Intraperitoneal glucose measuring using amperometric glucose sensors and intraperitoneal fluid samples in an animal model

Marte Kierulf Åm[1,2,6], Anders Fougner[1,3,6], Patrick Bösch[1,3], Ilze Dirnena-Fusini[1,2], Konstanze Kölle[1,3,6], Øyvind Stavdahl[1,3], Reinold Ellingsen[1,4], Dag Roar Hjelme[1,4], Sverre Christiansen[1,2,7] and Sven Magnus Carlsen[1,2,5,7]

marte.k.am@ntnu.no anders.fougner@ntnu.no patrick.c.bosch@ntnu.no ilze.dirnena-fusini@ntnu.no konstanze.koelle@ntnu.no oyvind.stavdahl@ntnu.no reinold.ellingsen@ntnu.no dag.hjelme@ntnu.no sverre.christiansen@ntnu.no sven.carlsen@ntnu.no

[1]Artificial Pancreas Trondheim – The APT research group (www.apt-norway.com)
[2]Department of Cancer Research and Molecular Medicine
[3]Department of Engineering Cybernetics
[4]Department of Electronic Systems
[5]Unit for Applied Clinical Research, Faculty of Medicine

Norwegian University of Science and Technology (NTNU), Trondheim, Norway

[6]Helse Midt-Norge – The Central Norway Regional Health Authority, Norway
[7]St Olav's University Hospital, Trondheim, Norway

Motivation

Subcutaneous (SC) glucose sensing:

Limited by slow response and poor robustness towards local temperature effects, mechanical pressure, foreign body reaction etc.

Intraperitoneal (IP) glucose sensing:

Faster dynamics than SC glucose sensing [1,2] and less prone to local tissue effects such as temperature changes, mechanical pressure, etc.

- Explore a possible difference in the glucose homeostasis at different locations in the peritoneal space.
- Investigate if an adapted commercially available glucose sensor can be used as a reference sensor for testing a long term IP glucose sensor.

Methods

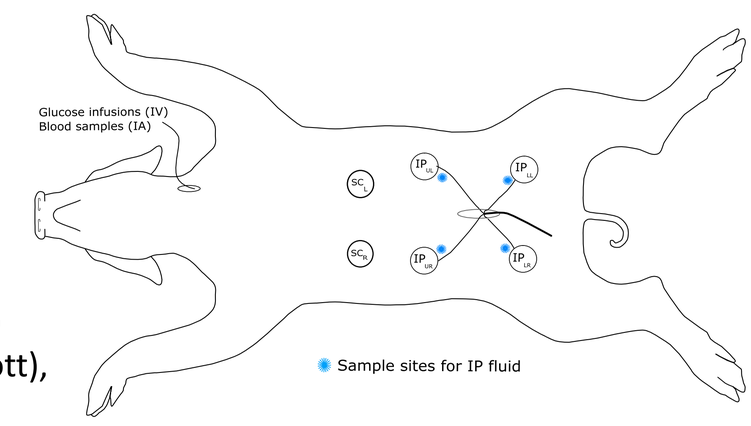
Animal experiments:

- 3 anaesthetized, non-diabetic farm pigs.
- Intravenous glucose challenges.

Sensors used:

- **Intraperitoneal (IP):**
  One amperometric enzyme-based (glucose oxidase) glucose sensor (adapted FreeStyle Libre Flash, Abbott), was inserted in each quadrant of the abdomen through a common site in the abdominal wall (figure).
- **Subcutaneous (SC):**
  Adapted FreeStyle Libre Flash (figure).
- **Arterial blood and peritoneal fluid:**
  Analysed on a blood gas analyser (BGA) (Radiometer ABL 725) for reference.

Sensor placement and sampling sites:



Data:

Glucose values presented in this poster are values measured by the pre-calibrated FreeStyle Libre glucose sensors, but single outlier values have been removed. No further calibration is performed.
For technical details of the sensor set up, please see separate poster – Paper poster board no. 50.

