Structured patient information management for efficient treatment and healthcare quality assurance in oncology

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Referat

Die Behandlung von Patienten mit Tumoren im Kopf-Hals-Bereich gestaltet sich als komplexer und herausfordernder Prozess sowohl für den Patienten als auch für die behandelnden Ärzte und Chirurgen. Zur Gewährleistung der bestmöglichen individuellen Therapie werden vor Beginn der Behandlung zahlreiche diagnostische Verfahren durchgeführt. Hierzu zählen unter anderem medizinische bildgebende Verfahren wie z.B. Computertomographie (CT) oder Magnetresonanztomographie (MRT) sowie die Entnahme von tumorverdächtigem Gewebe während einer Panendoskopie zur exakten Bestimmung der Tumorart (Histologie, Grading, TNM-Klassifikation nach UICC, genaue Lokalisation des Primärtumors, der lokoregionären Metastasen und ggf. Fernmetastasen). Die gewonnenen Informationen bilden anschließend die Grundlage für die Entscheidung über die durchzuführende Therapie und stehen in unterschiedlichen klinischen Informationssystemen sowie auf Papierakten zur Verfügung. Leider werden die Daten im klinischen Alltag häufig nur unstrukturiert und schwer auffindbar präsentiert, da die führenden Informationssysteme nur unzureichend in den klinischen Arbeitsprozess integriert und untereinander schlecht vernetzt sind. Die präzise und erschöpfende Darstellung der jeweiligen individuellen Situation und die darauf aufbauende Therapieentscheidung sind aber entscheidend für die Prognose des Patienten, da der erste, gut geplante „Schuss“ entscheidend für den weiteren Verlauf ist und nicht mehr korrigiert werden kann.

In dieser Arbeit werden neue Konzepte zur Verbesserung des Informationsmanagements im Bereich der Kopf-Hals-Tumorbehandlung entwickelt, als prototypische Software implementiert und im klinischen Alltag in verschiedenen Studien wissenschaftlich evaluiert. Die Erlangung eines tiefgreifenden Verständnisses über die klinischen Abläufe sowie über beteiligte Informationssysteme und Datenflüsse stellte den ersten Teil der Arbeit dar. Aufbauend auf den Erkenntnissen wurde ein klinisches Informationssystem *oncoflow* entwickelt. *Oncoflow* importiert vollautomatisch relevante Patientendaten von verschiedenen klinischen Informationssystemen, restrukturiert die Daten und unterstützt Ärzte und Chirurgen im gesamten Therapieprozess. Das System wurde anschließend in unterschiedlichen Studien evaluiert und der klinische Nutzen in Bezug auf effizientere Arbeitsabläufe und eine verbesserte Informationsqualität gezeigt. Im folgenden Teil der Arbeit wurden Machine Learning Methoden genutzt um von Daten in der elektronischen Patientenakte auf den aktuellen Prozessschritt im Therapieprozess zu schließen. Der letzte Teil der Arbeit zeigt Möglichkeiten zur Erweiterung des Systems zur Nutzung in weiteren klinischen Fachdisziplinen auf.

Danksagung

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Contents

List of Figures

List of Tables

Chapter 1

Introduction

1.1 Motivation

Head and Neck Squamous Cell Carcinoma (HNSCC) is the fifth-leading cause of cancer incidence in Germany with 16.500 patients in 2010 [1]. Head and neck cancer occurs in organs such as the oral cavity, oro- and hypopharynx, the nasopharyngeal zone or in the larynx and is closely related to a variety of risk factors which include amongst others nicotine or alcohol abusus, exposure to chemicals, and also certain viruses such as the human papillomavirus [2]. The tumor therapy has a profound impact on the patient's quality of life due to partly severe surgical interventions such as the removal of the larynx in combination with radiation therapy. Additionally, the Eurocare-4 and Eurocare-5 cancer studies analyzed the survival rates of tumor patients from all over the European Union between 1995 and 2007 and present sobering result. The relative 5 year survival rate for adult patients with HNSCC is at 42% [3, 4].

The detection and the treatment of HNSCC is a complex task that requires a high degree of interdisciplinary cooperation between different specialized medical disciplines [5]. Involved disciplines are head and neck surgery, maxillofacial surgery, radiation oncology, oncology, pathology, radiology and nuclear medicine. However, a crucial prerequisite to find the best possible therapy for the patient and to increase its outcome is that all physicians and surgeons have a common understanding of the patient case. Therefore, patient-specific information such as risk factors, blood-count, examination results of biopsy samples or medical images have to be available and conveniently accessible for the clinical staff.

Unfortunately, the information that is currently acquired lacks standardized contents, a structured documentation, and is distributed and encapsulated across different clinical information systems [6]. Hereby, the Hospital Information System (HIS) is the leading information system for text-based information and medical images originating from e.g. Computer Tomography (CT) or Magnetic Resonance Imaging (MRI) scans are stored in the Picture Archiving and Communication System (PACS). Also further department-internal information systems are used in daily clinical routine for special-purpose tasks [7]. These proprietary systems are commercial or originate from scientific

projects and are slightly or not integrated into the existing clinical IT-infrastructure.

This situation leads to several implications in daily clinical routine. Existing information is not instantly usable in electronic form, e.g. the automated creation of clinical documents such as physician letters or quality management reports is not possible. Currently, the physician has to login into different information systems, browse paper forms and manually aggregate relevant information in a time-consuming and error-prone copy & paste process. Due to proprietary database systems, users also don't have the possibility to directly access the database and perform a bulk export of patient data to transfer important information from the HIS to statistic tools for statistical evaluations. The heterogeneous information base serves at the moment as basis for therapy decisions, quality management and clinical studies but in fact these tasks require structured information within a centralized database [8, 9].

Especially in tumor boards where physicians from different medical disciplines meet to find together the best possible therapy for the patient a common understanding or common mental model based on structured information would be beneficial [10]. However, the management of these meetings is not well integrated into the existing IT infrastructure [11]. Furthermore, existing patient-specific information is not processed adequately to improve a common understanding of the actual case and the environment where tumor board meetings take place is not designed as a collaborative platform for knowledge-sharing and a productive decision-making process.

The presented work aims to develop basic requirements for the information management in the field of oncological head and neck surgery and to transfer this theoretical knowledge into a prototypical web-based clinical information system *oncoflow*. The work focused on the following topics:

1. Standardized and structured information acquisition
2. Integration of patient information
3. Clinical workflow support and automation
4. Tumor board support
5. Quality management and clinical certification

The *oncoflow* system has been deployed at a clinical site and the development was attended by clinical studies. The goal of these studies was to evaluate the *oncoflow* system in daily clinical routine with regard to the improvement of information acquisition, information quality and workflow support compared to the information systems that were used so far. The trade-off between the involved resources for improving information quality (e.g. an increased consultation time) and the noticeable advantages in daily clinical routine are weight by the clinicians and decide on the acceptance or refusal of the new *oncoflow* information system [12].

In the scope of this doctoral thesis the clinical workflow was analyzed and corresponding workflow assistance systems were realized for the clinical anamnesis, panendoscopy, tumor board and

follow-up process steps. The therapy process step that includes radiotherapy, chemotherapy and surgical intervention was not considered in this work and is subject of further research.

1.2 Clinical setting and system context

The clinic of Otolaryngology, head and neck surgery at the University Medical Center Leipzig is an independent clinic with ambulance, ward, phoniatry and operation rooms. About 200 patients per year with primary diagnosis head and neck cancer are treated with full in-house services for cancer therapy from pre-op consultation to post-op evaluation, check-up and therapy. Each patient passes through a treatment process consisting of a diagnostic, a therapy and a follow-up phase with a total time of at least 5 years. This work focuses on the treatment process, clinical information systems used in each process step and the overall integration into daily clinical routine (see Figure 1.1).

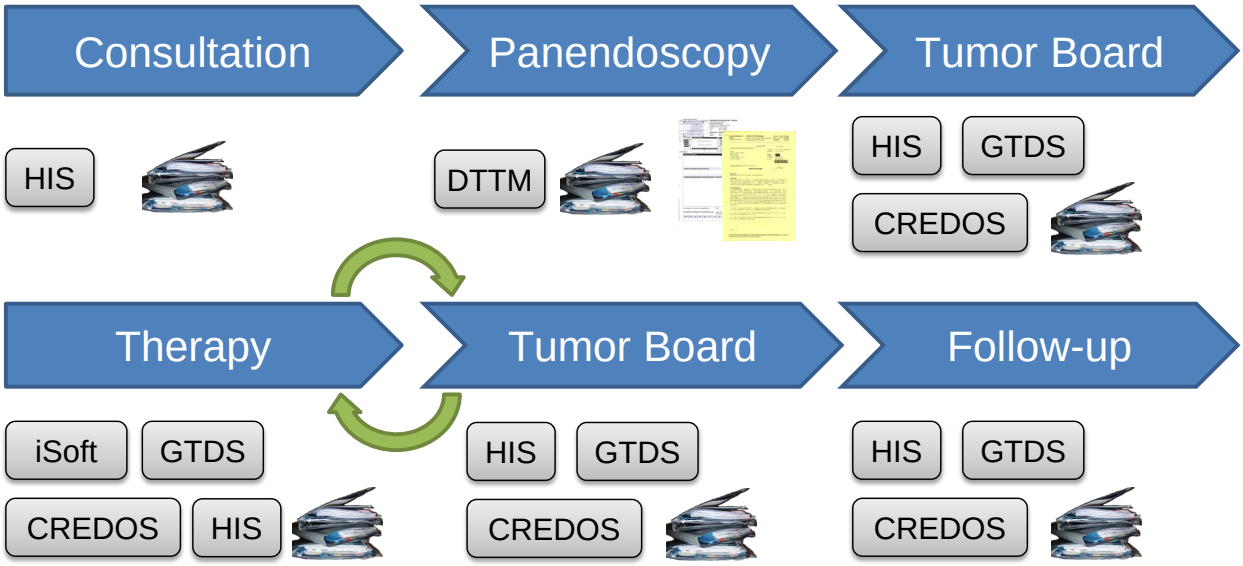

Figure 1.1 – Treatment process in head and neck surgery with major clinical information systems[1] supporting daily clinical routine. A panendoscopy is a routine comprehensive endoscopic examination of the upper aerodigestive tract in total anesthesia. The figure illustrates the heterogeneity of supporting information systems

The General Practitioner (GP) is frequently the first contact person when patients develop clinical symptoms such as difficulties in swallowing which do not disappear after a short time period. If the disease can not be cured within an adequate time frame or if the GP immediately suspects cancer the patient is referred to a specialized clinic or to a university hospital. In the depicted

[1] The leading information system is the Hospital Information System (HIS). Supporting systems during therapy are Picture Archiving and Communication System (PACS), Dornheim Tumor Therapy Manager (DTTM), iSoft laboratory documentation and the Treatment Planning System (TPS) for radiation therapy. Cancer Retrieval Evaluation and DOcumentation System (CREDOS) and Giessener Tumordokumentationssystem (GTDS) support the tumor documentation

example case the patient may be referred to specialists from head and neck surgery. Subsequently, the patient arrives in the department of head and neck surgery where a patient record in the HIS is created. During a first consultation the actual status of the patient is documented. The consultation consists of an anamnesis where the physician asks questions concerning current medical conditions, past interventions and way of life and a clinical examination where the physician examines ears, nose, oropharynx and larynx and performs a palpation and an ultrasound examination of neck lymph nodes. When a tumor is assumed morphological as well as functional medical imaging such as CT, MRI or Positron Emission Tomography (PET) is also performed and a panendoscopy, an examination for better contouring of the tumor extension under total anesthesia, is performed. During panendoscopy samples of potential tumor tissue are taken and sent to pathology for a histopathological examination. Subsequently, the DTTM supports the surgeon in reporting the biopsy locations, creating a clinical TNM Classification of Malignant Tumors (TNM) classification as well as a 3d tumor reconstruction [13, 14, 7]. Based on a positive histopathological result the patient is scheduled for the next tumor board. The head and neck tumor board in Leipzig takes place every Thursday where about 12 to 15 patients are discussed. Tumor board invitations and result protocols are created with MS-Word templates and sent via email to all participants. The complete scheduling process for one patient is very time-consuming for the attending physician. Information gathering from HIS and paper-based records and the creation of invitation and protocol take up to 30 minutes. After the first tumor board took place data export to additional information systems such as the GTDS and CREDOS are mandatory. Necessary information is manually reentered from HIS, the laboratory software iSoft and paper records by tumor documentation assistants for usage as tumor documentation and retrospective clinical studies. The therapy phase consists of a combination of chemotherapy, radiotherapy and surgical intervention depending on the decision in the tumor board. After each therapy, the patient is scheduled once more for the tumor board to discuss the therapy outcome, further therapies or the release of the patient into follow-up. During the follow-up phase the patient is scheduled for regularly meetings over the next five years where a clinical examination is performed and the current patient status is documented into the paper-based patient record and afterwards in the HIS.

1.3 Scope of the work

The concepts and information systems that are presented in this doctoral thesis aim to improve the oncological treatment process in terms of information integration, structured information acquisition, information quality, clinical workflow support and automation as well as quality management. The information system *oncoflow* and the Treatment Planning Unit (TPU) have been developed in close cooperation with physicians and surgeons from the department for head and neck surgery at the University Medical Center Leipzig and are tailored to the specific requirements in this medi-

cal discipline. However, the presented concepts are generally accepted for cancer treatment in all medical disciplines and are not solely tailored to head and neck cancer treatment. The information systems have been developed in a modular and easily extensible fashion with a facilitated modification, integration and application in other clinical disciplines in mind.

This work focuses on clinical workflows, information models and assistance functions to relieve clinical personnel from time-consuming and error-prone tasks. Additional information systems which are considered throughout this thesis only serve as information sources or information sinks. These systems such as SAP i.s.h.med or the DTTM are important with regard to information exchange between them and *oncoflow* and their role in the oncological treatment process. The functions which these systems provide are not in the scope of this work and thus, are not analyzed or described in detail.

1.4 Goals of the work

The major goals of this thesis are depicted in detail in the following subsections and are briefly illustrated in Figure 1.2. Gaining a deep understanding of the clinical workflow for tumor patient treatment in head and neck surgery was the first goal. Therefore, it was necessary to understand the process steps, actors and their roles, and the information flows as well as to identify clinical information systems that are used.

The second goal was the development of a web-based information system *oncoflow* that automatically imports patient-specific information, provides convenient and user-friendly access to this information and allows a structured documentation of treatment results.

The information system was then deployed at a clinical site and used by the physicians and surgeons in daily clinical routine. Hence, the database contains a growing amount of structured information that is the basis for workflow support, process automatization and quality assurance. Thus, the third and fourth goal use the information base for the development of intelligent workflow assistance systems and efficient tumor board support.

The improved assistance functions were evaluated in daily clinical routine in goal number five. The recognition of clinical workflows by using machine learning approaches is goal number six. Finally, concepts for the generalization of the aforementioned methods for a usage across different clinical disciplines have been developed.

1.4.1 Information management in oncology

Goal 1 A deep understanding of underlying clinical workflows, involved physicians and surgeons as well as necessary patient-specific information and the information systems or paper records where this information is stored is crucial. Hence, a detailed workflow analysis resulting in a precise documentation of the clinical setting was the first goal.

Figure 1.2 – Major goals of this doctoral thesis

Goal 2 The access to relevant patient-specific information in the previously identified information systems and an automatic integration into one central database is the prerequisite for clinical workflow assistance and the second goal. For this purpose an appropriate information system with a central database was developed and electronic communication interfaces to the information sources were established.

1.4.2 Clinical workflow support

Goal 3 Based on centralized available information the development of assistance systems for physicians and surgeons in daily clinical routine are the third goal. Therefore, a web-based information system *oncoflow* was implemented which aggregates and structures existing patient-specific information and provides convenient access and workflow support functions for physicians and surgeons.

Goal 4 The fourth goal was the improvement of the decision-making process in the tumor board. Therefore, existing conditions in the tumor board meeting room were analyzed in detail and an appropriate room design as well as useful assistance functions to support the decision-making process were implemented.

Goal 5 The next goal was the evaluation of the implemented workflow assistance functions in daily clinical routine. Therefore, the *oncoflow* system was deployed in the clinical computer network at the department of head and neck surgery and used in daily clinical routine. Within different quantitative and qualitative evaluation studies the benefit of *oncoflow* compared to the existing clinical information systems was evaluated.

1.4.3 Clinical workflow recognition

Goal 6 In order to provide appropriate clinical workflow assistance, quality management, and foster clinical certifications patient-specific information has to be structured according to the actual treatment phase and enriched with meta-information. Hence, the sixth goal was the development of probabilistic models which allow the prediction of the patient's current step in the treatment process based on information available in the EPR.

1.4.4 Generalization and multidisciplinary usage

Goal 7 Finally, the concepts developed in this work and the information system *oncoflow* should be generally accepted and not be tailored to a specific medical discipline. Thus, the last goal was the enhancement of the system for a more generalized usage.

1.5 Thesis outline

This thesis is divided into eight chapters representing the scientific methods and evaluation results in chronological order.

Chapter 1 presented in detail the motivation, the clinical context, the scope, the goals and the outline of this work. In Chapter 2 a detailed overview on existing scientific research projects and commercially available software products is given. The chapter is divided into four sections covering the topics electronic patient records, tumor board support, workflow recognition and distance measures for workflow evaluation.

Chapter 3 provides detailed information on the technical realization of the *oncoflow* clinical information system. Within the *oncoflow* system all scientific methods which are developed in this thesis were realized as prototypic implementation. Hence, *oncoflow* is the basis for all subsequent chapters and clinical studies which were performed in this work. The first section of this chapter

presents the *oncoflow* information model which is the basis for the backend database scheme. The second section gives a brief overview on the system architecture of the web-based application.

In Chapter 4 all functionalities for supporting physicians, surgeons and clinical staff in daily clinical routine which are already implemented in *oncoflow* are described in detail. The assistance functions are described in the same order as they appear in the actual treatment process starting from the first consultation until the final data aggregation and data export for clinical studies. The scientific evaluation of these assistance functions in daily clinical routine is presented in Chapter 6.

A concept of a sophisticated multimedia tumor board, the TPU, is presented in Chapter 5. The TPU provides workflow assistance for the management of tumor boards including the scheduling of patients and invitation and result mailings. Furthermore, the TPU consists of a wide variety of technical equipment that is installed in the team meeting room at the clinical site and helps to improve the decision-making process during tumor board conduction.

The *oncoflow* system has been deployed at a clinical site and is still used in daily clinical routine. Different clinical studies were conducted in a tight cooperation with physicians and surgeons to evaluate the advantages of the new information system. The results of these studies are presented in detail in Chapter 6.

The information management in clinical information systems is rarely tailored to the needs of physicians and surgeons. Thus, in Chapter 7 a completely new approach for clustering patient-specific information is presented. Hidden Markov models are used to enrich information with meta-data about the therapy process step from which this information originates. The developed algorithms are evaluated in a leave-one-out cross-validation study.

In Chapter 8 a concept for extending the methods which were originally developed for head and neck surgery to a broader area of application is presented. This concept aims to generalize the existing EPR in *oncoflow* to enable the usage of the system in a broader field of application. As an example an approach for the integration of radiation therapy planning into *oncoflow* is discussed.

Finally, in Chapter 9 the contents of this thesis are briefly summarized and the degree of goal achievement from Chapter 1 are presented. Furthermore, experiences gained from the development of *oncoflow* and the usage of the system in daily clinical routine are discussed in Section 9.3. Additionally, future work items are presented and final conclusions are made.

Chapter 2

Related work

2.1 Introduction

This chapter gives a brief introduction to existing research projects and commercially available software products related to the topics of this thesis.

Various kinds of existing EHRs and approaches for EHR design presented in Section 2.2 are a considerable information base for the development of clinical information systems. Most of the existing systems focus on very specific clinical disciplines or surgical intervention types and are not suitable for the usage in oncological head and neck surgery. However, information which is important for oncology and acquired in CREDOS and GTDS is available in *oncoflow* in order to support the clinical workflow, studies and certifications. The usage of those systems itself is not possible due to limitations accessing the information from the databases, because these systems are commercial products.

The support of tumor boards is covered in Section 2.3. The solutions presented in this section partly provide important assistance features such as the scheduling of patients for tumor boards, web-based presentation or teleconferencing. The TPU in combination with *oncoflow* implements much of the presented functions within one integrated system but provides many additional features especially during tumor board conduction as depicted in Chapter 5.

The recognition of workflows in the field of medicine is mostly applied to specific surgical interventions as depicted in Section 2.4. Theoretical approaches are mostly based on HMMs or Bayesian networks and were inspiring for the workflow recognition presented in Chapter 7. However, the approach presented in this work differs significantly from the related work projects and has not been investigated before to the best of our knowledge.

Section 2.5 presents research projects focusing on the comparison of documentation workflows in the field of medicine. The conclusion of all presented papers is that precise and complete documentation of medical information is crucial for the improvement of therapy outcome and the conduction of clinical studies. In order to compare clinical workflows Schumann et al. investigated in finding the most appropriate algorithm for comparing clinical workflows. Hence, the resulting Levenshtein

algorithm was applied to results from a clinical study presented in Section 6.6 in order to compare workflows for the documentation of the first consultation in head and neck tumor therapy.

Finally, one can conclude that many research projects and available software products already address aspects that are also in the focus of this thesis. However, a combination of these aspects that are integrated into one clinical information system which supports efficiently the treatment process of tumor patients and is well integrated in daily clinical routine is not available at the moment. Thus, the *oncoflow* system and the concepts presented in this thesis provide a basis for the development of future EPRs and clinical workflow assistance systems.

2.2 Electronic health records

2.2.1 Requirements of EHRs

Yu et al. investigated in requirements for EHRs especially for oncology [15]. The authors state that EHRs are not a digital copy of a paper-based medical record but provide flexibility in data presentation and the possibility to perform data mining, data analysis and generate new knowledge. EHRs should actively assist in the delivery of more efficient and higher quality health care.

In 2006 the US federal government provided an initial funding for the Certification Commission for Health Information Technology (CCHIT) to certify EHRs for functionality, interoperability, privacy and security. Unfortunately, those requirements do not meet the specific needs for EHRs in oncology. Thus, in 2009 an overview document has been released which describes specific requirements for oncological EHRs [16]. The whitepaper describes functional requirements and clinical data elements. A cancer data standards repository (caDSR) was established that contains common definitions for structured data elements to facilitate information exchange between different clinics and information systems.

Functional requirements cover all kinds of patient-specific information that is relevant in the scope of tumor documentation. The complete list of requirements is available in [16]. In Table 2.1 a summary of the most important functional requirements is shown, which serves as reference for an ideal oncological EPR.

2.2.2 Nationwide solutions

The GTDS provides a German large regional tumor database primarily for follow-up documentation funded by the German Federal Ministry of Health [17]. The goal of GTDS is to facilitate the documentation of the course of the disease including secondary diseases and long-term side-effects with respect to the actual disease and primary therapy. The documentation is performed by clinical staff as soon as a patient receives a histological confirmed tumor classification. The development of GTDS started in 1991 and is until now connected to 40 cancer centers in Germany so that during

Table 2.1 – Functional requirements for EHRs in oncology (Source: [16])

Category	Requirements
Cancer Treatment Plan	• Demographic information • Diagnosis • Tumor staging • Pathology findings • Co-morbid conditions • Prior treatment • Current treatment plan • Clinical trial protocol number
Cancer Treatment Summary	• Information from treatment plan • Delivered chemotherapy • Delivered biotherapy • Major experienced toxicities • Palliative care and hospice plans • Follow-up care provider • Tasks & timelines for disease recurrence monitoring • Long-term adverse effects form treatment
Oncology-specific Documentation	• Tumor staging • Radiation reports • Chemotherapy records • Pathology reports • Pain assessment • Patient consent forms • Eligibility for clinical trials • Clinical trial summaries • Patient education materials • End-of-life documents
Oncology-specific Functionality	• Chemotherapy and drug management • Dose calculations based on weight and lab results • Scheduling functions e.g. visits, infusions, etc. • Support clinical trials and research • Integration of bar-coding or RFID technology • Generation of quality metrics and other reports • Patient portal with Personal Health Record (PHR)

the past 24 years a huge amount of tumor data was collected. On the other hand, the age of the system, a lacking integration into the clinical workflow and only few assistance functions make the system less appealing for the usage in daily clinical routine.

The university medical center Ulm developed an extensive and certified cancer documentation tool CREDOS based on the SAP infrastructure [18]. The CREDOS system provides a standardized

tumor documentation, the import of little patient master data from the HIS, an automatic export to the GTDS as well as basic functions for supporting the certification to a cancer center. However, the system is lacking meaningful data import capabilities from the HIS which leads to time-consuming copy & paste work for the documentation assistants. Additionally, information entered in GTDS or CREDOS is not verified so that information quality is dependent on the work of the documentation assistant and can not be assured.

2.2.3 Monocentric or multicentric solutions

Wu et al. developed a comprehensive database management system for the organization and evaluation of mammography data sets [19]. The system is designed for the collection of consecutive mammography reports to develop reliable decision support systems and the implementation of accurate medical audits. Therefore, standardized, well-documented and transparent methods according to Brest Imaging Reporting and Data System (BI-RADS) and the Mammography Quality Standards Act (MQSA) are used to ensure data accuracy and facilitate data sharing and communication. Between 2006 and 2011 nearly 30,000 patients were accumulated in the database and 117 distinct pathologic diagnoses were cataloged for a pathology lexicon.

The university hospital in Dresden, Germany, developed an oncology information system MADOS4 for longitudinal basic tumor documentation [20]. The system implements six tumor notification forms for clinical diagnostics, tumor board, therapy, follow-up, recurrence and completion. The system contains additional documentation forms for breast, prostate and colorectal cancer. Histopathological information which is necessary for tumor documentation can be directly entered in the system or automatically imported from different pathological information systems via Health Level 7 (HL7) interface.

Segagni et al. developed an integrated infrastructure, the *ONCO-i2b2* platform, for the integration of clinical and research data to support translational research in oncology [21]. The platform integrates data originating from different information sources, stores them into a data warehouse and allows facts to be hierarchically structured as ontologies. The system actually manages data of more than 6500 breast cancer patients which were collected between 2001 and 2011 at the Fondazione Salvatore Maugeri hospital in Pavia, Italy.

Holzner et al. developed a comprehensive system for Patient Reported Outcome (PRO) documentation [22]. The system is based on tablet computers where patients can enter treatment-related information themselves. Thus, the routine collection of patient data with a reduced amount of human resources is possible in daily clinical routine. The information that is captured is e.g. related to quality of life, fatigue, depression, medication side-effects or disease symptoms. These are important parameters for medical research or daily clinical practice. The software allows to administer questionnaires and present the results. The software is widely used in various institutions in Austria, Switzerland, and the UK. About 5000 patients participated in the usage of the system.

Weiner et al. developed an EPR system which automatically notifies physicians about eligible patients for prospective clinical studies in realtime [23]. A clinical trial study at the Children's Hospital Boston compared the notification about eligible patients before and after the introduction of the new system. During an eleven month time-frame without the system the investigator was notified in 56% out of 61 patients, within a study time-frame of ten months with the notification system the investigator was informed in 84% out of 49 patients.

2.2.4 Scientific research projects

The Surgical Data Recorder developed by Rockstroh et al. aims at the structured documentation of intra-operative device information in a central database [24]. This approach targets the full-automatic collection of information generated by clinical devices which are available on the OR bus; hence, basically low-level information such as vital signs, device parameters or video streams are recorded. This information may be useful for the *oncoflow* system after a postprocessing phase so that only high-level information about the course of the intervention is available.

Documet et al., Le et al. and Deshpande et al. developed electronic patient record systems for minimally invasive spinal surgery and prostate cancer treatment [25, 26]. These systems are tailored to specific intervention types and provide automatic vital sign documentation, video documentation of endoscopic video devices as well as support for pre-operative planning and post-operative activities.

Zhang et al. developed a hierarchical radial approach for the visualization of patient information [27]. This approach uses a tree data structure for the storage of the main diseases as parent nodes and child nodes for more detailed information instead of using a timeline for information visualization.

The implications of German law on the implementation of cross-institutional health records and the application at the Thoraxklinik Heidelberg are presented from van der Haak et al. [28]. Safran et al. present a whitepaper of a national framework for the secondary use of health data as well as a summary of the experiences with online medical records during one decade [29, 30].

The role and importance of information systems in healthcare is the main research topic at the Institute for Medical Informatics, Statistics and Epidemiology (IMISE) at the Universität Leipzig [31]. Winter et al. provide detailed concepts of the implementation of health information systems within a multi-tier architecture reaching from physical devices in the IT department until the modeling of organizational processes. Besides technical realizations the work also focuses on the users of these systems as well as the behavioral and societal changes originating from an increasing IT support of all tasks in daily clinical routine.

2.3 Tumor board support

Patkar et al. investigated in the effectiveness of tumor boards on improved therapy outcome and suggested the usage of advanced clinical decision support systems to realize the full potential of tumor boards [11]. The first part of this work focused on the evidence on the impact of tumor boards. Therefore, scientific articles on the evidence of tumor boards have been reviewed. The respective outcomes were categorized into nine categories like survival rate, quality of life or time to intervention. The authors identified one randomized controlled trial study that shows no significant differences between cases discussed in tumor boards and the control group. Eight observational studies in different cancer domains reported improvements for tumor board patient cases. Only one study focused on cost-effectiveness of multidisciplinary melanoma care at large academic medical centers in the United States compared to traditional community-based treatment. Unfortunately, Patkar et al. found that the study design of almost all articles was poor but the authors did not suggest to interpret the absence of good-quality evidence as the evidence of ineffectiveness of tumor boards. Finally, the authors felt confident that health information technology could assist in structural and administrative aspects of tumor boards such as preparation, data collection, presentation and consistent documentation of decisions.

Eisner et al. provide detailed insight into organisational and technological changes at the "Steiermärkische Krankenanstaltengesellschaft m.b.H." in order to implement integrated tumor board management into the local HIS SAP i.s.h.med [32]. Prior to the integration relevant patient-specific information was transferred to the tumor board moderator via phone, fax or email. Afterwards, the moderator created tumor board invitations which were then sent to all participants via email. During the meeting the moderator noted the results and created meeting protocols which were sent few days later as email to the board participants. Additionally, the moderator transferred the results into the HIS. The complex process has been improved significantly by integrating the entire registration and documentation process into the HIS. Physicians and surgeons are now able to schedule their patients themselves at every hospital computer which has access to the HIS. The tumor board registration is then automatically completed with patient demographic information as well as existing tumor documentation. Tumor board invitations can then be immediately sent to all participants. Therapy decisions are complemented after the board meeting, so that also the tumor board protocols are instantly available in the HIS, centrally available for the attending physicians and surgeons and ready for the distribution across the board participants.

Bumm et al. and Siess et al. established a comprehensive IT infrastructure for tumor board management, results documentation and clinical study management at the university hospital "Klinikum rechts der Isar" in Munich [33, 34]. Firstly, the entire tumor board management process has been analyzed and requirements for an appropriate IT infrastructure have been derived. Afterwards, a centralized, web-based information system *Onkofile* was developed. The system has been installed in the local clinic network and provides tumor board management, patient registration and par-

ticipant invitation. Scheduled patient cases can be enriched with textual information as well as medical images. The system also provides an instant results documentation during the tumor board meetings and an automatic mailing of tumor board invitations and results. Furthermore, a clinical study management provides important parameters of ongoing studies during the tumor boards.

Li et al. developed a web-based teleconference system to support distributed tumor conferences at multiple locations [35]. The system provides a web-based tumor board management with a centralized availability of patient-specific information such as Word documents or Powerpoint presentations. During the video conferences the moderator is responsible for presenting the available information to the participants. The tumor conference participants are able to edit presented information in real-time which enriches the interaction and discussion possibilities between the remote locations.

Summarizing the shortcomings and goals of the shown literature leads to the following requirements on tumor boards:

- Automatic creation of tumor board invitations and protocols
- Automatic import of as much patient-specific information as possible for invitation and protocol creation
- Ensuring the consistent collection of crucial data such as disease staging and outcomes
- Consistent online documentation of tumor board decision and consent
- Ensuring that tumor board recommendations are followed in the practice
- Ensuring active patient participation
- Improving information exchange and regular communication flow between team members
- Establishing robust mechanisms for prospective assessment of tumor board performance
- Ensuring adherence with standards including evidence-based guidelines
- Establishing reliable interfaces with primary care to ensure continuity of care
- Achieving right balance of educational and care delivery objectives of this forum
- Allow patients the ability to fully explore all their available therapy options
- Eligibility of patients for recruitment into ongoing trials could also be screened in real time during the board
- Access for all participating physicians on patient data, tumor board invitations and protocols

Further requirements for cancer center certification postulated by the Deutsche Krebsgesellschaft (DKG) are discussed in Section 5.2.

2.4 Model-based workflow recognition

Knowledge of workflow information from surgical interventions and from perioperative processes is important for the development of intelligent clinical workflow assistance systems. Therefore,

statistical models such as HMMs [36] are appropriate for the recognition of workflow steps and are commonly used in the medical field.

The course of a surgical intervention can be represented as a sequence of 5-tuples, the individual Surgical Process Models (iSPMs), which contain process step information such as activity, actor, surgical instrument, target structure and time [37]. Subsequently, multiple iSPMs can be merged into a generalized Surgical Process Model (gSPM) [38]. A gSPM represents an averaged course of the corresponding intervention type. Based on the aforementioned theoretical basis, Schumann et al. investigated mathematical approaches for comparing iSPMs and gSPMs and assessing the quality of surgical processes [39]. Franke et al. developed a representation of surgical interventions based on Markov theory [40, 41, 42]. Based on the process knowledge that can be acquired from gSPMs, the surgical intervention can be partitioned into different phases. Subsequently, the gSPM can be used in combination with Markov theory to predict the actual high-level phase of an ongoing intervention with the help of low-level tasks such as sensor information. Based on these models, intelligent workflow assistance systems, such as systems that present surgical process information in the operating room, can be developed. This method has already been applied to surgical interventions in eye, neuro and ENT surgeries.

