

29. CHIRURGISCHE FORSCHUNGSTAGE

MAGDEBURG

Abstracts

Mit Zugkraft ins Zeitalter der Surgeomics

24. – 26. September 2026
Magdeburg

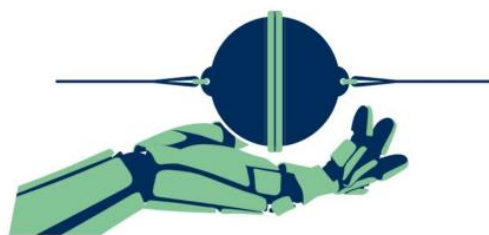


WIR DANKEN DEN SPONSOREN FÜR DIE UNTERSTÜTZUNG DER CHIRURGISCHEN FORSCHUNG



ABSTRACTS

ABSTRACTS



**29. CHIRURGISCHE
FORSCHUNGSTAGE**
MAGDEBURG

Immunologie an den Schnittstellen der Chirurgie

Neutrophil-Mediated Immunomodulation in Surgery: Friend and Foe of Tissue Repair

PD Dr. Luis Munoz
Universitätsklinikum Erlangen
Prof. Dr. Martin Herrmann
Friedrich-Alexander Universität Erlangen-Nürnberg

Neutrophils are the first immune cells recruited to sites of surgical injury and play a central role in orchestrating postoperative inflammation and tissue repair. Beyond their classical antimicrobial functions, neutrophils actively regulate immune responses through cytokine secretion, interactions with adaptive immune cells, and the formation of neutrophil extracellular traps (NETs). While these mechanisms are essential for host defense and wound healing, excessive or dysregulated neutrophil activation may contribute to postoperative complications, including impaired healing, thrombosis, infection, and organ dysfunction. Emerging evidence suggests that neutrophils exhibit remarkable functional plasticity, balancing pro-inflammatory and pro-resolving activities depending on the surgical context. A deeper understanding of neutrophil-mediated immunomodulation may reveal novel therapeutic strategies to optimize recovery, reduce complications, and improve surgical outcomes. This presentation will provide an overview of current concepts regarding neutrophil biology and its clinical relevance in modern surgery.

pH dependent neutrophil extracellular trap degradation by human macrophages

Maximilian Göbel, Yangfan Li, Melike Tombaz, Tina Histing, and Sabrina Ehnert

Background/research question

More than 200,000 people in Germany suffer from chronic wounds, which are often caused by dysregulation of the distinct phases of wound healing. During the inflammatory phase, immune cells such as neutrophils and macrophages play a crucial role in host defense. However, excessive inflammatory responses can impair healing. Neutrophil extracellular trap formation (NETosis), a specific form of neutrophil cell death, has been shown to delay wound healing. Chronic wounds often exhibit neutral-to-alkaline pH that drives excessive NETosis and hinders healing. While DNases and phagocytes normally clear NETs in healthy tissue, little is known about how pH modulates NET degradation. Therefore, this study explored pH-dependent NET clearance by macrophages, to develop pH-targeted therapies for chronic wounds.

Methods and statistics

Primary peripheral blood mononuclear cells (PBMCs) were isolated from human venous blood and differentiated into macrophages over 7 days in the presence of 50 ng/mL macrophage colony-stimulating factor (M-CSF). NETs were generated from neutrophils following stimulation with 100 nM PMA. Differentiated macrophages were treated with NETs at concentrations of 0.5, 1.0, and 5.0 ng/ μ L. Cell viability was assessed using live/dead staining and mitochondrial activity assays under different pH conditions (6.4, 7.4, and 8.4). Gene expression was analyzed by RT-PCR following RNA isolation. In addition, supernatants were collected for quantification of inflammatory cytokines. Finally, a NET degradation assay was established to assess the breakdown of NET structures. Statistical analysis was performed using and groups were compared by Kruskal-Wallis test with an α of 0.05.

Results

NET concentrations of 1.0 and 5.0 ng/ μ L reduced macrophage viability, as demonstrated by both live/dead staining and resazurin conversion assays, while pH had no significant effect over a 3-hour incubation period. Gene expression analysis revealed a 1.5-fold decrease in proinflammatory gene expression (IL1 β , CD86) under acidic conditions, whereas DNase1L1 expression was downregulated 1.5-fold in alkaline pH, compared to pH 7.4. Other markers, including TNF α and CD206, were not significantly affected by pH alone. Treatment with low NET concentrations (0.5 ng/ μ L) had only minor effects on macrophage viability, particularly under alkaline conditions. However, pH-cultured macrophages reacted to NETs treatment by releasing proinflammatory cytokines, including IL1 β . Fluorescence imaging showed uptake of NET structures into the macrophage cytosol (SYTOX Green-positive signals), with no apparent differences between pH conditions after 3 hours. Notably, NET degradation by DNase1 was reduced by approximately 5-fold under alkaline conditions compared with physiological and acidic pH.

Conclusion and Discussion

These findings provide new insights into the role of pH in regulating NET degradation during wound healing. The alkaline environment characteristic of chronic, non-healing wounds appears to inhibit NET degradation, potentially leading to their persistence and contributing to tissue damage. While these results highlight a previously unrecognized pH dependency of NET degradation, further studies with extended incubation periods are required. In particular, the effects of NET exposure on gene expression warrant deeper investigation.

Overall, modulation of wound pH may represent a promising therapeutic approach to improve chronic wound healing.

Klinische Studien und Fallbeobachtungen

The Biliary Microbiome in Symptomatic Cholelithiasis: a prospective comparison across microbial niches

PD Dr. med. Ulrich Wirth

Klinik für Allgemein-, Viszeral-, und Transplantationschirurgie, LMU Klinikum, LMU Medizin, Ludwig-Maximilians-Universität München

Dr. rer. nat. Ramiro Vilchez-Vargas

Medizinische Klinik und Poliklinik II, LMU Klinikum, LMU Medizin, Ludwig-Maximilians-Universität München

Franziska Fuchs

Klinik für Allgemein-, Viszeral-, und Transplantationschirurgie, LMU Klinikum, LMU Medizin, Ludwig-Maximilians-Universität München

PD Dr. med. Christian Schulz

Medizinische Klinik und Poliklinik II, LMU Klinikum, LMU Medizin, Ludwig-Maximilians-Universität München

Prof. Dr. med. Joachim Andrassy

Klinik für Allgemein-, Viszeral-, und Transplantationschirurgie, LMU Klinikum, LMU Medizin, Ludwig-Maximilians-Universität München

Introduction

The biliary tract was long considered physiologically sterile. However, recent studies have demonstrated the presence of a complex microbial community in both healthy individuals and

patients with biliary diseases. Bacteria are increasingly recognized as important contributors to gallstone formation and inflammatory diseases of the biliary tract. Nevertheless, high-resolution microbiome data on benign biliary disorders such as symptomatic cholelithiasis, acute and chronic cholecystitis, and choledocholithiasis remain limited.

Research Question

This study aimed to investigate the role of the biliary microbiome in benign biliary diseases, including symptomatic cholelithiasis, acute and chronic cholecystitis, and choledocholithiasis, and to compare the biliary microbial niche with adjacent microbial ecosystems of the oral cavity and the gut.

Methods

In this prospective study, bile, gallstone, saliva, and stool samples were collected from patients undergoing elective or emergency cholecystectomy for symptomatic cholelithiasis or cholecystitis, as well as from patients undergoing endoscopic retrograde cholangiography (ERC) for choledocholithiasis. Participants additionally completed a standardized questionnaire addressing dietary habits, physical activity, alcohol consumption, and smoking status. Transcriptionally active bacterial communities were characterized using 16S rRNA gene-based microbiome analysis. Microbiome sequencing data were analyzed using established pipelines.

Statistics

Comparative analyses of microbial community composition and diversity across anatomical niches and disease entities were performed, and associations with clinical characteristics were assessed using biostatistical methods.

Results

A total of 81 patients were included, comprising 28 patients with symptomatic cholelithiasis, 22 with chronic cholecystitis, 21 with acute cholecystitis, and 10 undergoing ERC for choledocholithiasis. Overall, 227 biological samples were analyzed. No significant associations were observed between microbiome composition and lifestyle factors or patient comorbidities. Distinct microbial clustering was identified according to anatomical niche, with the biliary microbiome showing greater similarity to the upper than to the lower gastrointestinal tract. The predominant bacterial genera detected in bile were *Escherichia/Shigella*, *Serratia*, *Pseudomonas*, and *Enterococcus*. Further analyses identified *Enterococcus*, unclassified *Enterobacteriaceae*, *Serratia*, *Pseudomonas*, *Escherichia/Shigella*, and *Porphyromonas* as relevant opportunistic pathogens associated with symptomatic gallstone disease. Notably, *Escherichia/Shigella* was strongly associated with inflammation in patients with acute cholecystitis.

Discussion

This study provides the first comprehensive characterization of the biliary microbiome in patients with symptomatic cholelithiasis and offers a comparative analysis of multiple microbial niches within the same individuals. The findings suggest that distinct opportunistic pathogens contribute to lithogenesis and the development of symptomatic gallstone disease.

Conclusion

These results improve our understanding of the biliary microbial ecosystem and may support the development of microbiome-based diagnostic and therapeutic strategies for benign biliary diseases.

Evaluation of MRI-Derived Indices and Spinal Malalignment in Patients with Pectus Excavatum

Müller LM¹, Stefanescu MC¹, Werner, E¹, Tural S¹, Rohleder S¹,

¹ Department of Pediatric Surgery, University Medical Center Mainz, Germany

Introduction

Pectus excavatum (PE) is the most common congenital chest wall deformity in pediatric surgery and is frequently associated with alterations in spinal alignment. The severity of the thoracic deformity can be quantified using magnetic resonance imaging (MRI)-derived parameters such as the Haller Index (HI), Correction Index (CI) and Asymmetry Index (AI). Radiation-free surface topography DIERS 4D Motion Lab System additionally enables assessment of spinal posture and alignment. However, the relationship between MRI-derived thoracic morphology and surface topography based spinal parameters remains insufficiently investigated.

Research Question

The objective of this study was to assess the relationship of AI, CI, HI and surface topography-based spinal measurements in motion using MRI and radiation-free surface topography.

Methods

This retrospective single-center study evaluated MRI-derived thoracic parameters and surface topography-based spinal measurements in preoperative patients with pectus excavatum. HI, CI and AI were determined from MRI scans. The scoliosis angle was assessed in upright position and motion using the DIERS 4D Motion Lab system.

Results

Twenty-two preoperative patients with pectus excavatum were included (median age 16 years; range 13–22 years). Mean HI was 5.64 ± 1.74 (range: 2.61–9.15, 95% CI: 4.86–6.40), mean CI: $33.94 \pm 9.89\%$ (range: 12.2–58.6, 95% CI: 29.56–38.33), and mean AI -0.029 ± 0.124 (range: -0.392–0.203, 95% CI: -0.084–0.026). Mean scoliosis angle (SA) was $-5.59 \pm 14.66^\circ$ (range: -29- +20, 95% CI: -12.09–0.91). A moderate positive correlation was observed between HI and SA ($r = 0.414$, $p = 0.055$). Significant correlations were identified between CI and SA ($r = 0.52$, $p = 0.01$) as well as between AI and SA ($r = -0.54$, $p = 0.01$).

Conclusion

Surface topography systems facilitate a radiation-free evaluation of potential correlations between chest wall deformities and spinal misalignments. This study offers preliminary evidence of a potential association between spinal misalignment and asymmetric malformations with high CI. However, these results need to be verified in a larger patient population and monitored over time following surgical correction.

Long-term complications following endovascular repair of infrarenal abdominal aortic aneurysms using Anaconda™ stent-graft prostheses

Tobias Röthig

Prof. Dr. med. Frank Meyer

(Department of General, Visceral, Vascular and Transplantation Surgery, University Hospital Magdeburg)

Dr. med. Udo Barth

(Division of Vascular Surgery, Department of General, Visceral, Vascular and Transplantation Surgery, University Hospital Magdeburg)

Introduction: Endovascular aortic repair (EVAR) has become the predominant treatment for infrarenal abdominal aortic aneurysms. Its short-term advantages in mortality, morbidity and perioperative complications in comparison to open surgical treatment are offset by the requirement for lifelong surveillance and by the risk of device-related complications and reinterventions during long-term follow-up.

Objective: Presentation of long-term outcomes of EVAR using Anaconda™ stent-graft prostheses at a tertiary referral centre under routine clinical conditions (“real-world data”).

Patients and Methods: Single-centre, retrospective observational case study (design) of all patients who underwent EVAR with an Anaconda™ stent-graft between 2008 and 2016, conducted as a systematic clinical audit for vascular-surgical quality assurance and as a contribution to health-services research. Patient-specific, procedure-related and outcome-relevant variables were recorded in a computerised registry and compared with data from the medical literature including statistical testing to identify significant influencing factors.

Results: Between 2008 and 2016, sixty Anaconda™ stent-grafts were implanted for infrarenal abdominal aortic aneurysms (follow-up period: 15 ± 2 years). The male-to-female ratio was 54:6 (9:1); mean age was 72.5 years. Twenty-seven endoleaks of any type occurred (45,0 %). Incidence of type I and type II endoleaks was 8.33 % ($n = 5$) and 36,67 % ($n = 22$), respectively; no type III or IV endoleaks were observed. Pronounced graft migration occurred in five cases (8.33%). A markedly elevated rate of thromboembolic limb occlusions was documented ($n = 10$; 16,67 %). Late open surgical conversion was required in eight patients (13.33%) — four cases (6.67 %) for recurrent embolic events and four cases (6.67 %) for stent - graft migration. When compared with two recent publications (Insernia et al., 2021*; Abatzis - Papadopoulos et al., 2024**), revealing noticeably higher rates of thromboembolic events and conversion to open surgical treatment.

Discussion: The investigation was prompted by a frequent cluster occurrence of prosthesis migrations, particularly involving Anaconda™ stent-graft prostheses, observed during medium- to long-term postinterventional follow-up.

Conclusion: The temporal clustering of stent-graft migrations following EVAR, observed within the first decade post-implantation, indicates a sustained upward trend in their incidence.

Definitive treatment usually requires open vascular surgery, as dislocated grafts may present in grotesque configurations and positions. The elevated incidence of thromboembolic limb occlusions relative to contemporary literature likewise supports consideration of late open surgical conversion and an age - adapted decision-making process that may favour primary open aneurysm repair in selected patients.

Surgical treatment of adrenocortical carcinoma in Germany – a model-based approach considering distribution and various levels of center expertise from 2020 to 2024

A. Mikl¹, M. Berlet¹, S. Schorn¹, M. Kießler¹, M. C. Weber¹, D. Wilhelm¹, H. Friess¹, C. Chiapponi¹

Introduction Adrenocortical carcinoma (ACC) is a rare, aggressive malignancy in which complete resection by an experienced team is the key prognostic factor. The European Society of Endocrine Surgeons (ESES) recommends at least six adrenalectomies (AE) per surgeon per year for benign disease and at least twelve AE per year for ACC. We evaluated whether German ACC surgery is concentrated in centres meeting these thresholds and how the geographic distribution of care evolved between 2020 and 2024.

Research Question How did the surgical treatment of ACC in Germany vary by geographic distribution and level of centre expertise from 2020 to 2024?

Methods Using the purpose-built Geo::Surg modelling framework, which integrates hospital quality data with geographic and census information, we analysed the annual minimal volume and spatial distribution of adrenalectomies (OPS 5-07[1/2]) and surgically treated ACC cases (ICD-10-GM C74.0) for 2020–2024. Overall case and procedure numbers were retrieved from the InEK database.

Statistics All analyses were descriptive; continuous variables are reported as mean $\pm$ standard deviation and categorical variables as counts and proportions. Departments were stratified by annual AE volume using the ESES thresholds (≤ 6 , ≥ 12 , and ≥ 30 per year), and the share of ACC cases below each threshold was compared between 2020 and 2024. Spatial distribution and minimal annual volume were estimated with Geo::Surg.

Results Between 2020 and 2024, 581 adrenalectomies were performed for ACC (mean 116 ± 8 per year; 3.2% of all AE), across 94 ± 4 departments per year and 229 hospitals - 54.1% of which treated ACC in only one of the five years. Overall, 60.0% of cases in 2020 and 52.8% in 2024 were managed in departments below the recommended twelve AE per year, while 26.9% (28.3% in 2024) were treated in very high-volume centres performing at least 30 AE per year.

Discussion ACC surgery in Germany is not systematically centralised: a consistent majority of patients were treated below the ESES-recommended twelve AE per year, and care was both geographically dispersed and fragmented, with sporadic single-year institutional exposure unlikely to sustain the multidisciplinary infrastructure ACC requires. This matters because the index operation is the principal determinant of outcome, and low-volume surgery is associated with higher recurrence. The rise in cases meeting the threshold (40.0% to 47.2%) indicates only a slow drift toward concentration, driven by informal referral rather than system-level

steering. Defined referral pathways, minimum-volume regulation, centre certification, and networked models could accelerate appropriate centralisation. Key limitations are the reliance on administrative coding -precluding data on resection margins, stage, or outcome - and the use of institutional rather than surgeon-level volume.

Conclusion The surgical treatment of ACC in Germany remains insufficiently centralised despite the strong volume - outcome relationship for this rare tumour. Care is geographically dispersed and fragmented across many low-volume providers. Practicable strategies for centralising interdisciplinary ACC treatment are needed.

Video-Assisted Thoracoscopic versus Open Thymectomy for Myasthenia Gravis: Impact of Tumor Size on Surgical Approach and Outcomes

H Wolfer, G Friedel, C Schlensak, V Steger, A Nemeth

Department for Thoracic and Cardiovascular Surgery, University Hospital Tübingen, Tübingen, Germany

Correspondence Author:

Dr. med. Himatur Wolfer Department for Thoracic and Cardiovascular Surgery,
University Hospital Tübingen, Hoppe-Seyler-Str.3, 72076 Tübingen, Germany

Background

Thymectomy improves acetylcholine receptor antibody–positive (AChR-ab+) myasthenia gravis even without visible thymic masses. Despite guidelines supporting early intervention, surgery is frequently delayed until mediastinal masses develop, potentially necessitating sternotomy. We hypothesized that early intervention enables video-assisted thoracoscopic surgery (VATS) with improved perioperative outcomes.

Methods

We conducted a retrospective cohort study of 45 consecutive myasthenia gravis patients who underwent thymectomy between 2014 and 2024 (VATS, n=35; sternotomy, n=10). The VATS cohort included 12 ocular myasthenia gravis patients (34%) and 15 patients (43%) without discrete masses. All sternotomy patients had generalized disease. AChR-ab+ prevalence was 77% versus 80%. Primary outcomes were perioperative complications and hospital length of stay.

Results

Among patients with discrete masses, those undergoing sternotomy had larger lesions (median diameter, 47mm [IQR, 30-53] vs. 27mm [IQR, 11-44]; $P=0.05$) and more frequently required resection of adjacent structures (60% vs. 14%; $P=0.007$). Median operative time was shorter with VATS (78 minutes [IQR, 66-106] vs. 163 minutes [IQR, 126-262]; $P<0.001$). Fewer VATS patients required ICU admission (11% vs. 60%; $P=0.014$). VATS was associated with reduced hospital stay (median, 3 days [IQR, 2-3] vs. 8 days [IQR, 5-11]; $P<0.001$) and chest-tube duration (mean, 1.6 ± 0.7 vs. 7.1 ± 8.0 days; $P<0.001$). Perioperative complications occurred in 14% after VATS versus 60% after sternotomy ($P=0.007$). R0 resection was achieved in 97% with VATS versus 60% with sternotomy ($P=0.004$).

Conclusions

In patients with myasthenia gravis, video-assisted thoracoscopic thymectomy was feasible in the majority of cases, including those without discrete thymic masses, and was associated with substantially lower perioperative morbidity compared with sternotomy. Larger thymic lesions necessitated open surgical approaches with increased complications. Given randomized evidence supporting thymectomy in AChR-ab+ myasthenia gravis regardless of visible thymic pathology, these findings support guideline-adherent early surgical intervention to preserve candidacy for minimally invasive techniques and minimize perioperative morbidity.

Prospective randomised study to evaluate the impact of post-procedural therapy individually tailored to the patient's resistance to antiplatelet agents, on treatment outcomes following interventional therapy for peripheral arterial disease (PAD) – a trial concept

Nicolas Kühnle,
Division of Vascular Surgery; Dept. of General, Abdominal, Vascular & Transplant Surgery;
Dr. Udo Barth,
Division of Vascular Surgery; Dept. of General, Abdominal, Vascular & Transplant Surgery;
Prof. Dr. Frank Meyer,
Dept. of General, Abdominal, Vascular & Transplant Surgery;
Dr. Katrin Borucki,
Department of Clinical Chemistry and Pathobiochemistry
Dr. Anke Lux,
Institute for Medical Data Science Magdeburg University Hospital, Magdeburg, GERMANY

Introduction:

Treatment with antiplatelet agents represents a well-established part of the standard management of symptomatic peripheral arterial disease (PAD). The indication for prescribing these agents in patients with claudication and (chronic) limb-threatening ischaemia is undisputed. Numerous studies conducted predominantly in cardiology patients have shown a high prevalence of treatment failure with antiplatelet therapy using ASA and clopidogrel.

Materials and methods:

The primary objective is to evaluate the benefits of a Multiplate-based testing strategy (Multiplate® test using the Multiplate® Analyser, Dynabyte, Munich/Germany) performed by the Institute of Clinical Chemistry and Pathobiochemistry compared with standard care without testing. The test principle comprises a monocentric clinical case-control study with a prospective, randomised, controlled, two-arm study design, without blinding.

Results (study corner points):

The study is to be conducted as a clinical case-control study. This is a single-centre study with a prospective, randomised and controlled two-arm study design. Patients will be randomly assigned to the two treatment groups. This will be done using permuted block randomisation (100 patients per group). The sample size calculation is based on the assumption of a clearance rate of 65% in the control arm and a clinically relevant improvement to 80% in the intervention arm (difference of 15 percentage points), which, according to the standard formula for comparing two proportions at a two-sided significance level of $\alpha=0.05$ and a target power of 80%, would result in a sample size of approximately 138 patients per arm. For reasons of practical feasibility in a single-centre setting, a sample size of 100 patients per arm (200 patients in total) will be recruited ensuring that the study has sufficient power for larger effect sizes (e.g. improvement from 60% to 80%), whilst primarily serving a hypothesis-generating purpose for smaller effect sizes. Patient recruitment will take place via the Division of Vascular Surgery. Here, patients with symptomatic PAD will be examined and the appropriate primary diagnostic procedures will be initiated. Based on the clinical findings and individual confirmatory diagnostics (CT [computed tomography] angiography, MR [magnet resonance] angiography, transbrachial DSA [digital subtraction angiography], colour-coded duplex sonography), the indication for interventional revascularisation is determined on an interdisciplinary basis during the

vascular surgery-radiology conference (similar to the policy of a certified "Vascular Medicine Center"). Subsequently, patients, for whom an intervention is planned, are recalled to the Division of Vascular Surgery for further care. Only patients, who are already taking and are taking only 100 mg of ASA once daily as an antiplatelet agent alongside their baseline medication, are included in the study. The first Multiplate® test is performed here at this timepoint:

- If platelet inhibition with ASA 100 mg once daily is insufficient, the patient is switched to clopidogrel 75 mg once daily.

- If platelet inhibition is adequate, ASA is continued at the same dose.

Subsequently, clinical findings are documented by measuring i) ankle-brachial index (ABI) in all patients and ii) walking distance under standardised conditions on a treadmill, and photographing lesions in patients with stage-IV PAD.

Post-interventionally, patients of the "ASA response group" receive a loading dose of 300 mg clopidogrel once on the day of the procedure, followed by 75 mg once daily for 4 weeks. The clopidogrel group ("non-ASA response group") continues with 75 mg. On the third post-

intervention day, a repeat Multiplate® test is performed in the clopidogrel monotherapy group: -If platelet inhibition is sufficient after the intervention, the standard maintenance dose of 75 mg clopidogrel is continued;

- If platelet activity is insufficiently inhibited, the regimen is switched to 100 mg ASA once daily and

2.5 mg rivaroxaban twice daily, in accordance with the subgroup analysis of the "VOYAGER PAD study". Early postoperative outcomes are statistically analysed by comparing the ABI and walking distance (before and after), as well as patency and occlusion rates and the amputation rate (using Kaplan-Meier estimates).

