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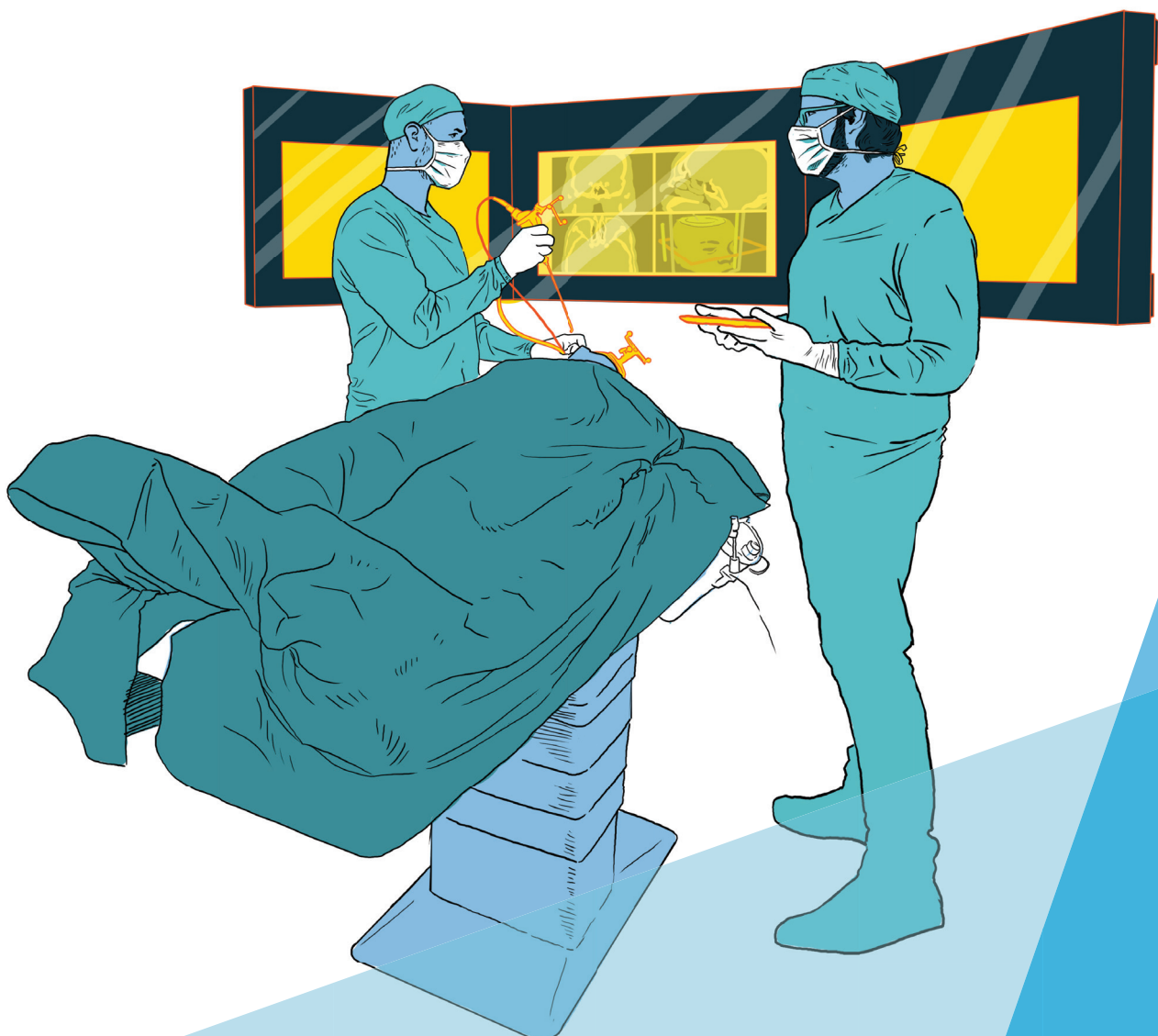
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FUTURE MED TECHNOLOGIES „INTELLIGENTE MEDIZINTECHNOLOGIEN AUF DEN WEG BRINGEN“

Doktorandenworkshop und Industriemesse

Abstract Book 2019

Herausgeber: Thomas Neumuth
Andreas Melzer



Future Med Technologies
Intelligente Medizintechnologien auf den Weg bringen
Doktorandenworkshop und Industriemesse
Abstract Book 2019

