Continuous intra-arterial blood glucose monitoring using quenched fluorescence sensing: a product development study

Oliver J Flower, Simon Bird, Lewis Macken, Naomi Hammond, Elizabeth Yarad, Frances Bass, Charles Fisher, Paul Strasma and Simon Finfer

In recent years, control of blood glucose (BG) in critically ill patients has been the most intensely investigated area of critical care practice and it is clear that management of BG has the potential to affect important clinical outcomes, most notably mortality. Hyperglycaemia is highly prevalent during critical illness[1] and is associated with increased morbidity and mortality in various patient groups.[2-5] Although intensive glucose control with intermittent glucose monitoring showed early promise, it has resulted in an increased incidence of severe hypoglycaemia[6] and, in the largest most externally valid trial to date, an increased risk of death.[7] As a result, the optimum target for BG in critically ill patients remains hotly debated.

Previous strategies to optimise BG concentration have focused on specific BG targets and mean BG concentration. However, the incidence of hypogly-caemia, increased BG variability and the degree of hyperglycaemia are all associated with adverse out-comes. To date, prospective studies of BG control and studies evaluating the association between BG and outcomes have relied on intermittent measure-ment of BG concentration and have used a variety of analysers. Use of point-of-care glucose analysers is no longer recommended, owing to concerns over their accuracy.[8] While intermittent monitoring using a blood gas analyser provides greater accuracy, it is time consuming, expensive and may not detect fluctuations in BG that are deleterious to patients.

Continuous glucose monitoring (CGM) allows observation of trends in BG concentration, provides the ability to intervene before the BG concentration enters an unacceptable range, and removes oper-ator error from both the timing of BG measurements and from the sampling and analysis of blood. Achieving better BG control that may translate to improved clinical outcomes requires an accurate CGM system.

A variety of systems are available for CGM, although none has yet entered routine clinical prac-tice in critical care. Options include intravascular and interstitial monitoring using an indwelling sensor, intermittent automated blood sampling with ex-vivo

ABSTRACT

Background: Continuous glucose monitoring (CGM) has the potential to improve the management of blood glucose (BG) and so improve patient safety and outcomes in intensive care units. The GluCath Intravascular CGM (IV-CGM) System (GluMetrics) uses a novel quenched chemical fluorescence sensing mechanism to measure BG.

Objective: We aimed to assess the safety and performance of the GluCath IV-CGM for a 24-hour period in 20 patients admitted to an ICU after cardiac surgery.

Methods: Heparin-bonded sensors were deployed via a standard 20-gauge radial arterial catheter inserted for routine care in 21 participants after cardiac surgery. Sensors were inserted shortly after ICU admission and BG was monitored for up to 24 hours. After an in-vivo calibration, the system recorded BG every minute. Ultrasound examinations checked for sensor position and the presence of thrombus. Outcome measures were qualitative (ease of use, interference with clinical care, blood pressure monitoring and blood sampling) and quantitative (accuracy in comparison with hourly measurements from a reference analyser). BG was managed according to usual protocols.

Results: Of 21 sensors deployed, one failed and one was malpositioned due to operator error. A total of 488 reference samples were collected, with BG concentrations ranging from 4.7 mmol/L to 13.4 mmol/L. Calibration samples, samples from the malpositioned sensor and six samples affected by technical errors were excluded. Of 437 paired sensor and reference measurements used to assess accuracy, 353 (80.8%) met International Organization for Standardization standard 15197: 2003 criteria (within 20% of reference when BG $\geq$ 4.2 mmol/L). The aggregate mean absolute relative difference (MARD) was 13.0%, with the MARD for individual sensors ranging from 4.7% to 33.5%. Preremoval ultrasounds detected clinically insignificant intravascular thrombus in five of 21 patients (23.8%). No sensor interfered with clinical care, haemodynamic monitoring or blood sampling. There were no device-related serious adverse events.

Conclusions: In this product development study, use of the GluCath system for 24 hours after cardiac surgery had no adverse effect on haemodynamic monitoring, arterial blood sampling or clinical care. Overall accuracy was acceptable in the context of the first phase of a product development study.

analysis (automated intermittent monitoring), and delayed indwelling monitoring via microdialysis. Of these options, the most attractive for critical care use is possibly intravascular monitoring using an indwelling sensor placed in an arterial catheter. Such a system can potentially provide truly continuous monitoring without the lag time inherent in subcutaneous monitoring, and without the risk of contamination from intravenous infusion of glucose-containing solutions, while the high flow in an artery should reduce the risk of thrombus formation. Possible drawbacks of such a system would be the remaining potential for thrombus formation, and the potential for the sensor to interfere with blood pressure monitoring and blood sampling.

