Using Digital Twins to Support Multiple Stages of the Patient Journey

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Abstract. New possibilities in personalized medicine need to be complemented by clinical decision support systems as well as context-specific applications to be used in clinical routine. We aim to implement a shared technical backend for a large variety of applications in personalized head-and-neck cancer treatment. The infrastructure is conceptualized as a multi-purpose digital twin for cancer treatment. A set of prototypes of clinical applications demonstrates the feasibility of using digital twins to support multiple stages of the patient journey.

Keywords. Oncology; Clinical Decision-Making; Clinical Decision Support Systems

1. Introduction

Healthcare is changing due to social challenges in the area of tension between increasing therapy effectiveness through personalization and standardization for cost efficiency. Relevant information, for example in interdisciplinary treatment of cancer, includes omics data, imaging and laboratory findings as well as living conditions among others [1]. For efficient treatment, case-related data must be available in daily clinical routine and decision support systems must seamlessly integrate into established workflows.

The work presented here aims to implement a common infrastructure for a large variety of applications in personalized head-and-neck cancer treatment. A common backend, a Digital Medical Twin (DMT), facilitates the integration of new models, novel products, and tailored treatments strategies thus shortening the time to market for innovations in personalized medicine. So far, digital twins in healthcare have been proposed focused on specific decision-making tasks in oncology [2], cardiology [3], and orthopedics [4] among others.

The possibilities of diagnostics and the variability of treatment strategies are ever increasing. Personalized medicine aims to provide the best diagnostic processes and treatments for each patient. To that end, reliable interoperability of data and biomedical systems, multimodal data analyses and user-centered assistance systems are essential for practical implementations. Although tedious and error-prone, media breaks, paper work, and manual documentation are still dominant in the healthcare sector. Most of the
established applications of personalized medicine target a specific work step or clinical function. In contrast to that, we aim to establish a common infrastructure that supports the whole patient journey while also addressing all relevant stakeholders.

2. Methods

The presented research and development aim to improve personalized care for patients with head-and-neck cancer. A comprehensive requirement analysis was conducted in close cooperation of clinicians, biomedical researchers, and healthcare companies. The interdisciplinarity ensures the development of practical solutions targeting actual clinical needs. Namely we focused on time-, device- and location-independent access to clinical data, multimodal data linkage and analysis, as well as context-aware, interactive visualization in daily routine. Each application involved in the clinical processes relies on a common infrastructure (the DMT). The implementation of the DMT follows the concept proposed in [5].

To realize an infrastructure that can support the treatment of cancer patients from the diagnostics through the decision making and therapy implementation to the long-term care, a technical platform and its interfaces were developed based on international standards, such as HL7 FHIR for health records [6], DICOM for imaging data, IEEE 11073 SDC for medical device data [7], and application-specific extensions. The platform aims to facilitate the development, evaluation and integration of novel medical applications. To that end, it provides a shared interface to case-related data currently distributed across a large variety of medical devices and information systems in clinical IT ecosystems. The interfaces are designed to be vendor-independent and provide reliable syntactic and semantic interoperability of data. We conceptualized the architecture around a Digital Medical Twin, a virtual representation of a patient by means of highly interconnected patient data. These data may include a large variety of modalities, e.g., measurements provided by Point-of-Care devices, medical reports, laboratory findings, molecular biomarkers, imaging, and patient reported outcome measures.

In its implementation, the DMT does not persist case-related data to avoid unnecessary duplicates and update issues. It rather dynamically loads and caches just the data required to answer the application’s request at hand. For some modalities, such as DICOM image series, only references are cached and provided. Hence, the interfaces of the DMT integrate easily with established standards. Most information systems provide their own set of data representations and ontologies, which can also be preserved by reference. In the DMT, case-related data is embedded into an extendible internal data structure based on the Resource Description Framework (RDF) called MPMResource. Each resource contains DMT specific metadata as well as an RDF representation of the original data resource (e.g., a FHIR-Resource) or a reference (e.g., for DICOM Image Series). An extendable internal representation based on RDF, combined with HL7 FHIR, the Web Annotation Data Model [8], and medical ontologies, allows for the semantic linkage of data points across various modalities. Even hardly structured data, e.g., documents, can thus be referenced on a segment level.

