

# ANNUAL REPORT 2018 Innovation Center

# Computer Assisted Surgery





# IMPRINT

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Prof. Dr. Andreas Melzer

## **CONCEPT & LAYOUT**

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### COVER

ICCAS's intelligent and fully networked demonstration operating room.

#### PHOTOS

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# GRAPHIC ARTS

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#### DISCLAIMER

All data in this report is to the Institutes specifications. **No responsibility can be accepted for the correctness of this information.** 

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# PREFACE

Dear Ladies and Gentlemen,

the year 2018 was very successful for ICCAS in terms of our research results, collaboration work and improved communication processes. Our research was targeted on two major areas: Computer Assisted Interventions and the projects on Model-based Medicine and intelligent OR.

Eight projects have been launched with a total amount of around 2.3 Mio Euro funding mainly provided by 'KMU-innovative' of the Federal Ministry of Education and Research (BMBF) and 'ZIM' of the Federal Ministry for Economic Affairs and Energy (BMWi).

The scientific output is reflected by 35 articles of prestigious journals and more than nine invited lectures and contributions to many panel discussions. For example, we took part in the Surgical Robot Challenge of the Hamlyn Symposium in London and supported the EU's largest civil protection exercise 'ModEX' in Bucharest in the scope of the project 'European Modular Field Hospital (EUM-FH)'. Furthermore, we hosted the 17th Annual Conference of the German Society for Computer and Robot Assisted Surgery (CURAC). Our 5th Digital Operating Room Summer School (DORS) attracted 16 international participants through a comprehensive five day program on computer assisted medicine.

We were able to host very important personalities. Among those were Saxony's Prime Minister Michael Kretschmer and the EU Commissioner for Humanitarian Aid and Civil Protection Christos Stylianides.

We would like to thank our partners, especially our clinical committee members, for their trust and great support and are looking forward to a successful and a pleasant new year.

Prof. mult. Dr. Andreas Melzer Director

Prof Dr. Thomas Neumuth Vice Director















# **INSTITUTIONAL FACTS**

- Germany's Minister of Education and Research visits ICCAS CURAC in Leipzig
- FIVE RESEARCH GROUPS:

Therapy Imaging and Model Management Systems (Dr. Oliver Burgert), Patient Model (Dr. Rafael Mayoral), Workflow and Knowledge Management (Dr. Thomas Neumuth), Assessment of Surgical Automation Systems (Dr. Werner Korb), Visual Computing (Prof. Dirk Bartz)

- ICCAS colloquium on Computer Assisted Surgery launched 2009
  - Establishment of the IRDC ICCAS as a pioneer and cooperation partner
- 2010

2008

- Surgical Planning Unit (SPU) opens ICCAS teams up with HTWK Leipzig – establishment of the Innovation Surgical Training Technology (ISTT) under professorship of Werner Korb
- ICCAS participates in the DICOM WG24 group 2011
  - ICCAS's demo OR 2.0 opens
    - RESEARCH AREAS: Model-Based Automation and Integration (Dr. Thomas Neumuth) and Standards (Prof. Heinz U. Lemke)
    - Advisory Board founded
- 2012
- ICCAS starts academic courses at HTWK RESEARCH AREA – Digital Patient Model (Dr. Kerstin Denecke) starts

2013

- TPU including ,oncoflow' launched at Leipzig University Hospital
  - PascAL (Patient Simulation Models for Surgical Training and Teaching) research project by Leipzig University and HTWK Leipzig
    - ICCAS plays a key role in the national BMBF research project 'OR.Net -Safe and Dynamic Networks in the Operating Room'
  - Honorary Professorship of Biomedical Information Systems at the HTWK Leipzig: Thomas Neumuth
  - Project 'HWS Structural Defect Classification and Modeling of the Cervical Spine' in cooperation with the Institute of Anatomy (Leipzig University) and the Fraunhofer IWU, Dresden
  - Researcher exchange programs with University of Southern California, ARTORG Center for Biomedical Engineering Research (University of Bern) and Fraunhofer MEVIS in Bremen

# 2014

- Prof. Andreas Melzer joins ICCAS as Director as well as professor of computer assisted surgery
- IT Innovation Award for ,oncoflow'
- First Digital Operating Room Summer School DORS 2014

# 2015

- Launching of cooperation with several scientific and clinical institutions Tenth anniversary of ICCAS with second DORS and ICCAS International Symposium
- Project OR.Net: Presentation of results in the complete demonstrator
  NEW RESEARCH AREAS: Noninvasive Image Guided Interventions (Prof.
- Andreas Melzer), Multimodal Intraoperative Imaging (Dr. Claire Chalopin) • Clinical Advisory Board founded
- New Advisory Board members: Prof. Ron Kikinis and Prof. Günter Rau

# 2016

- Final presentation of the flagship project OR.Net ICCAS receives ISO 13485 certification
- Federal health minister visits ICCAS
- 3rd Digital Operating Room Summer School DORS 2016
- Project start of Meta-ZIK SONO-RAY

# 2017

- ICCAS meets Federal Chancellor Angela Merkel at Digital Summit 2017
  4th Digital Operating Room Summer School consolidates its unique feature
- EUFUS 2017 & Preconference Workshop Experimental FUS and HIFU take place in Leipzig
- Successful non-invasive treatments with HIFU at Leipzig University Hospital
- RESEARCH AREA Life Support Systems with projects IMPACT and EMU launches
- Start of projects European Modular Field Hospital, PAPA-ARTIS and MoVE

# 2018

- ICCAS welcomes Saxony's Prime Minister Michael Kretschmer
- 5th Digital Operating Room Summer School inspired international participants
- ICCAS takes part at the Surgical Robot Challenge of the Hamlyn Symposium in London
- ICCAS hosts Steering Committee Meeting of the European Modular Field Hospital project
- ICCAS invites to the 17th Annual Conference of the CURAC-Society
- Launch of projects: ENSEMBLE, COMPASS and LYSiS
- EU Commissioner for Humanitarian Aid & Crisis Management Christos
  Stylianides visits ICCAS



















# **FACTS AND FIGURES**

### HEADCOUNT



	2014	2015	2016	2017	2018
Research Associates	23	23	23	32	39
Research Associates (FTE)	21	20	19	25	29
Research Assistents	19	16	17	14	18
Guest Researchers	6	5	13	10	20

### PUBLICATIONS



	2014	2015	2016	2017	2018
Total	28	40	31	42	35
First- and Senior Authorship	17	14	14	7	22
Co-Authorship	7	23	15	15	9
Book Chapters	4	3	2	0	4
Conference Proceedings	53	9	21	29	28

#### **GRADUATIONS**



	2014	2015	2016	2017	2018
Doctoral theses	3	4	1	3	0
Master theses	2	2	4	6	4
Bachelor theses	3	0	2	1	1

#### FUNDING



ICCAS is mainly funded by the BMBF Federal Ministry of Education and Research under its ZIK Centers of Innovation Excellence program and KMU-innovative program. Further external funding is received from the BMWi Federal Ministry for Economic Affairs and Energy for projects related to the ZIM Central Innovation Program for small and medium-sized enterprises as well as from the European Union. Leipzig University's Faculty of Medicine provides ICCAS with performance-based funding.



# ACTIVITIES

# **HIGHLIGHTS**



Harm-Bastian Harms (Johanniter), Gino Claes (Belgian Public Health Emergency), EU Commissioner Christos Stylianides, Dean of Studies of MedF Prof. Jürgen Meixensberger, Prof. Thomas Neumuth (ICCAS) and Prorector Prof. Erich Schröger discuss the operation mode of the modular field hospital on a model. (f.l.t.r.) © ICCAS, photo: Swen Reichhold

# EU COMMISSIONER CHRISTOS STYLIANIDES VISITED ICCAS

On November 23, 2018, ICCAS welcomed Christos Stylianides, EU Commissioner for Humanitarian Aid and Civil Protection. The Commissioner followed an invitation from the EUMFH project consortium around Prof. Thomas Neumuth, which presented the first results of the concept development of an European emergency hospital. Together with the EU Commissioner further steps to embed the EUMFH concept in the European framework for humanitarian aid and civil protection were discussed. Furthermore, he visited the ICCAS's Intelligent Operating Room and a surgical robotics application from the SONO-RAY group. In a statement, Stylianides emphasized the high importance of science for the EUMFH project and for further developments in disaster relief. ICCAS is the only partner of an European university. It participates with the electronic patient record and the networking of the information technology.

Nine European countries want to develop a modular hospital which can be transported to the scene of a disaster in very short time. Initial results from ICCAS have already been obtained and have been tested in the EU's largest civil protection exercise (ModEX) in Bucharest in November 2018.

# ICCAS WELCOMED SAXONY'S PRIME MINISTER MICHAEL KRETSCHMER

On January 18, 2018, Saxony's Prime Minister Michael Kretschmer, who visited Leipzig University for the first time since taking office, was warmly welcomed at ICCAS. Prof. Andreas Melzer, Prof. Thomas Neumuth and Prof. Andreas Dietz gave an insight into the current development of state-of-the-art OR technologies and let the Prime Minister lend a hand in the research operating room. In addition, Kretschmer was explained a robot-assisted therapy approach from the SONO-RAY project. Further guests were Rector Prof. Beate Schücking, the Prorectors Prof. Erich Schröger and Prof. Thomas Lenk and Dean Prof. Michael Stumvoll from Leipzig University, Prof. Wolfgang E. Fleig from Leipzig University Hospital as well as Prof. Markus Krabbes and Prof. Jens Jäkel from the Leipzig University of Applied Sciences for Technology, Economics and Culture (HTWK).



Guests of the Prime Minister visit at ICCAS.  $\mid$  @ ICCAS, photo: Christian Hüller

# ICCAS INVITED TO THE 17TH CURAC ANNUAL MEETING

In September, ICCAS invited to the 17th Annual Conference of the German Society for Computer and Robotic Assisted Surgery (CURAC). According to the motto 'Connected into the Future' experts in medical computer science, engineering and medicine jointly discussed possibilities and challenges on computer- and robot-controlled assistances in operating rooms.



Impressions of CURAC 2018 in Leipzig. | @ ICCAS, photos: Leonie Lang

# **EXTERNAL PRESENTATIONS**



# ICCAS'S 'INTELLIGENT OR' AT XPOMET© CONVENTION 2018 March 21 – 23, 2018, Leipzig

Dr. Stefan Franke explained the functionalities of ICCAS's 'Intelligent Operating Room' to Saxony's Minister for Social Affairs and Consumer Protection Barbara Klepsch at the XPOMET© Convention exhibition booth.



# ICCAS TOOK PART IN THE SURGICAL ROBOT CHALLENGE OF THE HAMLYN SYMPOSIUM June 24, 2018, London (UK)

Scientists from the SONO-RAY group competed with international leading research groups at the Surgical Robot Challenge of the renowned Hamlyn Symposium in London. They presented a robot system for supporting the ultrasound-guided removal of tissue samples.



# ICCAS SUPPORTED EU'S LARGEST CIVIL PROTECTION EXERCISE 'MODEX'

October 14 – 18, 2018, Bucharest (Romania)

Prof. Thomas Neumuth and Erik Schreiber supported the project team 'European Modular Field Hospital' (EUMFH) during the EU's largest civil protection exercise 'ModEX' in Bucharest. They evaluated the digital patient file for disaster relief developed at ICCAS under real conditions.

## **SELECTED EVENTS**



### GIRLS'DAY April 26, 2018 | ICCAS, Leipzig

On the occassion of the nationwide Girl's Day, Dr. Lisa Landgraf and Dr. Claire Chalopin gave female pupils an insight into research projects in the field of medical informatics at ICCAS.



# OPEN DAY

# June 6, 2018 | ICCAS, Leipzig

Leipzig University's Prorector for Development and Transfer Prof. Thomas Lenk and project coordinator Moritz Waschbüsch were two of the 100 visitors of the Open Day. ICCAS's scientists from all research areas had invited to demonstrate medical technologies in a close and simple way.



# LONG NIGHT OF SCIENCES June 22, 2018 | BBZ, Leipzig

At the Long Night of Sciences, the scientists of the Life Support Systems group experimentally explained the function of Electrical Impedance Tomography (EIT). Many guests came especially to fasten the measuring belt and to watch their own lung function in the live image.



# DIGITAL OPERATING ROOM SUMMER SCHOOL (DORS)

# August 27 – 31, 2018 | ICCAS, Leipzig

At the 5th Digital Operating Room Summer School, 16 international participants enjoyed varied insights into state-of-the-art medical technologies through the intensive support of the entire ICCAS team and physicians of the Leipzig University Hospital and the Heart Center Leipzig.

# **GUEST TALKS**



### INVITED TALK AT DGU CONGRESS September 27, 2018, Dresden

At the opening plenary of this year's Congress of the German Society for Urology, Prof. Andreas Melzer held an invited talk on aspects of the future operating room.



# KEY NOTE LECTURE AT BMT September 26, 2018, Aachen

At this year's Annual Conference of the German Society for Biomedical Engineering, Prof. Thomas Neumuth gave a keynote lecture on 'Patient Specific Model Guided Therapy'.



# PANEL DISCUSSION AT FRAUNHOFER INTERACTIVE EXHIBITION October 9, 2018, Berlin

At the Fraunhofer Interactive Exhibition ,Future Work', Prof. Andreas Melzer was one of the experts of the panel discussion ,Future Work Health'. Top-level representatives from science and politics talked about the workplace of the future in the fields of health and nursing care.



## PANEL DISCUSSION AT SZ CONGRESS September 25, 2018, Munich

Prof. Thomas Neumuth was one of the experts of the panel discussion on 'Smart Hospital' at the Süddeutsche Zeitung Congress 'Digital Health'. Together with participants from science, industry and medicine he discussed how digital technologies can simplify therapyand administration processes.

# **COLLABORATION WORKS**



# STEERING COMMITTEE MEETING OF EUMFH PROJECT

# July 10 – 11, 2018, Leipzig

Prof. Thomas Neumuth welcomed the international steering committee members of the project 'European Modular Field Hospital' (EUMFH). They met to promote the conception of a mobile hospital for emergency operations on behalf of the EU commission for humanitarian aid and civil protection.







# ICCAS MET TWINS IN JAPAN June 28 – July 31, 2018

For the second time, ICCAS scientists visited the Joint Institution for Advanced Biomedical Sciences of Tokyo Women's Medical University and Waseda University (TWIns) in Tokyo to discuss the topic 'open networking of medical devices and IT systems in operating room and hospital'.

# VISIT OF INTERACTIVE MEDIA LAB DRESDEN

#### March 1, 2018, Leipzig

Researchers from the Interactive Media Lab at Technische Universität Dresden met the DPM group to inform about the current research state on exploration and visualization of complex patient data. The two teams aim to collaborate in the area of decision support models for the tumor board.

# STATUS MEETING MOVE PROJECT September 9, 2018, Leipzig

The consortium of the project 'Modular Validation Environment for Medical Networks' (MoVE) met in Leipzig to check the current project status. Main topics of the BMBFfunded project are the approval, certification process and risk management of open networked medical products in integrated OR environments.

#### **PROJECT LAUNCHES**

#### **MR BIOPSY**

In January, the kick-off meeting of the BMBF-funded KMU-innovative project 'MRcompatible flexible biopsy forceps for minimally invasive tissue sampling' took place. Project partner is EPflex Feinwerktechnik GmbH. The goal is to research a worldwide first MR-suitable flexible biopsy forceps to improve the minimally invasive and image-guided removal of tissue samples without the previous high X-ray exposure. Under the direction of Prof. Andreas Melzer ICCAS deals with fundamental research of novel MRI and X-ray markers as well as experimental setups for the testing.



#### COMPASS

In September, the BMBF-funded joint project 'Cooperative immersive assistance system for minimally invasive surgery' – COMPASS started, in which ICCAS and several partners from science, clinic and industry develop an artificial navigation awareness for the intelligent support of minimally invasive endoscopic navigation.

#### ENSEMBLE

Since April 2018, ICCAS collaborates with the PHACON GmbH in the BMWi-funded ZIM-project 'Development of a scalable and magnetic resonance (MR)-compatible blood circulation model' – ENSEMBLE. The research object is a closed-loop system available as a self-contained training module, allowing the practicing of multiple surgical procedures, e.g. catheter-based operations. Hence, future surgeons can develop and expand their cognitive and motoric skills during the course of multiple practice sessions.

#### LYSIS



Partners involved in the LYSiS project: Jonathan Philip Takoh (UKL, Dept. of Visceral Surgery), Hannes Köhler (ICCAS and Diaspective Vision GmbH), Dr. Axel Kulcke (Diaspective Vision GmbH), Dr. Claire Chalopin (ICCAS), Prof. Ines Gockel (UKL, Dept. of Visceral Surgery), Prof. Thomas Neumuth (ICCAS), Sebastian Murad Rabe (UKL, Dept. of Visceral Surgery).

On October 9, the kick-off of the BMBF-funded KMU-innovativ project 'Innovative imaging for tissue differentiation in minimally invasive surgery – LYSiS' took place at ICCAS. In close cooperation with Diaspective Vision GmbH and the Clinic and Polyclinic for Visceral, Transplantation, Thoracic and Vascular Surgery ICCAS is researching on a computer-assisted method for the automatic characterization, recognition and presentation of tissue from intraoperative hyperspectral imaging data.

## HONORS AND AWARDS



### PROF. DR. ANDREAS MELZER

was appointed Chairman of the Advisory Board for Internal Affairs of the High Tech Surgery Association (HTC). It was founded in 2015 and brings together more than 9000 professionals worldwide in their specialties to exchange and promote knowledge about advances in surgical technology.

In November 2018, he has been appointed to the Board of the German Society for Biomedical Engineering (BMT) in the area 'Clinical Application'.



### PD DR.-ING. STEFFEN OELTZE-JAFRA

was elected as new member of the executive committee of the 'Visual Computing in Biology and Medicine Working' group. Furthermore, he earned the second place at the Karl-Heinz-Höhne Award ceremony of the German Informatics Society (GI).



# PROF. DR.

ANDREAS DIETZ

has been appointed to the Board of the European Head and Neck Society (EHNS) during the EHNS congress in Rome (Italy), for the next four years.



# JULIANE NEUMANN

won the Best Paper Award for her work 'Perioperative workflow simulation and optimization in orthopedic surgery' at the Medical Image Computing and Computer Assisted Intervention (MICCAI) satellite workshop 'OR 2.0 – Context-Aware Operating Theaters' in Granada, Spain.



