OC ToGo – Bed Site Image Integration into OpenClinica with Mobile Devices

Daniel Haak[a1], Johan Gehlen[a], Stephan Jonas[a], Thomas M. Deserno[a]

[a]Department of Medical Informatics, Uniklinik RWTH Aachen, Aachen, Germany

ABSTRACT

Imaging and image-based measurements nowadays play an essential role in controlled clinical trials, but electronic data capture (EDC) systems insufficiently support integration of captured images by mobile devices (e.g. smartphones and tablets). The web application OpenClinica has established as one of the world's leading EDC systems and is used to collect, manage and store data of clinical trials in electronic case report forms (eCRFs). In this paper, we present a mobile application for instantaneous integration of images into OpenClinica directly during examination on patient's bed site. The communication between the Android application and OpenClinica is based on the simple object access protocol (SOAP) and representational state transfer (REST) web services for metadata, and secure file transfer protocol (SFTP) for image transfer, respectively. OpenClinica's web services are used to query context information (e.g. existing studies, events and subjects) and to import data into the eCRF, as well as export of eCRF metadata and structural information. A stable image transfer is ensured and progress information (e.g. remaining time) visualized to the user. The workflow is demonstrated for a European multi-center registry, where patients with calciphylaxis disease are included. Our approach improves the EDC workflow, saves time, and reduces costs. Furthermore, data privacy is enhanced, since storage of private health data on the imaging devices becomes obsolete.

Keywords: Controlled clinical trials, Electronic data capture (EDC), Case report form (CRF), Mobile devices, mHealth, OpenClinica, Web services, Image management, Calciphylaxis

1. INTRODUCTION

Patient's data in controlled clinical trials is nowadays collected using electronic data capture (EDC) systems, which provide electronic case report forms (eCRF) instead of paper-based CRFs [1]. Errors during data acquisition are immediately prevented by automatic evaluation mechanism such as range checks or validations with more complex expressions. This avoids elaborative query processing, improves quality of data, saves time and reduces costs. In the last years, the open source software OpenClinica has been established as one of the world's leading EDC and clinical data management (CDM) systems [2,3]. The web application offers mighty functionality for collection, management, and storage of subject's data in multi-site clinical trials.

However, the healthcare sector seems to be ready for the next step, since a broad range of various mobile health (mHealth) applications joined in supporting medical personal and patients in various scenarios, such as health education and management, ambient assisted living, and health surveillance [4]. Although powerful mobile devices are available, usage of mobile applications seems to be not arrived in EDC systems for clinical trials yet: A mobile version of OpenClinica does not exists for smartphones or tablets.

Analogous to introduction of mobile applications in the healthcare sector, the role of imaging and image-based measurements in support of clinical trials, such as for development of neuropharamacological drugs, increased in the last years [5,6]. Hence, image integration and management have been improved in OpenClinica in previous work by small extensions: In [7] web services for transfer image and signal data into OpenClinica's eCRFs and invocation of automatic image and signal analysis have been proposed. Furthermore, context-related integration of binary large objects with (theoretically) unlimited file size into eCRFs has been shown in [8].

[1] Corresponding author: Daniel Haak, Department of Medical Informatics, RWTH Aachen University,
Pauwelsstr. 30, D - 52057 Aachen, Germany, email: dhaak@mi.rwth-aachen.de; phone: +49 241 80 85174, fax: +49 241 80 82426.

Medical Imaging 2014: PACS and Imaging Informatics: Next Generation and Innovations,
edited by Maria Y. Law, Tessa S. Cook, Proc. of SPIE Vol. 9039, 903909 · © 2014 SPIE
CCC code: 1605-7422/14/$18 · doi: 10.1117/12.2042847

However, OpenClinica still suffers in image integration via mobile devices, although image data is nowadays frequently available directly on smartphones or tablets, since they are used for image capturing. Thus, captured images are still stored on the mobile device or other temporal storage hardware, retrospectively attached to the eCRF and – hopefully – deleted afterwards. This workflow is particularly still performed, if data can be only collected on patient's bed site, which aggravates physician's workflow, costs time and leads to data privacy issues.

In this paper, we aim in enriching OpenClinica by a mobile application for instantaneous image data transfer into eCRFs. This will ensure close image integration in the clinical trial workflow. We demonstrate our concept and the resulting workflow by means of data collected for a medical register of the rare calciphylaxis (CUA) disease [9,10].

