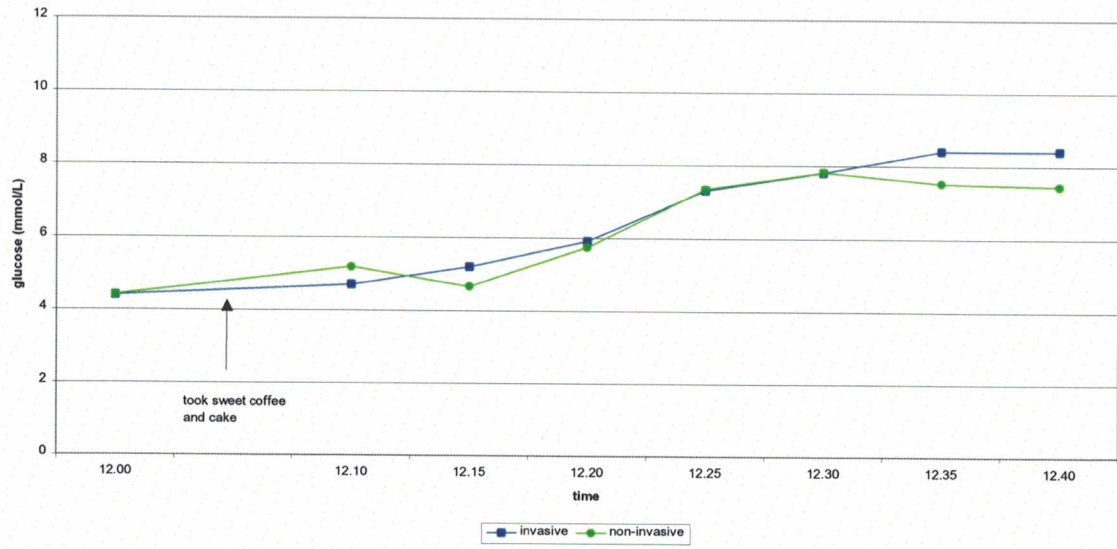


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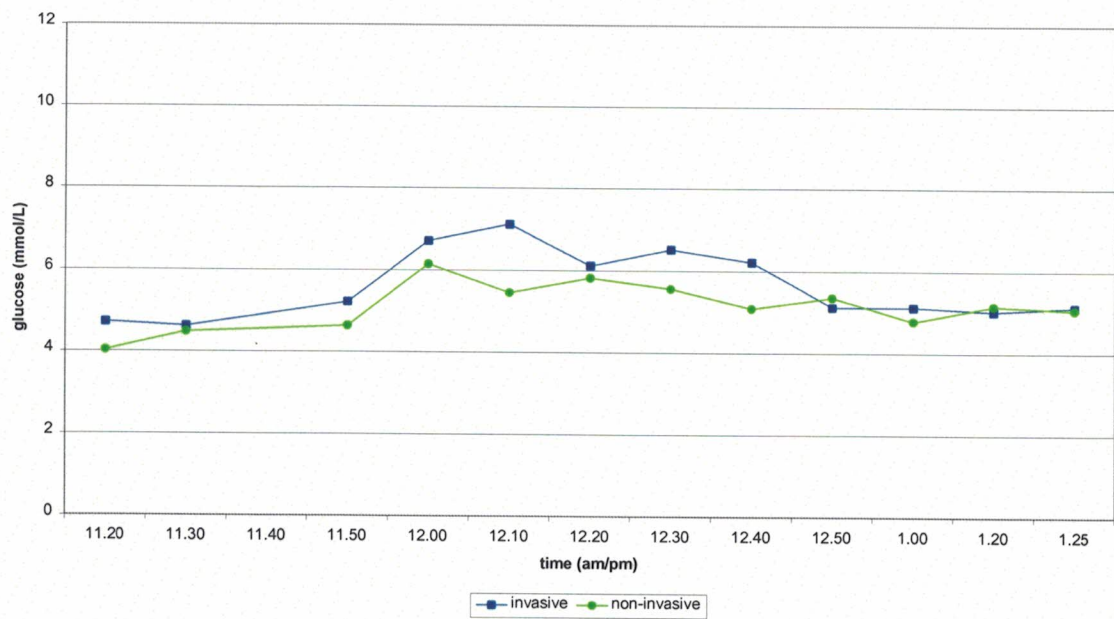
Whitland Research Limited

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Non-Diabetic Female, Day 1.



Non-Diabetic Female, Day 10.

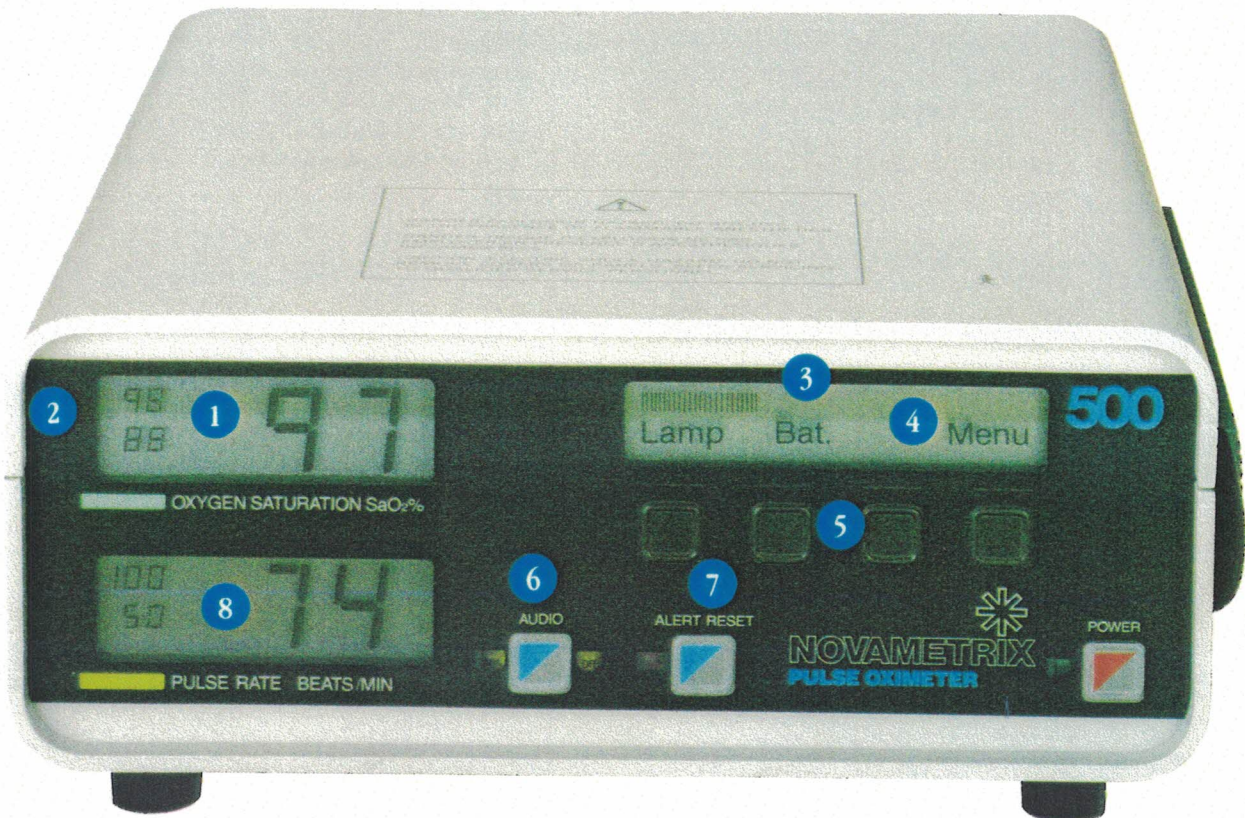


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NON-INVASIVE BLOOD GLUCOSE MONITOR

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Model 500 Pulse Oximeter



- 1 Large SaO₂ and pulse rate displays—easy to read.
- 2 Continuously visible high and low alert limits—keeps you informed of limits set.
- 3 Pulse amplitude bar graph—shows pulse signal activity.
- 4 High resolution message center—gives status indication and specific information regarding any alert condition.
- 5 Membrane keypad with tactile feedback.
- 6 *Two-minute silence* allows temporary silencing of audio alert, and AUDIO OFF disables audio alert with flashing indicator.
- 7 Alert reset—allows easy reset of all visible alerts once alert condition has been corrected.
- 8 Backlight of pulse rate, SaO₂, and message center displays for easy reading in dimly lit environments.

