DinamapBP-Automatic Data Acquisition System for Clinical Trials

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***Abstract* — The work presents a data acquisition system for blood pressure measurement in clinical trials based on pervasive computing approach. The system is devised with a view to minimise and probably eradicate input of erroneous data along with a number of other security measures.**

I. INTRODUCTION

Clinical trials. Newly developed medical therapies should be declared safe and effective prior to being introduced to the general public [1]. New medications are tested through clinical trials, a series of research studies using a limited number of volunteers and normally conducted Clinical Research Organisations (CRO). The clinical trial design depends on the type of therapy but normally includes initial health check of volunteers followed by regular checks, monitoring and testing during the trial, and keeping post trial contact.

Clinical trials are conducted in phases. The trials at each phase have a different purpose and help scientists assess possible health hazards and establish the efficacy of the proposed therapy. Regulatory bodies such as the Food and Drug Administration (FDA) decide whether to approve it based on the produced documentation and trial results.

Table 1 provides a short description for the first 3 phases of clinical trials. Phase I includes trials designed to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of a therapy. All trials in the first three phases are almost always conducted in inpatient clinics, where subjects can be observed by full-time medical staff. While Phase IV trials, that provide information on risks, benefits and optimal use, are normally conducted out of clinics.

Data collection. Data, collected during clinical trials, depend on the type of medical treatment tested. However, majority of Phase I trials require standard data such as blood samples and Vital Signs (blood pressure and temperature). All relevant information is always provided in a Clinical Trial Protocol, a document describing the organization of a clinical trial, objectives and methodology. The protocol usually also describes eligibility criteria for volunteers, the schedule of tests, procedures, medications and dosages, length of the study. An example of the schedule for a clinical trial Phase I is shown in Figure 1. All measurements are recorded on CRFs (Case Report Forms) - questionnaire specifically used in clinical trial research and found as a primary data collection tool from the investigator site. Provision of full and complete and accurate data and all associated documents is essential, hence the current paper based approach creates a number of problems including document storage and reliability of the collected data.

Generated Master Treatment Schedule (0000, P6, G1)

Location	Protocol Time	Task	Schedule Offset	Start/End Date	Assigned	Dil1	Dil2	Dil3	Dil4
Ward 1		Troubleshooting	00:00	28-Jan-2000 07:50 - 08:02	AB	07:50			
Ward 1	day 1 five min supine	Orthostatic Vital Signs	-00:10	28-Jan-2000 07:50 - 08:02	BJ	07:50	07:53	07:56	07:59
Ward 1	00:00	Dosing	00:00	28-Jan-2000 08:00 - 08:12	AB, MMo	08:00	08:03	08:06	08:09
Ward 1		Troubleshooting	00:00	28-Jan-2000 08:10 - 08:22	AB	08:10			
Ward 1	day 1 five supine	Orthostatic Vital Signs	00:10	28-Jan-2000 08:10 - 08:22	BJ	08:10	08:13	08:16	08:19

Figure 1. An example of a Master treatment schedule

TABLE I. CLINICAL TRIAL PHASES

	Phase I	Phase II	Phase III
Description	A Phase I trial is the first test of a new treatment to see if it is safe to use in people. The new treatment is tested because it showed promise in lab tests.	Once a treatment is found to be safe (often in a Phase I trial), it can be tested to see if it helps patients.	A Phase III trial tests a treatment that has been shown to help some patients (often in a Phase II trial). It usually compares a newer treatment to the standard or best known treatment.
Goals	Learn: Whether the treatment is safe. The best way to give the treatment (for example, as a pill or a shot). The right dose -- the amount that causes the fewest side effects	Learn: Whether the treatment works. Whether there are any less common side effects, which may appear when more patients get the treatment	Learn: Whether the new treatment is better than, as good as or worse than the standard treatment Phase III trials may be more complex and look at more aspects of treatment than Phase I or II trials.
Number of Patients	20-80	100 or more	Several hundred to several thousand

At Richmond Pharmacology, blood pressure measurements are taken using automatic blood pressure measurement device Dinamap (Figure 2. a). Nurses are responsible that correct data are input into CRF forms on scheduled time. The standard procedure is identical for every volunteer and requires

- Switching the device on,
- putting the cuff on a volunteer's arm and
- record the Blood Pressure values from the Dinamap at the scheduled time

Once the trial is finished, all collected data (CRFs) are entered manually and several independent checks are conducted to avoid data entry mistakes. Only then data records are presented in electronic format to a sponsor (organisation funding the study, normally a drug manufacturer).

