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ORIGINAL ARTICLE

Glucose Measurement of Intensive Care Unit Patient Plasma Samples Using a Fixed-Wavelength Mid-Infrared Spectroscopy System

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Abstract

Objective:

Glycemic control is a rapidly developing field in intensive care medicine with the aim of reducing mortality, morbidity, and cost. Current intensive care unit (ICU) glucose measurement technologies are susceptible to interference from medications, volume expanders, and other substances present in critically ill patients. We hypothesized that a fixed-wavelength mid-infrared (mid-IR) spectroscopy system would be accurate for measuring glucose levels of ICU patients.

Research Design and Methods:

This is a prospective investigation of plasma samples from two different institutions treating a heterogeneous population of ICU patients. The first 292 samples were collected from 86 patients admitted to Stamford Hospital, and the next 352 samples were collected from 75 patients from three ICUs at the University of Maryland. Plasma samples were measured on a Fourier-transform infrared or a proprietary spectrometer, with a glucose prediction algorithm to correct for spectral interference, which were compared with reference measurements taken using a YSI 2300 glucose analyzer.

Results:

Glucose values ranged from 24 to 343 mg/dl. Numerous medications and injury/disease states were observed in the patient populations, with metoprolol, fentanyl, and multiple organ failure the most prevalent. Despite these interferents, there was a high correlation ($r \geq 0.94$) and low standard error (≤12.8 mg/dl) between the predicted glucose values and those of the YSI 2300 STAT Plus reference instrument in the three studies. A total of 95.1% of the 644 values in the three studies met International Organization for Standardization 15197 criteria.

Conclusion:

These results suggest that a fixed-wavelength mid-IR spectrometer can measure glucose accurately in the plasma of ICU patients.

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Abbreviations: (APACHE) Acute Physiology And Chronic Health Evaluation, (FTIR) Fourier-transform infrared, (ICU) intensive care unit, (IRB) institutional review board, (ISO) International Organization for Standardization, (mid-IR) mid-infrared

Keywords: continuous glucose monitoring, intensive care unit, interference, spectroscopy

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Introduction

Existing technologies to manage blood glucose in the intensive care unit (ICU) rely heavily on handheld meters, which are still vulnerable to a wide variety of error sources that can put a patient at risk. Common sources of meter error include patient or methodology interferences, operator mistakes, environmental exposure, and device malfunction. It is well-known in the research community that meters are susceptible to interference (e.g., changes in hematocrit, oxygenation, uric acid, or ambient temperature, as well as the administration of dopamine, mannitol, maltose, or icodextrin) and that meter measurements are not taken frequently enough.[1–5] However, operators are typically unaware of these inaccuracies and risks, which has led to reports of patient deaths specifically related to inaccurate measurements involving elevated readings from the presence of non-glucose sugars.[6] In addition, capillary blood glucose measured by meters is not interchangeable with venous or arterial blood glucose,[7] and the agreement between meters and central laboratory analyzers is often poor, particularly at the low and high ranges.[8]

Beyond the specific limitations of handheld meters, all manual methods have the additional disadvantage of being time consuming,[9] resulting in reduced sample frequency[10] that can affect insulin dosing schedules.[11] An accurate, frequent, automated method of measuring glucose that can detect and correct for interferences would help critical care physicians achieve glycemic control in their patients.

Call for New Technology

There is substantial evidence that glycemic control should be managed in the ICU by avoiding hyperglycemia, mild hypoglycemia, and glycemic variability.[12,13] However, as cited earlier, the current state of the art has significant limitations in assisting clinicians in meeting these clinical goals, establishing the need for an automated, near-continuous glucose monitoring system for their ICU patients, with sufficient accuracy to provide reliable alarms for hyperglycemia, hypoglycemia, and variability.[14–16]

Background on Mid-Infrared Glucose Measurement

Pharmacological agents, their metabolites, and endogenous biochemical conditions that arise from an injury or disease state can all interfere with the accurate measurement of blood glucose. Fortunately, these substances can be detected with spectral analysis. Clinical and diagnostic applications of mid-infrared (mid-IR) spectroscopy have been one of the most active areas of research and development since the 1990s. Heise and colleagues demonstrated how the information-rich mid-IR spectra may be used to estimate clinically important blood analytes such as glucose, proteins, cholesterol, urea, triglycerides, and uric acid when measured in plasma.[17] With mid-IR spectroscopy, not only can glucose in plasma be identified, but quantified as well.[18]

Physiologically important analytes such as glucose have spectral bands in a limited range of the infrared spectrum, found most easily in the mid-IR region.[19] In principle, a limited number of bands within the mid-IR region can be used to estimate these analytes. Instead of covering the broad range of 4–12 μm of mid-IR, a specific set of 25 wavelengths between 7 and 10 μm was chosen for this investigation. Specifically, 11 of the filters are between 7 and 8 μm, 6 of the filters are between 8 and 9 μm, and 8 of the filters are between 9 and 10 μm. Wavelengths were specified to 0.001 μm. These 25 filter wavelengths were identified through mathematical modeling. This reduced coverage of the mid-IR region was tailored to the absorption of glucose in this region, as shown in **Figure 1**.

