Health Digital Twins with Clinical Decision Support and Medical Imaging

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Abstract As the concept of digital twins as virtual representations of physical entities is rapidly gaining popularity in healthcare, this paper studies the feasibility of incorporating clinical decision support (CDS), clinical data, and medical imaging into health digital twins (HDTs). A HDT is visualized in a web application, health data are stored in a FHIR-based electronic health record, computed tomography images are stored in a rudimentary DICOM-based picture archiving and communication system. An Arden-Syntax-based CDS system consisting of an interpretation and an alert service is connected. The prototype focuses on interoperability of these components. The study confirms the feasibility of CDS integration into HDTs and provides insight into possibilities for further expansion.

1 Introduction

In the last decades, the healthcare industry has witnessed significant advances in technology-driven solutions aimed at enhancing patient care, diagnosis, and treatment.

Clinical Decision Support. One such advancement can be observed in computerized clinical decision support systems (CDSSs), which over the past 25 years have evolved from simple stand-alone systems lacking meaningful interoperability to complex, integrated platforms [16].

Challenges remain regarding the universal implementation of CDSSs in clinical practice, such as a quickly evolving technological landscape leading to the need of

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processing vast amounts of various clinical data, the persistent difficulty in establishing standardized intra-organizational processes for knowledge engineering and management, and the need to further integrate seamlessly and efficiently into clinical workflows [16]. Nonetheless, a 2020 meta-analysis of controlled clinical trials by Kwan et al. [12] found that the use of CDSSs led on average to an overall absolute improvement in the proportion of patients receiving the desired care by 5.8% (CI_{95} 4.0% to 7.6%), albeit with significant heterogeneity between studies (I^2 = 76%). While this improvement may not seem revolutionary, no data regarding the speed at which the desired care had been delivered was collected. Furthermore, it is predicted that adoption as well as efficacy of CDSSs will continue to rise in the coming years as a result of continuing improvements in computational capabilities and knowledge discovery [16].

Other factors contributing to the predicted further rise in CDSSs' relevance to clinical practice is the ongoing adoption of Health Level Seven's (HL7) Fast Healthcare Interoperability Resources (FHIR) as a unified clinical data model as well as the evolution of standards representing clinical knowledge and clinical reasoning—like for instance the Clinical Quality Language (CQL) and Arden Syntax (both normative standards by HL7)—and their interoperability with the FHIR data model [19].

Health Digital Twins. Another concept rapidly gaining traction is that of the health digital twin (HDT). Originally emanating from the manufacturing industry, developments in information and communications technology have given rise to increasing research on how to apply digital twins as virtual representations of real-world entities to the healthcare sector [20]. While the classical approach to healthcare consists primarily of one-size-fits-all guidelines, tailored to a hypothetical average patient, HDTs bear the potential to facilitate a more individualized, patient-centered healthcare delivery [14]. A variety of research projects on utilization of digital twins in clinical care are underway [11, 14, 20, 21]. However, they tend to focus on a narrow field of medicine such as personalized disease management in multiple sclerosis [21]. Thus far, a more generalized approach is lacking.

Health Digital Twins and Clinical Decision Support. This study presents a prototype web application integrating the concept of the HDT with generalized clinical data stored in a FHIR-conformant electronic health record (EHR), medical imaging data stored in a picture archiving and communication system (PACS), and CDSSs.

Since a high-fidelity full-body HDT may be far from achievable due to technological limitations, the HDT aims to be a proof of concept of a full-body low-fidelity proto-HDT [11]. Low-fidelity in this context means that the underlying data are not updated in real time—e.g., by use of internet of things sensors—but only when new laboratory test results or medical imaging data of the patient are available and the medical professional actively uses the application. The prefix proto- denotes that the current implementation serves as an archetype for building more complex, individualized HDTs.

Furthermore, the prototype integrates state-of-the-art medical imaging visualization functionality. The application is intended to integrate into a hospital information

system as depicted in Figure 1. This integration is possible by adherence to industry-standard interfaces—namely FHIR as a standard data model as well as transmission of clinical data via the FHIR representational state transfer (REST) application programming interface (API) and Digital Imaging and Communications in Medicine (DICOM) for storage and transmission of medical imaging data.