Data collection and especially data entry are prone to mistakes, since they are monotonous and repetitive processes. Hence after double data entry there are some stages of quality control (QC) checks are performed.

Aims and objectives. The aim of this paper is to outline a pervasive computer system that successfully addressed the problems described above by directly recording measurements from device to a proprietary database without intermediate manual recording to CRF and subsequent manual data entry. In addition to that the system provides administrative control tools such as Online Schedule planning tasks and times for nurses; Administration unit providing the means to Study managers monitoring tasks completion and emergency situations.

II. System Design

Server and Database. Richmond Pharmacology has a number of servers installed for different purposes that are backed-up daily. Microsoft SQL Server 2000 is used as a back-end for database application. The system combines 3 databases from two of which are currently in use at RPL: Scheduler Database – containing all information from the Scheduler software, Volunteer Recruitment (VR) Database - containing information about volunteers and a database with Dinamap readings and authorised users of the system. Scheduler software is a tool for creating schedules for clinical staff based on knowledge, working hours and availability of employees. The software is designed to resolve possible clashes such 2 tasks assigned to same employee. VR database combines all information about volunteers taking part in clinical trials. Once a volunteer is registered, a permanent RPLid is assigned automatically. RPLid is a unique number for each volunteer consisting of 6 digits. Finally, the database for the Dinamap is designed to prevent data redundancy and incorrect data management such as deleting inaccurate records.

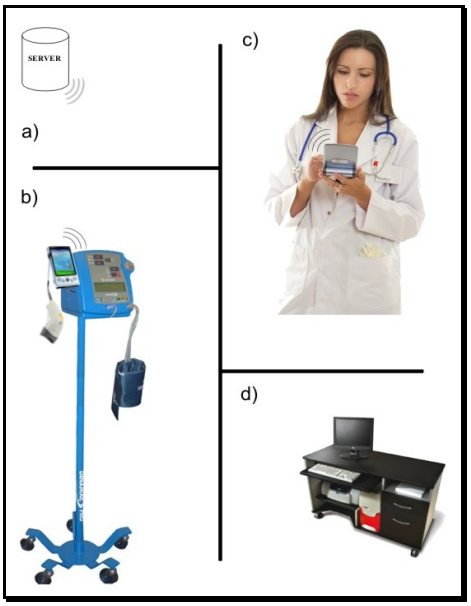

Figure 2. DinamapBP system design.

Hardware design. Dinamap is a portable blood pressure measurement device and can be carried around a ward using a stand on wheels (Figure 2. b). For added mobility Pocket-PC (PPC) with wireless connection is used as a host data acquisition device. PPC is attached to Dinamap communicating through a serial adapter. The system also uses barcode reader for scanning RPLids from volunteer's card, a security procedure introduced to ensure that blood pressure is taken from the right volunteer (Figure 2. b).

Currently, at Richmond Pharmacology, all nurses have printed version of schedules with them to ensure that they carry out their duties on time, extremely important for a successful completion of a costly trial. The presented system addressed this user need by proprietary software allowing cross-link to the Schedule online (Figure 2. c). Hence any nurse can install the relatively small software and view her schedule on the PPC. This not only allows viewing online her schedule but to also respond on time to any amendments made to her scheduled tasks. All of this is currently written and corrected on paper that needs to be distributed to all staff.