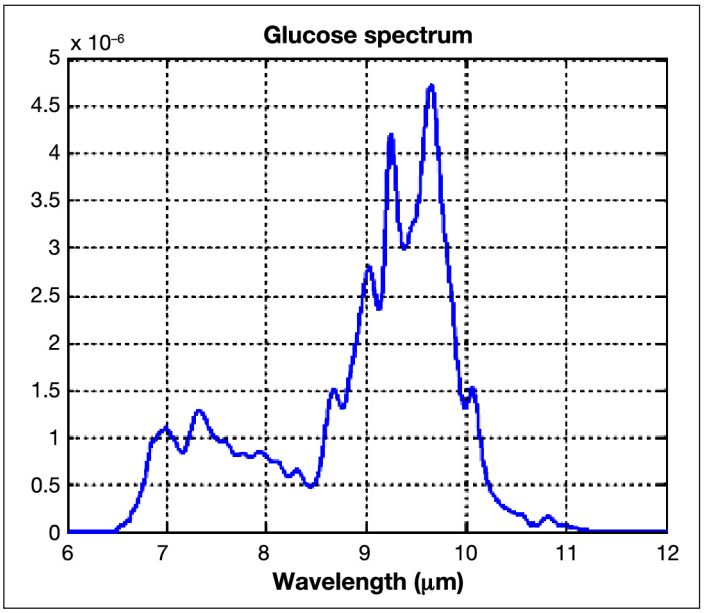

Figure 1. Mid-IR absorption of glucose.

Research Design and Methods

Study Objectives

The objectives of these studies were to evaluate the accuracy and performance of fixed-wavelength mid-IR technology and to optimize a glucose prediction algorithm for interfering substances, using samples representative of the intended use population. Plasma samples from ICU patients were analyzed with either an Fourier-transform infrared (FTIR; Perkin Elmer Spectrum One) with access to only 25 specific wavelengths, in the case of the Stamford study, or a proprietary mid-IR spectrometer, in the case of the Maryland studies. In all studies, glucose was measured on the plasma samples using the YSI 2300 STAT Plus (Yellow Springs Instruments, Yellow Springs, OH) as the reference standard.

Complete information on patient medication, disease status, and treatments were provided by the site staff in each location. When there were significant discrepancies between paired reference and fixed-wavelength mid-IR glucose measurement, analyses of the source documentation led to the investigation as to what substances could have affected the spectra from the plasma samples. Pure spectra of the identified interferents were then isolated and subsequently proven to interfere in separate laboratory experimentation. If subsequently verified, the interferent was added to the algorithm's library of interferences. (For example, it is common to use volume expanders in trauma patients. During one of the trials in Baltimore, a discrepancy was noted when the administration of hetastarch, in particular, was used. This substance contains a non-glucose sugar, which was subsequently corrected for.)

This process of adding validated interferences to the algorithm's library was used throughout the study. No filter wavelengths were added during any of the studies. With the exception of adding to the library of interferences, no changes were made to the algorithm during this study. Thus, the learning was to validate the design of a 25-wavelength mid-IR spectrometer, validate the algorithmic approach, as well as ensure that the library of interferences was robust, toward the goal of making glucose readings from an integrated system capable of adjusting to the wide range of medications and endogenous substances commonly found in critical care medicine.

For these studies, the instrument used a proprietary real-time algorithm to generate sample-specific calibration coefficients. A total of 303 normal volunteer blood samples were collected and scanned. Those spectra and their YSI reference standard glucose values are stored in the instrument. The instrument's calibration includes a database of 200 drug and endogenous substance spectra. For each hospital blood measurement, the composition of the blood sample is determined in real time, indicating if calibration adaptation is required or not. Following that determination, the onboard substance spectra table is queried for the specific spectra found in the sample and the normal subject calibration database electronically titrated with each compound to generate a sample-specific calibration data set. From that data set, an adapted calibration vector is constructed, in real time, and applied to the measured sample spectra to compute interference-free glucose concentrations.