The study concept will be applied for official German-wide study registration.

Conclusion:

The novelty of the study lies in the fact that, for the first time, the strategy involving Multiplate®-guided dose/medication adjustment is being tested against the standard strategy without testing, followed by a subsequent assessment of success. The study does not compare fixed medication regimens but rather the strategy of whether or not Multiplate® testing is used for individual adjustment. In the control arm, medication is administered in accordance with guidelines without test-based adjustment.

Opioids in patients with back pain: To initiate or to stop. Patients monitored over 6 years of care including a 7-year follow-up

Giselher Pfau G(1), Anke Lux (2), Frank Meyer(3)

1 Division of Pain Therapy, Dept. of Anesthesiology and Intensive Care;

2 Institute of Medical Data Science;

3 Dept. of General, Abdominal, Vascular and Transplant Surgery;

Otto-von-Guericke University with University Hospital, Magdeburg (Germany)

Background:In light of the 'opioid epidemic'described in numerous occasions in the U.S.A.,the question of why opioid consumption is rising in cases of non-cancer pain has become increasingly important.

Questions:Do patients experiencing pain always require opioids?

Does the specific pain diagnosis to be treated influence opioid prescription?Is oxycodone necessary?

Patients & methods:Using three different research approaches,patients with back pain admitted between 2010 and 2015 were followed up to seven years later to assess the quantities of opioids prescribed during the intermittent years and the relevant factors influencing this.

Results:During the observation period from 2010-2015,769 patients were treated.

Of these,267(34,7 %)had back pain(radicular and non-radicular).

Patients with back pain,in particular,require stronger opioids than those with other forms of pain(neuropathies,head/ facial pain).

With long-term use,the proportion of opioids>1,200 mg tilidine equivalent dose (TED)for back pain is 20%,which is higher in the overall group of diagnoses examined here than in the literature (9.9%).

Discussion:Patients with back pain represent a more difficult group of subjects to treat than the overall cohort of patients examined here.This is demonstrated by the clinical symptomatology in patients who have never received opioids or who did not receive opioids at the end of the observation period (38.2%vs.52.4 %).This is also evident in diagnoses such as headaches,in which no patient received the maximum dose of 1,200 mg TED.It should be noted critically that,in finding the 9.9%rate in the literature,it is unclear,which diagnoses contributed to this and to what extent.

It has also become clear that oxycodone is dispensable.

Conclusion:In future studies and reviews of the literature,attention must be paid to the pain conditions under investigation.

Da Vinci single-port-assisted subcostal esophagectomy (SP SC RAMIE)

Luca Bellaio, Vladimir J Lozanovski, Edin Hadzijušević, Evangelos Tagkalos, Franziska Renger, Olga Adamenko Meier, Suzanne S Gisbertz, Hauke Lang, Peter P Grimminger

Abstract

Introduction

Recent developments in robotic systems, such as the introduction of the da Vinci Single-Port (SP) Robot System allow for precise access to the esophagus through a small cervical and subcostal single-port incision. As previously demonstrated, the subcostal incision during the da Vinci Single-Port Subcostal RAMIE (SP SC RAMIE) is used for access to the thoracic cavity to dissect the esophagus, retrieve the specimen, and perform reconstruction. SP SC RAMIE offers advantages in esophageal cancer surgery but remains unfamiliar and requires a long learning curve.

Research question

Feasibility and Safety of the SP SC RAMIE procedure for esophageal cancer

Methods

The first 25 consecutive SP SC RAMIE procedures were analyzed. Patient demographics, neoadjuvant therapy, resection margins, lymph node yield, intraoperative parameters, postoperative recovery, complications, and mortality were assessed. Feasibility was defined by achieving RO resection and a lymph node yield exceeding benchmark recommendations.

Statistics

SPSS Version 30.0.0) was used for all analyses. Continuous variables are presented as mean $\pm$ standard deviation (SD) or median (range), while categorical variables are expressed as percentages.

Results

The cohort consisted primarily of male patients with adenocarcinoma of the esophagogastric junction, 72% of whom had undergone neoadjuvant therapy. RO resection was achieved in all cases, with a mean lymph node yield of 30 (SD $\pm$ 10), confirming procedural feasibility. Mean total operative time was 324 ($\pm$ 51) minutes, with an active console time of 79 ($\pm$ 17) minutes. No intraoperative complications or conversions occurred. No patient received epidural or intercostal catheter analgesia and mean postoperative pain scores were very low. By postoperative day five, 92% of patients were receiving analgesia on demand. Most patients ambulated on the first postoperative day, and the median hospital stay was seven days (range 5-40). Postoperative complications included two cases of pneumonia (8%) and two anastomotic leakages (8%), all managed endoscopically with an endoluminal vacuum sponge. In-hospital, 30-day, and 90-day mortality rates were 0%.

Discussion

The results show that SP SC RAMIE is feasible, allows effective intrathoracic esophageal mobilization, and enables adequate subcarinal and radical mediastinal lymphadenectomy in selected patients. These outcomes were achieved within operative times comparable to other minimally invasive esophagectomy techniques. An RO resection was achieved in all patients, with a high lymph node yield likely attributable to the enhanced visualization and precision of the robotic system. No in-hospital, 30-day, or 90-day mortality rates were observed, supporting the safety of this technique. These findings support SP SC RAMIE as a promising option for selected cases.

Conclusion

SP SC RAMIE is a feasible and safe esophagectomy technique for lower esophageal cancer resection, with a low complication rate and high lymph node retrieval. Rapid recovery, low pain scores, and a short hospital stay highlight its potential benefits.

Kolorektalbiologie im Wandel – Von molekularen Mechanismen zur klinischen Innovation

Redirecting Tregs to the inflamed gut: CAR-guided anti-inflammatory therapy in IBD

Jessica Kümmel, 1

Constanze Binder, 1

Hannah Nies, 1

Dr. rer. nat. Natalie Burkard, 1

Univ.-Prof. Dr. med. Nicolas Schlegel, 1

Dr. med. Johanna C. Wagner, 1

1: Department of General, Visceral, Transplantation, Vascular and Pediatric Surgery,
University Hospital Würzburg, Würzburg, Germany

Ulcerative colitis (UC) and Crohn's disease (CD) are the two major types of inflammatory bowel diseases (IBD). They are caused by a multifactorial pathophysiology involving genetic predisposition, altered immune function, microbiota changes, environmental factors, and loss of intestinal barrier integrity. Decreased barrier function plays an important role in the development of IBD. Altered expression of barrier proteins disrupts gut permeability, while impaired immune homeostasis leads to immune cell infiltration and elevated pro-inflammatory cytokines, including TNF- α , IL-12, and IL-23. Although complex in disease etiology, a defective regulatory T cell (Treg) compartment and the loss of immune tolerance are widely recognized drivers of IBD progression.

Since Tregs naturally possess tolerance-inducing and anti-inflammatory properties, they are promising therapeutic candidates for restoring immune tolerance in IBD. To engineer epithelial barrier-targeted Tregs, we developed a panel of chimeric antigen receptors (CARs) that recognize gut-specific antigens. Using an established in vitro model of intestinal inflammation, we verified the antigen-dependent activation of CD4⁺T cells expressing each gut-specific CAR by measuring the level of CD69 and the CD25 mean fluorescence intensity (MFI). In current ongoing work, we are evaluating the ability for gut-specific CAR Tregs to suppress gut-reactive conventional T cells and restore epithelial barrier integrity. Therefore, we will analyze anti-inflammatory cytokine signatures, including IL-10 and TGF- β , as well as the transepithelial electrical resistance (TEER) of an intestinal epithelial barrier model in a pro-inflammatory environment following co-culture with CAR Treg. The aim is to identify the CAR construct that best combines potent anti-inflammatory function with high target specificity. These findings will provide the basis for a preclinical strategy that aims to re-establish mucosal immune tolerance, promote endogenous tissue repair, and reduce chronic intestinal inflammation in a sustainable manner.

Unusual Differential Diagnosis of Acute Appendicitis in Central Europe – Right-Sided Diverticulitis (Clinical and Surgical Aspects of a Rare Localization)

Dergunov (Magdeburg) ... Rose C*, Croner RS, Meyer F

Dept. of General, Abdominal, Vascular and Transplant Surgery;

* Dept. of Radiology and Nuclear Medicine;

Otto-von-Guericke University with University Hospital, MAGDEBURG (Germany)

Background:In addition to acute appendicitis,which represents the most common cause of right lowerquadrant abdominal pain,uncommon differential diagnoses should also be considered.Owing to theirrelatively low prevalence and limited familiarity in routine clinical practice,these conditions may posediagnostic and therapeutic challenges.

Aim:By means of a case description,the diagnostic and therapeutic case management of a patient withright-sided diverticulitis is to be highlighted,a rare manifestation of diverticular disease,including thediscussion of case-specific management experiences.In addition,selected current literature is reviewed.**Method:**Scientific case report with selective literature review and discussion

Results:(case presentation including medical history,symptomatology,clinical findings,diagnostic work-up,diagnosis-finding,[differential]diagnosis/therapy,clinical course,outcome,and follow-up):

Medicalhx:-Current:A38-year-old woman presented with several days of right lower quadrantabdominal pain without associated fever,chills,dysuria,or disturbances of bowel function.**-Own:**Relevant comorbidities included arterial hypertension and an atrial septal defect.There was nohistory of previous abdominal surgery.

Clinical findings:The patient was in good general condition with obesity.Abdominal examinationdemonstrated tenderness in the right lower quadrant,most pronounced at McBurney's and Lanz's points,without guarding or evidence of peritoneal irritation.

Diagnostics:-Laboratory parameters:They revealed elevated inflammatory markers with a C-reactiveprotein(CRP)serum level of 158.73mg/Land slightly right-sided white blood cell count("leukocytosis"; $11.4 \times 10^9/L$).

-Abdominal ultrasound demonstrated inflammatory thickening of the intestinal wall in the aboral third ofthe ascending colon,with anilldefined diverticulum and a smallpericolic fluid collection suggestive of acontained perforation.

-Complementary computed tomography revealed(and,thus,confirmed)inflammatory wallthickening ofthe aboral third of the ascending colon extending over a length of approximately 6 cm,accompanied bysurrounding soft-tissue stranding,without definite evidence of perforation.

Differential diagnosis:Segmental colitis (nonspecific or infectious),Crohn's disease,ulcerative colitis,ascending colon diverticulitis,acute appendicitis,and psoas inflammation or psoas abscess.

Therapy:Conservative inpatient managemen including clinical assessment,laboratory and imagingdiagnostics,temporary bowel rest,intravenous(i.v.)fluid therapy,analgesic treatment,local cooling,pharmacological thromboprophylaxis,i.v.antibiotic therapy(piperacillin/tazobactam 4.5g three timesdaily),seria dinical and laboratory monitoring,gradual reintroduction of oral nutrition,and mobilization.

Clinical course:Under the above-mentioned measures,the patient remained clinically stable with goodtolerance of oral fluid intake.Abdominal pain improved rapidly,accompanied by amarked decline ininflammatory markers.Gradual reinitiation of oral nutrition was achieved

without complications. The patient was discharged in improved clinical condition after five days of inpatient treatment.

Outcome: At the time of discharge, only mild residual tenderness in the right lower quadrant was present, with an otherwise unremarkable abdominal examination.

Follow-up: Outpatient clinical and laboratory follow-up was recommended, including colonoscopy after 6-8 weeks.

Definitive diagnosis: Ascending colon diverticulitis Conclusion: Right-sided diverticulitis represents a relatively uncommon manifestation of diverticular disease in Europe but far more in Asia. In patients with a compatible clinical presentation and suspected diagnosis, complementary cross-sectional imaging should be performed to establish a timely and reliable diagnosis-finding. Accurate diagnosis is essential not only for distinguishing right-sided diverticulitis from other causes of right lower quadrant abdominal pain but also for initiating appropriate, findings-based, and above all timely treatment. Although the general principles of conservative, interventional, and surgical management largely correspond to those applied in left-sided diverticulitis, the optimal surgical approach remains a matter of ongoing debate. While limited and organ-preserving resections are generally preferred whenever feasible, right hemicolectomy continues to play an important role in published series. Potential explanations include diagnostic uncertainty, difficulties in differentiating inflammatory disease from malignant pathology (sometimes even intraoperatively), and the variable extent of inflammatory involvement. Consequently, the optimal surgical strategy for right-sided diverticulitis has yet to be clearly defined.

The role of reactive, adhesive, gonadal fat in the progression of anastomotic healing

Laura Charlotte Gloeck,
 Department of Surgery, University Hospital Bonn, Germany
 Dr. Patrick Leven,
 Department of Surgery, University Hospital Bonn, Germany
 Yasin M. Abdel Galil,
 Department of Surgery, University Hospital Bonn, Germany
 Dr. Dalila J.S. Ribeiro,
 Institute of Innate Immunity, Biophysical Imaging, University of Bonn, Germany
 Dr. Ernesto Picon-Galindo,
 Institute of Innate Immunity, Biophysical Imaging, University of Bonn, Germany
 Patrik Efferz,
 Department of Surgery, University Hospital Bonn, Germany
 Prof. Dr. Dagmar Wachten,
 Institute of Innate Immunity, Biophysical Imaging, University of Bonn, Germany
 Prof. Dr. Sven Wehner,
 Department of Surgery, University Hospital Bonn, Germany

Resection of diseased tissue during colorectal surgery requires the creation of an anastomosis by suturing transected bowel segments. In up to 27% of patients, impaired colon anastomotic healing (CAH) results in colon anastomotic leakage (CAL), which is associated with substantial morbidity and mortality. Obesity is a known risk factor for CAL. Clinical observations indicate that white adipose tissue frequently adheres to the anastomotic site; in mice, this is predominantly gonadal white adipose tissue (gWAT). However, its role in anastomotic healing remains unclear. Given the metabolic and inflammatory alterations of gWAT in obesity, we hypothesized that gWAT adhesions in obese mice are associated with impaired CAH.

This study aims to investigate the role of gWAT in CAH and the impact of obesity-associated alterations. A murine proximal colon anastomosis model was used, with healing outcomes assessed by an anastomotic complication score (ACS). Mice were fed either a low fat (LF), high fat (HF) or control diet prior to surgery. Bulk RNA sequencing was performed to compare adhesive vs contralateral fat in control diet fed mice. Flow cytometry and immunohistochemistry were used for in-depth immune cell phenotyping in anastomosis-adherent versus contralateral (non-adherent) gWAT. To evaluate the overall contribution of adhesive gWAT to CAH, mice underwent gWAT lipectomy or sham surgery prior to anastomosis.

Bulk RNA sequencing revealed significant transcriptomic differences between adhesive and non-adhesive gWAT. HF diet-fed mice exhibited impaired anastomotic healing compared to control diet-fed mice. Anastomosis-adherent gWAT showed an overall increase in immune cell infiltration relative to contralateral gWAT. Total T cells, including CD4⁺ and CD8⁺ subsets, as well as effector (CD44⁺CD62L⁻) and naive (CD44⁻CD62L⁺) T cells, and macrophages were increased. Neutrophil and monocyte counts differed significantly between adhesive and non-adhesive gWAT only in control diet-fed mice.

Notably, control diet-fed mice exhibited higher numbers of CD4⁺ and CD8⁺ T cells per gram of tissue in adhesive gWAT compared to HF diet-fed mice. Neutrophils, monocytes, and macrophages, including Tim4⁺CD11c⁺ classically activated macrophages, were also more abundant in adhesive gWAT from control diet-fed mice. These findings indicate obesity-

associated immune dysregulation. Immunohistochemistry confirmed the presence of neutrophils, monocytes, and macrophages in adherent gWAT. Lipectomized mice demonstrated higher CAL rates compared to sham-operated controls, highlighting a possible protective role of gWAT in anastomotic healing.

gWAT exerts a dual role in CAH. While its presence and adherence to the anastomosis supports healing, obesity-related immune alterations impair its protective function and increase the risk of CAL. These findings suggest that adipose tissue plays a modulatory role in intestinal healing and may represent a potential target for future therapeutic approaches.

CX-5461 sensitizes colorectal cancer cells to ATR inhibition by inducing transcription-replication conflicts

Hanna Deinlein 1,2,3

Carolin Kastner 1,3

Anica Maier 1

Christoph Otto 1,2

Ivana Paskov Škapik 4,5,6

Sarah Hahn 4

Chenrui Xie 4,5,6

Philip Claus 1,2

Jessica Kümmel 1,2

Elmar Wolf 7

Natalie Burkard 1,2

Nicolas Schlegel 1,2

Christoph-Thomas Germer 1

Armin Wiegering 4,5

Stefanie Schmidt 1,2

1)Department of General,Visceral,Transplant,Vascular and Pediatric Surgery,University Hospital Würzburg,97080 Würzburg,Germany

2)Experimental Visceral Surgery,University Hospital Würzburg,97080 Würzburg,Germany

3)Mildred Scheel Early Career Centre(MSNZ)for Cancer Research Würzburg,University Hospital Würzburg and University Würzburg,97080 Würzburg,Germany

4)Goethe University Frankfurt,University Hospital Frankfurt,Department of General,Visceral,Transplantand Thoracic Surgery,60590 Frankfurt am Main,Germany

5) Mildred Scheel Early Career Centre Frankfurt, University Cancer Center, University Hospital Frankfurt, Frankfurt am Main, Germany

6)Frankfurt Cancer Institute,Goethe University Frankfurt, Frankfurt am Main, Germany

7)Institute of Biochemistry,CAU Kiel,24118 Kiel,Germany

The majority of colorectal cancers(CRC)are characterized by loss-of-function mutation within the tumor suppressor gene APC leading to aberrant activation of the WNT signaling pathway. Consequently, APC loss-induced overexpression of the MYC oncogene is the major driver for CRC development. MYC is not only essential for inducing transcription by all three RNA polymerases (RNA Pol I/II), but also for the coordination of RNA transcription and DNA replication in highly proliferative cancer cells. In general, CRC shows elevated RNA Pol activity and, thus, enhanced transcription of ribosomal RNA genes compared to normal tissue. We show that the rDNA transcription inhibitor CX-5461 induces transcription-replication conflicts (TRCs) in ribosomal DNA regions in CRC, leading to cell cycle arrest and ATR/ATM-mediated DNA damage response (DDR). This results in cell cycle arrest and activation of ATR/ATM signaling indicative of a DNA damage response. Simultaneous inhibition of the elicited DNA damage response by the ATR inhibitor AZD6738 results in apoptosis in CRC cell lines as well as both murine tumor organoids and human patient-derived organoids. Combination treatment with CX-5461 and AZD6738 in a highly invasive colorectal liver metastasis (CRLM) in vivo model blocks tumor growth compared to single treatments, opening a therapeutic window for advanced CRC.

Microenvironment-Based Chemotherapy Response Profiling of Colorectal Liver Metastases

Asma Mourad,

Klinik für Allgemein-, Viszeral-, und Transplantationschirurgie, LMU Klinikum, LMU Medizin, Ludwig-Maximilians-Universität München

Ruonan Yang,

Klinik für Allgemein-, Viszeral-, und Transplantationschirurgie, LMU Klinikum, LMU Medizin, Ludwig-Maximilians-Universität München

Anna Christina Schmidt,

Klinik für Allgemein-, Viszeral-, und Transplantationschirurgie, LMU Klinikum, LMU Medizin, Ludwig-Maximilians-Universität München

Prof. Dr. Andreas Dendorfer,

Walter Brendel Zentrum für Experimentelle Medizin, LMU Medizin, Ludwig-Maximilians-Universität München

PD Dr. Julian Holch,

Medizinische Klinik und Poliklinik III, LMU Klinikum, LMU Medizin, Ludwig-Maximilians-Universität München

Prof. Dr. Hanno Nieß,

Klinik für Allgemein-, Viszeral-, und Transplantationschirurgie, LMU Klinikum, LMU Medizin, Ludwig-Maximilians-Universität München

Prof. Dr. Jens Werner,

Klinik für Allgemein-, Viszeral-, und Transplantationschirurgie, LMU Klinikum, LMU Medizin, Ludwig-Maximilians-Universität München

PD Dr. Ulrich Wirth,

Klinik für Allgemein-, Viszeral-, und Transplantationschirurgie, LMU Klinikum, LMU Medizin, Ludwig-Maximilians-Universität München

Introduction

Despite advances in multimodal treatment strategies and the development of targeted therapies, patients with metastatic colorectal cancer continue to have a poor prognosis. Ex vivo evaluation of treatment response using primary tumor tissue has emerged as a promising approach for developing individualized therapeutic strategies.

Research Question

This study aimed to establish high-precision cut tissue slices (PCTS) as an ex vivo model for evaluating the therapeutic response of colorectal liver metastases and to characterize treatment-induced alterations in the tumor microenvironment, including immune cell infiltration and cancer-associated fibroblast populations.

Methods

Fresh surgical specimens from patients undergoing resection of colorectal liver metastases were processed into 300-µm precision-cut tissue slices using a vibratome (Leica VT1000 S). Tissue slices were maintained in culture and treated on day 3 with a modified FOLFOX regimen for 48 hours. Treatment response was assessed using a resazurin-based viability assay and immunohistochemical staining for the proliferation marker Ki-67 and the apoptosis marker cleaved caspase-3, each compared with untreated controls. In addition, immunofluorescence analyses were performed to evaluate stem cell markers, cell cycle regulation, immune cell infiltration, and cancer-associated fibroblast (CAF) populations.

Statistics

Treatment effects were compared between treated and untreated tissue slices. Statistical significance was defined as $p < 0.01$. Receiver operating characteristic (ROC) analysis was performed to evaluate the ability of Ki-67 changes to discriminate between responders and non-responders.

Results

Precision-cut tissue slices were successfully generated from colorectal liver metastases of 11 patients and treated with FOLFOX for 48 hours. Chemotherapy resulted in a significant reduction in tissue viability compared with untreated controls ($p < 0.01$). Furthermore, treated samples showed significantly decreased tumor cell proliferation (Ki-67, $p < 0.01$) and increased apoptosis (cleaved caspase-3, $p < 0.01$). Changes in Ki-67 expression accurately discriminated responders ($n=8$) from non-responders ($n=3$), achieving an area under the curve (AUC) of 1.00. Responders additionally demonstrated reduced expression of FAP, VEGF, Cyclin D1, thymidylate synthase (TS), and ALDH1. Increased infiltration of CD3+ T cells, depletion of regulatory T cells, and co-induction of ATG5. In contrast, non-responders exhibited less pronounced treatment-induced changes and paradoxical upregulation of podoplanin.

Discussion

High-precision cut tissue slices represent a promising ex vivo platform for functional therapy testing in solid tumors. Although the model is limited by the requirement for surgical tissue specimens and a restricted culture period (< 14 days), it preserves the native tumor architecture, extracellular matrix, stromal compartment, and immune microenvironment. This enables the assessment of therapy-induced cellular interactions that cannot be replicated in conventional cell culture systems. Responders exhibited epithelial suppression accompanied by favorable immune remodeling and reduced CAF- and VEGF-associated signaling, highlighting the potential of this platform for personalized treatment prediction and translational cancer research.

Conclusion

High-precision cut tissue slices provide a physiologically relevant ex vivo platform that preserves the native tumor microenvironment and enables functional assessment of therapy responses, supporting their potential for personalized treatment prediction.

Targeting Metabolic Dependencies to Reverse Chemoradiotherapy Resistance in Locally Advanced Rectal Cancer

Maximilian Hellkamp

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Simon Gertken

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Jonas Buchloh

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Julius-Leonard Hellwig

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Lukas Ben Kowitzke

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

PD Dr. Michael Linnebacher

Molecular Oncology and Immunotherapy, Clinic of General Surgery, University Medical Center
Rostock, Rostock, Germany

PD Dr. Matthias Wirth

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Department of Hematology, Oncology and Cancer Immunology, Campus Benjamin
Franklin, Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin
and Humboldt-Universität zu Berlin, Berlin, Germany

Univ.-Prof. Dr. Stefan Rieken

Department of Radiotherapy and Radiooncology, University Medical Center
Göttingen, Göttingen, Germany

Prof. Dr. Jochen Gaedcke

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Clinic for General and Visceral Surgery, Städtisches Klinikum Karlsruhe, Karlsruhe, Germany

Prof. Dr. Michael Ghadimi

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Prof. Dr. Jürgen Wienands

Institute of Cellular and Molecular Immunology, University Medical Center Göttingen,
Göttingen, Germany

Prof. Dr. Günter Schneider

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Institute for Translational Cancer Research and Experimental Cancer Therapy, Technical
University Munich, Munich, Germany

Dr. Melanie Spitzner

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Prof.Dr.Marian Grade
 Department of General,Visceral and Pediatric Surgery,University Medical Center
 Göttingen,Göttingen,Germany

Introduction

Neoadjuvant chemoradiotherapy(CRT)followed by total mesorectal excision is the standard of care forlocally advanced rectal cancer(LARC).Pathological complete response rates of 20%to 30%remainlow because many tumors exhibit intrinsic resistance to radiation and chemotherapy,exposing patientsto unnecessary toxicity and ahigh risk of recurrence.Resistance to CRT is a multifactorial phenomenon driven by the interplay of tumor-intrinsic aberrations,the tumor microenvironment(TME),and metabolicadaptation.

