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Establishing an Interoperable Clinical Trial Information System Within MIRACUM

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Abstract. In the long-run we wish to demonstrate the power of linking clinical trial information to routine health records for straightforward patient recruitment – not only at each single hospital but in a large German consortium (called MIRACUM). In such architecture a hospital wide clinical trial registry (CTR) plays a major role. All such site specific CTR however, also need to be interoperable and support automated data provision for a central MIRACUM wide trial registry. Based on a survey of already existing trial information systems at each partner site and a comparison of their functionality, a joint requirement specification was created, a minimal MIRACUM wide trial core dataset was defined and an architecture was designed in which each MIRACUM partner could keep their autonomous system decision. Partners could however also join forces in a cooperative enhancement of a new open source trial registry. Thus, sites with no trial registry could be supported by the others and synergies used. Finally, the newly developed CTR will allow modular site specific add-ons and can also take over the function of the MIRACUM wide trial registry. In this paper we describe the process, how such a consortium-wide CTR was designed and developed, while always keeping cross-site interoperability as a major requirement.

Keywords: clinical trial registry, health information system, MIRACUM, MI-I

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1. Introduction

Optimal patient care relies on the results of clinical trials, as these are considered the gold standard for testing therapies and new diagnostic tools. The participation of patients is crucial for successful trial conduction. Many clinical trials fail due to insufficient recruitment of trial participants [1]. To improve the recruitment process with IT solutions, the MIRACUM consortium [2] in the German Medical Informatics Initiative (MI-I) strives to integrate clinical trial information containing inclusion and exclusion criteria in the hospital information system (HIS) of the partner sites and to map it to available routine data and in addition to share trial information via a consortium wide trial information system. Thus, local and inter-site interoperability is a crucial requirement. Furthermore, the trial information system needs to be connected to other systems, e.g. via import interfaces for trials from existing trial registries (German Clinical Trials Register (DRKS) [3,4], clinicaltrials.gov [5], and EU-CTR [6]) in order to achieve high data quality and allow a single point of entry. The university hospital sites were allowed their autonomy in selecting the respective local system, nevertheless providing synergies through joint development efforts for a new open source clinical trial registry (CTR). In this work we describe the basic components of an interoperable Clinical Trials Information System environment for the MIRACUM consortium and the process towards such a system.

2. Methods

2.1. Analysis of existing trials registries at participating sites

To detect and define requirements for local and consortium wide trial information systems, the status quo at each site was elicited with a structured interview using the consortium-wide Atlassian Confluence® Collaboration Platform for distribution and responses. Based on this survey, requirements for further development were discussed and evaluated in a face-to-face meeting and telephone conferences until unanimous agreement of the MIRACUM stakeholders was reached.

2.2. Requirement Specification

The MIRACUM data integration center architecture builds on an ecosystem of interoperable, (mostly) open source systems as components for dedicated tasks in the data integration scenario. This ecosystem is called MIRACOLIX [7]. The components do need to provide core functionalities and satisfy integration interfaces defined within the consortium, but besides this each site can still decide which system to apply for a certain functionality. One functionality is to include core information about all trials running at each hospital site and thus foster the design and implementation of an IT-supported patient recruitment system. For this purpose the minimal requirements for a site specific CTR and for its interoperability with a MIRACUM wide CTR were specified.

2.3. Definition of key parameters

A set of key trial parameters was derived from existing registries esp. the DRKS and defined in a consensus process, implemented on the Atlassian Confluence® Platform. Final unanimous agreement was reached in discussions at a face-to-face meeting and telephone conferences. Those key parameters shall be part of the MIRACUM wide CTR and local site specific CTR need to support export and mapping of their respective data into this central trial information system.

3. Results

3.1. Status quo

The current status of clinical trial information systems at each partner site is summarized in Table 1. Due to historical reasons and local requirements, the implementation of trial information systems at the MIRACUM partner sites is heterogeneous and ranges from inhouse developed home-grown systems (IHD) to commercial systems. Some of the sites did not yet have a comprehensive CTR (except e.g. Excel-based solutions within single clinics). Often existing CTRs only contained a subset of trials (e.g. oncological trials within a comprehensive cancer center). Four sites used commercial software products for trial management, whereas the other sites used in-house developments or lists based on Microsoft Excel®. Even within a single site (e.g. site 3) some clinics maintained their local system besides the hospital-wide CTR currently being established.