Results

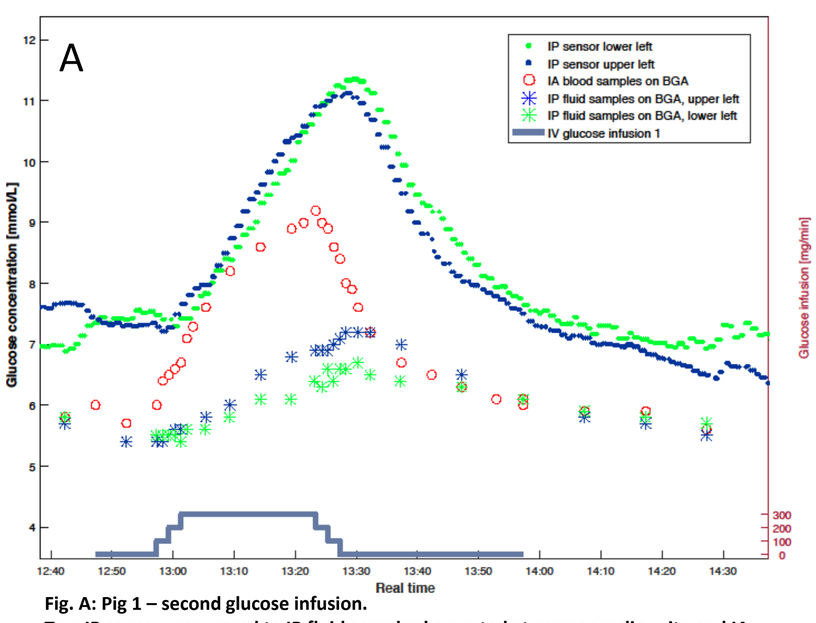


Fig. A: Pig 1 – second glucose infusion.
Two IP sensors compared to IP fluid samples harvested at corresponding site and IA samples.

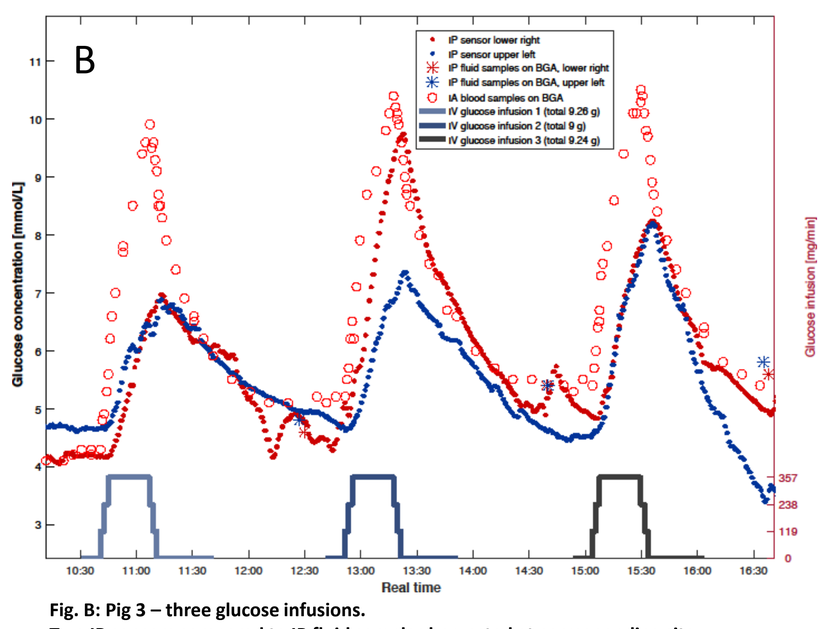


Fig. B: Pig 3 – three glucose infusions.
Two IP sensors compared to IP fluid samples harvested at corresponding site and IA samples during one day experiment

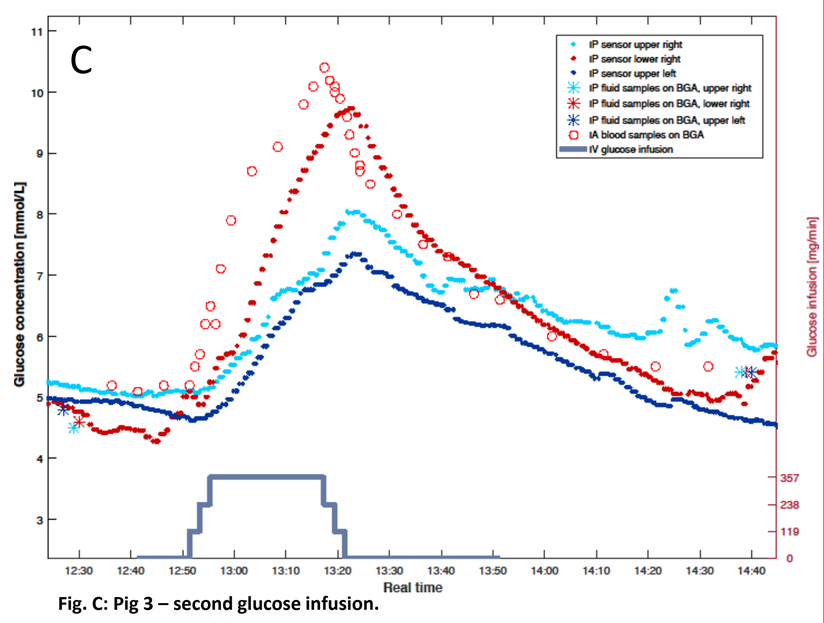


Fig. C: Pig 3 – second glucose infusion.
Detailed section of figure B. Three IP sensors compared to IA samples.