The goal of the algorithm and fixed-wavelength spectrometer is to recognize substances in the patient's plasma and then separate the glucose spectrum from all other spectra obtained from the patient's plasma. An example of this is shown in **Figure 2**.

Study Design

Three studies were conducted to develop and test this measurement technology. The initial work utilized 25 specific wavelengths in the mid-IR region and was used in study 1 at Stamford Hospital in Stamford, CT. The results provided the basis for the development of a proprietary mid-IR spectrometer, which was used in studies 2 and 3 at the University of Maryland in Baltimore, MD. This spectrometer utilizes the same 25 filter wavelengths that were initially validated in the Stamford study. All three studies were conducted under the approval of the institutions' institutional review boards (IRBs), and informed consent was obtained from each patient or legally authorized representative before any of the patients were enrolled into any of the studies.

In all studies, blood samples were obtained from critically ill patients. After separating the plasma, glucose values were estimated with either the 25 identified wavelengths of the FTIR or the proprietary technology (which had only 25 wavelengths) of the subsequently developed OptiScan spectrometer and compared with the YSI 2300 as a reference instrument. The samples contained a wide range of plasma expanders, pressure stabilizers, and other medications that can interfere with accurate glucose readings.

These were minimal risk, prospective studies. Samples were collected from patients admitted to a mixed medical/surgical ICU unit at Stamford Hospital for study 1 and

from patients admitted to the ICUs of one of three centers under the jurisdiction of the IRB at the University of Maryland for studies 2 and 3. A blood sample (4 ml in study 1, 10 ml in studies 2 and 3) was taken once daily from an existing arterial line or from a central line if available. In rare cases, venipuncture was used. The blood was then spun in a centrifuge to separate the plasma from the red blood cells.

In study 1 at Stamford, the plasma samples were measured on site using a single, reagentless FTIR spectrometer and the YSI reference device. In studies 2 and 3 at Maryland, the plasma samples were frozen at -70 °C and shipped to OptiScan Biomedical in Hayward, CA, for analysis. Upon receipt, the frozen plasma was thawed in a water bath and filtered through a micropore filter before processing on the FTIR and spectrometer as well as on the YSI.

Information regarding patients' laboratory values, medication, disease/trauma state, surgeries, procedures, and diagnostic tests were provided by the site staff and recorded on case report forms. This information was used by the algorithm scientists at OptiScan to assess the interferents likely to be present in each plasma sample.

Studies 2 and 3 conducted at Maryland followed similar procedures but had different study lengths and patient populations. Study 2 included 25 patients participating for 3 days, and study 3 included 50 patients participating for up to 7 days. Both studies included a single blood draw per day. Study 3 had the additional inclusion criteria of acute kidney or liver failure, without being on dialysis at time of enrollment. Patients from study 3 were categorized into three groups: complex cardiac (n = 20), isolated organ failure (n = 20), and complex surgical or sepsis (n = 10).

Study Populations

In study 1 at Stamford, 86 patients (70 from the ICU and 16 from the intermediate care unit, a subcritical care unit) were enrolled. Patient baseline characteristics and selected clinical outcomes are presented in **Table 1**.

A total of 75 subjects were enrolled at the University of Maryland: 25 in study 2 and 50 in study 3. There were 48 male and 27 female participants, with a mean age of 51.6 years. Critically injured patients were recruited from R Adams Cowley Shock Trauma Center, University of Maryland Medical Center, and the University of Maryland Veteran's Affairs Medical Center. Patients were at least 18 years old, were critically injured or ill, required intensive care monitoring, and had expected minimum