Other Model 500 features

- Compact size—easily fits on any anesthesia machine or cart.
- Lightweight (8 lbs.)—easily moved from one location to another.
- Low signal strength—eliminates inaccurate values when pulse signal is too low for reliable monitoring.
- Internal memory of programmed limits, audio volume and response times—even when unit is turned off all programmed information is retained.
- Digital circuitry—microprocessor-based and virtually maintenance-free.
- Audible pulse signal changes in tone—up or down—to reflect changes in SaO₂—vital information without taking eyes off patient.
- Array of ruggedly built sensors—easy application for any patient.
- Self Diagnostic—with POWER button on the unit performs a three-second self-diagnostic check and then it's ready to start monitoring.
- Service mode—provides further information for bio-medical engineer should a problem arise.

OPTICAL SPECTROSCOPY

BACKGROUND:

Pulse Oximetry

Cerebral Oxygenation

SIGNIFICANCE:

- **Optical path-lengths**
- **Arterial blood**

Pulsatile measurement

Heat

NON-INVASIVE MEASUREMENT APPROACHES

1. WAVELENGTHS 1552 and 1310nm

“...the current instrument could only be used for the monitoring of high blood glucose levels. To be of greater clinical value, lower concentrations would have to be measurable using this instrument.”

PhD Thesis 1992.

2. WAVELENGTH RANGE 5 - 11 μ m

“...optimal experimental arrangement gives a penetration depth in the skin of 10-20 μ m.”

3. WAVELENGTH RANGE 800-1050nm

- **Pulsatile approach**

Identifies arterial blood but poor signal to noise

- **Non-pulsatile approach**

Reflectance

TRANSMISSION

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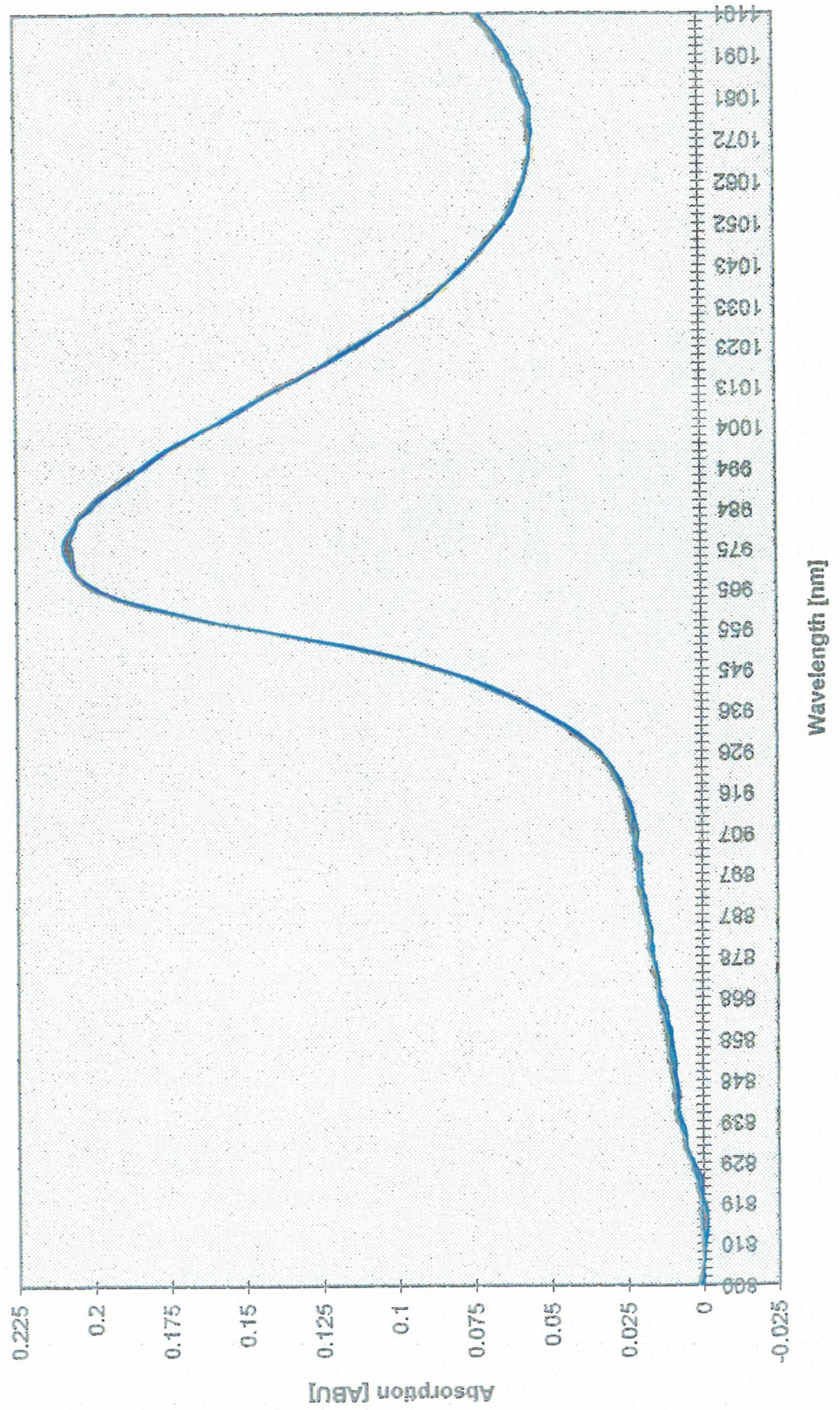
GLUCOSE IN WATER

Spectra determined in the range 800-1100nm when glucose concentration was increased from 0-40mmol/L (0-720mg/dl).

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0-40mM Glucose in Aqueous Solution



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MAJOR CONSTITUENTS IN BLOOD

Substance	Concentration (mg/dl)
Glucose	100
Water	≈ 75,000
Haemoglobin	15,000 (in red blood cell)
Albumin	4,000
Globulin	3,000
Total lipids	800
Triglycerides	300
Fibrinogen	250
HDL	200
Fatty acids	60
Urea	25
Lactic acid	20

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IN-VITRO DATA

GLUCOSE IN SALINE

No spectral change

GLUCOSE IN PLASMA

No spectral change

GLUCOSE IN HAEMOLYSED BLOOD

spectral change

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GLUCOSE IN WHOLE BLOOD

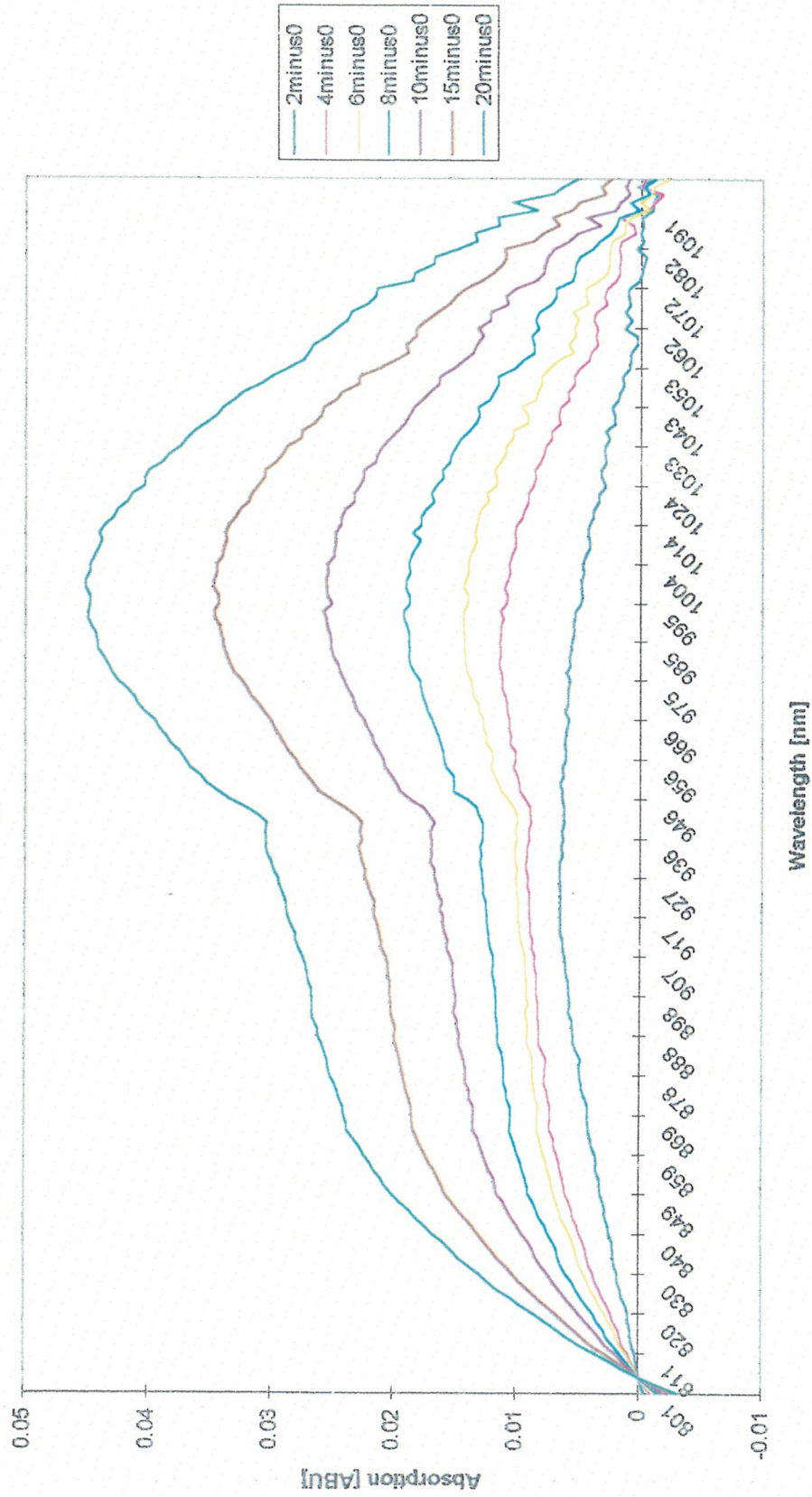
0-20 mmol/L (0-360mg/dl)