Here, we report our initial experience with an indwelling CGM sensor placed via a radial arterial catheter in patients who had undergone cardiac surgery. Our primary objective was to assess the safety and performance of the GluCath Intravascular CGM (IV-CGM) System (GluMetrics) for a 24-hour period in 20 patients admitted to an intensive care unit after cardiac surgery.

Materials and methods

Study objectives

The purpose of the study was to determine feasibility of use by assessing whether the sensor interfered with arterial blood pressure monitoring, blood sampling or any other aspects of clinical care, to document whether the sensor caused intra-arterial thrombosis detectable by vascular ultrasound examinations, and to evaluate the accuracy of the GluCath sensor in comparison with a reference blood gas analyser. The outcome measures are therefore separated into qualitative and quantitative data. Qualitative measures included records of interference with clinical care, blood pressure monitoring and blood sampling. Safety measures included regular ultrasound examinations to check for intra-arterial thrombus and clinical examination of hand perfusion distal to the sensor. Quantitative measures included the proportion of paired BG measurements compliant with the accuracy criteria of two

relevant standards — the older International Organization for Standardization (ISO) standard 15197: 2003 (In vitro diagnostic test systems — requirements for BG monitoring systems for self-testing in managing diabetes mellitus), and the newer Clinical and Laboratory Standards Institute (CLSI) standard POCT 12-A3 (point-of-care BG testing in acute and chronic care facilities). Under ISO 15197: 2003, BG concentration is required to be within 20% of a reference measurement when the BG level is at least 4.2 mmol/L (75 mg/dL) and within 0.8 mmol/L (15 mg/dL) of a reference measurement when the BG level is less than 4.2 mmol/L (75 mg/dL). Under CLSI POCT 12-A3, BG concentration is required to be within 12% of a reference measurement when the BG level is at least 5.6 mmol/L (100 mg/dL) and within 0.7 mmol/L (12.5 mg/dL) when the BG level is less than 5.6 mmol/L (100 mg/dL).

The study was conducted at the Royal North Shore Hospital ICU, Sydney, Australia. The study was approved by the Northern Sydney Local Health District Human Research Ethics Committee (Protocol Number 1105-170M). We included patients who were more than 18 years of age, scheduled to undergo cardiac surgery and who were expected to have a radial artery catheter inserted as part of their routine perioperative care. Each potential study participant provided written informed consent before their planned surgery and before any study-related activity. Patients were excluded if they were expected to stay in the ICU for less than 24 hours, were pregnant, had a known contraindication to heparin, or had any other condition that, in the opinion of the investigator, would interfere with their participation in the trial or pose an excessive risk to study staff.

The GluCath system

The GluCath system consists of a heparin-bonded sensor, monitor and a sterile calibration solution that is used for in-vitro calibration before sensor insertion. The system uses a quenched chemical fluorescence sensing mechanism, with the degree of fluorescence being determined by the glucose concentration in blood (Figure 1a). The sensor is
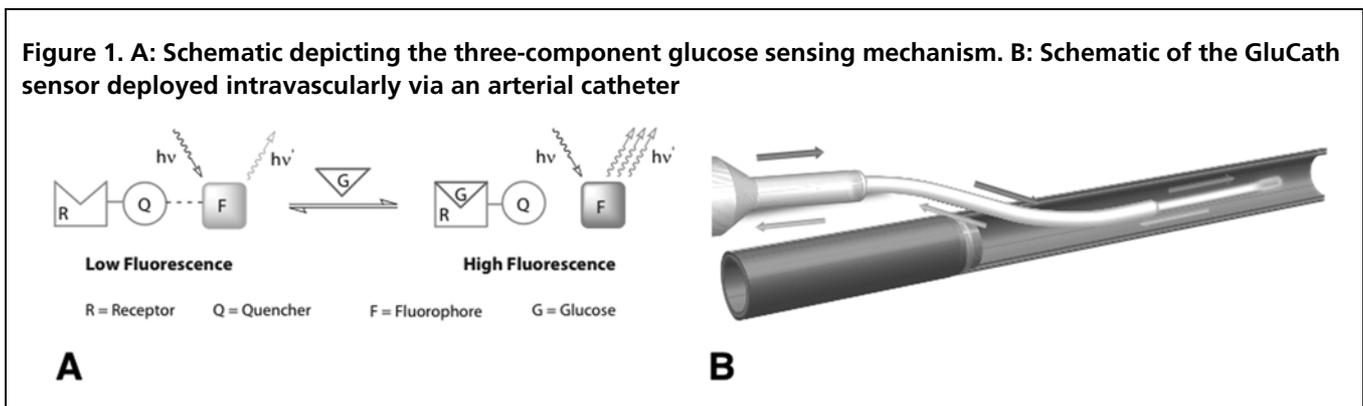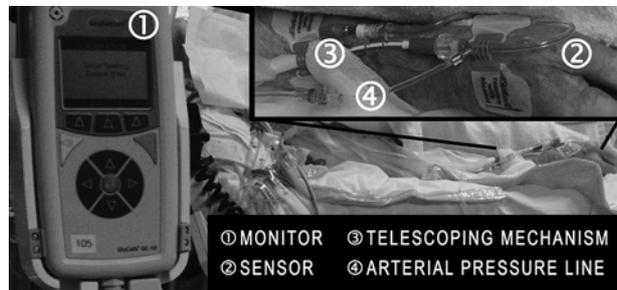
Figure 1. A: Schematic depicting the three-component glucose sensing mechanism. B: Schematic of the GluCath sensor deployed intravascularly via an arterial catheter