2. MATERIAL AND METHODS

We now first describe the components of our concept, namely OpenClinica as EDC system and OC ToGo as mobile application. After this, we present available interfaces for communication and their application in OC ToGo's workflow. In addition, we describe the CUA disease, which is used as example application to illustrate how OC ToGo can be applied on patient's bed site.

2.1 Components

2.1.1 OpenClinica

OpenClinica (Community Edition, Version 3.1.4.1) is an open source web application for EDC and CDM. The software allows data acquisition in clinical trials by user-defined eCRFs. OpenClinica maintains industry standards and is approved by regulatory authorities such as the Food and Drug Administration (FDA). The web application is based on a PostgreSQL database and developed using JavaServer Pages (JSP). This architecture allows access through modern web browsers and supports distributed data acquisition in multi-site trials. OpenClinica is structured in several packages such as OC Core and OC WS for core and web service functionality, respectively.

2.1.2 OC ToGo

OC ToGo is developed for mobile devices that are operated with Android using the Android Software Development Kit (SDK) [11]. Android is an operating system for mobile devices (e.g. smartphones and tablets) developed by Google, which is based on a Linux kernel. The Android SDK allows development of mobile applications in Java programming language and provides an application programming interface (API) including functionality for addressing hardware components of the mobile device. However, not all Java libraries are supported by Android, partly because Android uses its own virtual machine (VM) – called Dalvik – instead of the Java VM. Hence, several Android-specific libraries exists for various functionality. Our implementation is designed for Android version 2.3 ("Ginderbread"), since it is still compatible to newer versions, such as Android 4, but also supports older hardware.

2.2 Interfaces

Our systems uses web services and secure file transfer protocol (SFTP) for metadata and data transfer, respectively. Hence, it has to be ensured that both components of our systems provide suitable interfaces.

OpenClinica already offers several web service methods, which follow either the simple object access protocol (SOAP) or representational state transfer (REST) programming paradigm [12]:

- SOAP web service functionality is provided by OC WS component. SOAP services are based on a tightly coupled design and service calls are specified in web services description language (WSDL) contracts. This contract includes definitions of a remote function calls set, which specify via SOAP addressable methods and structure of transferable objects. SOAP methods include functionality for querying existing objects in an OpenClinica instance (e.g. studies, events and subjects) and for importing eCRF data in Clinical Data

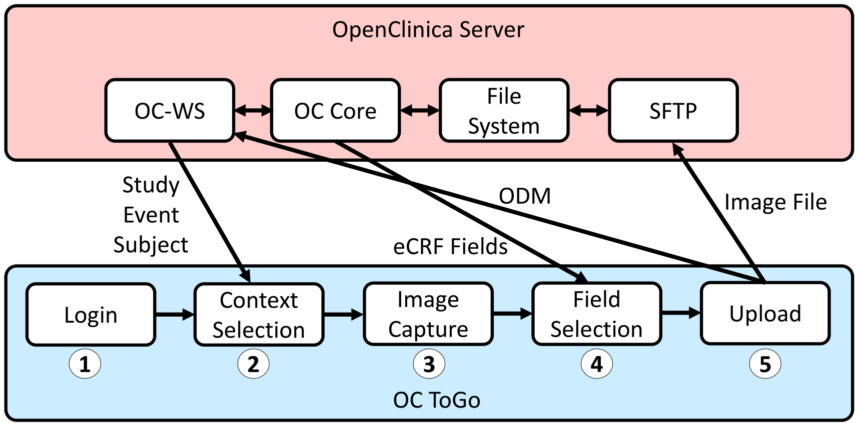

Figure 1: Architecture and workflow of OpenClinica and OC ToGo communication.

Interchange Standards Consortium Operational Data Model (CDISC ODM)[2] format. For authorization and data access, a security header based on the Spring WS-Security component[3] with user account information has to be added to each SOAP message.

- REST web services are embedded in the OC Core. REST services follow are more loosely coupled concept of design and are not based on specification contracts. REST methods are accessible as normal web pages by a stateless Uniform Resource Locator (URL). Communication with REST web service is based on hypertext transfer protocol (HTTP) methods, namely create, read, update and delete (CRUD). Using REST web services, the structure of an eCRF including defined fields and object identifier (OID) can be exported as ODM file.

Since OpenClinica is a web application, it typically runs on a web server. Hence, the operating system (e.g. Linux Debian 7.4) usually provides a SFTP server, too. If this is not the case, SFTP functionality can be included additionally, for instance, using software such as OpenSSH[4].