Change in haemoglobin concentration kept to a minimum.

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Difference Spectra for Increasing Glucose Concentrations with
Minimal Changes in Hb Concentration



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MANNITOL IN WHOLE BLOOD

0-40mmol/L (0-720mg/dl)

Change in haemoglobin concentration kept to a minimum.

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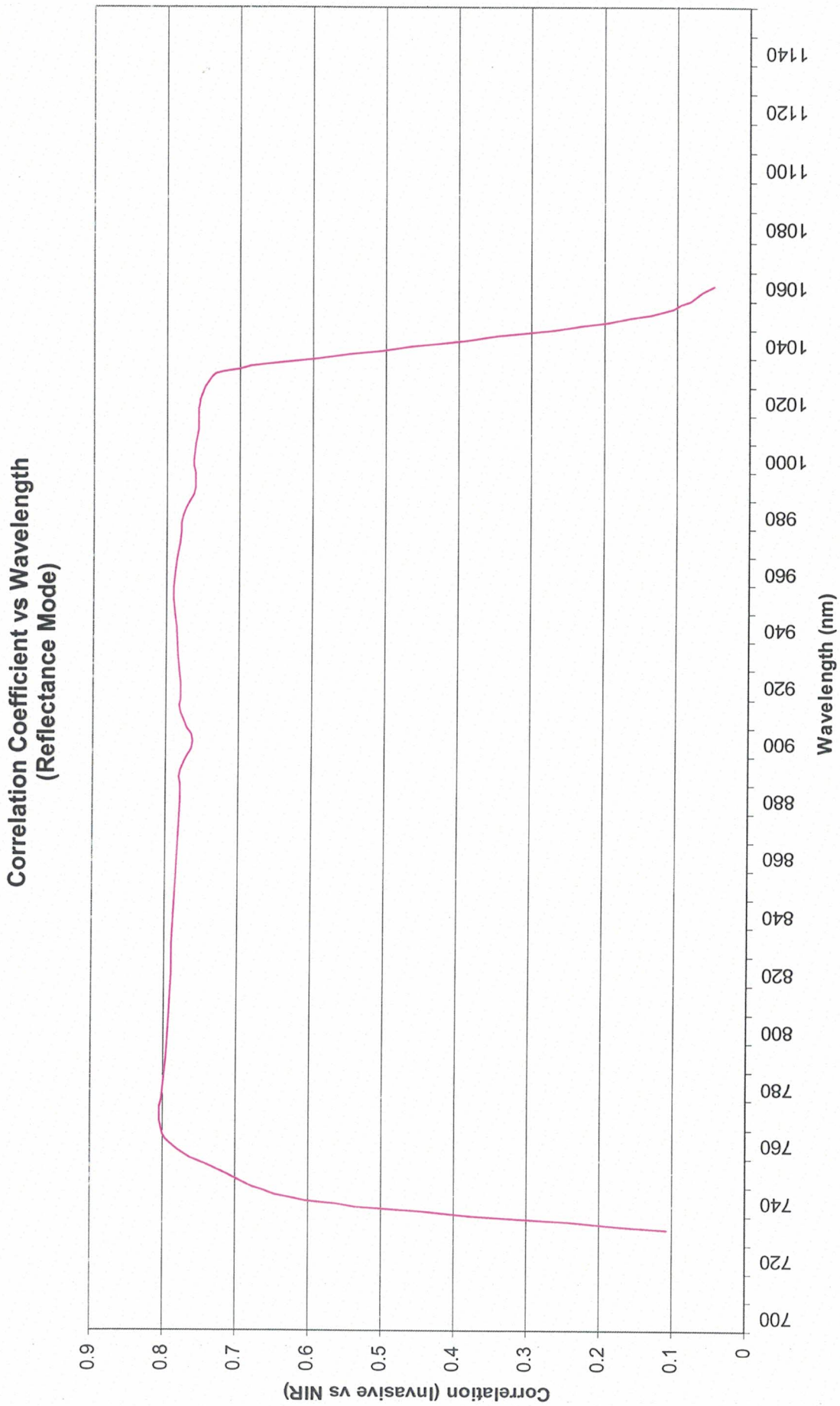
OBSERVATIONS

- A technique for measuring blood glucose concentration non-invasively should operate in the range 800-1050nm if it is to be produced as a low-cost monitor for use in the home.
- We have established that in the range 800-950nm there is a good correlation between the light transmitted through the finger and the glucose concentration.
- The most significant interferents we have identified in this spectral range are:

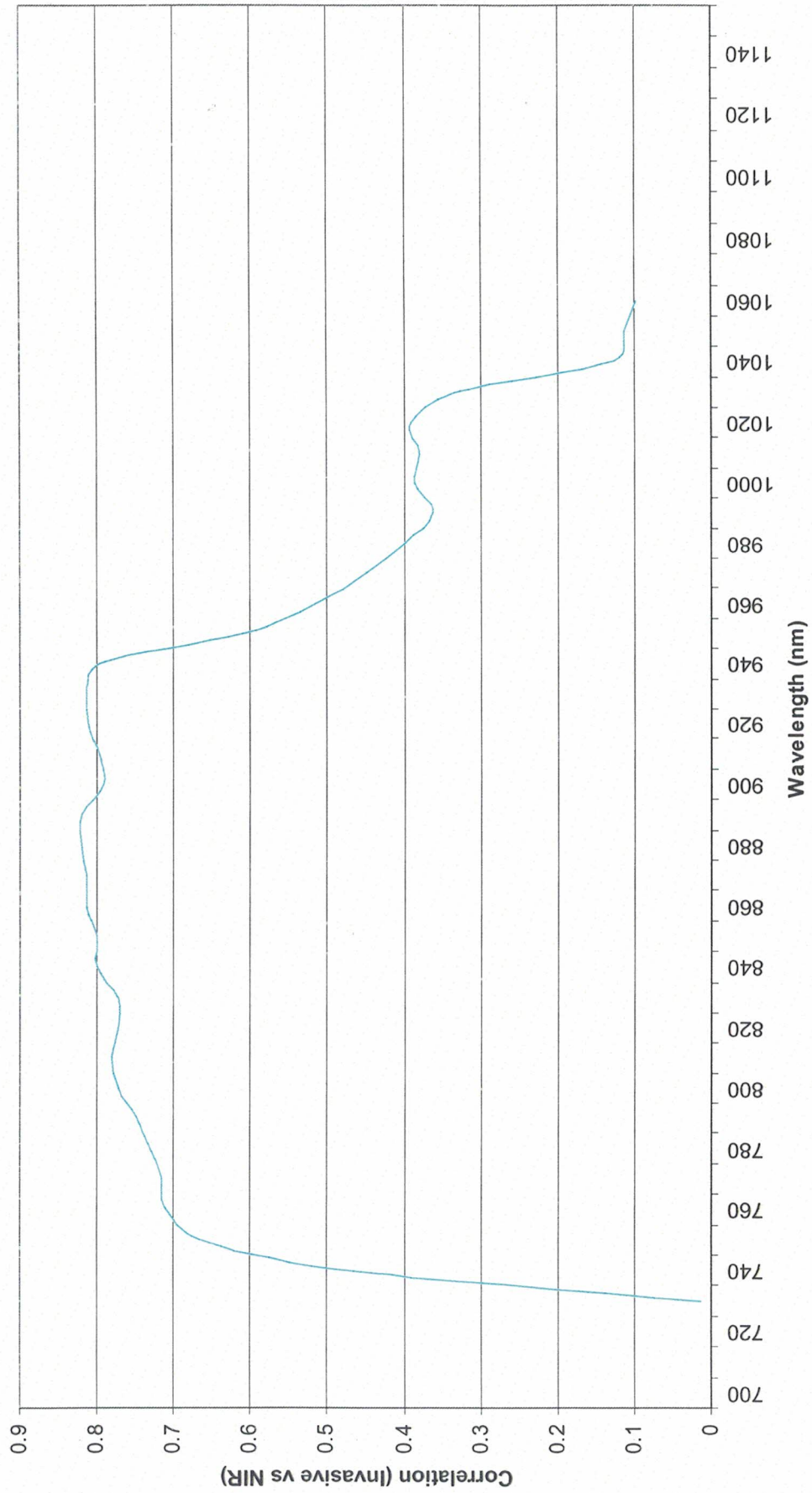
Water
Haemoglobin concentration
Oxygen saturation

