Integrated System for Individual Decentralized Monitoring for the Personalized Medicine*

Denise Junger, Natividad Martínez Madrid, *Member, IEEE*, Nisar P. Malek, Christian Thies

Abstract— **Integrating tools and applications into a clinically useful system for individual continuous health data surveillance requires an architecture considering all relevant medical and technical conditions. Therefore, the requirements of an integrated system including a health app to collect and monitor sensor data to support personalized medicine are analyzed. The structure and behavior of the system are defined regarding the specific health use cases and scenarios. A vendor-independent architecture, which enables the collection of vital data from arbitrary wearables using a smartphone, is presented. The data is centrally managed and processed by attending physicians. The modular architecture allows the system to extend to new scenarios, data formats, etc. A prototypical implementation of the system shows the feasibility of the approach.**

I. Introduction

Personalized medicine focuses on the person itself, its characteristics and needs. By enriching existing patient information through continuously collected health data, personalized medicine could be supported. Therefore, wearables can be used which are worn by the patients, for example, as a watch. Indications of the medical potential of unspecific health monitoring exist but are not yet thoroughly evaluated [1]. Furthermore, the increasing spread of patients using wearables for self-assessment is already affecting medical consultations.

For specific medical use cases such as cardiac monitoring [2] or activity data during chemoradiotherapy [3], integrated solutions for specific vital parameters are available. Understanding patterns of vital parameters and diseases is an emerging application for big data analysis and machine learning.

A flexible and user-friendly platform for the continuous monitoring of patients' health data, including medical data interpretation, should be developed together with a large-scale evaluation in the real clinical environment, in order to provide medical evidence and enable a systematic approach. This platform can be used to complement the current making of diagnosis, therapy planning, monitoring of the patient's condition as well as clinical evaluation and research.

A new project initialized by the ministry of social affairs and integration from the state of Baden-Württemberg in Germany called *bwHealthApp*, firstly addressed in [4], has the goal of developing a telehealth system for personalized medicine, including both a central server and decentralized gateway applications for body area networks (BAN). The system should provide tools for data recording by arbitrary commercially available wearables as well as examination and validation. Moreover, interfaces to systems for automated data analysis, alarming or deep learning for predictors should be developed. This work presents the requirements, the design and the architecture for such an integrated system, focusing on the central server.

II. Methods

Established approaches [5] were used for the requirements analysis and architecture definition. A showcase application of individual decentralized monitoring from the medical routine was selected. Its use cases and their particular scenario requirements were analyzed. The requirements were generalized towards a system architecture covering the principal needs for applications of individual continuous data collection as needed for the prototype.

Medical partners of this project are the Center for Personalized Medicine (CPM) and the Clinic of Internal Medicine of the university hospital of Tübingen (UKT), Germany. The users of the main showcase are patients undergoing chemotherapy treatment in medical oncological daycare units of the Clinic of Internal Medicine at UKT. Here, continuous monitoring of vital parameters can support the detection of critical situations or overall changes in the patient's condition [3]. These may require an adaption of the therapy regimen or therapy in general. Since one of the main goals of medical daycare is keeping a patient in his accustomed environment, the collection of data has to be as flexible as possible, with as little interference with daily life as possible. Besides the patient’s situation itself, the needed type, quality and quantity of vital data or patient-reported outcomes (PRO) relevant for monitoring as well as their correlation with pathophysiological processes are object of research [1, 2, 3]. The continuous use of available and user-friendly consumer wearables can provide medical data, with all limitations of unsupervised applications, from a so-far unavailable situation. Concerning the personal involvement of the patients, appropriate compliance considering the application of the tools can be assumed.

* This research is funded by the ministry of social affairs and integration, state Baden-Württemberg, Germany. The authors declare that they have no competing interests.

Denise Junger is with the School of Informatics of Reutlingen University, Germany; e-mail: denise.junger@reutlingen-university.de

Natividad Martínez Madrid is with the School of Informatics of Reutlingen University, Germany and with I.M. Sechenov First Moscow State Medical University, Russia; e-mail: nati@ieee.org

Nisar P. Malek is with Internal Medicine I, University Hospital Tübingen, and with the Center for Personalized Medicine, University of Tübingen, Tübingen, Germany.