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IMPRESSUM

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GRUßWORT

Liebe Leserinnen und Leser,

Liebe Teilnehmerinnen und Teilnehmer,

am 5. März 2019 veranstaltete das Innovation Center Computer Assisted Surgery (ICCAS) mit Unterstützung durch das Leipziger Amt für Wirtschaftsförderung den Doktorandenworkshop „Future Med Technologies“ mit begleitender Industriemesse auf dem Campus der Leipziger Universitätsmedizin. Unter dem Slogan „Intelligente Medizintechnologien auf den Weg bringen“, adressierte die Veranstaltung zum einen Unternehmen aus Sachsen, Sachsen-Anhalt und Thüringen, die sich mit ihren zukunftsweisenden Produkten und Stellenangeboten vorstellten und zum anderen Doktorand_innen aus der Region, welche in Kurzvorträgen ihre aktuellen Forschungsthemen und innovativen Ansätze im Bereich Medizin- und Biotechnologie vorstellten.

Der Workshop brachte den Teilnehmerinnen und Teilnehmern Kommunikationsmöglichkeiten und neue Impulse für ihr weiteres Wirken. Wir bedanken uns herzlich bei allen Referent_innen, Autor_innen und Co-Autor_innen, dem Organisationsteam sowie den Sponsoren für deren Engagement.

Die regionale Netzwerkveranstaltung begleiteten zudem das Dezernat für Forschungs- und Transferservice und der Career Service der Universität Leipzig sowie die Gründerinitiative SMILE.

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THEMENBEREICH: MODELLGESTÜTZTE THERAPIE UND OPERATIONSSAAL DER ZUKUNFT**An Electronic Patient Record for the European Modular Field Hospital**

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The project European Modular Field Hospital (EUMFH) aims to explore how the medical capacity of the Union Civil Protection Mechanism can be improved. Different Member States of the European Union combine their expertise and build a common deployable Emergency Medical Team (EMT) level 3 for disaster relief missions. Current developments show that there is a clear lack of active deployable level 3 Emergency Medical Teams i. e. referral hospitals in the field. Therefore, there is a need for a high-level medical module that can be deployed for a longer-term mission without putting the burden on one single Member State or organization.

During the project, ICCAS was commissioned with the conceptualization and provision of an electronic patient record (EPR) for EMTs. As first step, a comprehensive requirements analysis was conducted. Subsequently, a concept for an EPR was derived, taking the special demands (e. g. lightweight, high flexibility, robustness) of EMTs into account. After implementation, an early version of the EPR was tested during the MODEX exercise in Bucharest. The participating personnel was interviewed, regarding suitability, performance and operational capabilities of the developed EPR.

The EPR system was well received by the participants. Twenty-one team members have been interviewed. Fourteen of them with medical roles (physicians and nurse) and seven of them with supportive roles (Management, Logistics, or Training). Under the fourteen medical interview partners have been three medical team leaders and all participants came from nine different European countries. The overall feedback was very positive.

The evaluation of the EPR during the MODEX exercise was very successful, considering the positive user feedback. Despite of this success, there were various learned lessons on how to further improve the EPR to cope with the challenges of EMT missions. After EPR optimization, it will be tested under realistic conditions during another EMT exercise in the beginning of 2019.

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Cognitive Navigation Assistance in Minimally-Invasive Surgery

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Despite being a well-established practice, minimally-invasive surgery still causes the physical and operative restriction inherent to key-hole surgery. Decoupled hand-eye coordination, limited field of view and operating space, as well as decreased depth perception require exceptional performance of both surgeon and assisting technology. Navigating in an already complex environment, surgeons experience even higher cognitive workload when confronted with equipment of limited functionality and responsiveness. Maintaining spatial awareness and instrumentation skill can only be achieved through constant training and live operations. Because spatial cognitive and orientation capabilities vary individually, the ideal form of navigation assistance needs to address the surgeon, the patient and situational changes equally effectively. However, since the navigational support is an influencing factor for the surgeons' cognitive workload, we are investigating intelligent intraoperative assistance behavior that considers surgical cognition for navigational aid.