The following research studies investigated intraoperative workflow recognition during laparoscopic cholecystectomies and used HMMs for predicting surgical steps based on Operating Room (OR) sensor information. Padoy et al. used the process information to predict the remaining intervention time. The HMM in this project was developed from 12 recorded surgical interventions that consisted of 14 surgical phases. This model yielded a high prediction error (> 14 min) at the beginning of the intervention, but the error rate decreased significantly at the end (≈ 1 min) [43]. Blum et al. developed a HMM from 11 laparoscopic interventions that consisted of 14 process phases for the recognition of surgical phases during cholecystectomy interventions [44]. The evaluation of this model with a leave-one-out cross validation yielded a positive phase detection rate of 93%. Bouarfa et al. developed a framework to clean noisy sensor information with a Bayesian network approach to infer the correct low-level task [45]. Subsequently, a HMM was used to infer the corresponding surgical process steps based on the corrected low-level tasks with a prediction accuracy of up to 90%.

Modeling clinical workflows other than the OR is an emerging field of research for describing and optimizing clinical pathways. Huang et al. used dynamic programming approaches to summarize a clinical pathway from clinical event logs [46]. Medical behaviors in real-world event logs are very diverse and heterogeneous, but the authors demonstrated the applicability of the presented approach for creating condensed clinical pathway summaries in polynomial time. Subsequently, Huang et al. investigated the use of process mining techniques to extract explicit clinical pathway patterns from medical behaviors recorded in clinical workflow logs [47]. This research group focused on specific diseases, e. g. bronchial lung cancer, colon cancer, gastric cancer, breast cancer

and cerebral infarction. Based on classical sequence pattern mining algorithms, the authors developed an algorithm tailored to the specific scenario (*SCP-Miner*) and performed an evaluation against existing algorithms, such as *CloSpan* and *BIDE*. The results of the study demonstrated that the proposed approach provides better outcomes in terms of processing time, scalability and generated clinical pathway patterns. A later work of Huang et al. focused on improving the discovery of clinical pathway patterns from event logs through the use of probabilistic topic models [48]. The authors used a clinical event log from the cardiology department of the Chinese PLA General Hospital and successfully discovered the underlying clinical pathway patterns using the aforementioned method. The clinical pathway analysis can also be complemented by measuring the similarities between patient traces. Huang et al. employed latent Dirichlet allocation (LDA) to measure similarities between pairwise patient traces [49]. To evaluate the performance of the proposed approach, comparisons with the edit-distance-based similarity measure and a classical simple term vector-based method were performed. The precision of the LDA approach was 19% higher than those of the edit-distance and vector-based outcomes.

2.5 Distance measures for workflow evaluation

The improvement of clinical documentation as well as information quality in EPRs is already addressed in various research projects. Davis et al. developed a template within the EPR that improves significantly the documentation of asthma severity and the appropriate treatment [50]. Bordowitz et al. state that physicians underdocument and undertreat obesity and implemented an EPR that automatically calculates the body mass index and supports obesity documentation [51]. The documentation quality and also the treatment of obese patients have been improved significantly. Menke et al. implemented a computerized clinical documentation system in a pediatric intensive care unit resulting in an improved completeness of documentation, better accessibility and accuracy of information and no change in time spent for patient care by clinical staff [52]. An appropriate IT infrastructure is especially important in tumor documentation to provide physicians useful information, evaluate standards of care and get an impression about the effectiveness in cancer care [53]. Furthermore, the certification as comprehensive cancer center is important with regard to legal regulations and financial means [34]. Therefore, a centralized EPR and supporting tools for tumor therapy and cancer center certification have been developed at Innovation Center Computer Assisted Surgery (ICCAS) aiming at targeting the previously mentioned drawbacks [54, 55, 56].

Chapter 3

Information integration

3.1 The *oncoflow* information model

As a first step towards an improved information management an extensible, flexible and hierarchical information model has been developed. In a close cooperation with clinical partners paper-based records and clinical information systems involved in the oncological treatment process have been analyzed. Afterwards, important information entities were identified and grouped into different classes whereby each class represents a step in the clinical workflow (see Figure 3.1). Commonly accepted standards such as the Union Internationale Contre le Cancer (UICC) were used as theoretical basis during the design of the information model [57, 58]. The information model allows an instantiation of a temporal view of the patient history through a time stamped acquisition of diagnosis and therapy steps as well as an instantiation of a causal representation of stored information based on the logical sequence of activities in the care process. Details of the most important entities that can be directly mapped to process steps in the treatment process are listed in Table 3.1.

In the second step the information model has been converted into a relational database. This database is the heart of the *oncoflow* system and contains all available patient information in a structured manner. Furthermore, communication interfaces to relevant clinical information systems such as SAP i.s.h.med and the DTTM have been realized to exchange data electronically and relief the clinical staff from manually reentering necessary information into the central database (see Figure 3.3).

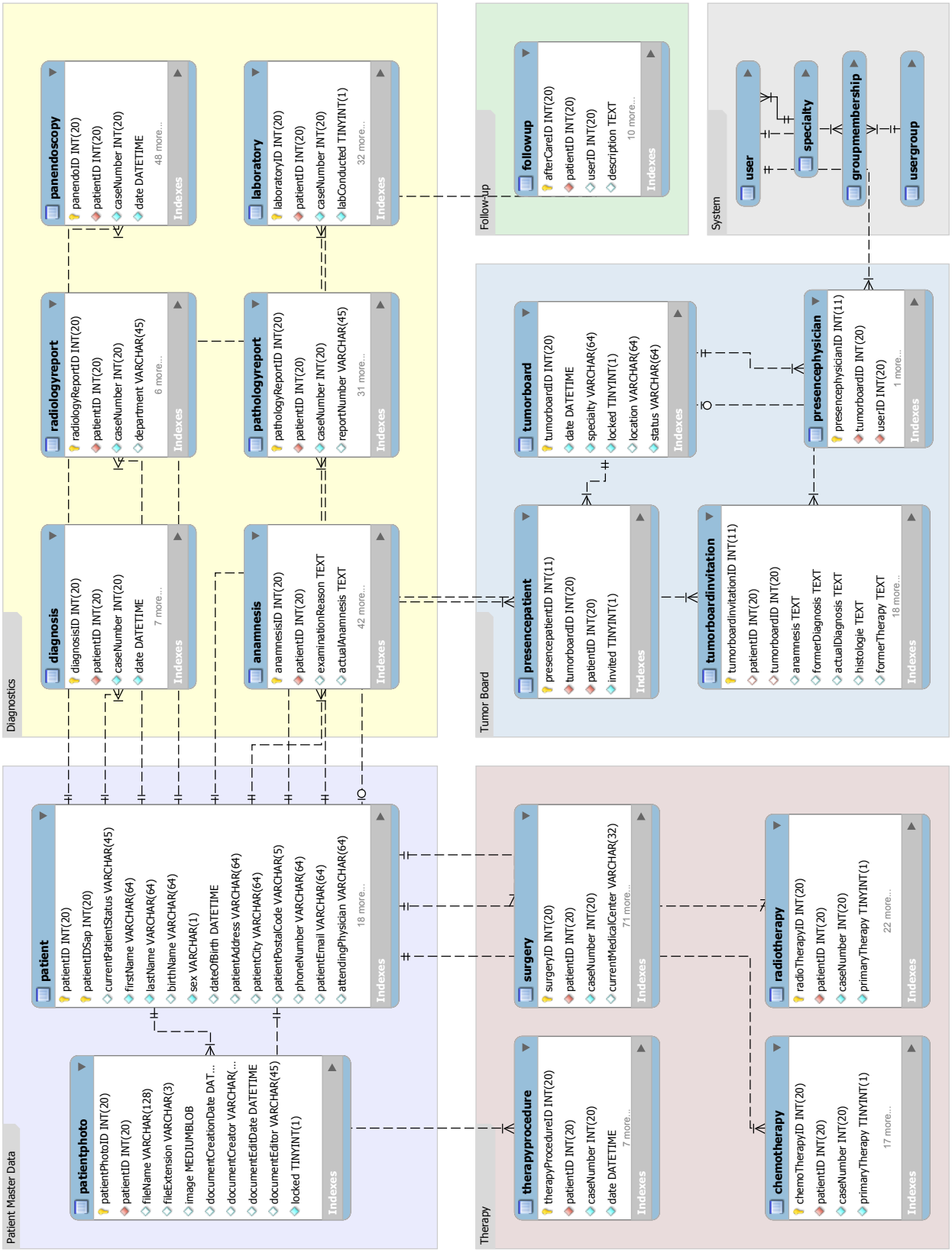

Figure 3.1 – Detailed information model depicting all information entities which are relevant in clinical diagnostics, tumor board, therapy, and after care

Table 3.1 – Detailed description of all information entities used in the *oncoflow* information model

Information class	Information entities	Primary data source
Patient	Name, Address, Date of birth, Referring physician Circumstances of death	HIS Family
Anamnesis	Nicotine, Alcohol, Risk factors, Family anamnesis, Profession, Medicaments	Anamnesis
	Karnofsky index, Pain, Teeth status	Examination
Diagnosis	Case number, Date, ICD10 code, Description	HIS
Procedure	Case number, Date, ICPM code, Description	HIS
Panendoscopy	Endoscopy images, Biopsy location, clinical TNM	DTTM
Histology	Localization, Grading, pathological TNM, Histopathological assessment	Histological report
Radiology	Evaluation report of radiological images	Radiological report
Intervention	Personnel (Surgeon, Assistants, Staff), Detailed intervention description, Neck-dissection levels	Intervention report
Chemotherapy	Drugs, Dose, Cycles	Chemotherapy report
Radiotherapy	Type, Target areas, Dose, Mucositis	Radiotherapy report
Follow-up	Date, Complications, Recidivisms	HIS
Laboratory results	Blood count	iSoft
Tumor board	Type, Time, Location, Participants, Patients Attended participants, Therapy decision	*oncoflow* TPU
User	Name, Group, Specialty, Mail address	*oncoflow*

3.2 System architecture

The *oncoflow* framework is designed as a modular system to support the extension with new functionalities and an easy integration with multiple external systems such as clinical information systems, databases or workflow management systems. The core framework is built as a three-tier-architecture according to the Model View Controller (MVC) design pattern (see Figure 3.2) [59].

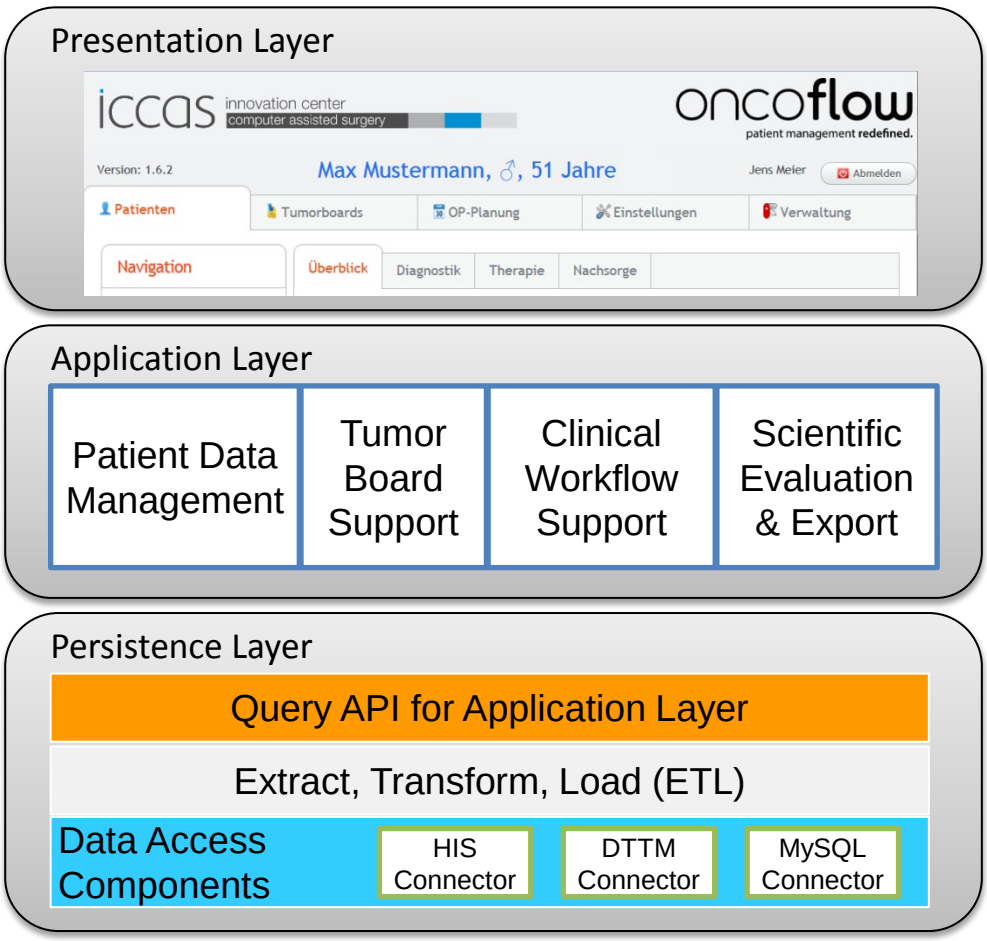

Figure 3.2 – The three-layer system architecture of *oncoflow* is built according to the MVC design pattern

3.2.1 Software components

Oncoflow was developed as a web-application based on the Vaadin application framework. Vaadin provides convenient integration of pure Java Enterprise (JEE) development with Google Web Toolkit (GWT) web technology. The software development takes place in Eclipse/Java and finally the Vaadin GWT compiler creates a web-application which can be deployed on application servers like Apache Tomcat. This approach has numerous advantages especially for software development in a scientific environment. Firstly, Java is widely taught at universities, hence, the entry barrier for researchers and student workers for maintaining the software is low. Furthermore, Vaadin relieves the developer from Hypertext Markup Language (HTML), Java Script and other web-related technologies and problems in favor of focusing on the specific programming problem. The entire *oncoflow* application is solely implemented with free software products. The used software, libraries and corresponding version numbers are depicted in detail in Table 3.2.

Table 3.2 – Software components used during *oncoflow* implementation

Component	Software	Version
Operating system	Debian Linux 6	Kernel 2.6.32
Database	MySQL	5.1
	Connector/J	5.1.31
Application Server	Apache Tomcat	8.09
Webserver	Lighttpd	1.4.28
Java	Oracle Java JDK	1.8.0_05
Encryption	OpenSSL	0.9.8
Web framework	Vaadin	6.14
Charts	Invient Charts	0.8.6
	HighCharts	2.3.3
IDE	Eclipse Kepler	SR 2

3.2.2 Persistence Layer (Model)

The persistent storage in *oncoflow* is realized with a MySQL database system. The connection between *oncoflow* and the database is established by the MySQL Connector/J library and the Apache Tomcat web application server. In the chosen setup the Tomcat server uses the Connector/J library, establishes connections to the database and maintains existing connections in a connection pool. The connection pool provides high performance in highly concurrent environments and performs the handling of idle connections so that the amount of open connections is dynamically adjusted depending on the actual requirements.

Object Relational Mapping (ORM) provides a transparent layer between application layer and database in *oncoflow*. Therefore, an ORM driver, the `DatabaseObject`, has been developed. The driver recursively translates Java class variables and values into Structured Query Language (SQL) statements and vice versa. A Java class that should be persisted in the database must inherit from `DatabaseObject`. Database tables to the corresponding Java class can be automatically created by using the method `DatabaseObject.createDatabaseTable()`. The `Query` class provides an interface between the `DatabaseObject` and the Tomcat connection pool.

In order to persist a Java object into the database the `Query` interface provides the methods `Query.insert(DatabaseObject)` and `Query.update(DatabaseObject)`. The `Query` class then acquires a database connection from the connection pool. Afterwards, the methods `DatabaseObject.generateInsertQuery()` or `DatabaseObject.generateUpdateQuery()` are used to create necessary SQL insert or update statements. Finally, the SQL statements are executed.

The `Query` class provides the method `Query.select(Class<?>, String)` to fetch information from the database. The first argument denotes the specific Java class which is inherited from `DatabaseObject`. The second argument is optional and may contain a MySQL `WHERE` clause to limit the results. Afterwards, the `Query` class executes the SQL statement and receives a SQL result set. The result set is then passed to `DatabaseObject` which in turn provides the method `getObjectFromResultSet(Class<?>, ResultSet)` to create a corresponding Java object. Each result object is finally stored in a table-like data structure, the `BeanItemContainer`, which is the return value.

The following paragraphs depict in detail the *oncoflow* communication interfaces and the implemented Extract (ETL) program logic. The interface to the HIS is unidirectional for security reasons. The interface automatically exports patient master data, diagnoses, procedures, histopathological results and radiological reports as comma-separated text files once a tumor diagnosis occurs for a specific patient. These files are stored on a network share and moved into an archive folder after successful import. The files contain the unique patient id, conduction date, International Statistical Classification of Diseases and Related Health Problems (ICD) or the German Operationen- und Prozedurenschlüssel (OPS) codes which are internationally denoted as ICPM as well as a textual description of the specific codes. Histological and radiological reports include additional information such as department, HIS-internal id codes and the detailed textual histological or radiological statement.

The second interface to the DTTM uses Hypertext Transfer Protocol (HTTP) for the exchange of patient master data, detailed tumor classification (TNM) and annotated endoscopic images. The

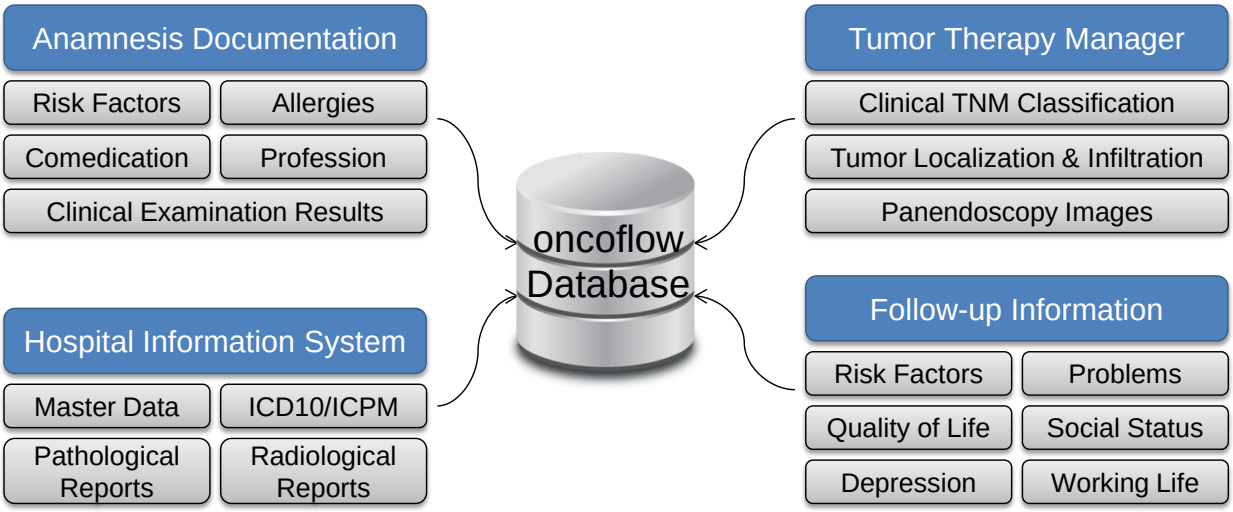

Figure 3.3 – The *oncoflow* system provides electronic communication interfaces for automatic data import as well as web-based documentation forms in order to assure structured information acquisition

DTTM is a local Windows application which can be opened from within the *oncoflow* patient record with the current patient id as parameter. Afterwards, the DTTM establishes a HTTP connection to *oncoflow*, transmits the patient id and *oncoflow* sends back the patient master data as Extensible Markup Language (XML) file. After the physician finished the panendoscopy documentation results are transmitted to *oncoflow* via a new HTTP connection. Textual results such as TNM classification or tumor grading are transmitted as XML file and endoscopic images are stored in a zip archive. Oncoflow then saves the information from the XML file, extracts the zip archive and adds the tumor classification and endoscopic images to the specific EPR. The entire panendoscopy and histopathological confirmation process is depicted in more detail in Section 4.3.

Information provided by the HIS is frequently unstructured continuous text. Hence, an extensive processing of the data during import has been implemented providing restructuring of given information and embedding the information into a semantic context inside the proposed information model. Thus, patient-related information is available in a structured manner within the central database and instantly usable for further electronic processing or complex search queries for retrospective clinical trial studies. Changes in reporting practice, e.g. changes in the meaning of ICD or OPS codes are not yet implemented in the information model due to the unavailability of this information in the data exported from the HIS. However, preserving the meaning of existing information despite of changing reporting standards is an important feature in a future release of *oncoflow*.

3.2.3 Presentation Layer (View)

The presentation layer consists of a rich Internet application within the web browser. A schematic representation of the User Interface (UI) is depicted in Figure 3.4. The UI has been designed according to the modular application framework requirements. Hereby the header shows patient demographic information such as patient name, gender and age as well as the username of the current logged-in user and a logout button. Subsequently, the main navigation bar has been implemented as a tab sheet where each application module is represented by one tab. Thus, each module is easily accessible and the system can be simply enhanced with new software modules. The module navigation bar is situated on the left side in the UI and contains module-specific contents. Even though there are no constraints for the included navigation items the usage of this navigation bar is mandatory for module developers. Finally, the module content area shows the actual module content. There are no restrictions for developers so that this area may contain text, tables, graphics or other content which can be realized with Java and the Vaadin application framework.

UI components such as buttons, text fields or tables are defined in Java (e. g. `Button button = new Button("Login")`) and are afterwards rendered with GWT as HTML elements. Based on the browser capabilities Asynchronous JavaScript and XML (AJAX) and the WebSocket protocol are used to exchange information between web-browser and application server, listen to user events such as button clicks or update UI elements where the content changed. A detailed diagram re-

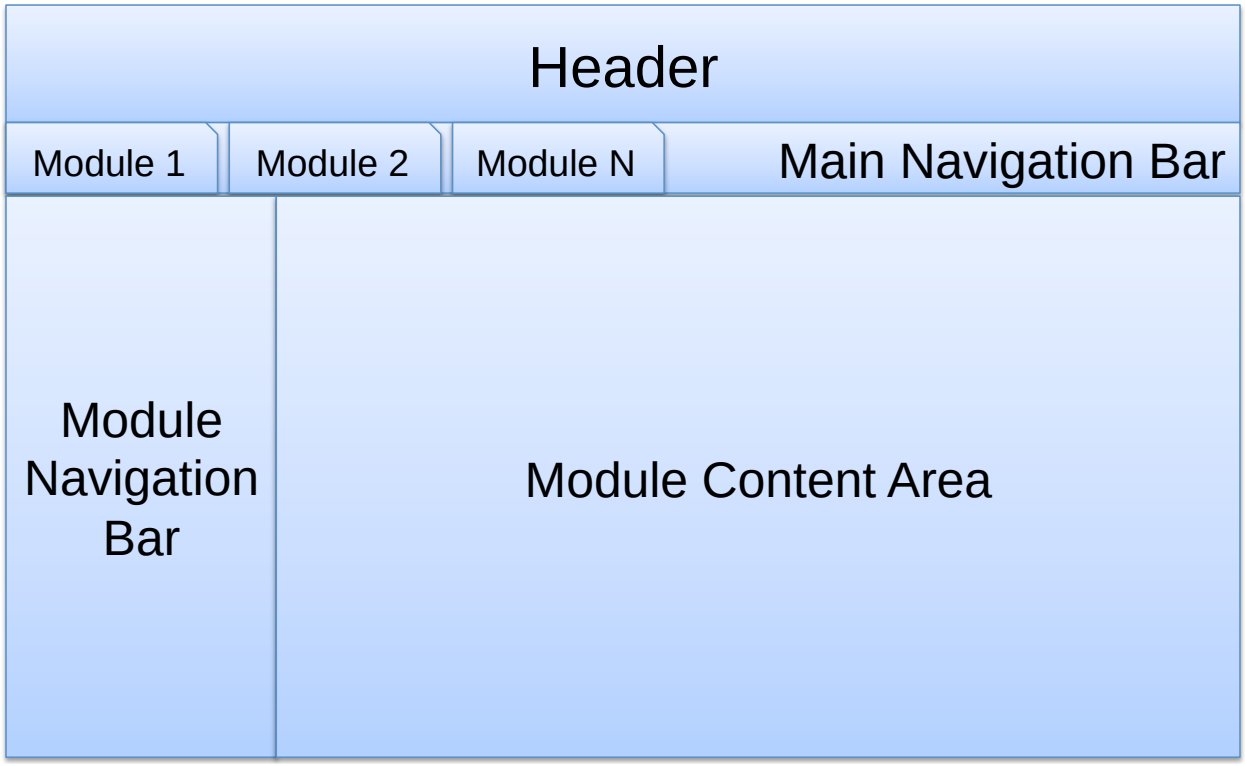

Figure 3.4 – Schematic representation of the *oncoflow* user interface

garding the client-side and server-side Vaadin architecture is provided on https://vaadin.com/book/-/page/architecture.html.

The "Look and Feel" of the UI is determined by the used theme. The standard theme *Runo* which is shipped with the Vaadin framework was mostly appropriate for the development of *oncoflow* in terms of font size, color palette and usability. Adjustments of theme elements were rarely necessary and could be achieved conveniently with Cascading Style Sheets (CSS) definitions in a user generated `styles.css` file. An impression of the final user interface is given in Figure 3.5.

3.2.4 Application Layer (Controller)

The *oncoflow* application layer consists of a variety of different special-purpose modules and is easily extensible by new functionalities. Each module consists of a module controller class responsible for the module initialization and the connection to the *oncoflow* framework or other modules if necessary. Each module gains access to the model via the previously described `Query` class (see Section 3.2.2) and is responsible for the creation of a module navigation bar as well as the module content (see Section 3.2.3).

Within the current development stage of *oncoflow* the system includes four modules for clinical workflow assistance and one system administration module. The patient data management module provides basic functionalities for *oncoflow* such as a patient list, search functions and the visual,

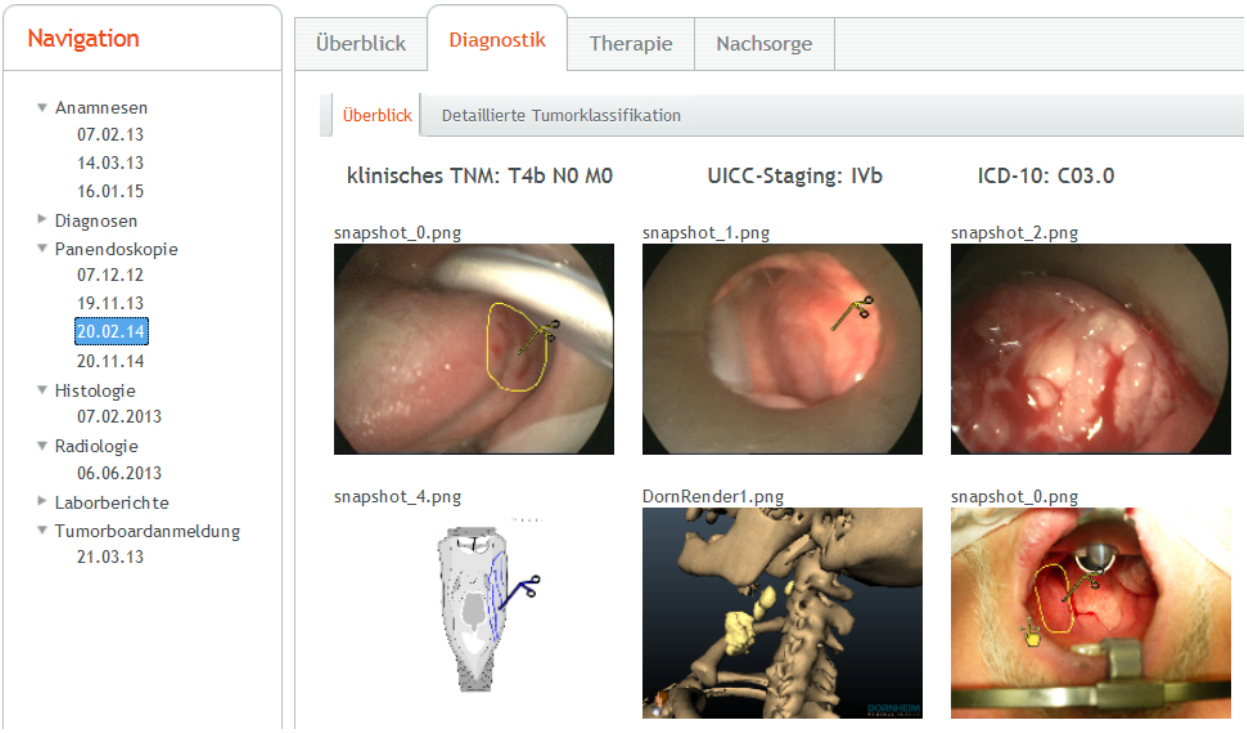

Figure 3.5 – The *oncoflow* user interface

structured representation of the EPR. The second module provides extensive tumor board support and is described in detail in Chapter 5. The clinical workflow support module covers several workflow assistance functionalities which are described in detail in Chapter 4. The scientific evaluation and export module provides support for physicians and surgeons for selecting, exporting and visual representation of information for retrospective clinical studies or quality management related tasks. The module is depicted in detail in Section 4.7.

Finally, the administration module comprises user management, system settings and service settings such as system variables or the activation or stop of data import services.

3.2.5 Data security

The *oncoflow* system deals with highly sensitive patient information. Hence, the information has to be protected from illegal access and eavesdropping. In order to protect the information from illegal access, user authentication is required. Each user must provide username and password on a login screen before access is granted. Users are enforced to change their passwords after the first login. The passwords itself are stored as hash value in the database, protecting the users privacy. A group-based rights management was implemented which significantly facilitates the assignment of access rights to multiple users simultaneously. The user can be assigned to different user groups with varying permissions which are listed in detail in Table 3.3.

Information transmitted over Local Area Networks (LANs) is prone to eavesdropping or illegal

Table 3.3 – Group-based rights management in *oncoflow*

Group	Permissions
Full administrator	The full administrator has access rights to patient information as well as to all technical settings.
Clinical administrator	The clinical administrator has access to all patient-specific information including the right to delete patient records.
Technical administrator	The technical administrator has access to all *oncoflow* settings such as user management, password reset and the data import services.
Physician	The physician has access to all patient-specific information and is able to change existing information.
Assistant physician	Assistant physicians can see all patient information, add new information entities e. g. documenting an anamnesis, but are not allowed to change existing information.
Manager	Managers have no access to patient-specific information. This group is only able to perform statistical evaluations.

access without appropriate security measures. The *oncoflow* application framework is completely web-based, hence, information visible on the users screen has been entirely transmitted over insecure network connections beforehand. Thus, security measures were put in place to protect sensitive information during the transmission in the hospital network. The transport security has been established with self-signed Secure Socket Layer (SSL) certificates which were created with the OpenSSL library. We decided to use the *Lighttpd* Web server as the primary communication endpoint for the user in favor of Apache Tomcat itself. The reasons were that the implementation of SSL encryption in Tomcat is rather complex but easily configurable in *Lighttpd* and that *Lighttpd* hosts further services such as a web-based SQL administration tool or a bug tracking system. However, *Lighttpd* forces the entire communication to be encrypted with SSL encryption so that login and patient-specific information is protected.

Chapter 4

Workflow assistance in daily clinical routine

4.1 Introduction

Physicians and surgeons follow the workflow which is described in detail in Section 1.2 in daily clinical routine. Unfortunately, they need to cope with all previously mentioned drawbacks originating from distributed information systems. The *oncoflow* system aims to improve these shortcomings by supporting the clinical staff during the complete patient treatment process. Therefore, *oncoflow* orchestrates a multitude of assistance functions originally provided by different information systems within a clear web-based user interface to efficiently support the clinical staff. This chapter describes all workflow assistance modules in detail which are implemented in *oncoflow* and which are already in use in daily clinical routine at the clinical site. A clinical study in which the process improvements were evaluated was conducted at the department of head and neck surgery. The study results are presented in Chapter 6.

4.2 Standardized anamnesis documentation

The first consultation of tumor patients reveal important information about the patient's current medical status. Based on this information the physician makes a diagnosis and prepares the following therapy. At the moment the results of anamnesis and clinical examination are documented as continuous text in the HIS into the so-called ambulance card. Most physicians use word templates containing relevant but slightly varying headlines for the structured documentation process. These headlines are transferred with copy and paste into the ambulance card and used as reference for the documentation process. However, important information e.g. about nicotine or alcohol abusus are lost in the free-form text, thus, are hardly usable for retrospective analysis, clinical studies or workflow assistance.

In order to find a standardized documentation of the first consultation we conducted several

interviews with all physicians and surgeons from the local head and neck department that are involved in tumor treatment. During these meetings the relevant questions to the patients, the order in which they are posed and all supporting documents have been acquired. The first part of questions covers the anamnesis process. During this phase the physician talks to the patient and documents relevant information simultaneously. Questions are related to the current problem, medication, profession, family anamnesis and risk factors such as nicotine or alcohol. Subsequently the clinical examination is performed with a detailed examination of ears, nose, oral cavity, hypopharynx and larynx as well as a palpation of the neck lymph nodes. Finally the results are documented in the HIS.