Meanwhile managers responsible for running a clinical study can monitor the process of blood pressure measurement from their offices using the Administration part of the software (Figure 2. d).

Interfacing. Figure 3. shows the system interfacing using different type of adapter cables to make possible the communication between devices. Since PPC(a) has only one USB port a hub(b) is used to increase the number of USB ports. USB to PS2 adapter (c) is then used to connect a Barcode reader (d) to the PPC. Barcode scanner is used for scanning barcode on Volunteer's cards for taking blood pressure measurements and to scan Employee's cards during logging in to the software. USB to Serial port adapter (e) is used for connecting Dinamap (g) through serial cable (f).

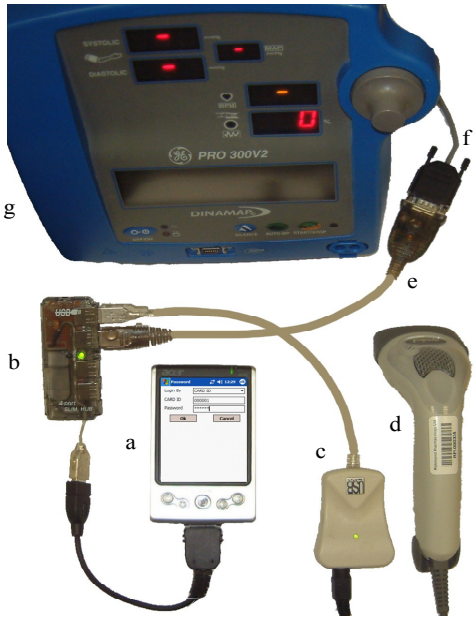

Figure 3. Hardware interfacing.

Software. Figure 4. represents a screenshot from the main window of the software built for Dinamap data acquisition system. For security reasons password method was implemented into the system conducting a user check prior to using the software. After 10 minute of inactivity system logs out automatically preventing unauthorised use.

The graphic interface replicates the Dinamap active buttons (becoming active after user is verified) and the readings on its screen display live all data obtained during its operation. However, no reading can be recorded unless the patient is identified and checked against the existing schedule. The patient is identified through the RPLid on the personal card. Barcode readers are implemented for this identification.

System was developed with intension to use intensively during clinical trials and created in a most simple and user friendly way. After starting the software schedule is shown on the screen and the system is already setup for use.

In cases when a nurse becomes unavailable for performing tasks, then second nurse (troubleshooter) can take over by identifying herself through scanning her ID card using the barcode reader. Similar solution is provided for a nurse who replacing another nurse; they can login and retrieve a schedule of a person whom replacing. All these are reflected in database, by keeping track of every operation.

Blood pressure is determined using the software in just 3 screen taps:

After nurse loges in to the system schedule is shown automatically on a screen and performs the next steps:

1) Nurse clicks on a task of a schedule.

2) Confirms Patient Id by using barcode reader.

3) Determination starts automatically after confirmation. After completion a record is created automatically.

The above 3 steps are performed for each scheduled patient. All consequent measurements for the same subject using the same scheduled task are recorded as repeated measurements with appropriate number.

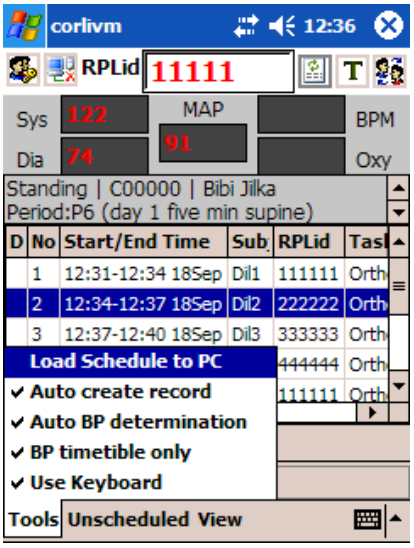

Figure 4. Software screenshot.

When unscheduled determination is needed the nurse simply clicks on the "Unscheduled" option, confirms relevant pre-entry information such as Study No and measurements starts automatically.

