Web-based Documentation System with Exchange of DICOM RT for Multicenter Clinical Studies in Particle Therapy

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ABSTRACT

Conducting clinical studies is rather difficult because of the large variety of voluminous datasets, different documentation styles, and various information systems, especially in radiation oncology. In this paper, we describe our development of a web-based documentation system with first approaches of automatic statistical analyses for transnational and multicenter clinical studies in particle therapy. It is possible to have immediate access to all patient information and exchange, store, process, and visualize text data, all types of DICOM images, especially DICOM RT, and any other multimedia data. Accessing the documentation system and submitting clinical data is possible for internal and external users (e.g. referring physicians from abroad, who are seeking the new technique of particle therapy for their patients). Thereby, security and privacy protection is ensured with the encrypted https protocol, client certificates, and an application gateway. Furthermore, all data can be pseudonymized. Integrated into the existing hospital environment, patient data is imported via various interfaces over HL7-messages and DICOM. Several further features replace manual input wherever possible and ensure data quality and entirety. With a form generator, studies can be individually designed to fit specific needs. By including all treated patients (also non-study patients), we gain the possibility for overall large-scale, retrospective analyses. Having recently begun documentation of our first six clinical studies, it has become apparent that the benefits lie in the simplification of research work, better study analyses quality and ultimately, the improvement of treatment concepts by evaluating the effectiveness of particle therapy.

Keywords: clinical studies, particle therapy, documentation system, DICOM RT, PACS

1. INTRODUCTION

Particle therapy as an innovative and relatively new technique is of increasing interest in radiation oncology. Compared to standard radiation therapy (RT) with photons, the main advantages lie in the distinct physical characteristics of particles enabling, in the case of protons, a more precise dose delivery to the target and thereby sparing of normal tissue and organs at risk.[1,2] Neutrons, especially carbon ions, do not have this improvement in dose distributions, but show a significant enhanced radiobiological effectiveness, potentially leading to an increase in local tumor control. Many clinical analyses have already shown promising results for several indications;[3] a variety of clinical studies are currently in progress and further studies are being planned in order to evaluate the benefits of ion therapy in tumor treatment.

The Heidelberg Ion-Beam Therapy Center (HIT) began patient treatment in November 2009,[1] with its main focus lying on clinical studies. Due to the fact that until now only a few ion centers are in operation, future centers are certain to profit from the progress at the HIT. Until now, particle therapy demands high organizational flexibility. Physicians and patients, desiring to use this new technology, are confronted with organizing complex treatment sequences. Naturally, it is necessary to be able to follow the course of treatment at all times to provide optimal patient care.[4] Especially for external patients, knowledge of previous treatment is vital for the responsible oncologist in order to plan ion radiation. Understandably, the referring physician is also interested in the progress of treatment, while both parties will be awaiting the follow-up results. To accomplish that,

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the key solution would consist in one central documentation system accessible by all involved parties, such as external/internal oncologists, physicists and researchers.

Within the framework of the European ULICE project (Union of Light Ions Centers in Europe), researchers at HIT are set before the task of developing a common database with transnational access to build a platform for international, multicenter clinical studies where all patient data is gathered by the participating institutions. During this process, increasingly large amounts of patient data must be analyzed. In general, analyzing clinical studies, in particular retrospectively, which contain large patient groups, is rather difficult, because of size and heterogeneity of the data and the different documentation style within different departments. Especially radiation oncology as an interdisciplinary field must deal with a large variety of voluminous datasets from various information systems in the hospital. This demands special coordination in data management. Therefore, we primarily need a documentation and management system integrated in the clinical environment, but preferably an additional, built-in possibility for immediate analysis of the collected data.

Nowadays, in the age of modern technology, the first choice exists in using Internet-technologies for transnational access. It is easiest and most common to network over the web. It has not only the advantage of having a high user acceptance and intuitive usability, but also to be platform-independent. Especially in healthcare, it is crucial to have all patient information on hand - even on mobile devices[5] - particularly in radiotherapy where one is always involved with imaging information.