A consolidated document which contains the standardized sequence of questions has been developed and finally verified by the participating physicians after the workflow analysis. Then the agreed set of questions has been implemented in *oncoflow* as a web-based form (see Figure 4.1). The form consists of free text fields for unstructured information as well as predefined checkboxes and dropdown fields for important therapy-related information such as nicotine consumption, pain or Karnofsky index. Some values especially for clinical examination questions are completed beforehand with standard values in order to relieve physicians from additional documentation effort. Form-based results documentation actually provides workflow support and improves information quality (see Section 6.6). Physicians are guided through the consultation process in a standardized manner and are relieved from using additional documents. Different text input fields and check buttons improve the user experience during the documentation and provide structured information storage at the same time. Hence, the information can be queried via SQL and is instantly available for further usage. There are also fields for unforeseen but relevant information available where the physician may add further notes that do not fit into existing categories. The EPR was also enriched with patient photos. Patient photos are an important means during tumor board discussions to give physicians which are not familiar with the patient an impression of its physical status. Especially for radiotherapists the patient's constitution is the basis for an optimal therapy planning.

A clinical study was performed to evaluate the presumed advantages of structured results documentation (see Chapter 6). The study focused on the overall satisfaction of the web-based system, the time needed for results documentation compared to the current workflow and finally the information density which should be improved with a structured documentation form.

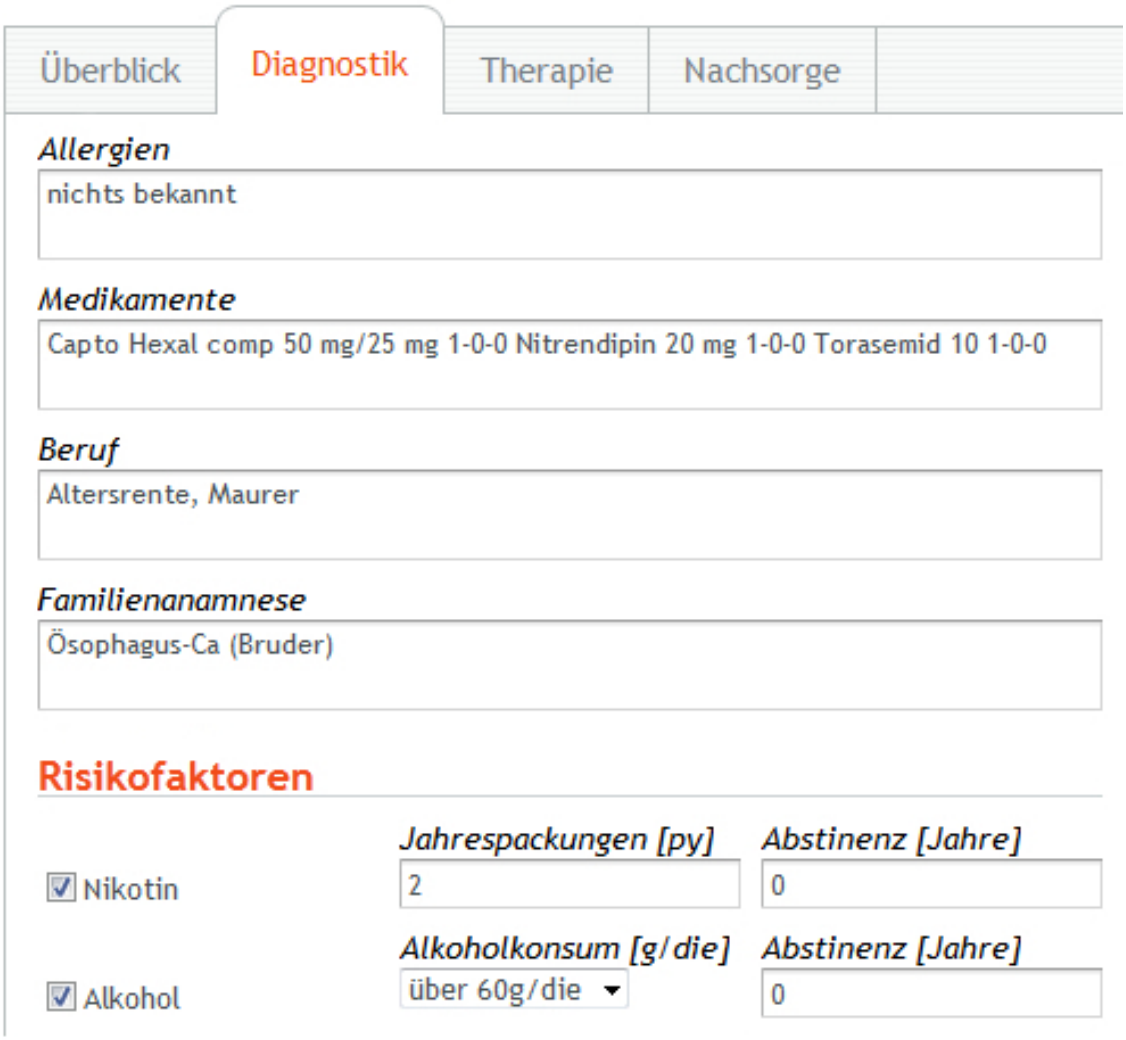

Figure 4.1 – Structured, web-based *oncoflow* anamnesis documentation form

4.3 Panendoscopy and histopathological confirmation

The panendoscopy is a diagnostic intervention under full anesthesia in order to perform a detailed examination of oral cavity, hypopharynx, larynx, esophagus and trachea. A panendoscopy consists of a combination of endoscopic examinations:

- Pharyngoscopy
- Microlaryngoscopy
- Tracheoscopy
- Bronchoscopy
- Esophagoscopy
- Epipharyngoskopy

Additionally, tissue samples of potential tumor tissue are taken during the intervention (see Figure

4.2). Each biopsy sample is pinned on a piece of cork and numbered consecutively by the scrub nurse. The nurse also denotes the biopsy location with the corresponding numbers in a histological request. Afterwards, the biopsy samples and the request form are sent to pathology department for histopathological confirmation resulting in a pathological TNM classification. The numbers are later used by the surgeons to map the histological findings to the corresponding biopsy samples. Right after the intervention the surgeon uses the DTTM to generate a clinical TNM classification and to create an intervention report enriched with endoscopic images as well as schematic representations from the larynx where the biopsy locations can be marked. An import of the DTTM report into the local HIS was not possible, thus, the surgeons created an additional intervention report within the HIS.

In order to facilitate and improve the aforementioned workflow and reduce documentation efforts an integrated workflow between *oncoflow*, DTTM and SAP i.s.h.med has been implemented (see Figure 6.2). Before a panendoscopy is performed, patient-specific information is already available in *oncoflow* through the SAP i.s.h.med data export. After the panendoscopy, the surgeon opens the EPR of the specific patient and creates a new panendoscopy data set. Subsequently, the surgeon is able to open the DTTM application directly within *oncoflow*. *Oncoflow* then automatically transmits

Figure 4.2 – Typical setting during a panendoscopy. The surgeon uses an endoscope and a biopsy forceps to obtain tissue samples through an esophagoscope

the patient master data and the current case number to the DTTM so that the surgeon is relieved from manually reentering existing information. Afterwards, the surgeon imports endoscopic images from the intervention, creates the clinical TNM classification and generates the intervention report as Portable Document Format (PDF) document in the DTTM. A dedicated network share for importing PDF documents into SAP i.s.h.med was established where the generated intervention reports are automatically stored. Based on the patient-specific case number which has to be the beginning of the PDF's file name the report is immediately imported by SAP i.s.h.med and included into the patient record. Hence, surgeons are relieved from a time-consuming creation of additional intervention reports within the HIS. Finally, the tumor classification, tumor location and endoscopic images are automatically transferred to *oncoflow* for a centralized availability.

Unfortunately, the entire process for histopathological confirmation is not yet fully integrated and supported. Further work will focus on the documentation of biopsy locations and corresponding numbers within *oncoflow* during the intervention. In combination with the structured reports from pathology department, assessments for the different biopsy samples which are clearly distinguishable according to their unique numbers could be directly mapped to the corresponding biopsy locations. A convenient visual representation of the results would surgeons allow to hover over the marked biopsy locations within the schema and see the corresponding pathological results for this tissue sample.

4.4 Follow-up consultation

Follow-up consultations are crucial in cancer treatment to assure tumor clearance and to recognize tumor recurrences at an early stage. This information is important for planning further therapies in time in case of recidivisms. The documentation is also valuable for a long-term assessment of therapy outcomes in order to perform retrospective clinical studies, hence, to improve tumor therapy. Consultations are taking place quarterly the first year after therapy and every 6 months the following 4 years. During the consultation the physician performs an examination of the oral cavity and the hypopharynx, performs a tracheostoma check if present and asks the patient about the current medical condition.

Patients with head and neck cancer experience partially severe functioning impairments after tumor therapy. In addition, the patient's way of life often does not change and risk factors such as nicotine or alcohol abuse remain even after a complex tumor therapy. However, functioning outcome and quality of life parameters are not regularly assessed in a standardized way in daily clinical routine. Patient-reported outcome monitoring is an efficient way to capture quality of life, fatigue, depression, medication side effects or disease symptoms for medical research and daily clinical practice [22]. The necessary technology such as tablet computers and web-based questionnaires are widely available in medical institutions so that the routine collection of patient

data with a reduced amount of human resources is possible. Thus, the follow-up consultation process has been enhanced with a tablet-based documentation system based on International Classification of Functioning (ICF) practice guidelines (see Figure 4.3) and an improved results documentation in *oncoflow* (see Figure 4.4).

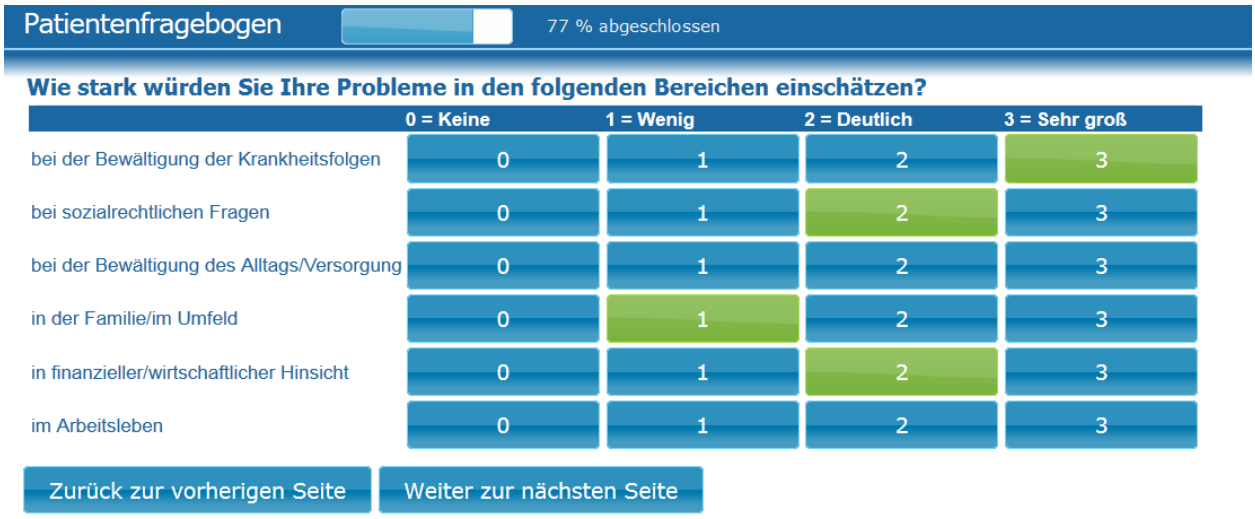

Figure 4.3 – A questionnaire concerning quality of life criteria is digitally answered by patients prior follow-up consultation with a tablet-based system

The assessment of the ICF based clinical practice guidelines was subject of a multicentric clinical study [60, 61]. A shortlist of outcome instruments based on predefined criteria has been evaluated by an interdisciplinary expert group. Afterwards, the experts agreed upon outcome measurement instruments for 3 application areas (screening, therapy evaluation/planning, clinical trials). Finally, a questionnaire has been developed based on the previous results and was implemented as Android tablet application in order to facilitate the electronic results documentation. The development of the Android application was realized by SWAN - Scientific Workflow Analysis GmbH.

Since then, the application is used before each follow-up consultation during the patient's waiting time which is frequently more than 30 minutes. During this time period nurses hand out tablets to the patients in order to answer the questionnaire. Afterwards, the questionnaire results are automatically imported into *oncoflow* and mapped to existing EPRs. Unfortunately, at the moment the information is not instantly usable by the clinical staff. Hence, an integration of follow-up information into the oncoflow user interface and an instant usability is work in progress.

The new approach enables the acquisition of information which is important for the evaluation of therapy outcomes, for the conduction of clinical studies focusing on aspects of functioning impairments after head and neck tumor therapy and finally for improving the therapy outcome significantly.

Subsequently, the patient enters the examination room for follow-up consultation. During the examination a nurse documents the results in SAP i.s.h.med (see Figure 4.4, left). Unfortunately,

the documentation is performed in a free-form text field and important questions concerning current nicotine or alcohol consumption are not asked. However, a structured follow-up documentation form has been developed in *oncoflow* to improve the clinical workflow and the information quality (see Figure 4.4, right).

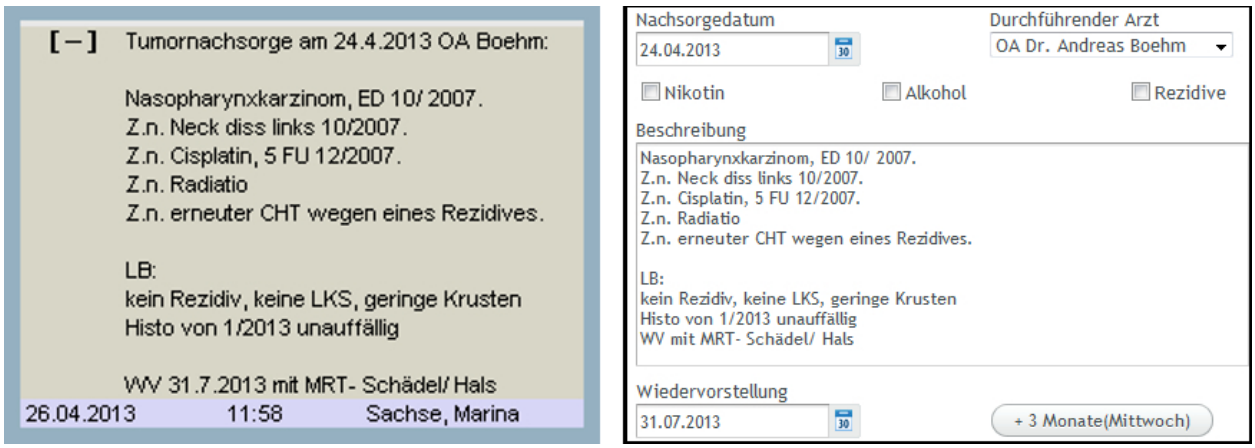

Figure 4.4 – *left:* The follow-up documentation in SAP i.s.h.med is conducted in an unstructured free-form text field; *right: oncoflow* provides a structured documentation of dates, actual risk factors and recidivism occurrence

Information availability and information quality are improved by 3 check boxes for alcohol and nicotine consumption as well as for tumor recurrence. This information allows retrospective clinical studies where tumor type, therapy, way of life and tumor recidivisms can be correlated over time. The clinical workflow is supported by using distinct date fields containing the consultation date as well as the date for reassessment. Particularly the reassessment date can be used for automatically generating patient lists for the upcoming follow-up consultation or to limit the number of patients scheduled for a specific date. A button `+3 Months (Wednesday)` increases the date for the next consultation each time by 3 months and facilitates the scheduling process. However, the tablet-based documentation and the structured follow-up documentation in *oncoflow* have to be merged so that only one consistent documentation will be used in the future.

4.5 Treatment guidance

The treatment guidance is rather a set of tools supporting daily clinical routine from the viewpoint of the attending physician than a single Web page in *oncoflow* and accompanies the patient throughout the entire treatment process beginning at the registration for the first consultation until the patient is released from follow-up meetings. Depending on the patient's current stage in the treatment process there are several tasks for the physician (see Table 4.1).

These tasks will be soon implemented in *oncoflow* as work list. Based on key events in the treatment process the patient status will be automatically updated in *oncoflow* and the patient

Table 4.1 – *oncoflow* work list items and corresponding tasks for the attending physician in daily clinical routine. Descriptions of the respective work list item are depicted in italic, physician's tasks in standard typeface

Work list items in *oncoflow*	Description and physician tasks
New patient	*Create new patient record* Schedule patient for anamnesis
Anamnesis	*Anamnesis and clinical examination performed* Creating diagnoses based on observations Schedule patient for panendoscopy
Panendoscopy	*Panendoscopy performed* Create intervention documentation Create TNM classification in DTTM Annotate endoscopy images in DTTM Upload tumor documentation to *oncoflow*
Pathology	*Histopathological report available* Schedule patient for next tumor board
Tumor board	*Therapy decision available* Schedule patient for therapy
Follow-up	*Follow-up consultation* Schedule patient for next follow-up Export patient information for survival analysis

moves to another work list item. These events may be an upload of panendoscopy information from DTTM into *oncoflow*, the availability of new histopathological reports or the discussion of the specific patient in the local tumor board. The work list supports the physician with an improved access to different groups of patients in daily clinical routine. An important use case example is the scheduling of patients for pre-operative tumor boards. Hereby, the trigger is the availability of histopathological results for the specific patient. Hence, *oncoflow* will provide an overview including all patients that have to be scheduled for upcoming tumor boards. The creation of tumor board invitations can be started immediately from this patient overview with the help of a new method described in Chapter 5.

4.6 Treatment summary

An overview of the current medical status of a patient is crucial, especially for physicians which are not familiar with their actual patient. The overview should present information important for physicians in the current treatment step. These information entities in the field of tumor therapy may be diagnoses, applied medical procedures, histopathological results as well as surgical intervention

or radiochemotherapy outcomes. This information is already available in digital form within the clinical information systems. Unfortunately, the information is not presented in an appropriate manner, hence, not visible for the physician at a glance.

In order to mitigate these drawbacks physicians and surgeons from the Inselspital in Bern, Switzerland, manually prepare relevant patient-specific information in a text document (see Figure 4.5). This patient summary is continued by each attending physician who manually reenters important information already available in the local HIS. The presented approach shows the significance of the problem but is also time-consuming and error-prone.

Max Mustermann 9-9-999

Diagnose **Wenig differenziertes Plattenepithelkarzinom der Nase inital Stadium cT4 cN0 M0**

- 20.04.2010 Tumor biopsiert Histologie: Wenig differenziertes invasiv nicht verhornendes Plattenepithelkarzinom mit hoher Proliferationsfraktion.
- 30.04. – 09.07.2010 4 Zyklen mit Induktionschemotherapie mit Taxotere, Cisplatin und Xeloda. Klinisch und radiologisch sehr gutes Tumoransprechen
- 21.07. – 10.09.2010: Kombinierte Radiochemotherapie mit Cisplatin

Noxen/Risikofaktoren: keine
Ernährung: per os gut möglich
Bildgebung **MRI vom 15.04.2010:** Raumforderdender Prozess in der Nasenhöhle mit infiltrierendem Wachstum und ossärer Destruktion des Ethmoids ausserdem Infiltration bis in die vordere Schädelgrube.
PET-CT vom 26.04.2010: Malignom typisch stoffwechselaktive Anreicherung der Nasennebenhöhlen mit Infiltration bis Sinus frontalis beidseits. Destruktion des harten Gaumens und keine Fernmetastasen
CT NNH vom 11.10.2010: Diskrete progrediente Schleimhaut der unteren Nasenmuschel links am ehesten posttherapeutisch. Kein Hinweis auf Tumorrezidiv.

Tumorsprechstunde 09.12.2010 – Dr. XY

Anamnese Dem Patienten geht es gut, keine Gewichtsabnahme. Eingeschränkte Nasenatmungsbehinderung, die schon vorbestehend war. Ansonsten problemlose Ernährung. Riechvermögen weiterhin eingeschränkt, dass Schmecken sei in der letzten Zeit zurückgekommen. Keine Doppelbilder.

Befunde Unauffällige Schleimhaut enoral. Unauffälliger Larynx, Pharynx bei guter Beweglichkeit der Stimmlippen. Endonasal feuchte Schleimhaut mit Sekret bei deutlichen Verwachsungen beidseits, die eine endoskopische Endoskopie erschweren. Hinter der Verklebung soweit Einsichtig kein Hinweis auf Rezidiv, keine Ulzeration bei feuchter Schleimhaut.

Beurteilung und Procedere
Aktuell locoregionär rezidivfreier Patient soweit beurteilbar ebenfalls im durchgeführten CT kein Hinweis auf Rezidiv. Der Patient erhält Anfang Januar ein PET-CT mit anschliessender Besprechung bei den Kollegen der Strahlentherapie, namentlich Herrn Bröhme, Ende Januar erneute Vorstellung auf der HNO-TU-SS zur PET-CT Besprechung und erneuten Untersuchung.

Figure 4.5 – A treatment summary used at the Inselspital in Bern which is generated and updated manually

The treatment summary in *oncoflow* addresses this issue and provides a condensed patient overview summarizing the most important information in the current treatment phase (see Figure 4.6). A prototypic rule-based implementation aggregates the latest information available originating from each process step into a one-page overview. The overview contains textual information as well as medical images from panendoscopy structured according to the oncological treatment process. The treatment summary should be more focused on the information which is relevant in the current treatment step. Thus, a dynamic framework which is aware of the patient's actual situation and which is able to restructure the visible content should be the next development step. However, the HMM-based approach presented in Chapter 7 builds the basis for further research in this field.

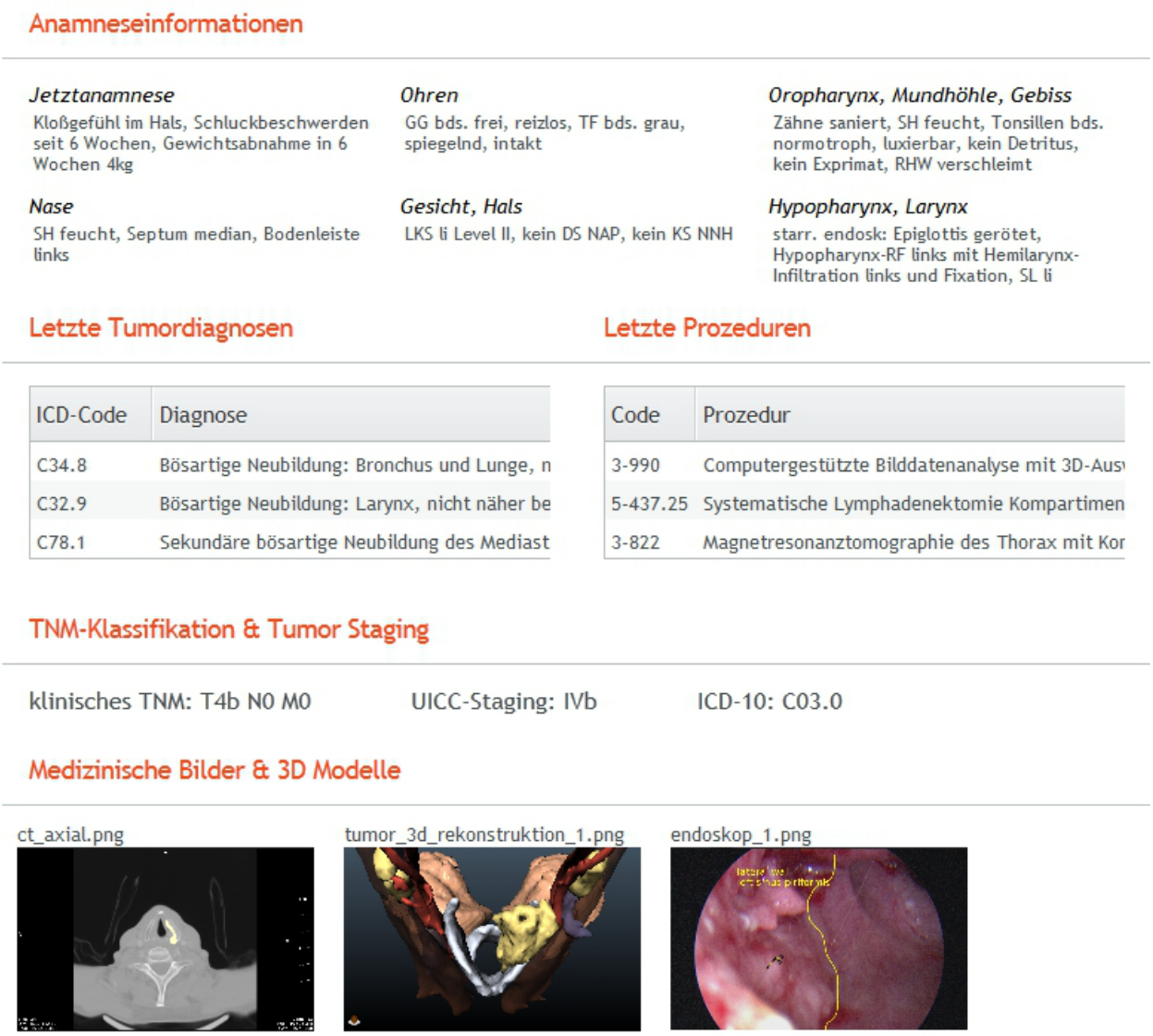

Figure 4.6 – The treatment summary gives a brief overview on the patient's current medical status. The automatically generated treatment summary in *oncoflow* has a clear structure and provides additional information in form of medical images

4.7 Information aggregation and data export

The support of clinical studies and quality management is one major requirement for *oncoflow*. Therefore, a full-automatic information import was established as depicted in Chapter 3 and new approaches were implemented and tested to acquire important information in a structured way as shown in Section 4.2, Section 4.3 or in Chapter 5. However, this information is only valuable for physicians and surgeons when they are able to select, aggregate and export relevant data according to their actual needs in a convenient way. Therefore, a module has been developed for *oncoflow* which allows a convenient access to existing information [62].

Requirements analysis The module development started with a detailed requirements analysis together with physicians and surgeons involved in head and neck tumor treatment. Hereby two major aspects for information export could be identified. In order to process huge amounts of patient data for statistical analysis the SPSS software suite is used. Therefore, the selection of patients with specific characteristics (e.g. blood count or alcohol consumption) within a defined time period and a following export as MS Excel sheet are needed. Within a second use-case scenario an online evaluation and processing of patient information is necessary where a predefined set of clinical questions is provided and the query results are immediately visible within the web-browser as depicted in Figure 4.7 for the average age of patients.

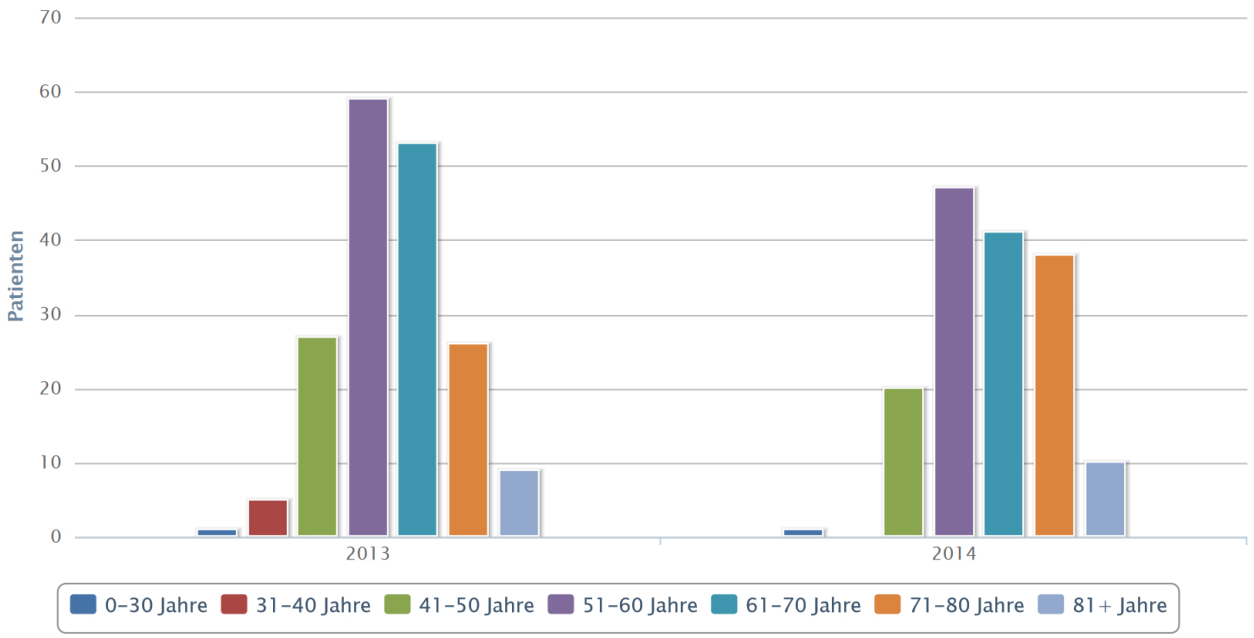

Figure 4.7 – The age structure of patients is instantly available in the web-browser

The questions for online evaluation could be divided into three categories and are depicted in detail in Table 4.2:

- Clinical workflow support
- Clinical studies
- Quality management and clinical certification

In the area of clinical workflow support the system helps physicians to keep track of patients that are temporarily treated in a different department in order to assure the subsequent treatment in the head and neck department. An example are patients which received a surgical intervention with subsequent adjuvant radiotherapy or chemotherapy. Sometimes, these patients are not sent back to head and neck department to be scheduled for follow-up consultations. The identification of these patients could be facilitated in *oncoflow* so that an appropriate follow-up care can be assured (see Table 4.2, question 10). Furthermore, all tumor patients should undergo a hearing test, hence, question 9 aims to identify patients with no test.

Table 4.2 – Relevant clinical questions from physicians and surgeons during the oncological treatment process

No.	Question	Description
1	Tumor boards (TB)	Patients cases discussed in pre- or posttherapeutic tumor boards compared to the number of all patients
2	First procedure	Date of the first applied procedure from patients whose first consultation was performed at most X days ago
3	No. of patients in TBs	Average number of patients in the tumor board per month
4	First consultation	Number of first consultations per month
5	HPV16 indicator	Histology reports containing information about the HPV16 status of a patient
6	TB decisions	List of therapy decisions in tumor boards including absolute and relative frequency of each decision
7	Time to first TB	Time in days between first consultation and first tumor board
8	Time to first therapy	Time in days between first consultation and first therapy
9	Aural examination	Patients which had no hearing test
10	Follow-up tracking	Identification of patients who had an adjuvant therapy but not yet a follow-up appointment or where the timeframe between the last therapy and the first follow-up consultation is larger than 5 month
11	ICD10 finder	Find all patients where a specific ICD10 code was assigned
12	ICD10 counter	How frequent was a specific ICD10 assigned, differentiated according to gender, alcohol or nicotine consumption

In the field of research and clinical studies the evaluation module supports the identification of patients with specific attributes. Latest research focuses on the connection between HPV16[1] status, smoking and alcohol habits and oropharyngeal cancer. Unfortunately, in the current information systems the identification of patients with HPV16 status is not possible, but the evaluation module allows the selection of patients with a HPV16 status in their histopathological results (see question 5).

Questions of the third category focus on quality management and clinical certification aspects. Clinical certification procedures, e.g. cancer center certification from the DKG [63], demand a structured documentation and evidence of time-frames during the tumor treatment as well as detailed information about tumor board conduction. Questions 7 and 8 focus on the time elapsed between the first consultation and the first tumor board or the time between the first consultation and the first applied therapy procedure. Question 1 evaluates the fraction of tumor patient cases discussed in the tumor board compared to all tumor patients. In this example the discussion of at least 95% of all patients in the tumor board is necessary to meet the DKG criteria.

Technical realization According to the results of the requirements analysis a new *oncoflow* module was developed that seamlessly integrates into the existing framework. A request catalog lists all clinical requirements depicted in Table 4.2. The questions are persisted in the *oncoflow* database and consist of a 3-tuple of information. The first part contains the SQL string which is later used for the database query. The second part of the tuple contains information about the user interface in the web-browser. Details such as parameter fields where the clinical staff is able to adjust query parameters or detailed descriptions of the current query are defined here. In the last part possible visual representations for the results and corresponding parameters such as axis labels for the charts are defined. Most results can be displayed as table, bar chart or pie chart. This modular concept allows an improved modification of existing queries as well as a facilitated implementation of new clinical requirements. All changes can be performed during live operation without a re-compilation and a re-deploy of the *oncoflow* system.

Entscheidung	Anzahl
Radiochemotherapie	5
Radiatio	5
adj RT	5
adj RCHT	4
adj RCT	4
adjuvante Radiatio	3

Figure 4.8 – Tumor board decisions sorted according to their frequency of occurrence

[1] Infection with the human papillomavirus (HPV) 16 are cause of a unique type of throat cancer

The results are presented tailored to the specific use-case. Figure 4.8 depicts results presented as table (see Figure 4.8).

Tables can also be saved as Excel file for further usage. The automatic aggregation of information is also conveniently usable for the creation of scientific publications or quality management reports. Therefore, bar-charts and pie-charts are automatically generated (see Figure 4.7 and Figure 4.9). The figures are instantly available for download as pixel graphic (jpg, png) or as vector graphic (svg). The HighCharts Java Script library is used to generate the figures.