- We have established that in the 820-830nm range the effects of these interferents are minimised.

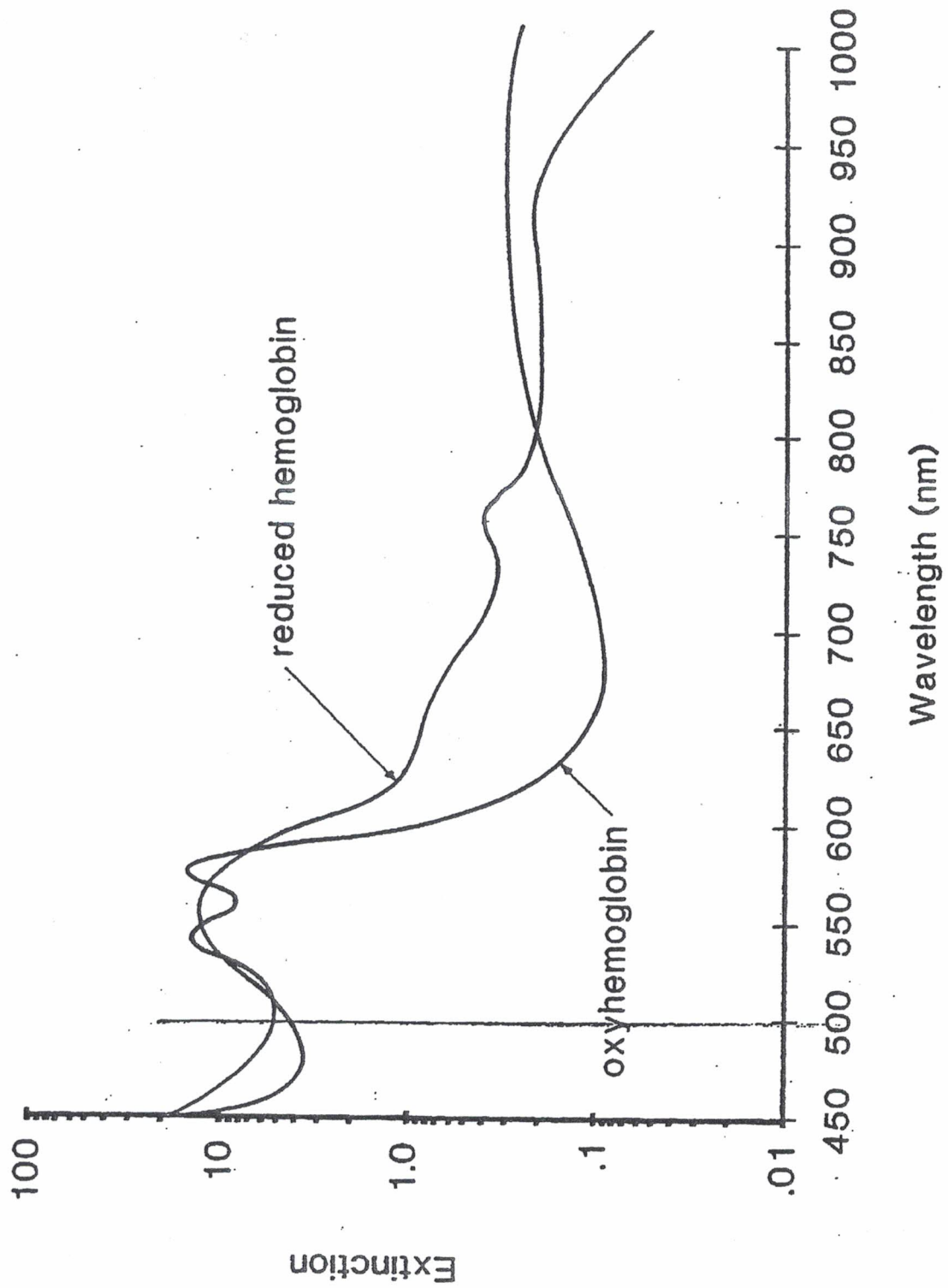
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Correlation Coefficient vs Wavelength
Showing influence of Water Peak



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Hemoglobin extinction curves.

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MEASUREMENT RANGE

Significance

- Away from the water peak at 970nm
- Effect of SO₂ changes minimised
- Effect of haemoglobin concentration changes minimised – by normalisation at 802nm
- Improved signal-to-noise

Factors above

Higher detector efficiency

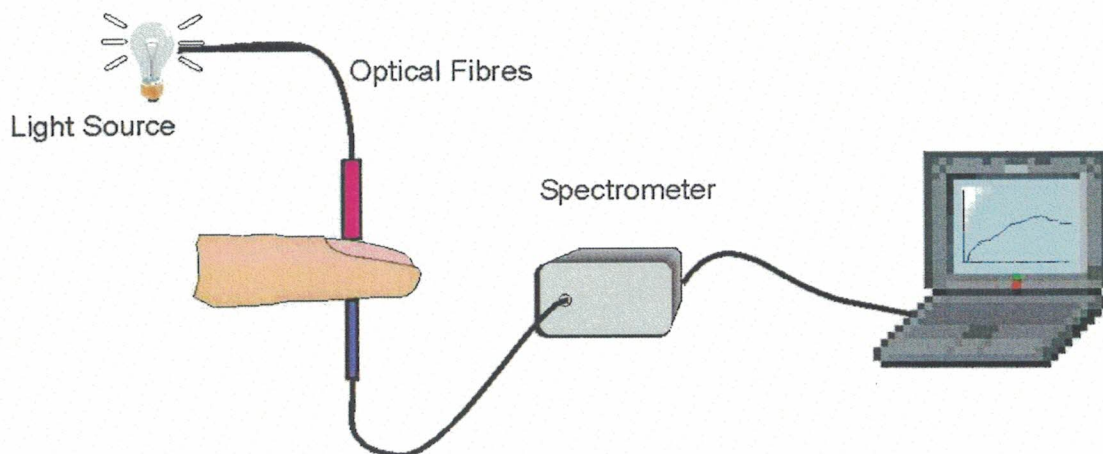
Light source characteristics

Potential

Narrow measurement range offers the possibility of an LED/Detector based monitor (no spectrometer).

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Schematic of Non-Invasive Blood Glucose Monitor



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MEASUREMENT TECHNIQUE

CALIBRATION

- Measure the transmitted light intensity through the finger and integrate in the range 820-830nm.
- Take finger-prick blood sample and analyse using a Glucotrend Blood Glucose Analyser (Boehringer Mannheim).
- Repeat these measurements at five or ten minute intervals for a period of 90-120 minutes.
- Plot integral above against invasive blood glucose concentration and determine two required patient-specific parameters.