In this paper, we describe our approach and first step for achieving an international web-based documentation system in particle therapy. With its main aim to transfer results, experiences with treatment concepts and ideas to new ion centers to be set up worldwide.

2. METHODS

It is still not unusual for clinical documentation to be achieved with collections of paper-based case report forms (CRFs), excel sheets and local copies of medical images. It is not necessary to explain the disadvantages of such unstructured and distributed documentation. The main goal of our approach is to provide a central web-based system, which has interfaces to the main existing information systems of the hospital for data import, to avoid double entries of patient and clinical wherever possible. Aside from this, all data is collected in specific modules, which can easily be adapted to individual needs. Security and data protection measures are implemented to fulfill the legal requirements.

2.1 General principles and architecture

The basis of the documentation system is built with an open source PostgreSQL database with standard interfaces to the PACS world.[6] It is based on the DICOM data model and can be dynamically extended with additional data structures. Interfaces allow the exchange and process of DICOM data as well as other information via HL7 messages. The underlying components are compliant with the IHE Framework and have been tested at four European IHE Connectathons.

A telemedicine record functioning as an extension is added with the characteristic of an electronic patient record (EPR) and a professional DICOM viewer (Class IIb; according the European Medical Devices Directive). It allows the user to exchange, store, process and visualize text data, all types of DICOM images and any other multimedia data.

This general infrastructure was originally developed by the CHILI GmbH, a company specialized in radiology systems with whom we are privileged to maintain a strong cooperation and to whom we attribute the technical know-how and experience.[7] Based on our vision for the ULICE project, we have planned and implemented additional functionality and customized the general setting, thus creating a specialized study documentation system.

2.2 Data import, handling and storage

On the one hand, data can be imported to the system automatically via the mentioned standard DICOM and HL7 interfaces. On the other hand, it can be imported manually by web-upload through an interface, which has been implemented as a Java applet running in any Internet browser. The Java applet can even receive and send data with DICOM C-Store. Moreover, DICOM CDs can also be read and written with the same interface.

Furthermore, a long-term archive (6 TB) is available to store and backup all DICOM and documentation data. This is realized with a SilentCube, which is a technology using a Network Attached Storage (NAS) with a RAID-1 hard drive system. It offers a modular solution that is not only easy scalable and highly redundant, but also highly available - the main requirement for long-term storage of patient data.

The web-based graphical user interface is independent both from the running operation system (e.g. MAC OS, Linux, MS-Windows) and the used browser (e.g. Safari, Mozilla, Internet-Explorer). Access to patient information is always patient-oriented. First, the system shows the list of all patients, which can be sorted or filtered to specific needs. Figure 1 shows the view on a single patient with the integrated radiation information. With a click on the thumbnail, the DICOM RT viewer is opened with the corresponding examination.