Table 1. Status quo of trial information systems at each MIRACUM site at project start. IHD: in-house development

Site	IT-solution	Applied in	Export formats	No of trials
	SecuTrial®	Hospital wide	SAS	Approx. 500
	IHD / SecuTrial®	Oncology	XML	800-900
	IHD: JAVA-based web application	Hospital wide	CSV, PDF	Approx. 2700
	Redmine®	Anaesthesia dept.		20
	Excel®	Oncology		n/a
	Desemo®			n/a
	not yet established			n/a
	not yet established			Approx. 200
	not yet established			Approx. 180
	centraXX®, currently being established	Neurology, Cardiology, hospital wide planned	SAS, STATA, XML, CSV	n/a

Since local requirements and CTR status quo varied among the MIRACUM partners (Table 1), agreeing on *one* IT solution to be used by all partners was not an option. The MIRACUM-wide exchange of trial information is designed to be independent of the site-specific IT solutions and foster patient recruitment among and across all MIRACUM partners. MIRACUM sites with already quite advanced and comprehensive systems for trial information, often commercial, decided to stay with those systems and configure them in accordance with the joint MIRACUM set of requirements. Others would join forces to further enhance and modularize a prototypical open source system that had already been developed at one of the sites. It is a JAVA-based prototypic system, where interfaces to import trial definitions

and characteristics from the DRKS and from clinicaltrials.gov were already planned and partly implemented. Together with some of the sites that did not yet have an established CTR, or didn't yet have implementation or development plans yet, they decided to start a joint MIRACUM team effort was initiated to further enhance this CTR and modularize it, allowing participating sites to adapt it to existing locally defined requirements

3.2. JAVA-based web application

Initially, a web-based software solution was used at site 3 to register their trial information. Its data structures and functionality were constructed on the foundation of the DRKS. Import functions for trials from the DRKS and from ClincalTrials.gov are already realized and an import function for trials from the EU-CTR is planned. Hence it will be possible to import all sponsor-registered trials from these three WHO-compliant registries without repeated manual input. All known trial identification numbers are used to filter out double entries. At site 3 hospital-wide LDAP-authentication is used, other identification/authentication mechanisms are possible.

Depending on the characteristics of a trial, additional custom parameters can be captured, which may include department or indication specific information. This customization can be performed individually by each MIRACUM partner. Trial parameters which were imported from DRKS/ClinicalTrials.gov are write-locked to always safeguard consistency with those trial information systems. In contrast the additional custom parameters, which are only persisted locally, can be modified over time. The defined set of key parameters (see next section) of each trial can be extracted from the data, shared with the MIRACUM partners and imported in the MIRACUM wide CTR (which will be realized early 2019 also based on this open source development).

3.3. Key parameters for MIRACUM-wide exchange of trial information

To establish exchange of trial information among all MIRACUM partners, a set of key parameters was defined containing a subset of the WHO Trial Registration Data Set (TRDS) (24 items) defined by the ICTRP [8] at the WHO with special emphasis on a structured way to describe inclusion- and exclusion criteria, while leaving out information not interesting for recruitment, e.g. sponsor information:

- Primary Registry and Trial Identifying Number (WHO item 1)
- Secondary Identifying Numbers (WHO item 3)
- Contact for Scientific Queries (Principal Investigator) (WHO item 8)
- Scientific Title (WHO item 10)
- Health Condition(s) or Problem(s) Studied including ICD-code (WHO item 12)
- Key Inclusion and Exclusion Criteria (incl. gender, age) (WHO item 14)
- Study Type (WHO item 15)
- Recruitment Status (WHO item 18)

The following further items were integrated into the MIRACUM key parameter set:

- participating institutions and departments,

- information about the last import and
- the date of the last changes.

4. Conclusions

Interoperability is an essential feature of large data sharing initiatives in order to leverage the value of sharing local data sets and joint software developments. Within this project the MIRACUM sites have illustrated that the definition and agreement of core datasets and core system functionalities of components within the comprehensive data sharing architecture allow sites to keep their autonomy in single component selection, while still able to interface with respective MIRACUM wide components, external resources (e.g. DRKS/ClinicalTrials.gov) and to share information across the network. Such an architecture is depicted in fig.1 that summarizes our ideas.

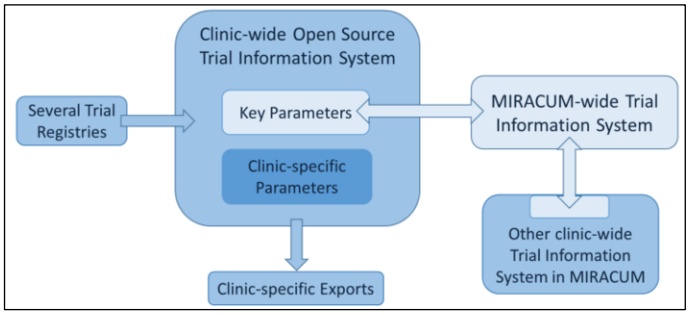

Figure 1. Embedding of hospital-wide trial information system. Trial information landscape.

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