#### ALEXANDER OESER

successfully presented his work on a novel system for assessing laboratory orders. He received the first price at the design challenge competition of the Visual Analytics in Healthcare (VAHC) workshop of the American Medical Informatics Association (AMIA 2018) in San Francisco.

# RESEARCH AREAS AND RELATED PROJECT PROFILES

LIFE SUPPORT SYSTEMS

INTRAOPERATIVE MULTIMODAL IMAGING





# MODEL-BASED AUTOMATION AND INTEGRATION

'Modern medicine is no longer conceivable without the use of technology: medicine, information management and biomedical technology converge to an ever greater extent. This development requires a combination of traditional medical devices with modern information systems.'

> Prof. Dr. Thomas Neumuth (group leader)



### **SCIENTIFIC STAFF**

Thomas Neumuth (group leader), Juliane Neumann, Nico Graebling, Stefan Franke, Erik Schreiber, Richard Bieck, Alexander Oeser, Lukas Schmierer (f.l.t.r.), Max Rockstroh

### **SELECTED PUBLICATIONS**

Neumuth T, Franke S. Clear oxygen-level forecasts during anaesthesia. Nat Biomed Eng. 2018; 2(10): 715-6.

Franke S, Rockstroh M, Hofer M, Neumuth T. The intelligent OR: design and validation of a context-aware surgical working environment. Int J Comput Radiol Surg. 2018; 13(8): 1301-8.

Unger M, Black D, Fischer NM, Neumuth T, Glaser B. Design and evaluation of an eye tracking support system for the scrub nurse. Int J Med Robot. 2018 [Epub ahead of print].

# PERIOPERATIVE WORKFLOW SIMULATION AND OPTIMIZATION IN ORTHOPEDIC SURGERY

### INTRODUCTION

Operating room management aims at the efficient coordination of surgical procedures by maximizing the number of surgical cases while minimizing the required surgery time, with the main goal of improving the patient outcome. Discrete Event Simulation (DES) can be utilized to describe, analyze and predict the impact of procedural changes in perioperative processes. The aim of this work is to provide a DES approach for a holistic perioperative process optimization with a focus on the combination of behavioral, temporal, operational and structural perspective. Two different process simulation techniques, namely Business Process Simulation (BPS) and 3D Process Flow Simulation were utilized. DES models were implemented with perioperative data from Total Hip Replacement (THR) and Total Knee Replacement (TKR) surgeries. The optimization objective is to increase the number of surgeries to three cases per day by reducing the intraoperative time through the optimization of the OR layout. Furthermore, the processes for surgery follow-up and OR preparation should be streamlined.

#### MATERIAL AND METHODS

For the intraoperative simulation 15 THR and 7 TKR surgeries and for pre- and postoperative simulation 30 (total or partial) knee- and hip replacement surgeries were recorded. The pre- and postoperative activities of all OR team members were modeled in BPMN format and simulated in different scenarios. The pre- and postoperative processes were streamlined with methods of Business Process Re-engineering and the simulation scenarios were repeated. In the second step, the intraoperative process optimization was performed. Afterwards, the simulation was repeated with improved intraoperative surgery times.

#### RESULTS

Firstly, the minimum, average and maximum process duration of the initial situation for different THR and TKR combinations were simulated (Fig. 1, light gray). The target of three surgeries per day could only be achieved with 3THR. All combinations with one to three TKRs widely exceed the maximum cycle time of 8h per day. Based on perioperative process optimization a decrease of the turnover times could be achieved (Fig. 1, dark gray).

The aim of the intraoperative process optimization was to shorten the surgery duration by



Fig. 1 - Cycle Time simulation results of THR and TKR combinations: 2 surgeries (left side) and of 3 surgeries (right side). The red line marks the 8h work time/ day boundary. The results after pre-, intra- and postoperative optimization (Target CT) are numbered.

improving the OR layout, instrument table positions and setups for THR and TKR. A 3D simulation environment was created with Delmia (Dassault Systems). The existing layouts and table positions were modeled and simulated based on the intraoperative recorded data (Fig. 2). Based on the simulation scenario, new setup suggestions are designed and compared to the initial setups.

The optimal setups for THR and TKR 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. The improved surgery times were included in the perioperative optimization and the BPS simulation study was repeated (Fig. 1, blue). The results of the perioperative optimization indicate that it would be possible to perform 3THR or 2THR+1TKR in the work time of one day.

#### **DISCUSSION AND CONCLUSION**

It could be shown that perioperative process optimization lead to improvement of OR utilization, reduction of turnover times and a decrease in personnel workload. Simulation techniques enable the determination not only that perioperative processes can be improved, but also in which way processes need to be adapted and how the process efficiency is changed due to the impact of different procedural, behavioral, structural, operational or temporal parameters. An objective time- and resource-saving assessment of different process alternatives and their impact on efficacy and potentials could be achieved.

#### **PROJECT TEAM**

Prof. Dr. Thomas Neumuth

Dipl.-Inf. Juliane Neumann

#### **PROJECT PARTNERS**

Leipzig University Hospital, Department of Orthopaedics, Traumatology and Reconstructive Surgery, Division of Joint Replacement and Orthopaedics, Prof. Andreas Roth

#### SELECTED PUBLICATIONS

Neumann J, Angrick C, Rollenhagen D, Roth A, Neumuth T. Perioperative Workflow Simulation and Optimization in Orthopedic Surgery. In: Stoyanov D, et al.: OR 20 Context-Aware Operating Theaters, Computer Assisted Robotic Endoscopy, Clinical Image-Based Procedures, and Skin Image Analysis. 2018; 3-11.

#### FUNDING

German Federal Ministry of Education and Research (BMBF)



Fig. 2 - 3D simulation scenario of the orthopedic OR modeled in Delmia (left TKR).

# CONTEXT-AWARE HUMAN-MACHINE INTERFACES IN INTEGRATED OPERATING ROOMS

#### INTRODUCTION

An increasing number of medical devices provide communication interfaces, but yet they only show very limited cooperative behavior. The lack of contextual information during surgery hinders autonomous intelligent system's adaptation. We implemented an intraoperative context-awareness pipeline and propose a modeling approach for the realization of online dynamic human-machine interfaces in the OR.

### MATERIAL AND METHODS

Context-aware automation usually bears severe risks that limit the applicability. Hence, we propose an additional layer of context-awareness, which dynamically assigns medical device functions to input devices and provides suitable configuration profiles depending on the surgical situation. By means of that, surgeon's direct control can be increased with a limited interaction complexity.

The automated assignment of device function to input devices is based on an on-the-fly analysis of the users' current and forthcoming needs. The algorithm maximizes the amount of functions provided with the limited number of input devices, such as foot switches and endoscope buttons. The optimization is also able to take user-specific preferences and device-specific limitations into account. The provision of configuration profiles, which can be applied with minimal user interaction, relies on a scoring algorithm that ranks predefined configurations according to the estimated usefulness in the given surgical situation.

The approaches were tested in a demonstration setup for Function Endoscopic Sinus Surgery including dynamic overlays to inform the user about new function assignments and configuration options (see Fig. 1).





Fig. 1- Control console with automated ranking of configuration profiles (above) and video overlay with the assignment of functions to the foot switch (below).

#### RESULTS

In the cross validations, 1245 work steps in 24 surgeries were analyzed. In the 1162 cases of input device usage, all interaction needs for the current work step and over 87 per cent (474 of 543) needs for forthcoming tasks could be provided with the dynamic function assignment. The context-aware ranking of configuration profiles reduced the required manual interaction for profile selection by over three quarters (156 to 708) in the 24 surgeries.

#### **DISCUSSION AND CONCLUSION**

The proposed methods extend the applicability of context-awareness beyond the automation of supportive tasks. With configuration ranking and dynamic function assignments, device adaptations and actions that require human confirmation due to risk management considerations, can be effectively assisted in addition to the automation of supportive tasks.

#### **PROJECT TEAM**

Prof. Dr. Thomas Neumuth

Dr.-Ing. Stefan Franke

Dipl.-Inf. Max Rockstroh

#### SELECTED PUBLICATIONS

Franke S, Rockstroh M, Hofer M, Neumuth T. The intelligent OR: design and validation of a context-aware surgical working environment. Int J Comput Radiol Surg. 2018; 13(8): 1301-8.

Franke S, Rockstroh M, Kasparick M, Neumuth T. A Method for the Context-Aware Assignment of Medical Device Functions to Input Devices in Integrated Operating Rooms. In: Stoyanov D, et al.: OR 20 Context-Aware Operating Theaters, Computer Assisted Robotic Endoscopy, Clinical Image-Based Procedures, and Skin Image Analysis. 2018; 12-19.

Franke S, Rockstroh M, Neumuth T. Context-awareness for control consoles in integrated operating rooms. Curr Directions Biomed Eng, 2018; 4(1): 291-5.

#### FUNDING

German Federal Ministry of Education and Research (BMBF)

# BIOPASS – IMAGE-, ONTOLOGY-AND PROCESS-BASED ASSISTANCE FOR MINIMALLY INVASIVE ENDOSCOPIC SURGERY

#### INTRODUCTION

In the BIOPASS project a novel localization approach for a markerless navigation system was developed to reduce the navigation hardware while assisting the surgeon with adapted navigation assistance. A critical aspect for the development of such an intelligent system was the definition of situational knowledge. Therefore, the goals of the project were: a multimodal acquisition of information in the OR, a comprehensive description as well as a consistent human-machine-interaction with a new navigation approach.

### MATERIAL AND METHODS

We combined a process modeling approach for temporal classification of visited anatomical landmarks during previous procedures with a semantic knowledge management system using an ontology framework. We used Hidden Markov Models (HMM) for the prediction of landmark sequences. For the ontological modeling the Foundation Model of Anatomy (FMA) as well as the Visual Concepts Ontology (VCO) were integrated to describe properties of the endoscopic view. This resulted in the definition of the BIOPASS Situation Ontology (BISON) which holds the semantic knowledge to describe a surgical procedure as a consecutive sequence of surgical situations. Both the process and ontology models were used in a BIOPASS demonstrator setup to predict landmarks and infer semantic information from them.



Fig. 1 - Overview of the BIOPASS System structure



Fig. 2 - Example screenshot of the BIOPASS System Demonstrator during evaluation.

#### RESULTS

A novel navigation method was implemented into a hybrid system with conventional optical tracking. In a first preclinical study, the hybrid system was used with continuous optical tracking and the new navigation algorithm in advance. Additionally, the line of sight for optical tracking was intermittently and permanently blocked resulting in a spontaneous and ongoing tracking assistance with the new navigation method. The Presented localization accuracy of the method was measured against the reference values defined in the CT model. Accuracy was calculated to have a mean error of 5 mm.

#### **DISCUSSION AND CONCLUSION**

We successfully integrated the novel navigation method into a conventional tracking setup and validated and evaluated the hybrid system in an ideal laboratory setup. Tracking functionality was identified to be comparable with conventional tracking technology. The missing quantitative navigation information, e.g. distance to regions of interest or CT-based allocentric localization, is substituted by an abstract qualitative navigation assistance, e.g. landmark-based egocentric orientation. How this new navigation assistance method actually benefits surgeon navigation experience and technology acceptance is still unclear. Further work needs to be done to enable better surgeon-machine-interaction along the navigation process.

#### **PROJECT TEAM**

Prof. Dr. Thomas Neumuth	_
M. Sc. Richard Bieck	

#### **PROJECT PARTNERS**

Zuse Institute for Information Technology, Berlin
LOCALITE GmbH, St. Augustin
 Dornheim Medical Imaging, Magdeburg

#### SELECTED PUBLICATIONS

Bieck R, Heuermann K, Hofer M, Neumuth T. From Passive Tool To Active Guidance: Requirements For Computational Navigation Intelligence In Computer-Assisted Functional Endoscopic Sinus Surgery. Int J Comput Assist Radiol Surg. [Epub ahead of print].

Heuermann K, Bieck R, Dietz A, Uciteli A, Franke S, Herre H, Neumuth T, Fischer M. Ein neuartiges Navigationssystem für die endoskopische funktionelle Nasennebenhöhlenchirurgie. 87. Deutscher HNO-Kongress, Düsseldorf, Germany; 2018.

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#### FUNDING

German Federal Ministry of Education and Research (BMBF)

# PIMPAP – PATIENT-BASED INDIVIDUAL MODELING OF PARASPINAL COLLATERAL NETWORK PERFUSION AFTER SEGMENTAL ARTERY OCCLUSION

#### INTRODUCTION

The repair of large thoracoabdominal aortic aneurysms (TAAA) is done by using endovascular minimally-invasive surgery with stent grafting. However, a successful intervention still poses risks of paraplegia or death due to ischaemic reactions in the spinal cord. The minimally-invasive, selective segmental artery coil embolization (MISACE) is a procedure employed to reduce these risks by preemptively closing supplying segmental arteries of the aorta before stenting. Since the procedure is still in an early application phase there exist no general guidelines and the effectiveness is currently being investigated in a multi-centric clinical trial in the PAPA-ARTIS EU-project. In the subproject PimPaP, a patient and an intervention process hybrid model is developed to investigate the influence of varying coiling patterns and their impact on the convalescence of spinal perfusion and the clinical outcome using computational modeling strategies.

#### MATERIAL AND METHODS

Multimodal patient-specific information is acquired in various stages including before, during and after the MISACE staging as well as one month and twelve months post-operatively after aneurysm repair. Using a digital patient modeling approach, a software-internal representation of the individual patient state is generated at different time points during the treatment



Fig. 1 - Overview of the PimPaP modeling approach and development stages.

process. Investigating the temporal changes of specific patient data (vital, pathological, and procedure parameters) leads to the abstraction of a more generalized representation of the treatment process and, furthermore, enables the comparison of new patients with this treatment representation.

#### **PROJECT TEAM**

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#### **PROJECT PARTNERS**

Saxon Incubator For Clinical Translation (SIKT)

PAPA-ARTIS Consortium (www.papa-artis.eu/project-partners)

#### FUNDING

This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No 733203.

# COMPASS – COMPREHENSIVE SURGICAL LANDSCAPE GUIDANCE SYSTEM FOR IMMERSIVE ASSISTANCE IN MINIMALLY-INVASIVE AND MICROSCOPIC INTERVENTIONS

#### INTRODUCTION

The surgical navigation process in minimally-invasive endoscopic surgery is time- and resource-constrained and in an intraoperative setup, conventional navigation assistance technology is reduced to a passive-supportive role. In the project COMPASS, a new technology for immersive assistance in minimally-invasive and microscopic interventions is developed to convert navigation systems into fully-acknowledged surgical actors. Since navigational support functions are influencing factors for the surgeons' cognitive workload, ICCAS research

#### RESULTS

The overall modeling approach is divided into five stages. We initially identified the components of a patient model representation including parameters, e.g. demographic background, imaging data, anamnesis, and diagnosis. Subsequently, the MISACE procedure is analyzed using workflow and process analysis steps to define a representative process model. Both the patient and the process model are then used to form a therapy model that is instantiated for the PAPA-ARTIS trial.

#### **DISCUSSION AND CONCLUSION**

We introduced our modeling approach for the simulation of the patient-individual intervention process for staged segmental artery occlusion as performed in a staged MISACE procedure. In a first step, the model components and relevant parameters were identified. With the start of the intervention phase in the PAPA-AR-TIS project, the model components will be instantiated and key patient and therapy process model parameters identified which correspond to the MISACE staging in a meaningful way.

in COMPASS is focused on the investigation of a modeling approach that considers surgical cognition for intelligent navigation assistance.



Fig. 1 - Overview of COMPASS project goals and their interconnection.



Fig. 2 - The modeling paradigm for intelligent computational navigation assistance behavior in minimally-invasive surgery.

#### MATERIAL AND METHODS

The modeling approach is based on the situation awareness theory from aeronautics and aerospace research, the cognition-guided surgery paradigm and knowledge from cognitive architectures development for autonomous robotics. The purpose is to extend a navigation assistance system so that it engages as a fully-acknowledged actor in the OR. This can induce automation-related drawbacks regarding human-machine interaction, e.g. decreased situational oversight and limited system predictability. In response, a parallel processing cycle mimics the human cognitive information processing cycle enabling the system to match a simulated navigation behavior with the real surgeon-individual navigation process.

#### RESULTS

We defined a dual information processing cycle model that uses both situation aware-

ness-based processing for situation comprehension and cognitive memory processing for the simulation of human-like behavior. The situation awareness cycle uses environmental perception as input for an inference step, in which the navigation situation is comprehended and projected into the future. The navigation cognition cycle based on an architectural framework mimics the human cognitive information processing cycle. The corresponding model maintains a working memory of relevant information for a current goal. It then evaluates and selects navigation steps that would lead to a specific navigation behavior. Simulated and real surgical navigation behavior are then compared to identify potential navigation support, e.g. goal-specific directions or possible work steps.

#### DISCUSSION AND CONCLUSION

The modeling approach for the development of an intelligent navigation assistance behavior will be thoroughly investigated in the recently started project. Furthermore, the performance of a cognitive architecture-based navigation cognition model is dependent on knowledge modeling, task definition and applied rulesets.

#### **PROJECT TEAM**

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#### FUNDING

German Federal Ministry of Education and Research (BMBF)

# MOVE – MODULAR VALIDATION ENVIRONMENT FOR MEDICAL NETWORKS

#### INTRODUCTION

The integration and networking of medical equipment has become an indispensable component of modern operating theaters. At present, the market is characterized by closed solutions, which are regulatorily approved as monolithic settings. The aim of the project is therefore to develop methods that support the development of openly integrated medical devices as well as the approval process by means of a test environment. The project aims to ease the access of SMEs to the market with innovative technologies.

#### MATERIAL AND METHODS

A simulation environment including communication infrastructure, simulated medical devices and test scenarios is being developed. The test platform will verify the networking of medical devices and software components and validate the communication regarding a large variety of parameters. Realistic, scenario-based simulations of an OR setup and its communication are implemented by a simulation engine and emulators of medical devices. Based on an integration with the IEEE 11073 SDC standards family, manufacturers can test their products against the virtual infrastructure early on in the development process.

In the frame of the project, ICCAS is responsible for the automated generation of realistic test scenarios from recordings of real interventions. Methods are developed that use already well-developed stochastic workflow modeling approaches to sample possible intervention courses and orchestrate the states and parameters of the emulated devices based on the estimated surgeon's behavior. To that end, a simulation engine is implemented, which reads formal descriptions of user and device behavior. A network of sampling components of various types, including Hidden Markov Models, Random Forests, and empirical distributions, is set up and frequently updated upon the run of a

scenario to generate realistic measurements, device parameter configurations, and remote procedure calls for the device under test. Fig. 1 summarizes the simulation approach.