The design is based on existing work on the situation awareness theory from aeronautics and aerospace, the cognition-guided surgery paradigm as well as information processing structures from cognitive architectures for autonomous robotics. The purpose is to extend a navigation assistance system so that it engages as a fully-acknowledged actor in the OR. The system attempts to mimic the human cognitive information processing cycle, enabling it to match a simulated navigation behaviour with the real surgeon-individual navigation process. Our research is focused on the investigation of a modelling approach that considers the various design principles to provide responsive situation-specific guidance and furthermore, to introduce a form of navigation awareness closely related to the surgical cognition process during spatial orientation and navigation.

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Development and Evaluation of an Instrument-Recognition-System for Intraoperative Activity-Tracking through a Multi-Sensor Armband

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Observing, documenting and anticipating a surgeon's actions have become a steadily growing field of interest. Many researchers have developed different methods for automatic instrument or action recognition. With the ulterior motive to automatically create a record of surgical actions, to activate medical systems based on scenario identification as well as to provide estimations of foreseeable consequences, researchers employ different methods to acquire information during procedures and put it into the surgical workflow context.

Recent published works focused on the analysis of endoscopic images, identifying instruments through markers or integrated RFID chips. This work proposes the use of biometrical data provided by sensors applied directly to the surgeon, thereby avoiding elaborate image classification and the installation of additional markers, cameras or sensors. By using preconditioned superficial electromyograms (sEMG) as input information, models acquired through machine learning algorithms are trained to find patterns between performed hand gestures and correlating muscle activation signals. In order to achieve this, a multi-sensor armband was employed, which allows measurements of the data and the subsequent feature extraction for the signal classification.

To reach this goal, the author employed the Myo Armband by Thalmic Labs, which allows the recording and transmission of eight sEMG-signals around the forearm. Signal analysis was done on datasets acquired in a laboratory environment. Different kinds of surgical instruments were used to allow for the recognition of a multitude of hand gestures. The recorded signals were filtered, analyzed and finally, well-established sEMG-features were extracted for the training of said classification models. In order to evaluate the feasibility of the approach, different kinds of classification models were trained on the same dataset. This aided in the evaluation of the method and the assessment on whether the identification of surgical actions and instruments by sEMG-Signals would be sufficient for further research.

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Herausforderungen bei der Prozessunterstützung im Operationssaal

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Durch die zunehmende Komplexität in der Gesundheitsversorgung, bedingt sowohl durch einen hohen Kosten- und Zeitdruck als auch durch die erhöhte Notwendigkeit technischer Systeme zum Erreichen des Behandlungszieles (minimalinvasive oder mikrochirurgische Eingriffe) sind zunehmend neue Ansätze zum Erreichen einer Interoperabilität verschiedener Systeme sowie auch der Einsatz von (semi-)automatischen Unterstützungssystemen notwendig. In einem ersten Schritt wurde ein theoretisches Vorgehensmodell auf der Basis eines geschlossenen Regelkreises für die intraoperative Prozessunterstützung entwickelt. Dabei steht der chirurgische Prozess im Zentrum. In weiteren Schritten wurde ein System zur Erfassung des aktuellen Arbeitsschrittes auf Basis der vorhandenen Videodaten (z. B. Mikroskopie, Ultraschall) [1], sowie eine zentrale Speicherlösung für den Operationssaal entwickelt [2]. Neben der indirekten Erfassung von Aktivitäten stellt auch die direkte Nutzung von Medizingerätedaten eine Möglichkeit der Zuordnung des Prozessschrittes dar. Im Rahmen der Arbeiten des Projektes OR.NET wurde mit dem IEEE 11073-SDC Standard eine Möglichkeit zur offenen Vernetzung geschaffen. Die Implementierung von Mehrwertdiensten auf Basis des Kommunikationsstandards ermöglichte die Entwicklung eines offen vernetzten Operationssaales [3]. Basierend auf dieser Basistechnologie wurden gemeinsam mit verschiedenen Partnern Mehrwertdienste entwickelt und mit Klinikern und Klinikbetreibern evaluiert [4]. Die Ergebnisse der Evaluation zeigen, dass durch eine syntaktische und semantische Interoperabilität neue, nutzbringende Funktionen umgesetzt und die Tätigkeiten der verschiedenen Nutzergruppen im Gesundheitssystem effektiv unterstützt werden können.