Beyond an aggregation of data, our DMT concept includes modules that provide trend analyses and abstractions based on various types of models. By design, the overall architecture of the DMT is agnostic to the analysis methods used. The aggregation of patient data from primary clinical information systems is performed by specialized
collector modules, thus simplifying the adaptation of the DMT implementation the additional clinical IT ecosystems. Each module is defined by its own RDF module description, specifying the type of data the module requires and, when invoked successfully, produces. This allows for the on-demand compilation of a modules’ call hierarchy for complex requests. The created module call hierarchy finally leads to collector modules to acquire the requested data on execution. For each successful module call, an execution fingerprint is calculated, allowing to reuse the result of the call if possible. The reusability of modules and results is increased by designing modules for subtasks rather than building a large self-contained model for a specific decision support task. For each request, the collector modules are always invoked as they have to check whether new data is present on the clinical information systems.

The DMT provides a GraphQL endpoint for third party applications to request needed information for the assistance task in the present clinical setting. The response, provided as an MPMResource, may include data from clinical information systems as well as abstracted information calculated by modules, e.g., scores or patient-specific risk factors. Additionally, MPMResources, especially data computed from modules, are always linked to all resources that have been used for its calculation. This allows to trace back the computation from each information used by an application back to the primary observations and knowledge-based. This traceability simplifies the construction of argument chains providing reason for given information and suggestions. This is especially important in computer-added clinical decision making [1]. Also, if observations become outdated or invalidated, it is also easily possible to invalidate all data derived from it.

The modular architecture allows to integrate knowledge-based as well as data-driven methods. Hence, the DMT implementation can be extended to account for new clinical knowledge, treatment strategies, or other diseases.

3. Results

With the DMT, we aim to provide a shared infrastructure as well as assistance functions for all stages of the patient journey. Data access should be syntactically and semantically interoperable and independent from the providing clinical IT system. Several assistance systems were implemented using the DMT (see Figure 1).

![Figure 1](image-url)
To support diagnostics, we implemented a seamless integration of experimental molecular biomarkers for head-and-neck cancer into the clinical decision making. To that end, the Modaplex platform by Biotype GmbH, Dresden (Germany), was integrated, which enables the quantification of up to 50 DNA and/or RNA markers per sample within 3.5 hours. The analysis results are seamlessly transmitted via the laboratory information and management system developed by qualititype GmbH, Dresden (Germany), and are provided as HL7 FHIR in the DMT context. The avoidance of media breaks and communication bottlenecks between departments and institutions, as they are still common in daily routine, ensures an instant and reliable availability of relevant diagnostic data. This implementation serves as an example of how the integration of diagnostics can improve decision making in practice.

Prior to major clinical decision making in interdisciplinary tumor boards, the DMT aggregates all relevant data, including anamnesis, laboratory findings, diagnostic reports, radiological images, and medication plans among others, from multiple clinical information systems. The CaseExplorer, a software tool, uses the DMT as a backend to visualize case-related data combined with clinical knowledge. Additional analysis modules provide abstracted, concise summaries across multiple information entities to prevent initial information overload. However, each section also allows for a deep dive into the data, retaining the details and reasoning behind the provided abstractions. This is essential to achieve user acceptance in the medical domain. Based on an explicit modeling of clinical knowledge, interdependencies between information entities, such as sections in reports and imaging, or laboratory findings and medication, are formally represented and can be interactively visualized by the CaseExplorer. For instance, we use Business Process Model and Notation (BPMN 2.0) and annotated html fragments as structured representations of clinical guidelines and hospital-specific standard operating procedures. The formal representations and knowledge management system were developed with Gesundheitsforen Leipzig GmbH, Leipzig (Germany). Furthermore, a module that can analyze the eligibility of a patient for participation in a clinical study was implemented. However, due to the text-based inclusion criteria for studies could not be parsed automatically.