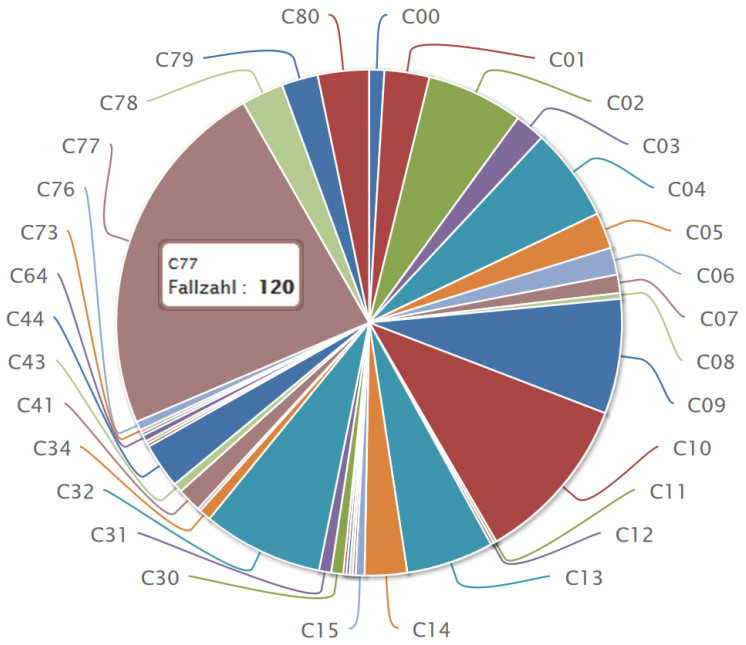

Figure 4.9 – The ICD10 counter gives a brief overview on the relative frequencies of used ICD10 codes. The diagram shows the distribution of ICD tumor codes for N=511 patients in 2013 and 2014. The exact numbers are displayed while hovering over the different segments of the pie. The ICD10 codes C00 – C32 denote head and neck tumors, C34, C78 denote tumors of the respiratory and digestive systems, C41 – C73 denote tumors of bone, skin, kidney and thyroid gland, C77 denotes tumors in the lymph nodes and C76, C78, C79 and C80 denote tumors that are not defined in detail

Chapter 5

Treatment Planning Unit

5.1 Introduction

Tumor boards are a generally accepted institution in tumor therapy so that upcoming clinical certifications from the German cancer association DKG make high demands on the conduction of tumor conferences [63]. On the other hand scientific research projects with varying results assessed whether the presence of tumor boards can be associated with improved treatment decisions or therapy outcomes [64, 65, 66]. The existing requirements to cancer centers and the few compelling studies about the outcome of tumor boards built the basis for the implementation of a comprehensive tumor board assistance module at the University Medical Center Leipzig [54, 67]. The module supports the entire tumor board management process including patient scheduling as well as invitation and protocol mailings. Intelligent results documentation during the board and automatic physician registration in the meeting room make the decision-making process more transparent and are first steps towards a clinical certification as cancer center (requirements of the DKG are depicted in detail in Table 5.1). In order to improve the common understanding additional patient information and medical images were included into the patient presentation based on the work of Simo et al. [68].

The following sections describe in detail all steps which were performed to efficiently support the management of our weekly tumor boards [69]. Furthermore, all technical assistance functions which are used during the tumor board conduction to support the decision-making process and to improve the information acquisition for cancer center certification are depicted.

5.2 Tumor board management support

The time-consuming process for tumor board management which includes invitation mailing, manual transcription of tumor board results and final tumor board protocol mailing has been improved significantly with *oncoflow*.

The weekly tumor board takes place on Thursday. The established process for scheduling patients

Table 5.1 – Requirements of the DKG on tumor boards. The description is highlighted in italic, the *oncoflow* support is depicted in standard typeface

Requirement	Description, *oncoflow* support
Tumor board cycle	*At least one tumor board must take place in a week.* The schedule of tumor boards is documented in *oncoflow*.
Tumor board preparation	*All patient-related information has to be gathered before the board.* The structured anamnesis and clinical examination as well as the automatic information import from HIS and DTTM guarantee the availability of all relevant patient-specific information in *oncoflow*.
Pretherapeutic board	*95% of all primary patients have to be presented in the pretherapeutic tumor board.* An evaluation of this characteristic number is possible with *oncoflow*.
Tumor board invitation	*Relevant patient information has to be distributed to all board participants beforehand.* A condensed view of existing patient-specific information helps the physician in the creation of board invitations. The invitation letters are afterwards automatically sent as PDF document via email to all registered board participants.
Tumor board participants	*Specialties from diagnosis, surgery, radio oncology, oncology, radiology and pathology must be present in each board.* All participants are registered via RFID in the TPU and stored in the *oncoflow* database for documentation purpose.
Medical images	*Patient-specific medical images (pathology, radiology) must be present and presented with an appropriate technical infrastructure.* Images from panendoscopy and 3d tumor reconstructions are available in *oncoflow* and presented within the TPU.
Tumor board protocol	*The tumor board protocol consists amongst others of an interdisciplinary treatment plan and should be immediately generated from the tumor documentation system.* *oncoflow* and the TPU are used for result documentation during tumor board conduction. Given information in the invitation letter are subsequently enriched with board decisions and automatically sent via email as a PDF document to all board participants.
Therapy deviation	*The tumor board therapy decision is obligatory. Therapy deviations and therapy changes at the will of the patient have to be documented.* The documentation of therapy changes is not yet implemented into the therapy workflow of *oncoflow* but scheduled for further development.

and sending invitations and protocols was as follows: Patients with histological confirmed tumor (ICD-O-M catalog) are scheduled for the next upcoming tumor board. Therefore, physicians from head and neck surgery used MS-Word templates, searched relevant information in the HIS and manually transferred the information into the template. Subsequently, the template was stored on a common network share. The deadline for patient scheduling is Wednesday noon. Afterwards, a

physician converted all Word documents into PDF format, created an email addressed to all tumor board participants, attached the PDF invitations and sent the mail. During the tumor conference an assistant physician presents the patient cases and documents the therapy decisions for each patient. Afterwards, the assistant physician manually reentered the therapy decisions into the existing Word files, created a second PDF file as tumor board protocol and sent the protocol to all participants. Unfortunately, the tumor board decisions were not centrally available in the HIS but only in the email inboxes.

In order to improve the workflow a dedicated tumor board module has been developed which assists the physician in each step. Firstly, the Word template has been implemented as structured form in *oncoflow* which is accessible within the EPR in the web-browser. The tumor board invitations are automatically pre-populated with existing information about recent diagnostic procedures and histopathological results. Additional information is visible at a glance so that the invitation form can be conveniently enriched with further patient details. Afterwards, on Wednesday noon the final invitation PDF files are automatically created with LaTeX with one button click in *oncoflow* and sent as email to all physicians and surgeons participating the tumor board. The email contains direct URLs to the specific electronic patient records in *oncoflow* and the PDF documents of all invitations. The therapy decisions during the tumor board are immediately documented by the assistant physician with an Android tablet and are stored in the particular EPR in *oncoflow*. Thus, the tumor board protocols can be immediately created and sent via email to all participants after the tumor conference has finished. The PDF files are also automatically imported into the patient's electronic patient record in the HIS to make the therapy decisions available for all attending physicians. Therefore, *oncoflow* saves a copy of each protocol into a dedicated folder from where SAP i.s.h.med regularly imports new documents.

5.3 A novel approach for meeting room design

The regular tumor boards take place in a meeting room at the radiology department of the University Medical Center Leipzig (see Figure 5.1). The room consists of two rearward projectors for displaying CT and MRI tomographic images on a large screen in front of the audience. The seating arrangements are chosen in a way that the audience view is directed to the screen. In the front right corner of the room a desk for the radiologist is situated from where the tomographic images are selected for presentation and the radiologist explains the diagnostic findings to the audience. During the meetings, the seats are manned according to the clinical hierarchy. Professors and senior physicians are sitting in the front while assistant physicians and students are sitting in the back of the meeting room.

The current setting reveals several drawbacks. The aim of a tumor board is an interdisciplinary discussion of possible therapy options in order to find the best possible therapy for the patient.

Figure 5.1 – Meeting room for regular tumor boards with strong hierarchical seating arrangements

However, the orientation of the seats in direction to the screen demands that the physicians on the front seats have to turn for discussing therapy options with their colleagues. But, unfortunately, the professors and senior physicians rather talk in direction of the screen and the radiologist. In combination with the noise of the projectors physicians and assistant physicians in the back are hardly able to follow the discussion or contribute their point of view. A detailed analysis of the influence of the clinical hierarchy was conducted by Lassalle et al. and served as important basis for this work [70].

Finally, the presentation of further patient-specific or therapy-decision related information is hardly possible, because the projectors are used by the radiologist. Actually, there is additional information available to facilitate the decision for a specific therapy. Endoscopic images showing the tumor may be more meaningful to medical disciplines like pathologists or radiotherapists than CT or MRI slices. A picture of the patient may give an impression of the patient's current constitution and decrease possible options for chemotherapy or radiotherapy. Unfortunately, this information is not available during tumor boards.

In order to improve the aforementioned drawbacks an entirely new concept for tumor board

meeting room design has been developed. Hereby, the meeting room concept and the engineering tasks such as hardware installation in the meeting room were conducted by my colleague Stefan Bohn [54]. A seating arrangement was developed with all medical disciplines which use the meeting room (see Figure 5.2). The V-style seating arrangement provides improvements for collaborative discussions and was accepted by all parties and could finally be realized. Apart from the seating arrangements further improvements in the meeting room are conducted such as the installation of two 50 inch plasma screens beside the large projector screens. On the screens additional information like patient information, panendoscopy images or medical images from nuclear medicine are shown.

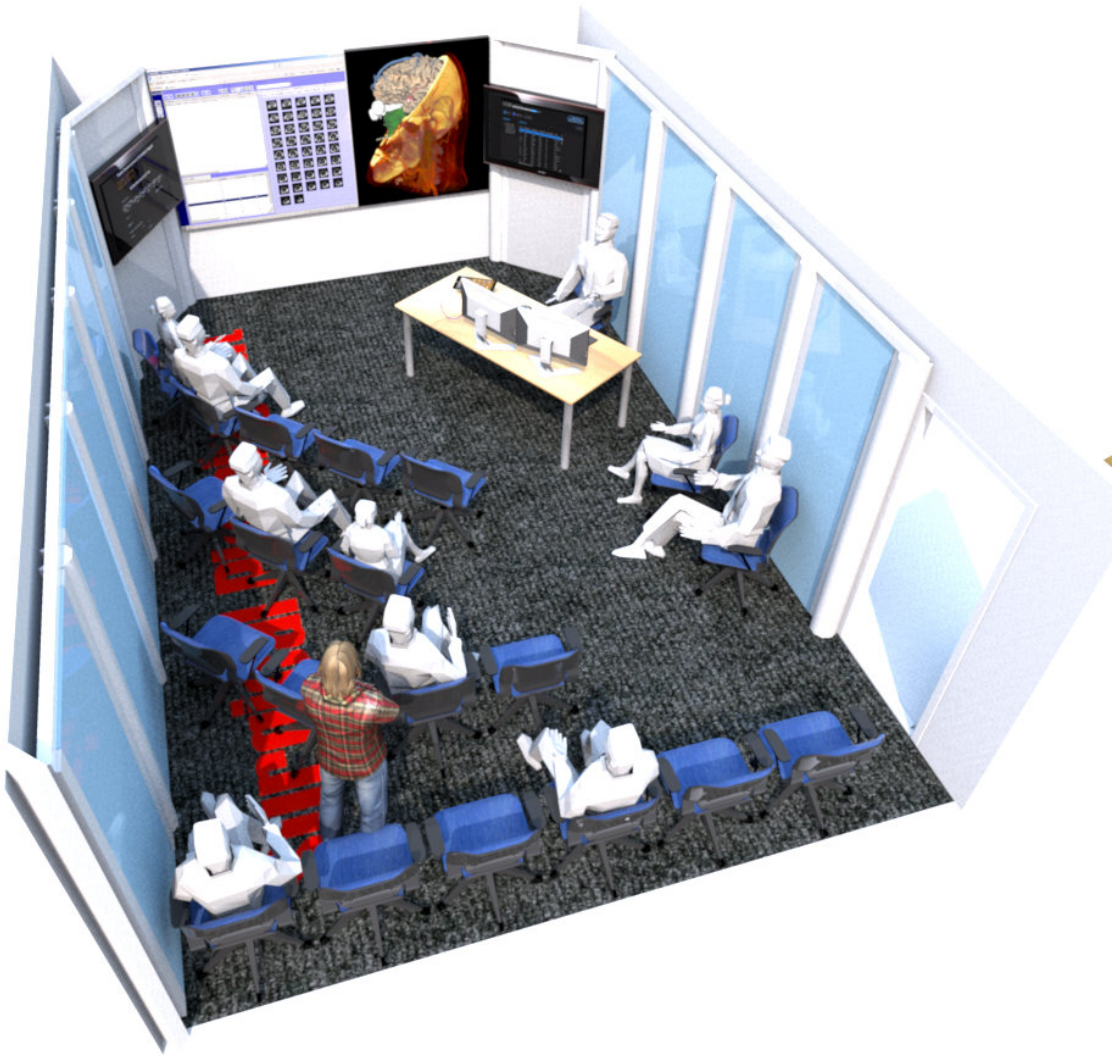

Figure 5.2 – A novel approach for meeting room design with V-style seating arrangement. Image printed with kind permission from Stefan Bohn

Finally, the automatic documentation of tumor board participants should be mentioned here. Requirements from the DKG are that specific clinical disciplines must join the regular tumor boards. In order to facilitate the documentation a RFID reader has been integrated at the meeting room entrance. The employee identification badges contain a RFID chip which transmits a unique identifier. Thus, physicians and surgeons put their badge on the RFID reader when they enter the room so that the presence is recognized in *oncoflow*. For the first time, a new physician or surgeon joins the conference, the unique badge identifier is shown in *oncoflow* and can be connected with an existing user profile or used to create a new user. Each user has assigned a clinical position (e.g. assistant physician or professor) as well as the associated department. Based on this information detailed reports about the presence of clinical disciplines and the hierarchy of the participating physicians can be generated for clinical certification purposes.

5.4 Conclusions

Figure 5.3 shows a photo of the new meeting room. In addition to the new plasma screens one can see a new light concept for the room. Initially, the idea was to support the decision-making process with different light schemes for the patient case presentation phase and the decision-making phase. A scientific evaluation of this concept with the help of psychologists is unfortunately pending due to a lacking interest on this topic.

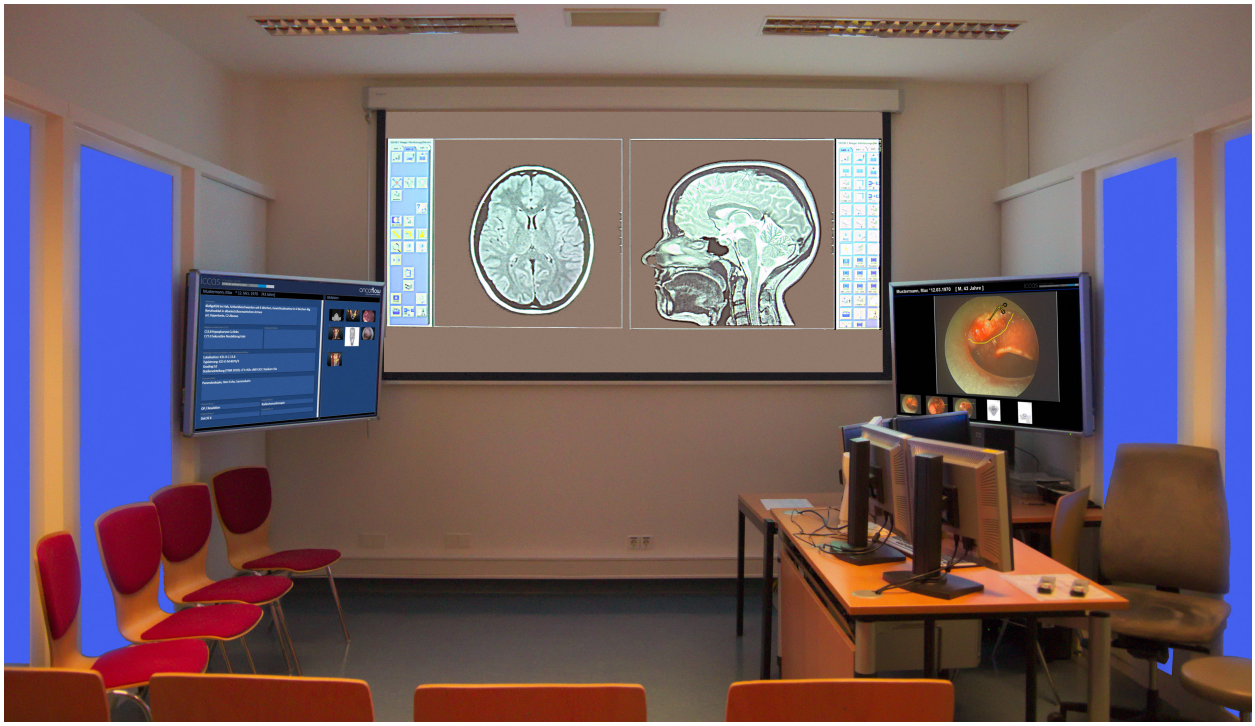

Figure 5.3 – The sophisticated tumor board design with additional screens for case and endoscopic image presentation and a new lighting concept

Comparing the functionalities of the TPU with the tumor board requirements depicted in Section 2.3 and Table 5.1 reveals that not all requirements are fulfilled. Fortunately, nearly all DKG requirements presented in Table 5.1 are met. There are weekly tumor boards where all patient-related information is presented in a structured way. Medical images from different imaging modalities are presented during the tumor board and a protocol with the therapy decision is sent to all participants. The requested documentation of a therapy deviation is not available at the moment.

The requirements in Section 2.3 cover a broader range of functions. At the moment, the TPU is lacking an active patient participation, a robust mechanism for prospective assessment of tumor board performance and reliable interfaces with primary care to ensure continuity of care. Furthermore, patients do not have the ability to fully explore all their available therapy options and the screening of eligible patients for recruitment into ongoing trials in real time is yet not possible and are topics of ongoing research and development.

However, the TPU is an entirely new approach to support the conduction of tumor boards and to make the results documentation process more efficient. The endoscopic images are very valuable to clarify the tumor location and the tumor extension so that all tumor board participants achieve a common understanding of the current medical situation and are able to contribute equally to find the best possible therapy for the patient. An example for the importance of endoscopic images are vocal fold carcinomas with extensions less than $5\ \mathrm{mm}$ which are not visible on regular CT scans (see Figure 5.4).

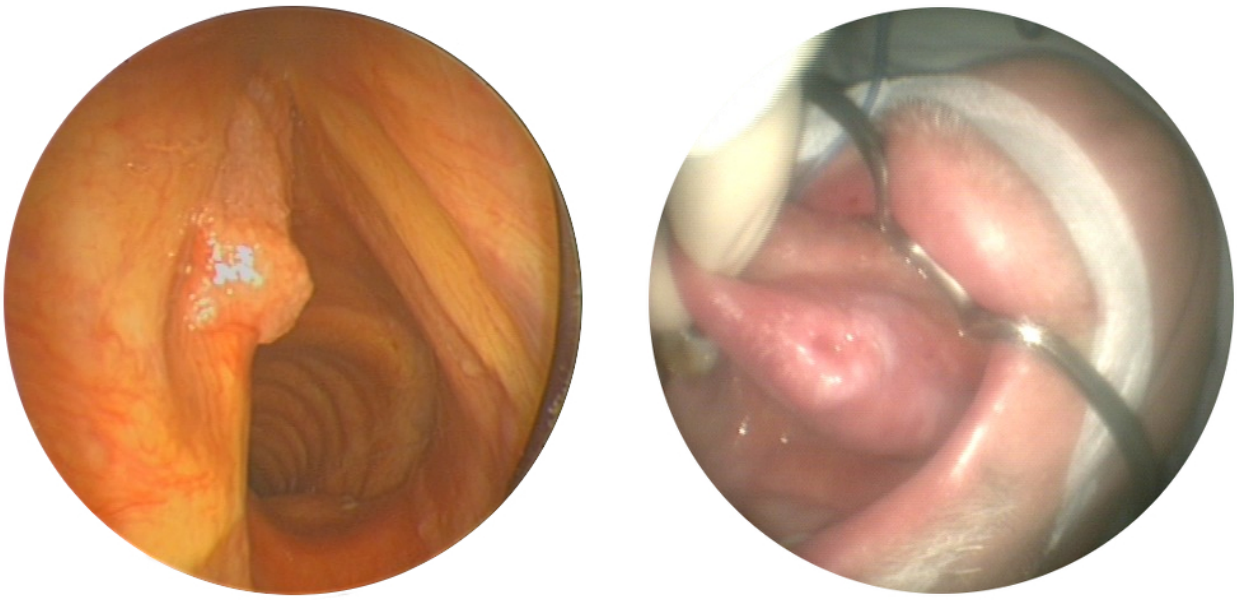

Figure 5.4 – Endoscopic image from carcinoma that are not visible on CT scans. *left:* a vocal fold carcinoma on the left vocal fold; *right:* tumor on the tip of the tongue

Chapter 6

Clinical application and evaluation

6.1 Deployment of *oncoflow* at a clinical site

The design and implementation of *oncoflow* has been realized in close collaboration with the department of head and neck surgery at the university medical center in Leipzig, Germany. The concept of a web-based central information base with clinical workflow as well as tumor board support started in 2011. The first prototype of *oncoflow* has been deployed for tests in daily clinical routine in October 2012. The system runs on a virtual Linux server at the IT department of the hospital and is accessible at each personal computer in the clinic via web-browser. During an initial trial phase at the clinical site shortcomings in the user interface, the HIS data export and the communication interface to the DTTM have been identified and fixed.

Since November 2012 *oncoflow* is being used in daily clinical routine for the documentation of anamnesis and clinical examination of patients with tumor suspect (see Figure 6.1, left) and the upload of panendoscopy results as well as the documentation of the intervention in combination

Figure 6.1 – *left:* documentation of anamnesis and clinical examination results in *oncoflow*, *right:* patient summary and endoscopic images are shown additionally to CT images in the tumor board

with the DTTM. Diagnoses, applied medical procedures, histopathological results and radiological reports are imported automatically so that all relevant information for the decision-making process in the tumor board are completely available inside the *oncoflow* EPR. The first usage of *oncoflow* together with the TPU to support the local head and neck tumor board was in February 2013 in the conference room at the radiology department of the university medical center Leipzig (see Figure 6.1, right). The new light concept with changing colors depending on the actual discussion phase, the presentation of endoscopic images and 3-dimensional tumor reconstructions at two 50-inch plasma screens and the new results documentation were well-accepted by the participating physicians and surgeons. Between March 2013 and August 2014 590 patient cases were scheduled for tumor boards with complete *oncoflow*, *Moboco* and TPU support.

The interconnection of *oncoflow* with all adjacent systems in the local hospital IT infrastructure is depicted in Figure 6.2. The Figure also shows the four main workflow steps improved with *oncoflow* and the TPU and the software products that are used in each process step. The model was created with the $3LGM^2$ toolbox developed at the IMISE at the Universität Leipzig [71].

6.2 Study design

The study focused on the documentation process of first anamnesis and clinical examination of patients with suspected head and neck tumor depicted in detail in Section 4.2. The clinical study has been performed in the department of head and neck surgery at the university medical center Leipzig between November 2012 and April 2013 and consists of three independent parts which are published in [72, 73].

The qualitative and quantitative parts of the study focus on the following three statements or hypotheses. Points one and two will be evaluated with the questionnaire and the third point will be quantitatively evaluated with the workflow analysis.

- The browser-based user interface will be accepted by the clinical staff due to a convenient handling and shorter response times compared to the HIS
- The provision of a structured form for result documentation gives the attending physician a guideline and relieves from using additional documents
- The usage of a web-based form for documenting first consultation results needs an equal amount of time than the documentation in SAP i.s.h.med

6.2.1 Quantitative evaluation

In the first part a detailed analysis of the current anamnesis workflow with the HIS as well as an analysis of the usage of *oncoflow* has been performed. Hereby the time stamps of each process step and the questions that were asked to the patient have been documented in detail. This part

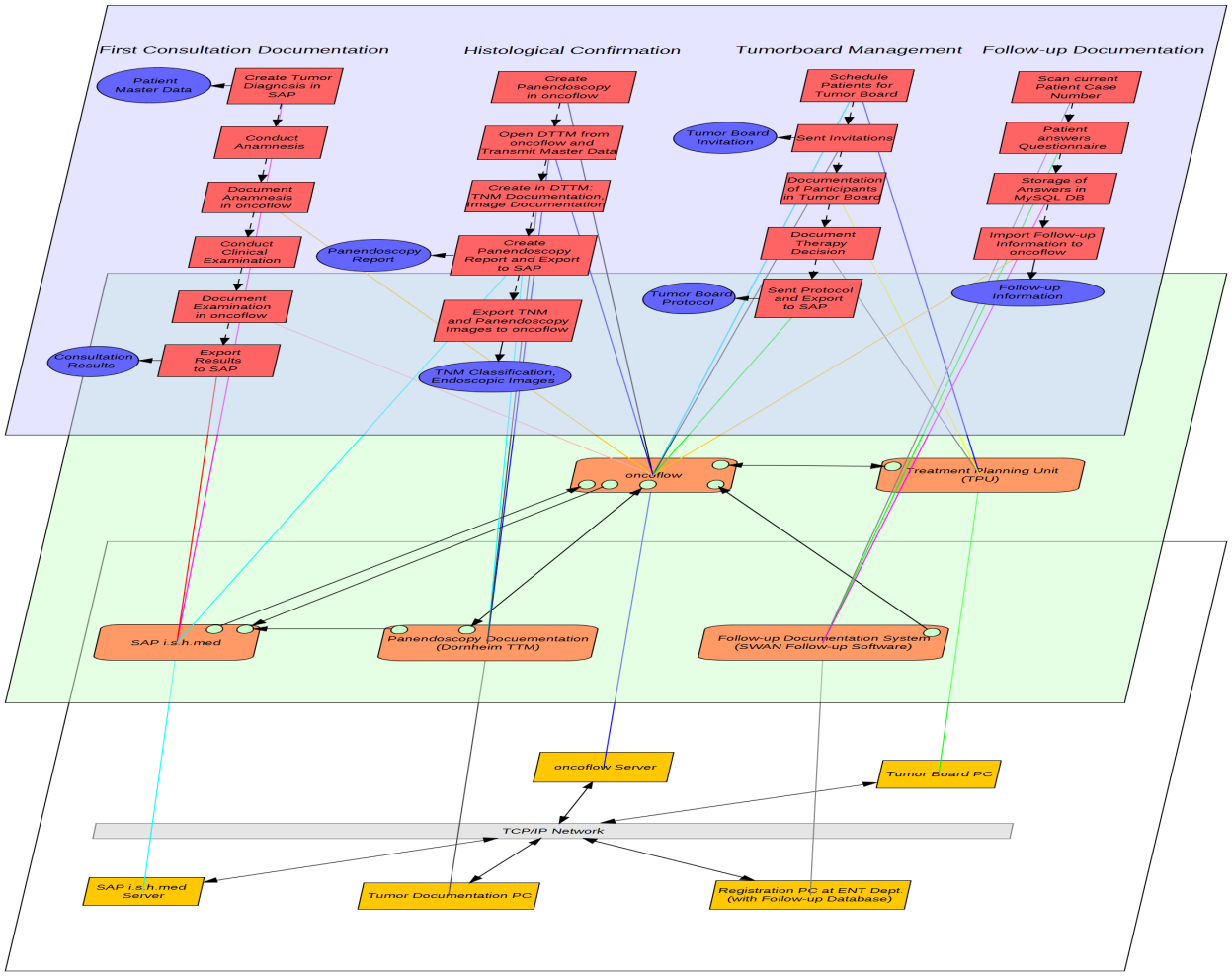

Figure 6.2 – The 3-tier architecture shows the interconnection of *oncoflow* with all adjacent systems on a physical layer (bottom), software layer (middle) and a functional layer (top)

of the study was performed using the s.w.an-Suite from SWAN – Scientific Workflow Analysis GmbH [74, 37]. The suite includes a workflow configurator that provides a graphical user interface for the definition of clinical workflows. These workflows consist of actors, activities and events. For this study one actor (physician) has been defined. Activities consisting of a start and end time as well as events representing one point in time can be assigned to each actor. Thus, based on the respective workflows depicted in the following paragraph about the questionnaire design, two different configurations for the documentation of the control group and experimental group have been created. The workflow recordings were performed with the workflow editor from the s.w.an-Suite on a Microsoft Windows XP tablet computer with a stylus pen as input device (see Figure 6.3, right). The documentation took place at the clinical site in an examination room at the head and neck department (see Figure 6.1, left). Therefore, the author of this thesis observed the anamnesis and clinical examination process and documented all occurring activities and events. The final workflows are stored as XML files that can be automatically imported into a PostgreSQL database

for further processing such as an automatic evaluation of activity times that can be used afterwards for statistical analysis.

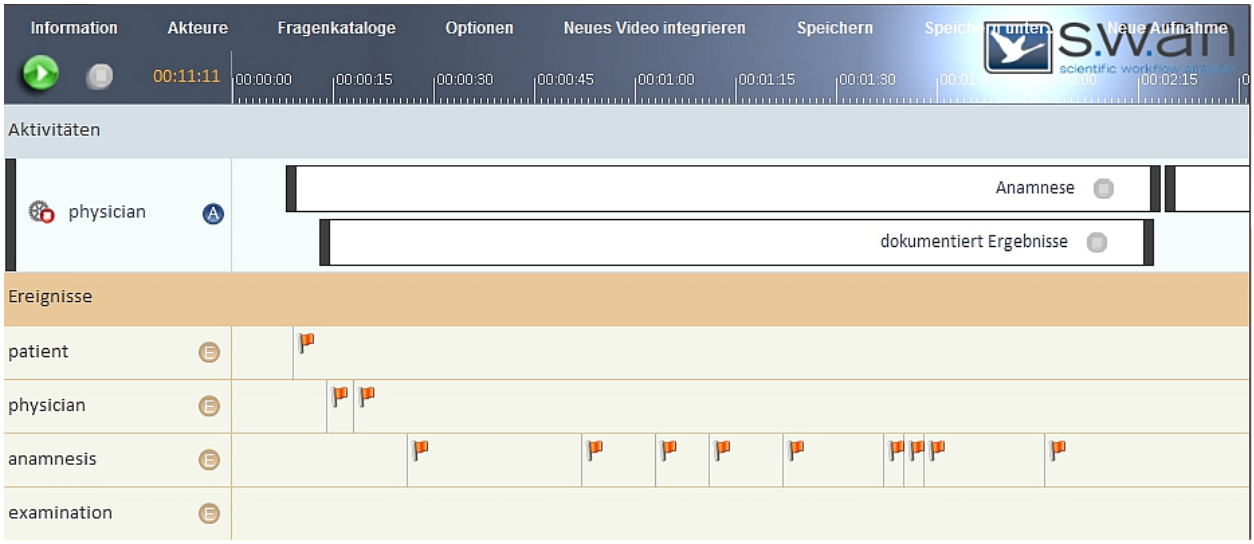

Figure 6.3 – User interface of the s.w.an workflow editor

6.2.2 Qualitative evaluation

A questionnaire-based investigation states the second part of the study and should evaluate a qualitative acceptance level of the new system compared to the current workflow. The questionnaire has been developed according to [75]. The questionnaire focuses on two major aspects with regard to the study hypotheses denoted in bullet points one and two:

- Acceptance of the structured web-based user interface compared to the unintuitive old-fashioned user interface of the HIS
- Does the structured documentation form of *oncoflow* improve the working process of the physician compared to a free-text field with the usage of additional helper documents in the conventional HIS

Hence, the questionnaire is separated into two major parts whereby the first part addresses the current working process with the HIS and the second part is focused on the usage of *oncoflow*. Each of these parts consists of eleven questions. An additional third part of the questionnaire aims to determine the overall satisfaction with *oncoflow*. The answers of the first two parts of the questionnaire were realized with a Likert scale consisting of five choices between 5 (strongly agree) and 1 (strongly disagree) [76]. The Likert scale of the last question part also consists of 5 choices but the answers range from 5 (very good) to 1 (very bad). The questions and corresponding answers are depicted in detail in Section 6.4.

6.2.3 Workflow distance evaluation

The third part of the study focused on the improvement of information quality which results from a structured documentation process. Therefore, the Levenshtein distance was applied to the data which originates from the clinical workflow analysis in order to show improvements in the documentation process so that the acquired data is more structured and exhaustive. The analysis focused on the points depicted as captions in the web-based anamnesis form (see Table 6.1).

The study hypothesis for the third part of this study is as follows: *"A structured documentation with a predefined set of questions results in a more structured and standardized clinical workflow, an EPR containing more relevant patient-specific data, hence, a higher information density."*

Table 6.1 – Study-relevant observation parameters depicted in ideal chronological order (*gold standard*)

Question type	Description
Actual anamnesis	Reason for going to the clinic and actual problems.
ENT anamnesis	ENT specific questions.
Common anamnesis	Information apart from ENT, e.g. herpes, cramps, etc.
Interventions	All former interventions.
Allergies	Information about existing allergies.
Drugs	Which drugs the patient uses regularly.
Profession	Profession of the patient, especially interesting in the case of potential tumor risk factors.
Family anamnesis	Diseases from family members, especially tumor diseases.
Nicotine	Nicotine consumption.
Alcohol	Alcohol consumption.

6.3 Experimental setup

6.3.1 Anamnesis and clinical examination process

The consultation consisting of anamnesis and clinical examination is actually performed by all physicians with a similar approach. If necessary the physician starts with a preparation of the consultation by opening the EPR, reading physician letters or importing medical images from a compact disc into the local PACS. Afterwards, the patient enters the examination room and the physician starts asking questions to the patient and simultaneously enters relevant information into the HIS. The clinical examination follows, then the patient leaves the room and finally the physician enters the examination results into the HIS.

The usage of *oncoflow* for results documentation leads to minor changes in the current workflow. During the preparation phase the physician opens the *oncoflow* patient record additionally to the HIS patient record. Unfortunately, due to lacking bi-directional communication interfaces from *oncoflow* to the HIS, the physician needs to copy & paste the consultation results from *oncoflow* to the HIS after the consultation (see Figure 6.4).