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Modular Infrastructure for Decision Models in ENT Oncology

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Computerized decision models based on Bayesian Networks promise to be a valuable addition to personalized medicine. Clinical decision support systems (CDSS) using these models can evaluate complex diseases, like head and neck cancer, and propose different suitable treatments. Their calculations must be based on routinely recorded patient data. Working with these systems must be associated with little to no additional efforts by the physicians.

To be fully integrated into the physicians' workflow, CDSS must also interlink smoothly with hospital information systems. We built a modular decision support system using web services to connect the different modules with the underlying information system. The four modules are: 1) a central processing unit containing methods from artificial intelligence to process the patient's status, 2) a model repository for storage and revision control of the patient specific decision models, 3) a data access unit connecting to several clinical data bases and 4) a connector to different user interfaces to provide the results in a suitable form. We prototypically implemented our infrastructure with a decision model for laryngeal cancer. Patient data is provided by a relational data base and processed in the central processing unit. Results, e. g. TNM-staging and personalized treatment options, are presented via a web application.

This modular infrastructure allows exchanging individual modules. For instance, the same processing unit could be connected to a different clinical data base or calculated results could be presented in another user interface, e. g., on a mobile device.

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Process Simulation Techniques for Perioperative Process Optimization

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The main goal of an efficient operating room management is the improvement of patient outcome while maximizing the number of surgical procedures and minimizing the surgery duration at the same time. Based on computer simulation techniques the perioperative processes could be optimized by determining in which way the processes need to be changed considering different procedural, behavioral, structural, operational and temporal parameters.

In this work, different simulation techniques of Discrete Event Simulation (DES) were utilized for the description, analysis, prediction and comparison of various perioperative process alternatives. Eventually, a holistic DES approach for perioperative process optimization in orthopedic surgery was developed. For this purpose, the underlying DES process models were implemented with perioperative data from Total Hip Replacement (THR) and Total Knee Replacement (TKR) surgeries. The optimization objective was the increase to three surgeries per day and OR by reducing the intraoperative time through the optimization of the OR layout. Simultaneously, the OR preparation and surgery follow-up processes were streamlined with methods of Business Process Re-engineering.

The simulation results were evaluated in the real intraoperative OR environment. This results in a decrease of surgery time of 9,45 min for THR and 3,25 min for TKR. In addition, a decrease of the surgery turnover times could be achieved based on perioperative process optimization. The simulation results also demonstrate the improvement of OR utilization, reduction of turnover times and a decrease in personnel workload.

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Semi-Automatic Generation of Bayesian Belief Networks in Oncology Using a Hybrid Modeling Approach

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The utilization of probabilistic models to support the decision-making process has been the focus of a variety of applications ranging from risk identification to stock market prediction and diagnostic support in healthcare. While automatic model generation through machine learning is a constant trend in a wide range of settings, it is very hard to adapt for the medical domain since the underlying system – namely the human organism – tends to be vastly complex and unpredictable. In combination with the diverse landscape of clinical documents that complicate automatic learning, alternative solutions need to be established.

Because there cannot be absolute certainty about a modality that involves an unpredictable system, a corresponding model that aims to represent the real world can only feature prior belief about a given situation and will then be instantiated when evidence becomes available. A way to gather the necessary domain knowledge (prior belief) is collaborative modeling. The approach features a single model instance that can be expanded or modified by a range of suitable contributors. The model structure based on causal relationships as well as the integrated values that depict the conditional probabilities of individual entities are entered manually by the users. Thus, the kind and amount of contributing experts directly correlates to the objectiveness of the resulting model which represents a crucial aspect of extensive acceptance among patients and health care representatives.

We have developed a novel concept for the assessment of clinical knowledge for an application in model-based decision support by utilizing a fragmented retrieval process (belief blocks) combined with a corresponding block-matching process. The underlying system supports the user by offering a variety of assistance features as well as structural data enquiry. Using this approach, we are able to combine information from various sources (expert interviews, study results, guidelines) into a single dynamic model instance that might then be instantiated with individual patient data to provide patient-specific decision-support.