Research question

We asked what actionable determinants drive CRT resistance in LARC and whether pharmacologicinhibition of identified targets can restore radiosensitivity of treatment-resistant cells.

Methods

We established a panel of fourteen patient-derived colorectal cancer celllines(PDCLs)obtained directlyfrom primary tumors,patient-derived xenografts,or patient-derived organoids.For mutationalcharacterization,panel sequencing was performed and all lines were phenotypically profiled usinglive-cell imaging.Therapy response was determined by colony-formation assays and ATP-basedviability after a 4Gy irradiation dose with or without standard CRT(5-FU+oxaliplatin).RNA-sequencingwas applied to elucidate molecular determinants of CRT resistance and a focused drug screen of 126compounds identified agents with selective activity in(chemo)irradiation(IR)-resistant PDCLs.SeahorseXF ATP-Rate analyzes quantified glycolytic and mitochondrial activity.

Statistics

Differential expression was analyzed with DESeq2(adjusted $p < 0.05$, $\log_2 FC \geq 1$).Gene-set enrichment(GSEA)used an $FDR < 0.25$.Metabolic read-outs were compared by two-tailed Student's t-tests($p < 0.05$).Drug-response was expressed as area-under-the-curve(AUC);a $\Delta AUC > \pm 0.05$ definedselective hits.Correlations between gene expression and tumor-regression grade(TRG)were assessedwith the Mann-Whitney U test.

Results

From 14 PDCLs,six cell lines were classified as IR-resistant.Transcriptomic profiling revealedenrichment of oxidative-phosphorylation and glycolysis pathways in IR-resistant PDCLs.The drugscreen uncovered only two compounds with selective efficacy in the IR-resistant cohort:the MCT1inhibitor AZD3965 and the GLUT1 inhibitor BAY-876.Both agents produced positiveirradiation-sensitization scores(ISS)in IR-resistant models,confirming a re-sensitization to therapy.Functionally,IR-resistant PDCLs displayed significantly higher basal oxygen consumption(OCR)andextracellular acidification rates(ECAR),leading to increased mitochondrial and glycolytic ATPproduction.Clinically,GLUT1 mRNA levels were significantly higher in non-responder patients (TRG 1)versus complete responder patients(TRG 4)in our retrospective Gottingen rectal cancer cohort,whichassociation was confirmed across two independent rectal-cancer datasets(MSK,TCGA).

Discussion and Conclusion

The data indicate that a metabolic-hybrid phenotype,characterized by concurrent up-regulation ofglycolysis,lactate export(MCT1)and glucose uptake(GLUT1),underlies intrinsic CRT resistance inLARC.Pharmacologic blockade of GLUT1,and to a lesser extent MCT1,re-sensitizes resistant tumorcells to irradiation,providing functional validation of the metabolic

dependency. Therefore, metabolic reprogramming seems to be a key driver of CRT resistance in rectal cancer. Targeting the glycolytic-lactate axis offers a promising strategy to improve response rates, enable organ-preserving treatment, and may provide a basis for stratifying patients who could benefit from more intensive, metabolism-targeted therapeutic approaches in locally advanced rectal cancer.

Towards standardized PIPAC Therapy: Development and preclinical validation of the first ready-to-use Doxorubicin-Cisplatin formulation

Dr.med.PhD Yaroslav Sautkin:

National Centre for Pleura and Peritoneum, University Hospital
Tuebingen, Tuebingen, Germany; Department of General, Visceral, Vascular and Transplant
Surgery, University Hospital Magdeburg, Magdeburg, Germany

PhD Ranjita Shegokar:

Capnopharm GmbH, Tuebingen, Germany

PhD Janek Kibat:

National Centre for Pleura and Peritoneum, University Hospital
Tuebingen, Tuebingen, Germany

Mona Kibat, MSc:

Capnopharm GmbH, Tuebingen, Germany

PhD Juergen Weinreich:

National Centre for Pleura and Peritoneum, University Hospital
Tuebingen, Tuebingen, Germany

PhD Hans Schoenfelder:

Capnopharm GmbH, Tuebingen, Germany

Prof. Marc André Reymond:

National Centre for Pleura and Peritoneum, University Hospital
Tuebingen, Tuebingen, Germany; Department of General, Visceral, Vascular and Transplant
Surgery, University Hospital Magdeburg, Magdeburg, Germany; Capnopharm
GmbH, Tuebingen, Germany

Objective

Pressurised Intraperitoneal Aerosol Chemotherapy (PIPAC) improves locoregional drug delivery for peritoneal metastases. However, no formulation has been specifically developed or approved for this application, and drugs are currently used off-label. Doxorubicin (DOX) and cisplatin (CIS) represent the most frequently applied PIPAC combination, yet their combined stability, compatibility, and performance under PIPAC conditions have not been systematically investigated. This study aimed to develop and preclinically validate the first ready-to-use, fixed-dose DOX-CIS formulation specifically tailored for intraperitoneal aerosol delivery.

Methods

A pharmaceutical development program compliant with IMPD principles was conducted, including formulation design, analytical method validation, drug-device compatibility, ex vivo performance testing, and stability assessment. The formulation was optimised for aerosolisation with the CE-certified CapnoPen nebuliser. Sprayability, volume optimisation, tissue uptake, and spatial drug distribution were evaluated using the enhanced inverted bovine urinary bladder (eIBUB) model and compared with the current clinical standard of separately nebulised DOX and CIS. Tissue drug concentrations were quantified using validated ICP-MS. Short-term in-use stability and long-term stability under ICH conditions were assessed by HPLC, pH, osmolality, and impurity profiling.

Results

The final ready-to-use aqueous formulation contained 0.131 mg/mL DOX and 0.656 mg/mL CIS in 0.9% sodium chloride, buffered to pH 4.0 ± 0.2. The formulation met predefined pharmaceutical specifications, demonstrated suitable viscosity and physicochemical stability, and showed no drug-device incompatibility. A total aerosol volume of 200

mL achieved optimal tissue uptake with the lowest aerosol sedimentation, outperforming 100 mL and matching reference drugs. Tissue concentrations of DOX and CIS were comparable to separately administered agents, with preserved dose proportionality and homogeneity of spatial distribution. The diluted formulation remained stable for up to 30 h at 2-8°C, while long-term storage at 5°C preserved CIS for 60 months and DOX for at least 9 months. Usability testing demonstrated simplified handling, reduced equipment needs, lower material waste, and decreased occupational exposure risk.

Conclusion

This study presents the first dedicated, ready-to-use DOX-CIS formulation specifically designed and preclinically validated for PIPAC. The formulation meets quality, stability, performance, and usability requirements, supporting its potential to standardise and improve intraperitoneal aerosol chemotherapy.

Funding

This research was funded by Capnomed GmbH, Tuebingen, Germany, and performed at the National Centre for Pleura and Peritoneum's research lab at the University Hospital Tuebingen, Germany.

Herz, Lunge, Surgeomics

Metabolomic, Immune, and Senescence Profiling for Biomarker Discovery in Coronary Artery Disease

Max Wacker, Frieder Neu, Cedrik Herlich, Frank Pessler, George Awad, Jens Wippermann, Anna Dittrich, Priya Veluswamy

Background & Objective: Coronary artery disease (CAD) is increasingly recognized as a chronic inflammatory disorder arising from the intricate interplay between metabolic dysregulation, vascular aging, and immune dysfunction. Endothelial senescence, a hallmark of vascular aging, promotes the secretion of senescence-associated secretory phenotype (SASP) factors that sustain chronic inflammation, endothelial dysfunction, and adverse vascular remodeling. Innate lymphoid cells type 2 (ILC2s), key regulators of tissue repair and immune homeostasis through the production of type 2 cytokines, have emerged as potential modulators of cardiovascular inflammation; however, their relationship with endothelial senescence and systemic metabolic perturbations in CAD remains poorly defined. Abscissic acid (ABA), an endogenous immunometabolic signaling molecule, has recently gained attention for its immunoregulatory and vasculoprotective properties. We hypothesize that alterations in systemic metabolism, including dysregulated ABA signaling, endothelial senescence, SASP-driven inflammation, and impaired ILC2 function, collectively contribute to promoting CAD pathogenesis.

Methods: Peripheral blood samples were obtained from patients with CAD and controls. Untargeted plasma metabolomic profiling was performed to characterize global metabolic alterations, followed by targeted quantification of ABA using liquid chromatography-tandem mass spectrometry. Circulating ILC2s will be comprehensively phenotyped by multiparameter flow cytometry, and their effector cytokines, including IL-5, IL-13, IL-4, and IL-9, were quantified. Endothelial senescence will be evaluated using established molecular markers, while circulating SASP mediators will be measured using multiplex immunoassays. Integrated multi-omics and correlation modelling will be employed to define the relationships among metabolic signatures, ABA, endothelial senescence, SASP factors, ILC2 phenotypes in CAD.

Expected Significance: This study will provide a comprehensive immunometabolic framework linking systemic metabolic remodeling with endothelial senescence and innate immune dysregulation in CAD. By integrating metabolomic, vascular, and immune phenotypes, the study aims to identify novel mechanistic pathways and biomarker signatures that may facilitate improved risk stratification and reveal potential therapeutic targets for the prevention and treatment of coronary artery disease.

Early Postoperative Outcomes Following Revascularisation for Peripheral Arterial Disease (PAD) at a Tertiary Referral Center Under Routine Clinical Conditions (A „Real-World Data“ Analysis)

Adamyan M, Meyer F, Barth U

Introduction: While endovascular and interventional modalities have progressed significantly, open revascularization remains a cornerstone in the management of complex peripheral arterial disease (PAD). Although the need for surgical treatment in Fontaine stage IIb PAD may decline further, particularly in light of the new 'S3 Guideline on the Diagnosis, Treatment and Follow-up of Peripheral Arterial Disease' recommendations, the number of patients requiring treatment for Chronic Limb-Threatening Ischemia (CLTI) is expected to remain constant.

Objective: To compare thromboendarterectomy (TEA), bypass surgery and hybrid procedures in the treatment of PAD in order to i) reflect everyday practice in vascular surgery, ii) optimise clinical decision-making, iii) ensure appropriate in-house vascular surgical quality assurance, and iv) contribute to clinical care research. **Method:** In this retrospective single-centre observational study, all consecutive patients with diagnosed PAD who had undergone open or hybrid vascular surgical treatment at a tertiary referral center between 2014 and 2023 were included. Case-related, perioperative, and outcome data were recorded in a registry and analysed for factors associated with early postoperative outcomes, particularly, patency, morbidity, and mortality.

Results: A total of 741 cases were included, in whom open vascular surgery was performed due to symptomatic PAD. Mean patient age was 69.0 ± 10.0 (range: 37-102) years, and mean body mass index (BMI) was 27.0 ± 5.3 (range: 13.9-53.1) kg/m^2 . The gender distribution showed 72.5 % male ($n=537$) and 27.5 % female ($n=204$) patients (2.64:1). Key cardiovascular risk factors included arterial hypertension (91.1 %), smoking history (78.7 %), hyperlipidaemia (61.1 %) and diabetes mellitus (42.8 %); interestingly, 61.6 % of patients presented with three or more of these factors. According to Fontaine classification, 3.1 % were treated in stage IIa, 41.2 % in stage IIb, and 12.3 % in stage III and 43.4 % in stage IV. Trend analysis demonstrated a 30.6 % increase in stage IV cases over the study period, comparing the 2021-2023 average to the 2014-2016 baseline. Bypass surgery was performed significantly more frequently at stage IV, whereas TEA with patch plasty predominated in stage IIb. Autologous graft material was used significantly more frequently in stage IV bypass procedures. Patients at stage IV had significantly higher complication rates, particularly pulmonary complications. A significant correlation was observed between PAD severity (Fontaine stage) and the risk of readmission (within 30 days [65.4 %] and 3 months [67.3 %]). In contrast, a comparison of the surgical modalities (TEA, bypass and hybrid) revealed no significant differences in postoperative morbidity, mortality or in the incidence of wound healing complications, haematomas or lymphatic complications.

Conclusion: Early postoperative outcomes of open surgical treatment for PAD were favourable and comparable to both institutional benchmarks and published literature. While these preliminary data are promising, they reflect early results that require further long-term follow-up.

Patients undergoing surgery at Fontaine stage IV remain at highest risk for perioperative complications and early readmission, with a marked increase in case numbers over the past decade. These findings underline the need for comprehensive management across all phases of surgical care:

- Preoperative optimisation(prehabilitation strategies,such as [respiratory therapy,physical conditioning,adequate nutritional support and weight optimisation], improvement of organ function [e.g.,blood pressure,glycaemic control,respiratoryfunction,functional capacity]and individualized adjustment of medication),
- Perioperative management(appropriate postoperative monitoring [incl.ICU whereindicated],tailored anticoagulation and antiplatelet therapy,targeted antibiotictherapy,continued respiratory therapy),and
- Postoperative care and follow up(intensified and structured follow-up, physiotherapy and functional as well as nutritional rehabilitation,psychological andsocial support,additional support measures [e.g.,occupational therapy,familyinvolvement where appropriate]).

This raises the question of whether the multimodal therapy mandated by the currentguideline,with a particular focus on exercise therapy,is sufficient to counteract thetrend of severe PAD stages.Consequently,long-term outcome analyses arewarranted to further characterise the quality and durability of open vascular surgerytreatment in PAD.

Video-Assisted Thoracoscopic versus Open Thymectomy for Myasthenia Gravis: Impact of Tumor Size on Surgical Approach and Outcomes

Dr.med.Himatur Wolfer, Prof.Dr.Godehard Friedel, Prof.Dr.Christian Schlensak, PD.Dr.med.Volker Steger, Dr.med.Atila Nemeth
Department for Thoracic and Cardiovascular Surgery, University Hospital
Tübingen, Tübingen, Germany

Background

Thymectomy improves acetylcholine receptor antibody–positive (AChR-ab+) myasthenia gravis even without visible thymic masses. Despite guidelines supporting early intervention, surgery is frequently delayed until mediastinal masses develop, potentially necessitating sternotomy. We hypothesized that early intervention enables video-assisted thoracoscopic surgery (VATS) with improved perioperative outcomes.

Methods

We conducted a retrospective cohort study of 45 consecutive myasthenia gravis patients who underwent thymectomy between 2014 and 2024 (VATS, n=35; sternotomy, n=10). The VATS cohort included 12 ocular myasthenia gravis patients (34%) and 15 patients (43%) without discrete masses. All sternotomy patients had generalized disease. AChR-ab+ prevalence was 77% versus 80%. Primary outcomes were perioperative complications and hospital length of stay.

Results

Among patients with discrete masses, those undergoing sternotomy had larger lesions (median diameter, 47mm [IQR, 30-53] vs. 27mm [IQR, 11-44]; $P=0.05$) and more frequently required resection of adjacent structures (60% vs. 14%; $P=0.007$). Median operative time was shorter with VATS (78 minutes [IQR, 66-106] vs. 163 minutes [IQR, 126-262]; $P<0.001$). Fewer VATS patients required ICU admission (11% vs. 60%; $P=0.014$). VATS was associated with reduced hospital stay (median, 3 days [IQR, 2-3] vs. 8 days [IQR, 5-11]; $P<0.001$) and chest-tube duration (mean, 1.6 ± 0.7 vs. 7.1 ± 8.0 days; $P<0.001$). Perioperative complications occurred in 14% after VATS versus 60% after sternotomy ($P=0.007$). R0 resection was achieved in 97% with VATS versus 60% with sternotomy ($P=0.004$).

Conclusions

In patients with myasthenia gravis, video-assisted thoracoscopic thymectomy was feasible in the majority of cases, including those without discrete thymic masses, and was associated with substantially lower perioperative morbidity compared with sternotomy. Larger thymic lesions necessitated open surgical approaches with increased complications. Given randomized evidence supporting thymectomy in AChR-ab+ myasthenia gravis regardless of visible thymic pathology, these findings support guideline-adherent early surgical intervention to preserve candidacy for minimally invasive techniques and minimize perioperative morbidity.

Evaluation of natural and synthetic Membranes for the Physiological Incubation Biosimulator (PIBS)

Lea Skrzypczyk 1, Britta Majchrzak-Stiller 1, Ilka Peters 1, David Wiedemann 1, Lisa Trzebiatowski 1, Chris Braumann 12, Waldemar Uhl 1, Johanna Strotmann 1, Philipp Höhn 1
 1 Department of General and Visceral Surgery, St. Josef Hospital Bochum, University Hospital of Ruhr University Bochum, Bochum
 2 Department of General, Visceral, and Oncologic Surgery, Evangelical Hospital Herne, Academic Teaching Hospital of Ruhr University Bochum, Herne

Fluid leakage from surgical wounds remains a major clinical challenge in visceral surgery and is closely associated with severe postoperative complications. Although surgical sealants are routinely applied to reinforce tissue integrity and support wound healing, aggressive biological secretions can compromise their stability and functionality. As a result, uncontrolled leakage into the abdominal cavity may occur, increasing the risk of infection, inflammation, and anastomotic failure.

The PIBS (Physiological Incubation Biosimulator) was developed as a model to investigate the field of surgical sealants allowing adjustment of temperature, humidity, and pressure to simulate physiological conditions within the human body. Hence, this system enables the reproducible evaluation and quantitative analysis of different membrane materials. This study investigated the applicability of different membrane model alternatives (porcine small intestine, porcine pleura and synthetic membrane material Nippi intestine) for burst pressure experiments using the PIBS, where a stepwise increase in pressure was applied to the membranes under controlled physiological conditions.

Porcine small intestine and porcine pleura show a high biological similarity to human tissue. Owing to their elastic and permeable properties, they are suitable for the investigation of mechanical stress effects. Because of their biological nature, porcine membranes show natural variations in contrast to a synthetic membrane material like Nippi intestine. However, porcine small intestine and porcine pleura appear as suitable membranes. The synthetic membrane material Nippi intestine on the other hand provides high reproducibility and controlled material properties because of its thin and flexible structure.

In contrast to the expectations, the results show that Nippi intestine is not a suitable membrane for standardized investigations of burst pressure sensitivity. Conversely, despite their inherent biological variability, porcine small intestine and porcine pleura yield reliable and highly applicable results.

The model successfully developed in this study enables the simulation of physiological conditions of the human body providing a basis for the analysis of sealants under the influence of different biological secretions as well as for other diverse potential applications.

Impact of Cultivation Parameters on the Structural and Mechanical Characterization of Bacterial Nanocellulose for Vascular Graft Applications

M.Sc.Saeed-Sharifpoor Kermani

-Department of Cardiac and Thoracic Surgery, Otto-von-Guericke University
Magdeburg, Magdeburg, Germany

PD. Dr. - Priya - Veluswamy

- Department of Cardiac and Thoracic Surgery, Otto-von-Guericke
University Magdeburg, Magdeburg, Germany

Prof.Dr.med.-Jens Wippermann

-Department of Cardiac and Thoracic Surgery, Otto-von-Guericke University
Magdeburg, Magdeburg, Germany

Dr.-Markus-Wilke

-Core Facility for Microscopy and Materials Analysis CMMA, Otto-von-Guericke University
Magdeburg, Magdeburg, Germany

Dr.-Axel-Boese

-Institute for Medical Technology, Chair „Medical Technical Systems“, Otto-von-
Guericke University Magdeburg, Magdeburg, Germany

M.Sc.-Marcel-Eisenmann

-Department for Biomedical Magnetic Resonance, Otto-von-
Guericke University, Magdeburg, Germany

PD.Dr.med.-Max-Wacker

-Department of Cardiac and Thoracic Surgery, Otto-von-Guericke
University Magdeburg, Magdeburg, Germany

Introduction and Objective: Bacterial nanocellulose (BNC) is one of the promising biomaterial candidates for small-caliber vascular grafts, owing to its excellent biocompatibility, high water content, and tunable mechanical properties. Optimization of BNC production requires a better understanding of how the composition of the culture medium, the addition of additives, and the bacterial concentration affect cellulose biosynthesis. In this study, the effects of ethanol, acetic acid (AA), magnesium sulphate (MgSO_4), the timing of addition, pH, and bacterial concentration on BNC production under static culture conditions were investigated.

Materials and Methods: BNC Samples were produced using *Komagataeibacter xylinus* cultured statically for 8 days in Hestrin-Schramm medium (HS) under a gradual temperature profile (24-28°C). Ethanol (0.5-2.0 %v/v), AA (0.4 vs. 1.5 %), MgSO_4 (0.05%), pH adjustment and supplementation timing (day 0 vs. day 2) were investigated individually and in combination. Subsequently, the bacterial concentration was increased from the standard inoculum (1.42×10^5 cells/mL) to 0.5×10^6 and 1.0×10^6 cells/mL. Wall thickness, elastic modulus, UV absorption, and hydration metrics were determined. **Results:** The addition of ethanol improved BNC production in a concentration-dependent manner, with approximately 1% ethanol resulting in consistent overall performance. Addition on day 0 consistently resulted in thicker BNC than delayed addition on day 2. MgSO_4 further enhanced cellulose formation, while AA reduced wall thickness and mechanical properties. An early pH adjustment reduced BNC production compared to the native HS medium. An increase in bacterial concentration led to a considerable rise in wall thickness, reduced biological variability, and partially offset the inhibitory effects of AA. The combination of

1% ethanol, MgSO_4 addition, early addition of the additives, and 1×10^6 cells/ml resulted in the thickest and most homogeneous BNCs

Conclusions: BNC production is not determined by a single parameter, but rather by the interaction of bacterial density, metabolic supplements, and cultivation conditions. Optimizing bacterial concentration in combination with early ethanol addition and the addition of MgSO_4 represents an effective strategy for improving cellulose biosynthesis and reproducibility, making it a promising approach for the production of a BNC small caliber vascular graft with improved structural quality.

A new model to study human angiogenesis ex vivo

Franka S.Krapp¹, Cyrielle Bouchez¹, Nikolai Schleussner¹, Naita M. Wirsik¹, Christian Goddemeier¹, Moritz Banse¹, Greta Ricken¹, Sören Blümer¹, Aram Abu Hejleh¹, Hans F. Fuchs¹, Hamid Kashkar¹, Christiane J. Bruns¹, Lars M. Schiffmann¹

¹ Department of General, Visceral, Thorax and Transplantation Surgery, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany.

² Institute for Molecular Immunology, Faculty of Medicine, University of Cologne, Cologne, Germany.

Introduction

Angiogenesis, defined as the formation of new blood vessels from existing ones, is a complex and tightly regulated process which is essential for vascular plasticity. Dysregulation of angiogenesis is associated with various pathological conditions, such as cancer, diabetes, and impaired wound healing [1]. To characterize human angiogenesis in surgically relevant diseases such as cancer or in wound and anastomotic healing new models for studying human angiogenesis are needed.

Research question

The aim of our project is to establish a human angiogenesis model to enable patient-specific investigation of vascular development. The established protocol will then be used to investigate several pro- and anti-angiogenic stimuli.

As a methodological basis for developing a human angiogenesis model, we used the 3D ex vivo murine aortic ring assay described by Baker et al.. In this assay, pieces of the murine aorta are cultivated to observe the development of micro vessels which undergo many key features of angiogenesis over a timescale similar to that observed in vivo [3]. To study human blood vessels, we used arteries harvested from patients during surgery and adapted the protocol for the murine aortic assay. Vascular growth was quantified using brightfield and fluorescence microscopy, and the acquired images were analyzed with ImageJ. To investigate the dependence of angiogenesis on mitochondrial respiration in endothelial cells, the used human blood vessels were additionally treated with rotenone, as an inhibitor of Complex I of the respiratory chain.