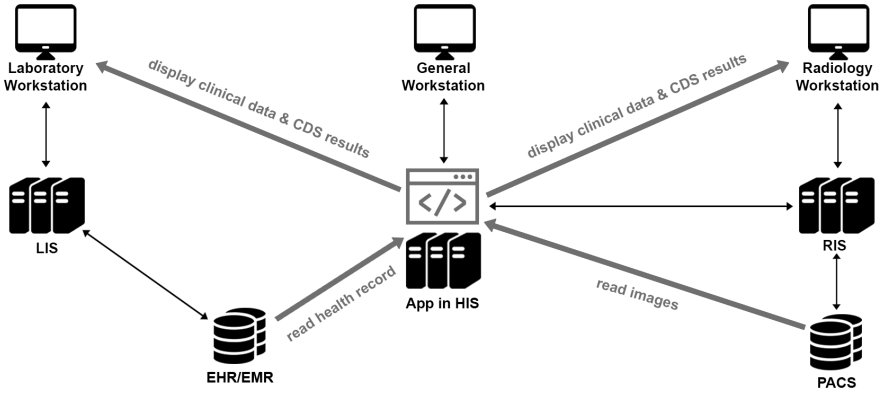

Fig. 1 Diagram of the proposed application's integration into a hospital information system (HIS). It reads the patient's clinical data—entered for example via a laboratory information system (LIS)—from an electronic health record (EHR) or electronic medical record (EMR) while reading image data from the picture archiving and communications system (PACS) without having to connect to the radiology information system (RIS). These images can then be displayed together with the clinical data and clinical decision support (CDS) results on any workstation in the hospital environment.

2 Methods

A literature research concerning the state-of-the-art of HDTs was conducted using the MEDLINE/PubMed database by the United States National Institutes of Health as well as Google Scholar and ResearchGate.

Next, a web application was implemented according to the Unified Modeling Language (UML) component diagram depicted in Figure 2. The frontend was developed using the Angular web development platform, the Angular Material user interface component library, the Tailwind Cascading Style Sheets (CSS) framework, and the WebStorm integrated development environment (IDE). Version control was achieved via GitLab. The application flow is depicted in the form of a UML sequence diagram in Figure 3.

The backend for the web application was developed using the Express web framework for Node.js and the WebStorm IDE. It functions as a rudimentary PACS by storing DICOM P10 instances and providing them to the frontend via the Web

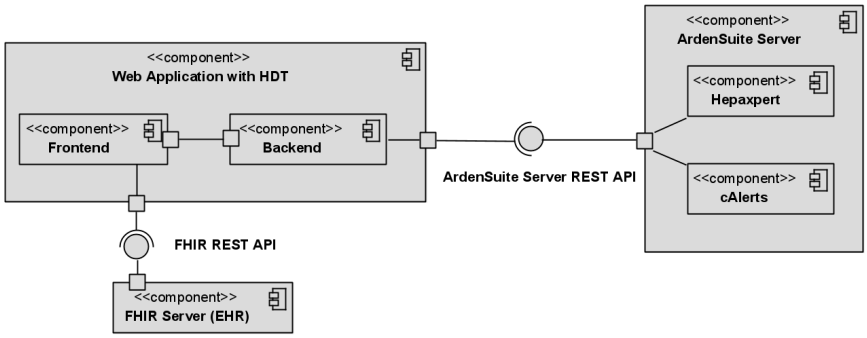

Fig. 2 UML 2.5 component diagram of the prototype system.

Access to DICOM Objects via Uniform Resource Identifiers (WADO-URI) communication mode described in chapter 6 of part 18 of the DICOM standard [18]. Furthermore, the backend statically serves a three-dimensional (3D) model acting as a full-body avatar of the patient.

DICOM images were obtained from the HCC-TACE-Seg dataset [17] via The Cancer Imaging Archive and are visualized in the frontend using the Cornerstone3D JavaScript library from the Open Health Imaging Foundation framework. The 3D avatar is displayed using the Three.js library. The full-body 3D model called "Nelly" was derived from digitized cryosections obtained by the The National Library of Medicine's Visible Human Project [15].