Fig. 1 - Schematic representation of the simulation approach of MoVE.

#### DISCUSSION AND CONCLUSION

The simulation approach is able to represent a large variety of devices' behavior, which is also directly derived from clinical use cases. Hence, manufacturers can test their novel devices and services in virtual settings without access to real medical devices and prior to a testing under wet conditions. Especially the development of high-level assistance services, such as dynamic OR allocation, semi-automated documentation, or workflow support, may profit from the developed simulation environment.

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#### FUNDING

German Federal Ministry of Education and Research (BMBF)

# ENSEMBLE – DEVELOPMENT OF A SCALABLE AND MAGNETIC RESONANCE (MR)-COMPATIBLE BLOOD CIRCULATION MODEL

#### INTRODUCTION

Medical residents accompany proficient staff in the operating room and fulfill a supporting role while observing and memorizing the procedure, in order to receive training in their surgical field. During this time, they start their surgical training by performing elementary suture and cutting tasks before moving on to more complex techniques and basic operations. In order to develop their surgical skills outside of real surgeries, trainees have the opportunity to simulate procedures on phantoms or specially prepared bodies. However, for the training of catheter-based surgery, they require a training model with a realistic vascular tree and an active blood circulatory system. The project EN-SEMBLE aims to provide such models, by using CT images and automatically segmented blood vessel areas throughout the combined data set. Together with a pump and a blood-like fluid, the resulting 3D representation will be used to manufacture an artificial vascular system.

### MATERIAL AND METHODS

The segmentation of the vascular system is to be performed by a segmentation algorithm, using a set of CT images as input.

The first step towards this goal was the acquire-

ment of a sufficient amount of anonymized data, which was used for preliminary development, testing and result comparison. Afterward, the project group engaged in further research, to establish an assortment of segmentation approaches by comparing their uses and results in state-of-the-art research. After the initial research, the team focused heavily on the use of active contour models and level-set algorithms. Furthermore, an additional manual segmentation was done, which is utilized as a ground truth that the employed methods will be compared to.



Fig. 1 - Merged CT images with segmented aorta volume; upper left – coronal plane, upper right – axial plane, lower left – sagittal plane, lower right – segmented aorta model.

#### RESULTS

Through the establishment of a database for further development, multiple CT image sets are available, in which segmentation will take place. The research phase of the project concluded in an assortment of possible segmentation approaches, such as the greedy snake algorithm or the level set method of Osher & Sethian. The manual segmentation yielded a model of an aorta, visualized in Fig. 1.

#### **DISCUSSION AND CONCLUSION**

In the early phases of the project, the group was able to take the first steps towards developing an automatic 3D modeling of the vascular system through a patient's CT images. By finishing data collection, research and manual segmentation of a ground truth model, the group is now in the process of using automatic segmentation to compare their corresponding results.

#### **PROJECT TEAM**

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#### PROJECT PARTNERS

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#### FUNDING

This project has received funding from the ZIM program of the German Federal Ministry of Economic Affairs and Energy (BMWi).

# EUMFH – BIOMEDICAL INFORMATION TECHNOLOGY FOR THE EUROPEAN MEDICAL FIELD HOSPITAL

#### INTRODUCTION

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.

#### MATERIAL AND METHODS

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.

### RESULTS

Twenty-one team members have been interviewed. Fourteen of them with medical roles (physicians and nurses) and seven of them with supportive roles (Management, Logistics, or Training). Among the fourteen medical interview partners were three medical team leaders and all participants came from nine different European countries. The system was evaluated very positive.

#### **DISCUSSION AND CONCLUSION**

The evaluation of the EPR during the ModEX exercise was very successful, considering the positive user feedback. Despite this success, there were various lessons learned 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 at the beginning of 2019.

#### **PROJECT TEAM**

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#### SELECTED PUBLICATIONS

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#### FUNDING

General Directorate for European Civil Protection and Humanitarian Aid Operations: ECHO/SUB/2016/739964/PREP14



# DIGITAL PATIENT- AND PROCESS MODEL

'The growing number of medical screening options and forms of treatment for complex diseases requires more patient-specific therapy decisions and treatment processes that increase the chance of a better clinical outcome. Digital patient and process models integrated in clinical decision support systems address these problems. They represent the disease-specific therapeutic decision-making and therapy processes and are instantiated with patient-specific data for personalized medicine.'

> PD Dr.-Ing. Steffen Oeltze-Jafra (group leader)


# **SCIENTIFIC STAFF**

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# **SELECTED PUBLICATIONS**

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# INTEGRATED SYSTEM ARCHITECTURE FOR MODEL-BASED DECISION SUPPORT IN ENT

# INTRODUCTION

Computerized decision models are a necessary tool to achieve personalized medicine. Clinical decision support systems (CDSS) using these models can process information about complex diseases, like cancer, and propose different suitable treatments. Their calculations must be based on routinely recorded patient data. Working with such 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.

## MATERIAL AND METHODS

We built a modular decision support system. This system adheres to technical and clinical

standards and adopts concepts from IHE. It uses 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.

# RESULTS

We prototypically implemented our infrastructure with a decision model for laryngeal cancer. Patient data is provided by the hospital information systems (SAP i.s.h.med among others) as well as a relational data base for validation purposes. The processing and therapy calculation is realized by a server-based implementation of the SMILE engine (a framework for probabilistic



Fig. 1 - Patient-specific data and clinical knowledge integrated into decision model.

models). Different model types are stored in a model distribution system. Calculation results, e.g. TNM staging and personalized treatment options, are presented via specialized web applications.



Fig. 2 - Requirement analysis for model application.

# DISCUSSION AND CONCLUSION

This modular infrastructure allows exchanging individual modules. For instance, the same processing unit could be connected to a different clinical data base. This is especially important when translating this kind of specific decision support to clinical practice, since different clinics use different information systems. Calculated results on the other hand might be presented in another user interface, e.g., on a mobile device depending on the clinical setting.

#### **PROJECT TEAM**

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#### SELECTED PUBLICATIONS

Gaebel J, Schreiber E, Oeser A, Oeltze-Jafra S. Modular Architecture for Integrated Model-Based Decision Support. Stud Health Technol Inform 2018; 248: 108–15.

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#### FUNDING

German Federal Ministry of Education and Research (BMBF)

# STRUCTURED EXPLORATION OF LARGE CAUSAL BAYESIAN NETWORKS WITH CHANGING EVIDENCES

## INTRODUCTION

Causal Bayesian networks (CBN) are frequently applied for modeling probabilistic causal relationships between components of complex systems in various domains such as biomedicine, risk analysis, and healthcare. Instantiated with given evidences, they have the potential to infer probabilities of the unknown and are thus particularly suited for reasoning under uncertainty. Apart from their functional promises, the visual presentation of such networks is equally important. Based on their graph-based structure, Bayesian networks have a natural visual representation in node-link diagrams. Thus, one can easily recognize potential correlations between nodes by the presence of edges. However, there are still some challenges in the visual presentation of especially large graphs which are applicable to the visualization of CBNs, too.

## MATERIAL AND METHODS

To develop a more suitable visual presentation for the investigation of large CBNs, we have defined several requirements, such as maintaining the graph-based structure, patient-specific information (evidences) need to be presented sorted by their relevance of influence, and evidences can be simulated. The requirement gathering process was based on our experience with CBNs in clinical decision support and a literature review.

Based on these requirements, an interactive visual tool has been developed. The uncertainty within the nodes' states is presented through probability distribution glyphs and the investigation of local structures and causality flows within CBNs is designed by placing the parent and child nodes on the left and right side of the node for investigation, respectively. Furthermore, exploration techniques were developed to investigate the whole structure of the network.

During a one-to-one blind study with 14 participants, the usefulness and usability of the developed tool has been verified.

## RESULTS

The newly developed interactive visual presentation technique enables a structured exploration of large CBNs. The goal is to help physicians in comprehending the structure and belief propagation of the investigated CBN. Furthermore, by providing a visual depiction of all available patient information sorted by their relevance of influence on the chosen target node, the users are provided with a familiar presentation which helps generating their own mental model and, thus, helps gaining trust in the system.



Fig. 1 - Structured exploration visualization approach using a CBN for TNM staging. On the right and bottom side, meta-information of the current set of evidences and a legend are displayed, respectively.



Fig. 2 - An overview of all observed patient-specific information is given in a special presentation. The evidences are sorted by their relevance of influence on the outcome of specified target nodes, e.g., N\_state\_patient.

## **DISCUSSION AND CONCLUSION**

The representation is currently limited to the depiction of only local structures. The next step is to provide a global view of the network.

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#### FUNDING

German Federal Ministry of Education and Research (BMBF)

# THE ICCAS TUMOR DASHBOARD – OPTIMIZING INFORMATION REPRESENTATION IN MULTI-DISCIPLINARY DECISION-MAKING

## INTRODUCTION

The treatment of complex diseases like cancer is an interdisciplinary process that involves the participation of various clinical departments and experts. In multi-disciplinary team meetings – so-called tumor boards – the presentation of case-related information for the decision-making process is based on a variety of different media components ranging from specialized information systems to paper-based records. In order to provide a complete and consistent overview on the respective case, we have developed a responsive, non-stationary system that provides realtime feedback about each case on a variety of devices.

## MATERIAL AND METHODS

Prior to the technical implementation of the system, we have conducted a qualitative survey with all current tumor board participants (surgery, pathology, radiology, medical and radiological oncology) at the Leipzig University Hospital. The goal of this survey included the determination of necessary metrics for the decision-making process as well as the classification in regard of their importance. The results of the survey were then directly translated into the design and development of the application.

## RESULTS

The system is built around a component-based structure which emphasizes the integration of different specialized views that each share a unified data access. In this way, information about the state of the disease or the patient's overall condition can be linked, e.g. to diagnostic results or laboratory findings, by following an effect-to-cause relationship. The current state of the application includes four components: [1] patient overview, [2] digital patient model, [3] laboratory findings and [4] therapy process. To meet the specifications of anywhere-anytime usage, the user interface (UI) comprises a responsive design paradigm that allows the automatic scaling of UI elements based on the screen size available.

## DISCUSSION AND CONCLUSION

While currently being tailored specifically to the use case of head and neck tumor boards, the system can be adapted to a variety of scenarios that involve multi-source information clustering for clinical cases. We are currently working on the connection of the system to the hospital information system (HIS) in order to provide an optimized representation layer to preferably single-source documentation.

#### PROJECT TEAM

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#### SELECTED PUBLICATIONS

Oeser A, Gaebel J, Dietz A, Wiegand S, Oeltze-Jafra S. Information architecture for a patient-specific dashboard in head and neck tumor boards. Int J Comput Assist Radiol Surg. [Epub ahead of print]. Oeser A, Gaebel J, Müller J, Franke S. Design Concept of an Information System for the Intuitive Assessment of Laboratory Findings. 9th Workshop on Visual Analytics in Healthcare (VAHC). San Francisco, USA; 2018.

#### FUNDING

German Federal Ministry of Education and Research (BMBF)

# CROSS-ENTERPRISE MODEL SHARING

## INTRODUCTION

Sharing data across work stations, wards and healthcare enterprises is crucial for treatment efficiency and success. The IHE profile 'Cross-enterprise document sharing' (XDS) provides a standards-based specification for sharing clinical documents between healthcare enterprises. XDS supports all kinds of documents that are bound to a specific patient. Thus, documents which are not linked to a specific patient, cannot be shared via XDS. Nevertheless, there are plenty of patient-independent documents, which are worth sharing for a greater benefit.

## MATERIAL AND METHODS

To resolve this discrepancy, ICCAS developed a generalized data model within a new integration profile named Cross-Enterprise Model Sharing (XMS). XMS covers all kinds of clinical documents, irrespective of whether they are bound to a specific patient or not. Within the scope of a requirements analysis, document types available in medicine were identified and examined. All documents can be classified into four categories: segmentation models, workflow models, patient models and others. Each category contains patient-specific as well as patient-independent document types (see Fig. 1).

## RESULTS

XMS is based on the XDS architecture but expands its potential by stripping off limitations. A model source (e.g. a physician) provides new documents by registering and uploading them into a repository.

The new documents are registered in the registry and can now be queried by model consumers.



Fig. 1 - Overview of specific and abstract document types in medicine. While IHE XDS includes only patient-specific documents (blue), XMS can handle patient-independent documents (green) as well.



Fig. 2 - Scheme of all XMS actors and transactions. The Patient Identity Source is only required, when handling patient-specific document types.

In case of patient-specific documents, the patient identity source identifies the according patient. When retrieving a document, a model consumer will query the registry for a required document. The registry provides the model consumer with information about the document's storage repository and other metadata. Subsequently, the model consumer is capable of retrieving the required document directly by using the information provided by the registry (see Fig. 2).

An XMS registry contains entries referencing documents in a repository. New entries can be submitted by a repository as single entry or in a submission set together with other entries. Entries may be associated with one or more folders to group them. Furthermore, each entry belongs to a clinical affinity domain (e.g. a specific hospital) and may reference a specific patient.

## DISCUSSION AND CONCLUSION

Hence, XMS systems allow to share all kinds of clinical documents between work stations, wards or healthcare enterprises as well as communicating patient-specific data with XDS-compliant systems. XMS is further developed continuously, to be utilized in other ICCAS projects (e.g. for sharing of process models, digital patient models, anatomic models. etc.)

#### **PROJECT TEAM**

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#### FUNDING

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# INTRAOPERATIVE MULTIMODAL IMAGING

'Intraoperative imaging plays a crucial role during surgery to improve the outcomes of the operations. Innovative non-ionizing and non-invasive modalities, like hyperspectral imaging, are beneficial for patients and medical staff. Artificial intelligence approaches can significantly support the surgeon in the analysis of the non-standard images.'

> Dr. Claire Chalopin (group leader)



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## SELECTED PUBLICATIONS

Barberio M, Maktabi M, Gockel I, Rayes N, Jansen-Winkeln B, Köhler H, Rabe SM, Seidemann L, Takoh JP, Diana M, Neumuth T, Chalopin C. Hyperspectral based discrimination of thyroid and parathyroid during surgery. Current Directions in Biomedical Engineering 2018; 4(1): 399-402.

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# THE AUTOSON PROJECT: IMPROVEMENT OF A NEURONAVIGATION SYSTEM FOR NEUROSURGICAL PROCEDURES

## INTRODUCTION

The use of intraoperative ultrasound (iUS) imaging supports the neurosurgeon during brain tumor operations. The US device can be integrated into a neuro-navigation system. Such system performs the visualization of the iUS image data overlapped on preoperative image data. However, the limitations are the lack of communication between the devices and of tools for the annotation of the image data. Therefore, the purpose of the project is the development of an improved neuronavigation system.

## MATERIAL AND METHODS

Firstly, an image-based connector was developed to automatically identify the values of the US parameters set during the acquisition. These parameters, for example the probe and the image depth, are only accessible through the monitor of the US device and are variously represented using characters, digits, symbols and geometrical shapes. Therefore, an approach based on template matching was implemented. Secondly, semi-automatic tools were developed to segment the brain tumor, the ventricles and vascular structures in the preoperative MR images. Moreover, an approach to automatically enhance the brain tumor contours in the iUS data was included. It consisted in registering a brain tumor model with the iUS image data. The three tools were implemented on a research platform using MeVisLab. The latter is connected with the US device through a video connection and with the neuronavigation system using a local network.

## RESULTS

The demonstrator was tested. Firstly, the live 2D iUS images of a phantom were visualized in comparison with the corresponding slices in the preoperative CT and 3D iUS data for a given image depth. The latter was modified by the user. The visualization was not correct anymore (Fig. 1a). The connector tool detected the change and communicated the new depth to the navigation system which updated the visualization (Fig. 1b). The second test consisted in segmenting the object using the tool of the research platform (Fig. 2a). The segmentation was sent to the navigation system which displayed the contours on its monitor (Fig. 2b).

## **DISCUSSION AND CONCLUSION**

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



Fig. 1 - a) The image depths are different in the live iUS image (right upper frame) and the corresponding slices of 3D iUS and CT data (left frames); b) The change of the depth value was detected by the connector tool and communicated to the navigation system which updated the visualization.



Fig. 2 - a) Segmentation performed on the research platform; b) The segmented object was sent to the navigation system which displayed it on the monitor.

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#### FUNDING

This project has received funding from the ZIM program of the German Federal Ministry of for Economic Affairs and Energy (BMWi).

Mexican National Council on Science and Technology (CONACyT) of Mexico (Grant number: 302481)

# EXTRACTION OF BRAIN TUMOR CONTOURS IN INTRAOPERATIVE ULTRASOUND IMAGING: COMPARISION OF DIFFEERENT METHODS

## INTRODUCTION

Intraoperative ultrasound (iUS) imaging is commonly used to support brain tumor operations. The extraction of the brain tumor contour can support the surgeon in the interpretation of the iUS data. A comparison of two approaches is presented in this paper.

#### MATERIAL AND METHODS

The first approach uses registration methods. First, a tumor model is obtained by a neurosurgeon from the preoperative MR data. Second, a local registration is performed over the MR and 3D-iUS images using different similarity measures (NGF, LC2) and rigid and affine transformations. Finally, the tumor model is aligned with the 3D-iUS data and its contours are shown. This approach was performed in MeVisLab and the ImFusion Suite (Fig. 1 left and middle).

For the segmentation approach, we used an Interactive Segmentation tool integrated in the ImFusion Suite. Here, we put landmarks in the brain tumor and the background, and then run the integrated algorithm to obtain the segmented tumor (Fig. 1 right).



Fig. 1 - Segmentation of brain metastasis of six patients using the three proposed methods in 3D-iBmode and 3D-iCEUS data. The ground truth is depicted in green and the obtained tumor contour result in red.

## RESULTS

The three methods were evaluated on datasets of 33 patients with glioblastoma and 33 patients with metastasis, including 3D-iBmode and 3D-iCEUS data. The brain tumors extracted with the algorithms were compared with manual extractions using the Contour Mean Distance (CMD) and the Dice Similarity Index (DSI).

US Image	Initial	Image Registration (MeVisLab)	Image Registration (ImFusion Suite)	Interactive Segmentation (ImFusion Suite)
3D-iBmde Metastasis	0.5253	0.7713	0.6022	0.8374
3D-iCEUS Metastasis	0.4781	0.7359	0.5477	0.8357
3D-iBmode Glioblastoma	0.4612	0.6814	0.5349	0.8515
3D-iCEUS Glioblastoma	0.4215	0.6506	0.5301	0.8276

Fig. 2 - Average DSI for every method. For the image registration approaches, the DSI was calculated before and after registration, and only the results obtained with the rigid transformation are presented.

