

Photographic Documentation by Mobile Devices Integrated into Case Report Forms of Clinical Trials

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Abstract. Subject's medical data in controlled clinical trials is captured in electronic case report forms. We present a mobile application (App) that utilizes the smartphone-integrated camera for integrating photographic documentation directly from subject's bed-side. Color reference cards are placed next to the wound and used for geometric and contrast registration. This ensures high image quality with the inexpensive consumer hardware. In addition, a code is detected from the card for subject identification. The App connects to an image analysis server and looks up the code-study-subject relation. Then, the smartphone connects with OpenClinica, an open source and electronic data capture system for clinical trials, which has been approved by the US Food and Drug Administration (FDA). The App is demonstrated by an ongoing clinical trial, where wound healing after a vascular surgery is followed up photographically. All 205 images collected in the study so far have been identified and integrated into subject's eCRF correctly. Avoiding manual mapping of photographs to study subjects avoids errors and latency, decreases costs, and improves data security and privacy.

1 Introduction

In clinical trials, the subject's data is captured in electronic case reports forms (eCRFs), which are hosted in electronic data capture (EDC) systems [1, 2]. Compared to the traditional paper-based method, EDC reduces errors, latency, and costs [3]. However, today's EDC systems insufficiently support integration of binary data such as medical signals or images. Some approaches have been published to extend EDC systems, either using a hypertext transfer protocol (HTTP)-based file upload [4] or the digital imaging and communications in medicine (DICOM) standard [5].

With OC ToGo, a mobile health (mHealth) application (App) has been developed [6]. The App integrates image data from subject's bed site via smartphones into the popular EDC system OpenClinica (OC). Using inexpensive consumer hardware with the smartphone-integrated camera, the photographs are calibrated regarding geometry, color, and contrast. For this, a standard color card is placed in the camera's field of view next to the area of interest. However,

the research nurse manually maps the images to the corresponding subject in the EDC system. This process is manual, relies on paper-based notes, and is therefore error-prone, complicated, and time-consuming.

OC ToGo has been extended and connected to an image analysis server (IAS) [7]. On the server, (i) the images are calibrated, (ii) the code printed on the card detected and (iii) mapped to the subject identifier (ID) of the corresponding study. After this, (iv) the photographs are automatically assigned to the corresponding study and subject via a look-up table. In this work, the architecture and the communication between the mobile App, OC, and the IAS is presented. The workflow of the entire system is demonstrated by an ongoing clinical trial, where an incision management system (IMS) for the reduction of groin wound infections after a vascular surgery is investigated.

2 Methods and material

2.1 OpenClinica (OC)

The open source project OC is one of the world's most famous EDC systems [1, 2]. The web applications offers rich functionality for collecting, managing, and storing of data that is captured in controlled clinical trials. OC is composed of a core and a web service package (OC-WS). OC-WS provides simple object access protocol (SOAP) and representational state transfer (REST) interfaces for data exchange.

2.2 OC ToGo

The mobile application OC ToGo integrates images taken with mobile device-integrated camera into OC's eCRF [6]. Via SOAP web services, studies, subjects, and events are queried from an OC instance after image capture. The research nurse then identifies the correct context of the images in the App. The images are transferred via the secure file transfer protocol (SFTP) to the EDC system.

2.3 Imaging equipment

A low-cost consumer color reference card (CameraTrax, USA) has been extended with an unique identifier printed as optical character recognition (OCR)-readable text and bar-code next to the color plates. The unique identifier is composed of 8 numerical digits in 3 blocks, which are separated by hyphens. The bar-code is generated using an ISO/IEC 16388:2007 encoding and includes a start and stop sign. The card has a size of 2 x 3 inches and is placed next to the wound within the camera's field of view. A smartphone-integrated 20,7 megapixel camera (Galaxy K Zoom, Samsung Electronics GmbH, Germany) with ten-fold optical zoom lenses (Carl Zeiss, Germany) is used.

Table 1. Card codes are mapped date-dependently to a study and a subject ID.