An EHR was implemented using a Docker image of the HAPI FHIR JPA server based on FHIR Release 4, the first release containing normative elements approved by the American National Standards Institute (ANSI) [7]. This version of FHIR is the data model and API standard mandated by the United States 21st Century Cures Act [1]. Furthermore, FHIR is to be adopted as a common standard in the European Union as decided by the European Union eHealth Network in early 2023 [2, 13].

Exemplary FHIR resources—i.e, a Patient resource containing demographic data and Observation resources containing clinical data—were created using the HAPI FHIR Java library. For semantic interoperability, all information in the resources is based on the reference terminologies Logical Observation Identifiers Names and Codes (LOINC), Systematized Nomenclature of Medicine Clinical Terms (SNOMED CT) and Unified Code for Units of Measure (UCUM).

The CDSS was implemented using the ArdenSuite CDS Platform [5], which is based on version 2.9 of the HL7 Arden Syntax [4, 8, 10, 19]. In the current prototype, it consists of two separate subsystems: *Hepaxpert* [3] for the automated interpretation of hepatitis serology laboratory test results as well as *cAlerts* [22] for providing context-sensitive clinical alerting. While *cAlerts* consists of multiple different packages, currently only one regarding myocardial infarctions via monitoring of blood levels of the cardiac troponin enzyme is implemented in the prototype application.

Since the application is in the proof-of-concept stage, merely the clinical data required for the CDSS are retrieved from—as well as initially saved in—the EHR,

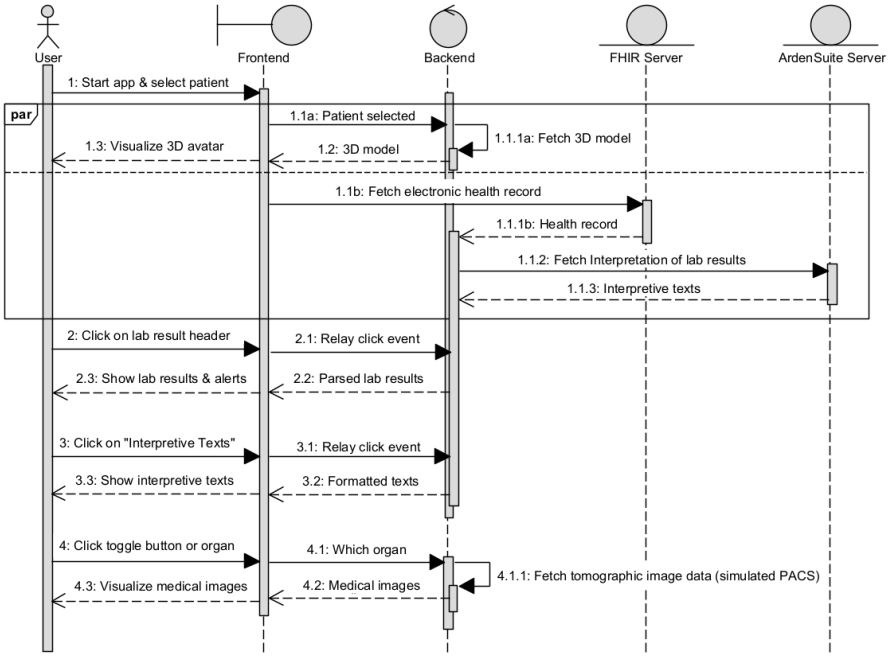

Fig. 3 UML 2.5 sequence diagram of the application where the frontend is shown as the system's boundary towards the user, the backend as controller, and the FHIR and ArdenSuite servers as entities.

namely FHIR Observation resources containing laboratory test results regarding hepatitis and cardiac troponin serology. Nonetheless, it is designed to facilitate generalization via expansion of the CDS modules or just by acquisition and display of a wider range of clinical data.

3 Results

The proposed prototype was established as described in section 2 and the components were successfully interconnected. Upon starting the application, the Visible Human Project HDT is visualized showing its anatomical parts separately and colored for easier differentiation. The patient's clinical data is fetched from the FHIR-based EHR, parsed, and visualized in tabular form besides the avatar upon a click on the heading "Laboratory Test Results", as visualized on the left side of Figure 5. At the same time, the CDSS is queried with the parsed clinical data, and alert messages derived from the results are displayed on the respective organs as depicted in the left part of Figure 4.