6.3.2 Postprocessing and analysis

The time measurement study investigated the influence of a new approach for results documentation on the amount of time a physician needs for performing anamnesis and clinical examination. The study will show that the new documentation system does not impair this process step. Therefore, the statistical evaluation focuses on the overall duration of the process and the amount of time needed for results documentation. The documentation time in the experimental group consists hereby of the sum of the time needed for documentation in *oncoflow* and the transfer time to the HIS. The following approach was used for the statistical evaluation of both overall workflow times as well as only documentation times. The open source software environment R has been used for all statistical calculations [77, 78].

Given two samples $x_1, \ldots, x_m$ and $y_1, \ldots, y_n$ that denote time measurement values from the control group and the experimental group, respectively. It has to be shown that both samples do not differ significantly from each other, hence, are from the same population. At first the Shapiro-Wilk test with significance level $\alpha = 0.05$ was applied in order to show the normality distribution for both samples [79].

The F-test is then used for the evaluation of the variances of the given populations [80]. If the variances are equal (F-value between lower critical value f_{low} and upper critical value f_{up}) the T-test, otherwise the Welch-test has to be used for the final comparison of both distributions. Both T-test and Welch-test are designed for small sample sizes [81]. The final result parameter of these tests is the t-value. The goal is to show that $|t| < t^*$ is true, where t^* is the critical parameter, meaning that the two sample groups are from the same population. For *oncoflow* this would mean that there is no significant impact on the anamnesis and clinical examination workflow of the physician. The critical parameters for the Shapiro-Wilk, F, T and Welch-test with significance level $\alpha = 0.05$ can be found in reference tables [79, 82].

The evaluation part for the Levenshtein distance measure study has been performed with a text-based Java application and a study file format especially developed for this project. The input file consists of a gold standard describing the ideal order of questions in the first line and the patient-specific observations in the following lines. The ideal order of questions equals the order used in Table 6.1 with a total number of 10 observations. The Java program processes two separate input files containing SAP i.s.h.med and *oncoflow* results and calculates the Levenshtein distance for each patient-specific observation with respect to the gold standard. The program also performs a statisti-

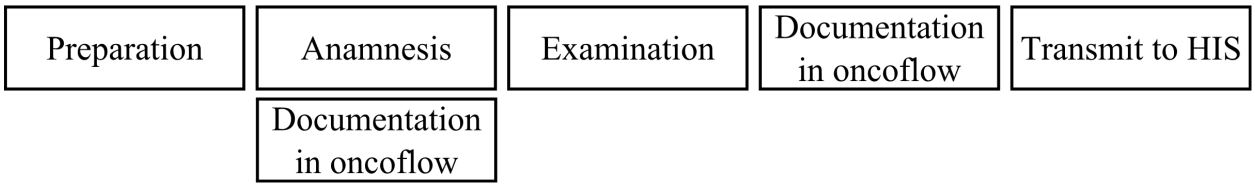

Figure 6.4 – The workflow for anamnesis and clinical examination during the clinical study with *oncoflow*

cal evaluation of the results. It calculates mean and median values, variance, and standard deviation. Afterwards, a Mann-Whitney U test is performed in order to show the statistical significance of the results.

6.4 Qualitative evaluation of the therapy process

The following three figures depict in detail the questions, results and median values of the questionnaire.

During the study five physicians used *oncoflow* and participated in the survey $(n = 5)$. In each

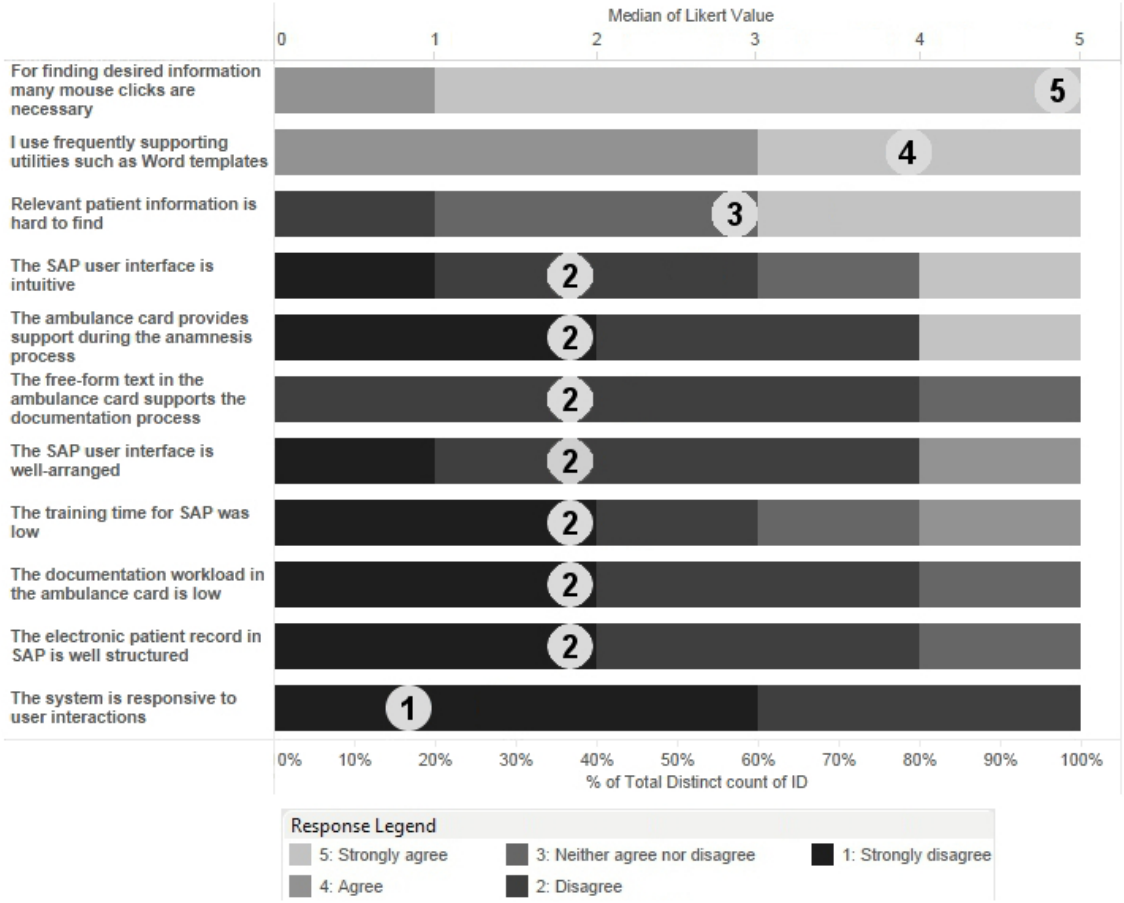

Figure 6.5 – Questions concerning the conventional HIS (SAP i.s.h.med)

figure the questions are depicted on the left side and the corresponding answers in percent are shown as horizontal bars on the right side. The scale on the bottom corresponds to the answers. The gray circles included in each horizontal bar show the Likert median value of the respective question.

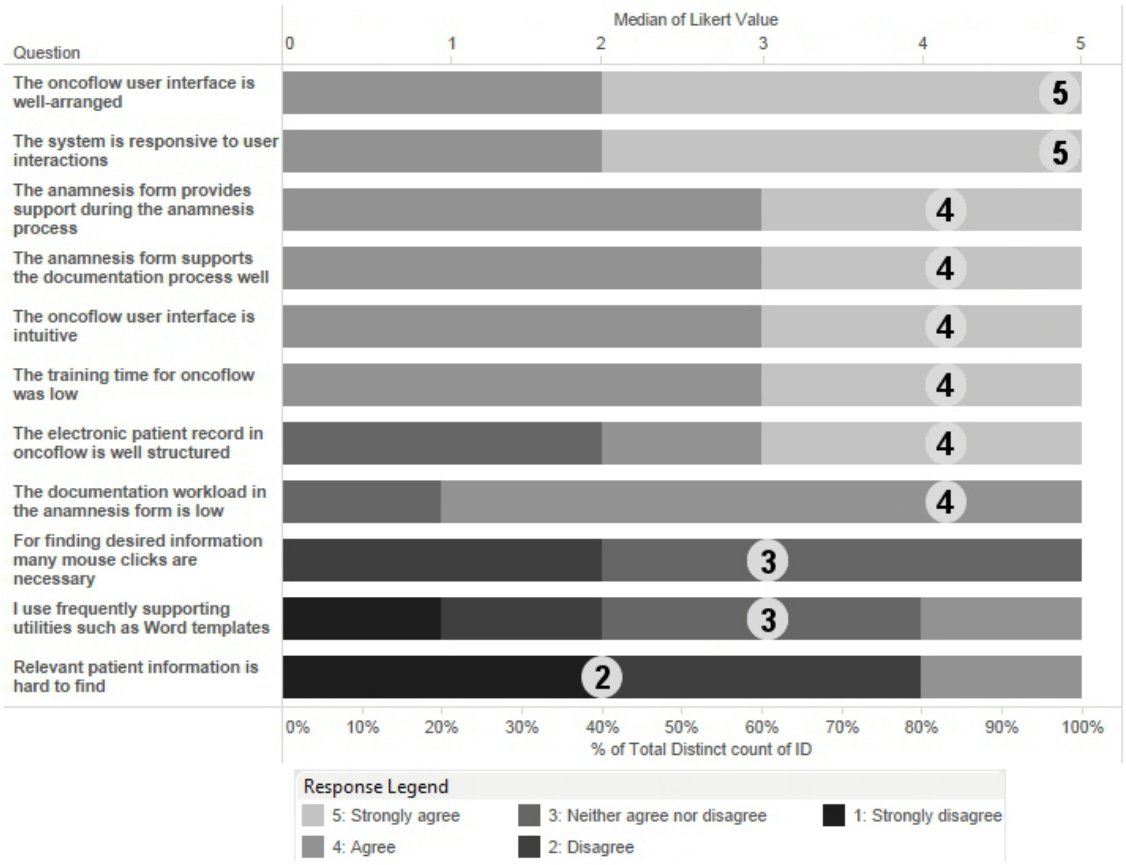

Figure 6.6 – Questions concerning the usage of *oncoflow*

The answers are sorted descending according to the Likert median value. The first three questions in Figure 6.5 address the topics usability and support. The results show that the user needs many mouse clicks in SAP i.s.h.med ($m = 5$), that relevant patient information is hard to find ($m = 3$) and that the physician frequently uses additional documents for anamnesis and clinical examination documentation ($m = 4$). Compared to the results depicted in Figure 6.6 exactly these three questions gain actually the lowest average ratings in *oncoflow* ($m = 3; m = 3; m = 2$). Questions focusing on the user interface in Figure 6.5 depict that SAP i.s.h.med receives low ratings for an intuitive ($m = 2$), well arranged ($m = 2$), and responsive ($m = 1$) user interface. The *oncoflow* user interface however has been judged as well arranged ($m = 5$), responsive ($m = 5$) and intuitive ($m = 4$) as can be seen in Figure 6.6. The remaining sets of five questions evaluate the workflow support for both systems. The SAP i.s.h.med ambulance card does not provide documentation support ($m = 2$) and the free-form text field is less helpful for information documentation ($m = 2$) and

the documentation workload is high $(m = 2)$. Also the training time for getting familiar with SAP i.s.h.med was relatively high $(m = 2)$ and the electronic patient record is unstructured $(m = 2)$. The new developed anamnesis and clinical examination documentation form in *oncoflow* supports the clinical process well $(m = 4)$, supports the documentation process $(m = 4)$ and minimizes the documentation workload $(m = 4)$. The electronic patient record in *oncoflow* is well-structured $(m = 4)$ and the training time for the system is low $(m = 4)$.

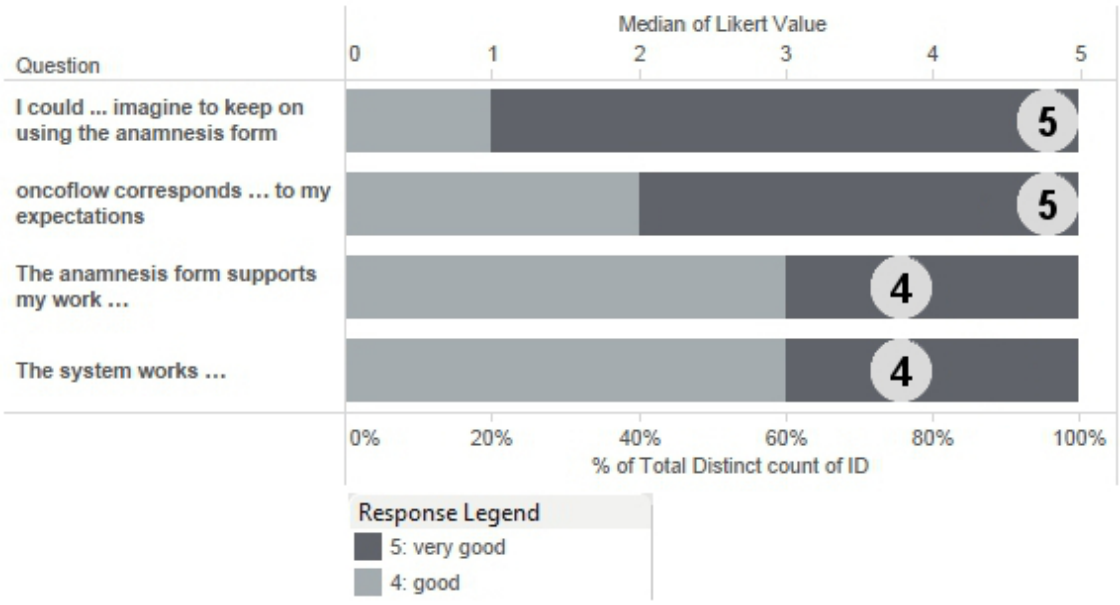

Figure 6.7 – Four questions evaluated the overall satisfaction of the surgeons with the *oncoflow* system whereby the three points denote space for the chosen answer

Finally, the questions regarding the overall user acceptance of *oncoflow* depicted in Figure 6.7 show that the users are very satisfied with the new information system. *Oncoflow* works well $(m = 4)$ and corresponds very well to their expectations $(m = 5)$. All users could imagine keeping on using the system in the future for the documentation of anamnesis and clinical examination $(m = 5)$. The new designed documentation form supports the work of the physician $(m = 4)$.

6.5 Quantitative evaluation of the therapy process

The detailed investigation of workflow times for anamnesis and clinical examination has been conducted within a control group that used the conventional documentation method with the HIS and an experimental group that used *oncoflow* for the results documentation. Altogether 25 workflows have been documented and are depicted in Table 6.2 (control group, 14 workflows) and Table 6.3 (experimental group, 11 workflows). Eleven additional workflows had to be excluded from the evaluation because they were incomplete or faulty because of the unpredictable daily clinical routine such as the arrival of emergency patients. The column “Overall duration” in Table 6.2 and Table

6.3 is not the sum of the following table columns. The column depicts the time between the start and the end of the workflow recording and includes small time slots between the different process phases. This is e.g. the time after the finished anamnesis part when the physician goes to the patient and begins the clinical examination.

Table 6.2 – Overall time and times for the different process steps recorded during the usage of SAP i.s.h.med for results documentation. All times are depicted in minutes

Workflow number	Overall duration	Preparation	Anamnesis	Exmination	Documentation in HIS	Interceptions
1	11:06	00:00	02:09	03:28	03:57	00:00
2	14:10	00:00	05:33	05:49	07:17	00:00
3	17:44	00:00	05:20	05:02	10:26	00:11
4	19:03	02:00	09:19	04:29	08:43	00:28
5	20:17	00:00	04:28	05:11	07:15	00:34
6	20:37	05:20	00:41	06:06	01:08	00:22
7	22:04	00:36	08:10	04:55	13:34	01:08
8	22:24	01:00	09:46	07:03	12:55	03:27
9	23:07	01:24	07:08	03:41	01:36	01:53
10	24:24	03:11	03:15	11:24	06:49	01:23
11	28:41	08:21	05:10	06:13	06:27	00:59
12	31:26	00:21	06:26	13:57	10:13	07:20
13	32:01	13:32	08:00	05:37	06:47	01:21
14	43:49	09:12	11:49	07:04	14:17	00:46
Mean	23:38	03:13	06:14	06:26	07:57	01:25
Std. dev.	08:17	04:17	03:04	02:54	04:05	01:56
Median	22:14	01:12	06:00	05:43	07:16	00:53

The mean values for the overall duration are 23:38 minutes for HIS and 25:48 minutes for *oncoflow* and the median values are 22:14 minutes and 22:10 minutes respectively. Despite an additional copy & paste step during the usage of *oncoflow* the HIS documentation is only 8.4% faster in the mean and actually 0.3% slower in the median value. The pure time where the physician is sitting in front of the computer and enters information is in the main focus for time measurement (see gray shaded result values in Table 6.2 and Table 6.3). Comparing the median values from 7:57 minutes with the HIS and 8:40 with *oncoflow* shows that the documentation in *oncoflow* lasts 8.1% longer. The median value for the documentation in the HIS is 7:16 minutes and in *oncoflow* 7:21 minutes which means that the documentation in *oncoflow* is 1.1% or 5 seconds slower than in the HIS. When the additional time for the transfer of the information from *oncoflow* to the HIS is considered the overall documentation in *oncoflow* is 17.9% slower in the mean and 8.5% slower in in the median value. Statistical tests as depicted in section Section 6.3.2 are now used to evaluate if the recorded workflow samples show significant differences. The Shapiro-Wilk-test, which had to be applied first, proved the normality distribution for all samples. Subsequently the F-test has been

Table 6.3 – Overall time and times for the different process steps recorded during the usage of *oncoflow* for results documentation. All times are depicted in minutes

Workflow number	Overall duration	Preparation	Anamnesis	Exmination	Documentation in *oncoflow*	Transfer to HIS	Interceptions
1	29:13	05:18	08:47	09:02	02:59	02:13	00:00
2	19:18	03:54	05:41	03:49	07:21	00:36	01:51
3	36:17	08:52	11:27	06:12	16:34	02:13	00:35
4	31:46	04:49	04:36	02:04	05:28	01:41	16:31
5	24:19	01:48	06:41	06:54	10:44	02:05	02:36
6	19:41	02:59	04:10	08:13	05:20	00:18	03:33
7	22:10	00:00	08:20	06:19	11:23	00:22	03:00
8	16:25	00:55	03:17	06:32	07:00	00:08	01:34
9	43:13	03:01	10:03	07:53	12:47	01:43	15:17
10	20:34	01:08	08:16	05:57	09:27	00:07	00:17
11	20:48	06:20	06:34	03:02	06:12	00:00	03:35
Mean	25:48	03:33	07:05	06:00	08:40	01:02	04:26
Std. dev.	08:21	02:39	02:33	02:11	03:57	00:56	05:48
Median	22:10	03:01	06:41	06:19	07:21	00:36	02:36

used for comparing the samples standard deviation. The F-values (1.0148 for the complete workflow, 1.1072 for documentation only) have been between the critical values $f_{low} = 0.308$,$f_{up} = 3.25$; hence, the standard deviations are not differing significantly. Based on the F-test results the T-test has to be used for finally comparing the workflows. Both T-test results show that $|t| < t^*$ $[t_1 = -0.6451, t_2 = -1.0344, t^* = 1.714]$ whereby t^* is the critical value of 1.714; thus, there is no significant difference between the workflows.

6.6 Workflow evaluation using Levenshtein distance

6.6.1 Background: Levenshtein distance

The Levenshtein distance has been developed to compare the similarity between two strings, thus also denoted as string edit distance [83]. Schumann et. al. compared the Levenshtein distance, the Jaccard distance [84], the Adjacency distance [85] and the graph matching distance [86] with regard to the application in quantitative workflow evaluation [39]. The authors conclude, “that the Levenshtein and Adjacency distances are best suited for measurement of distances between the activity sequences of surgical process models”. Thus, the Levenshtein distance was used for the similarity evaluation of clinical processes beside surgical interventions. The Levenshtein distance measure, however, takes into account the minimal number of insert, delete or replace operations to

convert one string into another one.

$$d^L = \begin{cases} 0 & \text{if equal} \\ +1 & \text{replace} \\ +1 & \text{delete} \\ +1 & \text{insert} \end{cases}$$

The following example also depicted in Figure 6.8 should clarify the chosen approach. Given two strings $X = ABCDEF$ with $|X| = 6$ and $Y = ABBCDM$ with $|Y| = 6$. To convert string Y into string X the following procedure could be applied. At first the second B from string Y has to be removed. Afterwards the M has to be replaced with an E and finally a F has to be added to string Y. The applied operations are not unique so that there may exist different ways for string transformation. The Levenshtein distance in this example equals $d^L = 3$ and is calculated as the minimal number of necessary operations.

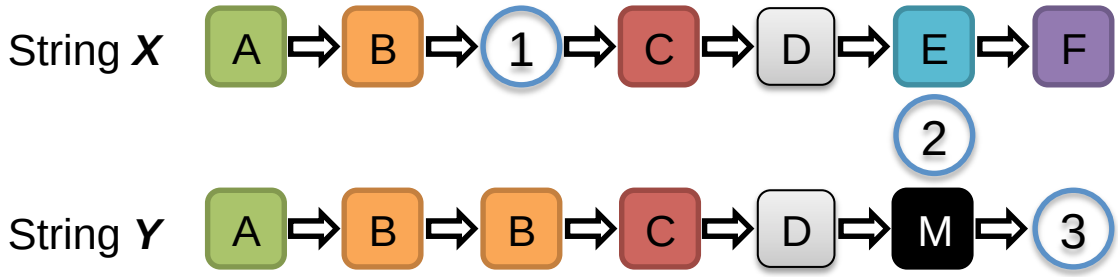

Figure 6.8 – Conversion of string X into string Y using Levenshtein algorithm. Numbers denote: 1 – delete, 2 – replace, 3 – insert

6.6.2 Distance measurement results

The clinical study encompasses 16 anamneses documented within the SAP i.s.h.med free text field as control group as well as 11 anamneses documented with the structured *oncoflow* form as study group. In Table 6.4 the number of documented information entities, the Levenshtein distance for each anamnesis compared to the ideal sequence of questions, the mean value and the standard deviation are depicted. The Levenshtein distance of SAP i.s.h.med will be denoted as d^L_{sap} and for *oncoflow* it will be referred to as d^L_{of}.

Mann-Whitney-U tests have been applied to the number of documented information $(p = 0.0023)$ and the Levenshtein distances $(p = 0.0001)$ which means that the populations show significant differences. However, the Levenshtein distance without additional knowledge provides no information about the real differences between the gold standard and the actually documented amount of information in the current observation set. Hence, the number of documented data entities has

Table 6.4 – Levenshtein distances comparing gold standard with anamneses from SAP i.s.h.med and oncoflow

	SAP i.s.h.med		oncoflow	
Anamneis	# data	d^L_{sap}	# data	d^L_{of}
1	1	9	7	5
2	2	8	10	2
3	10	9	11	1
4	5	7	11	2
5	9	6	14	6
6	4	9	10	2
7	11	7	10	0
8	9	6	9	3
9	0	5	10	0
10	0	5	10	0
11	8	4	10	0
12	8	4	-	-
13	8	6	-	-
14	9	7	-	-
15	8	5	-	-
16	9	7	-	-
Mean	7.44	6.50	10.18	1.91
Std. dev.	2.87	1.67	1.66	2.07

to be considered in the evaluation. The results for the documentation in SAP i.s.h.med show a mean Levenshtein distance with $\mu = 6.50$, thus, a significant difference to the ideal documentation workflow. Considering the mean number of documented data entities ($\mu = 7.44$) less information as defined in the optimal workflow has been documented. The *oncoflow* results show significant workflow improvements. The usage of the web-based anamnesis form results in a reduction of the mean Levenshtein distance by 4.59 to $\mu = 1.91$. The mean number of documented information entities increased to $\mu = 10.18$ which shows that basically all questions, which are important for the treatment process, are asked by the physician.

In Figure 6.9 the recorded information and Levenshtein distances are depicted in a boxplot representation. The boxplots show that the number of datasets increased through the usage of *oncoflow*, but also that the standard deviation strongly decreased. Hence, one can see that the Levenshtein distance shows a high decrease in *oncoflow*, but the standard deviation is equally high as in SAP i.s.h.med.

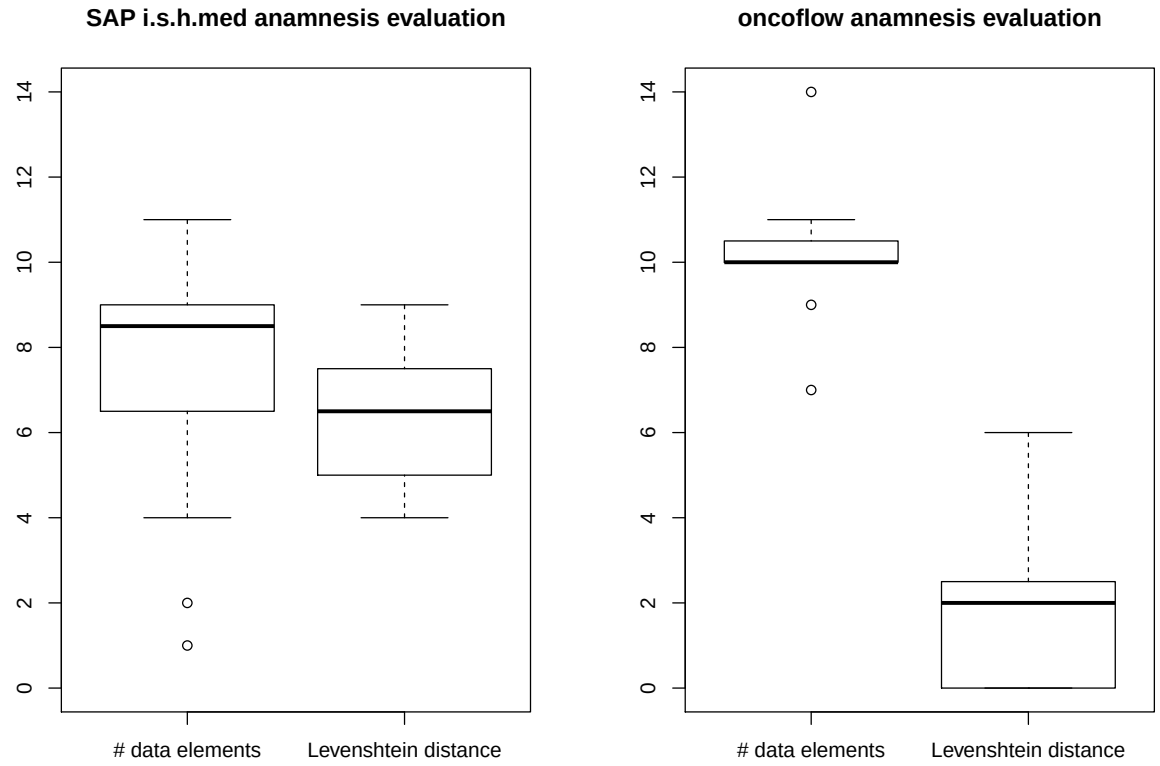

Figure 6.9 – Boxplot representation of *left:* # of data elements recorded during the anamnesis; *right:* Levenshtein distances

6.7 Discussion

The study presented in this paper confirms that a clinical information system developed in close cooperation with clinicians and tailored to the daily clinical routine is well accepted by the physicians and supports efficiently the clinical workflow. The study also shows that routine tasks that have been formerly supported by other information systems are not retarded significantly by the introduction of a new information system. The clinical study focused on anamnesis and clinical examination. In this process step the physician makes extensive use of the new user interface and workflow assistance functions during results documentation. However, only anamnesis and clinical examination with *oncoflow* is directly comparable to the existing workflow in daily clinical routine and can serve as an objective quantitative and qualitative evaluation of *oncoflow*. The time measurement part of the study quantitatively depicts that both approaches for results documentation are not differing significantly. The respective Table 6.2 and Table 6.3 show especially in the median values that documentation in *oncoflow* needs only few more time than the usage of SAP i.s.h.med. Based on the fact that only few samples exist in each sample population the empirical mean and median values are less representative. Thus, statistical tests that are tailored to the evaluation of studies with

small sample sizes have been applied to prove that both observations are not differing significantly. The equality of both workflow times is important for further usage of the system in daily clinical routine because it shows that the new system does not impair the efficiency of anamnesis and first clinical examination.

Furthermore, the complete anamnesis workflow was standardized. Our evaluation using Levenshtein distance measure revealed that the physicians follow the standardized set of questions. Hence, more patient-specific information is recorded within the new system. The number of documented information entities could be increased from 7.5 questions with SAP to 10 questions in oncoflow. This is an improvement of 25%.

The results of the questionnaire evaluation show that *oncoflow* supports the work of the physician very well in contrast to SAP i.s.h.med. The electronic patient record of *oncoflow* has been judged as well-structured; hence, the possibility for quickly accessing relevant information has been improved. Also the structured report form for results documentation makes this process step more efficient because the usage of additional supporting word documents is now obsolete and each physician uses a standardized set of questions that were agreed among all senior physicians. The other set of questions in the questionnaire addressed the user satisfaction of the physician with SAP i.s.h.med and *oncoflow*. Finally, the results show good ratings for *oncoflow* and low ratings for SAP i.s.h.med, respectively. The questionnaire evaluation also provides potential for improvements. The small number of five participating physicians and the usage of *oncoflow* in only one specific hospital is not sufficient for strong and objective results. The clinical processes that have been considered in the time measurement study have not been completely identical. The physicians in the experimental group needed one additional process step as workaround for transferring the documented information into the HIS. This time frame has been regarded as additional documentation time and directly compared with the documentation time in SAP i.s.h.med. Future work should focus on the implementation of a bi-directional communication interface between SAP i.s.h.med and *oncoflow* so that this process step is obsolete. Afterwards, this study should be performed again with two identical workflows. This second study should also include a higher number of workflows as well as a larger number of participating physicians. The conduction of a study that also includes physicians and processes from a different hospital would make the results much stronger.

6.8 Conclusions

We developed a comprehensive electronic patient record that automatically imports and restructures information from existing clinical information systems. The information is centrally available for the physician via a well-designed web interface and is instantly usable for further electronic processing. Furthermore, the *oncoflow* system provides different assistance functions such as a *Treatment Summary* and the automatic creation of physician letters based on existing patient information. The

tumor board is an important step in the oncological patient treatment process. All physicians and surgeons that take part on the patient treatment meet there for discussing possible treatment options and finding the best therapy. The *oncoflow* system together with the TPU provides extensive support for the tumor board. The system supports the creation of invitation letters, tumor board protocols, enriches the board discussion with endoscopic images and 3d tumor reconstructions and provides a voting system to make the decision making process more transparent. Within a clinical study that focused on the user acceptance of a completely redesigned electronic patient record and the usefulness of assistance features supporting daily clinical routine the new information system has been evaluated.

A time measurement study has been conducted to evaluate if the usage of the new system influences the time needed for conducting an anamnesis and clinical examination. This study showed that the overall time needed with the new information system is only 8.4% slower in the mean value and actually 0.3% faster with regard to the median value. A questionnaire-based evaluation study focused on the evaluation of the process improvement and user acceptance of the new system. The results show that physicians appreciated the new assistance functions and find information faster in the new electronic patient record. The new user interface received very good ratings and all physicians could imagine using the system furthermore in daily clinical routine.

Standardized and transparent workflows are important for the certification as cancer center, outcome documentation and quality management, and finally for evidence based medicine. Due to the usage of a structured documentation form physicians perform an anamnesis whose structure could be improved by 71%.

Due to the promising results future work will focus on the establishment of systematic and patient-oriented tumor documentation. Follow-up results are especially important for the evaluation of previous tumor therapies. Thus, standardizations in this area seem to be very fruitful.

Chapter 7

Workflow recognition

7.1 Motivation

The substantial amount of patient-specific information in clinical information systems helps physicians and surgeons obtain increasingly comprehensive overviews of patients. This information is available but is insufficiently structured and poorly searchable, particularly in the large HISs such as SAP i.s.h.med. There are several reasons for the poor structuring of this information, but it is mainly due to the primary economy-driven documentation goals of hospitals. Mature IT solutions are still lacking for a primary focus on treatment decision making, for hierarchically organizing patient-specific results, and for summarizing the results of relevant pretreatment investigations. This situation leads to inefficient processes in daily clinical routine and to considerable time spent searching documents that are relevant in the current treatment phase. Unfortunately, physicians do not have the ability to simply and quickly obtain the most relevant documents for the specific therapy phase. Furthermore, scientific questions such as "Show me all of the clinical documents that are generated during surgical interventions for patients with laryngeal carcinoma" cannot readily be answered using the currently available clinical information systems.

To improve clinical workflows, to relieve physicians and surgeons from time-consuming activities, to improve patient safety and to reduce costs, developing user-friendly and intuitive capabilities for searching and accessing clinical data is of critical importance. A fundamental prerequisite is knowledge of treatment processes in general, as well as specific knowledge regarding the current treatment phase of the patient. Knowledge of the overall treatment process can be acquired through a workflow analysis in the specific clinical disciplines or departments. Statistical models such as Hidden Markov Models (HMMs) are good methods for subsequently transferring the workflow analysis results into a mathematical representation that can subsequently be used to infer workflow phases from given patient-specific information that originates from clinical information systems, i.e., the so-called observations [36].

In this work, a completely new approach for automatically inferring the current step of a clinical patient treatment process from clinical data is presented. First, patient-specific information from

different clinical information systems is used as training data for creating a probabilistic model of the underlying treatment process. Subsequently, patient-specific information that was not a part of the training process can be provided to the model for predicting the most likely treatment step. Finally, each patient-specific information entity, such as disease codes, procedure codes or laboratory results, contains additional meta-information regarding the originating process step. This meta-information is very valuable for the development of sophisticated workflow assistance or clinical decision support systems.