Card Code	Study ID	Subject ID	Expire Date
03-15-0003	S_IMS	SS_0001001	31.08.2015
03-15-0013	S_IMS	SS_0001002	31.08.2015
07-15-0005	S_IMS	SS_0002001	01.01.2016
07-15-0003	S_VITAV	SS_0001001	01.01.2016
07-15-0023	S_EVIE	SS_0001001	31.12.2020

2.4 Image analysis server (IAS)

The IAS is a sub-component of a Web-based clinical trial management system [4]. It has been developed with the Google Web Toolkit (GWT). The IAS integrates black-box algorithms for image analysis. It supports Java and Matlab programming languages. A RPC-interface is offered allowing (mobile) systems to send images and parameters, and to trigger the analysis. Resulting images and measurements are sent back to the requesting system through the same interface.

On the IAS, the algorithm described by Jose et al. [8] is applied for geometric and color registration. The image processing pipeline starts with the lattice detection algorithm by Park et al., which is based on a mean-shift belief propagation in a Markov random field. This ensures robust localization of the card, which actually can be placed anywhere in the image and within a wide range of sizes and perspectives. Based on the a-priori known card geometry, the character printed code field is extracted and parsed by using the ocr-method of Matlab. A look-up table on the server maps the code to the corresponding study and subject ID. An expiration date allows multiple applications of cards within and between different trials (Tab. 1).

2.5 System interaction

The OC ToGo App stepwise interacts with OC and IAS (Fig. 1):

1. After recording the image, it is sent via SFTP to the IAS and calibration and OCR are performed. This yields an additional transformed image and processing parameters. Based on the OCR-extracted identifier, study and subject IDs are queried from the look-up table in the database.
2. The original and the transformed image, as well as the looked up IDs are sent back to the OC ToGo App via SFTP and web services, respectively.
3. The user confirms study and subject identification.
4. The events of the study are queried from the OC instance via web services.
5. The original and the transformed images are transferred to the OC server via SFTP and references to their location on the file system are stored in the eCRF via web services.

2.6 Evaluation study

In the IMS study (ClinicalTrials.gov #NCT02395159), the reduction of groin wound infections after a vascular surgery by negative pressure is investigated. A wound is recorded photographically at baseline (after surgery) and during the follow-up visits at week 1, 2, 5, and 7. In total, five images are captured sequentially from all the study subjects. Until now, 41 subjects have been included in the ongoing trial, partially recorded, and 205 images are available.

3 Results

The workflow for smartphone-based documentation of wounds is illustrated in Fig. 2. The research nurse captures images with the smartphone-integrated camera while placing a personalized color card next to the wound (Fig. 2, Step 1). The system suggests IDs for the study and the subject (Fig. 2, Step 2). After confirmation, the research nurse selects the current event according to the study protocol (Fig. 2, Step 3), and the image data is transferred to OC (Fig. 2, Step 4).

After successful transfer, the original and the calibrated images are embedded in the eCRF, which corresponds to the identified subject and chosen event of the study. In case the identification fails, the user can manually choose from existing studies and subjects of the OC instance. If no internet connection is available, the photographs are securely stored on the device and are embedded in the eCRF as soon as an internet connection is established.

So far, 205 images of wounds have been captured in the IMS study. For all images, the study and subject identification has been successfully performed and the photographs have been integrated into the correct eCRF.

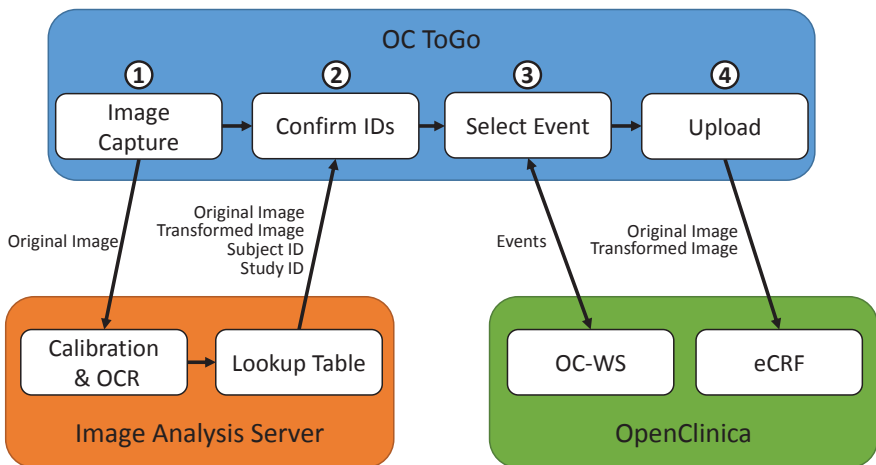


Fig. 1. System architecture and workflow of OC ToGo.