Low Fluorescence · High Fluorescence

R = Receptor   Q = Quencher   F = Fluorophore   G = Glucose

A   **B**

Figure 2. GluCath System after insertion into Patient 05

① MONITOR   ③ TELESCOPING MECHANISM
② SENSOR   ④ ARTERIAL PRESSURE LINE

deployed through the radial arterial catheter (Figure 1b). Blue light travels down an optical fibre to the sensing chemistry at the distal tip of the sensor, which fluoresces green in proportion to the glucose concentration of the blood. The sensor also measures, and corrects for, blood temperature and pH.

The GluCath monitor is portable, battery-operated and reusable (Figure 2). The user interface consists of a display and keypad for operating the device. The user enters reference BG and pH values after sensor insertion, completing the calibration in vivo. Optical signals are processed in the monitor where the fluorescence intensity is converted to a prospectively calibrated glucose value, which is recorded every minute. The device is enabled with alarms that request an additional reference sample if the measured BG value is less than 4.2 mmol/L (75 mg/dL) or greater than 10.0 mmol/L (180 mg/dL).

Device deficiencies were defined according to ISO standard 14155: 2011 (Clinical investigation of medical devices for human subjects — good clinical practice) as malfunctions, use errors or labelling inadequacies that affect device safety, durability or performance. Device malfunctions were determined by a technical review of recorded optical and temperature signals by the sponsor. Use errors were identified by a review of the study activity log and photographs.

Potential participants had a standard 20-gauge radial arterial catheter inserted before surgery as part of routine perioperative care. After surgery and subsequent admission to the ICU, if clinically stable, the patient was enrolled and the sensor was deployed via the radial arterial catheter with its tip located within the artery at least 14 mm beyond the arterial catheter tip (Figure 3a). This procedure was conducted using sterile technique by a trained study investigator.

After 30 minutes, the system was calibrated in vivo using an arterial sample analysed in an ABL800 Flex blood gas analyser (Radiometer Medical ApS). A calibration check was performed an hour later, and the system was recalibrated if the glucose concentration differed by 20% or more from the reference analyser. Other than during calibration, clinical staff and study personnel were unaware of the glucose concentration being recorded by the GluCath system. For up to 24 hours, hourly reference samples were drawn from the arterial catheter, through which the sensor was deployed. The volume of blood withdrawn from the patients was minimised by use of a Venous Arterial Blood Management Protection (VAMP) System (Edwards Lifesciences). The arterial line flush solution was normal saline containing 1 U/mL of unfractionated heparin.

The patient's BG level was managed according to the existing protocol for patients in the ICU and based on the measurements from the reference analyser. Treatment decisions were not made based on the glucose values recorded by the GluCath system.