Additionally, a mathematical representation of clinical workflows provides an important basis for a wide variety of analyzes. The model can identify both the most likely course of treatment as well as outliers for patients with complex cases. Subsequently, this information provides the basis for improving clinical pathways or for serving as a metric for clinical quality management [87].

7.2 Goals of this work

The primary objective of this work is to develop a new method for predicting single phases of the oncological treatment process based on patient-specific information entities originating from clinical information systems. The first step is to develop a probabilistic model based on HMM that is able to represent clinical workflows in different granularity levels. This model should then be able to predict the current treatment phase for a set of unknown clinical patient-specific information entities. We developed two types of HMM models with 3 and 7 therapy phases and with additional exception-handling approaches to address different types of variations in clinical workflows. The exception-handling approaches consider both the hierarchical properties of ICD10 and ICPM codes, as well as others, to improve the HMM prediction rates. These models are then trained with anonymized real-world clinical datasets from patients with primary head and neck tumor diagnoses. Finally, two types of HMM models are evaluated in terms of their recognition rates and the results of their exception-handling algorithms.

7.3 Theoretical background

Statistical models such as HMMs provide the theoretical basis for a wide range of applications and are also appropriate for modeling clinical workflows [88, 89, 90, 91]. Hence, this section will provide a brief introduction to HMMs and the algorithms used in this work.

We first wish to briefly discuss why we decided to use HMMs and to compare HMMs to neural networks and decision trees [92, 93]. The HMMs is a well-established method for workflow recognition with proven mathematical foundations. Additionally, many studies have previously employed HMMs for the recognition of surgical workflows, as depicted in detail in Section 2.4, with promising results. In our case, HMMs provide several advantages compared to neural networks

and decision trees. First, a substantial amount of training data is required to train neural networks. Furthermore, neural networks do not operate on transition and observation probability matrices, which is an important feature of HMMs. These matrices provide transition and observation probabilities in human-readable form, which provides a basis for further research, such as analysis of clinical workflows. Decision trees are a method for rule-based classifications: Each node in the tree represents one rule. Following the tree from the root node to the leaves, it provides exactly one answer to a specific question. The disadvantages of decision trees include their size when rules are very complex and their relatively low recognition rates compared to other algorithms [94, 95]. Finally, we decided to use a HMM in this case, but we will eventually perform the study with other algorithms in the future to compare the results.

7.3.1 Hidden Markov Model

A HMM describes a process over time. This process is characterized by a sequence of states that change by chance. The state change is modeled with a random variable X_t, where the transition probability between the states only depends on the current state, not on the past states. This property is called the "memorylessness" or Markov property. The states are not directly observable in a HMM because they are hidden, but each state yields so-called observations that are used for inferring the most probable state at time t. Observations can also be described with a random variable Y_t. A HMM is a 5-tuple $\lambda = (S; M; A; B; \pi)$, where:

- $S = \{s_1; \ldots; s_n\}$ Number of hidden states and values of X_t
- $M = \{m_1; \ldots; m_m\}$ Number of possible observations and values of Y_t
- $A \in \mathbb{R}^{n \times n}$ Transition matrix; $a_{i,j}$ denotes the probability of changing from state i to state j
- $B \in \mathbb{R}^{n \times m}$ Observation matrix; $b_{i,j}$ denotes the probability of observing m_j in state s_i
- $\pi \in \mathbb{R}^n$ Initial state distribution; $\pi_i = P(X_1 = s_i)$ denotes the probability that s_i is the initial state.

7.3.2 Viterbi algorithm

To find the most likely state sequence $Q = \{q_1; \ldots; q_T\} \in S$ for a given HMM λ and observation sequence $O = \{o_1; \ldots; o_T\} \in M$, the Viterbi algorithm can be used [96]. The Viterbi algorithm incorporates the transition and observation probabilities of individual states as well as the probabilities previously calculated for all states $t - 1$. This makes the Viterbi algorithm more robust to zero probabilities ($a_{i,j} = 0$ for some i and j) [36]. However, lacking probabilities in the underlying model may lead to serious problems. Two approaches for solving these drawbacks are presented in Section 7.4.3.

7.4 Materials and methods

7.4.1 Data acquisition

Integration of patient information

Clinical information is not stored within a central database but is rather distributed across multiple information systems, such as HIS, Radiology Information System (RIS), PACS or research-driven department-internal solutions [7]. This leads to inefficient clinical workflows and hinders the execution of clinical studies due to the lack of patient-specific information and error-prone copy-paste procedures. To mitigate the aforementioned drawbacks, a web-based clinical information system, *oncoflow*, has been developed [72]. The *oncoflow* system has been tailored to support physicians and surgeons in daily clinical routine during the treatment of patients with head and neck carcinoma. Therefore, electronic communication interfaces have been developed to import therapy-related information into a central database (see Figure 3.3). There are two main information sources, the HIS and the DTTM, that provide the majority of relevant patient-specific information. The first consultation reveals important therapy-related details, such as personal habits like alcohol or nicotine consumption, comedication or former surgical interventions. This information is acquired using a structured web-based documentation form. Finally, a broad set of information is acquired during follow-up consultations through the use of an Android tablet-based screening tool for functional disorders [60, 61].

Physicians and surgeons at the Leipzig University Medical Center have used the *oncoflow* system in daily clinical routine as a scientific prototype since March 2013. To train the HMM, only an EPR that contains at least a first consultation, a panendoscopy, a tumor board and a follow-up dataset is used to ensure that the patient already underwent the entire treatment process. Available tumor therapy-related ICD10 and ICPM datasets serve as important training data for the HMM.

Data selection, export and processing

The patient-specific information in the *oncoflow* database is not instantly usable as training data for the HMMs. Hence, an appropriate EPR must be identified, after which relevant information entities can be extracted. First, the patient datasets, which contain at least one entity of consultation, panendoscopy, tumor board and follow-up, were identified in the database. The resulting 40 available EPRs that met the required criteria provided the basis for creating the HMMs. Subsequently, the previously mentioned information entities and the tumor therapy-related ICD10 and ICPM codes from the specific patients were selected and exported in chronological order as a Comma-Separated Values (CSV) file, which serves as the input for the HMM. Detailed numbers are presented in Table 7.1. An information entity is also referred to as an observation.

The ICD10 and ICPM codes provide a hierarchical mapping of health conditions or operation

Table 7.1 – Distribution of observations in the selected EPRs.

total # of EPRs	total # of observations	average # of observations per EPR	minimum # of observations per EPR	maximum # of observations per EPR
40	2208	55	19	100

procedures to generic categories. To reduce the complexity of the HMMs and to increase the hidden state recognition rate, two different approaches are evaluated in this paper. The first approach is to construct the HMMs with full ICD10 and ICPM codes, which results in a more complex model with a larger number of observations. The second approach is to reduce the depth in the hierarchy by shortening the ICD10 and ICPM codes to a coarse granularity.

In the following examples, the ICD10 code *C32* and the ICPM code *5-303* should clarify the procedure. *C32* denotes a malignant tumor in the larynx and can be viewed as a parent node in the ICD10 classification. In the selected EPRs, more specific descriptions of this disease are used, such as *C32.0*, which denotes a malignant tumor in the glottis, or *C32.3*, which denotes a malignant tumor in the cartilage of the larynx. The same holds for the ICPM code *5-303*, which encodes a laryngectomy. In more fine-granular representations, *5-303.0* denotes a simple laryngectomy, and *5-303.01* denotes a reconstruction with local mucosa.

To evaluate the influence of the aforementioned code lengths on the prediction results, a post-processing of the exported information was performed. Therefore, all of the ICD10 and ICPM codes were shortened to their hierarchical parents and stored in a second CSV file for later use. Using the shortened disease and procedure codes results in fewer observations and more robust transition probabilities in the HMM.

7.4.2 Model properties

The oncological treatment process can be represented by different levels of granularity. At the finest-grained level, the process can be characterized by information entities in the EPR, such as ICD10 or ICPM codes. Unfortunately, this information is not readily usable by physicians or surgeons for obtaining a quick overview on the current medical status of the patient or for identifying the relevant information entities in the current treatment step. Hence, a presentation of the process in an adjustable granularity must be developed for the specific clinical or organizational needs.

In this study, two types of HMMs with different numbers of hidden states were developed in close cooperation with physicians and surgeons from the local head and neck department (see Figure 7.1). The 3-state model is a coarse representation of the workflow as described in Section 1.2 and allows existing patient data to be divided into three different categories. The finer-grained 7-state model is actually more helpful for physicians in daily clinical routine because the current treatment steps, such as panendoscopy or therapy, are clearly identifiable and existing patient data from the current

step can be acquired instantly.

To train the HMM, each of the 2208 observations were manually tagged with the correct state for the 3-state model and for the 7-state model. The appropriate states for the specific observations were identified by studying the specific EPRs in the HIS and receiving support from physicians and surgeons to clarify observations in which the actual state was not clearly identifiable. Finally, four CSV files were created for generating the HMM:

- 3-state model with full ICD10/ICPM codes
- 3-state model with short ICD10/ICPM codes
- 7-state model with full ICD10/ICPM codes
- 7-state model with short ICD10/ICPM codes

Based on the tagged observations, the initial state distribution π, the transition probability matrix A and the observation matrix B can be created. The length of the initial state distribution vector $\pi \in \mathbb{R}^n$ is equal to the number of hidden states of the HMM. For each data set included in the model, the hidden state of the first observation is assigned to the vector element of this hidden state in π. Finally, the initial state distribution is calculated. The transition matrix $A \in \mathbb{R}^{n \times n}$, where n denotes the number of states, is generated by assigning each state transition to the corresponding element in the matrix. If no state transition occurs from the observation at time t to the observation at time $t + 1$, then the matrix element $A_{j,j}$, where j denotes the current state, is increased by 1. Let *n* be the number of states and *m* be the number of observations; then, the observation matrix is given by $B \in \mathbb{R}^{n \times m}$. The matrix is generated by assigning each observation and its hidden state to the corresponding matrix element. The final probability distributions for A and B are row

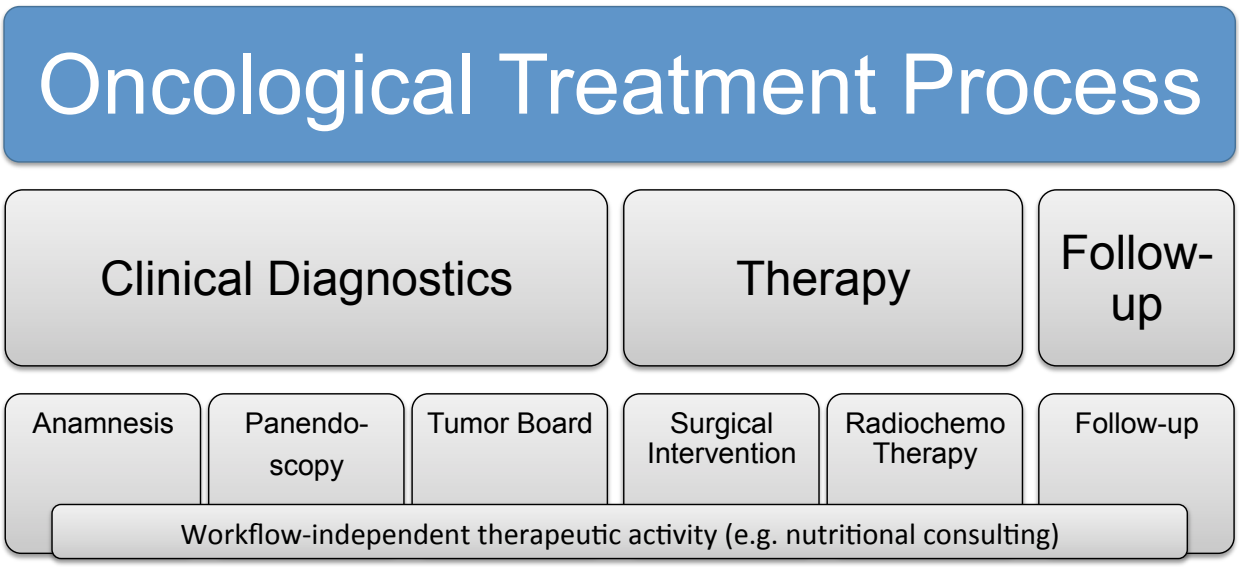

Figure 7.1 – Oncological treatment process in different granularity levels for patients with head and neck carcinoma. In the scope of this work, each step represents a hidden state in the HMM.

stochastic and calculated for each row in the matrix such that $\sum_{j=1}^{n} A[i,j] = 1 \; \forall_i \in \{1 \ldots n\}$ and $\sum_{j=1}^{m} B[i,j] = 1 \; \forall_i \in \{1 \ldots n\}$ hold.

7.4.3 HMM exception handling

Exception sources

Statistical models such as HMMs are based on probability distributions for predicting hidden states from given observations. Thus, specific observations may be misclassified or not classified at all due to missing transitions or observation probabilities. The exception handling presented in this section focuses on observations that are not classified by the HMMs and are thus tagged as *unclassified* (see Figure 7.2). There are two reasons why observations may not be classified.

The first reason is that a specific observation is only present in one EPR. Hence, when this patient record serves as test object during the leave-one-out cross validation, the specific observations are not included in the HMM generation, the respective elements in the B matrix have zero probability, and the model fails during the study. This situation is mitigated beforehand, and the specific observations are tagged as *unclassified*. A detailed description is given in Section 7.4.3.

Unfortunately, the classification with the Viterbi algorithm also fails in the case of specific observation sequences in which transition and observation probabilities are given. This case occurs when the study observation sequence significantly differs from the observation sequences used to generate the model. The respective observations are also tagged as *unclassified*.

To improve the overall recognition rates of the HMMs, two algorithms for exception handling were developed. The algorithms are applied to the state sequence produced by the Viterbi algorithm and aim to identify and re-classify the existing *unclassified* observations.

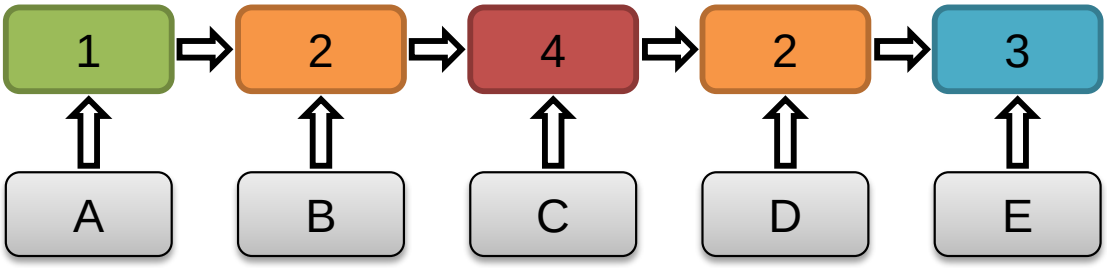

Figure 7.2 – Exemplary state sequence as a result of the Viterbi algorithm applied to the observation sequence A–E. States 1–3 are classified by the HMM. State 4 denotes *unclassified* and will subsequently be treated by the exception-handling process.

Previous recognized state

The first exception-handling algorithm sequentially parses a given state sequence for *unclassified* states and remembers the last classified state. If an *unclassified* state is found, it is assumed that

the model is still in the same state as predicted for the previous observation, and the previous state is assigned to the actual observation. This approach has two major drawbacks: the first is that this algorithm is not applicable if the first observation is already *unclassified* - in this case, the first and all immediately following *unclassified* observations remain unchanged. The second drawback is that this approach can only be applied to models in which consecutive states are equal for a certain number of observations. If the hidden states change frequently in consecutive observations, this approach may yield poor outcomes.

Observation-specific State Estimation

The Observation-specific State Estimation (OSE) approach is more sophisticated and aims to overcome the drawbacks of the *previous recognized state* algorithm described in Section 7.4.3. OSE incorporates knowledge about the hierarchical structure of ICD10 and ICPM codes in combination with modified parts of standard HMM algorithms to finally acquire hidden states for observations in which the standard HMM failed. The input parameters for OSE are the state sequence produced by the HMM's Viterbi algorithm $\vec{\nu}_{\text{Viterbi}}$, the corresponding observation sequence $\vec{\omega}$ and the underlying HMM, including the A, B and π matrices; the set of hidden states S; and the set of observations M (see Algorithm 1).

Initially, the given sequence of resulting states $\vec{\nu}_{\text{Viterbi}}$ is sequentially parsed to locate *unclassified* states (see Algorithm 1; line 1). If an *unclassified* state ν_i is found, the corresponding observation ω_i is acquired from the observation sequence. To find the most probable state for ω_i, the OSE algorithm is applied to all states s in the actual model (see Algorithm 1; line 7). Then, two different cases must be distinguished. In the first case, the current observation is part of the HMM, which means that this observation was part of the learning process of the model and has transition and state probabilities in the corresponding matrices. Hence, these probabilities can be immediately used to calculate the highest state probability (see Algorithm 3). In the second case, the observation is not part of the model training; hence, there are no transition and observation probabilities available. Thus, in the case that the observation is an ICD10 or ICPM code, similar observations are searched within all available observations M (see Algorithm 2), and the highest state probability for these observations can be subsequently computed (see Algorithm 1; lines 11, 12). Subsequently, the highest probability and the corresponding state are updated.

However, there is still a possibility that no appropriate similar observations can be found, and thus, the hidden state remains *unclassified*. In this case, the previous recognized state is selected as the fallback solution, as depicted in Section 7.4.3 (see Algorithm 1; lines 19, 20). Finally, the state of the current observation is updated.

Algorithm 2 shows the procedure for finding observations that are similar to a given observation. Here, the hierarchical structure of ICD10 and ICPM codes is utilized. First, a regular expression is used to ensure that the given observation ω_i is an ICD10 or ICPM code (see Algorithm 2; line

Algorithm 1 The Observation-specific State Estimation (OSE)

input: observation sequence $\vec{\omega}$, Viterbi result sequence $\vec{\nu}_{\text{Viterbi}}$, HMM λ

```
1:  for each ν_i ∈ ν⃗_Viterbi | ν_i = unclassified do
2:      highestProbability = 0
3:      mostProbableState = unclassified
4:      observation ω_i = ω⃗[index(ν_i)]
5:      HiddenStates S = λ.S // get list of hidden states from HMM
6:
7:      for each s ∈ S do
8:          if ω_i ∈ λ then
9:              _prob = calculateHighestStateProbability(ω_i, s, λ)
10:         else
11:             _simObs = findSimilarObservations(ω_i)
12:             _prob = calculateHighestStateProbability(_simObs, s, λ)
13:
14:         if _prob > highestProbability then
15:             highestProbability = _prob
16:             mostProbableState = s
17:
18:     // fallback solution
19:     if highestProbability = 0 then
20:         mostProbableState = usePreviousRecognizedState()
21:
22:     ν_i = mostProbableState
```

3). Then, a search string is created from the observation. During each iteration in the while-loop, the search string is shortened by one character, which means that the resulting string matches a wider set of ICD10 or ICPM codes, as described in detail in Section 7.4.1. Subsequently, the current search string is compared to all observations in the given HMM. When the search string matches a given observation code for the first time (longest prefix match), the corresponding code is saved in an array Θ, and the while-loop is stopped for the next iteration (see Algorithm 2; lines 11-13). The for-loop processes the remaining observations in M such that the most similar observations may be found.

Algorithm 3 aims to find the highest probability for observation ω_i being in state s at time t. Therefore, the transition probabilities from all states $k \in S$ at time $t-1$ into state s at time t are multiplied by the probability of the observation being in state s. This procedure is performed for all observations Θ, and finally, the highest probability is returned. Unlike the forward variables $\alpha_t(i)$ in [36], the HMM model probabilities for being in state k at time $t-1$ are not included in the actual calculation to avoid the influences of any incorrect calculations from the Viterbi algorithm.

Algorithm 2 `findSimilarObservations`

input: observation ω_i, hidden state s, current HMM λ
output: array of observations Θ

```
1:  Observations M = λ.M\ω_i // get list of observations from HMM w/o ω_i
2:
3:  if (ω ∈ ICD10) or (ω ∈ ICPM) then
4:
5:     found = false
6:     searchString = ω_i
7:     while searchString.length > 1 and ! found do
8:        searchString.removeLastCharacter
9:
10:       for each m ∈ M do
11:          if m.startsWith(searchString) then
12:             Θ.add(m)
13:             found = true
14:
15: return Θ
```

Algorithm 3 `calculateHighestStateProbability`

input: array of observations Θ, hidden state s, HMM λ
output: probability for being in state s

```
1:  TransitionMatrix A = λ.A // get transition matrix from HMM
2:  ObservationMatrix B = λ.B // get observation matrix from HMM
3:  HiddenStates S = λ.S // get list of hidden states from HMM
4:  highestProbability = 0
5:
6:  for each θ ∈ Θ do
7:     observationProbability = B[s][θ]
8:
9:     for each hidden state k ∈ S do
10:       transitionProbability = A[k][s]
11:       currentProbability = observationProbability ∗ transitionProbability
12:
13:       if currentProbability > highestProbability then
14:          highestProbability = currentProbability
15:
16: return highestProbability
```

7.5 Case study

7.5.1 Software design

To apply a HMM to a given observation sequence for predicting the corresponding sequence of hidden states, additional mathematical algorithms, such as the Viterbi algorithm (see Section 7.3.2), are necessary. Therefore, the open source software library `jahmm` (https://code.google.com/p/jahmm/) was used. This library implements the basic Forward and Viterbi HMM algorithms as well as the Baum-Welch and K-Means structure learning algorithms. A Java-based command line application was developed to implement the model generation process (see Section 7.4.2), to include the `jahmm` library and to perform the HMM exception handling (see Section 7.4.3. The software also performs the statistical calculations presented in Section 7.6.

7.5.2 Study execution

The aforementioned theoretical approaches for HMM model generation, hidden state prediction and exception handling were conducted in an evaluation study. The study was performed with a command line Java application (see Section 7.5.1) and four CSV files containing the input observations and the corresponding hidden states (see Section 7.4.2). Each input file contained $N = 40$ EPRs with the specific observations in exactly the same order but in a different granularity or as a different model type (3-state or 7-state).

To estimate the accuracy of the HMM and the presented exception-handling methods, the *leave-one-out cross validation* technique was used [97]. This approach uses $N - 1$ observation sequences and the corresponding hidden states (known data) as a training data set. The N^{th} observation sequence serves as an independent validation sample (unknown data) against which the model is tested. Hence, the study must be performed N times for each CSV input file. Within each iteration, one HMM is generated with the training data and then tested against the left-out observation sequence.

However, some observations are only included in one EPR. These observations are presented in detail in Section 7.6.1. This leads to significant problems during the execution of the study if the specific EPR serves as the validation data set. In this case, the lacking probabilities in the transition and observation matrices cause the Viterbi algorithm to yield incorrect state prediction results. To mitigate these shortcomings, the validation observation sequence is checked prior to the Viterbi processing. Therefore, each observation of the validation sample is checked against all observations included in the HMM, which are processed during training of the model. If the validation sequence contains such singular observations, the corresponding index is stored and the observation is removed from the original test sequence. Subsequently, the test sequence serves as an input for the Viterbi algorithm such that the processing can be finished without failure. Then, the

resulting state sequence is restored to the length of the original observation sequence by inserting the state *unclassified* at the index positions of the previously removed observations. The resulting state sequence then immediately serves as input data for exception handling or can be used directly for postprocessing.

The resulting state sequences of each iteration are stored for later postprocessing. After postprocessing, the results are compared to the states of the previously tagged observations, and both the correct and incorrect predicted states are counted in different granularities, including for each iteration, for each hidden state and for the entire cross validation. The recognition rates are subsequently calculated. The results are depicted in detail in Section 7.6.

7.6 Results

7.6.1 Model recognition rates

Table 7.2 presents the recognition rates of the Viterbi algorithm without any exception handling. The median values of 86.3% and 86.6% for long ICD10 and ICPM codes (in contrast to 89.6% for short codes) show that the pure HMM is more sensitive to the code length than to the number of hidden states. The minimum recognition rates for long codes are lower than those for short codes. One can also observe that the recognition of at least one observation sequence in the 7-state HMM completely failed because the minimum recognition rate is 0%. This also leads to a significantly higher standard deviation in the 7-state model with long codes.

Table 7.2 – State recognition results for the use of a pure HMM without exception handling. All values are depicted in %.

	3-State-Model		7-State-Model	
	long codes	short codes	long codes	short codes
Recognition rate	85.37	88.54	82.20	87.14
Minimum	60.00	64.94	0.00	63.64
Maximum	96.83	100.00	97.50	100.00
Median	86.32	89.66	86.59	89.58
Std. deviation	8.89	7.69	16.45	9.04

The first applied exception-handling algorithm that uses the last known state improves the recognition rates in all model types (see Table 7.3). In particular, the median value increased to 90% for each type, which thus indicates that the dependency on the length of the underlying ICD10 and ICPM codes could be mitigated. The minimum recognition rates increased significantly from 7%

to 10%. Unfortunately, this exception-handling approach is unable to correct observation sequences that are completely *unclassified*; therefore, the minimum recognition rate of the 7-state model with long codes is still 0%. The average and maximum recognition rates are slightly increased, and the standard deviation shows a slight decrease, except for the 7-state model with long codes.

Table 7.3 – State recognition results for the use of a HMM with additional exception handling. In this case, the last known state is used for observations with no state assigned by the plain HMM. All values are depicted in %.

	3-State-Model		7-State-Model	
	long codes	short codes	long codes	short codes
Recognition rate	89.31	90.35	85.78	88.72
Minimum	70.00	75.00	0.00	70.21
Maximum	100.00	100.00	98.08	100.00
Median	89.53	90.62	90.05	90.77
Std. deviation	6.75	6.13	16.15	7.68

The results for the OSE approach are presented in Table 7.4. The overall, median and maximum recognition rates are actually quite similar to those of the previous state exception-handling approach. A major improvement is the increase in the minimum recognition rate of the 7-state model with long codes from 0% to 66.7% and a decrease in the standard deviation from 16% to 8.6%. This result indicates that the OSE approach is able to correct hidden states of observation sequences even if the Viterbi algorithm completely fails.

Table 7.4 – State recognition results for the use of a HMM with additional exception handling. In this case, an observation-specific state estimation algorithm is used for the recognition of observations with no state assigned by the plain HMM. All values are depicted in %.

	3-State-Model		7-State-Model	
	long codes	short codes	long codes	short codes
Recognition rate	88.99	90.31	86.78	88.81
Minimum	63.33	73.33	66.67	70.21
Maximum	100.00	100.00	98.28	100.00
Median	89.83	90.62	89.54	90.40
Std. deviation	7.52	6.34	8.65	7.76

Finally, in Table 7.5, the number of states that were corrected by the previous state and the OSE exception-handling algorithm are presented. This table shows that both algorithms handled the

same number of *unclassified* observations. Furthermore, it can be observed that the OSE approach failed for eight specific observations, which are characterized by the following six ICD10 codes: *L02.1 (skin cheek abscess), K44.9 (Hernia diaphragmatica), C43.0 (malignant lip malignoma), C64 (malignant renal tumor), F33.2 (depressive dysfunction)* and *B37.81 (Candida oesophagitis)*. Within all 2208 observations, the observation *L02.1* was present three times in one EPR, and the other observations were present only one time. For these observations, the OSE algorithm could not find similar observations, and thus, the fallback solution was chosen.

Table 7.5 – Number of observations handled by error-correction algorithms.

	3-State-Model		7-State-Model	
	long codes	short codes	long codes	short codes
Previous state exception handling	110	49	140	49
OSE classification	102	41	132	41
Previous state fallback for OSE	8	8	8	8

7.6.2 Model accuracy

In this section, the results regarding the model accuracy are shown, which means that the recognition rates differed according to the hidden states in the HMM.

Table 7.6 presents the recognition rates for the 3-state model grouped by the different code lengths and exception-handling mechanisms. As shown, the recognition rates are equally distributed for the diagnostic and therapy phases. The recognition rates during the follow-up phase range between 3% and 7% lower. However, although there is no significant difference between the percentage values, there is no model-phase combination in which the recognition rate reaches 100%.

The result from the therapy-phase based evaluation for the 7-state model is presented in Table 7.7. The results for the anamnesis, panendoscopy and follow-up phases are homogeneous within the same ICD10 and ICPM code length but show better results for short codes. The tumor board and radiochemotherapy states show high recognition rates for each model type, in which the tumor board state yields recognition rates up to 100%. Finally, the recognition rates for the intervention and the other care phases are less than those of the aforementioned phases. These findings are discussed in detail in Section 7.7, in which the connection to the specific observation in these phases is established.

Table 7.6 – Hidden state-centered view of the recognition rates for the different 3-states model therapy phases. All values are given in %.

observation type	long observations			short observations		
exception handling	w/o	last state	OSE	w/o	last state	OSE
Diagnostic phase	87.30	89.42	88.15	89.56	90.13	89.70
Therapy phase	85.38	90.86	90.70	88.62	91.53	91.61
Follow-up phase	80.68	82.71	84.07	85.76	86.10	86.44

Table 7.7 – Hidden state-centered view of the recognition rates for the different 7-states model therapy phases. All vales are given in %.

observation type	long observations			short observations		
exception handling	w/o	last state	OSE	w/o	last state	OSE
Anamnesis	82.02	85.39	84.27	89.89	91.01	89.89
Panendoscopy	83.14	85.01	85.71	86.18	86.42	86.18
Tumor board	95.74	95.74	100.00	100.00	100.00	100.00
Radiochemotherapy	89.49	93.09	92.69	91.62	93.75	94.02
Intervention	69.03	81.86	87.17	78.76	84.51	84.96
Follow-up	79.24	81.31	83.39	88.93	89.27	89.62
Other care	75.13	76.72	77.51	80.69	81.48	81.48

7.6.3 Model comparison

The study results are presented in side-by-side boxplots in Figure 7.3. Each plot shows a single HMM type, the corresponding recognition rates for the plain Viterbi algorithm and the exception-handling approaches. In general, all of the plots show quite similar recognition rates for the different model types and exception-handling approaches (as previously discussed in detail in Section 7.6.1). Comparing the interquartile ranges reveals that the spread of the 7-state model results is considerably greater than that of the 3-state model. The median value in the 3-state model is situated in the center of the boxplot and exhibits a symmetric probability distribution. In contrast, the median value in the 7-state model is situated at the top of the box, which shows a high skewness or asymmetric probability distribution. Regarding the interquartile ranges between the long and short codes, plot A and plot B do not show significant differences, which indicates that the algorithms perform identically for the 3-state model regardless of the code length. The interquartile ranges in plot C and plot D show a considerably larger difference, which leads to the conclusion that the code length

plays a larger role when the model consists of more states.

Finally, the outliers in the boxplot provide important information about the different algorithms. The 3-state model in plot A and plot B show the most outliers for the plain HMM. Plot A shows additional outliers for the exception-handling algorithms, whereas the 7-state model shows less outliers for the model with long codes in plot C. This plot also shows the two observation sequences that are completely misclassified by the plain HMM but corrected by the OSE approach. The 7-state model with short codes in plot D shows more outliers for all model types.

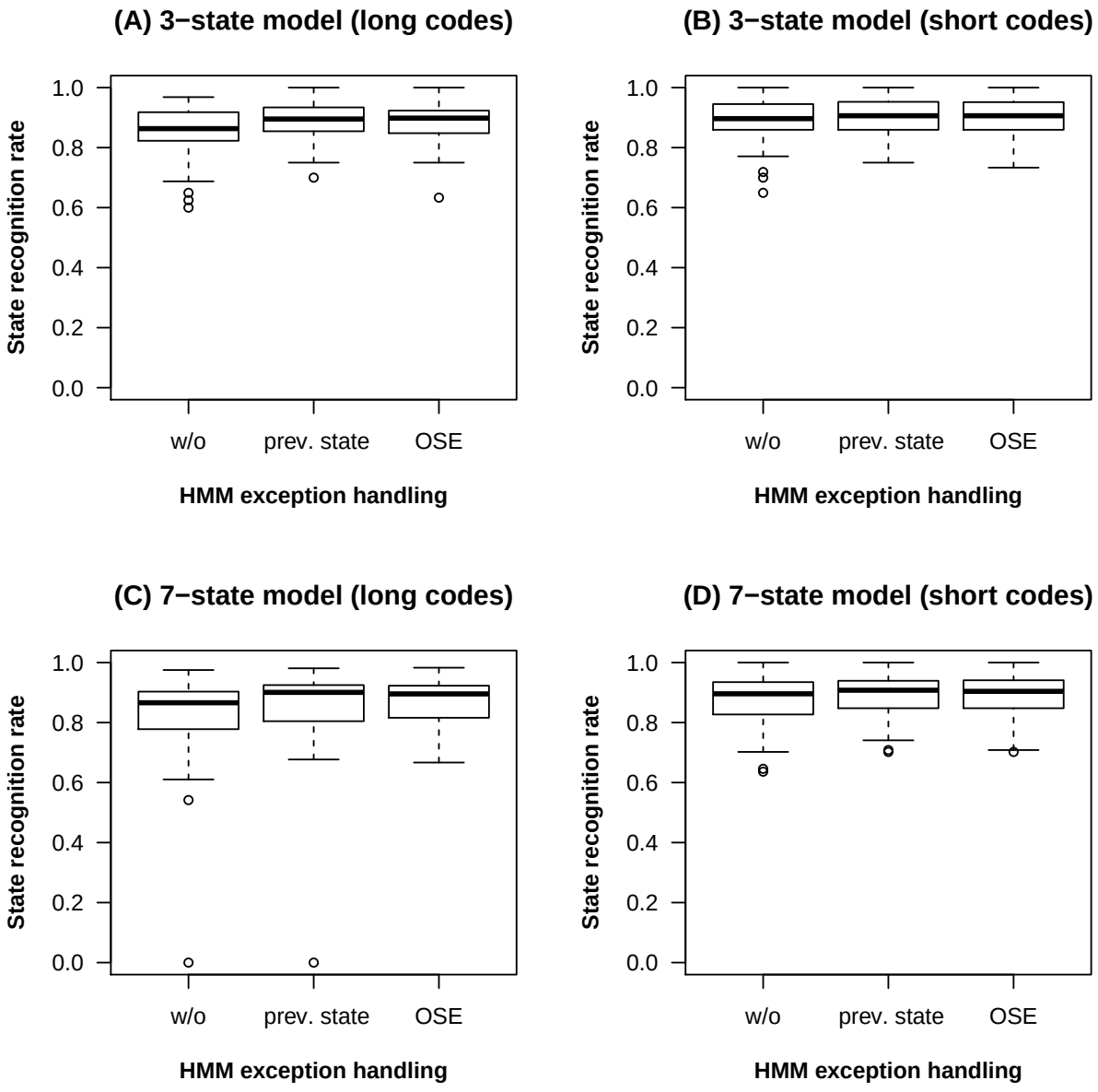

Figure 7.3 – Boxplots of the HMM recognition rates.