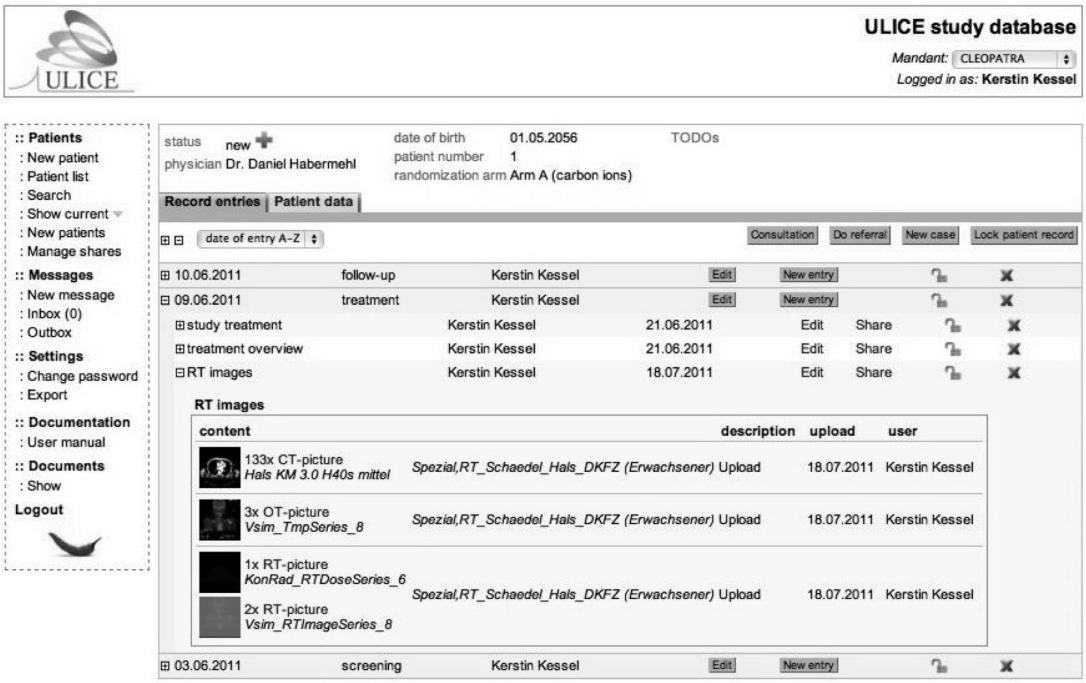

Figure 1. Screenshot showing a patient record with imaging information linked to the study documentation

2.3 Workflow integration

The system is connected with the Hospital Information System (HIS), the Laboratory Information System (LIS), the Picture Archiving and Communication Systems (PACS) and the Oncology Information System (OIS) in order to acquire automatic input via HL7 messages and DICOM (see Fig. 2). Interfaces to the HIS provide the initial setting of patients with HL7-ADT messages. Laboratory findings such as blood results are automatically imported via HL7-ORU messages from the LIS, and interfaces to the PACS reveal radiation data by DICOM RT and DICOM RT ion (e.g. DICOM RT image/structure set/plan/dose/treatment record, Computer Tomography (CT) and Magnetic Resonance Imaging (MRI) data). The OIS supplies further radiation information such as first and last day of irradiation, radiation method and the applied particle-type over HL7-DFT messages. These messages are also used to trigger a DICOM Q/R (Query/Retrieve) on the different PACS to import radiation data into the documentation system and map it to the corresponding patient when it is available.