A dedicated study nurse was present for the duration of the patient's participation in the study. The role of the study nurse was to assist with insertion of the sensor, to collect and analyse hourly arterial reference samples, to record

Figure 3. A: Ultrasound of Patient 05's, radial artery showing the correct positioning of the sensor tip distal to the arterial catheters. B: Ultrasound of Patient 17 showing the sensor tip inside the arterial catheter, resulting in measurement error
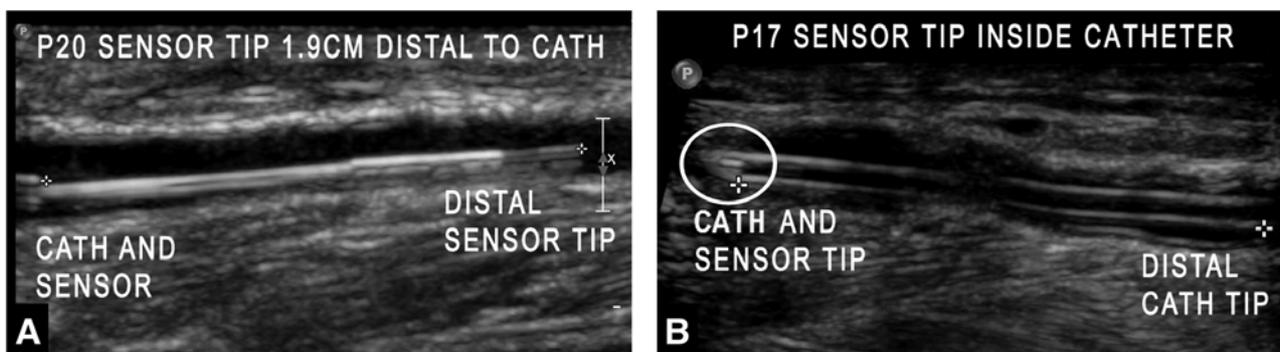
ease of blood draw, arterial flush and evidence of arterial waveform dampening, and to log medications and patient activity that could potentially affect sensor readings.

The sensor was approved for use for up to 24 hours but was removed earlier if deemed clinically necessary or when the radial arterial catheter was removed.

Ultrasound examinations of the radial artery and ipsilateral ulnar artery were performed by trained vascular ultrasound technicians before sensor insertion, immediately after sensor insertion and before sensor removal. Data recorded from the ultrasounds included vessel patency and diameter, blood-flow velocity, the presence or absence of thrombus and sensor positioning (Figure 3). Hand observations were performed within 24 hours of sensor removal and data collected included the presence or absence of erythema, oedema, bruising, pain or numbness.

Statistical analysis

We planned to study a convenience sample of 20 patients with dropouts being replaced. An initial run-in cohort of five patients was studied to establish the feasibility and safety of study procedures. The planned number of paired BG measurements between the GluCath sensor and reference analyser was 400 (20 per patient). Additional reference samples during times of unstable BG concentration could potentially increase this total up to a maximum of 600 points (30 per patient). The BG concentration measured by the reference analyser was compared with the last BG concentration recorded by the GluCath sensor before blood was drawn for analysis by the reference analyser; these two measurements were referred to as paired measurements.

The extent of agreement between the GluCath system measurements and the corresponding reference analyser values were evaluated by the following composite difference statistics: SD of the differences, the mean absolute difference (MAD), and the mean absolute relative difference (MARD). We also present the data in a modified Bland–Altman plot of the reference concentration minus the sensor concentration plotted against the reference concentration. A Clarke error grid is not provided, as it is an inappropriate method to evaluate accuracy of glucose measuring devices in critically ill patients.[8]

Results

We enrolled 21 patients between November 2011 and March 2012. In one patient (Patient 15), the sensor malfunctioned and was removed, and no data were collected. In a second patient (Patient 17), the sensor was malpositioned with the sensor tip inside the arterial catheter because of user error (Figure 3b). This sensor was retained in the patient's radial artery but the data were discarded. Nineteen sensors resided in patients' radial arteries for 20–

24 hours and provided data for the accuracy analysis. After excluding initial in-vivo calibration measurements, 443 paired measurements were obtained, of which six were excluded from the analysis — four because of sensor malfunction, one because of incomplete initial calibration and one because of monitor power failure (Figure 4).