Methods/Statistics

Results

The protocol modifications for adaptation to human tissue include various adjustments, ranging from seeding media and cell culture media to tissue handling. The most relevant adaptation of the protocol is the matrix used to embed the vascular rings. While murine aortas show best sprouting results in collagen, Matrigel appears to be the most suitable embedding medium for human tissue. Human arteries with diameters ranging from 0.8 to 3.8 mm were included from different visceral surgical operations. Our protocol is effective for all tested patient parameters regardless of gender or age.

First analysis of mitochondrial respiration in our human angiogenesis model shows that inhibition of complex I in human blood vessels leads to a reduced number and length of sprouts. Although inhibition of mitochondrial respiration impedes the formation and growth of new blood vessel sprouts, it does not reduce the number or length of existing sprouts.

Discussion/Conclusion

The results indicate that human arteries can be used as an in vitro model for angiogenesis as they show similar behavior to the already established mouse model, making it a valuable tool for translational research. Furthermore, the inhibition of complex I shows that angiogenesis in

the established human model as well as in the murine model is dependent on mitochondrial respiration. Investigations are ongoing to determine the underlying process during the metabolic switch in angiogenesis.

The usage of blood vessels from patients in our angiogenesis model could open new possibilities in the future for patient-specific therapeutic approaches. For example, predicting wound and anastomotic healing, or as a therapeutic target in cancer treatment through the inhibition of tumor-associated angiogenesis.

Modified Johannesburg technique sets the standard – superior biomechanical stability in chest tube fixation

Dr.med.-Tobias-Schöbel

-Universitätsklinikum Leipzig, Klinik und Poliklinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Leipzig, Deutschland

Dipl.-Ing.-Ric-Meißner

-Universitätsklinikum Leipzig, Klinik und Poliklinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Leipzig, Deutschland; ZESBO-Zentrum zur Erforschung der Stütz- und Bewegungsorgane, Leipzig, Deutschland

Dr.rer.med.-Stefan-Schleifenbaum

-Universitätsklinikum Leipzig, Klinik und Poliklinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Leipzig, Deutschland; ZESBO-Zentrum zur Erforschung der Stütz- und Bewegungsorgane, Leipzig, Deutschland; Frauenhofer-Institut für Werkzeugmaschinen und Umformtechnik IWU, Dresden, Deutschland

Prof.Dr.med.-Christian –Kleber

-Universitätsklinikum Leipzig, Klinik und Poliklinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Leipzig, Deutschland

PD Dr.med.habil.Dr.rer.med.-Isabella-Metelmann

-Universitätsklinikum Leipzig, Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie, Leipzig, Deutschland

PD Dr.med.habil.-Sebastian-Krämer

-Universitätsklinikum Leipzig, Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie, Leipzig, Deutschland

Introduction

Chest tube dislodgement is a frequent and potentially life-threatening complication after thoracic trauma. Reliable fixation is essential, particularly in emergency and combat casualty care. Several suture techniques exist, but comparative biomechanical evidence is limited.

Research question

How do suture technique, chest tube size, and tube material influence the biomechanical stability of chest tube fixation?

Methods

This prospective biomechanical cadaveric study compared three fixation techniques - PurseString (PS), Roman Sandal (RS), and Modified Johannesburg (JO) technique - across three tube sizes (20, 24, 28 Charrière) and two materials (polyvinyl chloride (PVC) and silicone). A total of 360 tests were performed on porcine thoracic wall specimens under standardized conditions. Specimens were subjected to vertical load-to-failure testing with continuous measurement of force and elongation.

Statistics

Statistical analyses were conducted in R (version 2025.09.0+387; R Core Team, Vienna, Austria). Data distribution was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Group comparisons were performed with the Kruskal-Wallis test and Dunn's post hoc test with Bonferroni correction or, where appropriate, the Mann-Whitney-U-test. Associations between categorical variables were analyzed with the Chi-square test. Effect sizes were reported as $r = |zN|$, and significance was set at $p < 0.05$.

Results

The Modified Johannesburg technique consistently demonstrated the highest pull-out strength across all tube sizes and materials, significantly outperforming both RS and PS ($p < 0.0001$). RS ranked second and showed significantly greater stability than PS in all conditions ($p < 0.0001$). Effect size analysis revealed large differences between JO and PS ($r = 0.87$) and between RS and PS ($r = 0.50$), and a medium effect between JO and RS ($r = 0.36$). PVC tubes provided significantly greater pull-out strength than silicone tubes ($147.0 \pm 54.2\text{N}$ vs. $128.5 \pm 42.2\text{N}$, $p = 0.01071$), although silicone tubes exhibited greater elongation prior to failure. Tube size had a modest influence on stability, with larger tubes tending toward higher pull-out strength, but pairwise differences did not reach significance. The predominant failure mechanism was suture rupture (78.9%), followed by tube rupture (11.1%), knot loosening (8.1%), and skin failure (1.9%).

Discussion

The modified Johannesburg technique should be considered the preferred method in high-risk environments, including military and emergency care, to minimize dislodgement and enhance patient safety. Suture rupture as the predominant failure mechanism hints at the suture material as the limiting factor of mechanical stability in chest tube fixation. We are currently investigating this hypothesis in follow-up trials.

Conclusion

The Modified Johannesburg technique offers superior biomechanical stability for chest tube fixation, regardless of tube size or material. PVC chest tubes show higher pull-out forces than silicone tubes. Chest tube size appears to have little influence on fixation strength.

Effects of the Nerve Growth Factor (NGF) on bronchial fibroblasts and epithelial cells in 2D and 3D airway models for allergic asthma

Helen Cording

Prof.Dr.Thorsten WallesDr.Cornelia Wiese-Rischke

Institute: Otto-von-Guericke-University Magdeburg,Department for Cardiac and Thoracic Surgery,Laboratory for Experimental Thoracic Surgery

Introduction:Asthma is a chronic inflammatory disease of the airways,affecting about 5%of thepopulation.There is a wide variety of treatments available,but in about 10%of patients they arenot sufficiently controlling the symptoms.Over time,chronic inflammation can lead toirreversible airway remodelling,which consists,among other aspects,of hyperplasia of thebronchial fibroblasts and epithelial cells.Nerve growth factor(NGF)as well as the T-helper type IIinterleukins,IL-4and IL-13,play asignificant partin the inflammatory process in allergic asthma.

Research question:Our work focusses on the effect of NGF,IL-4 and IL-13,on proliferation andactivation of fibroblasts and epithelial cells.

Methods:Bronchial fibroblast and epithelial cells of patients with(ast.Fb./EC.)and without(heaL.Fb./EC.)allergic asthma were cultivated in a 2D cell culture with NGF(10,50,100 ng/ml),L-4 and IL-13(each 10ng/ml)and in combinations.The proliferation rate was measured byusingan Alamar Blue assay,with measurements taken every 24 hours over 4 days.Ki-67immunostainingwas used to determine the number of proliferating cells after 24-hour incubationwith either NGF,IL-4,IL-13 or combinations.Further,we plan to look at the proliferation andactivation of fibroblast and epithelial cells in a 3D airway model.We also did qPCR to comparethe expression of the NGF receptors,TrkAand p75NTR,after incubation with NGF(100 ng/ml).

Statistics:For the statistical anaysis,we put the results in relation to the control and used the t-tests and alternativet-test,as well as the Mann-Whitney test.

Results:The proliferation rates for heal.Fb.,after NGF (50 ng/ml)incubation,were slightlyincreased,whereas rates for ast.Fb (50,100 ng/ml)were significantly increased on the secondday.Similar results were obtained for ast.EC(50 ng/ml)on day one.After incubation with NGF,IL-4 and IL-13,and combinations,significant increases were found in ast.Fb ater NGF(50 ng/ml)incubation on day three,and NGF/IL-4/IL-13 incubation on day two.For heal.Fb significantincreases were found after IL-4 and IL-13 incubation on day one.Results of the Ki-67immunostaining were divided nto low and high fluorescent cells.A significant rise in highfluorescent cells was found in every combination,whereas rates of low fluorescent cells wereincreased after IL-4 and NGF(50 ng/ml)incubation.So far,qPCR results have not shown anysignificant differences concerning the expression of the receptors between ast.Fb/EZ andheaLFb/EZ.

Discussion:The data from our 2D-models indicates a difference in the proliferative behaviourbetween ast.Fb/EZand heaL.Fb/EZ.The complex 3D airway model is going to simulate the in vivoairway more realistically by enabling cell differentiation,activation and cell-cell interactions andmakes acquired results more appliable.

Conclusion:Ourfindingscould potentiallybe used asabase for newtreatment developments anda more in-depth understanding of the ongoing processes in allergic asthma.

Grenzen verschieben in der Organtransplantation

Robotic liver surgery: enhancing immune competence and minimizing postsurgical inflammation

Frederike Stelter, Julia Nagelschmitz, Konstantina Varvareizou, Thomas Wartmann, Severin Gylstorff, Ahmed Sanin, Ronny Otto, Jörg Arend, Mareike Franz, Mirhasan Rahimli, Andrew AGumbs, Ulf D Kahlert, Roland S Croner

Robotic liver surgery: enhancing immune competence and minimizing postsurgical inflammation

Background: Robotic-assisted liver resection (RLR) has emerged as a minimally invasive alternative to open liver resection (OLR), offering short-term benefits such as reduced blood loss and shorter hospital stays. However, the differential immune response between these approaches remains unclear. This pilot study investigates systemic and local inflammatory responses in 22 patients (11 RLR, 11 OLR) undergoing liver surgery.

Methods: Clinical and laboratory parameters, leukocyte activation (L-selectin shedding assay), cytokine/chemokine levels (FACS multiplex analysis), and apoptosis (Caspase-3 staining) were assessed in peripheral blood, liver, and peritoneal tissue before and after parenchyma dissection.

Results: RLR demonstrated significantly lower perioperative levels of IL-6 and IL-10 systemically and locally compared to OLR. Laparotomy in OLR elevated baseline liver tissue levels of IL-6, IL-8, CXCL10, IFN γ , TGF β 1, and IL-1 β . Apoptosis induction in liver parenchyma was reduced in RLR, attributed to minimized trauma of the capnoperitoneum. Post-dissection, RLR patients exhibited lower liver levels of IL-6, IL-8, IFN γ , MCP1, IL-1 β , TGF β 1, and CXCL10. In the late postoperative phase (POD 5–20), systemic MCP1 and CD4+/CD8+ lymphocyte counts were reduced in RLR, alongside increased L-selectin shedding capacity.

Conclusion: This pilot study suggests that RLR preserves immune competence more effectively than OLR, with reduced systemic and local inflammatory and apoptotic responses. These findings suggest that robotic systems minimize tissue trauma, offering a clinically advantageous approach for liver resection.

Neu vernetzt – Organ-, Generation- und Landesübergreifende Forschung in der Chirurgie

Feasibility of an OPS-Based Coding Approach to Quantify Surgical Training Activities and Associated Time Expenditure: A Multicenter Prospective Pilot Study

Schaaf (Koblenz)

Feasibility of an OPS-Based Coding Approach to Quantify Surgical Training Activities and Associated Time Expenditure: A Multicenter Prospective Pilot Study

Background:

High-quality surgical training is essential for maintaining healthcare standards, yet training activities are insufficiently captured within current hospital documentation and reimbursement systems. In operative disciplines, training is associated with additional supervision and procedure time, but these efforts are neither systematically measured nor transparently represented. In 2025, the German Society of Surgery (DGCH) proposed a dedicated OPS code to document surgical training procedures. This pilot study aims to evaluate the feasibility and practical applicability of such an OPS-based approach.

Methods:

This multicenter prospective observational pilot study will be conducted across German surgical departments of different care levels and specialties. Over an 8-week period, all surgical procedures will be prospectively documented using routine OPS coding. For each procedure, participating centers will record whether substantial operative steps were performed by a surgical trainee under specialist supervision and whether a hypothetical training-related OPS add-on code would have been assigned. Additional time expenditure attributable to training will be categorized into four predefined levels (≤ 10 min, >10 -20 min, >20 -30 min, >30 min). Primary endpoints are feasibility and practicability of OPS-based documentation in routine clinical practice. Secondary endpoints include the proportion of training procedures, distribution of additional time expenditure, differences between surgical specialties and hospital care levels, and exploratory estimation of structural workload associated with training.

Results:

Data collection is scheduled for the third quarter of 2026. Results will provide the first multicenter prospective dataset on the frequency and time-related impact of surgical training procedures in Germany.

Conclusions:

This study will evaluate whether an OPS-based coding strategy is a feasible tool for standardized documentation of surgical training activities. The findings may support the development of future quality indicators and provide evidence for health policy discussions regarding the recognition and structural consideration of postgraduate surgical training.

The BZKF Lighthouse Project „Preclinical Models“: Building a Collaborative Infrastructure for Translational Cancer Research

Anne Rech
 Felix Engel
 Gabriele Büchel
 Gloria Lutzny-Geier
 Jessica Maas
 Kathrin Renner-Sattler
 Kirsten Lauber
 Maximilian Reichert
 Stefanie Schmidt
 Christoph Otto
 Nicolas Schlegel

The Bavarian Cancer Research Center (BZKF) is a consortium of the six Bavarian university hospitals and medical faculties with the aim of providing all citizens of Bavaria access to innovative cancer therapies. A distinctive feature of the BZKF is its lighthouse structure, which builds on the specific strengths of each participating site and focuses on specialized technologies and expertise.

The BZKF Lighthouse Project “Preclinical Models” was established in early 2024 to create a sustainable network for resource sharing across all BZKF sites. A central component of the lighthouse project is a REDCap-based database that integrates a broad range of preclinical model systems, including human and murine organoids, animal models, and various ex vivo systems for both tumor- and tumor-associated inflammatory models. Currently, the database contains 168 organoid models and 31 animal models representing different tumor entities. To provide user-friendly access to available datasets, the web-based platform [Praeklinische-Modelle.ukw.de](https://praeklinische-modelle.ukw.de) was established. The public search interface is free without registration. Relevant search parameters are mirrored from the REDCap database. Access to the protected area of the platform is restricted to registered users with a valid email from a German academic institution. Additional resources available after registration include standard operating procedures (SOPs) for laboratory animal procedures, educational videos on laboratory animal science, target validation resources, and details about the lighthouse structure.

Within the Target Validation Unit, we are currently developing an innovative platform for targeted protein degradation that utilizes, among others, the auxin-inducible degron system (AID). Our primary objective is the rapid degradation of promising “undruggable” protein targets that lack suitable pharmacological inhibitors. This platform facilitates target validation by enabling the induction of selective protein depletion, thereby allowing us to characterize the resulting anti-tumor phenotypes and mechanistic consequences of acute target loss. In conclusion, the Lighthouse Project “Preclinical Models” provides a framework for efficient translational research by enabling easy access to diverse preclinical models, bringing together complementary expertise, creating synergies, and accelerating the transfer of scientific discoveries into clinical practice.

German, Swiss, and Italian Medical and Surgical Specialty Training: A Comparative Overview of Curriculum Structure, Training Quality, and Practical Experience

A. Kraus; Dept. of Plastic, Aesthetic and Hand Surgery; *F. Meyer;
Dept. of General, Abdominal, Vascular and Transplant Surgery; Otto-von-Guericke University
with University Hospital; Magdeburg, Germany

Background: Postgraduate surgical training in Europe varies widely in structure, supervision, and educational philosophy, influencing the quality and consistency of resident formation.

Aim and Methods: This paper compares surgical specialty training in Germany, Switzerland, and Italy across several key parameters: access and selection processes, time spent in the operating room, theoretical instruction, opportunities and requirements for research, supervision and mentorship, rotation structure, training duration and flexibility, assessment and certification methods, simulation-based training, autonomy in clinical practice, work-hour regulation as well as financial and contractual conditions.

Results (corner points): -In Germany and Switzerland, training access is decentralized, with candidates applying directly to hospitals through job interviews and training regulated by medical chambers or scientific societies.

-Italy, in contrast, follows a centralized system governed by the Ministry of Education, with an entry based on a national competitive exam and residency conducted within university-based programs.

-Swiss training is characterized by a high degree of standardization and structured evaluation, while Germany offers greater institutional variability.

-Italian programs benefit from national curricula but often show heterogeneity in operative exposure and research integration.

Conclusion: This comparative analysis highlights strengths and limitations within each system, offering perspectives on harmonizing surgical education and promoting mobility within the European training landscape.

Feasibility of an OPS-Based Coding Approach to Quantify Surgical Training Activities and Associated Time Expenditure: A Multicenter Prospective Pilot Study

Schaaf (Koblenz)

Background:

High-quality surgical training is essential for maintaining healthcare standards, yet training activities are insufficiently captured within current hospital documentation and reimbursement systems. In operative disciplines, training is associated with additional supervision and procedure time, but these efforts are neither systematically measured nor transparently represented. In 2025, the German Society of Surgery (DGCH) proposed a dedicated OPS code to document surgical training procedures. This pilot study aims to evaluate the feasibility and practical applicability of such an OPS-based approach.

Methods:

This multicenter prospective observational pilot study will be conducted across German surgical departments of different care levels and specialties. Over an 8-week period, all surgical procedures will be prospectively documented using routine OPS coding. For each procedure, participating centers will record whether substantial operative steps were performed by a surgical trainee under specialist supervision and whether a hypothetical training-related OPS add-on code would have been assigned. Additional time expenditure attributable to training will be categorized into four predefined levels (≤ 10 min, >10 -20 min, >20 -30 min, >30 min). Primary endpoints are feasibility and practicability of OPS-based documentation in routine clinical practice. Secondary endpoints include the proportion of training procedures, distribution of additional time expenditure, differences between surgical specialties and hospital care levels, and exploratory estimation of structural workload associated with training.

Results:

Data collection is scheduled for the third quarter of 2026. Results will provide the first multicenter prospective dataset on the frequency and time-related impact of surgical training procedures in Germany.

Conclusions:

This study will evaluate whether an OPS-based coding strategy is a feasible tool for standardized documentation of surgical training activities. The findings may support the development of future quality indicators and provide evidence for health policy discussions regarding the recognition and structural consideration of postgraduate surgical training.

Innovation in Surgical Training Based on Anatomically Accurate Phantoms

Heike Walles, Kilian Kirsten, Moritz Lange, Khaled Alnazer, Pia Landschulze, Paula Sachs

Background:

Surgical training faces the challenge of meeting the increasing demands of modern surgical procedures. In particular, minimally invasive and robot-assisted techniques such as Video-Assisted Thoracic Surgery (VATS) and Robot-Assisted Thoracic Surgery (RATS) require the confident use of complex technology and specialized manual skills. The acquisition of these skills should increasingly take place outside the operating room. However, currently available training models often have shortcomings: They are not anatomically realistic enough, only partially replicate relevant anatomical structures, and are often made of materials that do not allow for the realistic performance of surgical procedures, such as skin suturing techniques.

Methods:

CT-based, anatomically accurate phantoms developed from clinical imaging data were used for surgical education and training. In addition to full-body and organ phantoms, specialized skill-training models were developed for different levels of training. The areas of application ranged from basic skills such as skin suturing techniques to more complex procedures such as pericardial puncture and the placement of a chest drain. The models were tested in various course formats with medical students, physicians in training, and experienced practitioners. The evaluation was based on standardized surveys regarding realism, practicality, and perceived learning success.

Results:

The phantoms used enabled the realistic representation of relevant anatomical structures and the implementation of practice-oriented training scenarios. In particular, the opportunity to practice surgical techniques under anatomically correct conditions was rated positively by the participants. Preliminary results from the surveys indicate high acceptance, improved subjective confidence in performing procedures, and a high perceived benefit for surgical training. Detailed evaluation data will be presented during the lecture.

Conclusion:

CT-based, anatomically accurate phantoms represent a promising addition to existing training approaches. They enable standardized, realistic, and risk-free training of surgical skills and can help bridge the gap between theoretical education, simulation training, and clinical practice.

Pankreasforschung jenseits bekannter Grenzen

Pancreatic proteomics: Workflow development for tissue and secretion analysis in postoperative pancreatic fistula

D. Wiedemann¹, B. Majchrzak-Stiller¹, L. Trzebiatowski¹, I. Peters¹, L. Skrzypczyk¹, J. Strotmann¹, S. Rozanova^{2,3,4}, K. Marcus^{2,3}, W. Uhl¹, C. Braumann^{1,5}, P. Höhn¹

¹Department of General and Visceral Surgery, St. Josef Hospital Bochum, University Hospital of Ruhr-University Bochum, Bochum

²Medizinisches Proteom-Center, Medical Faculty, Ruhr-University Bochum, Bochum ³Medical Proteome Analysis, Center for Protein Diagnostics (PRODI), Ruhr-University

Bochum, Bochum ⁴Core Unit for Bioinformatics (CUBiMed.RUB), Medical Faculty, Ruhr-University Bochum, Bochum ⁵Department of General, Visceral and Oncologic Surgery, Evangelical Hospital Herne, Academic Teaching Hospital of Ruhr-University Bochum, Herne

Postoperative pancreatic fistula (POPF) is one of the most frequent and clinically relevant complications after pancreatic surgery. Severe cases can lead to inflammation, infection, bleeding, organ failure, and, in some instances, fatal outcomes. POPF develops when pancreatic digestive fluid leaks into the abdominal cavity at the site of anastomosis, where its high enzymatic activity, often driven by premature protease activation, can damage surrounding tissue and blood vessels. Although several clinical risk factors have been described, the underlying molecular mechanisms and reliable early biomarkers remain unclear. The wide range of clinical manifestations suggests that individual biological differences may play an important role. Identifying molecular patterns associated with POPF could help improve perioperative management and enable earlier detection of high-risk patients.

In this project, both healthy pancreatic tissue and intraoperatively obtained pancreatic fluid are analyzed, as each may contain complementary information about tissue integrity, secretion dynamics, and patient-specific vulnerability. To explore these aspects, a proteomic workflow is established. The aim is to generate a robust and reproducible methodology that allows the systematic comparison of protein signatures across different patients and sample types.

The methodological work focuses on optimizing sample handling, protein extraction, cleanup, digestion, and LC-MS/MS analysis. Pancreatic tissue and pancreatic fluid differ in viscosity, enzymatic activity, and extracellular content, making them challenging biological samples, that require adapted processing steps. Standardized protocols for homogenization, lysis, and peptide preparation are tested with the goal of maximizing protein recovery while maintaining compatibility with mass spectrometry. Particular attention is given to reducing sample loss, improving reproducibility, and achieving sufficient proteome depth to enable meaningful analyses. This aims to provide a comprehensive overview of the samples' proteome and its variations, enabling further, more profound and pinpointed protein studies. First pilot experiments indicate that the workflow produces consistent peptide yields and allows for the detection of a broad range of proteins.

The proteomic platform is designed to be combined with future functional studies using patient-derived organoids and primary fibroblasts. These models will later help investigate how pancreatic secretions influence epithelial viability, fibroblast behavior, and extracellular matrix remodeling. Together with clinical data, these

functional insights may complement the proteomic findings and contribute to a more comprehensive understanding of POPF.

In summary, this work establishes a scalable and reproducible proteomic framework for analyzing pancreatic tissue and pancreatic fluid in a clinical context. The ongoing pilot studies form the basis for identifying molecular patterns associated with POPF and for linking individual proteomic signatures with functional and clinical parameters.

Impact of Fibroblasts on PDAC Subtype Maintenance and Chemotherapy Response in Patient Derived Organoids

Lisa Trzebiatowski¹, Lea Skrzypczyk¹, Dr.rer.nat. Britta Majchrzak-Stiller¹, Dr.rer.nat. Ilka Peters¹, David Wiedemann¹, Prof.Dr.med. Waldemar Uhl¹, Prof.Dr.med. Chris Braumann^{1,2}, Dr.med. Johanna Strotmann¹ and Dr.med. Philipp Höhn¹

¹ Department of General and Visceral Surgery, Division of Molecular and Clinical Research, St. Josef-Hospital, Ruhr-University Bochum

² Department of General, Visceral and Vascular Surgery, Evangelische Kliniken Gelsenkirchen, Akademisches Lehrkrankenhaus der Universität Duisburg-Essen

Pancreatic ductal adenocarcinoma (PDAC) is characterized by a very poor prognosis, mainly due to late diagnosis and rapid development of therapy resistance. Transcriptomic analyses have identified two major molecular subtypes, the classical and the basal-like subtype, which differ in clinical outcome and therapeutic sensitivity. Patient-derived organoids (PDOs) are increasingly used as preclinical models for individualized drug testing; however, preservation of primary tumor characteristics in vitro remains challenging. Emerging evidence suggests that tumor microenvironmental signals, including fibroblast-derived cues, may contribute to subtype plasticity and influence therapeutic response. This study investigates whether and how activated cancer-associated fibroblasts (CAFs) influence subtype-specific characteristics and drug response profiles in PDAC PDOs.