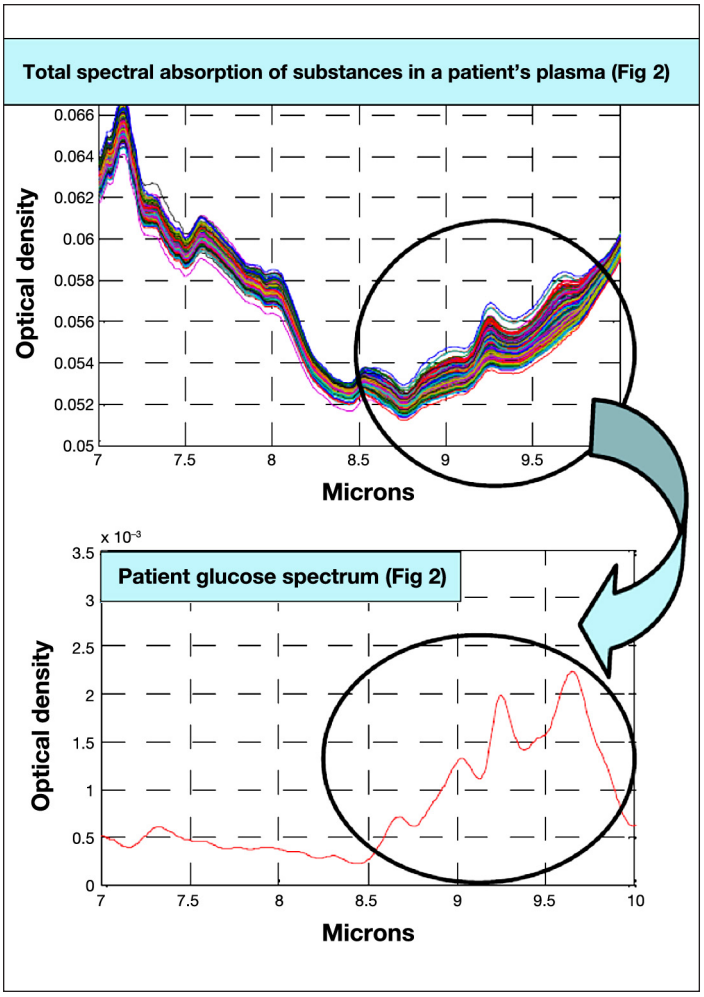

Figure 2. Total mid-IR spectral absorption of substances in a patient's plasma reduced to absorption of glucose alone.

Table 1.
Patient Baseline Characteristics and Selected Clinical Outcomes from Study 1, Stamford Hospital[a]

Number of subjects	86
Number of samples	292
Medical (%)	68.2
Mechanical ventilation (%)	45.5
Diabetes mellitus (%)	19.7
Autoimmune polyglandular syndrome	44.9 (35.3)
ICU length of stay (median)	2.5 (1.3–6.5)
ICU length of stay	5.4 (6.6)
APACHE IV predicted mortality (%)	23.1 (29.3)
Mortality (%)	18.2

[a] Data displayed as mean (standard deviation) or median (interquartile range) where noted.

ICU stays of 3 days (study 2) or 7 days (study 3). Pregnant women were excluded. Patient baseline characteristics and selected clinical outcomes are presented in **Table 2**.

Table 2.
Patient Baseline Characteristics and Selected Clinical Outcomes from Studies 2 and 3, University of Maryland

	Study 2	Study 3
Subjects		
Number of subjects	25	50
Number of samples	75	302
Gender		
Male	80%	56%
Female	20%	44%
Race		
Caucasian	16%	68%
African-American	84%	30%
Hispanic	0%	2%
Patients requiring		
Blood transfusion	60%	86%
>10 U blood/day	24%	36%
Surgeries	80%	68%
Dialysis	8%	42%
Vasopressors	28%	84%
Plasma expanders	32%	62%
Outcome		
Discharged	96%	64%
Expired	4%	36%

Data Analysis

Plasma samples in study 1 at Stamford were measured on the FTIR, with analysis limited to 25 particular wavelengths. Samples in studies 2 and 3 were measured using a proprietary fixed-filter wheel with 25 unique wavelength filters, as is illustrated in **Figure 3**. Linearity, correlation, and standard deviation were computed for predicted values against the measured YSI values. Statistical analysis was performed using MathWorks MATLAB 7 (MathWorks, Natick, MA).

Results

Study 1 at Stamford Hospital showed that using only 25 wavelengths of the FTIR yielded acceptable results. The correlation coefficient was 0.96 and the standard error was 9.75 mg/dl when compared with the YSI readings. A linear regression plot of predicted glucose values versus YSI values is presented in **Figure 4**. This result met International Organization for Standardization (ISO) 15197 criteria, as 96.6% (282/292) of the data points were within the specified range, exceeding ISO criteria for acceptance of 95%. Of the 292 data points, 42 were less than 75 mg/dl, of which 41 met ISO criteria. Of the 250 data points ≥75 mg/dl, 241 met the criteria. A total of 194 different medications were identified in the samples, and the numerous disease states were observed, including end-stage renal failure, with accompanying high levels of