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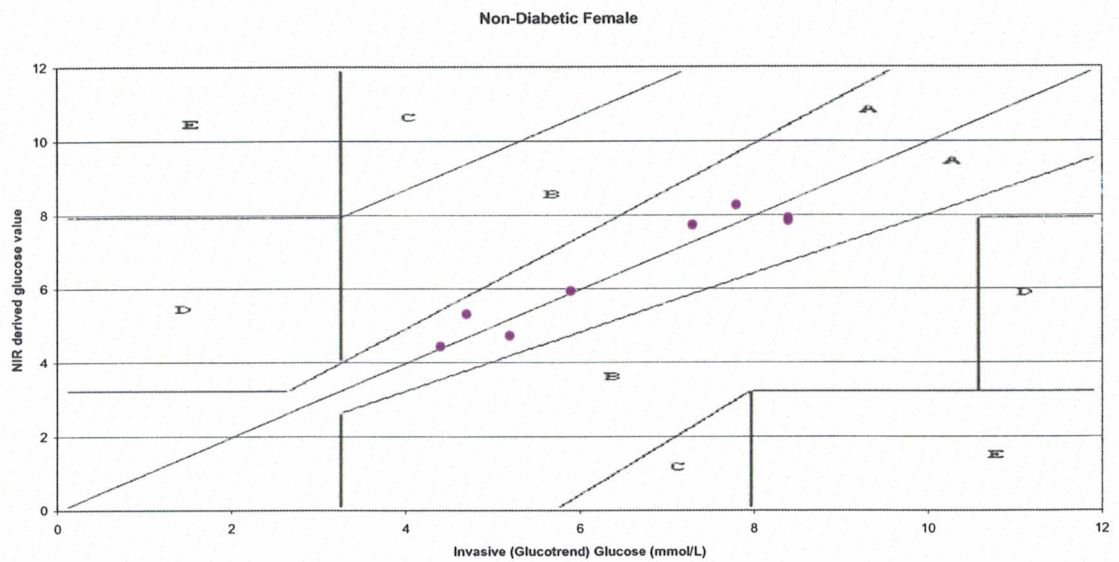
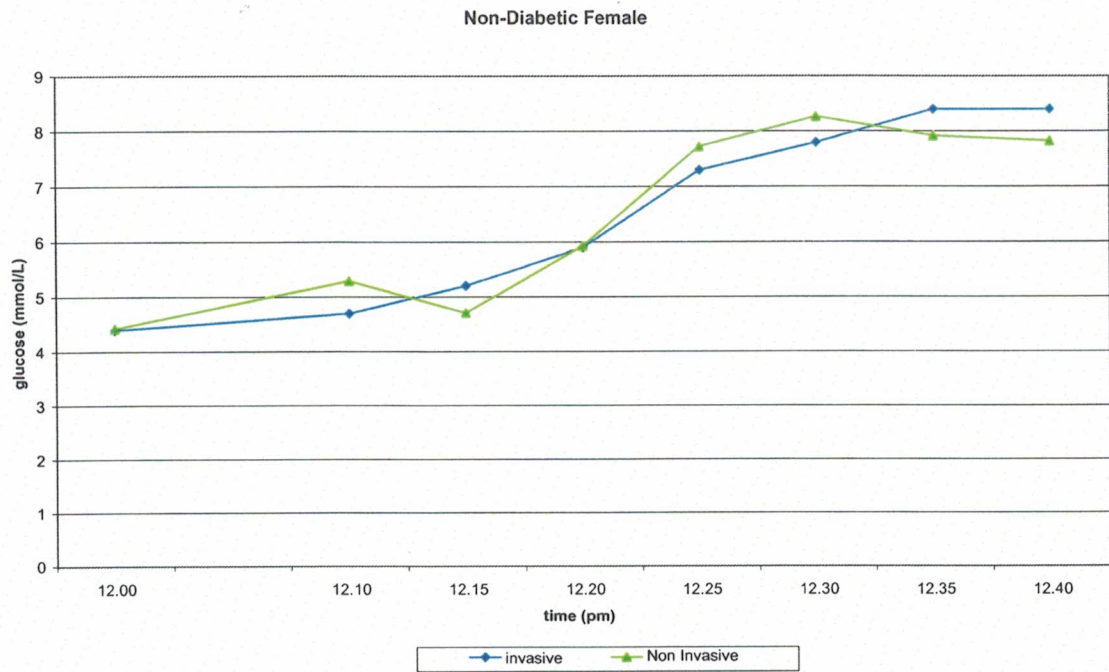
MEASUREMENT TECHNIQUE

PREDICTION

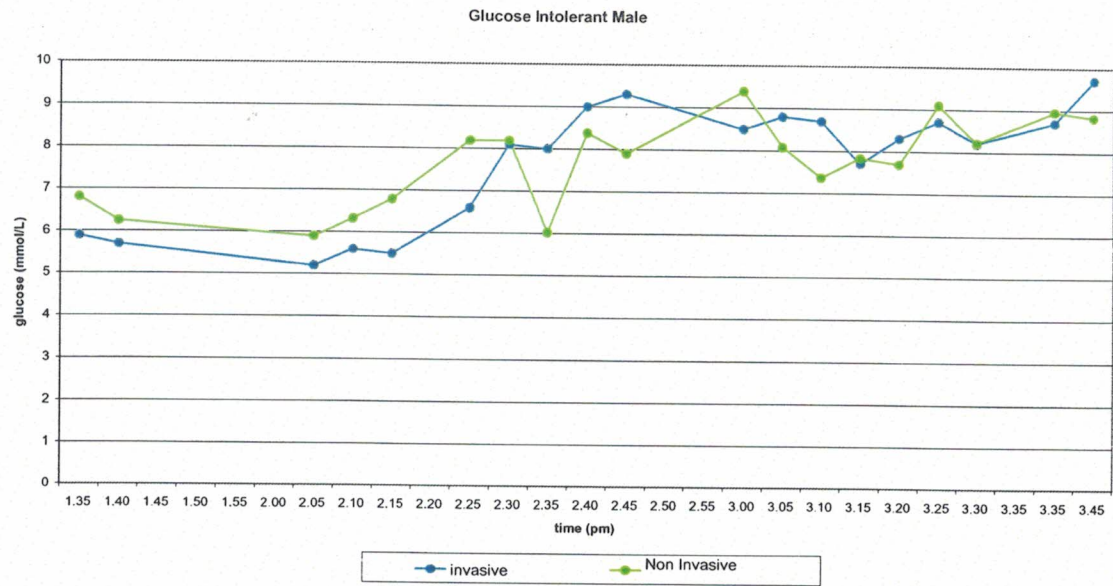
- Enter two previously determined parameters into monitor.
- Volunteer inserts finger in sensor
- Monitor predicts blood glucose concentration