Natively, the Android SDK does not offer support for web services or SFTP functionality. However, icesoap[5] provides SOAP web service functionality for Android-based mobile devices. REST web services can be accessed using HTTP. Furthermore, an SFTP client is offered by the Java Secure Channel (JSch)[6] library, which is also supported by Android.

2.3 Workflow

The OC ToGo communication interface is composed of 5 steps (Fig. 1):

1. The address of the targeted OpenClinica instance with username and appropriate password account information are queried from the user, which are stored during the session. According to OpenClinica, the password is encrypted by the MD5 hash algorithm and included in the security header, which is added to all SOAP web service messages sent to OC-WS.
2. Using icesoap, OpenClinica is queried via SOAP web services for existing studies, events and subjects, which are visualized to the user for selection and setting up the context of the image.
3. The mobile device's photo picker is triggered, and an image is captured by the user.
4. Based on the context information, the eCRF structure of the chosen event is accessed in ODM format via REST web services. On receive, the ODM file is parsed, specified file upload fields are extracted and offered to the user for selection.

---

[2] http://www.cdisc.org/odm
[3] http://goo.gl/dyklzZ
[4] http://www.openssh.com/de/
[5] http://code.google.com/p/icesoap/
[6] http://www.jcraft.com/jsch/

5. Image integration is started and image data is transferred to the OpenClinica server via SFTP using JSch. For authentication on the web server, same credentials as for web service access are used. Meanwhile an ODM file is generated, which includes study, event, subject and target field OIDs from the context and the location of the transferred image on the OpenClinica server's file system. The final ODM file is encapsulated into a SOAP web service message, which is send to the import-endpoint of OC-WS.

After image transfer is completed successfully, temporally stored image data is deleted from the mobile device. The visualization of the transferred image in OpenClinica is done by JavaScript code, which is embedded into the eCRF.

2.4 Example application

Calciphylaxis (calcific uremic arteriolopathy, CUA) is a rare disease, which is still not completely explored and understood. Pathomorphologically, media calcification of cutaneous arterioles and extracellular matrix remodeling are the hallmarks of the disease, which leads to painful, ischemic, partly necrotic skin ulcerations. CUA has devastating conditions associated with high morbidity and a mortality rate > 80% [13].

For investigation of this disease, data of CUA patient's is currently collected in a medical register at Uniklinik RWTH Aachen [9,10]. Continuous photographic documentation and monitoring of the wounds has been recently suggested towards quantitative assessment of CUA disease [14]. Since skin lesions of CUA patients are often accompanied by a great deal of pain, in particular on patient's movement, hospitalization of CUA patients is aggravated. Hence, CUA patients are often – at least in early stages of the disease – under physician's care on patient's bed site, where also data capturing and photographic documentation takes place. However, CUA cases are treated in multiple centers nationwide.

3. RESULTS

OC ToGo has been implemented as proposed, resulting in a prototype of the mobile application, which will used by medical personal (e.g. study nurses) for integration of captured skin lesion images of CUA patients into OpenClinica directly on patient's bed site.