Christian Thies is with the School of Informatics of Reutlingen University, Germany; e-mail: christian.thies@reutlingen-university.de

In the first step, principal use case scenarios considering the routine operation of the system were obtained by interviews and workshops with the stakeholders from the CPM. Within the specific use cases, important functionalities for changeability, extendibility, configurability and flexibility were considered. System characteristics, as well as functional and quality requirements, were defined covering the core task and general goals needed for the new approach. Influential factors and boundary conditions were defined for a more specific system presentation. The requirements analysis leads to components as well as professional and technical interfaces to define a comprehensive concept of the entire system architecture. The concrete architecture was developed, and a functional prototype demonstrates the feasibility of the approach via system tests. It focuses on the recording of wearable data and configuration options to allow changeability, extendibility and configurability.

III. Results

A. Use cases scenarios

Patient registration

The first step for using the app in treatment is patient registration and configuration. The attending physician registers a patient to be monitored in the medical daycare unit. Therefore, the smartphone application is installed on the patient's phone. After the installation, the authentication of the patient takes place for the initial registration (e.g., QR code scans). The patient's personal information is linked with the smartphone to be used as the BAN gateway via the international mobile subscriber identity (IMSI). This makes the patient and sensor data as associable as possible. The IMSI is also used for identification during operation. For specifying the use case of the monitoring scenario, the attending physician configures the functionalities, which are needed by the patient.

Device initialization and measurement

For the first usage of the smartphone app, the devices and measurements need to be configured. If the medical question does not need uniform devices, the patient can use the wearables he prefers if they provide the necessary interface and parameters. The app checks which characteristics are covered by which connected device. Missing components are notified, and feedback is requested. Regarding the configuration created by the physician, background services are constructed for each health care parameter (e.g., characteristic). The services are configured for each specific sensor data separately to collect the characteristic data continuously.

Data collection

By starting the data transfer, the sensor data is recorded from the wearables in the defined interval within the background. For each characteristic, the received raw data is interpreted, saved and visualized. The saved data contains the characteristic UUID, the sample ID, the raw and interpreted value, a timestamp, the personal ID and the IMSI number. The patient is reminded of questionnaires like forms or single values through a pop-up or message in the defined interval. After entering the information, he can save the data to be transferred to the server for storage. Event data in the form of event recording or status reporting like confirming actions are saved the same way.

Connectivity and operation

During data collection, further functionalities are needed to handle broken connections, error feedback and reconnects. These have to be realized by the BAN. In contrast to current more supervised monitoring approaches (e.g., Holter monitor), this will need to be evaluated with respect to clinical viability. Data synchronization with the central server also has to be realized. A fundamental challenge will be general usability for people with limited capability to operate the smartphone app. In case of need, the smartphone app informs the user about relevant issues or messages from the attending physicians. If available and sufficiently evaluated, even alarms may be issued.

Flexibility and further use cases

The parameters to be recorded by the smartphone app, as well as their configuration, aggregation, evaluation and valid wearables, may be changed, updated or deleted during operation. This requires a flexible software infrastructure for the efficient deployment of the connected patient's smartphone app. Here, app stores provide well-established concepts for version management and stable deployment mechanisms. Further use cases concerning functionality, reliability, usability, efficiency, changeability and transferability, like data safety and security, error handling as well as system administration and operation are not considered here.

B. System characteristics and requirements

The core task of the bwHealthApp system is the centralized recording of individual health data from decentralized data sources i.e. BANs. The wearables should be combined individually with respect to medically required parameters and independent of specific vendors. To record the data, an individualized smartphone application should take control of the processing of the data from the wearables so that it can be stored and transferred for further processing to a centralized clinical server. This data will be used for diagnostic purposes and to enrich existing patient data available in other health information systems. All data should be provided for treating physicians. The paradigm for data monitoring on the smartphone is continuously and unlimited in contrast to classical limited approaches (e.g., Holter monitor). The whole system should be generic, modular, integrative and open. High flexibility and configurability, as well as changeability and extendibility, should be the main features of the system. Other aspects and related quality requirements are important as well but are not the focus of this work.