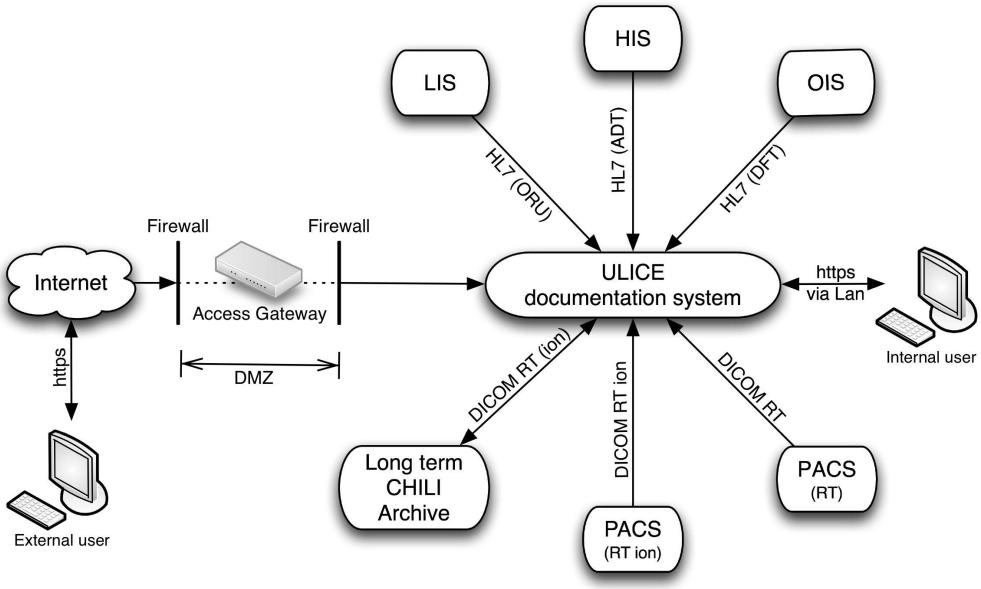

Figure 2. Connected systems and used protocols

One external user is, for example, a referring physician possibly from a cooperating partner from abroad. He can upload all existing imaging information and detailed treatment data (e.g. surgery findings, blood results) from the patient's previous treatments into the documentation system over the Internet. The physician at the HIT will review the case and decide if an indication for particle therapy is given and possible a study inclusion. If the patient is accepted for an irradiation in Heidelberg, all further essential data is documented in the system. After the particle therapy, the referring physician continues the common documentation during the follow-up period for a complete treatment overview. As external PACS are not connected, there is always the possibility for manual upload for DICOM or any other multimedia data.

2.4 Security concept

As the system is used in a clinical environment, specific privacy and security mechanisms are required. The system uses the https protocol to exchange data between the central server and other systems (see Fig. 2). This enables an encrypted data transfer. Thus, a user can, for example, open a browser somewhere on the Internet and connect to the documentation system. He then has a DICOM C-Store provider running in the browser, which receives DICOM data from the user's local environment and sends it encrypted via https (through several firewalls) to the central data repository. Additionally, client certificates are used to provide more host-to-host security and to verify authorized browsers of external project partners.

Users need an account and password to access the system. A roles-and-rights concept has been established to configure access to each study or client of the system separately. The roles of a user can change dynamically and are study-dependent, i.e. being a leading physician (level 1) for one study, and for another a standard user with only reading rights. So far, we created the main roles physician (level 1, level 2), study nurse / case manager, physicist, standard user (e.g. student) and admin. Additionally, we can merge users into user groups, for example, all users from a specific institution.

Communication with external users from participating study centers is realized by an intermediate application gateway in the demilitarized zone (DMZ) which receives https-requests, checks them and sends only valid requests to the server in the intranet of the hospital (see Fig. 2).

Furthermore, all data can be pseudonymized by a PID-Generator by the TMF (Technology, Methods, and Infrastructure for Networked Medical Research),[8] when it is imported into the system. The original patient information is then kept in a separate database. When a user has the right to view all data of a patient, the data

is de-pseudonymized instantaneously - but only for the specific user. One user is typically the treating physician with full access to all data. Other users, e.g. researchers or external physicians, only have restricted access to pseudonymized data.

2.5 Module design

The documentation system has a advanced graphical administration tool, which includes a form generator for designing and adjusting specific modules for individual clinical studies (XML based). This covers both the extension of the data structures and the graphical user interface. A major advantage is that this tool can be used by the local system administrators and does not need new developments by the computer experts. A test system has been set up where new modules can be created, validated and tested before they are used in the productive environment.

Very early, we decided not only to document study patients, but also patients not participating in clinical studies (non-study patients), meaning all patients ever treated at the Heidelberg facility, because, of course, not every patient fulfills the inclusion and exclusion criteria of a particular study. This can only be achieved by similar basic documentation for each type of patient (study or non-study) and led us to develop different kinds of modules. Some modules are used for all patients, and some are specifically designed and unique for individual studies to document specific parameters that are required by the study protocol and / or CRF.

The basic modules include vital patient information, e.g. basic data and treatment overview as well as radiation data and case management information. Depending on the location of the tumor region, a specific region module (e.g. head and neck, brain/skull base, upper GI, lower GI, spine, pelvis and extremities) must be used for documentation during screening, treatment and follow-up periods. These modules contain information that is again similar for all types. However, corresponding symptoms and side-effects are documented individually. Other common denominators in all studies include a recurrences/metastases module and a module to document the death of patients.

2.6 Usability

Clinical documentation and analyses is crucial for an optimal patient treatment and medical research. However, this is not a particularly popular task. For this reason, we aim to replace manual input with automatic documentation wherever possible. Several features are implemented to support the documentation process and prevent double entries of patient information. Certain modules are only selectable if predefined conditions are fulfilled. Some modules are only selectable once for each patient or depending on a previously created file entry. So-called listeners are implemented to fill data fields automatically, such as the time interval between surgery and the particular day or the age at study entry. Links to existing file entries within the documentation system help to switch between corresponding information. A patient-related link accessing the HIS from the documentation system makes it easy to search for additional patient information that is not part of the documentation system. Furthermore, a web-based ICD-O selector is implemented as an add-on feature for a standard documentation of diagnoses only allowing the search and insertion of valid encodings. We added a consultation feature for physicians to review findings or to obtain a second opinion. With the lock-option, a module-entry, a group of entries or even a whole case can be locked and thereafter cannot be changed again by anyone. This is necessary for monitoring studies.