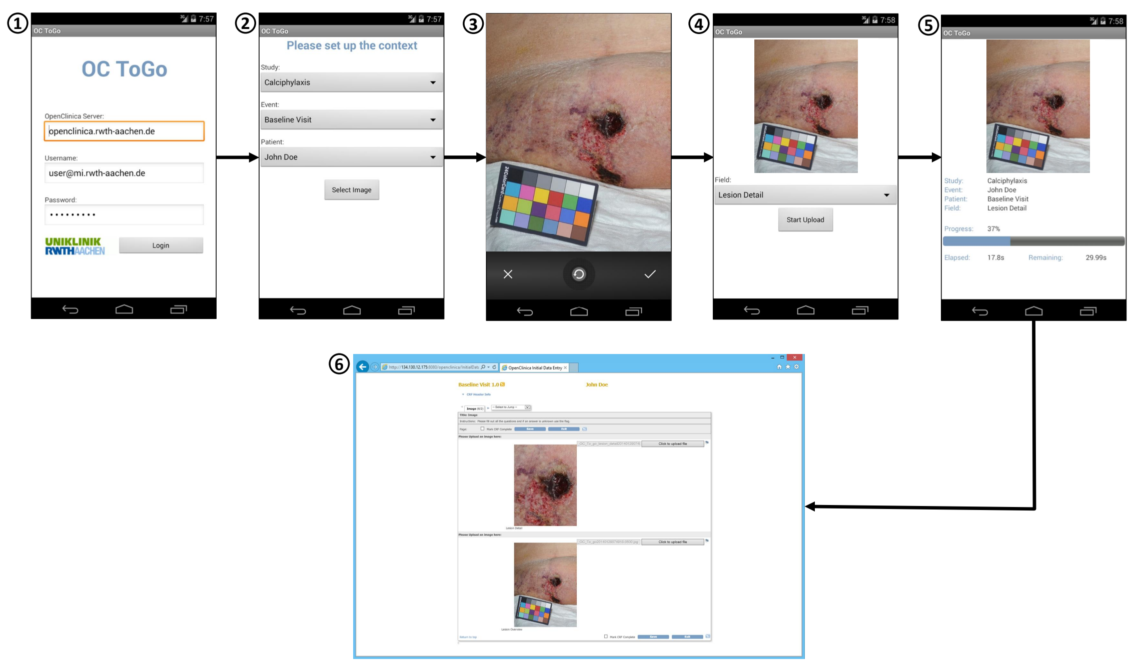

Figure 2: OC ToGo applied on skin lesion image collection of CUA patients.

Using our approach, the workflow is simplified. Equipped with a smartphone-based camera, the study nurse visits the CUA patient. Following a written standard operation procedure (SOP), photographic documentation is started and images are integrated directly into the eCRF (Fig. 2):

1. After starting the OC ToGo app, the start screen appears and the study nurse enters the address of the target OpenClinica server and corresponding account information.
2. After authorization, all existing studies, events, and subjects stored in the OpenClinica instance are displayed to the study nurse, who sets up the context of the image by selection.
3. The camera component of the smartphone is started and the study nurse captures images of a certain skin lesion. Several attempts may be needed until the nurse is satisfied with the image and confirms it.
4. The eCRF field, where the captured images should be integrated, is chosen.
5. The image transfer is started automatically, and progress information (e.g. estimated transfer time) is visualized. In addition, a summarization of the context is shown to the study nurse during transfer. Meanwhile, the study nurse is allowed to start the camera component again for capturing and transfer of additional images. Ending the patient's visit, the study nurse closes the mobile application.
6. On return to the web-based front end of OpenClinica, the captured images are already visualized.

Using OC ToGo, under restricted internet access for the mobile device on patient's home (UMTS connection), the transfer of a photograph typically compressed to 1.6 MB is lasting approximately 50 seconds.

4. DISCUSSION

OC ToGo provides a user-friendly and easy integration of image data into OpenClinica's eCRFs directly after capturing images with the mobile device's camera. Since stable image transfer and integration is ensured, patient's data has not to be stored on the mobile device or other temporal storage devices, retrospectively attached to the eCRF, and thereafter explicitly deleted. This avoids human errors, simplifies the workflow of the study crew, and increases patient's data privacy. In addition, the image is directly visible in OpenClinica for the medical staff in the clinical center, who can immediately give feedback to the study nurse during patient's visit, if necessary. Also, automatic quality checks for such images may be performed immediately, and communicated to the study nurse using the mobile devices. On insufficient data quality, the examination may be instantaneously repeated.

However, for querying OpenClinica for context information and image transfer, an internet connection has to be available, which may not always the case at patient's bed site. Hence, image capturing in offline settings should be supported in future version of the application. Then, data transfer will be triggered automatically as soon as the smartphone or tablet is connected to the internet again.

Without adapting OpenClinica's implementation, OC ToGo has been implemented using already available interfaces. This ensures compatibility with new releases of OpenClinica. However, some configuration is necessary on OpenClinica and the server before OC ToGo is ready to use. So far, OC ToGo supports image data only. Plain text and numerical data, typically captured in eCRFs, still has to be captured temporally on paper, and retrospectively entered into the eCRF. Alternatively, OpenClinica's eCRFs may be filled with OpenXData[7] or Mi-Co's Mi-Forms[8], which already have been successfully connected to OpenClinica[9,10]. However, OpenXData provides a user interface based on the Google Web Toolkit (GWT) and a Java-based mobile application for cell phones. Since the GWT project is a web application similar to OpenClinica and the Java-based application is designed for cell- instead of smartphones, it seems to be not really applicable on modern mobile devices. In contrast, Mi-Forms provides a broad range of software for various devices, including a mobile application for Android. Furthermore, Mi-Forms is also usable in offline settings. However, Mi-Forms is a commercial product, which may not be suitable for low-budget clinical trials, and OpenClinica's eCRFs have to be transformed to Mi-Forms designs first, which requires preparatory work. Hence, a low-budget solution supporting direct data entry into OpenClinica's eCRFs via mobile devices is still missing. Such an application would in special be