## **DISCUSSION AND CONCLUSION**

The interactive segmentation method is more robust and has a lower computing time than the registration approach. However, it is not automatic. On the other hand, the NGF similarity measure used in MeVisLab is more robust than the LC2 used by the ImFusion Suite.

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#### FUNDING

National Council on Science and Technology (CONACyT) of Mexico (Grant number: 819157)

# AUTOMATIC 2D BRAIN TUMOR SEGMENTATION USING INTRAOPERATIVE PERFUSION ULTRASOUND DATA AND THE UNET ARCHITECTURE ON DCNN

## INTRODUCTION

Intraoperative Ultrasound (iUS) imaging is standardly performed to support the surgeon in the visualization of brain tissue during brain tumor operations. US perfusion consists in recording the flow of a US contrast agent through the tumor. The area including the brain tumor is needed for a further analysis. Many brain tumor segmentation methods have been proposed in preoperative Magnetic Resonance (MR) data. Deep Convolutional Neural Network (DCNN) is one of the most powerful computer vision techniques. It has been directly inspired by the classic notions of simple and complex cells in the visual neuroscience. Recently, new DCNN architectures are emerging and are establishing themselves at the forefront of image segmentation.

## **MATERIAL AND METHODS**

The UNet architecture was originally proposed by Ronneberger et al. It consists of a special encoder-decoder network. The encoder network takes raw inputs and extracts representations of features using four modules. Each module is formed by two serial 3x3 convolutional layers and one 2x2 maxpooling operation. In order to extract the most relevant features, a dimensional reduction (stride 2) is involved. The extracted features of each module become the input of the next module, the final output of the encoder network is the output of the decoder network. Moreover, the decoder network is composed of four new modules, each module contains the first layer, a 2x2 upsampling operator. This operator increases the map size by a factor of 2, followed by two 3x3 convolutions. The last layer of each module is convoluted with the output module having the same size level than the encoder network. This is done four times for each map that has the same size. At

the final layer, a 1x1 convolution is used to map each feature vector to the wanted number of classes. This description is presented in Fig. 1.



Fig. 1 - UNet Architecture. Applied to brain tumor segmentation using perfusion ultrasound image data.

## RESULTS

The input iUS perfusion images and their corresponding ground truth were used for the network training and validation. The Nesterov Adam optimizer (Nadam) was implemented in Keras with Tensorflow as backend scheme. The error was computed pixel-wise over the final feature map by means of the binary cross-entropy loss function. Acceptable results were obtained with a pixel level accuracy of 72.63% using one k-fold cross-validation. The result is presented in Fig. 2.



Fig. 2  $\,$  - (a) Intraoperative US image, (b) Ground truth of US image, (c) Results obtained.

## DISCUSSION AND CONCLUSION

The UNet architecture achieved a satisfactory performance for the segmentation of the brain tumor in the iUS perfusion images. As future work, perfusion parameters derived from dynamic contrast-enhanced iUS perfusion will be used to improve the results.

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#### FUNDING

Mexican Council of Science and Technology (CONACyT), PhD grant number 455203.

# AUTOMATIC DETECTION OF SKIN PERFORATORS IN INFRARED THERMOGRAPHY USING UNSUPERVISED CLASSIFICATION METHODS

## INTRODUCTION

In reconstructive surgery the intraoperative mapping of the blood vessels (perforators) supplying a particular skin region supports the surgeon in the selection of the graft. Dynamic infrared thermography (DIRT) has several advantages over currently used invasive imaging modalities. After the application of a short and mild cooling to the skin area, the rewarming reveals the perforators on the DIRT recording. Automatically identifying and highlighting these perforators can speed up and increase the confidence of decision-makings.

## MATERIAL AND METHODS

The clustering of the perforators is performed in several steps: 1) Pre-processing of videos, such as image stabilization and smoothing. 2) The segmentation of the cooled region of interest (ROI), shown on Fig. 1. 3) Clustering the ROI using the unsupervised K-means algorithm. Two reheating parameters derived from the time-temperature curves (TICs) in DIRT were used as features: the first derivative of the TIC taken at the start of the rewarming period and the integral of temperatures of the first 25 seconds. 4) Identifying the cluster(s) containing the perforators with the maximal regions' mean temperature.

## RESULTS

Fig. 1 shows one example of a mask (right) created from an IR image extracted in the video after cooling (left). The task was challenging, as clothing and surgical equipment were present. Fig. 2 shows the result of the clustering (middle) of a DIRT video (left) and the clusters selected that are most likely to contain the perforators (right). The edges of the ROI exhibit strong reheating which were falsely identified as perforators. The developed algorithms were tested on a randomly selected set of 20 DIRT videos.



Fig. 1- Segmentation of the cooled skin area (right) depicted in the DIRT video (left).



Fig. 2 - Results of the K-means classification to extract the perforators. The arrows show examples of perforators.

## DISCUSSION AND CONCLUSION

The segmentation step separated the cooled ROI from the rest of the video very well. While the current clustering approach produces promising results, its main shortcoming is its low specificity. Perforators are not always identified individually, but often only as part of larger areas. Moreover, the problem of selection of the ROI edges should be addressed. Different machine learning approaches will be tested in the future. **PROJECT TEAM** 

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## FUNDING

ERASMUS+ Traineeship

# EVALUATION OF HYPERSPECTRAL IMAGING (HSI) FOR THE MEASUREMENT OF ISCHEMIC CONDITIONING EFFECTS OF THE GASTRIC CONDUIT DURING ESOPHAGECTOMY

## INTRODUCTION

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. Previous methods used for the analysis of preconditioning concepts in patients and animal models have shown several limitations.

## **MATERIAL AND METHODS**

Intraoperative hyperspectral images of the gastric tube through the mini-thoracotomy were recorded from 22 patients, 14 patients underwent laparoscopic gastrolysis and ischemic conditioning of the stomach with two-step transthoracic esophagectomy and gastric pull-up with intrathoracic anastomosis after 3 to 7 days. The tip of the gastric tube (later esophago-gastric anastomosis) was measured intraoperatively with HSI (Fig. 1). The analysis software provides an RGB image and four false color images representing physiologic parameters. These parameters are tissue oxygenation (StO2), perfusion- (NIR Perfusion Index), organ hemoglobin- (OHI) and tissue water index (TWI). A circular region of 25 mm diameter around the later anastomotic site was analyzed for each patient and tissue parameter.



Fig. 1 - RGB image with marked ROI at later anastomosis location (left) and false color image of tissue oxygenation (right).

## RESULTS

Intraoperative HSI of the gastric conduit was possible in all patients and did not prolong the regular operative procedure due to its quick applicability. HSI showed significant differences in tissue oxygenation of gastric sleeves between patients with and without ischemic conditioning (StO2<sub>Precond.</sub> = 78%; StO2<sub>NoPrecond.</sub> = 66%; p = 0.03) (Fig. 2). Also the NIR Perfusion Index showed clear differences for both patient groups (NIR<sub>No-Precond.</sub> = 62%; NIR<sub>Precond.</sub> = 68%).



Fig. 2 - Distribution of the index average inside the ROI among patients with and without ischemic preconditioning for tissue oxygenation (left) and NIR Perfusion Index (right).

## DISCUSSION AND CONCLUSION

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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#### SELECTED PUBLICATIONS

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## FUNDING

This project has received funding from the ZIM program of the German Federal Ministry for Economic Affairs and Energy (BMWi).

# MULTIPARAMETRIC SPECTRAL PATIENT IMAGING – ASSESSMENT OF PATIENT STATUS BASED ON CONTACT-FREE AND NON-INVASIVE MEASUREMENT OF CUTANEOUS PERFUSION AND SURFACE MOISTURE BY USING HYPERSPECTRAL IMAGING

## INTRODUCTION

The assessment of peripheral artery occlusion situation and the correct and clear estimation of patient status contribute significantly to the patient safety. In the SPIN project a camera-based system was developed to detect patient status information by including HSI information.

## MATERIAL AND METHODS

We used a non-invasive hyperspectral imaging system (TIVITA, Diaspective Vision GmbH) working in visible and near infrared spectral range to measure the patient status. The camera system is designed for optimal mobility in the clinical domain. The camera system is combined with an intraoperative workstation to process the received imaging data. The absorbance spectra as well as the HSI-perfusion-parameter values (tissue haemoglobin index, oxygen saturation, near-infrared perfusion, and tissue water index) were analyzed in different medical applications: the measurement of organ perfusion and cutaneous moisture. Together with the departments of anesthesia (changes of tissue perfusion after anesthesia during surgeries), ENT (patients with gustatory sweating) and angiology (peripheral skin perfusion of patients with circulatory disorder) the applicability of HSI was investigated to improve the treatment of the patients.

## RESULTS

ENT: Patients with gustatory sweating showed a higher perfusion in the sweating face area after stimulation. The moisture was not measureable with the HSI camera system.

Anesthesia: First recordings showed that the perfusion of organs was correctly visualized during surgeries (Fig. 1).

Angiology: Patients with circulatory disorders were examined. The calculated perfusion-indices showed differences between healthy and diseased areas.



Fig. 1 - Setup to evaluate the hyperspectral imaging system in a clinical environment (here: during a visceral surgery).

## DISCUSSION AND CONCLUSION

The reliability of this non-invasive and contact-free monitoring system for perfusion was demonstrated. The camera system may characterize the peripheral artery occlusion fast and objectively to support physicians in daily routine. During surgeries this technology provided a fast and accurate imaging technology to perfectly show the perfusion. Albeit, in the case of gustatory sweating the surface moisture was not measurable with the HSI camera system. In our study we could only measure the increase of perfusion in the examined area.

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#### SELECTED PUBLICATIONS

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#### FUNDING

This project has received funding from the ZIM program of the German Federal Ministry for Economic Affairs and Energy (BMWi).

# SUPERVISED TISSUE DISCRIMINATION DURING THYROID AND PARATHYROID SURGERY BASED ON HYPERSPECTRAL IMAGING

## INTRODUCTION

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 surgery. 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).

## MATERIAL AND METHODS

HSI data of 7 patients were acquired during open neck surgeries. Those resemble 3D data that includes spectral (500 – 1000 nm) and spatial (640 x 480 pixels) information. 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 neighbors (kNN) and Neural Networks. Each model was then tested on the classification of HSI data of two patients who have both glands present.

## RESULTS

More than 30,000 and nearly 4,000 spectra of the thyroid and parathyroid were used for the training and test of the classification methods. The best performing algorithm was SVM with a linear kernel. The overall accuracy of the method was 95.77 %. Tab. 1 shows the results of sensitivity, specificity and accuracies of the thyroid, parathyroid and muscle during the testing of the model. Fig. 1 shows the results of the classification for the two patients. The computing time was 0.33 s and 0.36 s.

	Thyroid	Parathyroid	Muscle
Sensitivity (%)	90.4	91.8	94.3
Specificity (%)	98.1	98.2	99.3
Accuracy (%)	<mark>96.9</mark>	97.2	98.5

Tab. 1 - Performance of the Support Vector Machine (SVM) algorithm for the classification of the thyroid, parathyroid and muscle based on hyperspectral imaging (HSI) data.

## DISCUSSION AND CONCLUSION

Machine learning methods are suitable to automatically discriminate thyroid and parathyroid using HSI. The computing time is acceptable for intraoperative use. The visualization of the classification results can be improved by smoothing the labeled classified regions. The performance of leave-one-patient-out testing has to be estimated. This would resemble realistic operation conditions where the patient's data is totally unknown.



Fig. 1 - Result of the classification of the HSI data of two patients using SVM. The colors depict: purple-thyroid, pink-parathyroid, green-muscle.

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#### FUNDING

Erasmus+ Traineeship



## INTRODUCTION

Hyperspectral imaging (HSI) is a non-invasive optical technique that shows potential to aid pathologists in cancer tissue diagnoses. In this study, cancer tissues from different patients were imaged by an HSI system to detect spectral differences between normal, metaplasia and esophageal adenocarcinoma (EAC) tissues (Fig. 1). It is important to distinguish between EAC and Metaplasia, because EAC involves cancer tissue, while Metaplasia is associated with an increased risk of cancer. Therefore, an automatic tool could help pathologists to get a good diagnosis for prevention and treatment. Tissue classification is performed using recurrent neural networks (RNN).

## MATERIAL AND METHODS

The tissue approach is performed through four stages. (1) Data collection: the pathologists acquired HSI data of 46 patients' samples and annotated the tissues (normal, metaplasia and EAC). (2) Database generation: the absorbance spectra corresponding to the three tissue classes were extracted from the HSI data, getting normal = 74,000, metaplasia = 5,727 and EAC = 333,275 spectra samples, using 5,727 from each class to train the network. (3) RNN implementation: We have developed an architecture using Long Short-Term Memory (LSTM) neural networks which are a special kind of RNN (Fig. 2). This kind of neural networks is very used in sequence prediction (or sequence learning) problems. (4) Finally, new data will be used to test the performance of the system.



## RESULTS

The proposed neural network provides with the current architecture accuracy values of 89.35% in Normal vs EAC-Metaplasia and of 91.18% in EAC vs Metaplasia tissue classification respectively. These results are the average of 10-folds cross validation process. This metric is used to give us an idea of the performance of LSTM architecture to classify these kinds of data (Fig. 2).

## DISCUSSION AND CONCLUSION

It is necessary to perform more tests to obtain the best architecture of the networks. Then, the real performance of the algorithms will be evaluated using the sensitivity. Finally, a tool to classify the HIS data of unknown samples and to visualize the results has to be implemented.

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Fig. 2 - Architecture implemented.

Fig. 1 - Absorption spectrum of each tissue

# LYSIS PROJECT: DEVELOPMENT OF A LAPAROSCOPIC HYPERSPECTRAL IMAGING SYSTEM

## INTRODUCTION

Laparoscopic procedures are essential for modern surgical oncology and visceral surgery. However, the field of view is limited in minimal invasive methods and the recognition of anatomical risk and target structures depends on the surgeon's expertise. Several imaging methods have been established to support these complex procedures in clinical routine. Ultrasound is used for the intraoperative identification of lesions, but is not suitable for the inspection of hollow organs like the intestine. Further methods involve the use of contrast media, which should be avoided if possible. Hyperspectral imaging (HSI) is a new method in medicine which showed promising results for the detection of anatomical structures and the evaluation of tissue perfusion in visceral and thoracic clinical research. HSI combines spectroscopy with imaging and enables contactless chemical analysis of tissue areas without the need of contrast media.

## MATERIAL AND METHODS

The aim of this project is the development of a new laparoscopic imaging prototype to support the identification of risk structures and lesions intraoperatively and non-invasively based on HSI technology in visceral and thorax surgery. Beside the construction of the laparoscopic system, machine learning classification approaches will be implemented to automatically recognize organs and tissue. Also, visualization approaches to optimally display the HSI data and the extracted structures in the videos have to be developed. The obtained prototype will be evaluated on ex-vivo tissue samples resected during patient operations.

The LYSiS project has a budget of 1 million Euro. It started on October 1st, 2018 and will last three years.

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## FUNDING

This project has received funding from the KMU-Innovative program of the German Federal Ministry of Education and Research (BMBF).



Fig. 1 - Schematic overview of the intraoperative estimation of tissue perfusion with laparoscopic hyperspectral imaging.



# COMPUTER-ASSISTED IMAGE-GUIDED INTERVENTIONS

'ICCAS researches on new technologies for imageguided procedures and therapeutic assistance systems in the field of MRI-guided and non-invasive interventions – MR-guided endomyocardial biopsy – novel application of focused ultrasound (FUS) under the guidance of magnetic resonance therapy (MRgFUS) – robotic-assisted MRgFUS and interventional techniques under PET-MRI guidance – combined FUS and radiation therapy to support the treatment of cancer (SONO-RAY, BMBF project).'

> Prof. Dr. Andreas Melzer (group leader)



# **SCIENTIFIC STAFF**

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Chalopin C, Landgraf L, Melzer A, Neumuth T, Oeltze-Jafra S, Salz P. Was gibt es Neues in der computerassistierten Chirurgie? In: Jähne J, Königsrainer A, Schröder W, Südkamp N: Was gibt es Neues in der Chirurgie? 2018; 51-68.

# 1 META CENTER FOR INNOVATION COMPETENCE (ZIK) BETWEEN ICCAS (LEIPZIG) AND ONCORAY (DRESDEN):

SONO-RAY – Combination Therapy of MR-Guided Focused Ultrasound-Hyperthermia (FUS-HT) and Radiation Therapy (RT) for the Treatment of Cancer | project part ICCAS

## INTRODUCTION

Image-guided procedures gain more and more clinical acceptance, especially in the field of cancer diagnosis and treatment. The imaging via ultrasound (US), X-ray computed tomography (CT) or magnetic resonance tomography (MRI) allows for minimal- and non-invasive procedures like biopsies, thermal ablation, embolization as well as minimally invasive surgery. The imaging leads to smaller incisions and thus reduces side effects like inflammation and shortens the time of hospitalization.

Focused ultrasound or high intensity focused ultrasound (FUS/HIFU) describes a unique technique using ultrasound beams to heat a target tissue inside the body in a totally non-invasive way. In contrast to diagnostic ultrasound imaging, a special form or e.g. an array of multiple transducers submit a large number of ultrasound waves into the focus point. The ablation of tissue using HIFU is already approved by the Food and Drug Administration (FDA) for the treatment of benign tumors of the uterine, of prostate carcinoma, in palliative treatment of bone metastasis and for therapy of essential tremor. During these procedures, treatment planning and control can be performed either by US-guidance or by MRI-guidance (MRgHIFU). In 2016, the MRgHIFU system Sonalleve (Profound medical), funded by ICCAS, was installed at the Leipzig University Hospital. Fourteen patients with uterine fibroids were treated in 2018 in Leipzig as teamwork of interventional radiology and gynecology. Furthermore, the first desmoid tumor was successfully treated with MRgHIFU. At the side of our project partner OncoRay in Dresden, the transurethral ultrasound system TULSA-PRO (Profound medical) was successfully installed into the clinical PET/MRI. In 2018, the progress of the SONO-RAY project at ICCAS in Leipzig included the further investigation of radiosensitizing effects of FUS-induced hyperthermia in vitro and the development of a next generation in vitro cell applicator together with Fraunhofer IBMT (St. Ingbert). In collaboration with oncology in Leipzig (Prof. Lordick, Prof. Hacker), first tests for immunostimulating events caused by FUS are underway.