2.7 Analyses

This task is still work in progress. Presently, any data entries from the database can be exported as an Excel sheet. Thus, one can produce statistical reports within seconds. To allow this, a query builder has been implemented that supports the user to generate individual queries very intuitively. Additionally, these can be saved and reused again for a continuous overview on the data.

3. RESULTS

All access to the documentation system takes place via the web. Thus, no software needs to be installed on clinical computers, as a web-browser is standard, and therefore the system can be immediately accessed everywhere on the Internet. The only prerequisite is an installed Java Runtime Environment (JRE). Each study can be designed and adjusted as needed. The web-based approach with its strong security measures allows the usage of the system for multicenter studies within the ULICE project and enables the essential patient referral functionality.

By using a standard SQL database, it is possible to start queries at any time to avoid incomplete information. Moreover, with the implemented export mechanism, any kind of data sheet can be exported for treatment-related questions by physicians - always up-to-date with the current status of information. Case managers are using this functionality to monitor upcoming patient visits and to ensure complete documentation.

Documentation started in May of 2011 and to date, we documented more than 250 patients in six clinical studies. Approximately the same amount of patients treated prior to the system's implementation is being documented retrospectively. By documentation of all patients ever treated at the HIT, we can evaluate single studies prospectively and gain the possibility for overall large-scale, retrospective studies.

The usage of the documentation system is very simple and user-friendly as proven by first feedback from study nurses, case managers and physicians. Upon the first contact with a potential new patient at the outpatient clinic, the initial information (e.g. insurance information, radiation planning appointments, treatment overview etc.) is entered into the database and the documentation begins.

In the environment of radiotherapy, it is essential that any DICOM RT data can be processed and visualized by all systems. Processing and display of RT data is today not yet a standard functionality of PACS or teleradiology systems. However, our system is able to exchange and store all kinds of DICOM RT data. The integrated web-based DICOM viewer ensures examination of radiation plans from every single computer in the hospital. This enables physicians to quickly review images without having to go to a PACS or even a radiation therapy planning station.

4. CONCLUSIONS

Many others have already said there is no "one-size-fits-all" solution for web-based documentation of clinical studies.[9] It is the large number of requirements and circumstances for the system that make an individual approach necessary. Our solution differs from other systems, which only manage and organize patient treatment[10,11] and other numerous approaches only documenting a single clinical study electronically.[12–15] Up to today, it is complex and time-consuming to run clinical studies with a large patient group and a multicenter structure, because of the amount and heterogeneity of data as well as the different ways of documenting in different formats within participating institutions. Especially in the field of radiation oncology, one must deal with distributed data in various information systems. On the one hand, we developed a platform that allows us to document clinical studies in radiation oncology, and on the other hand, we linked it to all other mandatory information system to combine the two.

The major benefit of this system lies in the fact that imaging information, i.e. RT, CT and MRI data is directly linked to the rest of the study, or rather treatment documentation (see Fig. 1) and can be simply accessed with standard web-browsers. This, in turn, simplifies the process of conducting multicenter studies distributed all over Europe. It gives us the opportunity to extend the analysis functionality to a more complex level. With the main aim to reduce the effort for future clinical studies, we are planning a separate functionality for prospective and retrospective data analyses. It will not only be able to answer simple statistical questions, but also taking imaging information into account. MR imaging and dose distribution are to be compared before and after treatment and thus reveal their direct correlation with clinical endpoints (e.g. overall survival, disease-free survival, recurrence location).

In conclusion, the documentation system of today simplifies the research work, ensures a better quality of study analyses, and ultimately improves patient treatment concepts and supports the evaluation of the role and effectiveness of particle therapy.

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