[7] http://www.openxdata.org/
[8] http://www.mi-corporation.com/
[9] https://trac.openxdata.org/wiki/OpenClinica
[10] http://www.mi-corporation.com/blog/8766/

interesting for EDC in developing countries, where mHealth applications are particularly suitable, due to the low costs of mobile devices [15].

Although Android seems to be the dominating operating systems installed on mobile devices worldwide. According to Gartner market research[11], 81,9% of mobile devices sold in third quarter of 2013 use Android. Hence, Android camera devices should be available in most clinical centers. However, OC ToGo versions for other mobile operating systems (e.g. iOS) will be developed in future.

5. CONCLUSION

Mobile applications conquer the health sector, but EDC seems to be still not well supported by mobile devices. With OC ToGo, an application for direct integration of images into the most popular EDC system OpenClinica by smartphones and tablets, a first step has been made. The application improves the workflow of medical personal on data capturing of patients with CUA disease and enhances data privacy. Support of offline settings and automatic generation of forms for other typical EDC data types will be implemented in future.

REFERENCES

[1] Pavlović I, Kern T, Miklavcic D. Comparison of paper-based and electronic data collection process in clinical trials: costs simulation study. Contemp Clin Trials. 2009 Jul;30(4):300-16.

[2] Leroux H, McBride S, Gibson S. On selecting a clinical trial management system for large scale, multicenter, multi-modal clinical research study. Stud Health Technol Inform 2011;168:89-95

[3] Franklin JD, Guidry A, Brinkley JF. A partnership approach for electronic data capture in small-scale clinical trials. J. Biomed. Inform. 2011;44:103-8

[4] Boulos M, Wheeler S, Tavares C, Jones R. How smartphones are changing the face of mobile and participatory healthcare: an overview, with example from eCAALYX. BioMed Eng OnLine 2011; 10(1):24..

[5] Uppoor RS, Mummaneni P, Cooper E, Pien HH, Sorensen AG, Collins J et al. The use of imaging in the early development of neuropharmacological drugs: a survey of approved NDAs. Clin Pharmacol Ther 2007; 84(1):69–74.

[6] Analoui M. Quantitative medical image analysis for clinical development of therapeutics. In: Deserno TM. Biomedical Image Analysis. Springer, Berlin, 2011, p. 359-75

[7] Deserno TM, Haak D, Samsel C, Gehlen J, Kabino K. Integration of image management and analysis into OpenClinica using web services. Proc SPIE 2013; 8674:0F1-10.

[8] Haak D, Gehlen J, Sripad P, Marx N, Deserno TM. Extension of OpenClinica for context-related integration of large data volume. Proc GMDS 2013 (in German).

[9] Brandenburg V, Specht P; Floege J, Ketteler M. Seven years of experience with the German CUA Registry. Abstract Presentation. American Society of Nephrology Renal Week. 2013

[10] Brandenburg VM, Sinha S, Specht P, Ketteler M. Calcific uraemic arteriolopathy: a rare disease with a potentially high impact on chronic kidney disease-mineral and bone disorder. Pediatr Nephrol. 2014 Jan 29. [Epub ahead of print].

[11] Meier R. Professional Android Application Development. Indianapolis: John Wiley & Sons; 2009.

[12] Zur Muehlen M, Nickerson JV, Swenson KD. Developing web services choreography standards-the case of REST vs. SOAP. Decision Support Systems 2005; 40(1):9-29.

[13] Brandenburg VM, Kramann R, Specht P, Ketteler M. Calciphylaxis in CKD and beyond. Nephrol Dial Transplant 2012; 27(4):1314-8

[14] Deserno TM, Sarandi I, Haak D, Jonas S, Specht P, Brandenburg V. Towards quantitative Calciphylaxis. Proceedings SPIE 2014; 9035: in press

[15] Akter S, Ray P. mHealth - an Ultimate Platform to Serve the Unserved. Yearb Med Inform 2010:94-100.

[11] http://www.gartner.com/newsroom/id/2623415