PDOs and fibroblasts were successfully isolated from primary PDAC tissue. Fibroblasts were characterized by immunofluorescence, and organoids were analyzed using whole-organoid immunofluorescence. Organoid subtype classification was performed using qRT-PCR analysis with subtype-specific marker panels. Preliminary data indicate that fibroblasts may contribute to the maintenance of subtype-associated features within PDO cultures and may influence treatment response patterns. Co-culture experiments with autologous and heterologous CAFs are ongoing, alongside drug sensitivity profiling using clinically relevant chemotherapeutic agents. Early observations suggest potential shifts in subtype-associated marker expression and corresponding differences in therapy response under varying culture conditions. These findings support the hypothesis that microenvironment-derived signals play a relevant role in regulating PDAC subtype plasticity in vitro. Incorporating stromal components may therefore improve the physiological relevance of PDO models.

This study highlights the importance of fibroblast-tumor interactions in maintaining PDAC subtype characteristics and shaping therapeutic response in organoid models. Optimizing culture conditions to better reflect the tumor microenvironment may enhance the predictive value of PDO-based precision oncology approaches.

Pancreatic prolylendopeptidase (PP) acts as a novel oncogenic factor of pancreatic islets

Alexander P.Steinhoff^{1,2},Cedric Wilden^{1,2},Caroline Bickelmann^{1,2},Selina Wrublewsky^{1,2},Matthias W.Laschke^{1,2},Emmanuel Ampofo^{1,2}

¹ Institute for Clinical and Experimental Surgery,Saarland University,PharmaScienceHub(PSH),66421Homburg,Germany

² Center for Gender Specific Biology and Medicine(CGBM),Saarland University,66421 Homburg,Germany

Introduction:

Pancreatic polypeptide(PP)is a neuropeptide which binds to neuropeptide y receptor 4(NPY4R)andis synthesized and secreted by PP-cells of islets of Langerhans.Its main functions are the regulation of satiety,insulin sensitivity and inhibition of pancreatic exocrine hormone secretion.However,whether PP has further specific function within the endocrine pancreas is still unknown.In the present study,we found that PP is crucially involved in the regulation of angiogenic processes.

Research question:

Does PP support angiogenesis within pancreatic islets?

Material and methods:

Human endothelial umbilical vein cells(HUVEC)and human pericytes from placenta(hPC-PL)weretreated with PP or in combination with a NPY4R antagonist as negative control.We investigated the angiogenic effect of PP by a panel of functional assays,including WST-1 assay,scratch assay and tube formation assay.Moreover,we studied the underlying molecular mechanisms by proteome array and Western Blot analyses.Ex vivo,pseudo-islets consisting of microvascular fragments(MVF)from murine epididymal fat pads and dissociated murine pancreatic islets were generated by liquid overlay technique.Subsequently,they were exposed to PP and the outgrowth of MVF was assessed by spheroid sprouting assay.

Statistics:

Data analyses were performed using GraphPad Prism.Statistical comparisons were conducted by one-way or two-way ANOVA when using more than two groups followed by a Tukey-post hoc test.A p-value of $<0,05$ was considered as statistically significant.

Results:

Our results clearly showed that PP increases mitochondrial activity,proliferation,and migration of HUVEC and hPC-PL.In addition,we found an improved angiogenic potential of both cell types as demonstrated by enhanced tube formation.The analyses of the underlying mechanism revealed that this was mediated by induction of Akt and Erk signaling pathways as well as an upregulated expression of specific angiogenic proteins such as vascular endothelial growth factor and tissue factor.As expected,the exposure of PP to pseudo-islets markedly stimulates the outgrowth of vascular cells into the surrounding collagen matrix.

Discussion:

The pancreatic vasculature proves crucial for the supply of oxygen and nutrients of the islets of Langerhans.While the endocrine hormones insulin,glucagon,somatostatin,and ghrelin have been shown as potentially angiogenic,the role of PP in angiogenesis is still unknown.Based on our findings showing that PP has angiogenic functions,additional in vivo experiments are required to confirm our in vitro results.

Conclusion:

Here we show for the first time that PPIs not only limited to regulation of digestion and satiety, but also significantly impacts vascular cell migration and proliferation leading to enhanced angiogenesis.

BAMBI and WNT Signaling Activity in Pancreatic Ductal Adenocarcinoma (PDAC) – A Study in Patient-Specific Tumor Organoids

Paul Valentin Winter¹, Thomas Wartmann¹, Katrin Hippe², Ludwig Wilkens², Roland S. Croner¹, Ulf D. Kahlert¹

¹ Molekulare und Experimentelle Chirurgie (MEC), Universitätsklinik für Allgemein-, Viszeral-, Gefäß- und Transplantationschirurgie

² Universitätsklinikum Magdeburg A.ö.R. Institut für Pathologie

Abstract:

Pancreatic ductal adenocarcinoma (PDAC) is among the most aggressive malignant tumors, offering limited therapeutic options, and is frequently diagnosed only at advanced stages due to its nonspecific symptoms. The WNT signaling pathway plays a major role in tumor progression by regulating the proliferation, differentiation, and stem cell-like properties of tumor cells. BAMBI (BMP and Activin Membrane-Bound Inhibitor) acts as a pseudoreceptor that competitively inhibits the TGF- β signaling cascade – a pathway of central importance in pancreatic carcinogenesis. Previous work by our group demonstrated a significant overexpression of BAMBI mRNA in pancreatic tumors, with clinical and prognostic relevance.

The aim of the present study is to characterize BAMBI expression and WNT signaling activity in patient-specific pancreatic tumor organoids (PDOs). For this purpose, intraoperatively resected, pathologically confirmed tumor samples as well as corresponding healthy primary tissue were used to establish PDOs. The PDOs were validated using a pancreas-specific tumor NGS panel and mass spectrometry-based proteomic analysis, whereby characteristic mutations, including KRAS, were detected both in the organoids and in the tissue of origin. PDAC-PDOs, together with five established PDAC cell lines, were subsequently characterized by Western blot and qPCR with respect to BAMBI expression and WNT activity, and were treated with two clinically applied WNT inhibitors. The results confirm the structural and molecular concordance of the PDOs with their respective tissue of origin and underscore their suitability as a preclinical model system. Tissue microarray analyses and Western blots revealed increased BAMBI expression in tumors, and particularly in metastases, compared with healthy tissue. Initial treatment experiments suggest that cell models with comparable BAMBI expression display similar sensitivity to WNT inhibitors, and that a decrease in BAMBI expression is observed under treatment.

This study provides initial evidence of a functional link between BAMBI expression and WNT signaling activity in PDAC and supports the potential of PDOs as a translationally relevant model system. Further validation experiments have been initiated. Future investigations aim to confirm the identified associations in larger patient cohorts and to evaluate the clinical applicability of BAMBI as a predictive marker for WNT inhibitor therapies.

Inflammatory cytokines impair glucagon expression and secretion in pancreatic α -cells

Caroline Bickelmann,

Institute for Clinical and Experimental Surgery, Saarland

University PharmaScienceHub (PSH), 66421 Homburg, Germany; Center for Gender Specific Biology and Medicine (CGBM), Saarland University, 66421 Homburg, Germany

Cedric Wilden,

Institute for Clinical and Experimental Surgery, Saarland

University, PharmaScienceHub (PSH), 66421 Homburg, Germany; Center for Gender Specific Biology and Medicine (CGBM), Saarland University, 66421 Homburg, Germany

Univ.-Prof. Dr. Leticia Prates-Roma,

Biophysics Department, Center for Human and Molecular Biology (ZHMB), Saarland

University, 66421 Homburg, Germany; Center for Gender Specific Biology and Medicine (CGBM), Saarland University, 66421 Homburg, Germany

Univ.-Prof. Dr. med. Matthias W. Laschke,

Institute for Clinical and Experimental

Surgery, Saarland University, PharmaScienceHub (PSH), 66421 Homburg, Germany; Center for Gender Specific Biology and Medicine (CGBM), Saarland University, 66421 Homburg, Germany

Prof. Dr. rer. nat. Emmanuel Ampofo,

Institute for Clinical and Experimental Surgery, Saarland

University, PharmaScienceHub (PSH), 66421 Homburg, Germany; Center for Gender Specific Biology and Medicine (CGBM), Saarland University, 66421 Homburg, Germany

Dr. rer. nat. Selina Wrublewsky,

Institute for Clinical and Experimental Surgery, Saarland

University, PharmaScienceHub (PSH), 66421 Homburg, Germany; Center for Gender Specific Biology and Medicine (CGBM), Saarland University, 66421 Homburg, Germany

Introduction: Insulin resistance and obesity-associated inflammation are key drivers in the pathogenesis of type 2 diabetes mellitus (T2DM). While inflammatory cytokines are well known to impair β -cell function, their impact on pancreatic α -cells and glucagon (GCG) regulation remains poorly understood. In this study, we investigated the effects of the pro-inflammatory cytokines interleukin (IL)-1 β , tumor necrosis factor (TNF)- α and interferon (IFN)- γ on GCG expression and secretion.

Methods: The viability and endocrine function of the α -cell line aTC1 and isolated islets were investigated by water-soluble tetrazolium (WST)-1 assay, lactate dehydrogenase (LDH) assay, quantitative real-time (qRT)-PCR, Western blot analysis and enzyme-linked immunosorbent assay (ELISA). The transcriptional activity of the GCG promoter was analyzed by reporter gene assays. The cellular composition of isolated islets was assessed by immunohistochemistry.

Results: We found that exposure of the α -cell line aTC1 to a mix of these cytokines activates cellular stress responses characterized by induction of the nuclear factor kappa-light-chain-enhancer of activated B-cells (NF- κ B) pathway and the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway. Moreover, cytokine treatment markedly reduced GCG gene expression and secretion through repression of GCG promoter activity. Mechanistically, this was associated with a disrupted transcriptional network. These findings were confirmed in isolated mouse islets, where cytokine exposure significantly reduced GCG expression and secretion in islets of both male and female donors.

Conclusion: Taken together, these findings indicate that inflammatory cytokines are potent modulators of α -cell function as well as GCG secretion and provide novel insights into inflammation-driven dysregulation of the endocrine function of pancreatic islets.

Transcriptional Regulation of GLS2 by LSD1 Reprograms Glutaminolysis to Drive Tumor-Specific Chemotherapeutic Responses in Pancreatic Cancer

Dr.Zhefang Wang,

Department of General,Visceral,Thoracic and Transplantation Surgery,UniversityHospital of Cologne

Qiu Huang,

Department of General,Visceral,Thoracic and Transplantation Surgery,University Hospital ofCologne

Dr.Jiangang Zhao,

Department of General,Visceral,Thoracic and Transplantation Surgery,UniversityHospital of Cologne

Zicheng Lyu,

Department of General,Visceral,Thoracic and Transplantation Surgery,University Hospital of Cologne

Dr.Feng Ju,

Department of General,Visceral,Thoracic and Transplantation Surgery,University Hospital of Cologne

Dr.Bo You,

Institute of Otolaryngology Head and Neck Surgery,Affiliated Hospital of Nantong University

Dr.Jie Wang,

Institute of Pathology,University of Cologne

Prof.Dr.Qiongzhu Dong,

Key Laboratory of Whole-period Monitoring and Precise Intervention of Digestive Cancer,Minhang Hospital,Fudan University

Prof.Dr.Margarete Odenthal,

Institute of Pathology,University of Cologne

Prof.Dr.Alexander Quaas,

Institute of Pathology,University of Cologne

Dr.Kalliope Nina Diakopoulos,

Comprehensive Cancer Center München,Institute for Tumor Metabolism,Technical University of Munich

Prof.Dr.Hana Algül,

Comprehensive Cancer Center München,Institute for Tumor Metabolism,TechnicalUniversity of Munich

Prof.Dr.Maximilian Reichert,

Department of Medicine II,Technical University of Munich

Prof.Dr.Christiane J.Bruns,

Department of General,Visceral,Thoracic and Transplantation Surgery,University Hospital of Cologne

PD Dr.Yue Zhao,

Department of General,Visceral,Thoracic and Transplantation Surgery,UniversityHospital of Cologne.

Introduction:Pancreatic ductal adenocarcinoma(PDAC)is one of the deadliest malignancies worldwide andacquired drug resistance is one of the main limitations to therapy outcomes.Increasing evidence suggests thattumor heterogeneity contributes to chemoresistance in PDAC,but the underlying mechanisms remain poorlyunderstood.Lysine-

specific demethylase 1 (LSD1/KDM1A) is an epigenetic regulator and has been implicated in multiple oncogenic processes. Previous studies have shown that LSD1 regulates glycolysis and lipid metabolism but its role in glutamine metabolism has not been fully characterized. Research question: In this study, we investigated the effect of LSD1 on chemoresistance in different subtypes of PDAC, and we analyzed how LSD1 regulates glutamine metabolism and whether targeting LSD1 could provide a subtype-specific therapeutic strategy for PDAC.

Methods: We combined analyses of publicly available datasets with mechanistic studies in PDAC cell lines. Drug responses were assessed using 3D organoid cultures, and apoptosis was measured by flow cytometry. ChIP-qPCR was performed to examine LSD1-mediated epigenetic regulation of target genes. C13 tracing was used to evaluate glutamine metabolic flux. Mitochondrial function was assessed using Seahorse XF mitochondrial stress assays and mitophagy analyses.

Statistics: Data are presented as mean $\pm$ SEM. Statistical significance was determined using two-tailed Student's t-tests or one-way ANOVA, as appropriate. A p-value < 0.05 was considered statistically significant.

Results: LSD1 demonstrates opposite effects on chemotherapeutic responses in different PDAC subtypes. Knocking down LSD1 increased sensitivity to gemcitabine and paclitaxel in RSK-subtype cells but reduced sensitivity in KRAS-subtype cells. Targeting mitochondrial respiration or mitophagy effectively overcomes LSD1-mediated, subtype-specific chemoresistance. Metabolic tracing analyses showed that LSD1 promoted glutamine oxidation in RSK-subtype cells, whereas glutamine-derived carbon was preferentially directed toward reductive carboxylation in KRAS-subtype cells. Interestingly, LSD1 suppressed GLS2 expression through regulation of H3K4me3 at the GLS2 promoter. GLS2 function differentially regulates chemotherapeutic responses, promoting resistance in RSK-subtype cells while enhancing sensitivity in KRAS-subtype cells.

Discussion: Our findings show that LSD1 affects chemotherapy response in a subtype-dependent manner. Distinct mitochondrial states in KRAS- and RSK-subtype tumors influence glutamine metabolism and determine the outcome of LSD1-GLS2 signaling.

Conclusion: This study identifies LSD1 as a subtype-dependent regulator of chemoresistance in PDAC. Our findings highlight the potential application of LSD1 targeting for overcoming chemotherapy resistance in RSK-subtype PDAC.

The Role of LNPK in Endoplasmic Reticulum Stress and Perineural Invasion of Pancreatic Ductal Adenocarcinoma

Nino-Javakhishvili

-Department of Visceral, Vascular and Endocrine Surgery, Martin-Luther-University Halle-Wittenberg, University Medical Center Halle, 06120 Halle (Saale), Germany

PD Dr.-Bogusz-Trojanowicz

-Department of Visceral, Vascular and Endocrine Surgery, Martin-Luther-University Halle-Wittenberg, University Medical Center Halle, 06120 Halle (Saale), Germany

Dr.-Yoshiaki-Sunami

-Department of Visceral, Vascular and Endocrine Surgery, Martin-Luther-University Halle-Wittenberg, University Medical Center Halle, 06120 Halle (Saale), Germany

Prof. Dr.-Jörg-Kleeff

-Department of Visceral, Vascular and Endocrine Surgery, Martin-Luther-University Halle-Wittenberg, University Medical Center Halle, 06120 Halle (Saale), Germany

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is an exceptionally aggressive malignancy with a dismal prognosis. Multiple factors influence its development and progression while many of the mechanisms are poorly understood. Endoplasmic reticulum (ER) stress and perineural invasion (PNI) are two of the prominent phenomena accompanying and driving the PDAC progress. In our previous study we developed an ex-vivo perineural invasion model and established a consensus transcriptome of PNI in PDAC using cancer cell lines and rat vagal nerves. The enriched genes included an upregulated LNPK. Since then, LNPK, encoding a protein Lunapark, has been identified as an ER structural protein, while its dysregulation has been linked to ER stress. LNPK loss-of-function is also responsible for a rare autosomal recessive neurodevelopmental syndrome and studies of this syndrome identified LNPK's role in central nervous system (CNS) development.

Research question: Our previous data and the recent studies linking LNPK to important PDAC-related processes prompted us to study its role in more depth in pancreatic cancer.

Methods: The LNPK expression in pancreatic tumor and normal tissues and survival analysis were explored using public GEPIA2 database. The expression was also tested using pancreatic cancer cell line and pancreatic whole tissue samples. 6 cancer cell lines and 10 cancer and cancer-adjacent pancreatic tissue samples were used for qPCR experiments. Protein Lunapark expression was determined by immunohistochemistry (IHC) using 47 paraffin blocks from PDAC and adjacent normal pancreatic tissue. IHC analysis was performed using immunoreactivity scoring system (IRS) separately for nerve-invading and non-nerve-invading cancer cells, stroma, pancreatic intraepithelial neoplasia (PanIN) lesions, and normal ducts. LNPK knockdown was done on 2 PDAC cell lines. Annexin V and Propidium Iodide and FACS were used for apoptosis assay. MTT assay was used for viability. Bulk RNA sequencing analysis was used on knockdown and control samples.

Statistics: Statistical analyses and graphic presentations are being performed using GraphPad Prism 10. Experiments were done in triplicates and significance assigned by p value of <0.05 . RNA sequencing data analysis and significant differential gene and pathway enrichment significance was based on adjusted $p < 0.05$.

Results: The data revealed higher expression of LNPK in cancer compared to normal pancreas tissue in public database as well as our tissue samples with a mean RQ of 7.2 in cancer vs RQ of 2.28 in healthy pancreatic whole tissue RNA (P value = 0.04). IHC analysis displayed specificity of Lunapark in cancer cells where approximately 40% of cancer cells scored 4.8 and

another 40%, 9-12. Stroma and low-grade PanINs displayed negative immunoreactivity. 88% of normal pancreatic ducts were also negative. qPCR data showed high expression in PDAC cell lines especially Panc1 and Patu8902 which were selected for gene knockdown experiments. Downregulation resulted in decreased proliferation and increased apoptosis 72 hours after knockdown compared to control samples. RNA sequencing supported the decreased cell viability by a significant downregulation of Cell Cycle and DNA Replication pathways in both cell lines.

Discussion: The decreased cancer proliferation after LNPK knockdown as seen by phenotypic effects and RNA sequencing analysis indicates that the protein could have not only structural but a functional role that could contribute to PDAC progression possibly through its effects on intrinsic states like ER homeostasis but also by its effects on nerve invasion and cancer spread.

Conclusion: Our current results suggest that LNPK could have a more specific role in pancreatic adenocarcinoma and its underlying mechanisms. The ongoing experiments are focused on assessing its connection to ER stress and PNI in more depth.

More than Implants – Orthopädie im Zeitalter der Surgeomics

Calcium-phosphate Ratio as a Marker for the State of Osteogenesis In Vitro: Implementing a Measurement Method That Doesn't Require EDX

Dr.med.Jakob Hofmann,
Med.Fakultät d.Universitätsklinikums Heidelberg;
Dr.med.Tim Bewersdorf,
Klinik für Unfall-und Wiederherstellungschirurgie d.Universitätsklinikums Heidelberg;
Ulrike Sommer,
Klinik für Unfall-und Wiederherstellungschirurgie d.Universitätsklinikums Heidelberg;
Univ.-Prof.Dr.med.Gerhard Schmidmaier,
Klinik für Unfall-und Wiederherstellungschirurgie d.Universitätsklinikums Heidelberg;
PD Dr.med.Tobias Großner,
Klinik für Unfall-und Wiederherstellungschirurgie d.Universitätsklinikums Heidelberg

Introduction: To effectively research bone tissue engineering, it is imperative to be able to assess the progression of osteogenesis in vitro. To track the progression of the formation of the inorganic extracellular matrix (ECM), the measurement of the calcium to phosphate ratio (CaP ratio) can be used. While this ratio is typically small during the beginning of osteogenesis, it then increases towards a value of 1.66, which corresponds to mature hydroxy apatite. The gold standard for measuring the CaP ratio is energy-dispersive x-ray spectroscopy, an elaborate technique which is not readily available at every laboratory. We therefore aimed to develop an alternative strategy for determining the CaP ratio of mesenchymal stem cell (MSC) cultures in vitro.

Methods: MSCs were harvested from adult human donors during elective hip surgery after informed consent was given. Cells were seeded at a density of 8,300 cells/cm² into 35mm petri dishes. The following groups were formed: A1-osteogenic medium (OM) for 1 week, B1-control medium (CTRL) for 1 week, A2-OM, 2 weeks, B2-CTRL, 2 weeks, A3-OM, 3 weeks, B3-CTRL, 3 weeks. OM: DMEM LG + dexamethasone + β -glycerol phosphate + L-ascorbic acid. CTRL: DMEM LG. After the end of each culture, the dishes were incubated with 0,5 mol/L HCl for 2 hours, before the cells were scraped from the petri dish, transferred into a test tube and again incubated with 0,5 mol/L HCl for a total of 24h. After that, the tubes were centrifuged and the supernatant analysed for calcium and phosphate concentration by the central clinical laboratory of the Heidelberg University Hospital.

Results: Over the course of the 3-week culture, the calcium to phosphate ratio in the osteogenic groups increased steadily from 0.3 in week 1 (A1) to 1.02 in week 2 (A2) and further to 1.39 in week 3 (A3). For the control groups, the ratio remained similarly low for the first two weeks (B1: 0.36; B2: 0.42) before shooting up to 1.76 for week 3 (B3). The absolute amount of calcium and phosphate was as follows: Calcium: 0.17 μ mol (A1)/0.22 (B1)/0.44 (A2)/0.22 (B2)/1.81 (A3)/0.37 (B3); Phosphate: 0.55 μ mol (A1)/0.62 (B1)/0.45 (A2)/0.53 (B2)/1.32 (A3)/0.21 (B3).

Discussion: Our method for measuring the CaP ratio of MSC cultures in vitro was based on the dissolution of the inorganic ECM using hydrochloric acid. We found that the CaP ratio increased during the 3 weeks of culture before eventually reaching 1.32. This value is lower than the theoretical value for mature hydroxy apatite (1.66) but it is in line with the ratio typically observed for human bone (1.39-1.62). The relatively low ratio implies that the development of mature mineral might not be fully completed after 3 weeks of culture in

vitro. In the control condition, the CaP ratio remains low for the first two weeks before jumping up to 1.76. While this value would indicate the formation of a mature inorganic ECM, it has to be kept in mind that the absolute amount of calcium and phosphate is in fact very low. Perhaps cells can still incorporate calcium into the ECM under control condition while not being able to hydrolyse phosphate, leading to a low amount of mineral with a very high calcium content. The exact mechanisms will have to be looked at in further experiments.

Conclusion: The amount of calcium and phosphate in the inorganic ECM of cell culture in vitro can be assessed by solving the matrix using HCl. However, for a full picture regarding the state of the inorganic component of osteogenesis one must not only look at the calcium-phosphate ratio but also at the total amount of mineral formed.

First Clinical Experience with an Augmented Reality System (ARVIS) for Component Alignment in Primary Total Knee Arthroplasty

Lara Diéguez González, Orthopädische Universitätsklinik Magdeburg;
Prof. Dr. med. Christoph H. Lohmann, Orthopädische Universitätsklinik Magdeburg

Accurate positioning of femoral and tibial components is essential for successful primary TKA. Augmented reality has recently emerged as a novel navigation technology that provides real-time intraoperative guidance while maintaining a streamlined surgical workflow. However, clinical experience with AR-assisted TKA remains limited.