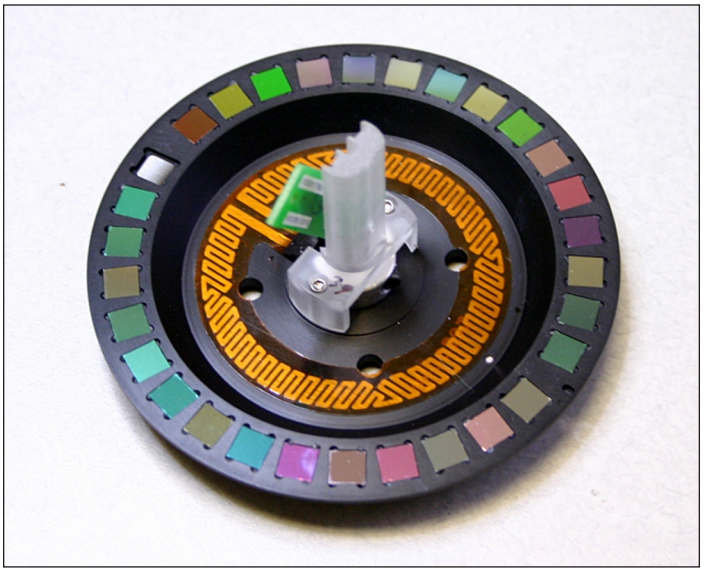

Figure 3. Fixed-filter wheel with 25 unique wavelength filters, used in the custom spectrometer.

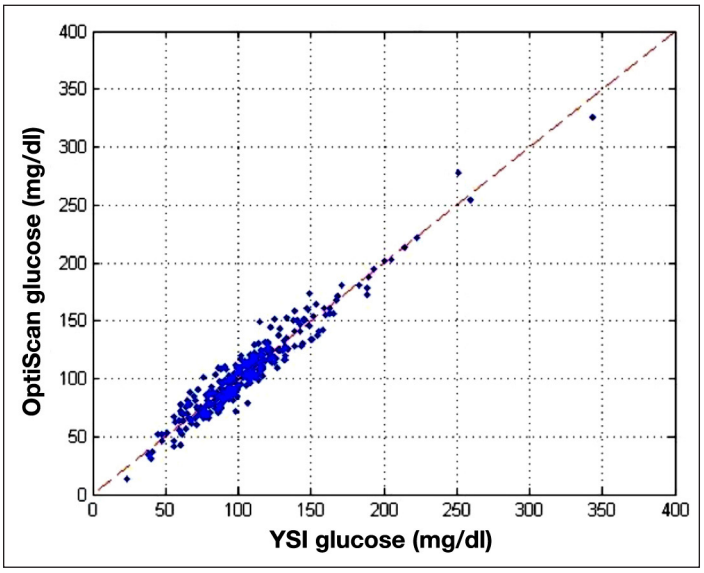

Figure 4. Linear regression plot, study 1, Stamford Hospital.

endogenous substances. The most commonly observed medications are listed in **Table 3**. Further study data are presented in **Table 4**.

Study 2 at Maryland showed that using a fixed 25-wavelength mid-IR spectrometer also yielded acceptable results. The correlation coefficient between predicted and observed reference values was 0.95, and the standard error was 10.1 mg/dl. This result met ISO 15197 criteria, as 98.7% (74/75) of the data points were within the specified range, exceeding ISO criteria for acceptance of 95%. Of the 75 data points, 1 was less than 75 mg/dl and met ISO criteria. Of the 74 data points ≥75 mg/dl, 73 met the criteria. A linear regression against the YSI is shown in **Figure 5.**

This was a relatively ill population, with a mean Acute Physiology And Chronic Health Evaluation (APACHE) II score upon admission of 19. Patient condition upon admittance is presented in **Table 5**. Anemia [median (interquartile range) nadir hemoglobin was 27.2% (5.1%)] and hyperlactemia (32% of patients had higher than normal lactate) were common. The observed patient values and normal laboratory ranges of selected substances are presented in **Table 6**. Laboratory values for all of the major categories were abnormal in this population.

Interferents present in the study 2 patients included colloidal and crystalloid plasma expanders, pressure stabilizers, antibiotics, pressors, and steroids. The colloid volume expander hetastarch was used in 24% of patients, and 29% of patients were on dialysis at the time of the study. A wide range of medications was used in these patients; the 20 administered most frequently are listed in **Table 3**.