Patient characteristics and outcome data on all 21 patients for whom data were collected and analysed, excluding data points where there was a confirmed device deficiency, are given in Table 1.
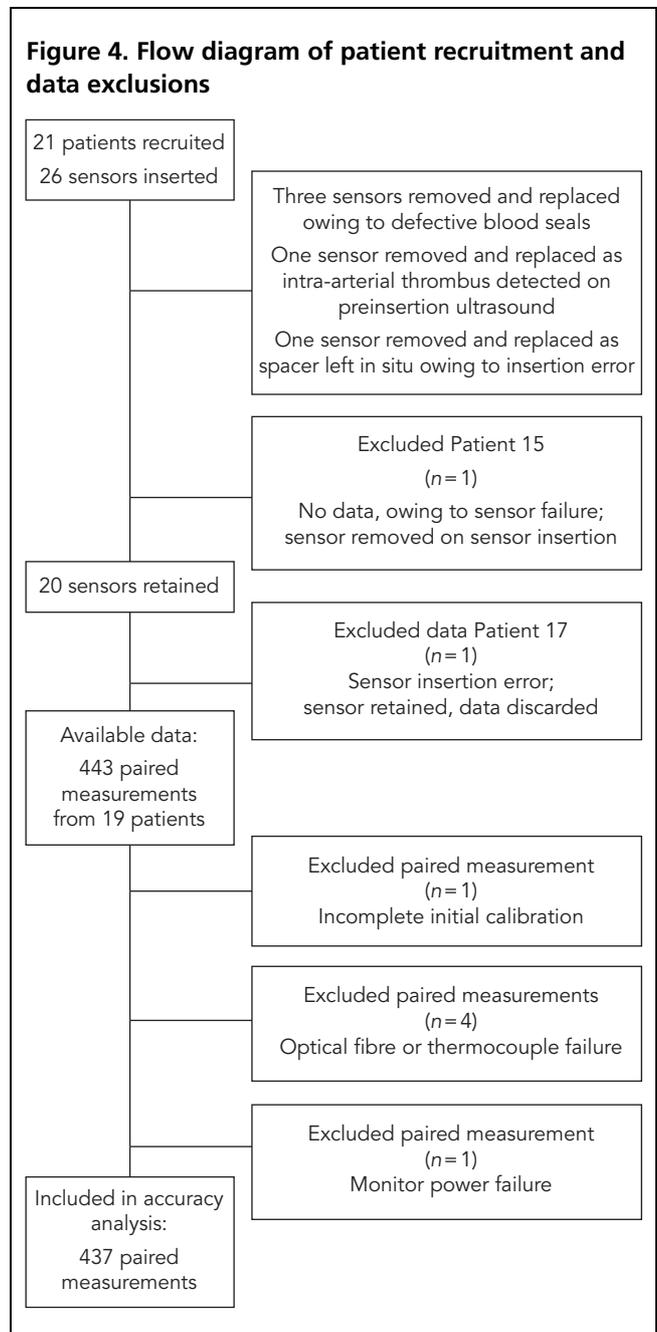
Figure 4. Flow diagram of patient recruitment and data exclusions

| Table 1. Patient characteristics and outcome data | | | | | | | | | | | |
| | | | | | | | | | | Number (%) of patient's paired values meeting criteria | |
Patient no.	Sex	Operation	Age, years	APACHE II score	Paired samples	Mean glucose (mmol/L)	SD (mmol/L)	Mean bias (mmol/L)	MAD (mmol/L)	MARD (%)	CLSI POCT 12-A3 (%)*	ISO 15197: 2003 (%)†
01	M	OPCABG	50	11	24	8.4	1.8	− 1.2	1.6	18.5%	11 (45.8%)	16 (66.7%)
02	M	OPCABG	67	11	22	9.0	0.8	0.4	0.7	7.7%	18 (81.8%)	21 (95.5%)
03	M	CABG	41	10	26	8.8	0.7	1.0	1.0	11.5%	16 (61.5%)	21 (80.8%)
04	M	MVR	61	7	25	8.7	0.6	0.1	0.5	6.0%	23 (92.0%)	25 (100.0%)
05	M	CABG	80	20	23	7.8	0.9	0.3	0.8	11.0%	14 (60.9%)	22 (95.7%)
06	F	OPCABG	81	18	24	8.7	0.4	− 1.0	1.0	11.4%	13 (54.2%)	24 (100.0%)
07	F	AVR	82	13	23	8.0	0.5	− 0.3	0.4	5.9%	20 (87.0%)	23 (100.0%)
08	F	OPCABG	53	17	22	7.9	1.2	− 1.2	1.2	15.9%	14 (63.6%)	15 (68.2%)
09	F	CABG	71	13	23	9.0	0.5	− 0.2	0.5	4.7%	22 (95.7%)	23 (100.0%)
10	M	OPCABG	41	14	23	7.4	0.6	− 0.3	0.5	6.3%	19 (82.6%)	23 (100.0%)
11	M	AVR	52	9	23	8.3	1.6	− 1.8	1.9	25.0%	7 (30.4%)	11 (47.8%)
12	F	MVR	54	15	21	7.9	1.0	− 2.7	2.7	33.5%	0 (0)	1 (4.8%)
13	M	CABG	49	10	23	6.7	1.7	0.2	1.4	21.0%	7 (30.4%)	15 (65.2%)
14	M	TVR	62	13	24	9.0	0.8	1.0	1.0	11.6%	12 (50.0%)	21 (87.5%)
15	M	AVR	72	13	No data available due to malfunctioning sensor							
16	F	OPCABG	80	16	23	8.8	0.9	0.6	0.8	9.8%	17 (73.9%)	20 (87.0%)
17	M	AVR	87	16	No data available due to malpositioned sensor							
18	F	MVR	75	12	23	8.1	0.6	− 0.9	0.9	11.0%	13 (56.5%)	23 (100.0%)
19	M	OPCABG	69	15	20	8.0	0.8	− 0.1	0.5	5.2%	18 (90.0%)	19 (95.0%)
20	M	AAG	74	9	24	8.5	0.5	1.1	1.1	13.1%	12 (50.0%)	22 (91.7%)
21	M	AVR CABG	84	14	21	8.1	0.7	− 1.7	1.7	19.9%	3 (14.3%)	8 (38.1%)
Overall			66 (14.5)‡	13 (3.3)‡	437	8.2	1.4	− 0.3	1.1	13.0%	259 (59.3%)	353 (80.8%)