For the realization of in vivo treatment in the SONO-RAY project in Leipzig, an MR-compatible small animal FUS probe was investigated in different preclinical MRI scanners in cooperation with Helmholtz Center (HZDR) and Fraunhofer IZI located in Leipzig. First steps for real-time MR-thermometry were implemented by a new postdoc. With regard to a clinical translation of observations in the SONO-RAY project new concepts for robotically assisted FUS treatment combined with radiation treatment were evolved.

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#### FUNDING

German Federal Ministry of Education and Research (BMBF)

# 1.1 RADIOSENSITIZATION OF CANCER CELL LINES BY FOCUSED ULTRASOUND HYPERTHERMIA IN VITRO

## INTRODUCTION

Hyperthermia describes the heating of tumor cells to temperatures ranging between 41-46°C. Radiosensitizing events like the reduction of non-oxygenated hypoxic tumor areals or a triggered drug uptake caused by hyperthermal heating were detected in different preclinical studies. Currently, there is no device for hyperthermia used in clinical routine based on the lack of real-time temperature control and heating which is only limited to the target region. In this context, image-guided focused ultrasound is for the first time a relevant method to generate hyperthermia precisely and non-invasively in the tumor region. Based on that knowledge, goals in Sono-Ray are the detection of optimal temperature for a pleasant short heating period but leading to radiosensitizing effects on cancer cell lines in vitro while avoiding necrosis. Furthermore, the impact of the time regime between the two treatment modalities FUS-induced hyperthermia and radiation (RT) needs to be investigated.

#### MATERIALS AND METHODS

Human head and neck (FaDu), glioblastoma (T98G) and prostate carcinoma (PC-3) cell lines were cultured in special ultrasound-penetrable 96-well cell culture plates (Greiner bio one GmbH, Germany) for high throughput FUS treatment. They were cultured in the desired medium in an incubator at 37°C and 5% CO2. To generate FUS hyperthermia in the well plates an existing FUS in vitro system (Imsat, Dundee) with a customized 1.14 MHz single transducer made by piezoelectric ceramic materials (Meggitt-Ferroperm Piezoceramics, Kvistgaard, Denmark) was modified to sonicate 3 wells in parallel at the acoustic intensity of 214 W/cm<sup>2</sup>. The transducer was mounted into a water container with circulating degassed water and a temperature of 34°C to avoid overheating. In preliminary studies, the target temperature of 45°C was the most homogenous temperature which could be held for a desired duration. Labview (National Instruments, Newbury, UK) and a motion system (VELMEX Inc., Bloomfield, NY, USA) were utilized to control the movement of the plate. An infrared thermal camera (PI450, Optris GmbH, Germany) and imaging software (PI connect version 2.10) monitored the temperature inside the wells in real time during FUS-HT treatment. A feedback loop from the camera to the motor enabled translation of the plate when the temperature reached the desired target. Hyperthermia in a thermal cycler (Mastercycler gradient, Eppendorf, Germany) worked as a control for the comparison of mechanical effects of FUS-HT and HT alone. To determine optimal temperatures of HT for radiosensitization and to analyze effects of different combinatorial time regimes, HT in the thermal cycler was performed at 43 and 45°C, for 30 and 60 min and with a time interval between HT and RT of 5, 60, 120, 240 and 360 min. Irradiation of cells in vitro was performed with an X-ray tube (DARPAC 150-MC) at a single dose of 10 Gy at Leipzig University Hospital. Cellular NAD(P)H levels (WST-1 assay, Roche Diagnostic GmbH) as a marker for cell viability and morphology analysis were evaluated 24, 48 and 72 h after treatment. Statistical analysis was done using one way-ANOVA with statistical significance at p<0.05 for three independent experiments.

## RESULTS

The combination of hyperthermia and radiation led to a significant reduction of cell viability (n=3, p<= 0.05) in all cell lines compared to RT alone. 72 h after the combination of thermal cycler HT+RT (60 min interval) the cell viability was decreased to 55 % (FaDu), 27 % (T98G) and 59 % (PC-3) (Fig. 1). The combination of FUS-HT + RT reduced the cell viability to 78 % (FaDu), 52 % (T98G) and 45 % (PC-3) (Fig. 2). In contrast, RT alone only led to a low reduction in cell viability to 84 % (FaDu), 64 % (T98G) and 75 % (PC-3). With regard to the optimal time sequence between HT treatment and RT a trend towards a shorter time interval of only 5 min could be observed (Fig. 1 (c)). However, this finding was not significant (n=3).

## **DISCUSSION AND CONCLUSION**

Our in vitro results suggest that a combination of FUS-HT and RT had additional benefits on head and neck, prostate cancer and glioblastoma cell lines compared to RT alone. The data suggest that a shorter interval time between the two treatment modalities may be more effective, which would be highly relevant for translation into the clinic. The less effective FUS-HT-RT in contrast to thermal cycler HT-RT is probably caused by non-constant heating in the currently applied FUS setup. There is a need for new in vitro systems, which allow simultaneous and homogenous heating in wells of a 96-well plate for high throughput molecular analysis. Such an innovative system was under development together with Fraunhofer IBMT and will be tested in 2019. Interestingly, glioblastoma is more sensitive to the thermal treatment than to irradiation, which needs to be clarified in future experimental work. The strong decrease in cell viability in all co-treated groups is probably caused by the impact of HT on DNA damage repair mechanisms, most likely due to protein denaturation caused by heating. The detailed underlying mechanisms need to be investigated in the future, in vitro as well as in vivo analysis will be performed in 2019 at ICCAS.



Fig. 1- Impact of different hyperthermia (HT) temperatures, treatment time and time regime during combination of HT and radiation therapy (RT) on the cellular NAD(P)H level of human head and neck (FaDu), prostate carcinoma (PC-3) and glioblastoma (T98G) cell lines 72 h after treatment. Relative cellular NAD(P)H levels were detected by a WST-1 assay. Combination of HT at 45°C for 30 min and RT with a variation of the time interval between HT and RT. Data were normalized to control values (no treatment), which were set to 100% NAD(P)H level.





120

FUS-HT+RT





Fig. 2 - Radiosensitization of human carcinoma cell lines by focused ultrasound hyperthermia in vitro. Human head and neck (FaDu), prostate carcinoma (PC-3) and glioblastoma (T98G) cell lines were seeded in ultrasound penetrable 96-well plates. FUS-HT was induced using an 1.14 MHz single transducer at the acoustic intensity of 214W/cm<sup>2</sup>. Target temperature was 45°C for 30 min which was controlled by a thermal camera. RT was performed with an X-ray tube at a single dose of 10 Gy. Cellular NAD(P)H levels were measured 24, 48 and 72 h after treatment. Data were normalized to control values (no treatment), which were set to 100% NAD(P)H level; n= 3, \*p< 0.05; \*\*p<0.01; #p<0.001; ##p< 0.001.

# 1.2 COMBINATION OF FOCUSED ULTRASOUND-INDUCED HYPERTHERMIA AND RADIATION IN VIVO USING PRECLINICAL MRI

## INTRODUCTION

Additionally to the investigation of molecular mechanisms of the radiosensitizing events occurring during FUS- hyperthermia in vitro a major goal in the Sono-Ray project is the analysis of effects of FUS-HT on the tumor microenvironment and the tumor growth after combination therapy of FUS-HT and RT in vivo. For MRIguided FUS-HT of human head and neck and prostate carcinoma tumors in a mouse model, an MRI-compatible FUS transducer needs to be installed in a preclinical MRI system. For non-invasive temperature control during the procedure temperature mapping based on the proton resonance frequency shift (PRF) thermometry needs to be realized in a small animal MRI or PET/MRI system.

## MATERIAL AND METHODS

Together with Fraunhofer IBMT a small animal MRI-compatible array transducer with 11×11 elements at a frequency of 960 kHz and aperture size of 10 mm x 10 mm was developed. For testing of MRI compatibility different spin and gradient echo sequences in a 1 T preclinical PET/MRI (Mediso Medical Imaging Systems, Hungary; at Helmholtz-Zentrum Dresden-Rossendorf, Institute of Radiopharmaceutical Cancer Research, Leipzig), in a 7 T preclinical MRI system (Bruker Corporation, USA; at Fraunhofer Institute for Cell Therapy and Immunology IZI, Leipzig) and in a clinical 3T MRI scanner (Philips GmbH, Germany; at Leipzig University Hospital) were measured. Bottle phantoms including water or agar were placed in the rat bed with rat body coil in the small animal systems or in the head coil of the clinical scanner.

PRF thermometry is implemented in clinical HIFU systems like the Sonalleve system (Profound medical). First steps towards real-time temperature mapping in the 7 T Bruker system were realized. An agar-milk phantom was heated via a warm water pad. During the heating and cooling period the temperature was monitored with the thermocouple of the Bruker system, and for reconstruction of MRI data in MATLAB images were acquired every 3 minutes ("T1\_FLASH" gradient echo sequence, Slice thickness = 1mm, inter-slice distance = 0.5 mm, Field of view (FOV) = 4.4 cm, Number of slices = 8, Echo time (TE) = 4.5 ms, Repetition time (TR) = 100 ms, matrix = 128×128).

## RESULTS

The in vivo transducer could be successfully installed into all three MRI systems. MRI measurements revealed some artifacts which are probably caused by antenna effects of the transducer electronics in the 3T clinical Philips and 7T preclinical Bruker scanner (Fig. 1). However, in the 1T preclinical Mediso PET/MR scanner, no images could be acquired when the transducer was present.

For temperature mapping, phase matrices from individual slices are calculated in MATLAB. It is known from two-dimensional (2D) Fourier analysis of signals that the phase of a complex number is normally wrapped onto the range of  $(-\pi,\pi)$ which does not reflect the true relative phase values across space. Thus, phase unwrapping is required before calculating the temperature difference ( $\Delta$ T). Here, Goldstein's brunch cut algorithm is used for 2D phase unwrapping from MR k-space raw data (Fig. 2).

## DISCUSSION AND CONCLUSION

So far, a platform consisting of an MR-compatible FUS-transducer allowing for hyperthermia in vivo was successfully installed in a 7T preclinical MRI in Leipzig. Further modifications of the transducer will be done to reduce artifacts generated by the array transducer. First steps for PRF thermometry calculation were performed and reconstruction of the data started. To enable real-time temperature mapping for MRg-FUS and RT combination treatments in vivo in the future more data need to be acquired using a mouse agar-milk phantom.



Fig. 1 - Measurement of the in vivo transducer in different MRI scanners. Transducer fixed to a 1.5 I water bottle phantom in the head coil of 3T Philips human MRI scanner. Gradient echo (T2W\_FFE), TE: 15 ms, TR: 200 ms. Transducer fixed to a phantom (agar and Lego) in the rat body coil of 7T Bruker MRI scanner. Sequence gradient echo (T1\_FLASH), TE: 15 ms, TR: 440 ms. White arrow shows position of the transducer.



Fig. 2 - Reconstruction of MRI data to enable non-invasive temperature mapping during in vivo FUS-HT. An agar-milk phantom with a thermocouple was placed into the rat bed of the 7 T Bruker MRI with a water heating pad. Reconstruction steps of phase images for temperature mapping based on PRF thermometry.

# 1.3 IN SILICO MODELING OF EFFECTS OF A COMBINED FUS-HT AND RT TREATMENT

## INTRODUCTION

Simulations of the cell behavior and growth under given circumstances allow for a better comprehension of the effects of hyper-thermal temperatures and radiation in cancer treatment. Mathematical models were already presented in the past, to examine and predict the

effects of heat on tumor cells. The most commonly used approach for this may be the Arrhenius model in combination with the calculation of t 43 equivalent minutes. Additionally, the Linear-Quadratic model provides good results in calculating the surviving fractions of cell cultures under given radiation doses. Yet, the research of combined therapies for ultrasound and radiation is still in an early stage of progress. Due to the sparse knowledge of the effects of such a combined treatment on the many different tumor cell types, only a few attempts could be made to combine both properties in an in silico model. Recently, an approach was presented to combine the two models for heat and radiation into a single one. Further developments in this domain pose great possibilities to improve predictions for cell behavior under specific circumstances and therefore the outcome of cancer treatment.

## MATERIALS AND METHODS

The previously defined framework for a cellbased simulation approach shown in Fig. 1 was implemented in a first cellular automaton version.

Similar to the work of Brüningk et al. 2018, cellular growth is calculated on a 2D or 3D regular grid, where for each cell the known cycle of G1, S, G2, and M states are simulated. During mitosis (M state), cells can proliferate into the 3rd-degree neighborhood, alternating between von Neumann and Moore neighborhood for a circular growth pattern. The direction of growth is chosen randomly for each cell division. Tumor cells go into arrest (additional state GO) and therefore stop division if all neighbors are occupied. Not taking into account any further properties like e.g. oxygenation, these first growth simulations result in a quadratic growth of cells in the 3rd-degree border of the tumor. Cell cycle times were adjusted according to example cell types from literature. Based on the work of Brüningk et al. (2017) as well, the OncoRay Team in Dresden provided a model for a combination of radiation and temperature to emulate a treatment with specific heat, radiation and time parameters. This model was included in the therapy calculations of the cellular automata. The implementation was done using C++ and parallelized with the OpenMP framework for parallel programming. Simulations were conducted in an exemplary 2D grid with a size of 100x100 and 500x500 elements with varying growth and treatment parameters and visualized with MatLab.



Fig. 1 - Calculation procedure for the cell simulation consisting of a growth and a therapy loop.

#### RESULTS

Results of both 100x100 and 500x500 sized calculations can be seen in Fig. 2. Both the amount of cells and their respective state after the last time step in the growth loop as well as after treatment with different temperature, radiation and time are visualized.



Fig. 2 - Cellular automata simulations on 100x100 and 500x500 grid size. Each grid element represents a cell, color-coded in its respective state (G1 - 1800s, S- 4800s, G2- 1500s, M- 900s). Treatment was simulated with 2 Gy radiation and 46°C hyperthermia for 10 min. a) Cells after growth in 100x100 grid. b) Cells after treatment in 100x100 grid. c) Cells after growth in 500x500 grid. b) Cells after treatment in 500x500 grid.

## DISCUSSION AND CONCLUSION

The presented cellular automaton is able to simulate a simplified cell growth (quadratic proliferation) and treatment outcome for different cell types and treatment modalities. It provides a solid base for further development to adjust the parameters for more realistic calculations. Factors like the amount of available oxygen and proliferation cycles before and after treatment, measured in experiments have to be taken into account.

# 1.4 CONCEPTS FOR ROBOTIC GUIDED FOCUSED ULTRASOUND HYPERTHERMIA AND RADIATION THERAPY IN THE CLINIC

## INTRODUCTION

Robotic systems become more and more important in medicine because they provide precise and reproducible positioning of surgical tools and equipment. In this context, robotic systems are used in clinics to assist, for example, during biopsies and ablation treatment. Regarding the non-invasive therapy applying FUS/HIFU in combination with radiation therapy for treatment of tumors at various locations or moving organs a precise positioning of the transducer is crucial for the efficacy and safety. Available HIFU systems like Profound Sonalleve only allow the treatment in very specific regions and are an uncomfortable procedure to realize a combination of FUS-HT and RT. Hence, a robotic arm positioning the FUS system according to the treatment planning is more versatile. For further studies on combined FUS-RT treatment. the robotic arm system needs to be integrated into existing clinical infrastructures like a PET-MRI system or radiation room.

# MATERIALS AND METHODS

To apply a combination of FUS-hyperthermia and RT (i) a robotic workflow consisting of an ultrasound-guided FUS system needs to be integrated into the radiation room or using MRI guidance into (ii) MR-guided radiation devices (e.g. MR-linac, Elekta).

To improve the usability and reduce complexity, collaborative robotics will be used to install a dual-arm robot setup (i). First evaluations were conducted with a mobile platform, utilizing a KUKA LBR iiwa 7 robotic arm and a Clarius L7 wireless ultrasound probe (Fig. 1) for the use case of ultrasound-guided biopsies. Touch gesture interaction concepts as well as a phantom study with 9 participants of varying technical and clinical expertise were performed. Vendor-independent communication with other devices was achieved using the surgical device communication protocol (SDC).

The realization of a FUS-RT combination in a PET/MRI-guided setup (ii) was achieved in Leipzig by integrating a PET/MR-compatible robot (InnoMotion by InnoMedic GmbH) into a Biograph mMR PET/MRI system (Siemens Healthineers) (Fig. 2). By virtualizing the hardware containing the planning software of the robotic arm with an Oracle VirtualBox, the system was successfully integrated into the clinical infrastructure. Placing the virtual machine on the post-processing and data storing Linux server attached to the PET/MRI system, image data can be transferred easily to the planning software which acts as a DICOM receiver.

## RESULTS

Regarding the first concept (Fig. 1 (a)) for US-guided FUS in a clinical radiation room based on use case-guided biopsies, the mean time for the localization of the target was 24 seconds and the mean time to hit the target was 42 seconds in case of the unassisted intervention. During the assisted procedure the mean time to plan the intervention was 23 seconds and the mean time to adjust the needle guide and hit the target was 51 seconds. Unassisted, the participants had to insert the needle two times on average to successfully hit the target, whereas the participants hit the target on the first needle insertion during the assisted intervention. The participants rated the needle guidance as an improvement of the workflow and rated the interaction concept as intuitive.



Fig. 1 - Concept for collaborative robot-guided focused ultrasound hyperthermia and radiation (a) and usability of a KUKA LBR iiwa 7 robotic arm with wireless ultrasound imaging probe (b). Touch gesture recognition tests of four touch gestures (Double Taps and Pushes) resulted in a total accuracy of 89.8% (c).

First steps for MR-guided FUS-HT and RT were made by successful modification of the MR-compatible Innomotion arm to fit in the Biograph mMR MR-PET system (Fig. 2 (a)) and the robotic arm system was integrated into the clinical IT infrastructure.



Fig. 2- Integration of the robotic arm into the MR-PET system (a). Attenuation map of the robotic arm visualized by two perpendicular maximum intensity projections of the linear attenuation coefficient of 511-keV PET annihilation photons (in 1/cm) obtained by a stand-alone PET scanner equipped with Ge-/Ga-68 rod sources (b). PET imaging of 5 MBq F18-FDG injected into a pomelo. PET data was reconstructed into a 256×256 matrix (voxel size: 1.40×1.40×2.03mm^3) using the built-in 3D ordered subset expectation maximization (OSEM) algorithm with 8 iterations, 21 subsets, and a 3-mm Gaussian filter (c).

