Architecture of a Wireless Personal Assistant for Telemedical Diabetes Care

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Abstract

Purpose
Advanced information technologies, joined to the increasing use of continuous medical devices for monitoring and treatment, have made possible the definition of a new telemedical diabetes care scenario based on a hand-held Personal Assistant (PA). This paper describes the architecture, functionality and implementation of the PA, which communicates different medical devices in a personal wireless network.

Description of the system
The PA is a mobile system for patients with diabetes connected to a telemedical center. The software design follows a modular approach to make the integration of medical devices or new functionalities independent from the rest of its components. Physicians can remotely control medical devices from the telemedicine server through the integration of the Common Object Request Broker Architecture (CORBA) and mobile GPRS communications. Data about PA modules' usage and patients' behavior evaluation comes from a pervasive tracing system implemented into the PA.

Results and discussion
The PA architecture has been technically validated with commercially available medical devices during a clinical experiment for ambulatory monitoring and expert feedback through telemedicine. The clinical experiment has allowed defining patients' patterns of usage and preferred scenarios and it has proved the Personal Assistant's feasibility. The patients showed high acceptability and interest in the system as recorded in the usability and utility questionnaires. Future work will be devoted to the validation of the system with automatic control strategies from the telemedical center as well as with closed-loop control algorithms.
1. Introduction

Current technologies employed in diabetes care have introduced new medical devices such as continuous insulin infusion pumps (1) and continuous glucose monitors to improve the patient’s health state and the decision making process affecting insulin-dependent diabetic patients (2). The integration of these devices into telemedicine systems could increase patients’ skill in managing their illness, contributing to the acceptance of these medical devices.

Telemedicine has shown a positive influence on diabetes care, providing innovative solutions for the diagnosis, monitoring and treatment of diabetic patients (3;4). Telemedicine services can electronically register diabetes monitoring measurements, such as Blood Glucose (BG) levels and vital signs. Earlier healthcare efforts at telemedicine management aimed at improving communication and cooperation between patients and doctors. Some of them were limited to the manual transmission of BG data (5) while others integrated automatic procedures for data sending, applied in wider scale experiences as a main tool for home care and diabetes education (6-8).

Some of the latest telemedicine systems are based on mobile telecommunication technologies to transfer glucose meter data to physicians (9). Other telemedicine systems are focused on manual transmission of BG results and real-time expert feedback by mobile phone (10). Also, manual sending of BG levels by mobile phone has been shown to motivate self-care management of diabetes (11;12). All these solutions provide diabetic patients with mobility, extending the features of conventional telemedicine services.

Regarding monitoring and treatment, there is a tendency to develop medical devices with continuous operation and communication capabilities. Some of the most advanced are the OmniPod system (13), an insulin pump which delivers insulin according to
instructions transmitted wirelessly from a hand-held personal diabetes manager, and new continuous glucose monitoring devices, which can transmit wirelessly glucose readings to a hand-held receiver (14-16). The possibility of communicating monitoring and insulin delivery data allows their integration with information systems and mobile technologies.

The consolidation of information technologies and the acceptance in clinical practice of new medical devices provide a new scenario that allows approaching the complex problem of diabetes care through different control strategies adapted to each patient’s characteristics, including the artificial pancreas as one of the possible automated control strategies. Closed-loop control algorithms have been tested in tightly controlled hospital scenarios (17-19), but their ambulatory use would require the integration of control algorithms with medical devices, communication capabilities and hand-held terminals to provide patients with mobility, decision support and feedback from health care providers.

This paper presents the architecture and implementation of a mobile Personal Assistant (PA) that supports personal and remote control strategies for insulin-dependent patients supervised by healthcare professionals through a telemedicine information system. The PA includes functionalities for data management and visualization and allows communication between different medical devices in a personal area network for automatic data download and device management. Usability and utility evaluation results have been obtained from a clinical experiment in Sant Pau Hospital, Barcelona.
2. **Telemedical diabetes care requirements**

Complex diabetes care in insulin dependent pump-treated patients can be optimized with different control strategies to be applied independently or in different periods of time according to each patient’s requirements (20):

1) *Patient control:* the patient decides to change his/her insulin pump programming using monitoring data coming from different medical devices (insulin pump, sensor glucose monitor, glucometer). The process is supervised *a posteriori* by doctors through the telemedical information system.

2) *Doctor control:* health care professionals suggest changes in the therapy after checking monitoring data with a remote access. Patients then operate the devices to follow doctor’s advice.