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THEMENBEREICH: ACTIVE ASSISTED LIVING (AAL)**Entwicklung eines Bewegungsunterstützungssystems für die Treppenüberwindung**

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Durch diverse altersbedingte Änderungen des menschlichen Körpers, wie Muskelkraftverlust oder Gelenkverschleiß, wird die Überwindung der Treppe zu einer täglichen Hürde für die Betroffenen. Infolgedessen treten Veränderungen im Gangbild, Balanceprobleme und eine erhöhte Angst vor dem Stürzen auf. Um diesen Problemen zu begegnen, wird ein am Körper zu tragendes Bewegungsunterstützungssystem (BUS) entwickelt. Ein derartiges, leicht an- und ablegbares System würde den Menschen in seiner Bewegung unterstützen, ohne dabei seine Muskelkraft zu ersetzen.

Neben der Analyse des Standes der Forschung und Technik sind die Bedürfnisse der Menschen beim Überwinden von Treppen zu spezifizieren. Dies beinhaltet die Ermittlung biomechanischer Anforderungen sowie akzeptanzorientierte Aspekte.

Durch die ermittelten Anforderungen können bereits abstrakte prinzipielle Lösungen synthetisiert und ausgewählt werden. Durch simulationsbegleitende Untersuchungen können optimale Parameter der unterstützenden aktiven und passiven Elemente quantifiziert werden. Dabei wird der menschliche Bewegungsapparat samt Muskeln sowie das BUS modelliert und die Bewegung des Treppenauf- und -abstieges simuliert.

Durch den Aufbau von Demonstratoren mittels additiver Fertigungsverfahren können Funktionen schnell und einfach getestet werden. Dabei stehen insbesondere die kinematische Kompatibilität des BUS, ergonomische Aspekte der Schnittstelle zum Menschen sowie eine intuitive Bedienung im Fokus.

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Wearables in der geriatrischen Pflege

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In den kommenden Jahren werden wir aufgrund des demografischen Wandels in Deutschland mit vielen Herausforderungen konfrontiert sein. Zu den Auswirkungen einer älter werdenden Bevölkerung gehört die steigende Zahl pflegebedürftiger und geriatrischer Patienten. Für das Jahr 2030 rechnen aktuelle Prognosen mit 6,2 Mio. Menschen in Deutschland, die das 80ste Lebensjahr überschritten haben, und 3,31 Mio. pflegebedürftigen Patienten, sowie einem noch steigenden Fachkräftemangel bei Pflegekräften.

Es sind neue technische Lösungen notwendig, um künftig die Arbeit der Pflegekräfte bestmöglich mit Informationen über den Patienten zu unterstützen. Wearables könnten eine Schlüsseltechnologie zur Erfassung von personenbezogenen Vitaldaten im geriatrischen Sektor sein.

Eine Marktübersicht zeigt, über welche Sensoren und Funktionalitäten die auf dem Markt erhältlichen Wearables verfügen. Um den tatsächlichen Datenbedarf der Pflegekräfte zu erfassen, wurden Experteninterviews mit Pflegefachkräften aus dem ambulanten und stationären Bereich durchgeführt. Die Ergebnisse zeigen, welche der mittels Wearables erfassbaren Vitaldaten sich die Befragten als Arbeitsgrundlage vorstellen können und welche sie sich in Zukunft noch wünschen.

Im Ausblick wird aufgezeigt, welche Anforderungen die befragten Pflegekräfte an Wearables haben, und wie ihnen die Daten perspektivisch zur Verfügung gestellt werden können

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THEMENBEREICH: NICHTINVASIVE BILDGEBUNG

Assessment of Automatic Perforator Detection in Infrared Thermal Images

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Knowledge of the location of the blood vessels supplying the skin and subcutaneous tissue is required during the planning of tissue transfer in reconstructive surgery. Computed tomography angiography and indocyanine green angiography are common imaging techniques but expose the patient to radiation or a contrast agent, respectively. Infrared thermal imaging was successfully used as a non-invasive alternative. To support the interpretation of thermograms, a method to automatically detect the perforators was developed and evaluated.

A system consisting of a thermal camera, a PC and custom software was developed. The temperature variations of the skin surface were analyzed to extract the perforator locations. To assess the performance of the algorithm a study comparing the detection results of the algorithm with manually labelled thermal images by two clinicians of the deep inferior epigastric perforator (DIEP) flap of 20 healthy volunteers was conducted.

The F-measure, precision and recall were used to evaluate the system performance. The median F-measure is 0.833, the median precision is 0.80, and the median recall is 0.907.