To correct for attenuation of gamma radiation by the robotic hardware in the PET field of view and test its performance, the integrated robot attenuation was measured with a stand-alone PET system equipped with Ge68-transmission sources emitting 511 keV gamma radiation (Fig. 2 (b)). MR-guided FUS-HT and RT therapy may be combined with PET imaging to evaluate the efficacy of these treatments during the procedure and further improve therapy strategies. An example of PET imaging is given in Fig. 2 (c).

## **DISCUSSION AND CONCLUSION**

We successfully implemented two previously developed interaction functions into a collaborative robotic assistance setup for interventional needle placement procedures. The interaction quality was evaluated in comparison with an unassisted needle placement.

With qualitative feedback on the interaction, it can preliminarily be assumed that collaborative robotic assistance with close-proximity intuitive control mechanisms benefits system acceptance and perceived guidance support. Using MR-PET imaging technique improves the evaluation of the efficacy of a combined FUS-RT treatment. Due to the early stage of these combined therapies, MR-capable robotic systems are hardly available. Therefore, these systems lack a standard for clinical integration. Studies with imaging and therapeutic ultrasound transducers will be conducted in 2019.

# 2 MR-SAFE FLEXIBLE BIOPSY FORCEPS FOR MINIMALLY INVASIVE TISSUE SAMPLING

## INTRODUCTION

The procedure of minimally invasive endomyocardial biopsy (EMB) under X-ray fluoroscopy guidance implies radiation, nephrotoxic contrast agent, and poor tissue contrast. Magnetic Resonance Imaging (MRI) guidance offers a promising option to overcome these disadvantages. So far, however, biopsy forceps are mostly metallic and as per ASTM/ISO regulation *MR* Unsafe because of radiofrequency heating. To improve the intervention, funding by the 'KMU-innovativ: Medizintechnik' program could be raised. Therefore, the objective of the joint project MR-Biopsy is the development and evaluation of a flexible and *MR Safe/Conditional* biopsy forceps along with a corresponding clinical workflow to realize MRI-guided EMB.

## MATERIAL AND METHODS

A design of the biopsy jaws has been realized that allows the processing of non-magnetic, non-metallic, and non-conductive materials. To enable MRI visibility and subsequently assess the opening state and spatial orientation of the jaw components under MR guidance, the jaws have been equipped with passive markers. Standard and real-time cardiac MRI sequences were obtained in an 1.5T MRI system (Siemens MAGNETOM Aera) and evaluated. For intensive ex-vivo suitability tests, a detailed and life-size phantom of the vessel system from groin to neck has been modeled and manufactured (Fig. 1). Therefore, anonymous medical imaging data of a patient was segmented (Materialise Mimics Innovation Suite) and served as blueprint for additive 3D printing.

## RESULTS

MRI visibility investigations show promising results 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 when comparing the prototypes 2 and 5 in Fig. 2.



Fig. 2 - A: test setup with opened jaw prototypes by EPflex GmbH of different materials, with various marker positions and concentrations (1-5), one jaw set without markers (6), and an equal sized reference volume (7). B: coronal MR image of the test setup with opened jaws in a saline solution. C: coronal MR image of the test setup with closed jaws in a saline solution. (TR= 40.95ms/ TE=1.1.6ms/ FA= $74^\circ$ / slice thickness=6mm/ matrix= $192\setminus00\96$ / pixel scaling= $1.77\setminus1.77$ mm<sup>2</sup>/ pixel bandwith=930Hz/ px). Below the image, the dimensions of the MRI artefacts of the opened/ closed jaws 2, 5, 6 are listed.

## **DISCUSSION AND CONCLUSION**

*MR Safe* jaw prototypes have been fabricated, equipped with passive markers, and evaluated under MRI, showing the feasibility to discriminate the opening state of the forceps. Further MRI and ex-vivo studies are currently conducted to ensure the applicability in terms of reliable MRI guidance and reproducible biopsy quality. Later, in-vivo investigations will be carried out



Fig. 1 - Left: 3D model of the phantom. Right: life size silicone phantom (55x25x20cm) by Phacon GmbH. A replaceable fresh porcine heart can be integrated into the phantom, as depicted in the computer model.

accordingly. Another task is to implement a clinical workflow for MRI-guided EMB, comprising optimized MRI sequences, MRI operation, intra-interventional communication, and patient safety.

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## FUNDING

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# 3 MRI-GUIDED FOCUSED ULTRASOUND IN THE TREATMENT OF UTERINE FIBROIDS AND BEYOND

## INTRODUCTION

In 2017 the Philips/Profound medical Sonalleve MR-HIFU System was put into operation at the Department of Radiology (Leipzig University Hospital) to establish an MR-HIFU service primarily to provide a clinical therapy option for cancer treatment and contribute to the growing body of evidence in the clinical as well as the research community. The Sonalleve MR-HIFU System is approved to treat uterine fibroids and bone metastases. We realized our aim by building up a multispecialty treatment center for uterine fibroids with MR-HIFU option. Our initial procedural and clinical experience with our first applications showed good results. Especially for young women in childbearing age, who are still wishing for a family, HIFU is important, e.g. to avoid uterine scars.

Beyond that, we extended the field of HIFU application on desmoid tumors. Desmoid tumors are locally infiltrative and may cause pain and dysfunction. Standard therapies, including surgical resection, radiation, and systemic therapy, suffer from excessive side effects when considering their limited efficacy for treating desmoid tumors. We were able to demonstrate that MR-HIFU treatment of desmoids is feasible and that this technique may be used to control the growth of symptomatic desmoid tumors, even of the abdomen and in analgesia without sedation.

## MATERIALS AND METHODS

#### Uterine fibroids:

A total of 60 patients with symptomatic uterine fibroids have been screened in our multispecialty Fibroid Center since 2017. After proper consultation and consensus for a therapy option, fourteen of them underwent MR-HIFU (Sonalleve, Profound Medical, Mississauga, ON) in a diagnostic 3 T MRI (Ingenia 3.0T, Philips Healthcare, Best, Netherlands). One patient with desmoid tumor was treated via MR-HIFU. Patients received an analgesic and sedative medication and their vital parameters were monitored continuously. T2-weighted and special bowel sequences were used for planning. Therapeutic and adverse tissue heating during sonication was controlled by multiplanar MR temperature mapping (6 slices in 3.5 s) in the treatment cell as well as the so-called near (skin) and far field (sacrum).



Fig. 1 - Diagnostic T2-weighted and contrast-enhanced MR images before and after MR-HIFU of a 32-year-old patient with multiple submucosal fibroids and conception difficulties. Primary HIFU treatment was preferred in this case because one-step surgical excision was considered likely to cause endometrial adhesion.

## RESULTS

## Fibroids:

Mean age (range) was 36 (28-52) years. Patients typically suffered from dysmenorrhoea, hypermenorrhoea, pollakisuria or conception difficulties; seven of them had large solitary and seven multiple smaller fibroids. Bowels frequently happened to lie in the beam pathway on the day of treatment only. Filling of the bladder, the rectum or both was then required to properly manipulate the bowel and uterus position. Five patients were treated successfully, taking 3–6 h, with non-perfused volumes ranging from 69 to 100%. There were no major complications - one patient developed an abdominal wall edema after cumulative near-field heating in a weakly thermosensitive fibroid minor complication; pain symptoms resolved completely after two months. All patients were discharged on the next day.

# Desmoid:

A 30-year-old patient with Gardnersyndrome, initially diagnosed in 2005, with desmoidal soft tissue tumors in both groins and in the right abdominal wall with infiltration of the subcutis, the M. rectus abdominis (incl. the left M. rectus abdominis) and long-stretched walling of the right lower costal arch presented in our clinic. The desmoid in the abdominal wall was symptomatic with pain and recurrent after a previous resection.

Another resection was rejected due to shortterm recurrence. Systemic therapy (Tamoxifen) showed no effect. Radiotherapy was also rejected due to adjacent risk structures (e.g. stomach) and side effects. Thus, therapy decision to multistaged MR-HIFU as compassionate use was made. The first session made 24% NPV (Non-perfused Volume) and was well-tolerated by the patient even though it was done under analgosedation and not in general anesthesia. Already one week after therapy subjective reduction of symptoms was observed and lasted for three months (today). Further HIFU therapy is planned for further volume reduction.

## CONCLUSION

We have successfully established a treatment center for symptomatic uterine fibroids and already performed the first MR-HIFU ablations. Patient comfort and compliance while and after the procedure in follow-up have so far been good. One future goal is to extend our service to other clinical entities as well, in particular to bone metastases.

MRgFUS can provide a safe and effective durable control of desmoid tumor growth and is an alternative to operative resection, radiation therapy and systemic therapy. MR-HIFU was, although performed only with analgosedation, well tolerated by the patient. Further HIFU therapy is planned.

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# 4 NEURO-MODULATION USING LIGHT INTENSITY FOCUSED ULTRASOUND

## INTRODUCTION

Several studies indicate that focused ultrasound can be used to non-invasively modulate neurons in the brain. This would have the potential of suppression and/or activation of neuronal activity. The goal is to use light intensity focused ultrasound pulses (LIFUP) to non-invasively modulate certain areas of the brain to treat e.g. stroke, addiction, chronic OCD (obsessive compulsive disorder), essential tremor and Parkinson's disease.

Fraunhofer IBMT (Tretbar, St. Ingbert) developed and provided a custom-made ultrasound system (Fig. 1), which allows LIFUP application to humans using freely programmable ultrasound parameters and transmission sequences, and that can be synchronized to EEG recordings. Ultrasound transmission is realized using a 3D ultrasound matrix transducer with a matrix of 11x11 elements, an active aperture of 35 mm x 35 mm and a center frequency of 650 kHz. This matrix array together with a special control software allows to position a focal ultrasound spot in a given volume with high spatial accuracy.

A first experimental trial with 20 participants was performed at the MPI (Villringer/Nierhaus) to evaluate if the maximum ultrasound energy provided by the LIFUP-system is sufficient for a neuro-modulatory effect that can be measured with EEG in terms of evoked potentials and/or event-related de-/synchronization. Therefore, LIFUP stimulation with ultrasound parameters tuned to maximum energy (Voltage amplitude: 150 V; Pulse width: 50 µs; Signal frequency (PRF): 500 Hz; Stimulus duration: 200 ms) was applied over the primary somatosensory cortex (S1) during EEG measurement.

The main general problem with transcranial LI-FUP application is that the transducer produces a clearly hearable sound (chirping) during excitation. Thus, possible ultrasound-induced neuro-modulatory effects are covered in the EEG by a large auditory evoked potential due to the auditory processing of the sound. A first solution for this problem is the application of auditory white noise over loudspeakers during EEG measurements. With this, we can show that the auditory evoked potential is eliminated as the white noise prevents a conscious auditory perception of the chirping sound. However, the resulting EEG recordings show no clear result of a neuro-modulatory effect due to the LIFUP stimulation so far. Currently, a second experimental trial is performed, after the LIFUP system was tuned to allow for ultrasound excitation with higher energy. In future, the elimination of the sound produced by the transducer would be a major technically progress.



Fig. 1 - LIFUP System with Matrix Transducer and UI (Fraunhofer IBMT, St. Ingbert).

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# LIFE SUPPORT SYSTEMS

'The non-invasive and radiation-free Electrical Impedance Tomography has the potential to offer direct insight into the patient's lung condition and lung function for physicians in emergency medicine, intensive care and neonatal care. We develop innovative analysis and monitoring algorithms to advance individualized therapy selection and steering for neonatal and adult patients with respiratory disorders in both the prehospital and the clinical setting.'

> Prof. Dr. Andreas Reske (group leader)



# **SCIENTIFIC STAFF**

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# ELECTRICAL IMPEDANCE TOMOGRAPHY ELECTRODE HANDLING WITH PARTIAL ACCESS TO THE THORAX

## INTRODUCTION

Electrical impedance tomography (EIT) is a functional imaging method capable of monitoring lung ventilation and can potentially be used as bedside application at intensive care units. In the IMPACT (Improved MultiPArametric monitoring of blunt Chest Trauma) project at ICCAS this imaging method is transferred to the use in prehospital emergency scenarios and a mobile EIT system is developed in collaboration with Fritz Stephan GmbH, ITP GmbH and the Leipzig University of Applied Sciences.

In emergency situations, such as car crashes, the emergency physician has to handle situations with trapped patients and only partial access to the thorax. In this case, only a part of the belt and few electrodes can be placed on the thorax, but the system is still required to detect problems with or missing lung ventilation.

## **MATERIALS AND METHODS**

In order to evaluate situations with a reduced number of electrodes, a virtual simulation study was conducted. A cylindrical phantom containing a single object with lower conductivity is created in a simulation environment. Simulating no access to the dorsal part of a patient, the electrodes on only one side of the object are gradually reduced and the same object is reconstructed in each step.

A prototypic phantom was built by the Leipzig University of Applied Sciences in order to test the developed EIT hardware functionality. For that reason, a cylindrical tank made from acrylic glass is equipped with 96 screws, acting as electrodes (see Fig. 1). The tank can be connected to the EIT hardware and test measurements can be recorded when the phantom is filled with conductive liquid, i.e. saline water.

# RESULTS

The first simulation results showed a severe reduction in image quality when reducing the number of electrodes on one side of the object. Even for a small number of missing electrodes the original simulated object was heavily distorted and could not be properly recognized (see Fig. 2).



Fig. 1 - Image of the EIT phantom, filled with saline water.



Fig. 2 - EIT image results of the simulation study of reduced electrodes on one side of the object. Results for 16, 14, 12 and 10 electrodes are depicted.

With the phantom, EIT measurements in different test situations can be created. Applying objects of different conductivity, impedance changes can be recorded, reconstructed and visualized. The connection of electrodes is variable and different electrode configurations of the 96 electrodes are possible.

## **DISCUSSION AND CONCLUSION**

Severe degradation of image quality was observed when simulating a reduced set of electrodes. Until now, purely virtual simulations were conducted. The developed EIT phantom is the optimal environment to generate actual measurements with varying electrode configuration. Consequently, next steps in the project are the evaluation of the simulation results with the developed EIT phantom, in order to develop algorithms handling a decreased and rearranged situation of electrodes.

### **PROJECT TEAM**

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### SELECTED PUBLICATIONS

Mrongowius J, Reske AW, Neumuth T, Salz P. Electrical Impedance Tomography Lung Imaging with partial access to the thorax: A simulation study. 17. Jahrestagung der der Deutschen Gesellschaft für Computer- und Roboterassistierte Chirurgie (CURAC). Leipzig, Germany; 2018.

## FUNDING

This project has received funding from the KMU innovative program of the German Federal Ministry of Education and Research (BMBF).

# PRELIMINARY STUDY RESULTS FROM THE IMPACT PROJECT WITH CLINICAL RELEVANCE

## INTRODUCTION

State-of-the-art approaches for recognition and regulation of impaired breathing and irregular ventilation encompass auscultation, sonography and spirometry. Yet, these methods are either insufficient for a conclusive detection and quantification of abnormal lung behavior or require time-intensive effort. Electrical Impedance Tomography (EIT) presents an alternative, visualizing pulmonary ventilation through a combination of small-voltage stimulations and measurements, performed by a multitude of electrodes around the patient's thorax. In IMPACT (Improved MultiPArametric monitoring of blunt Chest Trauma) the research group used EIT to establish a database for analyzing not well known artefacts during one-lung ventilation (OLV) or pneumothorax (PTX) and developing algorithms for their automatic detection.



Fig. 1: EIT-trend lines of left (grey) and right (black) image side.



Fig. 2: Left: Ventilation image reconstructed through EIT, Right: Delay Map acquired by compairing the pixels behavior to a global signal (blue – ventilation advance, red – ventilation delay).

# MATERIAL AND METHODS

The data was collected through a clinical trial with thoracic surgery patients, where OLV is necessary for the procedure and thoracotomy is leading to an intended and controlled PTX. An observational study with a current total of 12 patients was conducted.

EIT-reconstruction was done with EIDORS, an open source software employing the GREITalgorithm for ventilation reconstruction. The software returns a series of images at a resolution of 64x64 pixels, where image values represent the relative impedance change of each pixel of the reconstructed image. By analyzing each pixel's impedance change trend over time and subtracting the times of local maxima from those of an averaged impedance change signal, it was possible to calculate a matrix where each element represents a pixel's average delay. The resulting values are drawn on a 64x64 matrix, allowing the visualization through a colormap and leaving out pixels with little to no impedance change.

## RESULTS

Following the recording of the EIT-signals during the study, the group collected 12 EIT-datasets containing periods of time with one-sided-lung ventilation, represented through an EIT-trend (Fig. 1). During those periods of time an outof-phase signal occurred, which stopped when the thorax was closed and chest drains reestablished negative pleural pressure at the end of the operation.

The developed method of displaying and recognizing asynchronous ventilation patterns was partially based and tested on this dataset. Its resulting delay maps are images with 64x64 pixels and identify pixels / regions with a phase shift (Fig. 2). Sign and magnitude of the phase shift is distinguishable through the map's color and its intensity (positive-red, negative-blue).

# DISCUSSION AND CONCLUSION

Conclusions of the trial show that a unilateral lung collapse with open chest generates an ipsilateral out-of-phase ventilation like signal whose origin needs to be further investigated. One possible explanation could be the loss of contact between lung tissue and the inner chest wall, altering the path of electrical current while another explanation might be the passive movement of the collapsed lung in the thorax, caused by the moving mediastinum.

The proposed method to enable detection of unilateral respiration abnormities provides a visual feedback for the localized delay of ventilation in corresponding lung regions. This allows for a fast identification of regions affected by an impaired respiratory system. Following the conclusion of the study, the group will focus on further analysis of the delays, their sensitivity and specificity as well as the unknown out-of-phase signals.

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### FUNDING

This project has received funding from the KMU-Innovative program of the German Federal Ministry of Education and Research (BMBF).

# EMU – VENTILATION SYSTEM WITH ELECTRICAL IMPEDANCE IMAGING TO MONITOR PATIENT CONDITION AND TO OPTIMALLY VENTILATE THE PATIENT

# INTRODUCTION

Premature children and neonates often require support in ventilation for their first breaths or over a longer period of time, if the lungs are not properly developed yet. Especially for these small patients mechanical ventilation strategies need to be chosen carefully and due to a high risk of ventilator-induced lung injury (VILI), mechanical ventilation needs to be conducted in a gentle way. Since the individual adjustment of ventilation is not straightforward, the extent of ventilation needs to be assessed.