Table 3.
Top 20 Medications

Study 1	Study 2	Study 3
Metoprolol	Fentanyl	Insulin
Morphine	Propofol	Enoxaparin
Lansoprazole	Insulin	Heparin
Potassium chloride	Lorazepam	Fentanyl
Acetaminophen	Phenytoin	Pantoprazole
Pantoprazole	Enoxaparin	Piperacillin
Heparin	Vecuronium	Tazobactam
Furosemide	Cefazolin	Dobutamine
Famotidine	Pantoprazole	Hydrocortisone
Metronidazole	Furosemide	Furosemide
Piperacillin	Metoclopramide	Famotidine
tazobactum	Famotidine	Vancomycin
Lorazepam	Morphine	Norepinephrine
Magnesium sulfate	Dexmedetomidine	Vasopressin
Phenytoin	Midazolam	Albumin
Simvastatin	Heparin	Amiodarone
Salicylate,	Dobutamine	Morphine
acetyl salicylic acid	Ampicillin Sulbactam	Midazolam
Midazolam	Nafcillin	Milrinone
Vancomycin	Hydralazine	Methylprednisolone
Ampicillin/sulbactam		Propofol
Ciprofloxacin		

Table 4.
Study Data

	Study 1	Study 2	Study 3
N	292	75	302
Glucose range	24–343 mg/dl	66–219 mg/dl	36–304 mg/dl
r^2	0.93	0.91	0.89
Number of medications	194	76	228

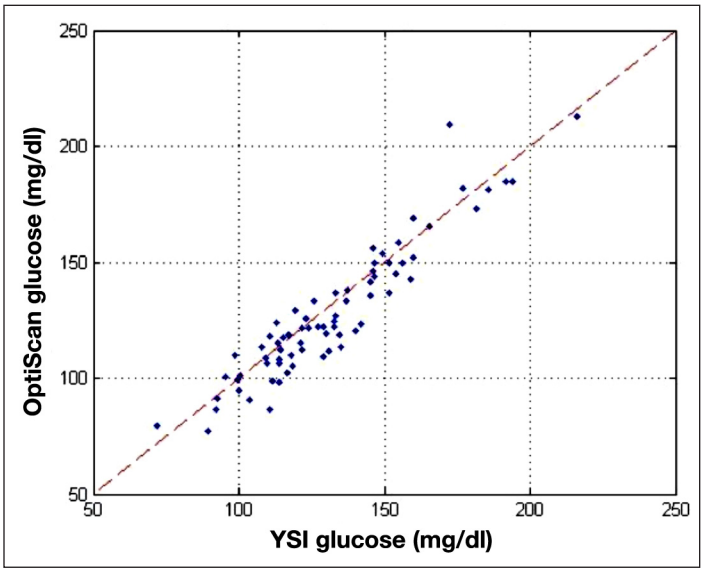

Figure 5. Linear regression plot, study 2, University of Maryland.

Table 5.
Patient Condition upon Admittance in Studies 2 and 3, University of Maryland

	Study 2		Study 3	
	Mean	Range	Mean	Range
Age	40.4 years	18–85 years	57.1 years	18–95 years
APACHE II	19	9–37	23.8	4–40
Sequential organ failure assessment	7.4	4–18	10.9	4–20
Systemic inflammatory response syndrome	2.76	1–4	2.92	0–4
Injury severity score	23.48	9–41	—	—

Study 3 at Maryland further validated that a fixed 25-wavelength mid-IR spectrometer also yielded acceptable results. The correlation coefficient between predicted and observed reference values was 0.94 and the standard error was 12.8 mg/dl. These data came close to meeting the ISO 15197 95% criteria, as 92.7% (280/302) of the data points were within the specified range. Of the 302 data points, 16 were less than 75 mg/dl, of which 15 met ISO criteria. Of the 286 data points ≥75 mg/dl, 265 met the criteria. A linear regression against the YSI is shown in **Figure 6.**

The mean APACHE II score of 23.8 was even higher than that observed in study 2, suggesting that, overall, the patients in study 3 were even more critically ill. This is supported by the higher mortality rate for the patients in study 3 (36%) versus study 2 (4%). Anemia and elevated lactate levels were common in patients in study 3, and these patients generally had a larger range of abnormal laboratory values relative to the study 2 patients. These patients also required transfusions, dialysis, vasopressors, and plasma expanders at higher rates than did the patients in study 2.

Table 6.
Patient Values and Normal Laboratory Ranges in Studies 2 and 3, University of Maryland[a]

	Study 2	Study 3	Normal laboratory range
Blood urea nitrogen	13.2 (6.9) mg/dl	39.6 (27.9) mg/dl	5.0–20.0 mg/dl
Creatinine	0.81 (0.27) mg/dl	2.18 (3.45) mg/dl	0.7–1.5 mg/dl
Total bilirubin	0.93 (0.42) mg/dl	6.5 (8.9) mg/dl	0.3–1.2 mg/dl
Platelets	144 (59) K/mcl	144(104) K/mcl	153–367 K/mcl
Hematocrit	29.5 (4.2)%	27.7 (4.0)%	35–50%
Lactate	1.78 (1.85) mg/dl	2.30 (2.19) mg/dl	0.5–1.6 mg/dl

[a] Study data presented are mean (standard deviation).