Influential factors for the system are the hardware and software infrastructure. Also, the performance of smartphone and server processors, as well as technical limitations of for instance battery lifetime, memory or network connectivity, must be considered. Different operating and database systems as well as middleware and communication servers between systems, their interfaces and protocols must also be taken into account. Other factors like handling offline and online modus for the app and essential external systems needed for the running system are relevant. For the programming, existing libraries, frameworks and systems (e.g., decision support), as well as existing interface specifications, data structures and models are to be used. The communication is based on standardized protocols as far as available. Effects concerning human life by monitoring health data and resulting diagnosis have to be identified and secured. All of these factors will be evaluated during the bwHealthApp project.

C. *System architecture*

The targeted solution is organized as a client-server system. The client-side includes a variable set of commercially available wearable devices and the smartphone application. The server-side consists of a gateway for the connection to the clients as well as the controller with access to internal systems. Each internal system may contain further subsystems and databases. In this paper, the server-side of the system will be described.

Wearables able to record information from the patients are combined into a BAN for which the smartphone app acts as data integration and preprocessing element. The data manager of the app initiates the data transfer to the gateway of the clinical server, ensuring authentication and data security.

Server-side

The gateway provides the interface between client and server, and manages authentication and access to the clinical infrastructure. Synchronous and asynchronous communication by standardized protocols, for instance exchanging configurations, is supported. The Fast Healthcare Interoperability Resources (FHIR) standard using JavaScript Object Notation (JSON) is applied as principal interface technology regarding system evolution, sustainability and interoperability.

The controller on the server dispatches data to the encapsulated application logic of the internal and external subsystems. The internal and specific subsystems of the bwHealthApp cover the administration of management data such as user identities, registered devices and individual parameter configurations, as well as runtime data such as assigned sensors and measured values. These are complemented by systems for data visualization, diagnosis support, and messaging for notifications. An identity manager provides authentication information for the gateway.

The bwHealthApp is designed for interoperability with external applications for clinical information processing like hospital information system (HIS) or tumor boards. It also serves as a data source for research applications such as machine learning excellences for predictor development or evidence-based medicine and provides the needed data warehousing tools.

D. *Functionality of the server-side*

The BAN and the app act as a patient frontend including storage, preprocessing and synchronization functionality. For the centralized management within the clinical infrastructure, all data is transferred to the gateway via specific FHIR service contracts.

Gateway and controller

Incoming messages are processed and evaluated regarding the validity, conformity, etc. Data security is ensured by encoded communication protocols and established authentication mechanisms (X.509). The messages are forwarded to the receiving controller. For communication, access information is configured within the internal components. The controller dispatches the administrative and health data to the integrated, encapsulated and clinical application logic. Therefore, the controller communicates with internal (e.g., identity management) as well as external subsystems (e.g., HIS) by providing medical standard interfaces (e.g., HL7, DICOM). This allows a flexible replacement of subsystems and even extendibility with other components.

Subsystems and databases

Internal, administrative subsystems take control of data management for user identities, device and measurement configurations, etc. The purpose is the management of individual monitoring cases. The system provides the visualization of individually monitored health data and in the first step is used by physicians for manual evaluation during individual consultations. Since there are yet no medical guidelines on how to use individual monitoring for personalized medicine, this marks the current system boundary. The further enrichment of a patient's electronic medical record (EMR) within a medical information system with a medical finding takes place in the respective external system. Interfaces are provided to transfer data, e.g., medical outcomes, to external subsystems for learning of predictors and ensuing automated alerting. Each internal and external subsystem manages persistency via its own database.

E. *Prototype of the bwHealthApp*

The proof-of-concept of the system has been tested with an initial prototype developed for the Android operating system.

Registration, configuration initialization, and data collection

The prototype provides a simple person model. The physician registers the patient in his role-specific GUI by associating a user ID and credentials to an existing person with a patient role. GUI modules for the patient are assigned regarding its specific medical question (e.g., a form for PRO questionnaires). The user ID is used for identification, login, measurement assignment, etc.

For the flexible and individual combination of data sources, the physician selects needed types of data from a list of identifiers for supported GATT characteristics as well as single items for manual data entry. Afterward, the sampling rate for each value as well as the synchronization schedule is configured. The configuration is saved.

Finally, the app is installed on the patient’s smartphone, where it can detect compatible wearables, establish the connections, and record the data according to the configured necessary characteristics for the patient.

Connectivity, operation and flexibility

If the connection is interrupted, the app automatically reconnects to the configured devices. Relevant issues and error situations are presented in specific status widgets.