This study showed that it is possible to automatically and reliably detect the skin perforators in thermograms despite their weak temperature signature. Therefore, IR thermal imaging is a suitable non-invasive and contactless approach for intraoperative use. Combined with a computer-assisted tool for the automatic detection of perforator vessels, it is a relevant alternative intraoperative imaging method to the standard indocyanine green angiography.

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Electrical Impedance Lung Imaging with Partial Access to the Thorax

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In prehospital emergency scenarios such as car crashes with trapped patients, the emergency physician needs to check the patient's vital state before taking further actions. Lacking alternatives that can be applied outside the hospital, physicians use auscultation for the examination of lung function. However, when executed in a noisy environment, this method is often not sufficient enough to allow for a proper analysis of respiratory functions.

An alternative non-invasive monitoring of lung function is achievable by employing Electrical Impedance Tomography (EIT). The current focus of the method's application is on lung monitoring in the intensive care unit as support and observation of mechanical ventilation.

In this project, in a simulation study, the potential use of EIT in prehospital emergency scenarios is examined. Existing EIT devices require a full enclosure of the thorax by the electrodes for the imaging process. However, in emergency scenarios this full enclosure may not be possible for trapped or injured patients.

Therefore, the imaging device must be able to handle a reduced number of electrodes, placed on only a part of the patient's thorax. To simulate this in a set of real animal EIT data, parts of the measured voltages are deleted. The modified data sets are then reconstructed and compared to the original image, reconstructed with the full data. The first results of this study show a reduction in the image quality and problems in the interpretability of the images even for a small number of reduced electrodes. In future work, different stimulation pattern need to be developed, to handle only partial access to the thorax.

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Evaluation of Hyperspectral Imaging on Measurement of Ischemic Conditioning Effects of the Gastric Conduit

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Hyperspectral imaging (HSI) is a relatively new method used in image-guided and precision surgery, which has shown promising results for characterization of tissues and assessment of physiologic tissue parameters. The aim of this study was to evaluate HSI for the measurement of ischemic conditioning effects during esophagectomy.

Intraoperative hyperspectral images of the gastric tube through the mini-thoracotomy were recorded from n=30 patients, 21 of whom underwent laparoscopic gastrectomy and ischemic conditioning of the stomach with two-step transthoracic esophagectomy and gastric pull-up with intrathoracic anastomosis after 3 - 7 days. The tip of the gastric tube (later esophago-gastric anastomosis) was measured with HSI. Analysis software provides a RGB image and 4 false color images representing physiologic parameters of the recorded tissue area intraoperatively. These parameters contain tissue oxygenation (StO₂), perfusion- (NIR Perfusion Index), organ hemoglobin- (OHI) and tissue water index (TWI).

Intraoperative HSI of the gastric conduit was possible in all patients and did not prolong the regular operative procedure. In particular, the tissue oxygenation of the gastric conduit was significantly higher in patients who underwent ischemic conditioning ($\overline{\text{StO}}_{2\text{Precond.}} = 79\%$; $\overline{\text{StO}}_{2\text{NoPrecond.}} = 64\%$; $p = 0.0025$).

HSI is suitable for contact-free, non-invasive and intraoperative evaluation of physiological tissue parameters within gastric conduits. Therefore HSI is a valuable method for evaluating ischemic conditioning effects and may contribute to reduce anastomotic complications. Additional studies are needed to establish normal values and thresholds of the presented parameters for the gastric conduit anastomotic site.

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Supervised Tissue Discrimination during Thyroid and Parathyroid Surgery based on Hyperspectral Imaging

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The parathyroid gland is located behind the thyroid. The number of glands and the position are individual. It requires an experienced surgeon to distinguish between the two glands and to not harm either of them during an open neck operation. Therefore, it would be beneficial to have a tool that can support the surgeons in their decision of removing one or both glands. This project concentrates on the discrimination of the parathyroid and thyroid using hyperspectral imaging (HSI).

The hyperspectral imaging system TIVITA™ Tissue (Diaspective Vision GmbH, Germany) was used for the acquisition of patient data sets. HSI data of 7 patients were acquired during open neck surgeries. A section of those images was identified as thyroid, parathyroid or muscle by the operating surgeon post-operatively. Those marked areas are then used in a selection of supervised machine learning logarithms: Support Vector Machine (SVM), k-nearest neighbours (kNN) and Neural Networks.

