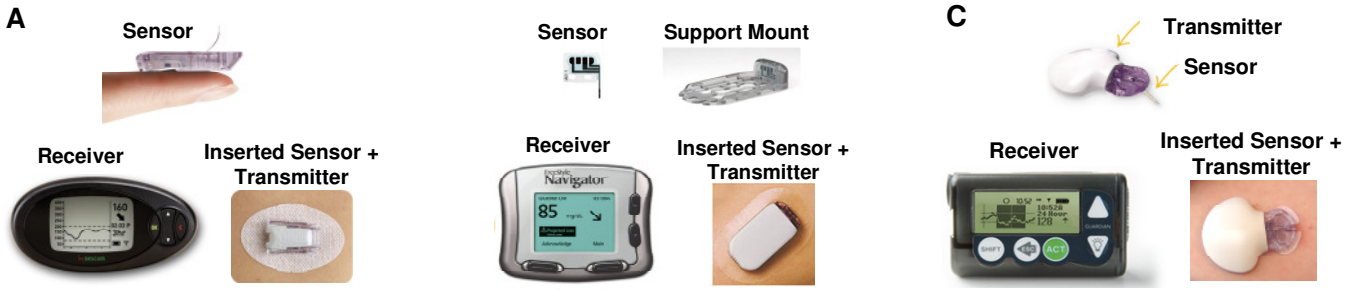
1. Publishable summary

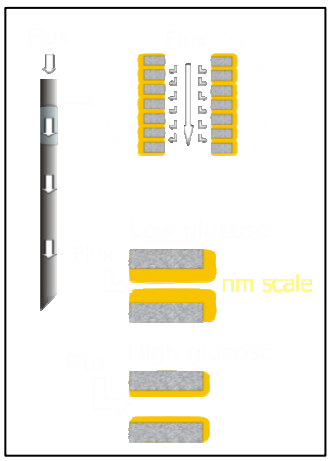
1.1 Description of the work performed

The major aim of the AP@home project is developing an Artificial Pancreas (AP) for "at home" use. This should allow patients with diabetes to live a close to normal live. One track of our project is focussed on developing and testing an AP system which uses an off-the-shelf continuous glucose monitoring (CGM) system and insulin pump (two-port system). In parallel we are developing in the second track a single-port AP system. This novel approach shall allow to monitor glucose and infuse insulin via the same port.
Our project has made good progress in its second year with respect to its aims and we performed several clinical studies:

In a small clinical-experimental study, patients with type 1 diabetes were asked to carry two Dexcom CGM systems. One of the systems was calibrated according to the manufacturers instruction (every 12 h), the other was calibrated only once after 48 h.
Two other clinical studies have been performed (one is not completely finished at all sites): in one the performance of different CGM systems was evaluated in a head-to-head comparison and in the other the performance of a conventional insulin pump was evaluated in comparison to that of the patch-pump used in the large AP study mentioned above.
In order to enable usage of an AP system under home conditions high safety requirements have to be fulfilled, e.g. in case the system signals an alarm (too low glycaemia for example) this information shall be transmitted to a physician via a Telemedicine approach.

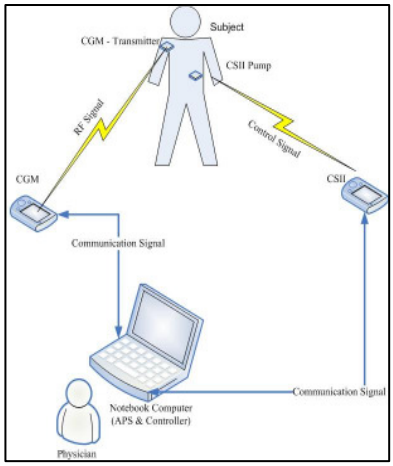


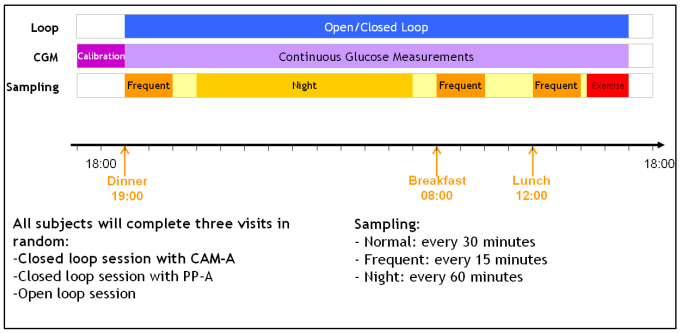
For the development of the single-port systems, which requires a single skin puncture as opposed to two punctures with the two-port system, the development made by Graz, Austria has resulted in five different prototypes (two different subtypes were developed: one with a glucose sensor outside the body and the other under the skin) that are currently tested in animal studies and first human studies.



The single-port system developed by Sensile in Switzerland has a membrane that is supposed to alter its properties according to the prevailing glucose levels. Such changes alter the characteristics of the insulin pulses applied via the same catheter. Analysis of these changes provides information about the glucose levels in the subcutaneous tissue and can be used to adjust the insulin infusion accordingly. It still has to be demonstrated that the membrane of these catheters truly respond to glucose under all circumstances and that the induced changes in permeability are large enough to allow a meaningful control of blood glucose levels.