The server includes prototypical implementations of required internal and external subsystems to test the data exchange between app and server. The server is implemented as a three tier Representational State Transfer (REST) architecture. Current functionalities provided by the REST server are, for instance, login, patient registration, receiving and storing measurement data. The application logic maps to the internal and external specific data models of the bwHealthApp. The data access layer provides a simple in-memory persistence solution, which covers the required data models.

Data model

The flexible handling of the measured data is the essential part of the data model. Therefore, the relation of device and characteristics is realized to represent the wearable configuration. Different value types for the characteristics (e.g., heart rate and RR interval for the heart rate measurement) are distinguished through data type description models that contain a unique identifier and are associated with the corresponding characteristic UUID. The combination of device, characteristic and data type descriptions is associated with the medical relevant values. This ensures the mapping of raw data to a semantic medical representation. The data model also represents manual, event, patient and user data, configurations, GUI modules, etc., necessary for the use cases.

System tests

The prototype has been successfully tested on an Acer Iconia One 10 tablet with a combination of one to three simultaneously connected sensors with different acquisition schedules. On the server-side, the patients were registered, and the needed characteristics and sampling requirements were configured. All seven sensor combinations and sampling schedules ranging from 1s to 120s yielded stable values over 30min. Connectivity and reconnections scenarios were also successfully tested.

IV. Discussion

Integrated and clinically approved solutions for specific vital parameters are just available for specific medical use cases and diagnosis. In contrast to these restricted monitoring applications, the depicted approach needs to combine changeable and case dependent sensor composition with medical data interpretation. The presented data integration solution was developed to enable the clinical validation of this open approach in the clinical environment. The designed system architecture depicts a vendor-free and open solution consisting of a centralized server and decentralized BAN gateway applications. The decoupling and separation between sensor data and value types allow handling varying sensor value combinations and sequential data representations (e.g., different sensor values within a GATT characteristic via BLE). The prototype was functionally evaluated and achieved the designated configurability and flexibility needed for the use cases.

For evaluation in the clinical environment, the prototype is currently finalized. Within the first evaluation phase, the reliability of connections, user acceptance, device handling, battery lifetime, and resulting data quality need to be assessed.

V. Conclusions

In conclusion, the work depicts the requirements analysis and architecture for the bwHealthApp, focusing on the server-side. The prototype's functionalities allow configuring required sensor data, synchronization schedules as well as connected devices for the patient's need. Via the app, data is continuously collected. The health data could support the making of diagnosis or therapy planning for personalized medicine. Flexibility and configurability, as well as changeability and extendibility, are central aspects of the system. This approach will need new medical, structural, organizational and administrative guidelines, which also have to be developed. To realize the comprehensive system, data security and protection mechanisms must be integrated.

Acknowledgment

This research is funded by the ministry of social affairs and integration, state Baden-Württemberg, Germany. The authors declare that they have no competing interests.

References

[1] J. Duscheck, "Wearable sensors can tell when you are getting sick", Stanford Medicine, 2017 [Available from http://med.stanford.edu/news/all-news/2017/01/wearable-sensors-can-tell-when-you-are-getting-sick.html, accessed on 28.06.2019].

[2] D. Dias, J. Paulo Silva Cunha, "Wearable Health Devices-Vital Sign Monitoring, Systems and Technologies", *Sensors* 2018, 18, 2414.

[3] N. Ohri, R. Kabarriti, W.R. Bodner, K.J. Mehta, V. Shankar, B. Halmos, M. Haigentz, B. Rapkin, C. Guha, S. Kalnicki, M. Garg, "Continuous Activity Monitoring During Concurrent Chemoradiotherapy", *Int J Radiat Oncol Biol Phys*, 2017, 97(5), 1061-65.

[4] D. Junger, Y. Möller, N.P. Malek, C. Thies, "Die bwHealthApp: Eine Plattform und Infrastruktur zum dauerhaften dezentralen individuellen Patientenmonitoring für die personalisierte Medizin", *Patientenzentrierte M-Health-Anwendungen für chronisch Kranke*, Springer, in print for 2020.

[5] H. Cervantes, R. Kazman, *Designing Software Architectures: A practical approach*, Addison & Wesley, 2016.