3) *Personal loop control algorithms:* closed-loop algorithms implemented in a portable device provide a real-time control of the insulin pump based on continuous glucose data.

4) *Remote loop control algorithms:* medical devices can be remotely programmed through a portable device according to doctors’ prescription, by automatic control procedures implemented in the telemedical information system.

The implementation of these personal and remote control strategies requires the development of a robust system (in terms of hardware and software) provided with bi-directional real-time communication to allow remote interaction with the patient’s medical devices either from the patient’s personal network or long distance from the hospital. At the same time, the system should be able to operate independently of public communications network availability.

According to these requirements, the PA has to run in a mobile device such as a PDA or a mobile smart phone using a mobile network to access the remote loop and supporting
telemonitoring, telecare and remote information services. The PA should be able to work as a stand-alone system, supported on its own local application and data repository, and should communicate with different medical devices through a personal wireless network which provides the patient with mobility and independence in his/her daily life.

Communications might be activated on user demand in two scenarios: i) to force bi-directional data exchange between the telemedical information system and the PA at any moment, and ii) to perform remote control of medical devices through the telemedicine server when demanded by patients or physicians through the Web access.

3. **The Personal Assistant Functionality**

The designed PA is a distributed agent that is able to act under patients' local request for information retrieval and medical device operation. Also, the PA is able to act under remote requests originated by physicians and to interact with remote components of the telemedical system at the Telemedicine Central Server (TMCS) without the intervention of the patient. The following sections specify the Personal Assistant user interface scenarios.

**A. Virtual user interfaces for medical devices**

Several virtual user interfaces allow the patient to set up each medical device (insulin pump, glucometer and continuous glucose monitor) and to download data from them.

The insulin pump virtual interface controls communications with the insulin pump, using the infrared port or Bluetooth™. This scenario allows insulin data downloading and configuration of pump parameters, setting current basal rates or date and time and reading the current parameters to verify that the configuration has been changed properly.

The glucose monitor virtual interface retrieves subcutaneous glucose measurements from a continuous glucose monitor using Bluetooth™. Glucometer values can be updated
to the monitor for calibration purposes.

The glucometer virtual interface allows downloading BG data and other information to the PA application through Bluetooth™ or the serial port.

B. Personal logbook

The patient logbook allows patients to manage their monitoring data, providing tools for data visualization and data entry (Fig 1.a). Most of the monitoring data are retrieved straight from the medical devices and values cannot be changed, but patients can complete the information for existing measurements or manually enter new values:

![Fig. 1 - PA user interface: (a) Personal electronic logbook; (b) Blood glucose measurement visualization](image)
- BG measurement editing allows specification of the moment of measurement (preprandial or postprandial) and time interval between measurements (breakfast, lunch, dinner, etc.) (Fig 1.b).

- Meal data include the amount of carbohydrates in units or grams, the type of carbohydrates and the intake moment.

- Insulin data consist of daily basal profiles coded with colors, daily bolus (bolus type and insulin amount) and total daily insulin.

- Additional data such as medication, stress, illness, physical exercise, etc.

Monitoring data stored at the TMCS can be downloaded at the PA local database through the synchronization process. Also, data registered manually at the PDA or downloaded automatically through medical devices can be updated in the Central Server Database via synchronization.

C. Visualization of graphs

The multiparametric graphical scenario presents a fast overview of the patient’s metabolic health state, providing information about exceptional events of interest and supporting the decision making process. This tool shows different representations of monitoring data (plot, pie or temporal graphs) (Fig 2.a). Variables such as BG, diet and administered insulin doses can be shown in a combined graph or separately.

D. Therapy viewing tool

The PA notifies the patient with a message whenever a new therapy is prescribed (Fig 2.b). The therapy viewing tool shows the current insulin and diet therapies proposed by the physician. Insulin therapy includes basal pump profiles with the recommended doses for each hour, a total of 24 rates, and bolus doses, showing the bolus type for each intake-
associated interval. Diet treatment presents the distribution of units associated with each daily intake, according to the type of carbohydrates recommended by the physician and the corresponding nutrient distribution (carbohydrates, calories, proteins and fats).