Second part of the software is a schedule for the clinical staff to ensure that all tasks are performed on time. The system is very similar to the Dinamap software but without Dinamap connection features. It replaces a paper copy of the schedule but sometimes the schedule is need an update and an online version of the Schedule using PPS becomes very practical showing immediately all changes.

Third part of the software is administrative module for data manipulations, monitoring and controlling the system (Figure 5. and Figure 6.). Study manager can monitor all processes and measurements taking place in a ward while in another office or even in a different hospital. Figure 5. shows the open dialog box for opening a ward presented as interactive graphical window with animations for added user friendliness. Screenshot of the software showing the layout of a ward is shown in Figure 6. . First the design of a ward is built then each bed is assigned to a patient where as each patients belong to some study. Designing window is very similar to most graphical applications, applying the same rules and techniques. So all objects in a ward are changeable and can be relocated as needed. After loading a ward, study manager can observe the location of each patient and find out which patient belongs to what study. Last 10 readings of blood pressure for a patient can be checked by simply moving the mouse cursor over the bed. As every study has thresholds for blood pressure, any reading out of those limits will be highlighter with a pink background. This allows monitoring and controlling all blood pressure readings and performing additional measurements if needed. Study managers are responsible for their studies only and hence cannot access patient's records from other studies. This is graphically expressed by fading the beds belonging to a different study.

Communication protocol. Communication protocol involves a sequence of commands sent through the serial port to obtain data from Dinamap such as device state, Diastolic and Systolic blood pressures. Serial communication is a popular means for transmitting data between a PC and peripheral devices. Serial communication uses a transmitter to send data, one bit at a time, over a single communication line to a receiver. This method can be used when data transfer rates are low or when transferring data over long distances.

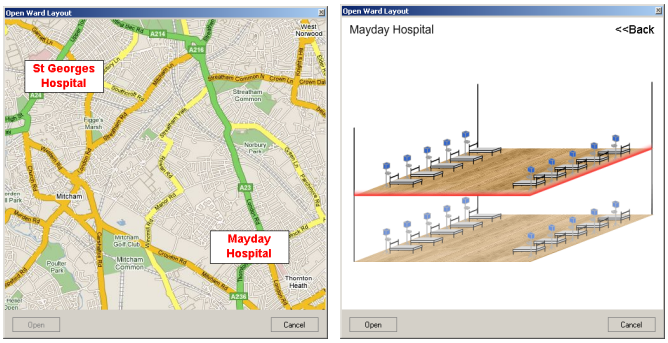

Figure 5. Animated graphical window for opening the ward for monitoring.

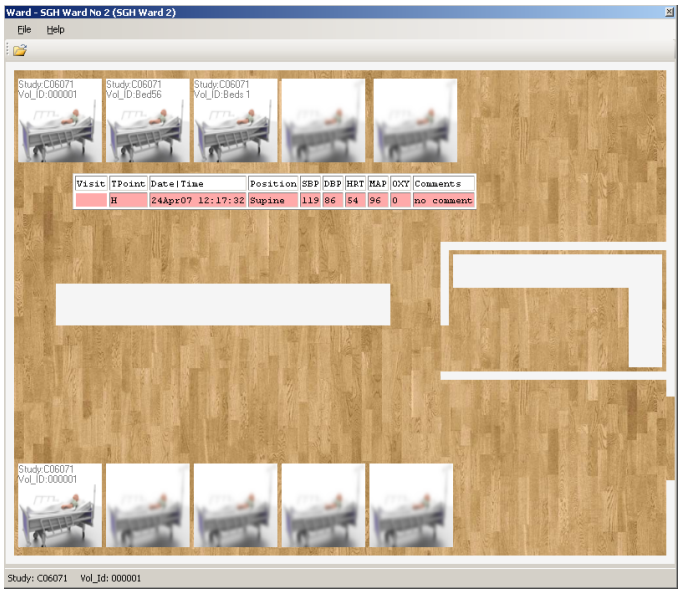

Figure 6. Interactive view of a ward for monitoring patient's vital signs.