For clinical decision making, we implemented an intelligent medical conference environment for tumor boards. The setting focuses on a structured, context-aware visualization of the case related data. The decision process for each patient is divided into three phases: a structured case presentation assisted by a wizard-like visualization, a discussion phase where all data are directly available on demand, and a decision phase assisted by case-specific references to clinical guidelines and a structured documentation. The visualization was designed and developed by Gesellschaft für Technische Visualistik mbH, Dresden (Germany). The conference environment also includes specialized hardware for audio recording, speaker differentiation, and context analysis. The system was developed by voice INTER connect GmbH, Dresden (Germany). Based on the context analysis, the visualization automatically reacts to discussed topics and can be controlled by directly by voice commands. The context aware medical conference environment is designed to reduce expenditure for preparation, reliably structured case presentation and data interaction, and it facilitates the necessary documentation.

Once the clinicians have recommended a therapeutic strategy, the patient needs to be educated accordingly. The patient compliance is positively influenced by clear explanations for which interactive visualization can be used. We integrated a tablet-based VR system developed by LeFx GmbH, Leipzig (Germany) that visualizes a multifaceted anatomical model, designed by Effigos AG, Leipzig (Germany). The setup uses two
tablets, one for the patient and another one for the clinician. The clinician can clarify explanations by controlling the visualization’s focus, by showing or hiding anatomic structures or by adding hand-drawn markers. The assistance system for patient education is designed to be more intuitive and interactive than the common paper-based approach.

The DMT can also be used to assist the surgical resection of tumors. A dedicated software module facilitates the initial configuration of medical devices and can personalize the setup. We integrated the module for the configuration of medical devices into an integrated operating room for demonstration purposes. The medical devices use the IEEE 11073 SDC standard family, hence, parameter setups can be done via network. The module compiles a case-specific configuration based on local standard operating procedures, team specific presets and preferences, and especially model-based case-specific device parameters derived from patient data. Additionally, selected patient data corresponding to the WHO Surgical Safety Checklist and an intervention-specific dashboard for case-related data are provided at the beginning of the intervention. The aim is to increase patient safety by increased awareness of potential risk factors.

Postoperatively, the DMT can be used to simplify the documentation process. A documentation module assesses workflow data provided by the device network using a model parameterized with case-related preoperative data. Based on the assessment, it detects process anomalies, which require additional documentation input from the surgeon, and finally compiles a case-specific intervention summary report. The report consists of structured sections and can be forwarded to clinical information systems via HL7 FHIR. We strive to objectify the reports and simplify documentation while still taking patient-specific factors into account.

The developed DMT also supports long-term treatment strategies. To that end, we integrate patient reported outcome measures. A digital pipeline for questionnaires on quality-of-life aspects was implemented. The data, either provided by digitization of paper-based questionnaires or digital acquisition, are integrated into the DMT using HL7 FHIR. Modules in the DMT can provide trend analysis across multiple questionnaires as well as combine patient reported outcomes with clinical data and medication plans. In the clinical setup, the gathered information on long-term treatments can be accessed and visualized during consultations on desktop systems, mobile devices, and smart mirrors.

4. Discussion

We developed various software applications that assist in multiple stages of cancer treatment. The applications are tailored to their contexts and target clinicians as well as patients. However, they all share the DMT as a backend to facilitate data access and data analysis. The realization of a digital twin with a specific focus on multi-purpose use and long-term support for cancer treatments extends its usage beyond a specific decision-making task. The vision is to establish a ‘One-Stop-Shop’ for the access to any case-related data as well as an extendible set of modules for data analysis that can be shared and updated whilst retaining the context-specific applications. The use of structured module descriptions and on-demand module call hierarchies in the DMT ensures the needed traceability of information in clinical decision making. Thus, software tools can create explanations for users and even use updated analysis models without the need for program adaptations.
The backend technology is currently applied to support clinical studies at the University Clinics Leipzig and we are in the first evaluation phase for selected applications. The interfaces based on international standards ensure a proper scalability of the approach in future realizations. The modular composition of models for analysis supports a continuous development process and facilitates step-by-step validation, deployment and evaluation. With the establishment of a common infrastructure, we aim to provide a long-term basis for the implementation and evaluation of new applications for personalized medicine as well as a faster integration into the clinical routine.

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References