E. Insulin Controller scenario

The insulin controller algorithm can work automatically in a continuous mode, providing a calculation for basal insulin rates every 15 minutes, or the patient can run the bolus advice mode before an intake or for a bolus calculation correction. The Insulin Controller scenario allows running the bolus advisor and starting or stopping the automatic algorithm. The implemented closed-loop algorithm is based on a non-linear MPC (Model Predictive Control) with Bayesian learning that has been previously tested (21). Input data required for closed-loop control include continuous glucose measurements, insulin history, meal intakes and the patient’s personal data. Any changes are presented to the patient in real time.
Fig. 2 - PA user interface: (a) Graphical representation of BG measurements associated to meals; (b) Synchronization scenario and Therapy change notification message.

F. Configuration scenario

The configuration scenario authenticates the user entering the login and password assigned at the TMCS. Patients can modify PA settings such as preferred language; blood glucose units (mg/dl or mmol/l); starting hour for visualizing monitoring data in his/her personal logbook; and other additional personal data such as weight, height, age, etc. The PA multilingual graphical user interface is available in English, Spanish and German.
4. Personal Assistant architecture and Implementation

The PA architecture follows a modular design to allow scalability and the easy integration of new functionalities. Fig. 3 shows the architecture's main modules and the software agents that support the communication process at the TMCS.

Two different security strategies control the access to the system assuring that only authorized patients can use the PA: a) Authentication: a login and password are required for application use and data synchronization. b) Device validation: the serial number of
every medical device is checked before any communication to assure that it matches the device assigned to the patient at the TMCS. To assure confidentiality and data integrity, the application provides data encryption, allowing data transmission and reception without changes.

The PA application has been implemented with the Java programming language to make the application platform-independent in terms of user interface and TCP/IP communications. The user terminal used for technical validation and clinical evaluation is an iPAQ hp2210 PDA with wireless communication facilities, such as infrared and Bluetooth™, and is provided with the AudioVox RTM 8000 module for mobile GPRS communication capabilities. The Java Virtual Machine CrEme v3.24 for embedded platforms has been chosen to run the application in the Windows CE environment.

This section describes in more detail the architecture modules for local and remote communications.

A. The Communication Device module

The Communication Device module provides the necessary methods to manage communications between the PA and several medical devices in the local loop. It is composed of three sub-modules for communication with the insulin pump, the glucose sensor monitor and the glucometer. Any submodule has to be programmed to support the specific device’s communication protocol. The modular architecture assures that the addition of another medical device does not affect the rest of the modules.

1) Insulin Pump communication

The insulin pump that is currently integrated in the PA is a Disetronic D-TRON™ plus. For the remote loop, a modified D-TRON™ insulin pump has been built by manufacturers
to make the pump remotely controllable via Bluetooth™ or infrared.

The communications between the PA and the insulin pump have been implemented using a Dynamically Linked Library (DLL) written in C++ for Windows CE and provided by the pump manufacturer. The library allows management of protocol communications and provides basic functions such as initialization, reading of events and setting of pump basal rates. The interaction between Java and the native library is implemented through the Java Native Interface, using a DLL bridge between the PA and the manufacturer DLL.

2) Continuous glucose monitor communication

Communications between the PA and the glucose monitor have been tested with a sensor prototype. The interaction between the PA and the glucose monitor is also achieved through a DLL similar to the pump’s, which manages protocol communications using Bluetooth™. The processes involved in the communications module require loading the DLL and invoking the functions to obtain continuous glucose data from the monitor.

3) Glucose Meter communication

The glucometer integrated in the system is a One Touch Ultra (Lifescan) which transmits BG measurements automatically to the PA application using a serial cable or Bluetooth™. Communications are supported by the Java Communications API javacomm, which allows interchange of data through serial ports. The communication between the PA and the glucometer is initiated by the patient through the virtual interface. The PA wakes up the glucometer, downloading the data stored in the memory to the PDA. After a basic data processing, the information stored in the glucometer is updated into the PA’s local database.
B. The User Interface module

The PA User Interface is based on the Java Abstract Windows Toolkit and offers a high scalability to the application. Several sub-modules can be distinguished: the ‘User Actions Log’ module registers the interaction of the patient with the User Interface; the ‘Access Control’ module is used for dealing with security and it is used for authentication methods; the ‘Bolus Advice’ module implements a bolus calculator tool; the ‘Closed loop algorithm module’ implements the Insulin Controller Algorithm; the ‘Devices Manager’ module provides access to the Virtual User Interfaces for medical devices; the ‘Therapy’ module allows the visualization of current insulin and diet treatment; the ‘Logbook’ and ‘Graphs’ modules allow visualizing monitoring data; and the ‘Settings’ module is needed to set user preferences and registers changes in personal data.