We performed the first large clinical trials with a two-port AP system. The algorithms (a calculation rule that translates the measured glucose levels in appropriate insulin infusion rates to keep blood glucose in the target range) were implemented into a platform that communicates with the CGM system (a Dexcom Seven plus sensor from Dexcom, San Diego, CA, USA) and the insulin pump (Omnipod, Insulet, Bedford, MA, USA). In a large clinical trial with six consortium centres two different versions of such an algorithm were studied versus conventional treatment (standard open loop) in 48 patients with type 1 diabetes. The patients remained in the clinical research centres for 24 h during the three study days. Aim of the study was to keep blood glucose within the target range (70-144 mg/dl (180 mg/dl after meals)) during the night and the experimental interventions. The performance of the two different algorithms (one was developed in Cambridge, UK and the other by Padua and Pavia, Italy) was challenged by disturbing factors like meals (dinner, breakfast and lunch) and exercise (30 min on a bicycle ergometer). On a control day the patients used their insulin pump according to their own insights.





1.2 Description of the main results achieved

Within the second year of the project the following main results were achieved:

A smaller trial which analyses the impact of calibration on the performance of a CGM system by comparing two identical CGM systems with different calibration procedures was performed successfully. With the results of this study a calibration algorithm was developed that diminished the number of false alarms by 30%. Also, accuracy can better be assessed in the clinical research center, where reference samples can be taken more frequently. One manuscript based on this study is accepted for publication and a second manuscript is in preparation.
The results of the two smaller studies about a head-to-head comparison of CGM systems and the performance of two different insulin pump types will become available soon.

In parallel a telemedicine platform was successfully developed. This allows data transfer from the AP system to a supervising clinical centre.

The first prototypes for the single-port AP systems were successfully developed for the Graz approach and tested in animal studies as well as in first human studies. For the other single-port AP system using a glucose responsive membrane numerous experiments and test have been performed in Lausanne and at Sensile. Sensile has demonstrated a high sensitivity of its measurement technique to changes in hydraulic resistances and Lausanne has provided first evidence of change in the hydraulic resistance with glucose concentration.

The first large clinical trial comparing the performance of the two different AP algorithms used to keep the blood glucose value in target range by using a conventional CGM and an insulin patch pump was performed in six participating centres throughout Europe. The main outcome of this study was that both algorithms were able to control glycaemia in a similar manner, i.e. in the intention-to-treat analysis the time spent in the target range was comparable. Time spent in hypoglycaemia was lower with closed-loop, and consequently glycaemia was a little bit higher on both study days with closed-loop active in comparison

to the control study day. The final analysis of the data collected in this study is expected to be finalized in May 2012. A manuscript shall be submitted shortly thereafter.

Also, all project management, dissemination and exploitation of the project activities are well on track, including publication activities (a first manuscript describing the AP@home project was published).

1.3 Expected final results

The results of the first clinical trials performed indicates that highly relevant information for optimization of the currently used algorithms will be gained, especially during challenging situations, that means after meals and during/after exercise. The analysis performed that far indicates that none of the two algorithms used in the large AP study is superior in comparison to the other to control blood glucose excursions under such circumstances. It also appears as if both algorithms were tuned to be conservative, i.e. the glycaeic control achieved was good but not optimal. The smaller scale clinical studies that has been performed also supports optimization of the algorithm development by providing relevant information about the performance of widely used CGM systems and insulin pumps. In summary, our achievements towards the final goal of our project, i.e. running a clinical trial with a two-port AP system at home, are very good. Also the development of single-port AP approaches has made very good progress, both regarding the GRZ approach which is based on commercially-available components and the exploratory SEN approach, which requires fundamental research work. The glucose responsiveness of the second approach could not be demonstrated under all circumstances yet.

1.4 Potential impact and use

The results of this project will lead to innovations benefiting European patients with diabetes, European health care and European industry for one of the major diseases presenting a massive challenge to European health care and society in general.

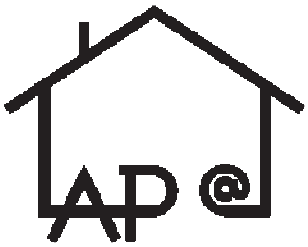
The outcomes of the project will have an impact on health care and scientific competitiveness. The knowledge on AP systems will increase significantly and improve significantly healthcare and patient comfort. The closed loop systems will allow secure, swift and seamless communication of health data from the device to the patient – continuous glucose trails, hypoglycaemia alarm – and to the health care provider. The links and interaction between patients and doctors will be improved and facilitating a more active participation of patients in the care process. The knowledge will increase the scientific competitiveness of scientists and clinicians in the diabetes field. This was clearly visible during the first open AP@home conference that take place early February 2012 at the occasion of a Diabetes Technology congress in Barcelona. This will lead to expansion of high-skilled jobs in pharmaceutical, therapeutics and related telemedicine services in European research and clinical organizations.

Due to the early stage after the second period there is no commercial outcome of the AP@home project; however, the scientific publications were published or are advanced in the review process.

1.5 Project website

Our homepage provides all relevant information about the AP@home project and is kept up-to-date regularly (www.apathome.eu). The internal part of this homepage is used extensively for data exchange within the consortium.

1.6 Project Logo



1.7 Contact details

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