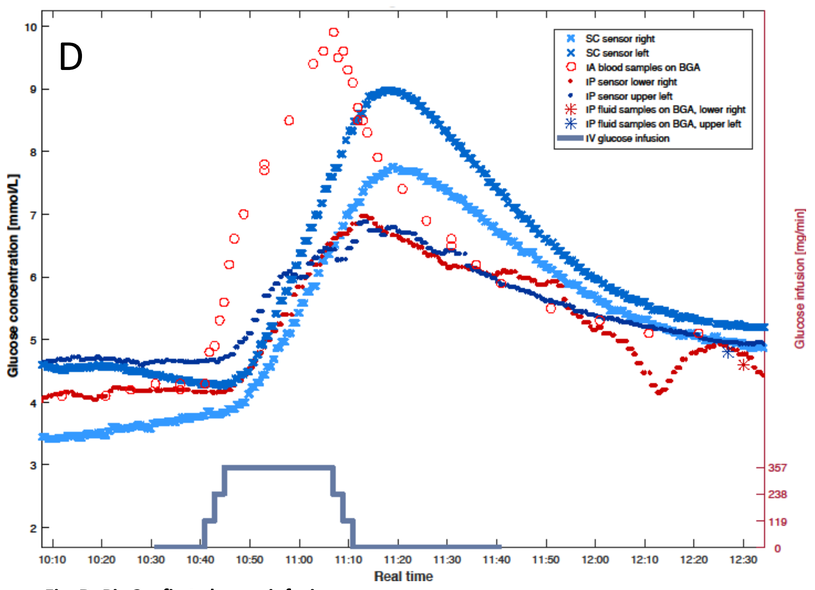


Fig. D: Pig 3 – first glucose infusion.
IP sensors compared to IA samples and SC sensors.

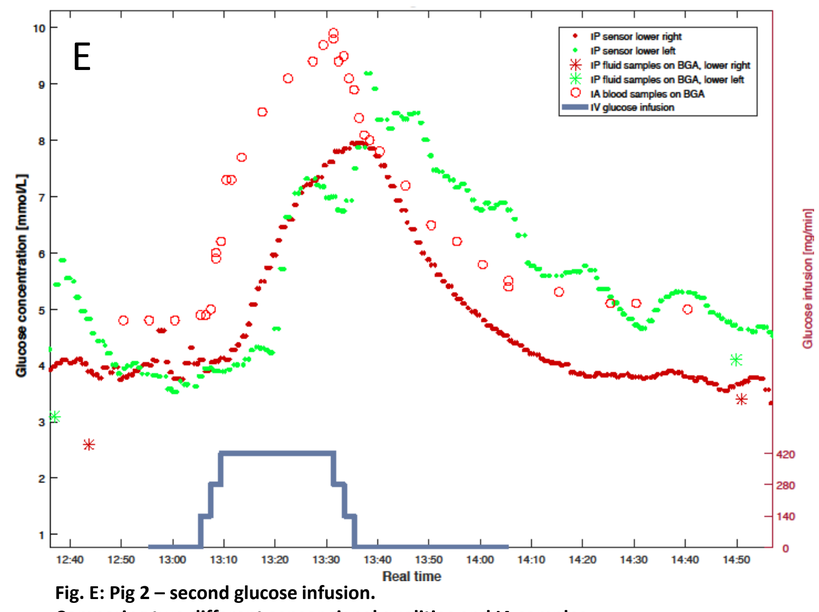


Fig. E: Pig 2 – second glucose infusion.
Comparing two different sensor signal qualities and IA samples.

Summary:

- IP sensors showed rapid response to decreasing glucose values (figs. B, C and E).
- IP sensors observed with shorter time to peak compared to SC sensors (fig. D).
- Great variation in signal quality (fig. E).
- Frequent IP samples in experiment no. 1 (fig. A) showed glucose rising faster and having a higher peak in the upper left part compared to the lower left part of the abdomen.
  This was not confirmed by corresponding sensor signals (fig. A).

Discussion

- IP glucose sensing enables fast detection of changes in blood glucose, and particularly the fast detection of descending blood glucose values is promising for a double IP artificial pancreas.
- The IP sensors need additional calibration, possible also the SC sensors, in order to give reliable glucose values under these experimental conditions.
- IP glucose sensing using amperometric enzyme-based sensors seems slower than previously shown with optical interferometric phenylboronic acid based sensor technology [1].
- There can be a possible difference in the glucose dynamics at different locations in the peritoneal space. This will be examined in upcoming animal experiments.

References

[1] Fougner, A.L., et al., Intraperitoneal glucose sensing is sometimes surprisingly rapid. Modeling, Identification and Control, 2016. 37(2): p. 121- 131.

[2] Burnett, D.R., et al., Glucose sensing in the peritoneal space offers faster kinetics than sensing in the subcutaneous space. Diabetes, 2014. 63(7): p. 2498-24505.