C. Remote communication module

The implementation of remote control strategies implies providing straight interaction with the patient’s medical devices from the remote Web access. The PA can behave as a server, receiving requests from the PA Remote Agent running at the TMCS to change the device’s programming or to start the remote database updating process by synchronizing automatically. The PA can also behave as a client to activate the remote access alternative and to register the PDA and its associated medical devices at the TMCS.

The client-server behavior has been achieved through the integration in the remote communication module of several CORBA (Common Object Request Broker Architecture) distributed objects implemented with the CORBA 3.0 standard (22). The object public interfaces have been described with IDL (Interface Definition Language).

Communications between distributed objects in the TMCS and the PA are handled through the Object Request Broker (ORB) provided by Inprise (Visibroker), which allows
interoperability and is completely java-based. The standard protocol IIOP (Internet Inter ORB Protocol) has been used to communicate distributed objects. The ORB allows initialization and publication of methods. The Visibroker naming service has been used to access distributed objects through the name assigned to the system.

D. The Data Access module

This module provides the PA with an access to the local database through a JDBC (Java Database Connectivity) driver. The personal local database contains different tables to allow interoperability between all the modules and to store the information necessary to manage the PA.

The database resides locally in the PDA. It has been implemented with Sybase’s UltraLite™ technology, as it needs very few memory resources and has the reliability and capabilities of the databases that implement the SQL standard. The two-way synchronization process with the TMCS Database is supported by MobiLink™. Communications between the MobiLink™ synchronization server at the Central Server Database and the local database at the PA are encrypted using the transport-layer security standard protocol.

E. Agents running at the TMCS

1) The Device Agent

The Device Agent controls access to the system by checking medical device serial numbers registered at the TMCS central database. Additionally, it pre-processes data coming from medical devices, especially data from the insulin pump.

The insulin pump registers single events that must be translated into understandable administered insulin doses. Due to limited resources in the PDA, it is of high interest to transfer these processing tasks from the PA to the telemedicine server, which helps
increase response times. The agent has been developed following the concept of a multi-access architecture (7). The Device agent is Java-based, and communicates with the PA through mobile GPRS communications.

2) The Remote Control Agent

The Remote Control Agent is located at the TMCS and acts as the intermediate element between the physician and the patient by notifying the PA of the new insulin pump configuration proposed by the physician. For security reasons, any changes require the patient’s express consent to change his/her current insulin therapy.

The Remote Control Agent calls the procedures exported by the remote communication module to obtain remote access to medical devices when it is required to modify the configuration or to start data synchronization automatically. The agent updates the physician’s prescription, communicating straight to the PA via GPRS using CORBA and remote invocation methods. The agent notifies the patient and the physician of any changes once the process has finished, through the virtual pump interface and the Web access.

The Remote Control Agent provides methods of calling the PA distributed objects and to allow registering the PA application and its associated devices, to obtain information about data updates in the PDA, or to send confirmation messages to the patient or physician.

The registering process of the PA implies sending the IOR (Interoperable Object Reference) code, which codifies the location of the object in the network and the methods that are exported. Once the IOR is available, the next step is to load the ORB into the remote server to allow the PA to be registered. After the necessary CORBA procedures are initialized, the remote agent waits for requests from the patient’s PA or from the physician through the Web Access.
5. Description of interactions in the system

The sequence of interactions between the PA application and the rest of components of the system can be summarized in the following (see Fig. 4):

A) The patient interacts with the PA to manage his/her diabetes, visualizing the PA personal logbook, updating monitoring data and modifying his/her preferred settings.

The physician monitors the patient’s health state interacting with the Web interface and he/she can propose a therapy change whenever any anomalous situation is detected. Any recommended change is stored at the TMCS central database and notified to the patient through the PA application.

After visualizing the insulin therapy modifications recommended by the physician, the patient can automatically reprogram the insulin pump using the virtual pump interface.

B) The patient can operate medical devices using the PA virtual interfaces to obtain administered insulin doses stored into the pump or to update glucose measurements coming from the glucometer or the continuous glucose monitor.

Depending on each patient’s requirements, the insulin controller algorithm can be used to provide bolus advice before a meal intake or as a continuous closed-loop controller that operates the insulin pump every 15 minutes.
C) When the patient wishes to update personal monitoring data at the TMCS or to download therapy changes or other data stored at the server, the synchronization process is started using a GPRS connection. The Device Agent authenticates the user and it has to pre-process data downloaded from the insulin pump to minimize the visualization time in the Web interface.