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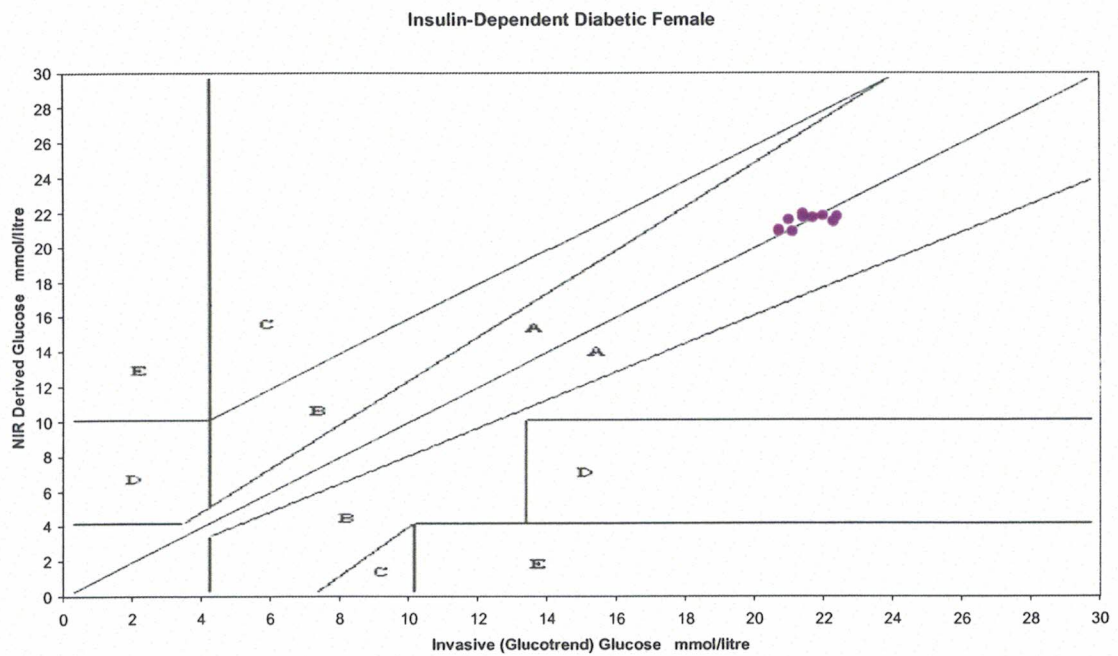
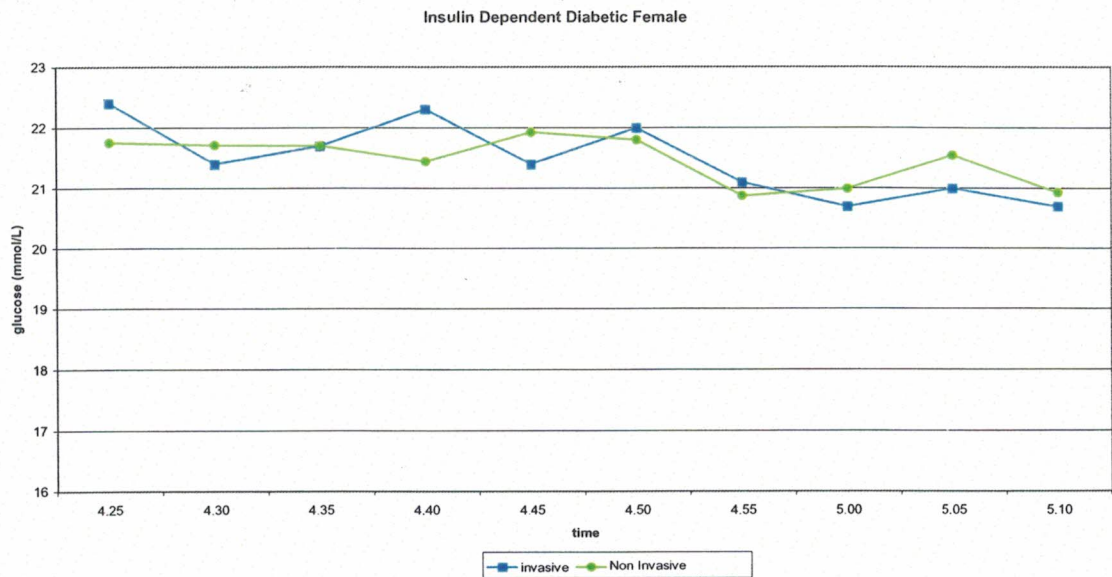
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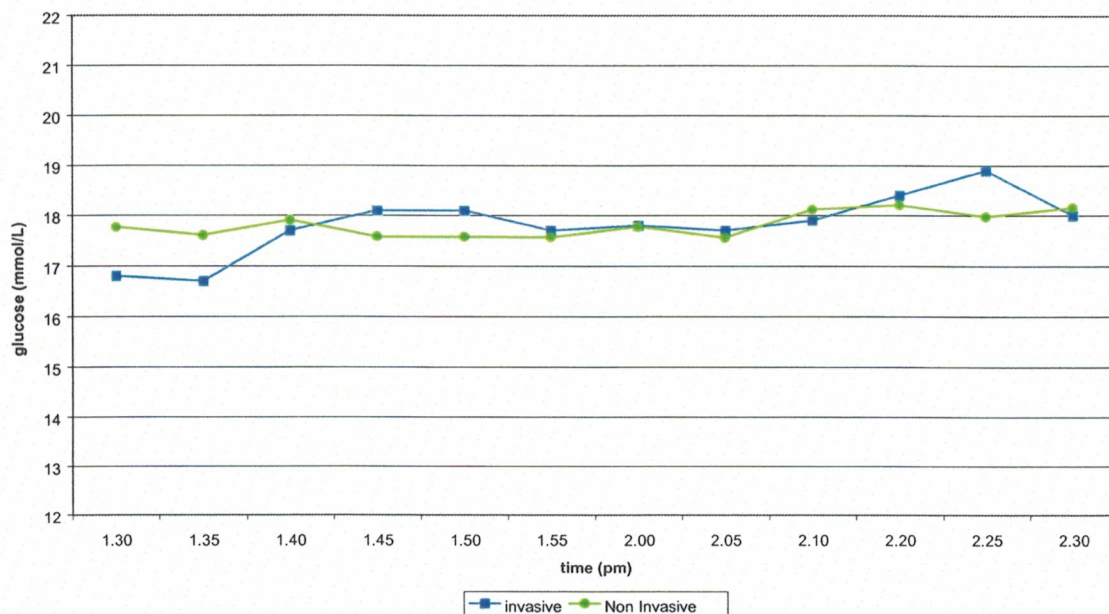
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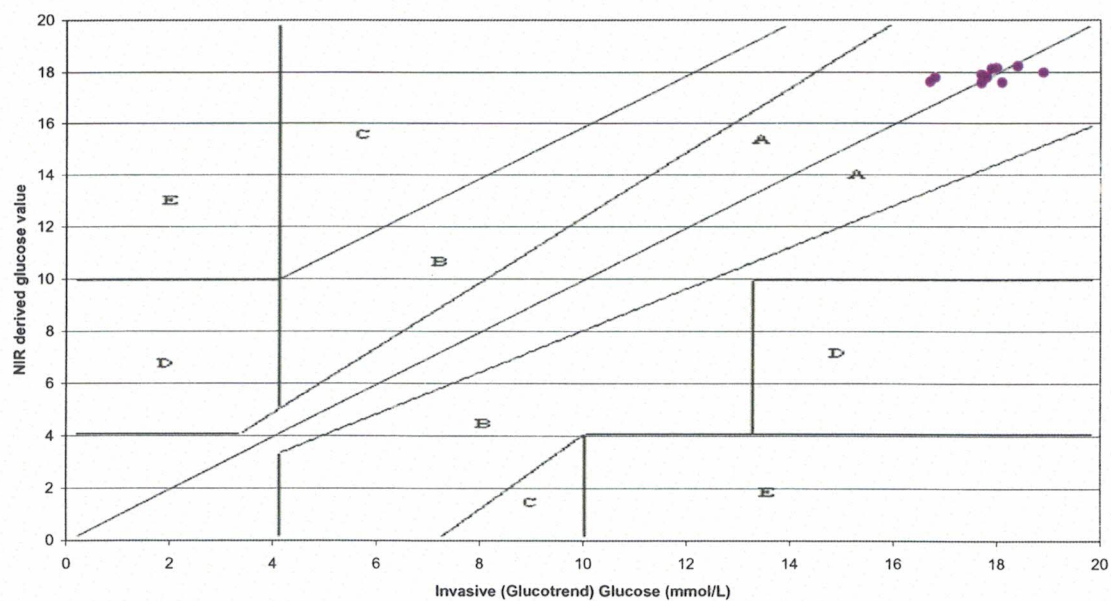
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Non-Insulin Dependent Diabetic Male