The non-invasive imaging method Electrical

Impedance Tomography (EIT) features the real-time visualization of lung functions without using ionizing radiation. In the EMU (Ventilation System with Electrical Impedance Imaging to monitor patient condition and to optimally ventilate the patient) research project at ICCAS, a combination of ventilator and EIT-device is developed in collaboration with Fritz Stephan GmbH. The aim of the combined device is the implementation of an improved ventilation strategy focusing on neonatal ventilation.

## MATERIAL AND METHODS

In order to capture the patient's response to the ventilation, EIT enables the visualization of ventilation and perfusion distribution. A special algorithm separates the ventilation- and perfusion-related EIT signals without any ventilation maneuver such as an apnea phase or the in-



Fig. 1 - Screenshot of the GUI for the joint visualization of ventilation and EIT signals.

jection of a saline bolus. Based on these distributions different parameters describing the patient's condition can be derived. Examples for these parameters are the extraction of regions with collapse and overdistension, the local delay and pendelluft phenomena, the heart rate and the regional overlap of ventilation and perfusion.

## RESULTS

A combined monitoring system consisting of the Sophie ventilator from Fritz Stephan GmbH, the Swisstom OEM EIT module and the Swisstom Baby EIT belt is developed and bundles the visualization of ventilator and EIT information in a joint "all-in-one" touch monitor. An innovative GUI (see Fig. 1) gives an easy access and analysis to the ventilator and EIT signals.

## **DISCUSSION AND CONCLUSION**

The developed device offers improved mechanical ventilation strategies for neonates without the requirement of X-ray and ionizing radiation. With this device, the aim of improved oxygenation with a reduced risk of VILI can be achieved through a real-time response with EIT. It even allows for monitoring of ventilation and perfusion in situations where standard oxygenation measurement is not available or of poor signal quality. This may be the case for sustained inflations in the first seconds after the delivery.

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## FUNDING

This project has received funding from the ZIM program of the German Federal Ministry for Economic Affairs and Energy (BMWi).

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# **CO-AUTHORSHIP**

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# **EVENTS**

# **IN-HOUSE EVENTS**

## **ICCAS STATUS SEMINAR 2017**

## January 18, 2018 | ICCAS, Leipzig

Presentation of ICCAS's research results and highlights in 2017

## **1ST SONO-RAY STATUS SEMINAR**

## January 18, 2018 | ICCAS, Leipzig

Presentation of the Meta-ZIK's (ICCAS and OncoRay) research results in 2017

# 14TH LEIPZIG RESEARCH FESTIVAL FOR LIFE SCIENCE

January 19, 2018 | Medical Study Center, Leipzig University

Jesús Guillermo Cabal Aragón | poster: 'Image based connector for the automatic configuration of 3D ultrasound data acquisition'

**Stefan Franke** | poster: 'Realization of context-aware technical assistance in integrated operating rooms'

**Reinhard Fuchs** | poster: 'Development and Evaluation of an Instrument-Recognition-System for intraoperative activity-tracking through a multi-sensor armband'

Jan Gaebel |poster: 'Modular Infrastructure for the Integration of Decision Models into Hospital Information Systems'

**Norbert Lang** | poster: 'Auditory feedback system for intraoperative navigation during craniotomy in neurosurgery'

Marianne Maktabi | poster: 'Hyperspektrale Untersuchungen von koagulierten tierischen Gewebeproben' Juliane Neumann | poster: 'Extending BPMN 2.0 Modeling Language for Surgical Interventions'

**Alexander Oeser** | poster: 'Development of a patient-specific dashboard application for decision-making in oncology'

**Max Rockstroh** | poster: 'Qualitative Evaluation of an integrated operating room based on the IEEE11073-SDC'

**Erik Schreiber** | poster: 'Prioritized Presentation of Surgical information to counteract information overload in the operating room' **Michael Unger** | poster: 'Integration of a MR-compatible robotic arm into the clinical infrastructure'

Jan Berger | poster: 'Scorpius – Robot assisted needle guidance and US monitoring'

**Richard Bieck** | poster: 'Towards Computational Navigation Intelligence In Computer-Assisted Minimally-Invasive ENT Surgery'

Julia Mrongowius | poster: 'Improved MultiPArametric monitoring of blunt Chest Trauma, IMPACT – a project presentation'

Juliane Müller | poster: 'Requirements and Visualization Methods for Visual Verification of Bayesian Networks'

**Xinrui Zhang** | poster: 'An in vitro study of ultrasound-induced HT combined with radiation therapy for glioblastoma cells'

# KUNSTSTOFF TRIFFT MEDIZINTECHNIK CONFERENCE

## January 31, 2018 | ICCAS, Leipzig

**Max Rockstroh** | presentation of ICCAS's Intelligent Operating Room

## **ICCAS COLLOQUIUM**

## March 12, 2018 | Leipzig University Hospital

**Ulf Leser** | invited lecture: 'PREDICT: Knowledge Management for Precision Oncology'

## SENIOR-ACADEMY

April 10, 2018 | Leipzig University Thomas Neumuth | lecture: 'Roboter in der Medizin'

# GIRLS'DAY

## April 26, 2018 | ICCAS, Leipzig

**Claire Chalopin, Lisa Landgraf** | Insight into medical informatics for female pupils

## ICCAS OPEN DAY

June 7, 2018 | ICCAS, Leipzig Presentation of ICCAS's research areas to the public

### LONG NIGHT OF SCIENCES

## June 22, 2018 | BBZ, Leipzig

**LSS group** | presentation of Electrical Impedance Tomography (EIT)

**Peter Salz** | lecture: From Idea to Device – Today's Medical Technology Production

## **5TH DIGITAL OPERATING SUMMER SCHOOL (DORS)**

August 27 – 31, 2018 | ICCAS, Leipzig University Hospital, Heart Center Leipzig

Unique introduction to various topics of computer-assisted medicine.

# 17TH ANNUAL CONEFRENCE OF THE GERMAN SOCIETY FOR COMPUTER AND ROBOTIC ASSISTED SURGERY (CURAC)

September 13 – 15, 2018 | ICCAS, Leipzig University Hospital and Medical Study Center

Andreas Melzer | welcome speech; session chair: 'Navigation'; lecture: 'Was gibt es Neues in iFUS?'

Thomas Neumuth | welcome speech; session chair: 'Workflowanalyse und Prädiktion'

Claire Chalopin | session chair: 'Navigation'

**Stefan Franke** | session chair: 'Chirurgische Assistenzsysteme'

Hannes Köhler | lecture: 'Intraoperative tissue characterization and classification in hyperspectral imaging: first results'

**Nico Graebling** | lecture: 'Generierung und Verwendung künstlicher Trainingsdaten für CNNs zur Erkennung von Operationsinstrumenten'

Julia Mrongowius | lectures: 'Electrical Impedance Tomography Lung Imaging with partial access to the thorax: A simulation study', 'Electrical Impedance Tomography for ventilation delay analysis'

**Johann Berger** | lecture: 'Kollaborative Interaktion für die roboterassistierte ultraschallgeführte Biopsie'

**Richard Bieck** | lecture: 'Simulating the Patient-Individual Intervention Process for Staged Segmental Artery Occlusion – A Modeling Approach

Marianne Maktabi | lecture: 'Eine Beurteilung der Anwendbarkeit von hyperspektralbasierter Bildgebungstechnologie bei viszeralonkologischen Eingriffen' Jesús G. Cabal Aragón | lecture: 'Development of an improved ultrasound navigation system for neurosurgical procedures'

Martin Reich | lecture: 'Interventionelle MR-geführte Herzbiopsie: Entwicklung einer innovativen MR-tauglichen Biopsiezange'

**Tobias Landeck** | lecture: 'One-lung ventilation and Pneumothorax detection using Electrical Impedance Tomography: a preliminary study report'

Jan Gaebel | lecture: 'Model-Based Imitation of Patient Scenarios for Oncological Decision Support'

# EUMFH PROJECT MEETING INCLUDING VISIT OF THE EUROPEAN COMMISSIONER FOR HUMANITARIAN AID & CRISIS MANAGEMENT

#### November 23, 2018 | ICCAS

**Thomas Neumuth** | member: steering committee; presentation of ICCAS and results of the project European Modular Field Hospital (EUMFH)

# CONFERENCES, SYMPOSIA, WORKSHOPS

# EUROPEAN ASSOCIATION FOR ENDOSCOPIC SURGERY AND OTHER INTERVENTIONAL TECHNIQUES (EAES) – TECHNOLOGY WINTER MEETING 2018

February 3, 2018 | Frankfurt am Main, Germany

**Prof. Dr. Andreas Melzer** | director symposium **Prof. Dr. Thomas Neumuth** | invited lecture: 'AI to Improve the Workflow in the OR. Fully Integrated OR – the German OR Network'

## SYMPOSIUM INTENSIVMEDIZIN UND INTENSIVPFLEGE

February 14 – 16, 2018 | Bremen Andreas Reske | invited lecture: 'Einsatz der Elektrischen Impedanztomografie im klinischen Alltag'

## VDE-TAGUNG 'SOFTWARE IN DER MEDIZIN'

February 28, 2018 | Goethe-Universität, Frankfurt a. M. Thomas Neumuth, Richard Bieck | presentation of ICCAS's research topics

### EUROPEAN CONGRESS OF RADIOLOGY (ECR)

February 28 – March 4, 2018 | Vienna, Austria Andreas Melzer | representation of ICCAS

# DGBMT IM VDE (FACHAUSSCHUSS OPTISCHE VERFAHREN IN DER MEDIZIN (OPTOMED) – WORKSHOP: 'VERGLEICHBARKEIT UND STANDARDISIERUNG OPTISCHER VERFAHREN IN DER MEDIZIN: WELCHE INFORMATIONEN BENÖTIGT DER ANWENDER? – WELCHE GRÖßEN MESSEN WIR?'

March 1 – 2, 2018 | Technische Universität Dresden, Dresden

**Dr. Claire Chalopin** | technical implementation of workshop: 'Dermatologie/Wunddiagnostik'

# CONFERENCE 'HOSPITAL CONCEPT' BY OSTBAYERISCHE TECHNISCHE HOCHSCHULE AMBERG-WEIDEN (OTH)

#### March 5, 2018 | Weiden

**Max Rockstroh** | invited talk: 'OR.NET: Safe and Dynamic Technology Integration in Operating Rooms and Hospitals'

# 48. KONGRESS DER DEUTSCHEN GESELLSCHAFT FÜR ENDOSKOPIE UND BILDGEBENDE VERFAHREN E.V. (DGE-BV) – 'ENDOSKOPIE LIVE 2018' & 'INTEGRATION'

March 15 – 17, 2018 | Munich

Andreas Melzer | member: board; opening and welcome speech; session chair: 'DGBMT – Bildgebung und -analyse in der Endoskopie und Chirurgie'; lectures: 'Computerassistierte Chirurgie und -therapie', 'Magic Lens AR and tablet based planning of surgical and interventional robotic assisted procedures'

# 23RD INTERNATIONAL CONFERENCE ON TELEMEDICINE AND EHEALTH (ISFTEH 2018)

### March 15 – 17, 2018 | Helsinki, Finland

Jan Gaebel | lecture: 'Probabilistic Patient Modeling for Therapeutic Decision Support in Oncology'

## EUROPEAN RESEARCH COUNCIL (ERC)

March 19 – 23, 2018 | Brussels, Belgium Andreas Melzer | member: ERC Starting Panel 2018

## FG-MEETING VISUAL COMPUTING FOR BIOLOGY AND MEDICINE (VCBM)

April 11 – 13, 2017 | Ulm Juliane Müller | invited talk: DPM Visualization

# CONNECTING HEALTHCARE IT (CONHIT)

## April, 17 – 19, 2018 | Berlin

**Thomas Neumuth** | session chair: 'Intelligente Technologie im Krankenhaus – Konvergenz von Medizintechnik und IT'

# 135TH CONCRESS OF THE GERMAN SOCIETY OF SURGERY (DGCH)

### April 17 – 20, 2018 | Berlin

**Andreas Melzer** | invited lecture: 'Computerassistierte Chirurgie'

Heinz U. Lemke | invited lecture: Model-based Surgery

## 42ND CONGRESS OF THE KOREAN SOCIETY OF ENDOSCOPIC & LAPAROSCOPIC SURGEONS (KSELS) & 8TH INTERNATIONAL SYMPOSIUM

April 19 – 21, 2018 | Jeju, South Korea

**Andreas Melzer** | session chair: 'AI in MIS'; invited keynote lecture: 'Artificial and Machine Intelligence in the OR of the Future'

## 29TH MEDICAL INFORMATICS EUROPE (MIE)

April 24 – 26, 2018 | Gothenburg, Sweden Jan Gaebel | lecture: 'System Infrastructure for Probabilistic Decision Models in Cancer Treatment'

# 14TH EUROPEAN CONFERENCE ON PEDIATRIC AND NEONATAL MECHANICAL VENTILATION (EPNV)

## April 25 – 28, 2018 | Montreux, Switzerland

**Peter Salz** | workshop presentation: 'The current EMU Prototype'

## **DEUTSCHER ANÄSTHESIE CONGRESS (DAC)**

### April 25 - 27, 2018 | Nuremberg

**Max Rockstroh** | lecture: 'Mehrwert durch Vernetzung – Der Patient im Fokus'

## VDE/DGBMT FOKUS-WORKSHOP 'MODELLGESTÜTZTE PERSONALISIERTE MEDIZINTECHNIK'

#### April 26, 2018 | Frankfurt a. M.

**Thomas Neumuth** | lecture: 'Grundidee, Zielstellung, Modellvarianten und-klassifikationen'

# RESEARCH SEMINAR AT UPC UNIVERSITAT POLITECNICA DE CATALUNYA

#### May 05, 2018 | Barcelona, Spain

**Steffen Oeltze-Jafra** | invited lecture: 'Therapy Decision Support'

## 12TH ANNUAL CONFERENCE ON HEALTH INFORMATICS MEETS EHEALTH (EHEALTH)

### May, 8 - 9, 2018 | Vienna, Austria

Jan Gaebel | lecture: 'Modular Architecture for Integrated Model-Based Decision Support'

## 99. DEUTSCHER RÖNTGENKONGRESS

## May 9 – 12, 2018 | Leipzig

Andreas Melzer | representation of ICCAS

## 18TH INTERNATIONAL SYMPOSIUM FOR THERAPEUTIC ULTRASOUND (ISTU 2018)

## May 14 - 17, 2018 | Nashville, TN, USA

Andreas Melzer | session chair: 'Thermal Therapies' Lisa Landgraf | session chair: 'Thermal Therapies'; lecture: 'In Vitro Effects of Ultrasound Hyperthermia and Radiation Therapy on Glioblastoma, Prostate and Head and Neck Cancer Cell Lines: Preliminary Studies'; poster presentation: 'Towards Integrating Robotics for Combined Focused Ultrasound and Radiation Therapy into the Treatment Process'

# 32ND ANNUAL MEETING OF THE EUROPEAN SOCIETY FOR HYPERTHERMIC ONCOLOGY (ESHO 2018)

### May 16 – 19, 2018 | Berlin

Xinrui Zhang | poster 'Flash' presentation: 'Ultrasound-induced hyperthermia – radiosensitisation in glioblastoma, prostate and head and neck cancer – preliminary studies'

# 26TH INTERNATIONAL CONGRESS OF EUROPEAN ASSOCIATION FOR ENDOSCOPIC SURGERY (E.A.E.S.)

## May 30 – June 1, 2018 | London, UK

Andreas Melzer | course director hands on: 'Ultrasound for Surgeons'; session chair: 'Gerhard Buess technology award'; invited lecture

Johann Berger | project presentation: 'SONO-RAY'

# 20TH EUROGRAPHICS WORKING GROUP ON DATA VISUALIZATION (EG/VGTC) AT CONFERENCE ON VISUALIZATION (EUROVIS)

June 4 – 8, 2018 | Brno, Czech Republic Steffen Oeltze-Jafra | presentation of Computer Graphics article

## **CHARITÉ INHOUSE EVENT 'INTENSIVE CARE'**

## June 6, 2018 | Charité Berlin

Max Rockstroh | invited lecture: ,Intensive Care of the Future'

# INTERNATIONAL CONFERENCE ON ENGINEERING, TECHNOLGOGY AND INNOVATION (ICE/IEEE ITMC) 19 – 20 June, 2018 | Stuttgart

# **Max Rockstroh** | session chair: 'IEEE Konferenz Workshop Regulatory Health'; lecture: 'OR.NET: Short introduction to medical device interoperability based on the IEEE11073-SDC standard family'

# 32ND INTERNATIONAL CONGRESS AND EXHIBITION OF COMPUTER ASSISTED RADIOLOGY AND SURGERY (CARS)

## June 20 – 23, 2018 | Berlin

Andreas Melzer | session chair: 'Clinical Decision Making'

**Thomas Neumuth** | session chair: 'Technical Standardization in the OR – Standards, Use Cases, Benefits and Potentials'; lectures: 'Medical information technology standards in the operating room', 'IEEE 11073 SDC and HL7 FHIR – Emerging Standards for Interoperability of Medical Systems' **Steffen Oeltze-Jafra** | lecture: 'Information Architecture for a Patient-Specific Dashboard in Head and Neck Tumor Boards'

**Claire Chalopin** | lectures: 'Measurement of moisture at skin surface with hyperspectral imaging', 'Image based connector for the automatic identification of ultrasound parameter values'

**Stefan Franke** | lecture: 'The intelligent OR – Design and validation of a context-aware surgical working environment'

**Chris Unger** | lecture: 'A Knowledge-based Data Entry Form for High Quality Clinical Data Collection'

**Erik Schreiber** | session chair: 'IHE Session'; lectures: 'Current Work Items for IHE Integration Profiles. Cross-enterprise Model Sharing (XMS) and Consistent Presentation of Surgical Information', 'IHE Surgery – Introduction, goals and current work items'

**Richard Bieck** | lecture: 'From Passive Tool to Active Guidance – Requirements for Navigation Intelligence in Computer-Assisted Endoscopic ENT Surgery'

Heinz U. Lemke | invited lecture: 'Machine Intelligence and CAS'

## 11TH HAMLYN SYMPOSIUM ON MEDICAL ROBOTICS

## June 24 – 27, 2018 | London, UK

**Andreas Melzer** | co-chair: 'Image Guided Therapies (IGT)'; invited talk: 'Ultrasound and MR Guided Focused Ultrasound Therapy: SONO-RAY'

Johann Berger, Johannes Keller | robotic presentation at 'Surgical Robotic Challenge'

# INTERNATIONAL SOCIETY FOR BAYESIAN ANALYSIS WORLD MEETING (ISBA)

## June 25 – 29, 2018 | Edinburgh, UK

**Jan Gaebel** | poster presentation: 'Bayesian Networks for Oncological Therapy Decision Support'

# SYMPOSIUM ON 'AI IN MEDICAL IMAGING' NATIONAL INSTITUTES OF HEALTH AND BIOMEDICAL IMAGING/ BIOENGINEERING (NIH/NIBIB)

August 24, 2018 | Bethesda, MD, USA

Heinz U. Lemke | panelist and speaker in session 'The Human-Machine System'

## TAG DER MEDIZINTECHNIK

September 12, 2018 | Fraunhofer Forum, Berlin Andreas Melzer | representation of ICCAS

# 21ST INTERNATIONAL CONFERENCE ON MEDICAL IMAGE COMPUTING AND COMPUTER ASSISTED INTERVENTION (MICCAI)

September 16 – 20, 2018 | Granada, Spain

**Stefan Franke** | lecture: 'A method for the context-aware assignment of medical device functions to input devices in integrated operating rooms'

**Steffen Oeltze-Jafra, Jan Gaebel** | tutorial: 'ModelsCDS: Digital Therapy and Patient Models for Clinical Decision Support'

Juliane Neumann | lecture: 'Perioperative workflow simulation and optimization in orthopedic surgery'

# CONFERENCE OF EUROPEAN CARDIOVASCULAR AND INTERVENTIONAL RADIOLOGICAL SOCIETY (CIRSE)

## September 22 – 25, 2018, 2018 | Lisbon, Portugal

**Lisa Landgra**f | poster presentations: 'Towards the integration of robotic concepts into the interventional oncology workflow of combined focused ultrasound and radiation therapy', 'Ultrasound therapy system for high throughput in vitro analysis'

# SZ-KONGRESS: 'DIGITAL HEALTH – GESUNDHEIT NEU DENKEN. WIE VERNETZUNG DAS GESUNDHEITSWESEN VERÄNDERT'

## September 25 – 26, 2018 | Munich, Germany

**Thomas Neumuth** | panel discussion: 'Smart Hospital: Wie digitale Anwendungen & Technologien Behandlungs- und Verwaltungsabläufe erleichtern'

# 52ND ANNUAL CONFERENCE OF THE GERMAN SOCIETY FOR BIOMEDICAL ENGINEERING (DGBMT WITHIN VDE) September 26 – 28, 2018 | Aachen

**Andreas Melzer** | chair: 'MR Safety and Compatibility of Medical Devices', lecture: 'New Devices for MR Interventional procedures'

Thomas Neumuth | keynote lecture: 'Patient Specific Model Guided Therapy'; session chair: 'Personalized model-based medical technology', 'Computer Assisted Surgery'; lecture: 'Context-aware medical technologies - relief or burden for clinical users?'