To evaluate the feasibility and initial radiographic outcomes of the ARVIS augmented reality system for femoral and tibial component alignment in primary TKA

A prospective case series of the first ten consecutive patients undergoing primary TKA using the ARVIS system was performed. The system provided intraoperative guidance for component positioning, including coronal alignment and tibial slope. Postoperative radiographic analysis was conducted to evaluate implant alignment relative to the planned surgical targets. Descriptive statistics were applied given the initial nature of this experience. All procedures were successfully completed using the ARVIS system. Postoperative radiographic analysis demonstrated accurate component positioning relative to the planned alignment targets. No device-related intraoperative complications or technical failures were observed. Detailed radiographic measurements will be presented at the congress.

This initial clinical experience suggests that ARVIS is a feasible and practical navigation system for primary TKA and integrates smoothly into the surgical workflow. While limited by small sample size, the preliminary findings support further clinical evaluation.

The ARVIS augmented reality navigation system appears to be a feasible and promising tool for component alignment in primary TKA. The first ten clinical cases demonstrate successful implementation and encouraging radiographic results. Larger comparative studies are warranted to confirm conclusion: The ARVIS system demonstrates promising accuracy and feasibility in early TKA cases, supporting further evaluation in larger, comparative studies.

Ag-Zn-PMEDM-Modified Ti6Al4V Implants for Preventing Periprosthetic joint infections

Daria Terens 1,M.Sc.Vadym Voropai 1,M.Sc.Adrian Buchholz 1,Dr.-Ing.Viet Duc Bui 2,Prof.Dr.-Ing.Andreas Schubert 2,Prof.Dr.rer.nat.Jessica Bertrand 1

1 Department of Orthopedic Surgery,Medical Faculty,Otto von Guericke University Magdeburg

2 Professorship Micromanufacturing Technology at the Faculty of Mechanical Engineering,ChemnitzUniversity of Technology

Introduction:Periprosthetic joint infections(PJI)are a serious complication following jointreplacement surgery and remain difficult to treat.Ti6Al4V alloys are widely used for orthopedicimplants.Their surface properties can influence susceptibility to infection.Antibacterial metalcoatings containing silver(Ag)and zinc(Zn)can reduce bacterial adhesion and biofilmformation.However,their combined effect on Powder Mixed Electrical Discharge Machining(PMEDM)-modified Ti6Al4V surfaces remains unclear.

Research Question:This study aimed to investigate the antibacterial properties andbiocompatibility of Ag-Zn-PMEDM-modified Ti6Al4V surfaces.

Methods:Ti6Al4V surfaces were modified using PMEDM with Ag-Zn concentrations of 0,2-2,5%.Unmodified Ti6Al4V and Electrical Discharge Machining(EDM)-modified Ti6Al4Vsurfaces(without Ag-Zn powder)served as controls.Surface roughness was measured by 3Dconfocal microscopy.Colonization by *S.capitis* and *E.coli* was assessed_by DAPIfluorescence staining($n = 6$).ROS production was quantified using CellROX Deep RedReagent($n = 8$).Biocompatibility was evaluated by analyzing the expression of inflammation-associated genes in Mono-Mac-6(MM6)cells.

Statistics:Data were tested for normality using Shapiro Wilk test and analyzed using one-wayANOVA.Significance was defined as $p < 0,05$.

Results:PMEDM increased the surface roughness(R_a)of Ti6Al4V.Ag-Zn-PMEDM-modifiedsurfaces significantly reduced *E.coli* colonization at high Ag and low Zn concentrations($0,97\%:0,23\%$, $p = 0,0139$).For *S.capitis*,colonization was significantly reduced with increasingAg-Zn concentration compared with the smooth Ti6Al4V control($p = 0,0076$),but not the roughEDM control.ROS production increased in *E.coli* on surfaces with a high Zn content($1,24\%:2,39\%$).In *S.capitis*,it increased significantly with increasing Ag-Zn concentration($p = 0,0456$).No significant changes were observed in the expression of FN,TGF β 2,IL-1 β ,or TNF- α by MM6 cells.

Discussion:The antibacterial effect against *E.coli* appears to be mainly associated with ahigher Ag content,whereas the reduced *S.capitis* colonization is likely influenced by theincreased surface roughness.As ROS production did not consistently correlate with bacterialcolonization,additional antibacterial mechanisms maybe involved.

Conclusion:Ag-Zn-PMEDM surfaces reduce bacterial adhesion without compromisingbiocompatibility.These findings highlight the potential of Ag-Zn-PMEDM surface modificationas a preventive strategy against PJI.

Generation of prevascularized spheroids for bone tissue engineering by fusion of microvascular fragments with ADSC

Dr.rer.nat.Selina Wrublewsky,
 Institute for Clinical and Experimental Surgery,Saarland
 University,PharmaScienceHub(PSH),66421 Homburg,Germany
 Caroline Bickelmann,
 Institute for Clinical and Experimental Surgery,Saarland University,PharmaScienceHub
 (PSH),66421 Homburg,Germany
 Prof.Dr.rer.nat.Emmanuel Ampofo,
 Institute for Clinical and Experimental Surgery,Saarland
 University,PharmaScienceHub(PSH),66421 Homburg,Germany
 Univ.-Prof.Dr.med.Matthias W.Laschke,
 Institute for Clinical and Experimental
 Surgery,SaarlandUniversity,PharmaScienceHub(PSH),66421 Homburg,Germany

Introduction:Three-dimensional spheroids represent promising building blocks for bone tissue engineering due to their enhanced cell viability,differentiation capacity and metabolic activity when compared to conventional two-dimensional culture systems. However,rapid vascularization of spheroids is of major importance to guarantee their survival after transplantation.To achieve this,we herein introduce the generation and differentiation of prevascularized spheroids by fusion of adipose tissue-derived microvascular fragments(MVF)with adipose-derived stem cells (ADSC).

Methods:MVF were isolated from C57BL/6J donor mice.For the generation of ADSC or ADSC+MVF spheroids,5,000 ADSC alone or 5,000 ADSC and 200 MVF were cultured in a liquid overlay system for 5 days.After generation,ADSC and ADSC+MVF spheroids were cultured under osteogenic or chondrogenic differentiation conditions for 0,7,14 or 21 days.Undifferentiated ADSC and ADSC+MVF spheroids served as controls.The diameters of the spheroids were assessed by bright-field microscopy.Viability,differentiation status,cellular composition and protein expression of the spheroids were determined by flow cytometry,immunohistochemistry,quantitative real-time(qRT)-PCR and Western blot.The angiogenic potential of the spheroids was analyzed using sprouting assays.All experiments were performed on days 0,7,14 and 21.

Results:After generation on day 0,ADSC and ADSC+MVF spheroids exhibited a round and compact shape.During the differentiation process,the diameters of all spheroids progressively decreased.The incorporation of MVF into ADSC spheroids did not affect their viability.However,the viability of all spheroids slightly declined from $92.2 \pm 2.3\%$ to $84.1 \pm 2.9\%$ between days 7 and 21.Von Kossa and Alizarin Red staining indicated a higher level of osteogenic differentiation in ADSC+MVF spheroids when compared to ADSC spheroids.In line with this finding,the incorporation of MVF into ADSC spheroids also promoted chondrogenic differentiation,as demonstrated by Alcian Blue staining.During the entire osteogenic and chondrogenic differentiation period,expression of the endothelial cell marker CD31 was detected in ADSC+MVF spheroids by means of Western blot analysis.Moreover,immunohistochemical staining showed that MVF effectively reassemble into new microvascular networks within the spheroids.Accordingly,ADSC+MVF spheroids also showed a high angiogenic sprouting activity in vitro.

Conclusion: These findings indicate that ADSC+MVf spheroids may ideally serve for bone tissue engineering due to their increased level of osteogenic as well as chondrogenic differentiation and high vascularization capacity.

Optimizing Posterior Pelvic Ring Fixation in Fragility Fractures of the Pelvis: A Classification-Based Comparative Study

Moeen Babayi,
 Department of Trauma and Orthopaedic Surgery, Asklepios Klinikum
 Wandsbek, Hamburg, Germany
 Dr. Med. Univ. Marie-Luise Paulsen,
 Department of Trauma and Orthopaedic Surgery, Asklepios
 Klinikum Wandsbek, Hamburg, Germany
 PD Dr. Christian Walter Müller,
 Department of Trauma and Orthopaedic Surgery, Asklepios
 Klinikum Wandsbek, Hamburg, Germany

Background. Fragility fractures of the pelvis (FFPs) are increasingly common in the elderly and are associated with pain, impaired mobility, loss of independence, and increased morbidity. The Fragility Fractures of the Pelvis (FFP) and OF Pelvis classifications support treatment decision-making by characterizing fracture morphology and instability. However, once surgical stabilization has been indicated, evidence guiding the optimal postero-fixation strategy remains limited. This study evaluates three commonly used percutaneous posterior pelvic ring fixation strategies and their impact on early postoperative functional recovery within comparable fracture patterns.

Methods. This retrospective comparative cohort study included consecutive patients who underwent surgical treatment for FFP type IIb and IIc fractures between January 2017 and June 2026 at a single Level I trauma centre. Preoperative radiographs and computed tomography scans were independently reviewed, and all fractures were classified according to both the FFP and OF Pelvis classifications.

Patients were stratified according to the posterior fixation strategy into (1) unilateral short iliosacral screw fixation, (2) single transiliac-transsacral screw fixation, and (3) bilateral short iliosacral screw fixation.

The co-primary outcomes were early postoperative pain reduction and functional recovery. Pain was assessed using the Visual Analogue Scale (VAS) preoperatively and on postoperative day 3. Functional recovery was assessed according to the documented ambulatory status. Secondary outcomes included time to surgery, operative duration, intraoperative fluoroscopy time, intraoperative and postoperative complications, implant-related complications, length of hospital stay, revision surgery, and discharge destination.

Between-group comparisons will be performed using appropriate parametric or non-parametric tests. Multivariable regression analyses will adjust for age, sex, fracture classification (FFP and OF), baseline pain, baseline mobility, ASA status, and time to surgery.

Results. Data collection and radiological classification have been completed. Statistical analyses are currently underway. The planned analyses will compare postoperative pain reduction, early functional recovery, operative characteristics, and complication rates among the three fixation strategies while accounting for fracture morphology according to both the FFP and OF Pelvis classifications.

Conclusion. This study is expected to provide comparative evidence regarding posterior fixation strategies for surgically treated fragility fractures of the pelvis. By integrating both the FFP and OF Pelvis classifications, the findings may contribute to a more individualized, classification-based selection of posterior pelvic ring fixation and improve early postoperative functional recovery.

Künstliche Intelligenz in der chirurgischen Versorgung

KI-gestützte 3D-Rekonstruktion in der Lungenchirurgie – Eine retrospektive Vergleichsstudie

Sayzana Kassahun
Katrín Hornemann
Waldemar Schreiner

Hintergrund

Die Segmentektomie hat einen neuen Stellenwert in der chirurgischen Behandlung des peripher lokalisierten, subsoliden und soliden nicht-kleinzelligen Lungenkarzinoms ≤ 2 cm. Neben funktionellen Vorteilen durch den Erhalt von Lungenparenchym konnte ihre onkologische Gleichwertigkeit zur Lobektomie in randomisierten Studien gezeigt werden. Aufgrund zahlreicher anatomischer Varianten der pulmonalen Gefäß- und Bronchialanatomie sowie der teilweise schwierigen präoperativen Zuordnung eines Tumors zu einem Lungensegment stellt sie jedoch weiterhin eine operative Herausforderung dar. Eine präzise Kenntnis der individuellen Anatomie ist entscheidend, um operative und onkologische Sicherheit zu gewährleisten. KI-gestützte 3D-Rekonstruktionen ermöglichen eine patientenspezifische präoperative Planung, werden jedoch bislang nicht routinemäßig eingesetzt.

Material und Methoden

Retrospektiv wurden Patienten analysiert, die zwischen Oktober 2023 und Dezember 2024 eine VATS-Segmentektomie mit präoperativer KI-gestützter 3D-Rekonstruktion erhielten. Eingeschlossen wurden Patienten mit präoperativ unklarer Diagnose, bei denen die Indikation zur Segmentektomie anhand von Tumorgröße, Morphologie und Lokalisation gestellt wurde. Insgesamt wurden 36 Patienten mit KI-gestützter 3D-Rekonstruktion mit einer Kontrollkohorte von 46 Patienten verglichen, die zwischen 2020 und 2023 ohne 3D-Rekonstruktion operiert wurden. Analysiert wurden Operationszeit, intraoperativer Blutverlust, intra- und postoperative Komplikationen, Clavien-Dindo-Grad-III-Komplikationen, Krankenhausaufenthalt sowie onkologische Resektionsqualität anhand des Sicherheitsabstands (≥ 2 cm) und der Margin-to-Tumor-Ratio ($M/T \geq 1$). Das verwendete KI-System (InferVision GmbH) erstellt auf Basis eines CT-Thorax innerhalb von etwa 280 Sekunden automatisiert patientenspezifische 3D-Modelle der pulmonalen Anatomie. Zwischen beiden Gruppen bestanden keine signifikanten Unterschiede hinsichtlich der präoperativen Patienten- und Tumorcharakteristika.

Ergebnisse

In der 3D-Gruppe wurden 29 % einfache und 71 % komplexe Segmentektomien durchgeführt. Anatomische Varianten fanden sich bei 26 % der Arterien und 13 % der Bronchien. In 17,3 % der Fälle führte die 3D-Rekonstruktion zu einer Anpassung der präoperativen Resektionsplanung. Das mediane Alter betrug 66,9 Jahre in der 3D-Gruppe und 66,5 Jahre in der Kontrollgruppe.

Patienten mit präoperativer 3D-Rekonstruktion hatten einen signifikant kürzeren Krankenhausaufenthalt (6 vs. 9 Tage; $p = 0,0015$). Intraoperative Komplikationen traten bei 5,9 % versus 2,2 % auf ($p = 0,828$), postoperative Komplikationen bei 28,6 % versus 35,3 % ($p = 0,884$). Schwerwiegende Komplikationen (Clavien-Dindo Grad III) waren ebenfalls seltener (9 % vs. 17,9 %; $p = 0,545$). Ein onkologisch empfohlener Sicherheitsabstand von ≥ 2 cm wurde in der 3D-Gruppe signifikant häufiger erreicht als in der Kontrollgruppe (41,2 % vs.

14,3 %; $p = 0,0219$; OR 3,44). Auch eine Margin-to-Tumor-Ratio ≥ 1 wurde häufiger erzielt (47 % vs. 31 %), ohne statistische Signifikanz ($p = 0,164$).

Schlussfolgerung

Die präoperative KI-gestützte 3D-Rekonstruktion verbessert die präoperative Operationsplanung und ist mit einem signifikant kürzeren Krankenhausaufenthalt sowie einer höheren Wahrscheinlichkeit verbunden, einen onkologisch empfohlenen Sicherheitsabstand von ≥ 2 cm zu erreichen. Die niedrigeren Komplikationsraten und die höhere Margin-to-Tumor-Ratio zeigten einen positiven Trend, erreichten jedoch keine statistische Signifikanz. Die Ergebnisse sprechen dafür, dass KI-gestützte 3D-Rekonstruktionen die anatomische Orientierung erleichtern und die onkologische Qualität anatomischer Segmentresektionen verbessern können.

LOPES (LLM-based Optimization of Patient Education in Surgery): an international multicenter cross-sectional study evaluating multilingual surgical patient education across ten languages

Ughur Aghamaliyev, Athanasios Zamparas, Javad Karimbayli, Dionysios Koliogiannis, Florian Kuehn, Jens Werner, Matthias Ilmer, Bernhard W Renz

Background

More than 300 million surgical procedures are performed worldwide each year. Increasing international migration has resulted in growing numbers of patients undergoing surgery in health systems where they have limited proficiency in the local language, challenging informed consent and equitable access to understandable surgical information. Large language models (LLMs) have emerged as a potential solution; however, their multilingual performance remains insufficiently evaluated. We assessed the performance of GPT-4o for surgical patient education across ten languages representing approximately 4.7 billion native speakers worldwide.

Methods

In this cross-sectional multilingual study, a previously published dataset comprising 120 frequently asked questions covering six general surgical procedures was translated from English into nine additional languages (Spanish, mandarin, Hindi, German, French, Italian, Greek, Turkish, Russian). Each language-specific dataset was entered into the publicly available GPT-4o model. Responses were independently evaluated by three native-speaking surgeons per language (30 reviewers; 3600 ratings) for factual accuracy, clinical relevance, coherence, and potential harm using standardized Likert scales. A structured survey assessed surgeons' attitudes towards multilingual LLM-assisted patient education.

Results

GPT-4o generated consistently high-quality responses across all evaluated languages. English responses achieved slightly higher ratings for factual accuracy and clinical relevance than non-English responses, whereas coherence and potential harm were comparable. Similar performance was observed for major and minor surgical procedures and for preoperative and postoperative questions. Although all participating surgeons considered LLM-generated responses useful for patient education, only about one-fifth considered fully autonomous AI-driven patient education ethically acceptable. Nearly half reported previous use of LLMs for patients who did not speak the local language.

Conclusion

GPT-4o demonstrated robust multilingual performance across ten languages and may improve access to understandable surgical information for patients facing language barriers. Multilingual LLMs may be particularly valuable when adequate multilingual patient education cannot otherwise be achieved. Current evidence supports their use as physician-supervised adjuncts rather than replacements for informed consent.

Organ Rescue: Innovative Ansätze bei Lungen- und Organversagen

A Flow-Defined Murine Liver Perfusion Model to Study Functional Vulnerability in Fatty Liver Disease

Dr.rer.nat.Peggy Stock

-Experimental hepatobiliary surgery Lab, Department of Visceral, Transplant, Thoracic and Vascular Surgery, University of Leipzig Medical Center, Liebigstraße 21, Leipzig, 04103, Saxony, Germany

Univ.-Prof.Dr.med.Thomas Ebert

-Department of Endocrinology, Nephrology and Rheumatology, University Hospital Leipzig, Leipzig, Germany

Univ.-Prof.Dr.med.Hans-Michael Tautenhahn

-Experimental hepatobiliary surgery Lab, Department of Visceral, Transplant, Thoracic and Vascular Surgery, University of Leipzig Medical Center, Liebigstraße 21, Leipzig, 04103, Saxony, Germany

Introduction: Steatotic liver disease is the most common chronic liver disease in industrialized countries. In addition to metabolic alterations, hepatic steatosis affects the sinusoidal microcirculation and may increase the susceptibility of the liver to perfusion disturbances. This is particularly relevant after major liver resection, as impaired perfusion of the remnant liver may directly affect postoperative liver function. However, the quantitative relationship between steatosis-associated structural alterations, intrahepatic perfusion, and resulting functional impairment remains insufficiently characterized.

Research Question: Establishment of a standardized in situ murine liver perfusion model to investigate whether steatosis-associated structural changes alter hepatic perfusion and thereby impair liver function.

Methods: C57BL/6N mice and steatotic Leprotvdo mice were perfused in situ via the portal vein. Perfusion was performed using oxygenated Williams' Medium E supplemented with 1% albumin at different flow rates. Normoperfusion of C57BL/6N mice (2 ml/min) served as the reference group. C57BL/6N and Lepr^{bb} mice were investigated under altered perfusion conditions to characterize perfusion- and steatosis-associated changes.

Indocyanine green (ICG) was used to assess hepatic excretory function. Time-dependent ICG clearance was quantified in the vena cava outflow and bile. Tissue integrity and hepatic zonation were evaluated by histological and immunohistochemical analyses, including hematoxylin and eosin (H&E) and glutamine synthetase (GS) staining. Metabolic characterization included quantification of triglycerides, free fatty acids, and lactate in liver tissue, as well as free fatty acids and lactate in vena cava outflow samples.

Statistics: All groups were analyzed using descriptive statistics. In the reference group, data were tested for normal distribution and potential outliers. Time-dependent changes in paired vena cava samples were analyzed using the Friedman test. Kendall's W was reported as an effect size. In the case of a significant global test, pairwise Wilcoxon tests with Holm correction were performed.

Results:Initial perfusion model-validation experiments in normoperfused C57BL/6N livers demonstrated reproducible ICG kinetics, with biliary ICG appearance occurring in close temporal proximity to first vascular detection. In parallel, histological and metabolic readouts were used to characterize tissue integrity, hepatic zonation, and perfusion-associated metabolic changes. Reference livers showed predominantly moderate parenchymal alterations with largely preserved pericentral glutamine synthetase expression. Metabolic measurements provided reference ranges for intrahepatic triglycerides, free fatty acids, and lactate. In vena cava outflow samples, free fatty acid concentrations remained largely stable over time, whereas lactate tended to decrease during perfusion.

Under reduced-flow conditions, ICG assessment remained feasible, while outflow lactate levels appeared higher than under the reference condition. In steatotic Lepr^{cb}h^{to} livers, ICG kinetics were more heterogeneous, including delayed biliary ICG transfer in the liver with more pronounced histological steatosis and higher intrahepatic triglyceride content. These preliminary observations suggest that the model can capture steatosis- and perfusion-associated alterations in hepatic excretory and metabolic function.

Discussion/Conclusion:The established in situ perfusion model enables standardized assessment of hepatic perfusion-function coupling using time-resolved ICG kinetics. Preliminary findings suggest that advanced steatosis may impair biliary ICG transfer despite preserved vascular ICG availability. Thus, future analyses should stratify steatotic livers according to steatosis severity. This model may help define functional reserve in steatotic livers and improve risk assessment after major liver resection.

Low-intensity ultrasound (LIUS) verstärkt IL-6/pSTAT3-Signale von murinen Hepatozyten

Dück E(1), Reich S(2), Keitel-Anselmino V(2), Wartmann T(1), Croner RS(1), Kahlert U(1), Stelter F(1)

(1) Universitätsklinik für Allgemein-, Viszeral-, Gefäß- und Transplantationschirurgie, Magdeburg

(2) Universitätsklinik für Gastroenterologie, Hepatologie und Infektiologie, Magdeburg

Einführung:

Die Regeneration des Lebergewebes nach Hemihepatektomie ist ein hochkomplexer und entscheidender Prozess, der insbesondere bei vorgeschädigter Leber (z.B. durch Chemo-/Radiotherapie oder chronische Lebererkrankungen) vermindert ist. Um ein postoperatives Leberversagen zu verhindern, sind regenerative Stimulierungsfaktoren erforderlich. Hierzu soll die ultraschallgestützte Stimulation der Interleukin-6 (IL-6)-Kaskade als Regenerationsstimulus untersucht werden, um die eingeschränkte Regeneration zu verbessern und postoperative Komplikationen zu reduzieren.

Zielsetzung und Methode:

Untersucht wurde, ob gepulste (LIPUS) und kontinuierliche Ultraschallstimulation (LICUS) die IL-6-induzierte STAT3-Phosphorylierung in murinen Hepatozyten verstärken. Dabei standen die Analyse der optimalen Ultraschallparameter und der Auswirkungen auf Apoptosemarker im Vordergrund. Hierzu wurden primäre Hepatozyten aus C57Bl/6J-Mäusen isoliert, kultiviert und am Folgetag mit rekombinantem IL-6 (10 ng/ml) stimuliert. Anschließend erhielten die Zellen eine 20-minütige Low-intensity ultrasound (LIUS)-Behandlung. Die Kontrollen erhielten IL-6 ohne LIUS. Gemessen wurden STAT3-Phosphorylierung sowie Caspase-3 und Cleaved-Caspase-3 mittels Western Blot-Analyse. Ergänzend wurden quantitative label-free Proteom- und explorative Phosphoproteomanalysen von nicht mit IL-6 behandelten LIPUS-, LICUS- und Kontrollproben durchgeführt, um native molekulare Effekte der Ultraschallstimulation zu charakterisieren.

Ergebnisse:

LIUS steigerte die IL-6-vermittelte STAT3-Phosphorylierung im Vergleich zu IL-6 allein deutlich. Der stärkste Effekt wurde bei LIPUS 100 mW/cm² beobachtet (ca. 9-fache pSTAT3/β-Actin-Intensität), während LICUS mit 200 mW/cm² die höchste Aktivierung zeigte (ca. 22-fache pSTAT3/β-Actin-Intensität). Die Analyse der Cleaved-Caspase-3 sowie Caspase-3-Level ergab bei diesen niedrigen Intensitäten keine Hinweise auf eine erhöhte Apoptose.