The best performing algorithm was SVM with a linear kernel. The overall accuracy of the method was 95.77 %. It was demonstrated in this study that machine learning methods are suitable to automatically discriminate thyroid and parathyroid using HSI. In our study, the computing time was acceptable for intraoperative use (less than 0.4 s). Despite of the less patient number, we calculated very promising results (accuracy of 96 %). In further works, the visualization of the classification results can be improved by smoothing the labelled classified regions. Finally, studies with larger patient numbers are required to better test the quality of the classification algorithms. Moreover, a classification of risk structures like nerves or tissues like lymph nodes will be crucial assist the surgeon during the operation.

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The AutoSon Project: Improvement of a Neuronavigation System for Neurosurgical Procedures

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The use of intraoperative ultrasound (iUS) imaging supports the neurosurgeon during brain tumor operations. Neuro-navigation systems perform the visualization of the iUS images overlapped on preoperative data. However, the limitations are the lack of communication between the devices and of image annotation tools.

An image based connector was developed to automatically identify the values of the US parameters set during the acquisition. These parameters are only accessible through the monitor of the US device and are variously represented. Moreover, semi-automatic tools were developed to segment the brain tumor, the ventricles and vascular structures in the preoperative MR and iUS images.

The tools were implemented on a research platform connected with the US device through a video connection and with the neuro-navigation system using a local network. A user modified the image depth on the US device. The connector tool detected the change and communicated the new depth to the navigation system which updated successfully the visualization of the images. Also, brain structures segmented using the tool of the research platform were sent to the navigation system and were successfully displayed on its monitor.

A commercial neuro-navigation system was improved by several tools facilitating the communication with the US device and performing the segmentation of target structures. A demonstrator including the neuro-navigation system, an US device and the research platform was built and tested. The next step is the evaluation in the operating room.

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THEMENBEREICH: BILDGESTUTZTE INTVERVENTIONEN**Alternative Treatment of Prostate Cancer: New Strategies using Focused Ultrasound**

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Prostate cancer (PCa) is common in men and some subtypes exhibit high metastatic rate. Hormone therapy with testosterone (T) could reduce invasiveness of androgen dependent PCa. Focused ultrasound (FUS) is reported to enhance effects of other treatment modalities. The aim of this study is to characterize thermal and mechanical effects of FUS on PCa and hormone metabolism.

Androgen independent (PC-3) and androgen dependent (LNCap) PCa cell lines were cultured in FUS penetrable 96 well plates (Greiner Bio-One) for treatment with a customized 1.14 MHz single focused transducer. To investigate mechanical effects, cavitation dose was evaluated with terephthalic acid method (Sigma) and via hydrophone (Precision Acoustic). For analysis of T metabolism, cells were treated with T (Sigma) at different concentrations for 12 days. Cell viability (WST-1 assay, Roche) was evaluated for both treatments.

Generation of free radicals (OH) serves as marker of cavitation dose and depends on the FUS intensity and duration (3 W, 40 s: 150 AU; 11.5 W, 40 s: 1500 AU). Different cavitation doses can lead to decreased cell viability to 87 % and 74 % in PC-3 24 h post treatment. Preliminary experiments of T metabolism lead to a concentration dependent loss in LNCap cell viability to 34 %, 25 % and 23 % for 1, 8 and 32 ng/ml, respectively. In contrast, no effect of T treatment was observed in PC-3 cells.

The first data suggest that cavitation can cause minor damage to PC-3 cells, mechanical effects will be further studied. In the future, cell sensitivity to T and metabolism combined with FUS treatment will be investigated.

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In Vitro Focused Ultrasound Hyperthermia for Radiosensitization of Human Cancer Cells

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Hyperthermia (HT; 40 – 46 °C) has been reported to sensitize cancer cells to radiation therapy (RT). Focused ultrasound (FUS) displays for the first time a suitable technique to generate local HT. In this study, impact of combined FUS-HT and RT treatment on human cancer cells was investigated in vitro.