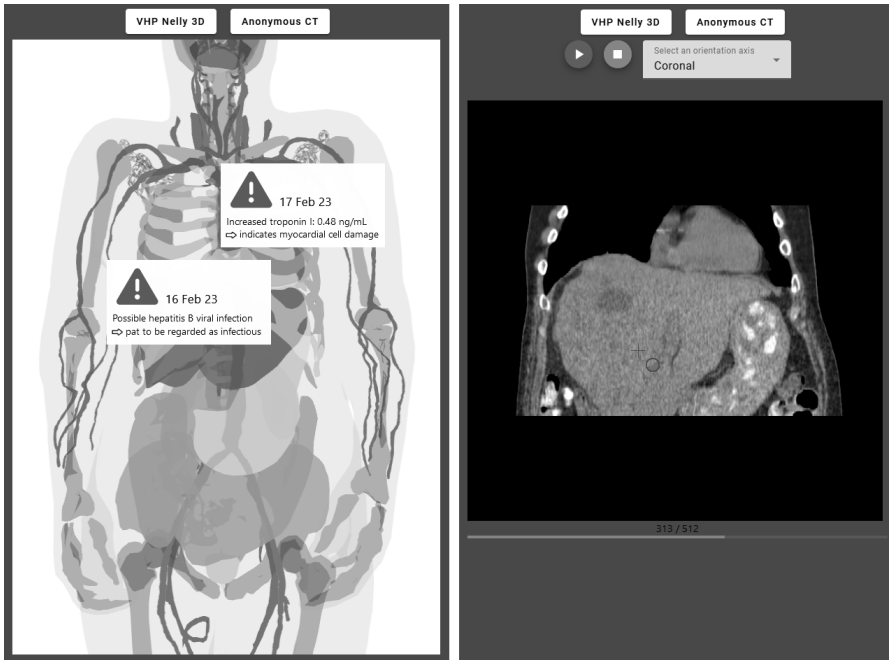

Fig. 4 Screenshots of the HDT component of the application. The full-body 3D avatar with the CDS alert messages visualized as tooltips on top of their respective organs is depicted on the left. Upon clicking on an organ or the heading "Anonymous CT", the avatar is replaced with a DICOM viewer showing recent images of the patient, in this case of the patient's liver. The DICOM viewer is depicted on the right and allows for manipulation of the window width and window center with the cursor to highlight the contrast of different tissues or materials, scrolling through a stack of slices with the mouse wheel or animating the stack scroll via the play and stop buttons, and multiplanar reconstruction via the choice box above the images.

If interested in a comprehensive summary of the laboratory test results' clinical significance, interpretive texts generated by the CDSS can be displayed in the rightmost column of the screen with a click on the heading "Interpretive Texts", as can be seen in the right column of Figure 5. Clicking on an organ of interest leads to the most recent diagnostic images to be fetched from the PACS and displayed instead of the full-body avatar. This is depicted in the right part of Figure 4, where a computed tomography (CT) series of the patient's liver consisting of 97 instances (i.e., slices) is visualized. Incorporation of the novel Cornerstone3D library for the DICOM viewer facilitates further inspection of the patient's anatomy by incorporating multiplanar reconstruction, meaning that the application has the ability to calculate the volume between the slices, enabling the series to be viewed from different orientation axes. Furthermore, the window width and window center of the displayed CT images can be easily adjusted with the mouse, allowing for different types of tissue to be inspected in sufficient contrast.