D) During a remote loop control strategy, the PA can be remotely programmed with automatic control procedures. If the physician detects any anomalies while visualizing a
patient's logbook, he/she can modify the therapy through the Web treatment scenario. Insulin therapy changes proposed are transferred to the Remote Control Agent, which notifies the new therapy to the patient in the PA interface. When the patient agrees to a therapy change, the PA application notifies to the Remote Control Agent that the process can be started. The patient and the physician are notified in real-time when the process is finished.

6. Technical Test and Validation

The PA application has been tested in the laboratory for technical validation of its hardware and software components, obtaining relevant information for the PA operation.

A. Personal Assistant autonomy

Commercial PDA devices have serious restrictions in the amount of battery run time. For this reason, we made a previous selection to look for the most appropriate device, in order to minimize the impact on PA autonomy.

The PDA chosen (iPAQ hp2210) has an estimated usage time for a fully charged battery of up to 12 hours, depending on the type of use of the PDA. This means that even for the worst case of battery consumption, the scenario of personal loop control which requires longer processing time, the PDA chosen would be suitable as long as the user is aware of the need to charge it every 12 hours. To assure that there is no data loss even if the battery is consumed, the PA data is stored in a Flash SD memory card.

B. Memory consumption

The memory used by the PA application and the rest of required software elements have been measured to estimate the consumed resources:

- Operating System (OS): 10,18 MB
- Java Virtual Machine(VM) + PA: 18.5 MB
- Bluetooth™: 19.6 MB
- GPRS communication + CORBA server: 22.4 MB

PA memory requirements are covered by the iPAQ hp2210, as it is provided with 64MB of RAM memory.

C. Synchronization time

The time to exchange data between the PA and the TMCS databases via synchronization is highly dependent on the amount of data transmitted and the type of connection. Laboratory tests have shown that the time can vary from few seconds to 4 minutes when using mobile GPRS communication. The longest synchronization time has been measured when transmitting monitoring data from over a long period such as three months of insulin pump memory.

7. Evaluation of feasibility and usability of the PA in a clinical scenario

The PA application has been tested in a randomized and cross-over clinical experiment with 10 type 1 diabetic patients (5 women, age 40.6 (21-62), diabetes duration 14.7 (3-52) years) from Hospital de Sant Pau (Barcelona, Spain) (23). All the patients were randomly assigned to start the experiment in one of the groups (control or intervention) for a month. After a month, all the patients were transferred to the other branch (intervention or control) for another month.

This experiment has provided the necessary data to evaluate the feasibility of the PA and the reliability of communications between the PA and medical devices in the personal loop and the components of the TMCS in the remote loop. The experiment allowed recording data related to frequency of use of the PA application by patients, utilization of
the provided functionalities, user satisfaction, usability and utility. The PA was tested for
*Patient Control* strategy with the PA application and for *Doctor Control* strategy with the
TMCS. Patients were recruited from those regularly attended in the outpatients’ diabetic
clinics of the hospital.

During the control phase, patients did not use the PA and did not receive any feed-back
from the medical center, but they sent glucose data for retrospective analysis.

During the intervention phase, patients used the PA and the telemedicine services to
send monitoring data (blood glucose measurements, insulin doses administered, diet and
other additional events) to the physician in charge. All the patients were provided with the
Disetronic D-TRON™plus insulin pump, able to communicate with the PA using the
infrared port. The physician (Dr. M. Rigla) analyzed data sent by patients through a Web
access, and could advise modifications of the basal rates and/or boli that the patient could
check with the PA. To reinforce the PA usage, an automatic SMS message was sent to
the patient’s cellular terminal after each therapy change.

Fructosamine and HbA1c were registered at the start and end of each period for
retrospective evaluation between periods. The clinical impact of the system has been
reported (23), showing that the usage of the wireless PA joined to the telemedicine system
allows better glycaemic control in pump treated type 1 diabetic patients due to a significant
reduction of fructosamine (393 ±32 vs. 366 ±25 umol/L; p<0.05). HbA1c tended to
decrease (8.0 ±0.6 vs. 7.78 ±0.6; p=0.073). Comparisons were made using nonparametric
tests for paired data (Wilcoxon’s test).

The evaluation of technical feasibility and usability of the PA application has been
carried out with two data collection procedures:
A. Objective evaluation: Automatically generated logs

In order to study how the patients perform their sessions with the PA, the system keeps a local record of usage traces. This enables registration of data in the application’s local database about the patient’s behavior (number of sessions, viewing of therapy changes, access to personal logbook, entering monitoring values, downloading data from medical devices, etc.). The automatically generated logs have been used to assess objective parameters.