M = male. F = female. OPCABG = off pump coronary artery bypass graft. CABG = coronary artery bypass graft. AVR = aortic valve replacement. MVR = mitral valve replacement. TVR = tricuspid valve replacement. AAG = ascending aortic graft. APACHE = acute physiology and chronic health evaluation. MAD = mean absolute difference. MARD = mean absolute relative difference. CLSI = clinical laboratory standards institute. POCT = point-of-care testing. ISO = International Organization for Standardization. * Within 0.67 mmol/L or 12.5%. † Within 0.83 mmol/L or 20%. ‡ Mean (SD).

Qualitative performance

Sensors were successfully deployed in 20/21 patients (95.2%). The device did not interfere with clinical care, blood pressure monitoring or blood sampling. Deployment of the sensor through the arterial catheter did not compromise arterial line function or patient care.

We successfully collected 488 blood samples over the sensors for analysis. Difficult sampling or dampening of the blood pressure waveform were observed on 17 occasions (3.5%) in five patients. In four of the five patients there was ultrasound evidence of thrombus in the radial artery being studied. Although a quantitative controlled analysis was beyond the scope of this study, the study staff concluded that the frequency of arterial catheter problems was similar to standard care. With the exception of Patient 19, all episodes of dampening or sampling difficulty were resolved by repositioning the hand or flushing the catheter. The catheter and sensor were both removed from Patient 19 after 20 hours of

monitoring, owing to loss of catheter patency. A new catheter was inserted without the GluCath sensor present and pressure monitoring was resumed normally.

Safety

In five patients (23.8%), thrombus or blood-flow abnormalities were detected on the preremoval ultrasound examination and documented as anticipated adverse events. One had thrombus in proximity to the sensor only, two had thrombus in proximity to the arterial catheter only and two had thrombus in proximity to both the sensor and catheter. No clinical signs or symptoms of hand ischaemia were observed and no treatment was necessary.

Unrelated to the study device, one patient suffered a cardiopulmonary arrest. In this patient, the sensor functioned successfully during cardiopulmonary resuscitation and urgent return to the operating room. Another patient experienced anaphylaxis that was assessed as being an

Figure 5. Bland–Altman plot, excluding Patients 15 and 17
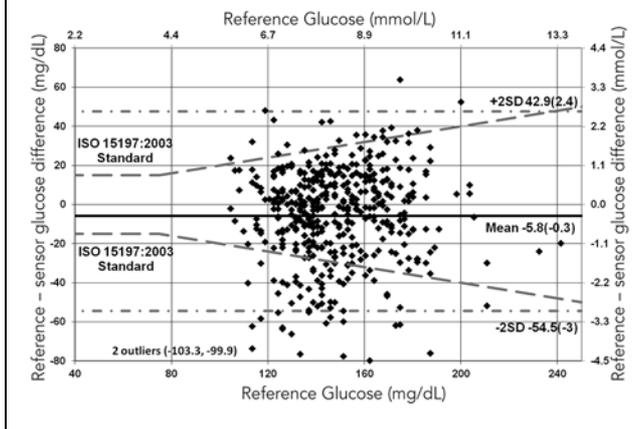
adverse drug reaction. Both serious adverse events were judged not to be related to the device or study procedure.

Device deficiencies

All 26 sensors inserted during the study were monitored for device deficiencies. As a result, 31 pairs of reference measurements and corresponding sensor readings were excluded from the accuracy analysis (Figure 4).