4 Discussion

The identification of subjects for mobile photographic documentation in controlled clinical trials is performed completely automatic. Based on a color reference card that is already used for geometric and color calibration, an OCR-based subject identification is performed. This process allows automatic transfer of the captured images into the eCRF. The system is composed of an App running on the mobile device (smartphone) with an integrated camera, an analysis server with embedded Java and Matlab algorithms, and the EDC system OpenClinica. Mapping of images with study and subject is performed seamlessly in the

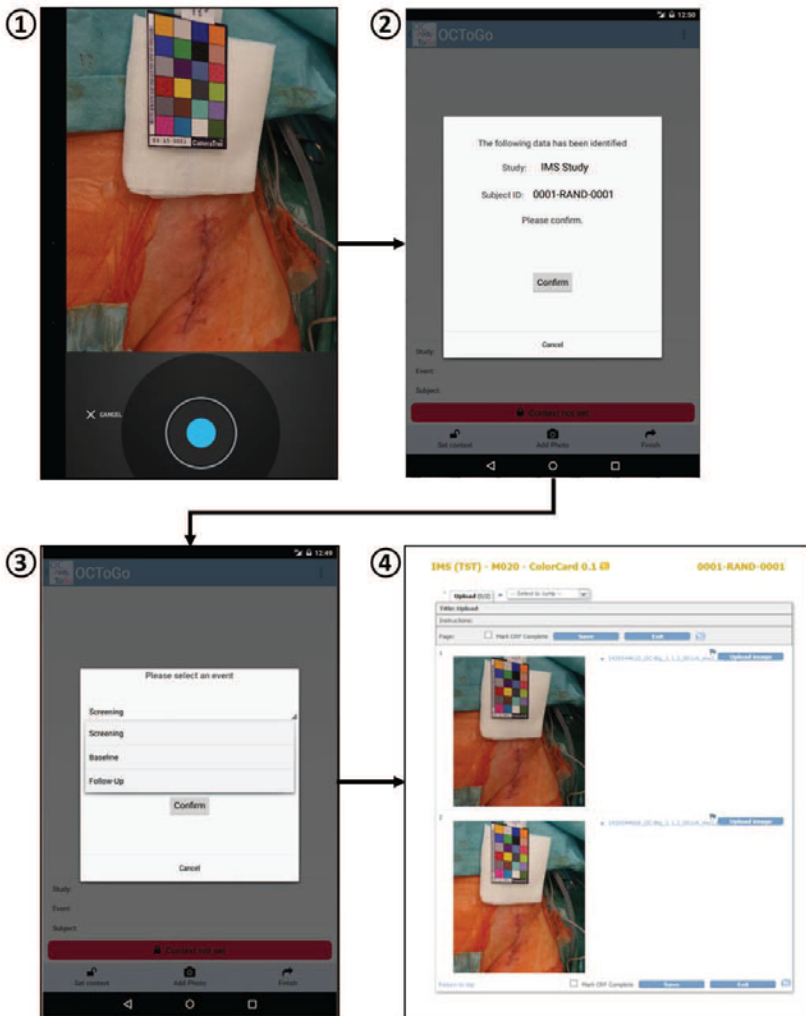


Fig. 2. Final workflow of OC ToGo.

workflow and completely automatic. This avoids any manual and error-prone steps for the study personnel, e.g., the research nurse. However, the automatic recognition still can be improved by introduction of an automatic recognition of the bar-code, which is already printed on the card, but not considered yet. Comparison of both codes further reduces errors, e.g., in case one of the codes is covered on the image. Labeling of material already has simplified the workflow in other medical processes, such as the identification of blood transfusion recipients [9]. In general, all kind of identification methods such as quick response (QR)-codes are applicable. However, a reliable image quality still has to be ensured by appropriate standard operating procedures (SOPs). This is another advantage of simultaneous recording and processing. If the automatic analysis fails, the research nurse is notified when still being at the subject's bed side and can re-capture the scene.

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