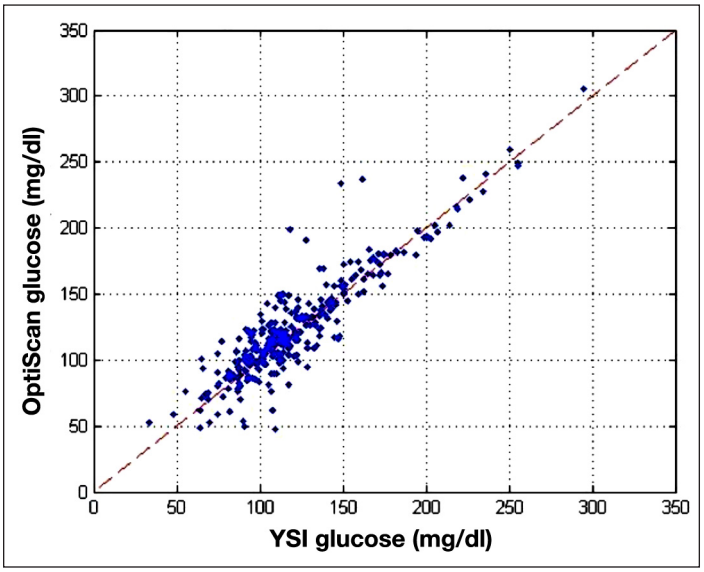

Figure 6. Linear regression plot, study 3, University of Maryland.

Discussion

These three studies demonstrate the feasibility of using fixed-wavelength mid-IR measurement technology to provide accurate measurements of blood glucose in varying ICU populations. The high correlation and the low standard error using the predicted values suggest that this technology compares favorably to reference analyzers such as the YSI. The measurement technology used an algorithm with an expanding library of verified and validated interferences to become insensitive to the variety of plasma expanders, medications, and the numerous injuries, illnesses, and complications present in the critically injured and ill patients in the three study populations from two geographically separate environments.

Study 1 at Stamford allowed the building of an initial reference library of interferents. These results were promising, justifying development of a proprietary spectrometer and further research into more severe ICU populations to ensure that a larger array of potential interferents was studied.

Building upon that initial feasibility demonstration, studies 2 and 3 at Maryland further tested the approach and measurement algorithm by using more critically ill patients. In both studies, all major laboratory values extended into the abnormal range. The higher APACHE II scores and mortality rate in study 3 relative to study 2 suggest that the targeted enrollment used in study 3 resulted in sicker patients and, as a consequence, a more challenging list of interferents. It is important to note that the plasma expander hetastarch was used on a large percentage of the Maryland patients, as this drug contains a non-glucose sugar specific to ICU patients.

One limitation of these studies is that the generation of plasma was done manually. This has been separately addressed and studied in a system that uses a reagentless cuvette and onboard spectrometer with storage of spectral data on interferents (the OptiScanner, OptiScan Biomedical, Hayward, CA).[20,21] A second limitation of this study is the possibility that not all interferents

were identified. This deficiency is being addressed by further clinical research in process. A third limitation of these studies is that they do not provide enough information within a particular ICU patient to validate patient-specific accuracy. That would have required more paired measurements per patient than was allowed by the IRB in any of the studies and would have required the integrated system to be connected to the ICU patient. This limitation is being addressed by clinical research now in process.

Conclusion

The current studies suggest that a mid-IR fixed-wavelength measurement system can be adapted to become insensitive to many types of interferents commonly observed in critically ill patients through a process of identifying interferents and adding them to a library that is part of the algorithm. Despite low hematocrit, high lactate levels, the presence of plasma expanders, pressure stabilizers, antibiotics, vasopressors, steroids, and myriad other drugs present in the ICU samples, the predicted glucose values closely matched the readings from the YSI reference instrument. Further work involving the attachment to ICU patients with an integrated, automated plasma-generation system is warranted.

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Disclosures:

Dr. Krinsley is an advisor to Roche Diagnostics, Medtronic, Edwards LifeSciences, Baxter, and OptiScan. Stamford Hospital was paid an honorarium for enrolling patients in the study. Dr. Krinsley received no direct compensation. Dr. Grant Bochicchio has performed studies for Edwards LifeSciences and for OptiScan. He has not received direct compensation from OptiScan.