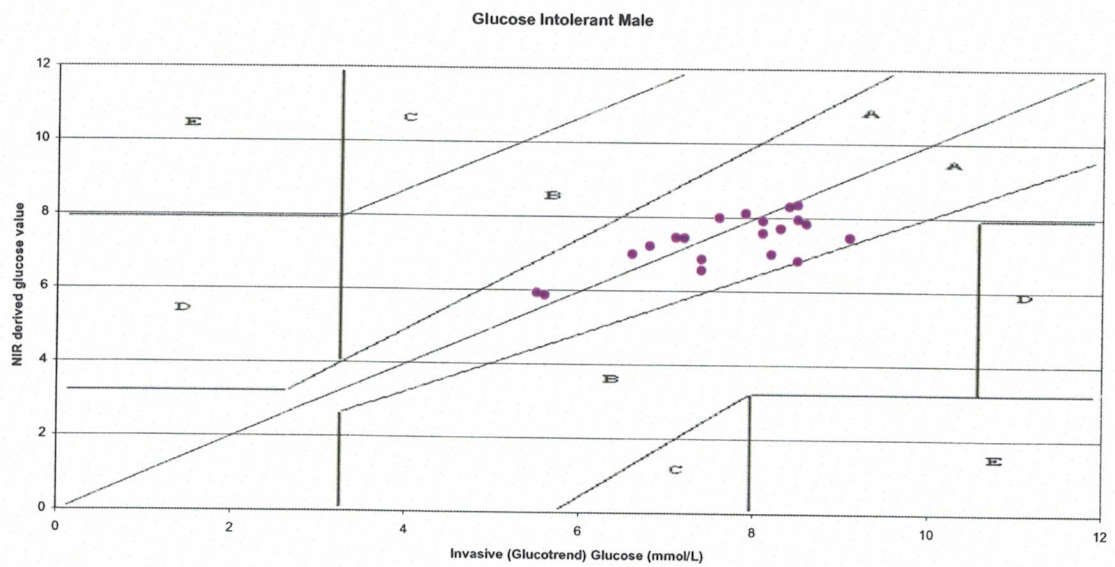
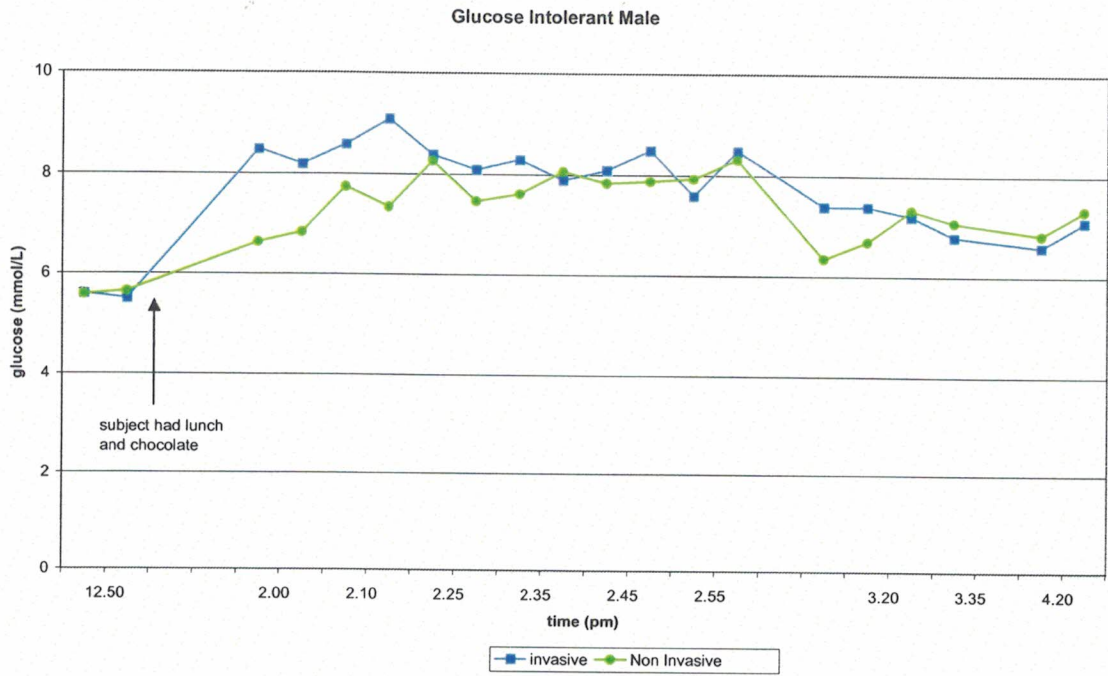
Non-Insulin Dependant Diabetic Male



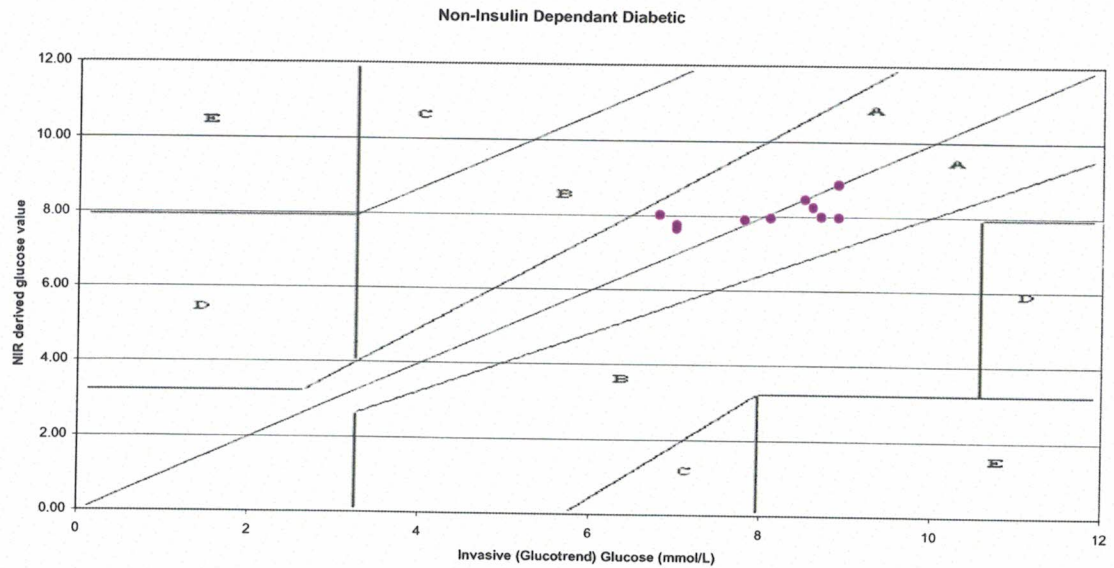
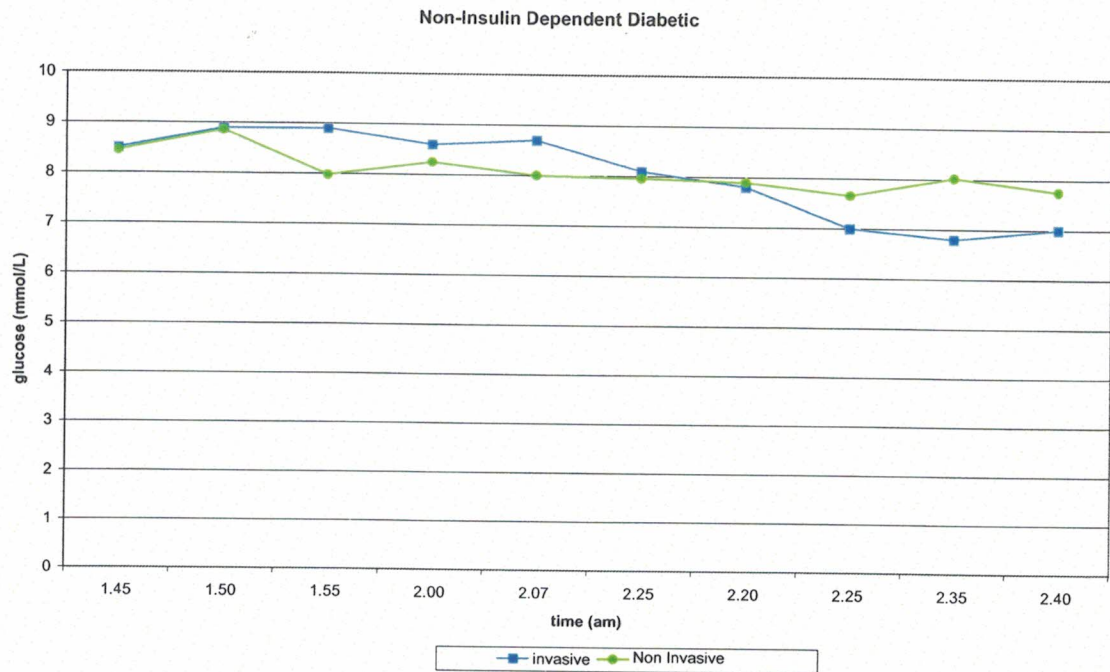
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SIMPLIFIED CALIBRATION

- Assume first calibration parameter is constant for everyone.
- Determine the second parameter from the first blood sample.
- Predict blood glucose concentration using this one-point calibration procedure.