Serial communication is the best choice most computers have one or more serial ports, so no extra hardware needed. The very small amount of data exchanged in the particular application rendered this protocol ideal. A serial cable was specially designed to connect the ports as required by Dinamap (Figure 2. f).

Figure 7. shows the block diagram of the communication between Dinamap and a PPC. Using a preset serial port PPC sends a command checking the device status every 5 seconds. If device is switched on, then set of commands are sent to device to obtain required values. In case of an explicit request for additional operations, appropriate command is sent to the device until respond is received. In case, when no data is received from Dinamap within 5 seconds, it is assumed that device is not responding or switched off and the software keeps checking Dinamap status every 5 seconds until response is received. A special technique is used to determine whether Dinamap acquired a reading from a patient as there is no explicit indication that measurement is done. However, Dinamap provides information on how many seconds ago was last determination is performed. Currently this operation is performed every 5 seconds and indication of a new determination can be found only by checking whether the value is different from the previous value.

System testing. The system passed 2 stages of tests for technical problems and usability features [2]. All users' proposed features were recorded and after further discussions changes were agreed and implemented into the system. Alpha release is issued for a final set of tests. The latest series of tests is being conducted on real studies by replicating (shadowing) standard manual procedures. Final assessment of the stem is to be conducted when all results are corrected, analysed and compared.

III. Discussion and Conclusion

Initial tests showed that the proposed system significantly reduces and even removes all customary errors normally occurring during manual recording.

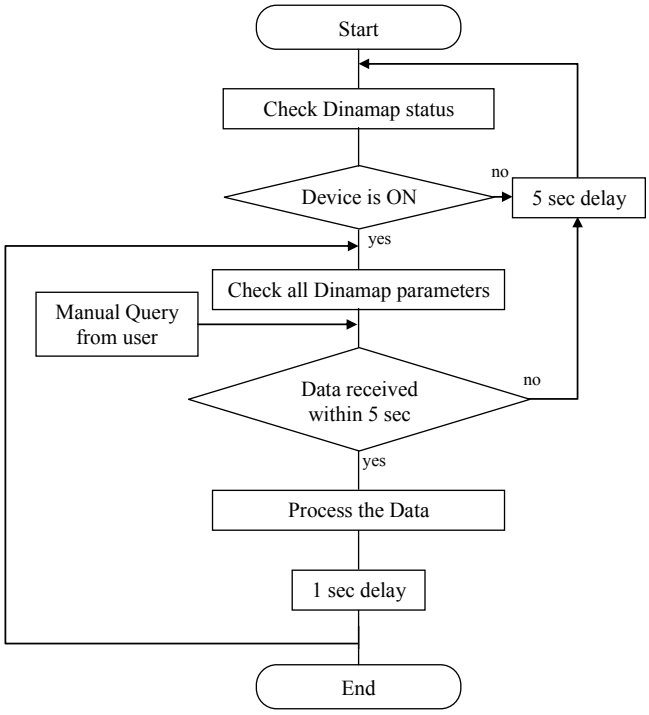

Figure 7. Communication schema of Dinamap with PPC.

At the same time, data entry process to the database is performed automatically avoiding the need for manual update of the study database, Current procedure require that i) acquired data forms are entered twice by independent operators for data protection and checked against each other and that ii) entered data are checked again for possible data entry errors.

Preliminary tests proved the advantage of the proposed advantage and consistency over the traditional way of acquiring vital signs. The system eliminated the possibility of invalid readings and saved significant amount of time on data entry and checking processes on mock studies. The system passed also the test for user friendliness as the nurses reacted positively commenting that it does not require preliminary knowledge on computers to be able to use it. The system is to be introduced in the practice in early 2008.

Acknowledgment

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[2] Myers Glenford J., "The art of software testing", 2nd ed., John Wiley & Sons, 2004.