Fig. 5 summarizes the average and standard deviation of data sent weekly with the PA during the intervention phase, as well as the average and standard deviation of the frequency of usage of the main scenarios per week. Patients’ behavior did not change along the intervention phase. The functionalities of the PA application preferred by patients according to their usage were: downloading insulin data (6.32 ± 3.1 per week), viewing the personal logbook (7.54 ± 6.4 per week) and synchronizing the PDA with the TMCS (7.98 ± 4.3 per week). The number of pump downloads shows that interaction between the PA and the insulin pump was frequent, whereas the number of synchronizations during the experiment gives an idea of the frequency of interaction between the mobile application and the TMCS.

Patients communicated with their physician more than once per week on average, and the physician made at least two modifications in current therapy, in contrast with traditional practice where changes are usually carried out during the visits to the healthcare centre.
Fig. 5 - Weekly average of data sending and most used functionalities of the Personal Assistant for ten type 1 diabetic patients.

B. Subjective evaluation: online questionnaires

An evaluation questionnaire was used to measure qualitative aspects of user satisfaction regarding the PA application at the end of the clinical experiment.

It allowed evaluation of the technical use of the telemedicine system in general and specifically the use of the PA application, reliability of the system, usability and utility. The usability and utility evaluation measured the subjective perception of ease of use and overall utility and satisfaction with the PA.
Table I - Evaluation with questionnaires: number of answers regarding usability and utility questions

<table>
<thead>
<tr>
<th>Usability</th>
<th>I Agree</th>
<th>I partially agree</th>
<th>I partially disagree</th>
<th>I disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>A The system helps me to collect data (BG, insulin, diet...) faster and more efficiently</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>B The system helps me to understand and analyze my monitoring data faster and effectively</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C It was easy to learn how to use the system and become familiar with it</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>D The system is convenient to use</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>E The use of the system has made my daily life more difficult</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>F I like the system</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Utility</th>
<th>I Agree</th>
<th>I partially agree</th>
<th>I partially disagree</th>
<th>I disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>A The system helps me to communicate with the physician quickly and effectively</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>B The system helps me to make decisions regarding my diabetes</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C The system increases the flexibility of my therapy</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>D The system has helped me to reduce the number of acute problems (hypoglycaemia, ketosis, etc.)</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>E The use of the system makes me feel more secure in handling my diabetes</td>
<td>6</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F I would recommend the use of the system to other diabetic patients</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table I reflects usability and utility questions related to the PA and the answers provided by the patients. Nine out of ten patients answered all the questions. In general, all patients had a positive opinion of the functionalities and utility of the system. Although some patients did not think that the system could help to reduce the number of acute problems, it is important to notice that all the patients considered the system easy to learn and they would recommend it for diabetes care.
8. Discussion

The system architecture proposed in this paper considers the implementation of four different control strategies based on local and remote area networks for multiple loop alternatives, which can be used separately or combined in different periods of time in an ambulatory environment. The wireless PA is supported by a telemedicine information system that optimizes the quality and quantity of the information registered by patients and improves patient-physician communication, enhancing the decision-making process for adjustment of therapy in a collaborative and supervised way.

The selection of a modular approach for the technical development and integration of each medical device independently from the rest of components allows adding new medical devices easily. Also, the structure of the system permits a continuous, separate evaluation of different modules. The tracing system of patient behavior when interacting with the application provides very useful feedback for the evaluation process, and it is required for making further improvements to the system. Improvement of existing functionalities and integration of new features help keep the system up to date.

Several alternatives have been considered for remote invocation procedures, such as CORBA and the Java Remote Method Invocation (RMI). Both enable the application to be executed on any platform. The main disadvantage of CORBA is its complexity, while the RMI architecture can only be used between Java applications. CORBA constitutes an ideal mechanism for the interoperation of objects written with different programming languages and it was preferable for building a portable system that can be adapted to most of the existing or future PDA or mobile platforms. Also, supporting the use of different programming languages might be required in the future to adapt the communication libraries provided by different medical devices.
The use of always-on networks such as mobile GPRS communications makes transparent data transmission to users possible, periodically updating at the PA data from medical devices and transferring new data to the TMCS. The main problems related with GPRS communication are that the connection can take some time when high amounts of data are transmitted or that there might be problems with connection coverage, as GPRS is not yet present and robust enough in some suburban areas. This situation might limit the use of automatic remote control strategies that could require real-time operation. The use of the TCP/IP transport protocol guarantees that the migration to new advanced communication technologies such as UMTS would be immediate.