Human glioblastoma (T98G), prostate (PC-3), and head and neck cancer cell lines (FaDu) were seeded in ultrasound-penetrable 96-well plates (Greiner Bio-One). We have used a special sonicator for cell culture plates developed at IMSaT (University Dundee) and modified by us comprised by a programmable VXM motor controller and a NEMA 17 stepper motor (VELMEX Inc.). FUS-HT (45 °C, 30 min) was induced using customized 1.14 MHz transducer at 214 W/cm². Temperature was monitored by thermal camera (Optris). HT (45 °C, 30 min) in thermal cycler worked as control. Single RT was applied at 10 Gy with an X-Ray device (DARPAC 150-MC; 1.28 Gy/min) afterwards. Effects on metabolic activity (WST-1, Roche) and DNA double-strand breaks (γH2A.X, Cell signaling) were evaluated.

Combination of HT+RT leads to a significantly ($p < 0.05$) decreased metabolic activity (T98 G: 27 %; PC-3: 50 %; FaDu: 55 %) compared to single RT (T98 G: 65 %; PC-3: 76 %; FaDu: 85 %) 72 h after treatment. Metabolic activity was also reduced in FUS-HT+RT group (T98 G: 52 %; PC-3: 45 %; FaDu: 88 %). FUS-HT+RT enhances the number of residual DNA double-strand breaks in PC-3 cells (8.57 foci/nucleus) compared to RT alone (5.32 foci/nucleus) 1 h post treatment.

Our data indicate that FUS-HT is an effective tool to radiosensitize cancer cells in vitro. Comparison to control group revealed importance of consistent temperature level. New in vitro FUS systems are needed and under investigation.

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Integration of Combined Radiation and Focused Ultrasound Therapy into the Clinical Domain

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Radiation therapy (RT) is commonly used for cancer treatment, however still causes negative side effects. Applying hyperthermia (HT; 40 – 45 °C) non-invasively in a target region with focused ultrasound (FUS) causes radio-sensitizing effects and improves treatment outcome. The aim of this work is, therefore, to present novel ideas for a combined FUS-HT-RT treatment and to propose concepts for an effective realization in two parts:

1. In silico simulations:

Preoperative decision support can be crucial in cancer therapy to apply the right treatment at the right time and place. By providing information on treatment outcome for specific tumor cell lines, surgeons can be supported immensely. Therefore in silico simulations to predict treatment outcome are performed, by performing ultrasound propagation calculations, as well as implementing an HT-RT model in a cellular automaton approach.

2. Collaborative robotics:

To provide precise treatments with low complexity and high user acceptance, collaborative robotics are introduced into the clinical environment. Utilizing novel interaction approaches and planning modalities, different frameworks for KUKA LBR iiwa 7 robots are developed. A first mobile platform was evaluated for the use case of ultrasound-guided biopsies. A user validation with an abdominal phantom (Triple Modality 3D Abdominal Phantom, CIRS Inc., USA) showed promising results for targeting precision and usability.

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Research and Development of a Forceps for MR-Guided Interventions with the Use Case Endomyocardial Biopsy

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Minimally invasive endomyocardial biopsy (EMB) is currently conducted under X-ray fluoroscopy guidance. This procedure implies radiation exposure, administration of nephrotoxic contrast agent, and poor soft tissue contrast. Magnetic Resonance Imaging (MRI) guidance offers a promising option to overcome these disadvantages entailing advantages as high soft tissue contrast and discretionary slice positioning. So far, however, biopsy forceps are mostly metallic and as per ASTM/ISO regulation MR Unsafe due to radio frequency heating. The objective of this project is the development and evaluation of an MR Safe biopsy forceps to realize MRI guided EMB. MR Safe jaw prototypes have been fabricated, equipped with passive MR markers, and evaluated under 1.5 and 3 Tesla MRI, assessing the visibility. The results are promising in terms of appropriate selection of size, position, and concentration of the markers to identify the opening state: a clear difference regarding the artifact sizes can be observed visually. For ex-vivo suitability tests, a life-size phantom of the vessel system has been modeled and manufactured. Further studies are currently conducted to ensure the applicability in terms of reliable MRI guidance and reproducible biopsy quality. Contemporarily, a corresponding clinical workflow for MRI guided EMB is developed, considering appropriate MRI sequences, MRI operation, intra-interventional communication, patient care, and safety.

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Dieses Abstract Book umfasst die wissenschaftlichen Beiträge von Doktorand_innen in den Themenfeldern: Modellgestützte Therapie und Operationssaal der Zukunft, Active Assisted Living (AAL), Nichtinvasive Bildgebung und Bildgestützte Intervention.

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