**Xinrui Zhang** | lecture: 'Combination of focused ultrasound hyperthermia (FUS-HT) and radiation therapy: Validation of in vitro effects in a preliminary study'

Johann Berger | lecture: 'Assessment of Natural User Interactions for Robot-Assisted Interventions'

**Claire Chalopin** | lecture: 'Hyperspectral based discrimination of thyroid and parathyroid during surgery'

# ANNUAL MEETING GERMAN SOCIETY OF UROLOGY (DGU)

### September 26 – 29, 2018 | Dresden

Andreas Melzer | invited keynote during opening plenary

**Stefan Franke** | lectures: 'Roboterassistierte OP-Techniken: Morgen'; 'Der OP-Saal von morgen'

## **12TH INTERVENTIONAL MRI SYMPOSIUM**

October 5 - 6, 2018 | Boston, MA, USA

Andreas Melzer | faculty member; chair: 'Special Session for European Focused Ultrasound Charitable Society'; invited talk: 'Novel Technologies and Applications of MR Guided FUS and HIFU'

## FRAUNHOFER INTERACTIVE EXHIBITION #ZUKUNFTSARBEIT

#### October 8 - 12, 2018 | Berlin

Andreas Melzer | panelist: panel discussion #Zukunftsarbeit Gesundheit

# ANNUAL CONGRESS EUROPEAN ASSOCIATION OF NUCLEAR MEDICINE (EANM)

## October 13 - 17, 2018 | Düsseldorf

Andreas Melzer | lecture: 'Trends in Computer Assisted Intervention'; talk: 'ROUND TABLE: Incorporating Imaging and Machine Intelligence in the Operating Room – Portable and/or Fixed Equipment? Will Interventional Workflows be Affected?'

**Heinz U. Lemke** | session chair: EANM-IFCARS Joint Symposium on Computer Assisted Radioguided Intervention in Surgery and Radiology

# EUROPEAN SOCIETY FOR MAGNETIC RESONANCE IN MEDICINE AND BIOLOGY (ESMRMB) SUMMER SCHOOL

October 18 - 20, 2018 | Vienna, Austria

Andreas Melzer | lecture: 'MR-safety issues in Interventional MR'

# 6TH INTERNATIONAL SYMPOSIUM ON FOCUSED ULTRASOUND

## October 21 - 25, 2018 | Reston, VA, USA

**Andreas Melzer** | poster presentations: 'Focused ultrasound-hyperthermia and radiation therapy for combined treatment of brain and prostate tumors – preliminary studies in vitro', 'Concepts for robot-assisted focused ultrasound to support radiation therapy'; representation of ICCAS at a booth

## INNOVATIONSFORUM FLEXMED

## October 24 – 25, 2018 | Dresden Alexander Oeser | representation of ICCAS

## TRI-ANNUAL IMAGE-GUIDED-THERAPIES (IGT) NETWORK AND MEETING

### November 1, 2018 | University of Dundee, UK

Andreas Melzer | welcome speech; session chair: 'Research Talks', 'Plenary Talk', 'Poster Prize and Final Words'

# ANNUAL SYMPOSIUM AMERICAN MEDICAL INFORMATICS ASSOCIATION (AMIA) AND 9TH WORKSHOP ON VISUAL ANALYTICS IN HEALTHCARE (VAHC 2018)

#### November 3 - 7, 2018 | San Francisco, CA, USA

**Alexander Oeser** | lecture: 'Design Concept of an Information System for the Intuitive Assessment of Laboratory Findings'

# 30TH CONFERENCE INTERNATIONAL SOCIETY FOR MEDICAL INNOVATION AND TECHNOLOGY (ISMIT 2018)

## November 8 – 10, 2018 | Seoul, South Korea

Andreas Melzer | international scientific committee member; invited lecture: 'Future Operating Room & Safety'

### NATIONAL CANCER CENTER KOREA

## November 12 – 14, 2018 | Goyang, Korea

Andreas Melzer | invited lectures: 'Intelligent OR solutions and intraoperative focused ultrasound', 'Ultrasound guided ultrasonic energy therapy and radiation support (SONO-RAY)

# 10TH NATIONAL SYMPOSIUM OF BARIATRIC AND METABOLIC SURGERY, 1ST NATIONAL SYMPOSIUM OF ROBOTIC SURGERY

## November 23, 2018 | Bucharest, Romania

Andreas Melzer | course director: 'Workshop: Surgeons Ultrasound'

# 104TH SCIENTIFIC ASSEMBLY AND ANNUAL MEETING

RADIOLOGICAL SOCIETY OF NORTH AMERICA (RSNA) November 25, 2018 | Chicago, IL, USA

Andreas Melzer | representation of ICCAS

# **DIGITAL SUMMIT 2018**

December 3 – 4, 2018 |Nuremberg Thomas Neumuth | representation of ICCAS

# PRESENTATIONS AT FAIRS

## XPOMET© CONVENTION

March 21 – 23, 2018 | Leipzig

**Thomas Neumuth** | invited lecture: 'Medical Device Interoperability in the OR of the Future'

**Stefan Franke, Max Rockstroh** | Showcase Construction: 'OR of the Future' and Use Case Session: 'Medical Device Interoperability in the OR of the Future'

### **CONNECTING HEALTHCARE IT (CONHIT)**

### April 17 – 19, 2018 | Berlin

**Thomas Neumuth** | session chair: 'Intelligente Technologie im Krankenhaus – Konvergenz von Medizintechnik und IT', representation of OR.NET e.V.

## **11TH HAMLYN SYMPOSIUM ON MEDICAL ROBOTICS**

## June 24 – 27, 2018 | London, UK

**Andreas Melzer** | co-chair: 'Image Guided Therapies (IGT)'; invited talk: 'Ultrasound and MR Guided Focused Ultrasound Therapy: SONO-RAY'

Johann Berger, Johannes Keller | robotic presentation at 'Surgical Robotic Challenge'

## MEDICA 2018

November 12 – 15, 2018 | Düsseldorf

**Prof. Thomas Neumuth** | panel speaker: 'Operating Theater 4.0 – The OR.NET approach to safe and dynamic device networking'; lecture: 'Medizintechnik und Künstliche Intelligenz [KI]'

## MITTELSTANDSKONFERENZ

November 19 – 20, 2018 | Berlin Richard Bieck | project presentation COMPASS

# **PROJECT- AND COOPERATION WORK**

KICK OFF MEETING PROJECT MRI-SUITABLE FLEXIBLE BIOPSY FORCEPS FOR MINIMALLY INVASIVE TISSUE SAMPLING

January 26, 2018 | Dettingen/Erms

# MR-INTERVENTION AND MR-HIFU AT CHILDREN'S NATIONAL MEDICAL CENTER

February 6 – 10, 2018 | Washington, WA, USA Andreas Melzer | MR-Interventions and MR-HiFu

# STEERING COMMITTEE MEETINGS OF PROJECT

EUROPEAN MEDICAL FIELD HOSPITAL (EUMFH) February 19 – 21, 2018 | Tallin, Estonia July 10 – 11, 2018 | Leipzig October 13 – 18, 2018 | Bucharest, Romania December 10 – 12, 2018 | Rome, Italy Thomas Neumuth | steering committee member

## DPM GROUP MEETS INTERACTIVE MEDIA LAB FROM TECHNISCHE UNIVERSITÄT DRESDEN

March 1, 2018 | Leipzig Alexander Oeser, Jan Gaebel | representation of ICCAS and the Digital Patient Model

## **EUROPEAN RESEARCH COUNCIL (ERC)**

March 19 – 23, 2018, June 18 – 22, 2018 | Brussels, Belgium

Andreas Melzer | member: ERC Starting Panel 2018

## FINAL PRESENTATION OF PROJECT BIOPASS

April 25 – 27, 2018 | Siegburg

# MR BIOPSY AND MR STENT AT GUYS' AND ST THOMAS HOSPITAL

April 26, 2018 | London, UK Andreas Melzer | cooperation talks

# GERMAN CANCER AID AT UNIVERISTY CANCER CENTER (UCCL) LEIPZIG

May 14 – 17, 2018 | Leipzig University Hospital, University Cancer Center Leipzig (UCCL)

**Thomas Neumuth** | presentation of computer assisted medicine in cancer therapy

# WORLD HEALTH ORGANIZATION (WHO) – REGIONAL CONFERENCE

#### April 18, 2018 | Brussels, Belgium

**Thomas Neumuth** | Presentation of research results on the development and application of digital medical records for emergency medical teams (EMTs)

# MR-INTERVENTIONS at CHILDREN'S NATIONAL MEDICAL CENTER

October 26, 2018 | Washington, USA Andreas Melzer | MR-Interventions

## **KICK-OFF MEETING PROJECT HEALTH EU**

June 27 – 29, 2018 | Lausanne, France

# RESEARCH STAY AT JOINT INSTITUTION FOR ADVANCED BIOMEDICAL SCIENCES OF TOKYO WOMEN'S MEDICAL UNIVERSITY AND WASEDA UNIVERSITY (TWINS)

June 28 – July 31, 2018 | Tokyo, Japan

Johann Berger, Max Rockstroh, Erik Schreiber | Scientific Exchange on open networking of medical devices and it systems in operating room and hospital

## PROJECT MEETING MOVE

September 13, 2018 | Leipzig

### EU CIVIL PROTECTION EXERCISE MODEX

October 14 - 18, 2018 | Bucharest, Romania

**Thomas Neumuth, Erik Schreiber** | Evaluation of digital patient record for disaster relief under real conditions in the scope of project EUMFH

## KICK-OFF MEETING PROJECT LYSIS

October 9, 2018 | Leipzig

# HYPERSPECTRAL IMAGING (HSI) WORKSHOP AT CLINIC OF VISCERAL SURGERY AT LEIPZIG UNIVERSITY HOSPITAL

## November 14, 2018 | Leipzig

Claire Chalopin | welcome speech Hannes Köhler | lecture: 'Clinical and technical developments'

# **UNIVERSITY COURSES**

## VISIT AT CHONGQING UNIVERSITY

November 4 – 5, 2018 | Chongqing, China Andreas Melzer | representation of ICCAS

# VISIT AT UNIVERSITY OF SHANGHAI FOR SCIENCE AND TECHNOLOGY

November 6 – 8, 2018 | Shanghai, China Andreas Melzer | representation of ICCAS

#### **REQUIREMENTS WORKSHOP OF PROJECT COMPASS**

December 4, 2018 | Leipzig

#### LEIPZIG UNIVERSITY

'Computer Assisted Surgery' Faculty of Mathematics and Computer Science practical course

'Development of Medical Products' Faculty of Mathematics and Computer Science lecture

'Introduction to Computer Assisted Surgery' Faculty of Medicine lecture

'Medical Planning and Simulation Systems' Faculty of Mathematics and Computer Science lecture

'Surgical Navigation, Mechatronics and Robotics' Faculty of Mathematics and Computer Science lecture

'System Innovation in Medicine' Faculty of Mathematics and Computer Science lecture and seminar

### **LEIPZIG UNIVERSITY OF APPLIED SCIENCES (HTWK)**

'Developing Medical Products' Faculty of Electrical Engineering and Information Technology lecture and seminar

'Project Management for Engineers' Faculty of Electrical Engineering and Information Technology, Mechanical and Energy Engineering lecture and seminar

System Engineering Faculty of Electrical Engineering and Information Technology lecture

# GRADUATIONS

## **MASTER DEGREES**

## Nico Graebling

'Generierung und Verwendung künstlicher Trainingsdaten für CNNs zur Erkennung von Operationsinstrumenten' Leipzig University

### **Karsten Brandt**

'Graphenbasierte Visuelle Analyse von Qualitätsberichten der Krankenhäuser' Leipzig University

## Norbert Lang

'Eine intraoperative Planungs- und Navigationssoftware für Kraniotomien unter der Verwendung eines Auditory Displays' Leipzig University

## **Chris Unger**

'Structured Collection of Patient Data for Decision Support Systems by the Example of a Probabilistic-Graphical Model for Laryngeal Cancer Therapy' Leipzig University

## **BACHELOR DEGREE**

## Moritz Lehnhardt

'Entwicklung einer Prozesskette zur additiven Herstellung von realitätsnahen Blutkreislaufmodellen' TU Darmstadt

# ORGANIZATION



# **EXECUTIVE DIRECTOR**

Melzer, Andreas

Human Medicine & Dentistry

# **STAFF**

Angel Raya, Erick	Electrical Engineering
Athner, Katrin	Business Management
Bailis, Nikolaos	Chemistry,
	Human Medicine
Bednarz, Anastasia Helena	Biology
Beil, Verena Maria	Molecular Life Science and
	Bioinformatics
Berger, Johann	Computer Science
Bieck, Richard	Computer Science
Blaschke, Vera Sophie	Medical Life Sciences and
	Human Medicine
Chalopin, Claire	Medical Imaging
Donig, Julian	Technical Radiology
Fischer, Marcus	Humanities
Fitzner, Anne	Office Communication
Franke, Stefan	Computer Science
Fuchs, Reinhard	Electrical Engineering and
	Information Technology
Gaebel, Jan	Computer Science
Gaunitz, Tristan Marvin	Biomedical Technology
Georgi, Christoph	Computer Science
Giri, Priya	Mathematics
Girrbach, Felix	Human Medicine
Graebeling, Nico	Computer Science
Hikal, Aisha	Human Medicine



## **VICE DIRECTOR**

Neumuth, Thomas	Computer Science,
	Electrical Engeneering

Hühn, Marius	Human Medicine
Ivanova, Margarita	Biomedical Engineering
Kazakova, Alina	Humanities
Keller, Johannes Alfred	Computer Science & Logic
Kindler, Johannes	Computer Science
Köhler, Conny	Biomedical Engineering
Köhler, Hannes	Medical Engineering
Kongtso, Patrick	Computer Science
Krabbes, Frederik	Humanities
Landeck, Tobias	Human Medicine
Landgraf, Lisa	Biology
Lang, Leonie	Communication and
	Media Studies
Leifels, Leonard	Human Medicine
Leipold, Maximilian	Human Medicine and
	Bioinformatics
Lenhardt, Moritz	Mechanical Engineering
Lepach, David	Computer Science
Lindner, Dirk	Human Medicine
López Ramírez, Jose Luis	Electrical Engineering
López Rodríguez, Pedro	Electrical Engineering
Luckert, Clemens	Physics
Maktabi, Marianne	Computer Science
Meschke, Tim	Business Information
	Systems

Mrongrowius, Julia	Medical Engineering
	Science
Müller, Juliane	Computer Science
Neumann, Juliane	Computer Science
Oeltze-Jafra, Steffen	Computer Science
Oeser, Alexander	Media Management
Pabst, Tobias	Computer Science
Patties, Ina	Biology
Pfahl, Annekatrin	Medical Engineering
Pogány, Gergely	Biomedical Engineering
Prägler, Stefan	Human Medicine
Reich, Martin	Sensorics and Cognitive
	Psychology
Rockstroh, Max	Computer Science
Rosenow, Simon	Media Management
Roy, Upasana	Physics
Salz, Peter	Computer Science
Schmierer, Lukas	Computer Science
Schneider, Dominic	Computer Science,
	Human Medicine
Scholz, Kathrin	Humanities
Schreiber, Erik	Computer Science
Seifert, Andreas	Physical Engineering
Selbmann, Lisa	Human Medicine
Troitzsch, Hanna	Jurisprudence
Tschachtli, Christine	Office Communication
Unger, Chris	Computer Science
Unger, Michael	Computer Science
Weber, Sebastian	Computer Science
Weiße, Karin	Humanities
Wermke, Ludwig	Computer Science
Wichmann, David	Industrial Engineering and
	Human Medicine
Wiegand, Ulrike	Human Medicine
Zeumer, Christoph	Humanities
Zhang, Xinrui	Pharmacology
Ziemann, Martin	Human Medicine

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