7.6.4 Correlation between observations and states

The recognition rates of the HMM significantly differ for different hidden states, particularly in the 7-state model (see Section 7.6.2). To explain the reasons for these differences, two overfitted HMMs with short observation codes, including all observation sequences, were created for the 3-state and 7-state models. In general, there are two different types of observations: the first type can be uniquely identified by the HMM; therefore, this observation only occurs within one hidden state. The second observation type consists of observations that occur along the entire treatment process and are present in multiple hidden states. To create an appropriate example, ten representative observations and their observation probabilities in the B matrix were chosen and transformed into levelplot diagrams. For comparison, the same observations for the 3-state model and the 7-state model were chosen and are explained in detail in Table 7.8.

Figure 7.4 shows the levelplot for the 3-state model observation matrix. The observations A–E are clearly assigned to the clinical diagnostics phase. These are the anamnesis, panendoscopy and tumor board observations that only appear in this phase. In addition to these clearly allocable observations, the following observations, F and G, were chosen. These observations are ICD10 codes, which are encoded every time a patient enters a clinical department throughout the entire treatment process. Thus, these observations are equally distributed across all treatment phases. Subsequently, observation H denotes a surgical intervention where neck lymph nodes are removed. This ICPM code primarily appears in the therapy phase, but it also appears in the diagnostics phase because lymph nodes are sometimes also removed during a panendoscopy. Observation I represents a radiation therapy that is only conducted during the therapy phase. Finally, observation J corresponds to a follow-up meeting, which is typically only performed in the follow-up phase; however, if recidivisms occur directly in the first meeting, the therapy phase is prolonged until the patient is tumor-free.

The levelplot in Figure 7.5 shows both the states and corresponding observations for the 7-state model. Only the differences between this model and the 3-state model should be mentioned here. Observations A–E are separated into 3 different states but are only present in exactly one state. Observations F and G are present in all states but not in the tumor board state because physicians and surgeons do not encode ICD10 codes when the tumor board discusses a patient. Due to the more fine-grained tagging in the 7-state model, observations H and J are only present in one state. Observation I is again only present in one state, which in this case is a radiochemotherapy state.

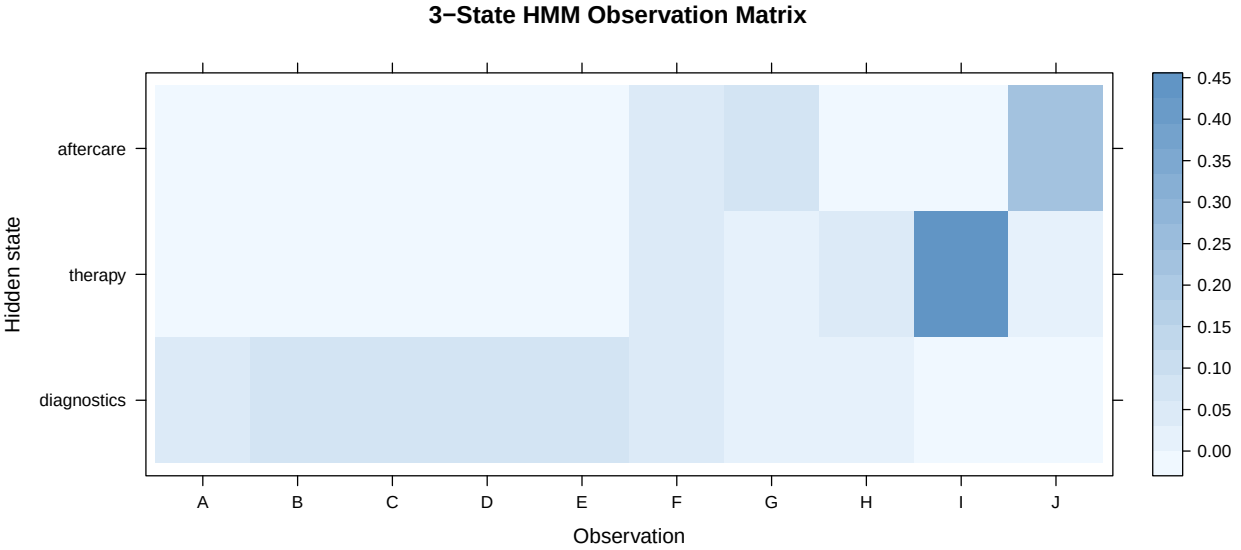

Figure 7.4 – Heatmap of the 3-State HMM observation matrix with selected observations. The map depicts the probability that an observation will occur in a specific state. For a detailed explanation of observations A–J, see Table 7.8

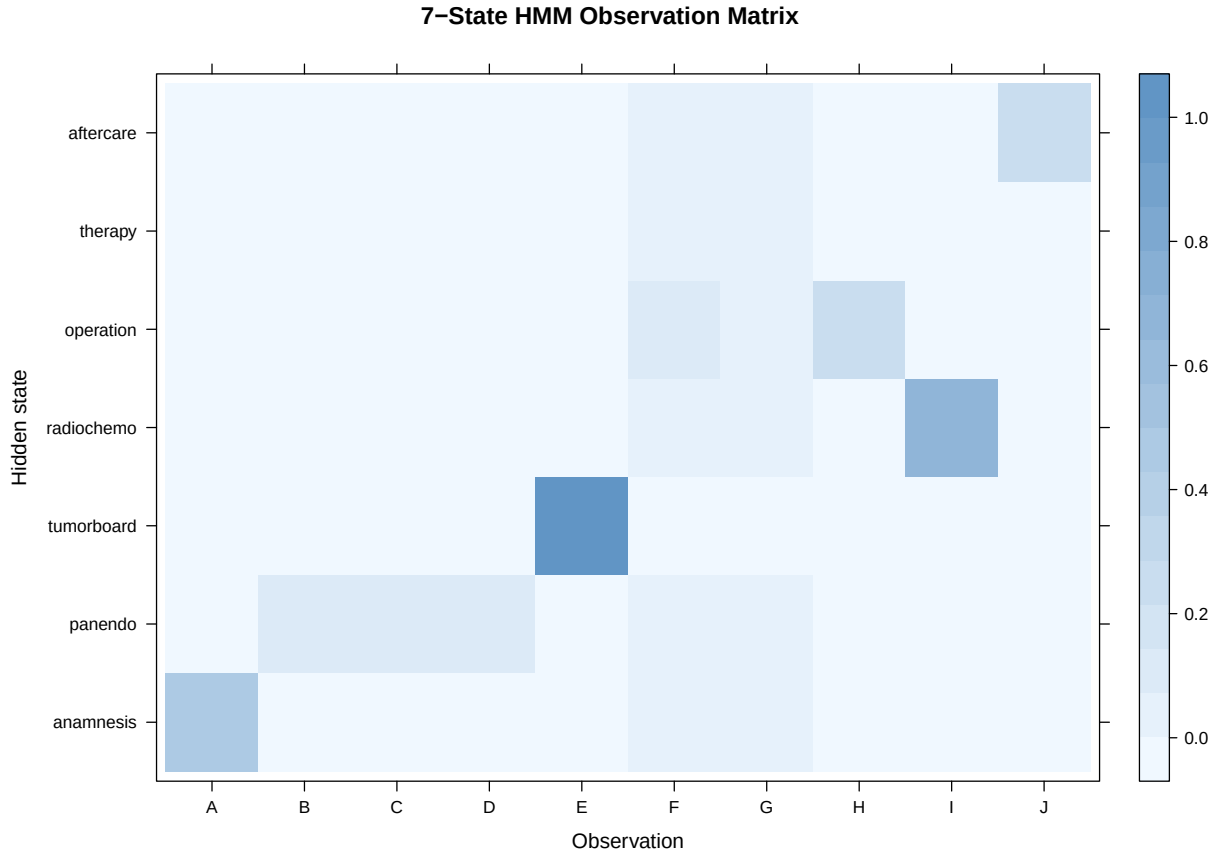

Figure 7.5 – Heatmap of the 7-State HMM observation matrix with selected observations. The map depicts the probability that an observation will occur in a specific state. For a detailed explanation of observations A–J, see Table 7.8

Table 7.8 – Detailed explanation of selected observations in the heatmap representation of 3-state and 7-state observation matrices (see Figures 7.4, 7.5).

Observation	Acronym	Description
A	anamnesis	An anamnesis observation occurs when the first anamnesis was documented with the structured report form in *oncoflow*.
B	panendoscopy	The panendo observation occurs when a surgeon uses the DTTM for OR documentation and uploads the results to *oncoflow*.
C	1-610	This ICPM code denotes a diagnostic laryngoscopy and is assigned by the surgeon after a panendoscopy.
D	1-630	This ICPM code denotes diagnostic esophagoscopy and is assigned by the surgeon after a panendoscopy.
E	tumor board	The tumor board observation occurs when a patient is scheduled for a tumor board with the *oncoflow* tumor board assistance module.
F	C77	The ICD10 code C77 classifies a secondary malignant tumor in the lymph nodes.
G	C32	This ICD10 code specifies a secondary malignant tumor in the larynx.
H	5-403	This ICPM code denotes a surgical intervention to remove lymph neck nodes (neck dissection)
I	8-522	This ICPM code specifies a high-voltage radiation therapy.
J	follow-up	This observation occurs when follow-up information is acquired with the tablet-based questionnaire system or directly entered in the specific *oncoflow* documentation form.

7.7 Discussion

This work presented a new methodology for predicting clinical workflow steps based on HMMs. The concepts and algorithms were developed and evaluated in a study with anonymized real-world patient data sets of 40 EPRs and a total number of 2208 observations. The performed study provided good results for the recognition of the patient's current therapy phase based on given observation sequences. The achieved recognition rates ranged between 82% and 90%.

Pros: The prediction results of a pure HMM's Viterbi algorithm primarily depend on the lengths of the used ICD10 and ICPM codes. The number of hidden states in the model does not exhibit a significant influence on the results. The developed exception-handling approaches improve the recognition rates and most notably minimize the influence of long and shortened ICD10 and ICPM codes. Both exception-handling results provide similar outcomes, as shown in Table 7.3 and Table 7.4. The previous recognized state algorithm uses a type of educated guess in combination with the hypothesis that the actual state of the process does not frequently change over time. In contrast, the OSE algorithm uses actual transition and observation probabilities from the current HMM along with knowledge of the hierarchical structures of ICD10 and ICPM codes to estimate the correct hidden state. Hence, this approach provides higher reliability and robustness; therefore, the OSE algorithm should be preferred over the previous recognized state algorithm.

The influence of an increasing number of hidden states on the recognition rates is an important factor for use in cases where the underlying workflows have variable granularity. Fortunately, the results of this study show that the recognition rates between a model with three states and a model with seven states do not exhibit considerable differences. Hence, this approach can be used in scenarios or use cases where models with a highly variable number of hidden states are necessary. The lengths of ICD10 and ICPM codes were also a subject of the evaluation study. In fact, the results of the study demonstrated that the hierarchical depth of the underlying codes primarily influences the recognition rates of the Viterbi algorithm. This behavior is reasonable given the model complexity. The model with long codes consisted of 185 observations, whereas the model with short codes consisted of only 117 observations. A smaller number of states results in a smaller observation matrix, higher probabilities for each observation and thus better prediction results. The use of exception-handling algorithms improves the recognition rates and increases the robustness of the model. The OSE approach incorporates the previous findings and reduces the model complexity by shortening the codes from *unclassified* observations. Thus, OSE makes the model less complex to find appropriate transition and observation probabilities.

Cons: However, although the number of observations used in the study is quite large, specific aspects in the results show that a larger number of observations would have made the model more robust against complex treatment processes. The outliers in Figure 7.3 plot C can be viewed as an

example for such an observation sequence originating from a rare complex medical case. A larger set of training data with a wider variety of treatment processes would result in models that are better fitted to cluttered workflows and thus provide better recognition results and a decreased need for exception handling.

Some remarks on the OSE algorithm are also necessary. Observations that are not ICD10 or ICPM codes can only be corrected by OSE when transition and observation probabilities are available in the corresponding matrices. A search for similar observations is not currently possible. Hence, if no probabilities are given for these observations, the last known hidden state is assigned. The search for similar ICD10 and ICPM codes works very well for the oncological therapy process in head and neck surgery. However, this approach cannot be immediately applied to treatment processes in other clinical disciplines. In different medical fields, a broader range of codes may be encoded such that supposedly similar observations actually yield an incorrect hidden state. Hence, future studies regarding therapy processes for different medical disciplines must be conducted.

7.8 Conclusions

The use of a stochastic model provides a reliable classification of patient-specific information entities with the corresponding workflow step in the treatment process. To the best of our knowledge, this is the first approach designed to infer clinical workflows directly from HIS information entities. There is only one similar approach available in the scientific literature, which was developed by Huang et al., who used clinical event logs for mining clinical pathway patterns [47, 46].

Workflow recognition and the automatic classification of patient-specific information are important for the development of assistance functions for different clinical use cases. The knowledge of the patient's current treatment step provides the basis for workflow assistance. With this knowledge, clinical information systems are able to provide physicians and surgeons with only the information necessary for a specific therapy phase such that less time is spent in searching the appropriate information entities. A second relevant use case in daily clinical routine is the acquisition of patient-specific documents. In existing information systems, physicians and surgeons browse through tens or hundreds of data sets and manually search appropriate documents. It is not possible to answer questions such as "Please give me all documents that have been created during radiation therapy". When each information entity is tagged with its corresponding workflow step, access to information generated during a specific step in the treatment process can be significantly improved.

Future work will focus on improving the presented approach and integrating it into daily clinical routines. First, the capabilities of the model must be extended. The current state of development does not support breaks in the process in the case of treatment abortion or death, which is very important for the use in daily clinical routines. Additionally, the time elapsed between two observations should be incorporated into the model to support the detection of potential process phase transitions. This

information can then be used to refine the transition and observation matrices of the model. Second, the ability to train the model for daily use is a crucial prerequisite. This could be realized using a feedback-based approach, in which experts correct failures of automatically tagged information entities. Furthermore, the HMM will be integrated into *oncoflow* (see Section 7.4.1) to enrich the patient-specific information with workflow information and to implement the aforementioned clinical workflow assistance functionalities.

Chapter 8

A concept for multidisciplinary clinical application

The treatment process of tumor patients is supported by different stand-alone EPR and Clinical Decision Support (CDS) systems. We developed a concept for the integration of a specialized EPR for head and neck tumor treatment and a Digital Imaging and Communications in Medicine in Radiotherapy (DICOM-RT) based CDS system for radiation therapy in order to improve the clinical workflow and therapy outcome [98]. A communication interface for the exchange of information that is only available in the respective other system will be realized. This information can then be used for further assistance and clinical decision support functions. In the first specific scenario radiation therapy related information such as radiation dose or tumor size are transmitted from the CDS to the EPR to extend the information base. This information can then be used for the automatic creation of clinical documents or retrospective clinical trial studies. The second specific use case is the transmission of follow-up information from the EPR to the CDS system. The CDS system uses the current patient's anatomy and planned radiation dose distribution for the selection of other patients that already received radiation therapy. Afterwards, the patients are grouped according to the therapy outcome so that the physician can compare radiation parameters and therapy results for choosing the best possible therapy for the patient. In conclusion this research project shows that centralized information availability in tumor therapy is important for the improvement of the patient treatment process and the development of sophisticated decision support functions.

8.1 Introduction

The therapy planning for tumor patients is a long-lasting and challenging process due to the complexity of disease patterns, manifold treatment options and the involvement of different specialized medical disciplines [99]. Actually, numerous assistance and decision support systems are used in daily clinical routine for relieving physicians and surgeons from recurring and time-consuming tasks as well as supporting in complex therapy planning scenarios. However, these systems do not

integrate well into the clinical workflow, are poorly integrated into the clinical IT landscape and have only limited possibilities for sharing patient-specific information with each other [6].

For improving the therapy planning, enhancing the possibilities to perform clinical trial studies and quality management as well as making the patient treatment process more safe and more efficient a cooperation project between the ICCAS at the Universität Leipzig and the Image Processing and Informatics Lab (IPILab) at the University of Southern California (USC) has been established. In the first step of the project two clinical information systems assisting physicians and surgeons in daily clinical routine have been analyzed in detail. The goal has been the identification of new and sophisticated solutions for systems integration, common usage of existing information and the development of valuable assistance functions that benefit from a broader information base.

The *oncoflow* EPR was the first system under consideration [55]. The second system which has been analyzed is an imaging informatics based decision support system that aims to lower radiation dose to organs at risk surrounding the tumor, in order to reduce radiation toxicity and improve patients' quality of life post-treatment [100]. This system has been developed at the IPILab in close cooperation with the Loma Linda University Medical Center (LLUMC) and the University of California at Los Angeles (UCLA). Based on a quantified patient anatomy and a knowledge base of existing information from retrospective treatment plans the system helps the radiotherapist to find the best possible treatment plan parameters and the most optimal dose parameters for the patient.

In this chapter a detailed analysis of the clinical workflows, information models and assistance functions of both information systems will be given. The analysis revealed very promising interconnections between the workflows and data models. Both systems depend on information entities which are available in each of the other, so that the implementation of communication interfaces seems to be very fruitful. Finally, a concept for systems integration and further common research will be given.

8.1.1 Clinical workflow for head and neck tumor treatment

The treatment process for patients with head and neck tumor and the most important clinical information systems used in each process step are briefly depicted in Figure 1.1. Most patients are referred from a general practitioner to the clinic with a suspected tumor. In a first consultation the current medical status of the patient such as pain, medication, allergies and way of life is documented and an examination of ears, nose and throat is performed. When a tumor is furthermore suspected the patient underwent an examination in full anesthesia, the panendoscopy, where samples from potential tumor tissue are taken. After a histopathological examination of the tissue samples confirming the presence of a tumor the patient is discussed in the regular tumor board for finding the best possible therapy. Common therapy options are surgical interventions, radiotherapy or chemotherapy. After each applied therapy the patient will be discussed again in the tumor board for results evaluation. In the case of remaining tumor tissue and further available therapy options

the patient is scheduled for the next treatment steps. Otherwise, when no more tumors persist the patient is released into follow-up phase.

8.1.2 Radiation therapy workflow for prostate cancer treatment

The workflow for planning and conducting radiotherapy is shown in Figure 8.1. At first the patient is referred to the radiology department for the generation of simulated CT images. These images are the basis for the treatment planning workflow. Afterwards, relevant organs or Region of Interests (ROIs), are manually contoured within each CT slice on a TPS. These ROIs include critical organs and structures surrounding the tumor, as well as target definitions. Subsequently, the initial parameters such as number and placement of radiation fields, adjustment of multi-leaf collimators, etc. are estimated for a first computation of a dose grid. The Planning Target Volume (PTV) and also the adjacent organs that are affected during therapy, the Organs at Risk (OAR), are depicted in Figure 8.2. Thereafter, the resulting Dose Volume Histogramss (DVHs), isodose contours, dose homogeneity, etc. are reviewed and re-adjusted within an iterative process until the radiation oncologist approves the treatment plan. Finally the patient receives the radiation therapy. The described workflow is embedded into a complete tumor treatment workflow as one specific therapy option such as depicted in Figure 1.1 and not performed stand-alone.

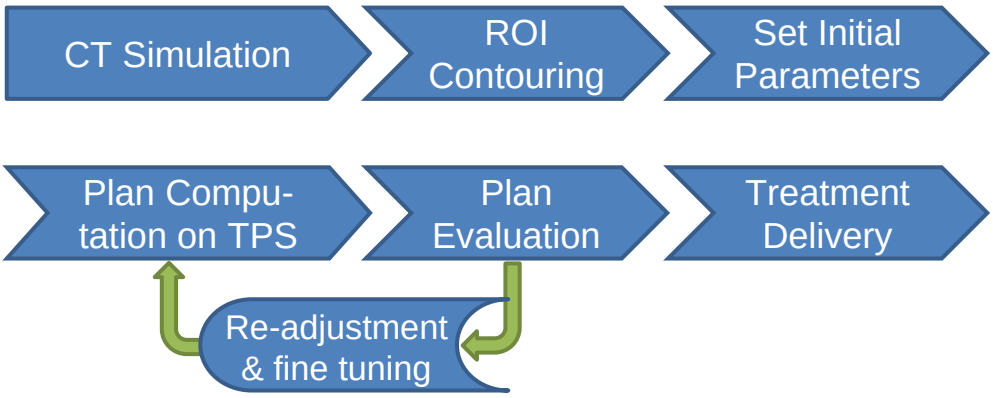

Figure 8.1 – Workflow for planning and delivering radiation therapy

8.2 Methods

In this section a detailed overview about both information systems will be given. Hereby the focus lies on the underlying workflows, information models, assistance functions and required information entities. The first system under consideration will be *oncoflow* because it covers the entire patient treatment process in oncological head and neck surgery. The workflow of the decision support

system for radiotherapy planning will be analyzed afterwards because its workflow represents one possibility of the therapy phase in the overall treatment process.

8.2.1 Analysis of the *oncoflow* information system

The clinical information system *oncoflow* aims to support the physician and clinical staff throughout the entire treatment process. A crucial prerequisite is that all necessary patient-related information is available in a centralized database. Therefore, communication interfaces to relevant clinical information systems such as the HIS or the DTTM have been established [18, 7, 101]. These interfaces provide an automatic import of therapy-related information into the central database and relieve physicians and clinical staff from error-prone and time-consuming copy and paste procedures. The underlying information model is briefly depicted in Figure 3.1 and shows the patient-specific information groups in the *oncoflow* database. The tumor board protocol and follow-up information entities are important in the scope of this project and already available in oncoflow. Hereby the tumor board decision is the key event where radiotherapy is started. The follow-up information contains long-term therapy outcome as well as the patient's survival status. Missing data in oncoflow is information generated during radiotherapy. Basically each information entity is stored in a structured way for further electronic processing, workflow assistance in daily clinical routine and usage in clinical trial studies or for quality management purpose. The information is conveniently accessible for the clinical staff within a structured web interface.

The usage of *oncoflow* for workflow assistance such as automatic generation of clinical documents, the support of retrospective clinical trial studies or improved quality management requires a broad information base. Information originating from anamnesis and clinical examination is important for the following therapy decision; hence, entered manually within a structured reporting form from the physician during this process step. The automatic data import enriches the underlying MySQL database with additional information such as patient master data, diagnoses, histopathological results, radiological results, tumor board decisions and follow-up information. Unfortunately, an automatic import of therapy-related information such as intervention reports or radiotherapy dose plans could not yet be established.

8.2.2 Analysis of the decision support system for radiation therapy planning

The aim of the decision support system is the creation of a patient model through mathematical quantification of relevant anatomical characteristics of patients in order to assist the clinician in identifying the treatment parameters that are likely to yield the most optimal outcomes and help in minimizing normal tissue complications. The underlying problem is depicted in Figure 8.2. The PTV must receive a homogeneous radiation dose. However, the adjacent OAR should only receive

the lowest possible dose from the overlapping radiation field. Unfortunately, the radiation field often includes many critical structures that should ideally be spared. The likelihood of an OAR being over-dosed varies in accordance with the volumetric spread of the OAR around the PTV. For instance, even with the same amount of volumetric overlap between OAR1 and OAR2 with the PTV, small shifts in radiation dose result in much more devastating effects for OAR2 as compared to OAR1 solely based on the geometric spread of the OARs around the PTV. The system quantifies certain patient-specific anatomical features and uses this information in refining the treatment plan by drawing upon the knowledge base of the decision support system to identify the most optimal, achievable dose end-points and treatment plan parameters.

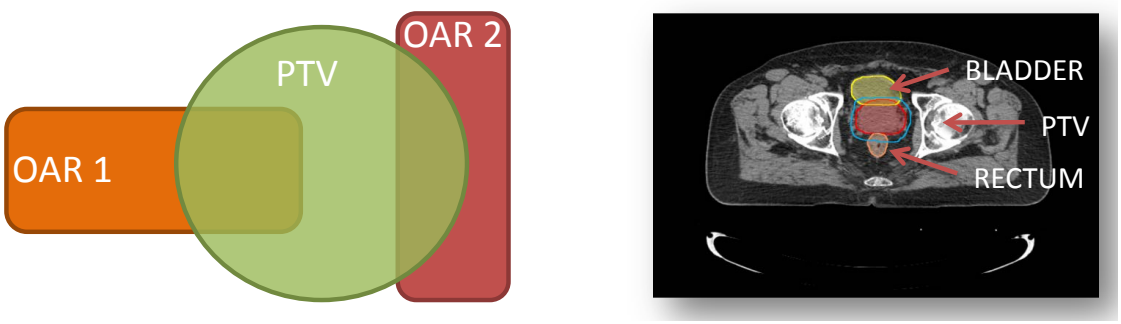

Figure 8.2 – The overlapping problem of PTV and different adjacent healthy organs during radiation treatment delivery

The decision support system acquires necessary information from four main Digital Imaging and Communications in Medicine (DICOM) files namely CT Images, DICOM-RT Structure Sets, DICOM-RT Dose Objects and DICOM-RT Treatment Plans (see Figure 8.3, left). Information in this context is always patient-specific; hence, each information entity is related to the patient. A patient may have multiple studies containing multiple series objects. The CT images hereby contain the image pixel and image plane metadata that help in registering the images in the patient coordinate system. The structure set contains a list or sequence of ROIs defined by a name and a number and a sequence of contours as well as associated CT images related to each ROI (see Figure 8.3, right). Dose objects contain a three-dimensional grid where pixel values represent dose measurements scaled by a dose grid-scaling factor, and different dose volume histograms belonging to the different ROIs. Finally, the plan object contains different technical details belonging to the actual treatment plan such as the amount of dose that has to be delivered to the target, maximum allowed deviations for ensuring patient safety or parameters describing the positioning of the patient with respect to the treatment machine. Furthermore, a knowledge object that is not part of the DICOM standard, but rather contains information that has been gathered and calculated from the raw DICOM data. At the moment, the database lacks follow-up information about therapy outcome, complications and survival rates. This information is important for further assistance functions such as proposing patients with similar anatomy with a good outcome to the radiotherapist for improved

therapy planning.

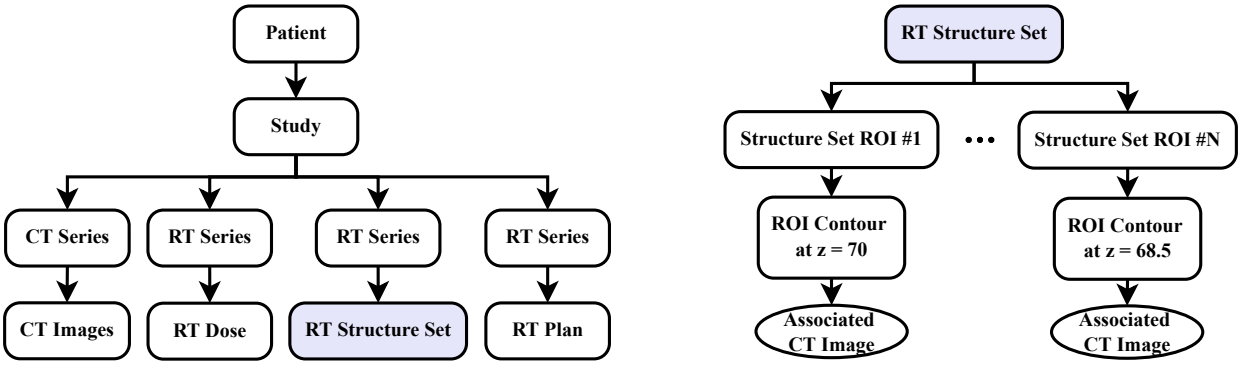

Figure 8.3 – *left:* Diagrammatic representation of the information model of the radiation therapy CDS system; *right:* Exemplary representation of a RT Structure Set object

8.3 Results

A concept for the integration of *oncoflow* and the CDS system has been developed (see Figure 8.4). The overall patient treatment process is depicted with blue chevrons. The workflow for radiation therapy is depicted with red chevrons; hence, one can see that both processes integrate well. Communication interfaces for sharing patient-specific information are shown as gray arrows and the data that is relevant in the specific workflow step is described in the round-cornered rectangles left beside the arrows.

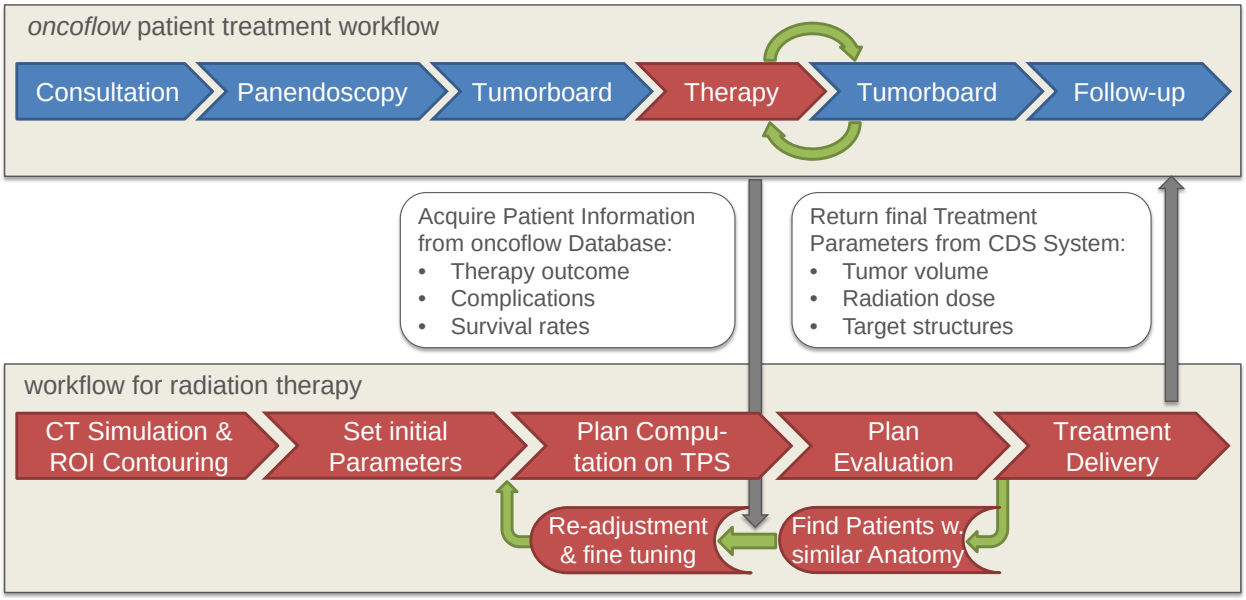

Figure 8.4 – Integration concept for *oncoflow* and the CDS system and communication interfaces with relevant information entities that have to be exchanged

Within this concept the CDS system is able to use additional information originating from previously conducted therapies for improving the radiation treatment plan. After the tumor and the adjacent organs at risk have been segmented, the radiotherapist creates the initial parameters, plans the computation on TPS and evaluates the plan. If the radiotherapist is dissatisfied with the plan evaluation step the CDS system is used for reducing further iterations. The system is able to find previously treated patients with a similar anatomy. Subsequently, the CDS system will acquire the respective therapy outcomes, complications and survival statuses from oncoflow. The radiation therapy plans and therapy outcomes can now be linked together for assisting the radiotherapist during the next planning iterations. Finally, the correct plan parameters are transmitted to *oncoflow* for further usage e.g. for the creation of a clinical report or the discussion of the patient in the following tumor board.

The decision support system was initially tested with proton therapy treatment planning data for prostate cancer. However, since the anatomical variations in the tumor location and tumor-OAR spatial relationships is very minute across patients, this system does not provide as much benefit to prostate cancer cases as it would to cancer sites with more complicated anatomies. The system is currently being used with head and neck cancer patients treated with conventional three-dimensional conformal radiotherapy (3d CRT) as well as Intensity Modulated Radiation Therapy (IMRT). Treatment planning for head and neck cancer involves a lot of small critical structures surrounding the PTV, with a lot of variation in tumor location.

8.4 Discussion

Patient-specific information is the basis for efficient clinical workflow assistance, decision support and personalized medicine especially in the field of tumor treatment. The both systems analyzed in this paper support the oncological treatment process, whereby they perfectly complement one another. The workflow for radiotherapy is a part of the whole patient treatment process. At the moment both systems are lacking different information entities that the respective other system owns. Oncoflow needs information about radiation therapy planning and treatment delivery that is important for tumor board discussion, further therapy planning and outcomes analysis within clinical studies or quality management. This information is available in the radiation therapy decision support system. The latter system in turn is able to group patient data according to anatomy, treatment plan and outcome; hence, it is able to provide the radiotherapist a set of patients that have already received their therapy for comparison with the current patient for finding the best therapy. However, an important information entity in this context is the therapy outcome that is not available to this system but inside the *oncoflow* database.

In the next phase of this project the decision support system will be evaluated in the field of head and neck surgery. Therefore, communication interfaces between both systems will be established

to facilitate the exchange of patient-specific information and improve the clinical workflow. Afterwards, therapy outcome information available in *oncoflow* can be used for improved radiotherapy decision support. Radiotherapy planning information such as the radiation dose enriches the *oncoflow* database and can be used for workflow and decision support or clinical trial studies. Due to the fact that both systems are web application based on a MySQL database a final integration of both systems and the database schemes seems appropriate eliminating redundant information storage and the creation of a more generalized electronic patient record for personalized medicine.