Device deficiencies were associated with the insertion procedure for seven sensors, resulting in six sensor removals, of which five were replaced. Malfunctions observed included retrograde blood flow into the sensor extension set, arterial catheter failure with persistent waveform dampening, and optical signal loss upon insertion (Patient 15). Except in patient 15, these sensors were removed and replaced within an hour of insertion. One use error occurred in two patients, where a spacer was inadvertently placed between the sensor extension set and the arterial catheter hub, resulting in the sensor tip residing inside the arterial catheter. This error was detected post-hoc in Patient 17, resulting in the exclusion of 25 paired measurements that were not obtained from undiluted arterial blood, but was discovered within an hour of insertion in Patient 19, in whom the sensor was removed and replaced.

Use errors involving sensor securement and in-vivo calibration may have affected the results from nine patients. In Patient 01, accidental traction was placed on the sensor cable during patient repositioning after 20 hours of monitoring. This resulted in the sensor being partially retracted back into the arterial catheter, causing contamination with arterial line flush solution and falsely low readings from the sensor for the last 4 hours of the study. Errors in recording the blood sample time on the monitor and calibrating the system resulted in erroneous reference BG values being entered into

the monitor for in-vivo calibration for two patients, and caused accidental recalibrations of current sensor readings for six patients and of reference readings for two patients. These results were all retained for the accuracy analysis.

Device malfunctions occurred during the monitoring period of four patients and resulted in the exclusion of readings from the accuracy analysis. In one patient (Patient 08), the monitor was accidently power cycled, resulting in one excluded reading while the monitor was restarted. In two patients (Patient 11 and Patient 12), the sensor thermocouple failed after 21 or 22 hours, resulting in four sensor readings being excluded. In the fourth patient (Patient 20), the initial in-vivo sensor calibration was not completed, resulting in one excluded reading before successful calibration.

There were no device malfunctions or use errors that led to serious adverse events during the study.

Quantitative performance

A total of 488 blood samples were collected from 21 participants, with reference BG concentration measurements ranging from 4.7 mmol/L to 13.4 mmol/L (85–241 mg/dL); 437 paired points from 19 successfully deployed and functioning sensors were available for performance analysis. Blood samples used for initial in-vivo device calibrations were excluded, as were 31 samples (6.4%) corresponding to device or procedural failures. Comparison of prospectively calibrated GluCath system glucose values to the reference values resulted in 353/437 (80.8%) of paired points meeting the ISO standard 15197: 2003 criteria (within 20%) and 259/437 (59.3%) meeting the CLSI standard POCT 12-A3 criteria (within 12.5%). Overall, aggregate results included an SD of 1.4 mmol/L (25 mg/dL), an MAD of 1.1 mmol/L (20 mg/dL), and an aggregate MARD of 13.0%. Individual sensor MARDs ranged from 4.7% to 33.5% (Table 1).

The Bland–Altman plot (Figure 5) of the reference BG levels against the difference between the GluCath system measurements and the reference levels shows a mean bias of − 0.3 mmol/L (− 5.8 mg/dL), the upper limit of agreement of 2.4 mmol/L (42.9 mg/dL) and the lower limit of agreement of − 3.0 mmol/L (− 54.5 mg/dL). No correlation is evident between the glucose difference and the reference glucose level. This plot also shows paired points meeting the ISO 15197: 2003 criteria.

Paired reference glucose values used for performance analysis ranged from 5.8 to 13.4 mmol/L; 404/437 (92.4%) were in the target glycaemic control range of 6.0–10.0 mmol/L (108–180 mg/dL), 27/437 (6.2%) were above 10 mmol/L (180 mg/dL), and 6/437 (1.4%) were in the range of 4–6 mmol/L (72–108 mg/dL). There were no values below 4.0 mmol/L (72 mg/dL).

Discussion

In this open-label, non-randomised, single site, product development study we evaluated the use of a novel system of CGM using a quenched fluorescence sensor deployed through a standard radial arterial line. We found the sensor simple to deploy, and it did not interfere with patient care or cause any significant adverse events.