Eine ergänzende Proteomanalyse identifizierte 3196 Proteine, von denen 52 signifikant reguliert waren. Diese waren überwiegend zytoskelett-, stoffwechsel- und translationsassoziiert. Hervorzuheben sind unter anderem das IQ Motif Containing GTPase Activating Protein 2 (IQGAP2; Zytoskelett/Signaltransduktion), das im Gegensatz zum eng verwandten ubiquitären Protein IQGAP1 vor allem in der Leber gebildet und als Tumorsuppressor in Bezug auf das hepatozelluläre Karzinom (HCC) diskutiert wird¹ und die Betain-Homocystein-S-Methyltransferase 1 (BHMT1) als Teil des Methioninstoffwechsels.

Explorative Phosphoproteomanalysen ohne vorherige Phosphopeptid-Anreicherung identifizierten zusätzlich 31 ultraschallspezifische Phosphorylierungsereignisse als posttranslationale Modifikation, unter anderem von Vinculin (VCL) und Cingulin (CGN) als Zell-

Zell-Kontaktproteine sowie mehrere mitochondriale Enzyme wie die ATPsynthase subunit alpha mitochondrial (ATP5F1A; Komplex V) und die NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 10 mitochondrial (NDUFA10; Komplex I), was auf eine Beteiligung von Mechanotransduktion und einer Anpassung des mitochondrialen Energiestoffwechsels hindeutet. Bemerkenswert war, dass die Adenosylhomocysteinase (SAHH/AHCY) sowohl in der Label-free-Proteomanalyse als auch in der Phosphoproteomanalyse durch Ultraschall reguliert wurde. Dieser doppelte Nachweis spricht für eine funktionelle Beteiligung des Methionin-/SAM-Stoffwechsels an der ultraschallinduzierten zellularen Antwort.

Schlussfolgerung:

Niedrigintensiver Ultraschall verstärkt die IL-6/STAT3-Signalübertragung in Hepatozyten, ohne Apoptose auszulösen. Ergänzende Proteom- und Phosphoproteomanalysen von nicht mit IL-6 behandelten Hepatozyten deuten darauf hin, dass LIUS als mechanobiologischer Reiz Veränderungen des Zytoskeletts, metabolische Anpassungen und dadurch regenerative Wirkungen induziert. Diese Befunde bestätigen die zentrale Rolle der IL-6/STAT3-Achse in der Leberregeneration^{23,4} und legen nahe, dass LIUS regenerative Signalwege gezielt verstärken kann. Damit stellt LIUS einen vielversprechenden nicht-invasiven Ansatz zur Förderung der Leberregeneration nach Leberresektion dar.

Investigating Immunological Effects of Ultrasound-Assisted Liver Regeneration Using a Translational Mouse Model of Partial Hepatectomy

Konstantina Varvareizou, Elias Dück, Maria Reich, Verena Keitel-Anselmino, Thomas Wartmann, Roland S. Croner, Ulf Kahlert, Frederike Stelter

¹ Department of General, Visceral, Vascular and Transplant Surgery, University Hospital Magdeburg, Otto von Guericke University Magdeburg, Magdeburg, Germany

² Department of Gastroenterology, Hepatology and Infectious Diseases, University Hospital Magdeburg, Otto von Guericke University Magdeburg, Magdeburg, Germany

A remarkable trait of the liver is its ability to regenerate after injury. However, this regenerative capacity is often impaired in patients with chronic liver disease or previous chemotherapy, increasing the risk of postoperative liver failure following major liver resection. Identifying new strategies to support liver regeneration therefore remains an important clinical challenge.

In this work, we investigate whether low-intensity ultrasound stimulation can enhance liver regeneration after partial hepatectomy. In preliminary in vitro experiments using liver organoids, we observed increased cellular proliferation following ultrasound treatment. Building on these findings, we employ a well-established two-thirds partial hepatectomy (PHx) mouse model to study the effects of low-intensity pulsed ultrasound (LIPUS) and low-intensity continuous ultrasound (LICUS) in vivo. Resection of the median and left lateral lobes triggers a regenerative response characterized by hepatocyte proliferation, immune cell recruitment, and systemic signalling pathways that restore liver mass within days.

To address age-related differences in regenerative capacity, young, middle-aged, and aged mice are included in the study. Sham-operated animals and mice undergoing PHx without ultrasound treatment serve as controls.

To gain further insight into the immunological changes during regeneration, multiplex cytokine profiling will be performed to assess inflammatory and regenerative signalling pathways associated with ultrasound treatment. This work aims to contribute to the understanding of ultrasound-mediated regenerative mechanisms and to the development of non-invasive treatments after major liver resection.

CD26/DPP4 inhibition reduces peribronchiolar fibrosis in a murine model of chronic lung allograft rejection

Dr.med.-Birte-Ohm

-Institute for Laboratory Animal Science and Experimental Surgery, Faculty of Medicine, RWTH Aachen University, Aachen, Germany; Department of Thoracic Surgery, Faculty of Medicine, RWTH Aachen University, Aachen, Germany; Department of Thoracic Surgery, Faculty of Medicine, Medical Center-University of Freiburg, University of Freiburg, Freiburg, Germany

Dr.med.-Martina-Haberecker

-Department of Pathology and Molecular Pathology, University Hospital Zurich, Zurich, Switzerland

Kathleen –Mertens

-Laboratory of Medical Biochemistry, Department of Pharmaceutical Sciences, University of Antwerp, Antwerp, Belgium

Prof.Dr.-Ingrid-De Meester

-Laboratory of Medical Biochemistry, Department of Pharmaceutical Sciences, University of Antwerp, Antwerp, Belgium

Prof.Dr.-Gernot –Zissel

-Department of Pneumology, Medical Center-University of Freiburg; Faculty of Medicine, University of Freiburg, Freiburg, Germany

Prof.Dr.-Sven-Diederichs

-Division of Cancer Research, Department of Thoracic Surgery, Medical Center-University of Freiburg, Faculty of Medicine, Freiburg, Germany

Prof.Dr.-Wolfgang-Jungraithmayr

-Division of Thoracic Surgery, Rostock University Medical Center, Rostock, Germany

Introduction:

Chronic lung allograft dysfunction (CLAD) is the principal factor limiting long-term survival after lung transplantation and is characterized histologically by fibrotic remodeling of the airways, parenchyma, and pleura. CD26/dipeptidyl peptidase-4 (DPP4) participates in immunological and profibrotic processes and has been detected in fibrotic areas of chronically rejected lung allografts.

Research Question:

This study examined whether pharmacological inhibition of CD26/DPP4 attenuates fibrotic remodeling in a murine model of chronic lung allograft rejection.

Methods:

Using an allogeneic orthotopic left lung transplantation model, BALB/c donor lungs were transplanted into C57BL/6 recipients. Recipients received cyclosporine A and methylprednisolone and were randomized immediately postoperatively to a control or an intervention group, the latter additionally receiving vildagliptin via the drinking water. After four weeks, serum and transplanted lungs were analyzed. Systemic DPP4 inhibition was

quantified fluorometrically. Fibrotic remodeling was assessed by Masson's trichrome staining separately for parenchymal, peribronchiolar, and pleural areas; profibrotic markers were examined by RT-qPCR, and CD26 and α -SMA expression immunohistochemically.

Statistics:

An a priori sample size calculation (two-tailed Student's t-test, Ashcroft score as primary endpoint, Cohen's $d=1.5$, $\alpha=0.05$, power=0.80; G*Power 3.1) yielded $n=10$ analyzable animals per group. Normality was assessed by Shapiro-Wilk test. Groups were compared using unpaired two-tailed Student's t-tests (normally distributed data) or the Mann-Whitney test (non-normal data), and survival by log-rank test. A p -value <0.05 was considered significant.

Results:

Surgical and early postoperative outcomes did not differ between groups, and survival to the four-week endpoint was comparable (log-rank $p=0.4833$). Oral vildagliptin treatment significantly reduced systemic DPP4 activity ($p<0.05$). Histologically, the intervention group showed a significant decrease in peribronchiolar fibrosis ($p=0.0381$), whereas parenchymal (Ashcroft score) and pleural fibrosis were not significantly affected. At the mRNA level, DPP4 expression was significantly reduced in lung allografts of vildagliptin-treated animals ($p=0.0281$). The expression of profibrotic markers, including Col1a1, Fn1, Acta2, Fap, Tgfb, Il1b, and Snai1, did not differ significantly between groups. Likewise, immunohistochemistry revealed no significant differences in the presence of peribronchiolar CD26-positive cells or in parenchymal α -SMA expression.

Discussion:

The effect was confined to the airway compartment, with parenchymal and pleural fibrosis, profibrotic marker expression, and CD26-positive cell and α -SMA immunoreactivity unchanged. This is consistent with a role of CD26/DPP4 in airway-centered remodeling, while redundant pathways likely sustain remodeling elsewhere. More potent or locally targeted delivery may strengthen the effect.

Conclusion:

Continuous CD26/DPP4 inhibition with vildagliptin did not prevent chronic rejection in this murine model, but selectively reduced peribronchiolar fibrosis. This compartment-specific effect supports further evaluation of CD26/DPP4 inhibition as a preventive approach to airway-centered fibrotic remodeling in CLAD.

Liquid Biopsie in der peri-chirurgischen Versorgung

Circulating Hsp70 in Thoracic Oncology: A Biomarker for Tumor Progression and Prognosis

Prof. Johannes Bodner,

München Klinik Bogenhausen (akademisches Lehrkrankenhaus der TU München)

Prof. em. Dr. rer. nat. Gabriele Multhoff,

Transla TUM (Zentralinstitut für Translationale Krebsforschung der Technischen Universität München)

Introduction: The identification of reliable biomarkers for assessing tumor aggressiveness, staging, and treatment response remains a major challenge in thoracic oncology, particularly in the context of surgical decision-making. The stress-inducible heat shock protein 70 (Hsp70) is frequently overexpressed in malignant tumors, expressed on the tumor cell membrane, and released into the circulation both actively and passively.

Research-Question: This study aimed to evaluate the diagnostic and prognostic relevance of circulating Hsp70 (eHsp70), with a particular focus on its potential role in preoperative risk stratification in thoracic malignancies.

Methods: This analysis is based on two independent studies: (1) a cross-entity cohort including 389 patients with various solid tumors and 108 healthy controls, and (2) a thoracic cohort comprising 178 patients with non-small cell lung cancer (NSCLC) and 35 patients with pulmonary metastases. Free and extracellular vesicle-associated Hsp70 levels were quantified using the Hsp70-exo ELISA. In the thoracic cohort, additional immunophenotyping of peripheral blood lymphocytes was performed.

Statistics: Statistical analyses included non-parametric testing (Kruskal-Wallis) and receiver operating characteristic (ROC) analyses to assess diagnostic performance.

Results: Circulating eHsp70 levels were significantly elevated in all tumor cohorts compared to healthy controls ($p < 0.001$). A consistent stage-dependent increase in eHsp70 concentrations was observed, ranging from early-stage to locally advanced and metastatic disease. Diagnostic performance was limited in early-stage disease but improved markedly in advanced stages (AUC up to ~0.83).

In the thoracic cohort, these findings were confirmed for NSCLC, with significantly elevated eHsp70 levels independent of histological subtype. Notably, eHsp70 correlated with clinically relevant parameters of tumor aggressiveness: patients with lymph node metastases exhibited significantly higher levels (AUC 0.82 for nodal involvement), and elevated preoperative eHsp70 levels were associated with an increased risk of early tumor recurrence. In addition, eHsp70 levels were linked to immunological alterations, including increased regulatory T cells and altered natural killer (NK) cell profiles.

Discussion: The observed stage-dependent increase in eHsp70 levels supports its role as a surrogate marker of tumor burden and biological aggressiveness. The association with lymph node metastases and early recurrence highlights its potential clinical relevance, particularly in the preoperative setting. Compared to established biomarkers, eHsp70 may provide additional information on tumor biology and could improve current staging strategies.

Conclusion: Circulating eHsp70 represents a promising non-invasive biomarker reflecting tumor burden and biological aggressiveness in thoracic malignancies. Although its diagnostic sensitivity is limited in early-stage disease, eHsp70 demonstrates strong clinical

potential in advanced stages, particularly for the prediction of lymph node involvement and early recurrence. Importantly, eHsp70 may support preoperative risk stratification, improve staging accuracy, and contribute to surgical decision-making. Its integration into multimodal biomarker strategies may further enhance personalized thoracic oncology.

Industriesymposium (AstraZeneca): Perioperative Therapien beim Lungen- und gastroösophagealen Karzinom — Status Quo

Innovation in Surgical Training Based on Anatomically Accurate Phantoms

Heike Walles, Kilian Kirsten, Moritz Lange, Khaled Alnazer, Pia Landschulze, Paula Sachs

Background:

Surgical training faces the challenge of meeting the increasing demands of modern surgical procedures. In particular, minimally invasive and robot-assisted techniques such as Video-Assisted Thoracic Surgery (VATS) and Robot-Assisted Thoracic Surgery (RATS) require the confident use of complex technology and specialized manual skills. The acquisition of these skills should increasingly take place outside the operating room. However, currently available training models often have shortcomings: They are not anatomically realistic enough, only partially replicate relevant anatomical structures, and are often made of materials that do not allow for the realistic performance of surgical procedures, such as skin suturing techniques.

Methods:

CT-based, anatomically accurate phantoms developed from clinical imaging data were used for surgical education and training. In addition to full-body and organ phantoms, specialized skill-training models were developed for different levels of training. The areas of application ranged from basic skills such as skin suturing techniques to more complex procedures such as pericardial puncture and the placement of a chest drain. The models were tested in various course formats with medical students, physicians in training, and experienced practitioners. The evaluation was based on standardized surveys regarding realism, practicality, and perceived learning success.

Results:

The phantoms used enabled the realistic representation of relevant anatomical structures and the implementation of practice-oriented training scenarios. In particular, the opportunity to practice surgical techniques under anatomically correct conditions was rated positively by the participants. Preliminary results from the surveys indicate high acceptance, improved subjective confidence in performing procedures, and a high perceived benefit for surgical training. Detailed evaluation data will be presented during the lecture.

Conclusion:

CT-based, anatomically accurate phantoms represent a promising addition to existing training approaches. They enable standardized, realistic, and risk-free training of surgical skills and can help bridge the gap between theoretical education, simulation training, and clinical practice.

Biologische Technologien der Tumorforschung für die Chirurgie

Characterization of Cholangiocarcinoma Organoids and Investigation of Magnetic Hyperthermia as an Oncological Therapeutic Approach for the Treatment of Cholangiocellular Carcinomas

M.Sc.Nikol Kodra*

-Department of General,Visceral,Pediatric and Transplant Surgery,RWTH UniversityHospital Aachen,Germany,

Dr.med.Julian Palzer*

-Department of General,Visceral,Pediatric and Transplant Surgery,RWTHUniversity Hospital Aachen,Germany,

M.Sc.Robert Pohlberger

-Department of General,Visceral,Pediatric and Transplant Surgery,RWTHUniversity Hospital Aachen,Germany,

M.Sc.Max Schoenen

-Institute of Medical Engineering,Helmut-Schmidt-University Hamburg,Germany,

Dr.-Ing.-Lennart Göpfert

-Institute of Medical Engineering,Helmut-Schmidt-University Hamburg,Germany,

Dr.-Ing.Benedict Bauer

-Department of Medical Textiles,Institute of Textile Engineering,RWTH AachenUniversity,Germany

Dr.-Ing.Caroline Emonts

-Department of Medical Textiles,Institute of Textile Engineering,RWTH AachenUniversity,Germany

Prof. Dr.-Ing. Thomas Gries

- Department of Medical Textiles, Institute of Textile Engineering, RWTHAachen University,Germany

Prof.Dr.med.Florian Vondran

-Department of General,Visceral,Pediatric and Transplant Surgery,RWTHUniversity Hospital Aachen,Germany

Univ.-Prof.Dr.rer.nat.Ioana Slabu

-Institute of Medical Engineering,Helmut-Schmidt-University Hamburg,Germany

Priv.-Doz.Dr.med.Dipl.Phys.Anjali A.Roeth

-Department of General,Visceral,Pediatric and TransplantSurgery,RWTH University Hospital Aachen,Germany

*Equal contribution

Introduction

Cholangiocarcinoma(CCA)is an aggressive malignancy localized in the bile ducts.Many patients are diagnosed at anadvanced stage,and the number of effective treatment options

remains limited. Consequently, research into novel therapeutic strategies is of great interest to improve patient outcomes. Due to organoids' high similarity to the primary tumor, CCA organoid cultures derived from human tumors were used to investigate nanoparticle-augmented stent-based magnetic hyperthermia as a therapeutic strategy for tumor reduction.

Research question

This study aimed to characterize the CCA organoid lines established from patients at our department and to investigate whether magnetic hyperthermia could provide promising potential for tumor treatment.

Methods

Patient-derived CCA organoids were established from patients undergoing surgical resection at RWTH Aachen University Hospital after informed consent. The resected specimen was minced to the mm² range and was digested enzymatically. After digestion, the cell pellet was embedded in ice-cold Geltrex⁷ and seeded using the 'hanging-drop' technique. CCA organoids were characterized using Immunohistochemistry (IHC) and testing CCA-specific markers: CK7, CK19, SOX9, and S100P. The effects of nanoparticle-augmented stent-based magnetic hyperthermia were investigated at different thermal conditions: mild hyperthermia at 43±1.5°C and intermediate hyperthermia 45±1.5°C. The cytotoxic effects were analyzed using the ATP-based CellTiter-Glo[®] Luminescent Cell Viability Assay.

Statistics

The average cell viability of the samples (n=3) and the standard deviation were calculated. The coefficient of variation was calculated based on these last two. Statistical significance was evaluated by Student's two-tailed t-test: p<0.05(), p<0.01(*), and p<0.001(**).

Results

Patient-derived CCA organoids could be successfully established and used as an in vitro model to evaluate the cytotoxic effect of magnetic hyperthermia treatment employing a nanoparticle-augmented stent. Upon establishment of stable patient-derived CCA organoid cultures, IHC-based characterization confirmed the biliary phenotype of our CCA organoids, exhibiting features of cholangiocarcinoma. In IHC staining of our CCA organoids, CK7, CK19, SOX9 and S100P were strongly expressed. Cell viability after magnetic hyperthermia treatment at 43±1.5°C was decreased to approximately 80%, while at 45±1.5°C it was reduced to approximately 50%. Investigations of different organoid lines further demonstrated heterogeneity in treatment response between different organoid lines.

Discussion

The difference in treatment efficacy between different CCA organoid lines under the same treatment conditions indicate altering vulnerability of different CCA organoid lines, hereby suggesting heterogeneous and patient-specific treatment response rates. The reduction at higher-range temperatures is greater compared to lower-range temperatures, indicating higher effectiveness for treatment at higher temperatures. The results suggest that magnetic hyperthermia could be a potential therapy for cholangiocarcinoma and highlight organoids as a valuable platform for preclinical therapeutics screening.

Conclusions

In this study, we demonstrate stent-based magnetic hyperthermia as a reproducible and effective treatment for patient-derived CCA organoids. Cell viability analysis showed a significant reduction in cancer cells in vitro. The application of different magnetic hyperthermia treatment protocols to CCA organoids showed results that varied with temperature and varied between patients.

Personalized fly avatars for investigating gastrointestinal cancers

Reiff (Düsseldorf)

Introduction

Surgical resection remains the definitive treatment for localized solid tumors, particularly with gastrointestinal oncology. However, despite macroscopically complete resections, therapeutic resistance and disease recurrence driven by distinct sub-clonal somatic mutations present a persistent clinical challenge. Traditional mammalian models, such as patient-derived mouse xenografts (PDXs), are constrained by prohibitive costs and prolonged generation times rendering them impractical for immediate clinical decision-making.

Research Question

Can patient-specific transgenic *Drosophila melanogaster* (fruit fly) models serve as a rapid, scalable, and translationally accurate functional screening platform to identify personalized adjuvant drug combinations within a clinically actionable window?

Methods

Biopsy from patients is analysed with NGS to map the patient's specific driving oncogenic mutations (e.g., Wnt, RAS/MAPK signaling pathways). Transgenic *Drosophila* strains can be rapidly generated to mimic precise multi-genic mutation profiles with Crispr/Cas9. These customized "fly avatars" can then be subjected to high-throughput, automated screening against a panel of FDA-approved chemotherapeutic agents to identify novel combinatorial therapies.

Statistics

Quantitative data regarding larval survival rates, adult eclosion frequency, and intestinal epithelial tumor-like overgrowth areas are achievable in high replica numbers.

Results

The transgenic multi-genic fly avatars successfully recapitulated key pathological features of the clinical disease, including profound stem cell hyperproliferation, disrupted intestinal architecture, and a significant reduction in overall survival (Zipper et al., 2022). In the future, high-throughput drug screens will identify synergistically effective, patient-specific multi-drug combinations that significantly rescued the lethal phenotype and normalized midgut proliferation (Bang et al., 2016/2019). Crucially, the entire experimental workflow is achievable in about 4 months.

Discussion & Conclusions

These findings demonstrate that *Drosophila* avatars effectively bridge the gap between static genomic sequencing data and dynamic functional drug response. For surgical oncologists, the primary barrier to incorporating personalized in vivo testing has always been time. Furthermore, the economic scalability of the *Drosophila* model permits the testing of multi-drug cocktails that would be cost-prohibitive in mammalian systems, thereby identifying novel therapeutic vulnerabilities tailored to the individual patient's tumor architecture. *Drosophila* avatars provide a rapid, cost-effective, and highly scalable functional precision medicine platform. By delivering patient-specific therapeutic insights within a highly

actionable timeframe, this model represents a viable strategy to complement surgical interventions and optimize personalized adjuvant oncology care.

Ösophaguskarzinom - Neue Evidenz, neue Strategien, neue Perspektiven

Characterization of the sodium-hydrogen-exchanger subtype 3 (SLC9A3) in esophageal adenocarcinoma cells

Dr.rer.med.Chuang Yang,

Department of Visceral, Transplant, Thoracic and Vascular Surgery, Leipzig University, Faculty of Medicine, Leipzig, Germany

PD Dr.med. Patrick S. Plum,

Department of General, Visceral and Transplant Surgery, University Hospital Tübingen, Tübingen, Germany

Dr.med. Stefan Niebisch,

Department of Visceral, Transplant, Thoracic and Vascular Surgery, Leipzig University, Faculty of Medicine, Leipzig, Germany

Prof. Dr. med. Ines Gockel,

Clarunis Universitäres Bauchzentrum Basel, Department of Visceral Surgery, Bouchentrum Basel, Switzerland

PD Dr.rer.nat.habil. René Thieme,

Department of Visceral, Transplant, Thoracic and Vascular Surgery, Leipzig University, Faculty of Medicine, Leipzig, Germany

Introduction: The incidence of esophageal adenocarcinoma (EAC) is steadily increasing, while prognosis remains poor due to diagnosis predominantly at advanced stages. Recently, SLC9A3 (solute carrier family 9 member 3) was identified in a genome-wide association study as a risk gene for Barrett's esophagus and EAC. SLC9A3 is involved in maintaining the sodium ion gradient and regulating intracellular pH homeostasis.

Research Question: This study aimed to characterize the functional relevance of SLC9A3 in EAC and to assess its contribution to tumor development and progression.

Methods: In an in vitro model of Barrett's esophagus and EAC, SLC9A3 expression levels were analyzed by qRT-PCR. siRNA-mediated knockdown of SLC9A3 was performed, and proliferation as well as cell death were assessed using live-cell imaging. In addition, migration assays were conducted. RNA sequencing of siSLC9A3 cells was performed, and glycolytic as well as mitochondrial function were evaluated using glycolysis and mitochondrial stress tests.

Statistics: Analyses were performed using GraphPad Prism 10. Results are presented as mean $\pm$ standard error (S.E.M.) and a p-value of less than 0.05 was considered statistically significant.

Results: SLC9A3 was highly expressed in the investigated EAC cell lines (FLO-1 and OE19). Live-cell imaging demonstrated decreased proliferation and increased cell death following SLC9A3 knockdown. Furthermore, siSLC9A3 cells showed reduced migratory capacity and increased E-cadherin expression. RNA sequencing revealed upregulation of immune-related pathways, including increased PD-L1 expression in siSLC9A3 cells. Mitochondrial stress tests

demonstrated reduced basal respiration and ATP production, while glycolysis stress testing showed decreased glycolytic activity after SLC9A3 suppression.