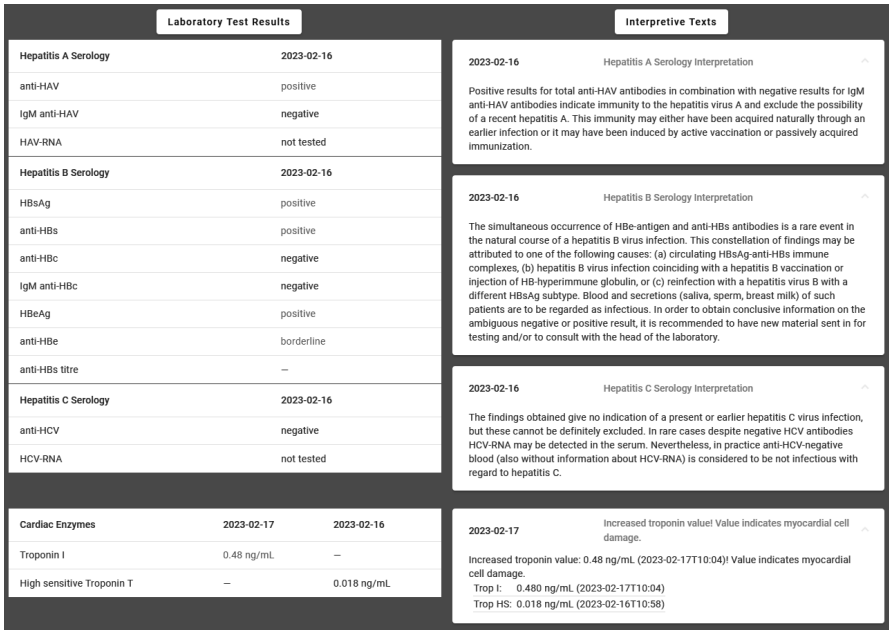

Fig. 5 Screenshot of the CDS component of the application. Laboratory test results parsed from FHIR Observation resources are displayed in the left column, while the CDS messages obtained from the ArdenSuite server are displayed in the right column. Both these columns are displayed to the right of the HDT component depicted in Figure 4. Laboratory Test results are color-coded for better readability, where "negative" is colored in green, "borderline" in orange, and "positive" as well as values leading to a clinical alert are colored in red.

4 Discussion

A prototype application integrating HDTs, EHRs, PACS, and CDSSs was presented, confirming the feasibility of combining these concepts. However, due to the archetypal nature of the application, there remain several possibilities for future work. For instance, it would be possible to expand the DICOM viewer functionality to perform volumetric rendering as well as the already implemented multiplanar reconstruction. This would enable display of a complete 3D model of the imaged body region. Moreover, DICOM segmentation objects could be visualized on top of the CT images. In conjunction with volumetric rendering, this feature could make the full-body avatar created from cryosections obsolete in the future, instead creating a HDT out of the patient's latest tomographic images.

Current versions of the Arden Syntax do not standardize data access from external sources. Instead, site-specific implementations are allowed and expressed within curly braces ({}) in medical logic modules (MLMs). Thus, sharing of clinical knowledge represented in MLMs reliant on accessing external databases requires manual adaption of each MLM, a challenge dubbed the the curly braces prob-

lem [4, 10]. This problem is avoided in the prototype by the application parsing the clinical data fetched from the EHR, converting the contents of the FHIR Observation resources into data types clearly defined by the standard, and querying the ArdenSuite server with those objects. The incorporation of FHIR as a unified data model in Arden Syntax version 3.0 [9] will allow for MLMs directly accessing data from FHIR resources [10, 19], thus facilitating substantial architectural simplification of the proposed application.

Integration of live sensor data is conceivable, increasing the fidelity of the proposed HDT and thereby broadening its field of application to include intensive or surgical care, as for example detailed in [14]. However, the collection and analysis of "big" data was outside the scope of this feasibility study.

The current prototype relies on a medical professional to actively engage in the application for querying the CDSS. A way of further integrating the application into clinical workflows would be the inclusion of CDS Hooks as a mechanism to automatically query the ArdenSuite server for CDS whenever a new laboratory result is added to the EHR [4, 6].

In order to allow for the HDT to be eventually used in clinical practice, execution of a qualitative usability study and subsequent quantitative validation of the proposed system will be the inevitable next steps in development.

5 Conclusion

The study confirms the feasibility of integrating clinically proven CDSS into a full-body HDT and demonstrates the clear potential for promoting patient-centered care as well as expediting clinical workflows. Nevertheless, more research is needed to adequately assess clinical usefulness as well as the system's impact quality of care.

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