Single-Port Artificial Pancreas
(or is a single skin perforation enough?)

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Little Arrows but Big Issues?
Where to Measure Glucose and to Deliver Insulin with AP-Systems?

- **Glucose measurement**
  - Intravenous (= blood)
  - Dermal (= intradermal interstitial fluid)
  - Subcutaneous (= interstitial fluid in adipose tissue) (most glucose sensors)
  - “Skin” (= mixture of compartments)

- **Insulin delivery**
  - Intravenous
  - Intraperitoneal
  - Subcutaneous
  - ARIA: Inhaled, Nasal, Dermal etc.
Critical Aspects of Glucose Measurement and Insulin Delivery

Glucose measurement
- Intravenous – risky, not long term (?)
- Dermal – time lags, freq. measurements?
- Subcutaneous – limited risks, long term?
- “Skin” – not available yet

Insulin delivery
- Intravenous – risky, not long term
- Intraperitoneal – limited risks, absorption
- Subcutaneous – limited risks, absorption
- Alternative routes of insulin application (ARIA) practicability?
Reasons and Issues with the sc-sc Approach

- Most AP-systems employ a two-port approach:
  - Subcutaneous glucose measurement
  - Subcutaneous insulin application

- Reasons:
  - Availability
  - Mature technologies
  - Relatively low risk for the patients
  - Relatively ease of use

- Patients have to carry around two devices all the time: CGM system plus insulin pump

- Patients don’t like this! Major reason for not using CGM systems in clinical trials/reality
How to Reduce the Hurdle?

- Single-port approach: Glucose sensing at the site of insulin delivery
Glucose Sensing at the Site of Insulin Delivery?

- Key question: Has the insulin infusion an impact on the measured glucose levels?
- Local drop in glucose levels in ISF by infused insulin?
- Deviation of the glucose levels measured in the interstitial fluid from plasma?
- Clinical experiments conducted by the University of Graz showed that a single-port approach is feasible
“we found that within 60 min after exposing adipose tissue of healthy humans to a standard 100 units/ml insulin preparation, insulin’s effect on the tissue glucose concentration saturates and a stable ratio between the tissue and plasma glucose concentration is attained.”

Lindpointer et al.  
Diabetes Care 2010b

- Insertion of a special indwelling catheter into subcutaneous adipose tissue of 10 patients with type 1 diabetes
- Using the catheter for simultaneous insulin delivery and glucose sampling
- Glucose concentration observed at the tissue site of insulin delivery correlates well with that seen in plasma.
Clinical Study with Single-port System

- Insulin Delivery
- Plasma Glucose
- Tissue Glucose

Oral Glucose (75g)

Glucose (mmol/l)

Insulin Delivery (U/h)

Time (h)

Subject 08
Single-port AP: Is this technically feasible?

Not experimental set-up but a practically usable product is required

No international activities to develop the necessary technology, but two different innovative approaches are followed within the EU-project AP@home

Aim is to have at least one functional single-port AP system at the end of the project
AP@home

Bringing the artificial pancreas home

EU Project, funded by 10.5 Million Euro
Started February 1st, 2010
Official Coordinator, L. Heinemann, Profil
AP@home consortium
Bringing the artificial pancreas home

Major tasks

- ICT Development
  - Algorithm
  - User Communication
  - TeleResponse
- Two-Port Prototype
- Prototype I
- Prototype II

Integration and Validation
Pre-Clinic → Clinic → Home

Dissemination & Exploitation
WP 2.1 Development of New Single-Port Artificial Pancreas Systems

Partners:

- P4 (GRZ), Medical University of Graz, Austria
- P8 (LAU), EPFL, Switzerland
- P10 (SEN), Sensile Medical AG, Switzerland
- P11 (STM), ST Microelectronics, Italy
- P13 (4A), 4a engineering GmbH, Austria
Single-Port Artificial Pancreas Systems

Two complementary approaches

1. Single-port AP based on insulin cannula with integrated glucose sensor
   • Combining off-the-shelf glucose sensor with insulin cannula
   • Two sensor placement concepts: ex-vivo and in-vivo
   • Advantage: proven sensing technology
   • Challenge: assembly of sensor and cannula

1. Single-port AP based on glucose-responsive membrane
   • Micro-fluidic approach: measure the flow of insulin through a glucose-responsive porous cannula
   • Adapt established glucose-responsive hydrogel formulations to porous cannula
   • Advantage: tailor responsivity to detection of hypoglycemia
   • Challenge: new measurement principle
TA 2.1.3: Insulin Cannula with Integrated Glucose Sensor
GRZ/4A Approach

- Two Sensor Placement Concepts
  - ex vivo:
  - in vivo:
TA 2.1.3: Insulin Cannula with Integrated Glucose Sensor
GRZ/4A Approach

- Cannulas with slanted insertion
TA 2.1.3: Insulin Cannula with Integrated Glucose Sensor

GRZ/4A Approach

- Cannulas with straight insertion
TA 2.1.3: Insulin Cannula with Integrated Glucose Sensor

GRZ/4A Approach

- Sensors from Dexcom
TA 2.1.3: Insulin Cannula with Integrated Glucose Sensor

GRZ/4A Approach

- Sensors from Abbott
TA 2.1.3: Insulin Cannula with Integrated Glucose Sensor
GRZ/4A Approach

- Sensors from Medtronic
SEN/LAU Approach

- **Principle:** monitor changes in the flow of insulin administration (pulsed) through a glucose-responsive porous cannula

- **Combine insulin administration (basal rate 0.25-1 IU/hr) with measurement of glucose concentration**

- **Core element:** An hydrogel trapped in the nanopores of a support membrane swells and shrinks responding to glucose variations.
Single-Port AP Based on Glucose-Responsive Cannula
SEN/LAU Approach

Glucose-responsive cannula

Glucose responsive hydrogel

Pores
Single-Port AP Based on Glucose-Responsive Cannula
SEN/LAU Approach

\[ \Delta V(t) \sim 250-500 \text{ nL} \]

Pump profile
3-6 min

\[ \Delta P(t) \sim 5-100 \text{ mBar} \]

Sensor response

High glucose

Low glucose
The Sensile Artificial Pancreas Concept
The Sensile Artificial Pancreas
Possible Embodiment

Artificial Pancreas

- Dialysis & Delivery Needle
- Micro Pump
- Nanoliter Control Device
- Insulin
Two-port approach for AP systems is the more widely used, patients don’t like that many systems are attached to them.

Single-port approach is an attractive and possible alternative!

Significant reduction barriers towards practical usage of an AP system.

Until now not studied in clinical studies but animal studies are on their way.

Recent developments are very promising.

Clinical data in 1-2 years will proof the validity of my statement.