References:

1. Fahy BG, Coursin DB. Critical glucose control: the devil is in the details. Mayo Clin Proc. 2008;83(4):394–7.
2. Tang ZP, Du XG, Louie RF, Kost GJ. Drug interference on glucose measurements with six handheld glucose meters and a portable analyzer for point-of-care testing in critical care. 51st Annual AACC Conference, New Orleans, LA, July 25–29, 1999.
3. Louie RF, Tang Z, Sutton DV, Lee JH, Kost GJ. Point-of-care glucose testing: effects of critical care variables, influence of reference instruments, and a modular glucose meter design. Arch Pathol Lab Med. 2000;124(2):257–66.
4. Karon BS, Griesmann L, Scott R, Bryant SC, Dubois JA, Shirey TL, Presti S, Santrach PJ. Evaluation of the impact of hematocrit and other interference on the accuracy of hospital-based glucose meters. Diabetes Technol Ther. 2008;10(2):111–20.
5. Nerhus K, Rustad P, Sandberg S. Effect of ambient temperature on analytical performance of self-monitoring blood glucose systems. Diabetes Technol Ther. 2011;13(9):883–92.
6. Garber JR. The FDA's Center for Devices and Radiological Health's Response. June 24, 2009. *www.nytimes.com/packages/pdf/health/20090717_MONITOR_1.pdf*. Accessed February 1, 2012.
7. Binette TM, Cembrowski GS. Diverse influences on blood glucose measurements in the ICU setting. Chest. 2005;128(4):3084–5
8. Kanji S, Buffie J, Hutton B, Bunting PS, Singh A, McDonald K, Fergusson D, McIntyre LA, Hebert PC. Reliability of point-of-care testing for glucose measurement in critically ill adults. Crit Care Med. 2005;33(12):2778–85.
9. Aragon D. Evaluation of nursing work effort and perceptions about blood glucose testing in tight glycemic control. Am J Crit Care. 2006;15(4):370–7.
10. Juneja R, Roudebush CP, Nasraway SA, Golas AA, Jacobi J, Carroll J, Nelson D, Abad VJ, Flanders SJ. Computerized intensive insulin dosing can mitigate hypoglycemia and achieve tight glycemic control when glucose measurement is performed frequently and on time. Crit Care. 2009;13(5):R163.
11. Boyd JC, Bruns DE. Quality specifications for glucose meters: assessment by simulation modeling of errors in insulin dose. Clin Chem. 2001;47(2):209–14.
12. Krinsley JS, Meyfroidt G, van den Berghe G, Egi M, Bellomo R. The impact of premorbid diabetic status on the relationship between the three domains of glycemic control and mortality in critically ill patients. Curr Opin Clin Nutr Metab Care. 2012. Epub ahead of print.
13. Krinsley JS. Understanding glycemic control in the critically ill: 2011 update. Hosp Pract (Minneap). 2011;39(2):47–55.
14. Fahy BG, Coursin DB. An analysis: hyperglycemic intensive care patients need continuous glucose monitoring-easier said than done. J Diabetes Sci Technol. 2008;2(2):201–4.
15. Egi M, Finfer S, Bellomo R. Glycemic control in the ICU. Chest. 2011;140(1):212–20.
16. Rybka J. [Glycaemia control in critically ill patients is justified and effective]. Vnitr Lek. 2010;56(9 Suppl):977–87.
17. Heise HM, Marbach R, Koschinsky T, Gries FA. Multicomponent assay for blood substrates in human plasma by mid-infrared spectroscopy and its evaluation for clinical analysis. Appl Spectrosc. 1994;48(1): 85–95.
18. Kruse-Jarres JD, Janatsch G, Gless U, Marbach R, Heise HM. Glucose and other constituents of blood determined by ATR-FTIR-spectroscopy. Clin Chem. 1990;36(2):401–2.
19. Kim YJ, Yoon G. Prediction of glucose in whole blood by near-infrared spectroscopy: influence of wavelength region, preprocessing, and hemoglobin concentration. J Biomed Opt. 2006;11(4):041128.
20. Magarian P, Sterling B. Plasma-generating glucose monitor accuracy demonstrated in an animal model. J Diabetes Sci Technol. 2009;3(6):1411–8.
21. Jax T, Heise T, Nosek L, Gable J, Lim G, Calentine C. Automated near-continuous glucose monitoring measured in plasma using mid-infrared spectroscopy. J Diabetes Sci Technol. 2011;5(2):345–52.