Use of the GluCath system appeared to be safe. The insertion of the GluCath sensor did not cause additional risk to patients beyond the anticipated risks of radial artery catheterisation. We did not observe any sustained arterial waveform dampening and there was no difficulty in withdrawing arterial blood over the sensor. In five patients, we observed non-occlusive thrombus in proximity to the sensor, the arterial catheter, or both, before sensor removal. In two additional patients, we replaced the radial arterial catheter because of ultrasound evidence of thrombus before sensor insertion. Although we do not have accurate data on the incidence of arterial catheter-related thrombus occurring within 24 hours of admission to ICU after cardiac surgery, it has previously been shown that a preoperative ultrasound examination detected abnormalities of the radial artery in 27.1% of patients awaiting coronary artery surgery.[9] Radial artery occlusion is a common and well recognised complication of radial artery catheterisation. One review reported that temporary arterial occlusion occurred after 831 of 4217 radial artery catheterisations (an overall incidence of 19.7%), and permanent occlusion occurred in 0.09% of catheterisations.[10] Despite careful examination, we did not detect radial artery occlusion or clinical signs or symptoms of thrombus or hand ischaemia in any of our patients. There were no unanticipated adverse device effects or device-related serious adverse events; and although we studied only 21 patients, our experience suggests that the presence of the sensor did not increase the risk of arterial occlusion or distal ischaemia.

The accuracy of the GluCath CGM system was assessed against a Radiometer ABL 800 FLEX blood gas analyser. This analyser is as accurate as a central laboratory BG measurement[11] and endorsed by recent recommendations that have specifically considered standards for assessing CGM.[8]

GluCath sensors were successfully deployed and functioned as intended in 19 of 21 patients, resulting in 437 paired glucose readings for the assessment of accuracy. Currently there are no agreed performance standards for CGM, although future standards are likely to demand assessment of both point accuracy and trend metrics.[8] In the absence of agreed standards, we reported the performance of the system using performance standards applied to intermittent sampling and measurement systems, ISO 15197: 2003 and CLSI POCT 12-A3. This assessment is in keeping with the recent recommendation that the point accuracy of CGM systems should be similar to that of intermittent measuring systems.[8] After excluding samples used for device calibration and six paired measurements affected by technical failures of the sensor or monitor, 80.8% of GluCath system measurements met the ISO 15197: 2003 criteria and 59.3% met CLSI POCT 12-A3. These values compare favourably with other CGM systems, such as a subcutaneous amperometric system that employs glucose oxidase, in which 68.1% of values met ISO criteria.[12] The point accuracy of the individual sensors varied and some of this variability was due to device deficiencies discovered during this study relating to routine use in the critical care environment.

CGM using a sensor inserted via an arterial catheter has potential advantages over some other methods. BG concentration measured in arterial blood should be consistent wherever measured, whereas venous and capillary measurements may vary from one vascular bed or venous system to another. Sensor insertion into an in-situ arterial catheter can be performed rapidly and the only interference with glucose monitoring is from occasional flushes of the arterial catheter after blood draws.

The system used in this study had a telescoping mechanism that allowed the sensor to be inserted to different depths, which would make the system adaptable to use with arterial catheters of different lengths. However, the telescoping mechanism was the source of a number of problems resulting in partial retraction of two sensors and back leakage of blood in three sensors. As a result of these observations, the telescoping mechanism has been removed from subsequent versions of the system. One sensor produced erroneous data owing to an insertion error when a spacer was accidentally left between the arterial catheter and the sensor-containing tubing. This resulted in the sensor being positioned within the arterial catheter, rather than the lumen of the artery, and measuring the

temperature, pH and glucose concentration of the arterial flush solution rather than blood. As a result, a design change has been made to eliminate the potential for this insertion error to occur in the future.

Our study had limitations. It was performed in a single centre and studied a single population of patients after elective cardiac surgery. During this study, there were no reference BG measurements of less than 4.7 mmol/L or greater than 13.4 mmol/L, therefore, we did not assess the performance of the GluCath system outside this range. We limited BG monitoring to 24 hours, which is shorter than a typical patient stay in an ICU and shorter than that desirable for a CGM system. We acknowledge that interference with clinical care is a subjective assessment and conclusions drawn about this have inherent limitations. Finally, alarm algorithms developed using the data from this study will be required to provide clinically relevant warnings in future developments of the system.

Future research using this technology may include assessing a larger cohort of patients for a longer duration and patient cohorts other than those who have undergone cardiac surgery.

Conclusions

This product development study has demonstrated that the GluCath system is a safe and practical system for continuously measuring BG in critically ill patients. Subsequent improvements in the design of the system should be evaluated for a longer period of time and in a broader population of patients.

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Author contributions and competing interests

All authors made substantive intellectual contributions to this study, in conception and design, acquisition of data, and analysis and interpretation of data. All authors have been involved in drafting and revising this manuscript for important intellectual content. All authors have given final approval of this version to be published.

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