fiberoptic sensor (the first clinical trials were performed with a 22 gauge IV introducer). After the sensor is inserted through the IV introducer, the introducer is removed and only the small fiberoptic sensor remains in the vessel. There is a one-point calibration 30 minutes after insertion. The sensor is intended to last for 48 hours, but the first clinical studies, conducted at the Sansum Diabetes Research Institute, were for 8 and 24 hours only. Subjects in the Sansum study were otherwise healthy volunteers with type 1 diabetes. Up to

two sensors were placed in peripheral veins in the arm. Venous reference samples were taken every 15 minutes from the opposite arm and measured with a laboratory glucose analyzer.

The GluCath findings far surpassed the ISO15197 standards for clinical accuracy under 75 mg/dl (± 15 mg/dl) and just barely met the standard for above 75 mg/dl (± 20 mg/dl) – we highlight that these studies were performed on 20 sensors in healthy volunteer subjects and we expect to gain more clarity on the accuracy. This system does not require any IV maintenance, flush solutions or blood aspirations. The company will next conduct a set of pivotal trials with a large number of subjects in the ICU as well as perform additional clamp studies in healthy volunteer subjects (in order to deliberately test the system at high and low glucose which would be unethical to do in ICU patients).

There seemed to be considerable enthusiasm from the audience as well as the FDA regarding the device's accuracy in the hypoglycemic ranges, however, GluMetrics must clearly demonstrate that the device can achieve the same high level of performance in critically-ill patients as in healthy volunteer subjects. One important unresolved issue for the entire field of ICU glucose monitoring is the appropriate accuracy standard. It's not known whether the FDA will accept ISO 15197, which is more stringent than currently available technologies, for this application or whether they will require a higher level of performance (we may hear more on thoughts from the FDA if DexCom/Edwards' inpatient continuous glucose monitor is submitted to the FDA, although we remain unclear on the specific timeline of this device in the US).

Moving forward, GluMetrics is developing a second-generation product with a 26-gauge introducer and a new point of care device with a modern user interface (e.g., large high-resolution display, graphs, and rate of change indicator). On the regulatory front, we are looking forward to hearing more data on GluCath in the hyperglycemic range, in which the device barely met the ISO 15197 guidelines. Following the meeting, the FDA was crowding 'round Dr. Peyser, which we felt was a positive.