Another restriction of the system is due to the use of hand-held devices with limitations such as energy consumption, which implies charging the system regularly. It is important to consider this problem when implementing critical applications. Also, PDAs increase complexity due to high constraints in terms of memory and processors. But even with these limitations, the technical validation of the architecture presented has shown the feasibility of using portable devices with any of the proposed control strategies. In the scenarios tested during clinical experiments, patients can use the PDA to run other personal applications, which increases the PA's appeal for them. However, when using the PA for remote loop control strategies, the chosen PDA (hp2210) is completely dedicated to monitoring tasks because the CORBA server consumes a high amount of memory resources. Newer versions of hand-held devices equipped with more RAM memory would improve this limitation.

The implementation of the PA application with the Java technology makes it portable to other platforms as long as the operating system supports a Java Virtual Machine. This feature makes easier the migration of the PA to existing or future portable devices, which
would improve features such as memory, battery runtime or wireless communication capabilities.

Security has been a key point for the development of the system, as medical data is a data category that requires special handling. The EU Directives (Directive 95/46/EC 24th October 1995) about security requirements have been followed to assure that medical data stored in the system is protected against non-authorized access, and that the transmission of data is performed in a secure way. Data transmission through GPRS is secured using the synchronization technology provided by Sybase’s Database Management System, which allows a strong database encryption and secure transmission through the transport-layer security. Additionally, the system provides access control and guarantees that only authorized users have access to services and stored data.

Electromagnetic interference (EMI) becomes an important factor to consider when using wireless devices to transmit medical data. It is well known that all electric devices have the potential to produce electromagnetic radiation, including PDAs, cellular phones and Bluetooth™ devices. However, medical devices such as glucose monitors or continuous insulin pumps include Bluetooth™ or wireless capabilities, and have to be tested for electromagnetic emissions and for immunity to EMI before being approved for clinical use. For critical scenarios, such as closed-loop control, or to use the wireless PA system in hospital areas, an environmental assessment should be performed to evaluate the susceptibility of devices to power levels of electromagnetic radiation as well as to avoid device malfunction.

The system was tested by patients over a wide age range lacking previous experience with similar systems, and all of them considered the system a useful tool for managing their illness. As a whole, patients were of the opinion that the system helped to improve
their communication with physicians and their decisions about diabetes daily adjustments. Patients feel more confident to handle the disease while using the system, increasing their sense of safety and they consider that this helps to understand and analyze their monitoring data faster and more efficiently. They did not find the system difficult to learn or to use, after receiving some training instructions. For all these reasons, patients are willing to recommend the use of the wireless PA application joined to telemedical care for diabetes. User's satisfaction is one of the most important points to take into account when considering the generalized use of this kind of systems.

The evaluation of two control strategies in a clinical environment has shown that all the patients used the PA to register and send data to the hospital on a regular basis, although the pattern of system usage varied between individuals. They had instructions to send data (blood glucose and insulin doses administered) to the TMCS at least once per week. Results have shown that they sent insulin data almost everyday. This was one of the most innovative features for patients and they had a big interest in viewing and analyzing these data daily. Patients kept communicating with the telemedical service once per day through the synchronization process for the intervention phase, which emphasizes that patients want to keep their physicians informed of their health state. Other scenarios of the PA application preferred by patients are viewing the logbook, which allows analyzing monitoring data or checking current therapy, both basic tools for their daily adjustments. The physician was also very motivated by the system, and analyzed the patient's monitoring data every day, making the corresponding therapy changes whenever required.

The unavailability of commercial medical devices with wireless capabilities and FDA approval for remote control limited the testing of the complete automatic closed-loop
solution in a clinical environment and was restricted to laboratory technical tests. In terms of clinical results, the PA application has shown that it contributes to improve glycaemic control (23), which joined to user’s satisfaction supports that the PA application together with the TMCS might constitute a new good tool for diabetes care.

Cost-benefit analysis of the system have been accomplished (24), based on HbA1c reductions obtained during clinical experiments, in order to evaluate its introduction in routine care. This has allowed estimating cost savings due to reduced probability of developing diabetes related diseases in a 30-year time frame. However, to improve cost efficiency of the system, the costs of system operation and especially the cost of continuous glucose measurements need to be notably lowered.