8.5 Conclusions

Two different information systems with clinical decision support have been analyzed with respect to their workflows, information models and assistance functions. The system *oncoflow* accompanies the entire treatment process of patients with head and neck tumors and provides automatic information import from different clinical information systems and clinical workflow support. The second system provides decision support during prostate cancer treatment planning. The detailed analysis of both systems revealed that they are lacking important information entities such as radiotherapy information or patient outcome amongst others. Hence, further research between ICCAS and IPILab in systems integration and information exchange provides a high synergy potential for making the entire treatment process of cancer patients safer and more efficient.

Chapter 9

Discussion & Conclusions

9.1 Resume

The oncological patient treatment is a long-term process where physicians and surgeons decide on complex therapies based on existing patient-specific information. Information about the actual patient case originates from different specialized medical disciplines during the clinical diagnostics phase. Involved are physicians performing the first consultation, radiologists conducting CT or MRI scans, surgeons taking biopsy samples and pathologists examining the tissue samples in order to receive a TNM classification. Some of the generated information is available in a central HIS or PACS, some information is stored across multiple department-internal information systems or noted in paper-based patient records. However, after clinical diagnostics physicians and surgeons participating in the treatment process meet in regular tumor boards to discuss the best possible therapy for the patient. The better tumor board participants are informed about the actual patient case the better is the therapy decision they agree upon.

This work aims to improve the information management and the quality assurance in oncology. Therefore, an analysis of the patient treatment process in oncological head and neck surgery was performed. The analysis revealed that the management of patient-specific information is a challenging task for surgeons and physicians. Existing clinical information systems are insufficiently integrated into daily clinical routine and stored information entities are distributed across different proprietary databases. Thus, existing information is hardly usable for further electronic processing, workflow support, clinical studies or quality management. Hence, a web-based clinical information system *oncoflow* has been developed which automatically integrates patient-specific information from different information systems into a multimodal digital patient model. Based on this centralized and structured information source assistance functions supporting physicians and surgeons in daily clinical routine and quality assurance measures were implemented. The system is a prototypical implementation and will be extended with further functionalities in the future.

Subsequently, the system was deployed at a clinical site and used in daily clinical routine for the documentation of first consultation results, panendoscopy reports and for the creation of tu-

mor board invitations and tumor board protocols. Additionally, the information visualization and seating arrangements in the meeting room were significantly improved to provide a collaborative environment, a common knowledge base about the actual patient case and decision-making support. A clinical study was performed in order to evaluate the advantages of the new information system compared to the previous situation. The study revealed that the new system efficiently supports the clinical documentation process, improves the information quality through standardized and structured documentation forms and is finally well-accepted because of a modern and responsive user interface.

Due to the usage of *oncoflow* in a productive environment for more than one year the database contains large amounts of patient-specific information. In order to improve the information quality in *oncoflow* to develop intelligent clinical assistance systems or to provide efficient access and export of information for clinical studies and quality management tasks a sophisticated approach to predict the current treatment step based on Markov models was developed. 40 patient data sets with more than 2000 information entities were used to build a stochastic model which represents the treatment process in multiple granularities. Afterwards, a leave-one-out cross validation study was performed to evaluate the prediction rates of the model. The study proofed that this model allows to predict the patients current treatment step based on data sets in the EPR with recognition rates up to 90%. The workflow recognition allows clustering of patient information and to answer questions such as “Show me all ICD10 codes which were generated during the therapy phase!”.

The *oncoflow* application was developed in close cooperation with physicians and surgeons from head and neck surgery. In order to provide a more generalized solution which is not tailored to a specific medical discipline a concept for a multidisciplinary clinical application of *oncoflow* was developed. Within this concept the usage scenario was extended from a primary surgical workflow driven application to support information exchange and integration of decision support for radiation therapy.

9.2 Goal achievements

The goals of this work are described in detail in Section 1.4. Fortunately, with the development of *oncoflow* and the TPU as well as the usage of both systems in daily clinical routine one can conclude that these goals have been fulfilled. However, regarding the seven work packages in Section 1.4 not all goals could be achieved completely.

9.2.1 Achievements: Information management in oncology

Goal 1 achievements The first goal was a deep understanding of the oncological patient treatment process in head and neck surgery. The entire treatment process and information systems which are used in each process step are depicted in Figure 1.1. A profound knowledge of all process

steps except the therapy could be achieved. The activities, people and information systems in each process step are described in detail in the corresponding sections for workflow assistance where the gained knowledge is immediately transferred into assistance modules. Intraoperative workflows or detailed information about radiotherapy or chemotherapy could not be achieved in this work.

Goal 2 achievements The next goal aimed at the centralization of important information into one database and the development of an information system that supports physicians and surgeons. The *oncoflow* information system provides an easily extensible infrastructure for clinical workflow support and communication interfaces to relevant clinical information systems. Patient-specific information is automatically imported where possible, acquired in a structured manner where necessary and stored into a central database.

Regarding the requirements on EHRs listed in Table 2.1 the EPR in *oncoflow* provides the demanded functionality in terms of the cancer treatment plan such as demographic information, diagnosis documentation or tumor staging. The system is lacking information entities requested in the category cancer treatment summary originating from the therapy phase. This is rather an organizational problem because of lacking data export interfaces to the leading clinical information systems than an issue with *oncoflow* itself and will be realized in future work. The same holds for the oncology-specific documentation. Parts of the oncology-specific functionality such as chemotherapy and drug management are not in the scope of this work. Other parts of this category such as bar-coding or RFID technology are already implemented within the TPU. Also the generation of quality metrics and other reports is possible in the current development stage to support workflow assistance and quality assurance.

9.2.2 Achievements: Clinical workflow support

Goal 3 achievements The development of efficient workflow assistance functions was the aim of the third goal. We developed support functions for the first consultation, panendoscopy and follow-up documentation as well as for tumor board management and scientific evaluation. The focus was on the assistance functions which were most favored by our clinical partners. A prototypic implementation of these functions was developed and is still in clinical use. However, the clinical studies performed with this modules and the experience gained through the daily usage showed that there is still room for improvements. The system is also lacking support for therapy-related workflow steps due to missing data. But finally, the existing assistance modules really help physicians and surgeons in daily clinical routine and are very appreciated.

Goal 4 achievements Goal number four was the improvement of the decision-making process during tumor board conduction. We implemented a new room concept and provide additional information as well as immediate results documentation. The new TPU is well-accepted from

all participating physicians and surgeons and the results documentation, invitation and protocol mailing with *oncoflow* saves physicians valuable time. A second clinical discipline could be won in May 2014. The department of maxillofacial surgery also uses *oncoflow* and the TPU for scheduling their patients for tumor boards. Unfortunately, the new V-style seating arrangements persisted only the first months and was then rearranged to the former style.

Goal 5 achievements The fifth goal was the evaluation of the new system in a clinical study. The first part of the study was a qualitative evaluation with a questionnaire in order to evaluate the satisfaction with the new system and to compare *oncoflow* with the HIS SAP i.s.h.med. The results were very promising and *oncoflow* received very good ratings compared to the HIS. The second and third part of the study focused on a quantitative evaluation in terms of usability and information quality. The results showed that the usage of *oncoflow* does not consume more time and the results also show that the information quality is much better with *oncoflow*.

9.2.3 Achievements: Clinical workflow recognition

Goal 6 achievements Goal number 6 aimed at the recognition of the actual process step based on patient-specific information. Therefore, a probabilistic model based on HMMs was developed. The model prediction rates were between 80% and 90%. Hence, this model can be used to classify patient-specific information in the EPR and provide a more structured information base for further clinical assistance and decision-support functions.

9.2.4 Achievements: Generalization and multidisciplinary usage

Goal 7 achievements Finally, the last goal was the extension of *oncoflow* to a more generalized system which is not tailored to a specific medical discipline. Therefore, a concept was developed to include radiation therapy decision-support and share important information in order to provide additional support functions. The actual integration of both systems and the extension of *oncoflow* to more clinical disciplines is part of future work.

9.3 Lessons learned

The development of a clinical information system that really integrates into daily clinical routine is a challenging task. The initial idea was the integration of all patient-specific information into a central database for realizing appropriate workflow assistance for the physician. In the first step only clinic-internal databases developed for clinical studies and the HIS have been considered because they contained information for every process step. Our experience showed that this information is not sufficient at all for supporting daily clinical routine. Hence, it is important for the implementation

of a comprehensive information model to not only rely on given information but to accompany each process step personally in daily clinical routine. One have to talk to the physician, gather all available questions that the physician asks the patient and examine paper-forms as well as information systems that are used during the treatment process.

The realization of interfaces to the existing HIS was a cost-intensive and time-consuming process. Therefore, legal agreements with the IT department and clinical directors had to be established concerning data security and an external supplier had to be engaged that extends the HIS with the desired data export features. The overall process until the export interfaces were working without errors lasted about 18 months whereby lacking or error-prone data exports made up the major issues. Faber presents different approaches for the design and implementation of EPR systems and carefully investigates the top-down and bottom-up approach [102]. He concludes that a strict top-down approach of the management leading the project into the right direction and a specific user involvement in the basic process steps seem to be a good approach. This approach has been successfully applied for the development of *oncoflow*. Hereby, the senior physician had the project lead from clinical side and defined and enforced the overall project goals. On the other side the detailed technical realization, the development of the user interface, the improvement of the user experience as well as the integration of the system into daily clinical routine has been performed self-reliant from ICCAS staff together with physicians from the head and neck department.

9.4 The Digital Patient Model, the Therapy Imaging and Model Management System and *oncoflow*

The *oncoflow* IT infrastructure implements one step towards a Digital Patient Model (DPM) within a Therapy Imaging and Model Management System (TIMMS) infrastructure [103].

A DPM is the orchestration of heterogeneous patient-specific information in order to assist physicians and surgeons and to provide clinical decision support by using machine-learning and big data approaches. In the scope of this work the basis for a DPM for head and neck surgery was created. The *oncoflow* database integrates textual information throughout the entire treatment process from anamnesis to follow-up consultation. This information is enriched by annotated endoscopic images originating from the DTTM. A further building block of the DPM are 3-dimensional models of the patients anatomy. The Dornheim Segmenter is a state-of-the-art tool that provides the creation of 3d models based on CT images, the segmentation of organs as well as precise volume measuring of anatomical structures [13]. The integration of this information into the *oncoflow* system is future work.

The TIMMS specifies basic requirements on an IT infrastructure for personalized medicine and the digital OR. A high-performance computer network connects different engines with model databases (see Figure 9.1). The *oncoflow* system already implements several aspects of a TIMMS.

The *oncoflow* database in the narrower sense or the *oncoflow* DPM in the broader sense can be seen as a TIMMS repository. Furthermore, the clinical workflow support in *oncoflow* implements the kernel for workflow and knowledge and decision management. The structured web-based user interface can be seen as the visualization and representation engine. The modeling engine is represented by the Dornheim Segmenter. Future work focuses on quality assurance, which also includes verification of information entities, so that *oncoflow* will implement a TIMMS validation engine.

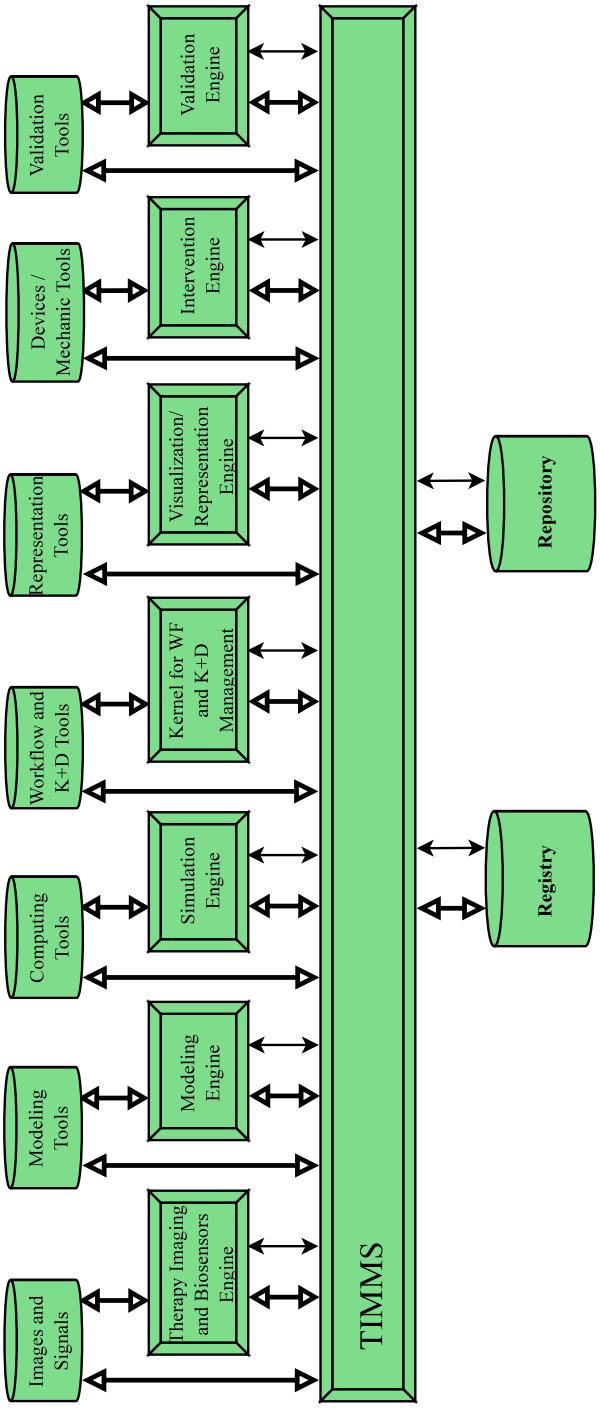

Figure 9.1 – Therapy Imaging and Model Management System (TIMMS)

9.5 Future work

Future developments of the *oncoflow* system focus on supporting the entire oncological treatment process in head and neck surgery by implementing the lacking support for the therapy phase. Therefore, the access to therapy-related information such as reports from surgical interventions, radiation therapy doses and chemotherapy cycles has to be established. Subsequently, the specific details of those workflow steps, participating physicians and information flows have to be evaluated in detail in order to provide efficient workflow support. Thus, further physicians from different clinical disciplines such as radiotherapists or chemotherapists may get involved in the usage of *oncoflow* and provide valuable input for making the system usable in a more generalized way.

With a growing amount of patient-specific information in the database the implementation of comprehensive evaluation features for secondary usage of the existing information for clinical trial studies, quality assurance as well as clinical certifications becomes more important. Hence, additional effort should be spent in extending the module for scientific evaluation and export presented in Section 4.7. Additionally, data mining and native language processing techniques are promising research areas in order to extract valuable information from free-form text and to develop an information base that is semantically connected. Summarized, the system must be smarter to really add value to daily clinical routine and administrative tasks.

Finally, the generalization of the system for multidisciplinary application is a major point of future work. This point is very important for the development of a commercial system instead of a scientific prototype.

9.6 Conclusions

The development of *oncoflow* lasted three years until the state that is presented in this work was achieved. During this time we had a tight collaboration with physicians and surgeons from the clinic for head and neck surgery at the university medical center Leipzig. This collaboration is very important to understand the requirements of such a system in daily clinical routine. Therefore, we spent much time to be present during first consultations, clinical examinations, panendoscopies, tumor boards and follow-up meetings in order to fully understand the clinical processes, see the forms which have to be filled out and to see how the physician works and interacts with the patient. I think, this was one major aspect why we were able to fully comprehend the clinical requirements and to develop an information system that fits to the users needs.

Our scientific prototype is in use in daily clinical routine since March 2013, is really appreciated by the physicians and surgeons and is steadily improved. The clinical studies and the constant usage show that the system is really accepted by the users because of the good usability. *Oncoflow* and the TPU received much attention at the worlds largest computer exhibition CeBIT 2013 in Hannover. Saxony's Minister-President Stanislav Tillich visited the exhibition booth and was en-

thusiastic about our research (see Figure 9.2). The systems also received much attention from the local newspaper “Leipziger Volkszeitung” with a great article about the new TPU (see Figure 9.3). *Oncoflow* was also nominated as one of the most innovative products in the field of E-Health in the year 2014 at the “Innovationspreis IT” which is a great achievement for this work (see Figure 9.4).

Finally, the presented systems are a great platform for further research in the field of oncology. *Oncoflow* will be the information basis for sophisticated assistance and decision-support systems due to the availability of a huge amount of patient information within a central database. A very promising research project in this field is the DPM which aims to integrate all patient-related information as well as scientifically based knowledge into a multi-dimensional model [104]. Eventually, *oncoflow* will be available as commercial product with certification as medical product according to the Medical Device Directive (MDD).

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Acronyms

AJAX Asynchronous JavaScript and XML

CCHIT Certification Commission for Health Information Technology

CDS Clinical Decision Support

CREDOS Cancer Retrieval Evaluation and DOcumentation System

CSS Cascading Style Sheets

CSV Comma-Separated Values

CT Computer Tomography

DICOM-RT Digital Imaging and Communications in Medicine in Radiotherapy

DICOM Digital Imaging and Communications in Medicine

DKG Deutsche Krebsgesellschaft

DPM Digital Patient Model

DTTM Dornheim Tumor Therapy Manager

DVH Dose Volume Histograms

ENT Ear, Nose & Throat

EPR Electronic Patient Record

EHR Electronic Health Record

ETL Extract

GP General Practitioner

GTDS Giessener Tumordokumentationssystem

GWT Google Web Toolkit

HIS Hospital Information System

HL7 Health Level 7

HMM Hidden Markov Model

HNSCC Head and Neck Squamous Cell Carcinoma

HTML Hypertext Markup Language

HTTP Hypertext Transfer Protocol

ICCAS Innovation Center Computer Assisted Surgery

ICD10 International Statistical Classification of Diseases and Related Health Problems

ICD International Statistical Classification of Diseases and Related Health Problems

ICF International Classification of Functioning

ICPM International Classification of Procedures in Medicine

IMISE Institute for Medical Informatics, Statistics and Epidemiology

IMRT Intensity Modulated Radiation Therapy

IPILab Image Processing and Informatics Lab

LAN Local Area Network

LLUMC Loma Linda University Medical Center

MDD Medical Device Directive

MRI Magnetic Resonance Imaging

MVC Model View Controller

OAR Organs at Risk

OPS Operationen- und Prozedurenschlüssel

OR Operating Room

ORM Object Relational Mapping

OSE Observation-specific State Estimation

PACS Picture Archiving and Communication System

PDF Portable Document Format

PET Positron Emission Tomography

PHR Personal Health Record

PRO Patient Reported Outcome

PTV Planning Target Volume

RFID Radio-frequency Identification

RIS Radiology Information System

ROI Region of Interest

SQL Structured Query Language

SSL Secure Socket Layer

TIMMS Therapy Imaging and Model Management System

TNM TNM Classification of Malignant Tumors

TPS Treatment Planning System

TPU Treatment Planning Unit

UCLA University of California at Los Angeles

UI User Interface

UICC Union Internationale Contre le Cancer

URL Uniform Resource Locator

USC University of Southern California

XML Extensible Markup Language

gSPM generalized Surgical Process Model

iSPM individual Surgical Process Model

Zusammenfassung der Arbeit

Dissertation zur Erlangung des akademischen Grades
Dr. rer. med.

Structured patient information management for efficient treatment and healthcare quality assurance in oncology

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Die Behandlung von Patienten mit Tumoren im Kopf-Hals-Bereich gestaltet sich als komplexer und herausfordernder Prozess sowohl für den Patienten als auch für die behandelnden Ärzte und Chirurgen. Zur Gewährleistung der bestmöglichen individuellen Therapie werden vor Beginn der Behandlung zahlreiche diagnostische Verfahren durchgeführt. Hierzu zählen unter Anderem medizinische bildgebende Verfahren wie z.B. Computertomographie (CT) oder Magnetresonanztomographie (MRT) sowie die Entnahme von tumorverdächtigem Gewebe während einer Panendoskopie zur exakten Bestimmung der Tumorart (Histologie, Grading, TNM-Klassifikation nach UICC, genaue Lokalisation des Primärtumors, der lokoregionären Metastasen und ggf. Fernmetastasen). Die gewonnenen Informationen bilden anschließend die Grundlage für die Entscheidung über die durchzuführende Therapie und stehen in unterschiedlichen klinischen Informationssystemen sowie auf Papierakten zur Verfügung. Leider werden die Daten im klinischen Alltag häufig nur unstrukturiert und schwer auffindbar präsentiert da die führenden Informationssysteme nur unzureichend in den klinischen Arbeitsprozess integriert und untereinander schlecht vernetzt sind. Die präzise und erschöpfende Darstellung der jeweiligen individuellen Situation und die darauf aufbauende Therapieentscheidung sind aber entscheidend für die Prognose des Patienten, da der erste, gut geplante „Schuss“ entscheidend für den weiteren Verlauf ist und nicht mehr korrigiert werden kann.

In dieser Arbeit werden neue Konzepte zur Verbesserung des Informationsmanagements im Bereich der Kopf-Hals-Tumorbehandlung entwickelt, als prototypische Software implementiert und im klinischen Alltag in verschiedenen Studien wissenschaftlich evaluiert.

Die Erlangung eines tiefgreifenden Verständnisses über die klinischen Abläufe sowie über beteiligte Informationssysteme und Datenflüsse stellte den ersten Teil der Arbeit dar. Hierfür wurden in Gesprächen mit den klinischen Partnern die Arbeitsabläufe, am Behandlungsprozess beteilig-

te Informationssysteme sowie die Datenflüsse detailliert dokumentiert. Die theoretisch erlangten Grundlagen wurden durch Hospitationen bei den einzelnen Prozessschritten während des Behandlungsprozesses ergänzt. Die Hospitationen ermöglichten einen umfassenden Einblick in den klinischen Alltag und offenbarten wichtige Details in den jeweiligen Prozessschritten welche durch die Arbeitsroutine der Ärzte und Chirurgen in den vorangegangenen Gesprächen unerwähnt blieben.

Aufbauend auf den Erkenntnissen aus der Workflowanalyse wurde das klinische Informationssystem *oncoflow* entwickelt. Hierfür wurden die Informationen über den klinischen Arbeitsablauf bei der Behandlung von Kopf-Hals-Tumoren strukturiert und die patientenspezifischen Daten, die während der Behandlung erhoben wurden, in ein technisches Datenmodell überführt. Dieses Datenmodell bildet die Grundlage bei der Entwicklung einer relationalen Datenbank die alle behandlungsrelevanten Informationen an zentraler Stelle speichert und die persistenzschicht für das *oncoflow* System darstellt. Das *oncoflow* System ist eine webbasierte Applikation, die es den Ärzten und Chirurgen ermöglicht, klinikweit per Webbrowser auf alle patientenspezifischen Informationen zuzugreifen. Die Informationen werden dem Arzt übersichtlich präsentiert, so dass der aktuelle Behandlungsstatus des Patienten sowie relevante Dokumente sofort ersichtlich sind. Das *oncoflow* System aggregiert vollautomatisch alle patientenspezifischen Informationen aus verschiedenen klinischen Informationssystemen wie z.B. dem Krankenhausinformationssystem (KIS) oder abteilungsinternen Unterstützungssystemen und speichert diese Daten strukturiert in der internen Datenbank. Der automatische Datenimport entlastet das klinische Personal sowie Ärzte und Chirurgen von zeitaufwändigen und fehleranfälligen Copy-Paste-Prozeduren.

Oncoflow bietet Ärzten und Chirurgen außerdem eine vielzahl von Assistenzfunktionen, um den klinischen Arbeitsablauf, das Qualitätsmanagement oder die Durchführung von klinischen Studien effizient zu unterstützen. Gleich zu Beginn des Behandlungsprozesses unterstützt das System bei einer strukturierten Durchführung und Dokumentation der Erstanamnese sowie der klinischen Untersuchung. In der anschließenden Panendoskopie wird die Dokumentation der Untersuchungsergebnisse und das Management der medizinischen Bilddaten, die bei der Endoskopie entsthen, unterstützt. Das Management des wöchentlichen Tumorboards wird komplett über *oncoflow* realisiert. Hierzu zählen unter Anderem die Einladung von Patienten zum nächsten Tumorboard, die Erstellung der Einladungsschreiben, der automatische Versand der Tumorboardeinladungen per EMail an die teilnehmenden Ärzte und Chirurgen, die Dokumentation der Ergebnisse sowie der Versand der Tumorboardprotokolle. Intelligente Abfragemasken ermöglichen es dem klinischen Personal vorhandene Informationen aus der Datenbank abzufragen und visuell aufzubereiten um Fragestellungen für klinische Studien, das interne Qualitätsmanagement oder klinische Zertifizierungen beantworten zu können.

Das System wurde anschließend in unterschiedlichen Studien evaluiert und der klinische Nutzen in Bezug auf effizientere Arbeitsabläufe und eine verbesserte Informationsqualität gezeigt. Der Fokus der durchgeführten Studien lag auf der Evaluation des Nutzen strukturierter Datenerhebun-

gen durch die Verwendung eines klinischen Informationssystems was perfekt auf den täglichen Arbeitsablauf in der Klinik angepasst ist. Während der Studien wurden Arbeitsprozesse in der Klinik einerseits mit *oncoflow* und andererseits mit dem bisherigen KIS durchgeführt, dokumentiert und anschließend qualitativ und quantitativ evaluiert. Die Studienergebnisse zeigen einen deutlich strukturierten Arbeitsablauf sowie eine erheblich höhere Informationsdichte bei der Benutzung von *oncoflow* verglichen mit der Benutzung des KIS.

Durch die Nutzung von *oncoflow* im klinischen Arbeitsalltag wurden Schwächen bei der Datenhaltung sichtbar. Informationen enthalten unterschiedliche Metadaten wie z.B. den Zeitpunkt der Erstellung oder den Autor. Die Abfrage von Informationen gruppiert nach dem jeweiligen Prozesschritt im Behandlungsprozess ist im Moment nicht möglich. Deshalb wurden im folgenden Teil der Arbeit Machine Learning Methoden genutzt um von Daten in der elektronischen Patientenakte auf den aktuellen Prozessschritt im Therapieprozess zu schließen. Hierfür wurden anonymisierte Patientendaten aus der *oncoflow* Datenbank herangezogen um auf Basis von Hidden Markov Modellen (HMMs) statistische Modelle des Behandlungsprozesses zu erzeugen. Mit Hilfe der Modelle lässt sich mit einer gewissen Wahrscheinlichkeit der Prozesschritt im Behandlungsprozess bestimmen, in dem das Datum erstellt wurde. Anschließend kann der Datensatz in der Patientenakte um zusätzliche Prozess-Metainformationen erweitert werden die zur Entwicklung weiterer Assistenzsysteme oder für erweiterte Datenabfragen genutzt werden können. Die Methoden wurden anschließend in Laborstudien wissenschaftlich evaluiert. Es konnte gezeigt werden, dass der aktuelle Behandlungsschritt mit einer Wahrscheinlichkeit von bis zu 90% korrekt bestimmt werden kann.

Die Methoden und Konzepte zur Verbesserung des klinischen Informationsmanagements und zur Unterstützung von Ärzten und Chirurgen während des klinischen Behandlungsprozesses wurden in dieser Arbeit am Beispiel der onkologischen Kopf-Hals-Chirurgie praktisch umgesetzt und evaluiert. Die entwickelten Methoden sind allerdings nicht auf eine spezielle klinische Fachdisziplin beschränkt. Im letzten Teil der Arbeit werden Möglichkeiten zur Erweiterung des Systems zur Nutzung in weiteren klinischen Fachdisziplinen am Beispiel der Strahlentherapie aufgezeigt. In dem Konzept wird die Einbindung eines Informationssystems zur Verbesserung der Bestrahlungsplanung in *oncoflow* evaluiert und es werden Vorteile für beide Systeme aufgezeigt.

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Auszeichnungen und Medienpräsenz

Abbildung 9.2 – Der Besuch des sächsischen Ministerpräsidenten Stanislav Tillich war das Highlight der *oncoflow* Präsentation auf der CeBIT 2013. Jens Meier hatte die Möglichkeit dem Ministerpräsidenten die Vorteile des neuen Informationssystems zur Behandlung von Tumorpatienten live zu präsentieren

Im Leipziger Uni-Klinikum stellten Andreas Dietz (Dritter v.l.) und Andreas Böhm (Zweiter v.r.) das multimediale Tumorboard-System vor. Foto: Andreas Döring

Das ist Leipzigs Zentrale gegen den Krebs

Spezial-Tumorboard am Uni-Klinikum ist in Betrieb – Mediziner versprechen sich bessere Therapie

Am Leipziger Uniklinikum ist gestern das multimediale Tumorboard in Betrieb gegangen. Es ist die neue Zentrale zur Bekämpfung von Krebs im Hals-Nasen-Ohren-Bereich (HNO).

Mit dem Tumorboard können Krebsbehandlungen im sensiblen Kopf-Hals-Bereich besser geplant werden. Die Neuerung hatten die Leipziger Ärzte mit Informatikern des Uni-Innovationszentrums für Computergestützte Chirurgie (ICCAS) entwickelt (wir berichteten). „Nächste Woche dürfen wir das Tumorboard auch auf der Cebit 2013 in Hannover vorstellen", erklärte Jens Meier, einer der Chefentwickler im ICCAS.

„Die Technik ist schon revolutionär", sagte Andreas Dietz, HNO-Chef des Uni-Klinikums. „Besonders im Rachen-Raum haben wir einen extremen Zuwachs an Tumorarten wie Kehlkopfkrebs, Mundhöhlen-, Zungen- oder Luftröhrenkrebs. Da spielen Viren eine Rolle und Lebensweisen wie etwa ein intensiver Tabak- und Alkoholgenuss. Mittlerweile stirbt auch jeder zweite Patient an diesen Krebsarten." Solche Erkrankungen seien sehr komplex, mit vielen Tücken behaftet. „Und das Problem ist, dass Therapie und Diagnostik weltweit noch nicht so interdisziplinär betrachtet werden, wie es sein müsste. Den Krebs einfach operieren reicht hier mitunter eben nicht."

Seit gestern läuft das in Leipzig anders: Im Operativen Zentrum des Uni-Klinikums wurde in einem Extra-Raum das Tumorboard-System installiert. Regelmäßig versammeln sich hier die an der Behandlung Beteiligten: HNO-Ärzte, Onkologen, Strahlenmediziner, Chirurgen, Pathologen, Psychoonkologen...

Dann schlägt die Stunde des Tumorboards: Neben Laborbefunden, Untersuchungsergebnissen sowie Arztberichten fließen dort alle Bilddaten ein – Röntgenaufnahmen sowie Bilder aus dem Magnetresonanztomografen (MRT) und Computertomografen (CT). Alle Daten eines Patienten werden auf den großen Monitoren zu dreidimensionalen Modellen des Tumors zusammengeführt. Dabei berechnet das System zugleich die Größe und Ausdehnung des Krebses. So lassen sich nun zum Beispiel Kehlkopf-Tumore auch von Seiten betrachten, die bislang nicht darstellbar waren – etwa von der Wirbelsäulenseite her. Alle am Tisch versammelten Experten werfen dann ihr geballtes Wissen in den Ring, um die optimalste Therapiemöglichkeit für den Patienten zu diskutieren.

Die weltweit einmalige HNO-Planungseinheit für Diagnose und Behandlung bekam bereits den Poster Award der Amerikanischen Kopf-Hals-Gesellschaft – der „Oscar in der Medizintechnik". Dietz, Meier und Kollegen stellen das Tumorboard nun auch den Gästen des heute beginnenden dritten Workshops zur HNO-Onkologie vor. Zu dem sind mehr als 100 Fachkollegen und Experten für Kopf-Hals-Tumoren aus Deutschland, Österreich, Schweiz und Frankreich nach Leipzig gereist. *Angelika Raulien*

Das HNO-Tumorboard

- Um das multimediale Tumorboard, einen Prototyp aus der Forschung, im Uni-Klinikum zu etablieren, wurde eine halbe Million Euro investiert – mit Fördergeld von Bund und Land.
- Von der neuen Einrichtung profitieren jährlich rund 600 Uni-HNO-Patienten.

Abbildung 9.3 – Zeitungsartikel aus der Leipziger Volkszeitung über das multimediale Tumorboard und die verbesserte Entscheidungsunterstützung. Der Artikel wurde mit freundlicher Genehmigung des Verlages abgebildet

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Karlsruhe, im März 2014

Beate Heider
Geschäftsleitung

Rainer Kölmel
Geschäftsleitung

be a part of IT

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Abbildung 9.4 – Zertifikat des “Innovationspreis IT 2014” für *oncoflow* als innovative Lösung im Bereich E-Health

Erklärung über die eigenständige Abfassung der Arbeit

Hiermit erkläre ich, dass ich die vorliegende Arbeit selbständig und ohne unzulässige Hilfe oder Benutzung anderer als der angegebenen Hilfsmittel angefertigt habe. Ich versichere, dass Dritte von mir weder unmittelbar noch mittelbar geldwerte Leistungen für Arbeiten erhalten haben, die im Zusammenhang mit dem Inhalt der vorgelegten Dissertation stehen, und dass die vorgelegte Arbeit weder im Inland noch im Ausland in gleicher oder ähnlicher Form einer anderen Prüfungsbehörde zum Zweck einer Promotion oder eines anderen Prüfungsverfahrens vorgelegt wurde. Alles aus anderen Quellen und von anderen Personen übernommene Material, das in der Arbeit verwendet wurde oder auf das direkt Bezug genommen wird, wurde als solches kenntlich gemacht. Insbesondere wurden alle Personen genannt, die direkt an der Entstehung der vorliegenden Arbeit beteiligt waren.

Ort, Datum Unterschrift