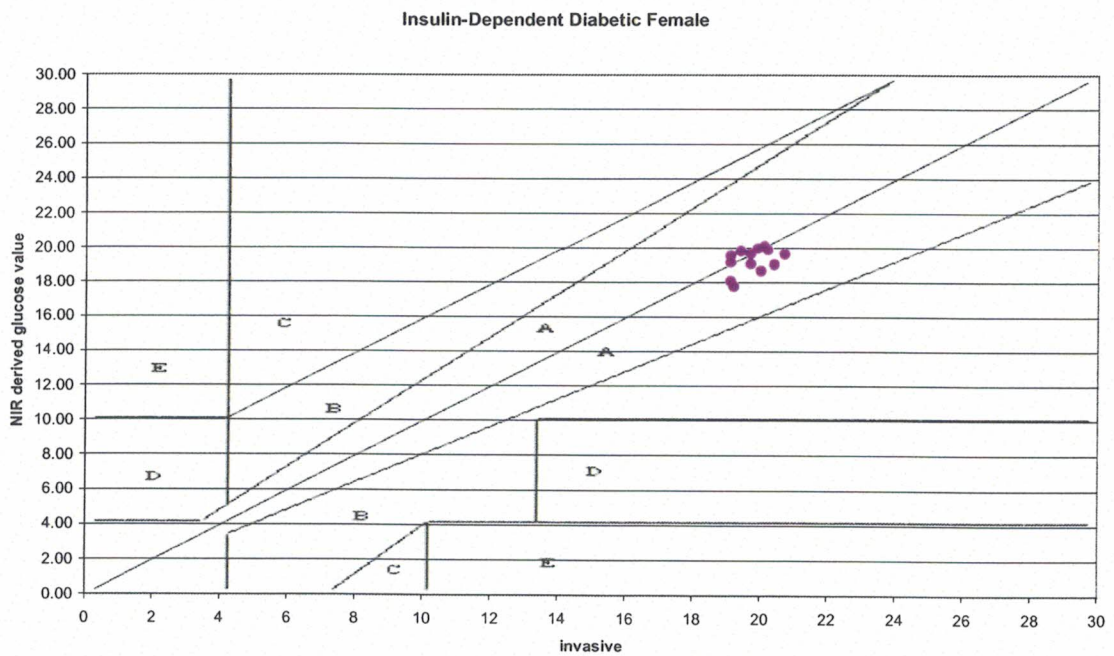
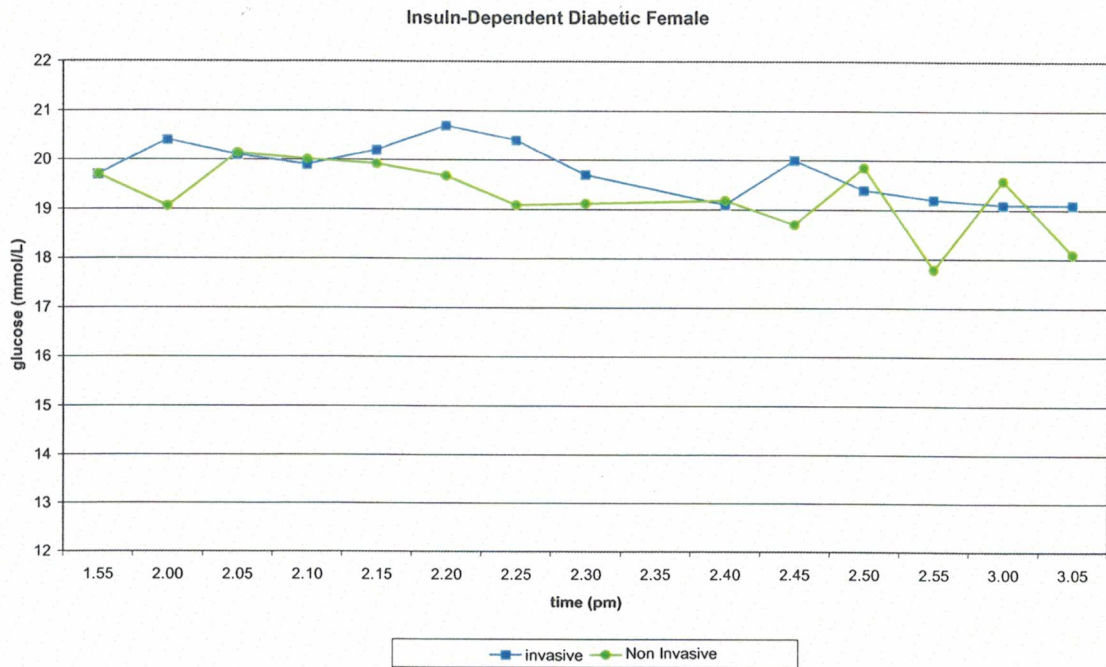


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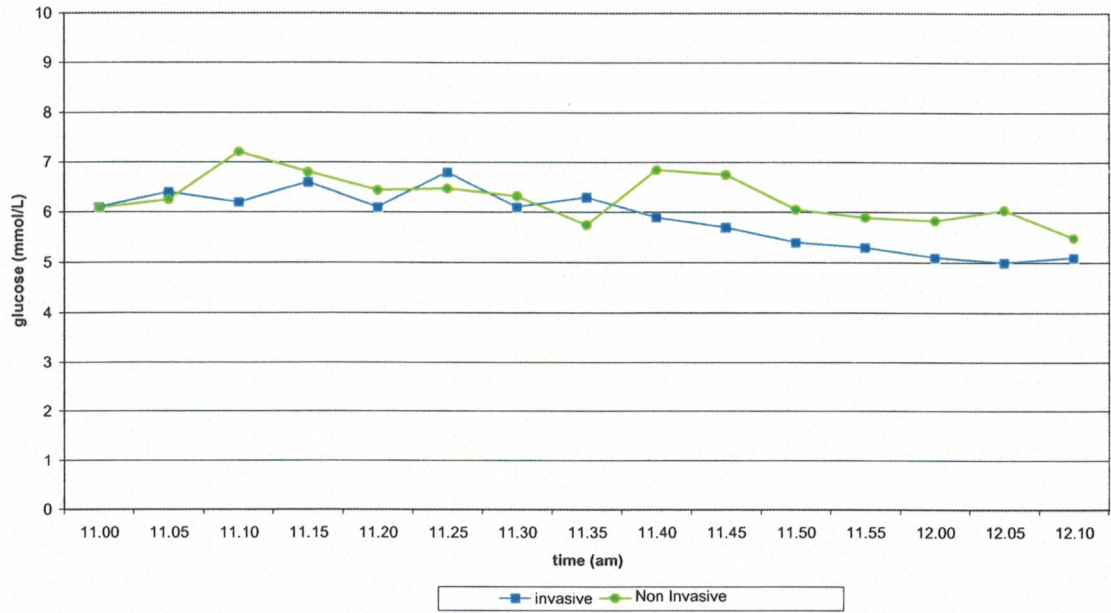
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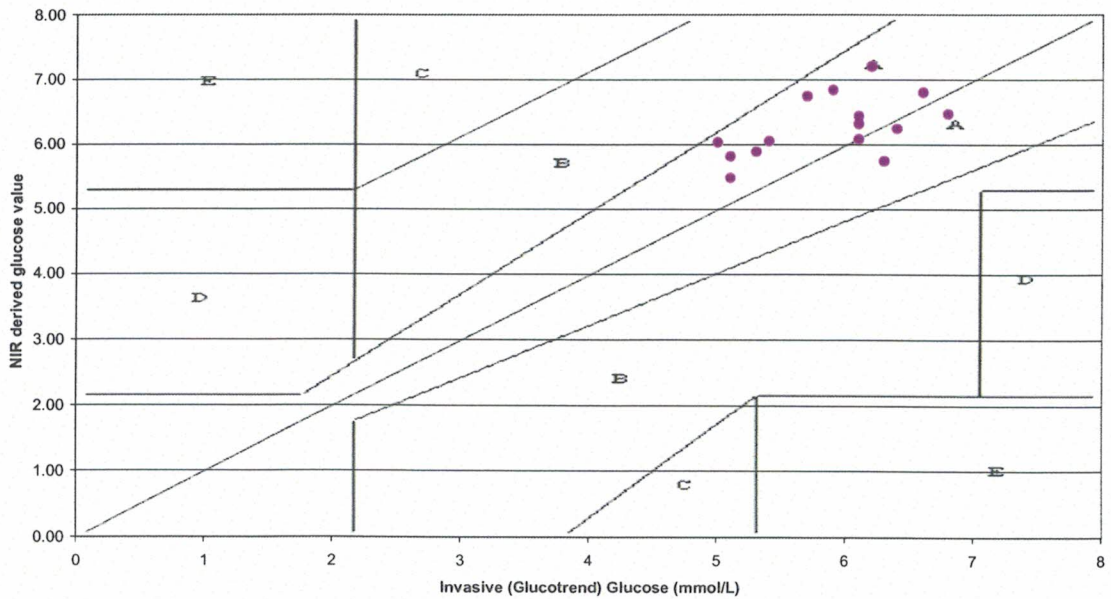
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Insulin-Dependent Diabetic Female (2)



Insulin-Dependent Diabetic Female (2)



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ARTERIO-VENOUS GLUCOSE DIFFERENCE

- Glucose in peripheral venous blood usually 3.9 - 6.1mmol/L (70-110mg/dl).
- Glucose in arterial blood usually 0.8-1.6mmol/L higher (15-30mg/dl).
- The difference is strongly dependent on glucose utilisation and blood flow.
- A-V glucose difference depends on nutritional and metabolic activity. Maximum difference of 2.5mmol/L reported (45mg/dl).

H.M. Heise *Biosensors in the Body* (1997)

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