The PA architecture provides support for several ambulatory control scenarios. The presented architecture shows the proof of concept of a suitable technical platform for a future ambulatory artificial pancreas, once wireless continuous glucose monitoring sensors and insulin pumps are commercially available, and closed-loop control algorithms are properly validated. However, in future implementation, the integration of the intelligence of the application into a more reliable and robust device might be considered. The modular proposal for the architecture will continue to be valid in this scenario. Meanwhile, the PA would be a practical tool during clinical validation of controlled algorithms in a supervised area such as a hospital, as it improves the patient’s mobility.

9. Conclusions

This paper has presented the architecture and implementation of a wireless Personal Assistant that supports different telemedical control strategies. The system integrates communications with three different medical devices (glucometer, insulin pump and
continuous glucose sensor) and presents a modular architecture that allows the easy integration of new features. The requirement of using distributed agents able to perform always-on bi-directional and real-time communication has been achieved with the CORBA standard.

The overall architecture of the system has been technically tested in laboratory and two scenarios of ambulatory control have been clinically evaluated. The evaluation experiment showed that the functionalities provided to patients and health care practitioners have been employed regularly and, according to the results of usability and utility questionnaires, the patients showed high acceptability of and interest in the system. Future work includes testing the closed-loop control and remote control strategies.

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Conflict of interest statement:
None of the authors of this article have competing financial interests or personal relationships with other people or organizations that could inappropriately influence their work.

Ethics statement:
The work presented in this article has been approved by the Sant Pau’s Hospital ethical committee, to assure that it safeguards the well-being of the subjects studied. All subjects participating in the study gave informed consent to the work.

Authors’ contributions:
- **Gema García-Sáez** has contributed to the design of the system and its implementation; to the technical evaluation methodology; to the user training and technical support during the clinical study; and to the analysis and interpretation of data. She also contributed to the clinical study definition. Also, she has contributed to the preparation of the manuscript and to revision procedures and she has approved the version submitted.
- **M. Elena Hernando** has coordinated the technical design and implementation of the system. She contributed to the clinical study definition; to the evaluation methodology; and to the analysis and interpretation of data. Also, she has contributed to the preparation of the manuscript and to revision procedures and she has approved the version submitted.
- **Iñaki Martínez-Sarriegui** has contributed to the implementation of the system and to analysis of data. He has contributed in the process of writing the article and he
has approved the final version submitted.

- Mercedes Rigla has contributed to the design and implementation of the clinical study; to the system functional specification; and to the interpretation of data. She has revised the article critically and she has approved the final version before submission.

- Verónica Torralba has contributed to the design of the system, to the implementation and to the analysis of data acquired. She has revised the article critically and she has approved the final version before submission.

- Eulalia Brugués has contributed to the user training and technical support during the clinical study and to the acquisition of data. She has revised the article critically and she has approved the final version before submission.

- Alberto de Leiva has contributed to the conception and design of the system; the definition of the evaluation methodologies; and to the analysis and interpretation of data. He has revised the manuscript critically and he has approved the final version before submission.

- Enrique J. Gómez has contributed to the conception and design of the system; the definition of the evaluation methodologies; and to the analysis and interpretation of data. He has revised the manuscript critically and he has approved the final version before submission.

Summary table:

a. What was already known on the topic:

- Information technologies are being employed to face new solutions for diabetes management. In this area, telemedicine systems involving daily monitoring of
clinical data, education, and personal feedback have shown to be successful in diabetes care.

- Handheld data-capture technology is more accurate than traditional paper-based recording of blood glucose values into a logbook. The use of new monitoring devices for diabetes management such as continuous insulin infusion systems and continuous glucose monitoring devices, provide additional alternatives which can be managed more efficiently with handheld technology.

- Closed-loop control algorithms are being tested in tightly controlled hospital scenarios, but their ambulatory use won’t be achievable if the integration of algorithms with medical devices, communication capabilities and hand-held terminals to provide patients with mobility, decision support and feedback from health care providers is not faced.

b. What this study added to our knowledge:

- The evaluation of the presented architecture in clinical practice with a group of patients with diabetes has proved the personal assistant’s usability and utility based on the patients’ opinion. Also, it has generated a wide acceptability, which allows spreading it out to a higher number of patients and the use of the system in other scenarios such as closed-loop control.

- The evaluation process of the Personal Assistant has been based on a tracing system of the patient behavior, which allows registering the patient interaction with the application transparently to the user. The tracing system provides useful feedback about the preferred scenarios and this information can be used to adapt new functionalities to the patient’s preferences.
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