Discussion: These findings demonstrate marked overexpression of SLC9A3 in EAC cell lines, suggesting a potential role in tumor progression. Functional assays indicate that SLC9A3 contributes to cell survival and migration, while its knockdown may suppress metastatic potential. Increased PD-L1 expression further suggests a role in immune evasion. Moreover, suppression of SLC9A3 impaired mitochondrial function and cellular metabolism.

Conclusion: Collectively, these results suggest that SLC9A3 plays a multifaceted role in EAC cell proliferation, migration, immune modulation, and mitochondrial activity, highlighting its potential as a therapeutic target in EAC.

INHBA Regulates EMT and Ferroptosis-Associated Cell Death in Esophageal Adenocarcinoma

Anne Zeug

-Department of Visceral, Transplant, Thoracic and Vascular Surgery, Leipzig University, Faculty of Medicine, Leipzig, Germany

Dr. rer. med. Chuang Yang

-Department of Visceral, Transplant, Thoracic and Vascular Surgery, Leipzig University, Faculty of Medicine, Leipzig, Germany

M.Sc. Anna-Katharina Matheis

-Department of Visceral, Transplant, Thoracic and Vascular Surgery, Leipzig University, Faculty of Medicine, Leipzig, Germany

Univ. Prof. Dr., FEBS, FACS (Hon.) - Christiane J. Bruns

-Department of General, Visceral, Thoracic and Transplant Surgery, University Hospital of Cologne, Faculty of Medicine, University of Cologne, Cologne, Germany

Priv.-Doz. Dr. rer. nat. Yue Zhao

-Department of General, Visceral, Thoracic and Transplant Surgery, University Hospital of Cologne, Faculty of Medicine, University of Cologne, Cologne, Germany

PD Dr. med. Patrick S. Plum

-Department of General, Visceral and Transplant Surgery, University Hospital Tübingen, Tübingen, Germany

Dr. med. - Stefan Niebisch

-Department of Visceral, Transplant, Thoracic and Vascular Surgery, Leipzig University, Faculty of Medicine, Leipzig, Germany

PD Dr. rer. nat. habil. René Thieme

-Department of Visceral, Transplant, Thoracic and Vascular Surgery, Leipzig University, Faculty of Medicine, Leipzig, Germany

Introduction:

The incidence of esophageal adenocarcinoma (EAC) rises continuously in Western countries, while patient prognosis remains poor, largely due to therapy resistance and metastatic disease. The tumor microenvironment is increasingly recognized as a critical determinant of tumor progression and treatment response, with cancer-associated fibroblasts (CAFs) playing a central role. Inhibin subunit beta A INHBA has recently emerged as a potential therapeutic target in EAC and has been implicated in tumor proliferation, survival, epithelial-mesenchymal transition (EMT), and the induction of a tumor-promoting CAF phenotype.

Research question:

This study aimed to investigate the role of INHBA and CAFs in tumor progression, metastasis, and chemoresistance in esophageal adenocarcinoma.

Methods:

The functional role of INHBA was analyzed in silico using TCGA datasets and investigated in vitro using siRNA-mediated knockdown in EAC cell models, primarily OE33 cells. Cellular proliferation and viability were assessed by live-cell imaging. Clonogenic capacity and molecular alterations were evaluated by colony formation assays, Western blotting, and RT-qPCR. Cell death was analyzed using Annexin V flow cytometry. In addition, indirect co-culture systems with patient-derived CAFs were established, and transwell migration assays were performed to assess migratory behavior.

Statistics:

Statistical analyses were conducted using GraphPad Prism. Depending on the experimental setting, paired or unpaired t-tests were applied to normalized datasets.

Results:

High INHBA expression in EAC specimens was associated with reduced overall survival in TCGA data as well as in the GEO dataset GSE19417. Knockdown of INHBA significantly impaired proliferation, clonogenic growth, and migratory capacity of EAC cells. These effects were accompanied by increased regulated cell death displaying molecular characteristics consistent with ferroptosis, including reduced GPX4 expression. Furthermore, INHBA suppression resulted in upregulation of the cell cycle inhibitor p21 and downregulation of the EMT-associated marker vimentin. In contrast, indirect co-culture with CAFs induced a mesenchymal-like transcriptional program in EAC cells and enhanced migratory activity.

Discussion:

These findings identify INHBA as a potential mediator of aggressive tumor behavior in EAC. Suppression of INHBA reduces tumor cell fitness and promotes ferroptosis-like cell death, whereas CAF-derived signaling independently enhances EMT-associated phenotypes and migration, indicating complementary pro-tumorigenic mechanisms within the tumor microenvironment.

Conclusion:

INHBA contributes to multiple oncogenic processes in EAC, including proliferation, survival, and EMT-associated cellular plasticity. In parallel, CAF-derived signals promote EMT-related transcriptional reprogramming, potentially facilitating metastatic dissemination and therapy resistance. Combined therapeutic targeting of INHBA and CAF-mediated signaling pathways may therefore represent a promising treatment strategy in EAC.

Evaluation of Circulating microRNA Abundance and Reference Gene Normalization in Patients with Esophagogastric Junction Cancer

Hongyu Li¹, Anna-Katharina Matheis¹, Patrick S. Plum^{1,2}, Stefan Niebisch¹, Ines Gockel³, René Thieme¹

¹ Department of Visceral, Transplant, Thoracic and Vascular Surgery, University Hospital Leipzig, Leipzig, Germany

² Department of General, Visceral and Transplant Surgery, University Hospital Tübingen, Tübingen, Germany

³ Clarunis-University Digestive Health Care Center, Department of Visceral Surgery, University Hospital of Basel, Basel, Switzerland

Introduction:

Esophageal adenocarcinoma (EAC) and gastric cancer (GC) represent major upper gastrointestinal malignancies and are associated with unfavorable prognoses. Chemotherapy resistance remains a major obstacle to successful treatment, highlighting the need for reliable predictive biomarkers. MicroRNAs (miRNAs) have emerged as important regulators of chemoresistance and may serve as minimally invasive biomarkers for treatment response. However, accurate analysis of circulating miRNAs is challenged by the lack of standardized normalization strategies for quantitative PCR (qPCR) data.

Research question:

This study aimed to investigate whether selected circulating miRNAs may serve as predictive biomarkers for therapeutic response and to establish a normalization strategy for qPCR-based circulating miRNA analyses using multiple endogenous reference genes.

Methods:

Based on prior reports, four circulating miRNAs (miR-19b-3p, miR-106a-5p, miR-21-3p, and miR-16-5p) were chosen for analysis. Their expression levels were quantified by quantitative real-time PCR (qPCR) in blood samples obtained from 40 patients with EAC and 28 patients with GC. For normalization of qPCR data, endogenous reference miRNAs (miR-16-5p, miR-484, miR-222-3p, and miR-107) described in previous studies were applied.

Statistics:

Statistical analyses and data visualization were performed using GraphPad Prism. Expression stability of candidate reference genes was assessed using geNorm and RefFinder. Depending on data distribution and experimental setting, Mann-Whitney U tests, Wilcoxon matched-pairs signed-rank tests, or paired Student's t-tests were applied. A p-value < 0.05 was considered statistically significant.

Results:

geNorm and RefFinder analyses identified miR-484, miR-222-3p, and miR-107 as the most stable reference miRNAs, while the less stable miR-16-5p was subsequently analyzed as a gene of interest. Patients undergoing perioperative chemotherapy exhibited significant alterations in the expression of miR-106a-5p, miR-21-3p, and miR-16-5p. In contrast, no

significant differences in circulating miRNA expression were identified between responders and non-responders to chemotherapy.

Discussion:

The observed upregulation of miR-21-3p and miR-106a-5p in non-responders supports their potential involvement in chemotherapy resistance mechanisms in esophagogastric malignancies. In contrast, reduced circulating miR-16-5p levels after treatment may reflect therapy-associated tumor dynamics. Furthermore, this study highlights the importance of using multiple endogenous reference miRNAs for accurate normalization, as reliance on a single reference gene may introduce substantial analytical bias.

Conclusion:

The present study establishes a strategy for qPCR normalization using multiple endogenous reference miRNAs in circulating blood samples from EAC and GC patients treated with chemotherapy. These findings may support future investigations exploring circulating miRNAs as biomarkers in upper gastrointestinal cancers.

Antibody-Mediated GDF 15 Neutralization Attenuates CAF-Associated Cisplatin Resistance in Esophageal Adenocarcinoma Cells

Pinwei-Deng

-Department of General, Visceral, Thoracic and Transplantation Surgery, University Hospital Cologne, 50937 Cologne, Germany

Dr.-Ningbo-Fan

-Department of General, Visceral, Thoracic and Transplantation Surgery, University Hospital Cologne, 50937 Cologne, Germany; Department of Thoracic Oncology, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Guangzhou 510060, China

Zicheng – Lyu

- Department of General, Visceral, Thoracic and Transplantation Surgery, University Hospital Cologne, 50937 Cologne, Germany

Lisa-Raatz

-Department of General, Visceral, Thoracic and Transplantation Surgery, University Hospital Cologne, 50937 Cologne, Germany

Prof. Dr. rer. nat. -Jörg-Wischhusen

-Department of Obstetrics and Gynaecology, Section for Experimental Tumor Immunology, University Hospital Würzburg, Würzburg, Germany

Univ.-Prof. Dr. med. -Christiane J.-Bruns

-Department of General, Visceral, Thoracic and Transplantation Surgery, University Hospital Cologne, 50937 Cologne, Germany; Center for Molecular Medicine Cologne, University of Cologne, 50931 Cologne, Germany

Priv.-Doz. Dr. - Yue – Zhao

- Department of General, Visceral, Thoracic and Transplantation Surgery, University of California, 50090 Californiabased University Hospital Cologne, 50937 Cologne, Germany

Introduction: Cancer-associated fibroblasts (CAFs) promote chemotherapy resistance in esophageal adenocarcinoma (EAC) cells through paracrine signaling. GDF15 is a potentially targetable component of the CAF secretome.

Research question: We investigated whether antibody-mediated GDF15 neutralization attenuates CAF-associated cisplatin resistance in EAC cells.

Methods: OE33 cells were exposed to TBE63 CAF-conditioned medium or transwell co-culture and treated with cisplatin together with a GDF15-neutralizing antibody or IgG1 isotype control. Cell viability, apoptosis, and mitochondrial membrane potential were assessed. Genetic GDF15 depletion, recombinant GDF15 rescue, mitochondrial respiration analysis, and oxidative phosphorylation inhibition were used for complementary mechanistic validation.

Statistics: Student's t-test or one-way ANOVA with multiple-comparison testing was applied as appropriate. A two-sided p value < 0.05 was considered statistically significant.

Results: CAF-conditioned medium and CAF co-culture increased OE33 cell viability during cisplatin treatment. GDF15 neutralization partially attenuated this protective effect, whereas the IgG1 control showed no comparable activity. GDF15 blockade also increased cisplatin-associated apoptosis and reduced TMRE fluorescence in surviving tumor cells. Consistently, genetic GDF15 depletion impaired mitochondrial respiration and treatment tolerance, whereas recombinant GDF15 partially restored the resistant phenotype. Low-

dose oxidative phosphorylation inhibition further sensitized EAC cells to cisplatin under CAF-supported conditions.

Discussion: GDF15 neutralization interferes with a functionally relevant component of CAF-mediated survival signaling and mitochondrial adaptation during chemotherapy stress.

Conclusion: GDF15 blockade partially reduces CAF-associated cisplatin resistance in EAC cells, providing a rationale for further preclinical evaluation in additional tumor-stroma models.

Intelligente Technologien und Chirurgierobotik

Wireless Microrobots: From Early Cancer Detection to Precision Therapy

Dr.Jiyuan Tian,

Division of Smart Technologies for Tumor Therapy,DKFZ Dresden.

Dr.Yue Gao,

Division of Smart Technologies for Tumor Therapy,DKFZ Dresden.

Dr. Meng Zhang,

Division of Smart Technologies for Tumor Therapy, DKFZ Dresden.

Jyothi Kumari Mariyanna,

Division of Smart Technologies for Tumor Therapy,DKFZ Dresden and TUDresden.

Dr.Moon Kwang Jeong,

Division of Smart Technologies for Tumor Therapy,DKFZ Dresden.

Ann-Sophia Müller,

Division of Smart Technologies for Tumor Therapy,DKFZ Dresden and TU Dresden.

Nicolas Schmitt,

Division of Smart Technologies for Tumor Therapy,DKFZ Dresden and TU Dresden.

Dr.Haoying Wang,

Division of Smart Technologies for Tumor Therapy,DKFZ Dresden.

Dr.Liyuan Tan,

Division of Smart Technologies for Tumor Therapy,DKFZ Dresden.

Prof.Dr.med.Martin Wagner,

Clinic and Polyclinic for Visceral,Thoracic and Vascular Surgery,University Hospital Carl Gustav Carus Dresden.

Prof.Dr.med.Tareq Juratli,

Department of Neurosurgery,University Hospital Carl Gustav Carus Dresden.

Prof.Dr.Tian Qiu,

Division of Smart Technologies for Tumor Therapy,DKFZ Dresden and TU Dresden.

Introduction

Microrobotic technologies enable wireless,minimally invasive,and precise operations at anatomically inaccessible sites,offering new opportunities across the cancer care continuum.A major challenge is achieving accurate navigation,deep-tissue locomotion,and clinically compatible operation.Previously,we demonstrated the first tissue-penetrating magnetic nanorobots capable of propelling through the vitreous humor to precisely target the optic disc of the retina [1].Building on this work,we develop microrobots for active propulsion and wireless sensing in deep biological tissues.

Methods

We develop wireless magnetic actuation and localization systems for precise microrobot navigation. Magnetic torque and gradient forces propel robots through confined lumens, such as the biliary duct, and soft tissues, such as the brain parenchyma. Microrobots are fabricated by two-photon lithography using biocompatible materials with micrometer-scale resolution. Permanent-magnet-based field generators provide a clinically relevant workspace and sufficient actuation strength, while multimodal imaging—including ultrasound, X-ray fluoroscopy, and our new magneto-oscillatory localization technique [2]—enables accurate closed-loop control.

Results and Discussion

We present multiple microrobotic platforms for cancer applications. A magnetically actuated upper gastrointestinal sampling robot performs minimally invasive tissue biopsy for early cancer detection by actively collecting epithelial cells from the mucosal surface [3]. A tissue-penetrating helical microrobot enables targeted biopsy, molecular diagnosis, and localized drug delivery in deep-seated brain tumors [4]. For minimally invasive surgery, a cooperative team of miniature robots transports an endoscopic instrument over ten times heavier than an individual robot through the biliary duct to perform electrocautery procedures [5].

Conclusion

Microrobots are emerging as versatile tools across the cancer care continuum, enabling early screening, precision diagnosis, personalized drug screening [6], and targeted therapy. By integrating physical access with molecular sensing and therapeutic functions, they could establish a new paradigm for precision cancer management, linking diagnosis, treatment selection, and targeted therapy.

References

- [1] Z. Wu, et al. *Science Advances*, 4, eaat4388 (2018). [2] F. Fischer, et al. *npj Robotics*, 2, 1 (2024). [3] J. Tian, et al. *IEEE/RSJ Int. Conf. on Intelligent Robots and Systems (IROS)*, (2025). [4] M. Zhang, et al. 4th German Cancer Research Congress, (2025). [5] M. Jeong, et al. *Advanced Science*, 11, 2308382 (2024). [6] Y. Gao, et al. *Advanced Robotics Research*, accepted (2026).

Disposable sensors for next-generation healthcare

Prof.Dr.Can Dincer-Technische Universität München

Abstract:

Disposable sensors are low-cost and easy-to-handle sensing devices for short-term or single-shot measurements. Over the last decade, they have become increasingly important for different applications, including from environmental, forensic, pharmaceutical, agricultural, and food monitoring to diagnostics, especially the point-of-care testing and wearables. In this talk, first a short introduction to disposable sensors will be given. Afterwards, a broad spectrum of different biosensing approaches for next-generation on-site testing will be presented: (i) Multiplexed on-site therapeutic drug monitoring of antibiotics from invasive and non-invasive samples toward personalized antibiotherapy, (ii) CRISPR-powered electrochemical biosensors for nucleic-acid-amplification-free, simultaneous and on-site detection of multiple RNAs and other biomolecules for COVID-19 management, (iii) wearable microfluidic immunosensing devices for lab-on-a-bird applications and beyond, (iv) low-cost electrochemical paper-based wearable sensors that can be integrated to any type of facemask for wearable and continuous monitoring of breath biochemistry and/or testing of the infectious diseases such as coronaviruses from exhaled breath, and (v) light-controlled dynamic bioassays using optogenetic switches (OptoAssays) for wash-and pump-free point-of-care diagnostics.

Accessible 3D-Printed Perfusion Platform for Patient-Specific Tumor Modeling and Real-Time Oxygen Monitoring in Surgical Oncology

Meghna Wilfred

-Chair of Measurement Technology, Otto-von-Guericke-University Magdeburg, Germany

Ahmed Y. Sanin

-Molecular and Experimental Surgery, Otto-von-Guericke-University Magdeburg, Germany

Arslan Ghazanfar

-Molecular and Experimental Surgery, Otto-von-Guericke-University Magdeburg, Germany

Josephine Müller

-Chair of Medical Systems Technology, Otto-von-Guericke-University Magdeburg, Germany

Dr. Liudmila Deckert

-Chair of Measurement Technology, Otto-von-Guericke-University Magdeburg, Germany

Dr.-Ing. Melanie Facht

- Chair of Medical Systems Technology, Otto-von-Guericke-University Magdeburg, Germany

Prof. Dr. rer. nat. Christoph Hoeschen

-Chair of Medical Systems Technology, Otto-von-Guericke-University Magdeburg, Germany

Univ.-Prof. Dr. rer. nat. Ulf D. Kahlert

-Molecular and Experimental Surgery, Otto-von-Guericke-University Magdeburg, Germany

Prof. Dr.-Ing. Ulrike Steinmann

-Chair of Measurement Technology, Otto-von-Guericke-University Magdeburg, Germany

Patient-derived organoids (PDOs) are increasingly used in surgical oncology to support personalized therapeutic decision-making by preserving patient-specific tumor characteristics. However, conventional static culture systems suffer from limited nutrient and oxygen transport, resulting in hypoxia and central necrosis that can compromise experimental outcomes. Although microfluidic perfusion systems address these limitations, many require complex cleanroom fabrication and irreversible device assembly, preventing retrieval of intact tissues for downstream histopathological analysis. To overcome these limitations, a cleanroom-free, reusable organ-on-chip (OoC) platform with reversible mechanical closure was developed for long-term perfusion culture and harvesting of intact 3D tissues without device destruction.

The platform architecture comprises four modular components engineered for sequential assembly and non-destructive sample harvesting. The foundation of the system is an open-bottom, autoclavable chamber body featuring an integrated bubble vent, fabricated via stereolithography (SLA) using Liqcreate Bio-Med Clear resin. The open base of this chamber body is permanently sealed against a borosilicate glass coverslip using biocompatible silicone adhesive, with the coverslip serving as the primary substrate for cellular deposition. Following culture seeding onto this glass substrate, a thin, gas-permeable PDMS membrane ($\sim 22 \pm 2 \mu\text{m}$, Sylgard 184, 10:1 ratio, validated via spectrophotometry) is cast onto a structural PDMS support ring, which is positioned directly over the chamber's upper sealing interface. The complete fluidic assembly is then securely enclosed using a

polypropylene(PP)screw-top lid printed via fused deposition modeling(FDM).A digital peristaltic pump drives continuous media perfusion through the chamber at 50 $\mu\text{L}/\text{min}$ within a controlled incubator environment (37°C ,5% CO_2 ,95%RH).Real-time,non-invasive oxygen telemetry of the tumor microenvironment (TME)is achieved via luminescence-based sensor spots fixed to the culture area and read by an optical oxygen measurement system.

Device integrity and physiological stability were verified during a 15-day continuous perfusion study using HepG2 hepatocellular carcinoma spheroids formed via the hanging-drop method(20%FCS,40%DMEM,40% methylcellulose)and embedded in Basement Membrane Extract(BME).The culture chamber maintained a highly stable dissolved oxygen air saturation profile of $\sim 86\%$ at the active culture site and $\sim 96\%$ in the fluid reservoir, contrasting sharply with the hypoxic degradation observed in static control groups reaching 64%.Serial brightfield microscopy confirmed the preservation of dense, compact, and structurally translucent spheroid morphologies over the 15-day window.To establish clinical utility within translational oncology pipelines,the system was used to culture primary patient-derived pancreatic ductal adenocarcinoma(PDAC)organoids isolated from resected tumor tissue.Following 10 days of continuous on-chip perfusion,brightfield tracking and Hoechst nuclear staining demonstrated robust cellular expansion,excellent structural integrity,and a complete absence of central necrotic core formation.

The developed 3D-printed perfusion platform provides a reliable and accessible approach for long-term ex vivo tumor culture while enabling non-destructive tissue retrieval for downstream analyses.Sustained tissue oxygenation and prevention of necrotic core formation demonstrate effective maintenance of physiologically relevant culture conditions.Combined with real-time oxygen monitoring,the platform offers a promising tool for functional oncology studies,patient-specific drug testing,and personalized treatment evaluation within translational surgical research workflows.

Feasibility of Autonomous Robot-Assisted Ultrasound of the Abdominal Aorta: A Pilot Study in Healthy Volunteers

Dr.Alexandra Scheibert,

Klinik für Chirurgie,UKSH Campus Lübeck

PD Dr.Mark Preuß,

Universitäres Herz-und Gefäßzentrum Hamburg,UKE Hamburg

Dr.Jonas Osburg,

Institut für Robotik und Kognitive Systeme,Universität zu LübeckJulia Schweifer,Klinik für Chirurgie,UKSH Campus Lübeck

Prof.Dr.Floris Ernst,

Institut für Robotik und Kognitive Systeme,Universität zu LübeckPD Dr.Marco Horn,Klinik für Chirurgie,UKSH Campus Lübeck

Introduction

Although ultrasound screening for abdominal aortic aneurysms is non-invasive,radiation-freeand cost-effective,it remains dependent on trained examiners.Autonomous robot-assistedultrasound could improve standardisation and increase the availability of screeningexaminations.

Research question

This pilot study investigated the feasibility of autonomous,robot-assisted ultrasound scanningof the abdominal aorta,comparing two image-based vessel-tracking methods.

Methods

Ten healthy volunteers underwent conventional and robot-assisted ultrasound examinations ofthe abdominal aorta.Two physicians performed repeated robot-assisted manual scans toassess operator-dependent variability.Subsequently,the robot moved the ultrasound probeautonomously along the aortawhile maintaining constant contact force.Vessel tracking wasperformed using eithertemplate matching or Doppler signal tracking.The probe trajectories,vessel-tracking accuracy,examination time and participant experience were then evaluated.One participant was excluded from the quantitative analysis due to atechnicalmalfunctionduring recording.The study was approved by the Ethics Committee of the University of Lübeck,Germany.

Statistics

Due tothe exploratory pilot design,the results were analyseddescriptively.Repeated physician-performed scans and autonomous robotic scans were compared in terms of probe trajectoryand tracking performance.

Results

Autonomous robotic scanning ofthe abdominal aorta could be performed on all participantswithout any safety-related terminations.Template matching produced more accurate andconsistent vessel tracking than Doppler-based tracking,especially over longerscan distances.The mean vessel tracking error was 5.5 ± 6.7 mm with template matching and 11.9 ± 5.5 mmwith Doppler-based tracking,indicating a 46%reduction in error with template matching.Deviations between autonomous and physician-guided scans were

comparable to the variability observed between different physicians. Doppler-based tracking was limited by intermittent switching to adjacent vessels as the target.

Discussion

The findings demonstrate the technical feasibility of autonomous abdominal aortic ultrasound scanning under controlled conditions. Tracking performance depended on the anatomical region and surrounding vascular structures. Template matching appeared particularly suitable for aortic tracking due to the vessel's characteristic cross-sectional appearance.

Conclusion

Autonomous robot-assisted ultrasound of the abdominal aorta is feasible. In this pilot study, template matching was more robust than Doppler-based tracking. However, further technical development and validation in patients are required before it can be used for abdominal aortic aneurysm screening or post-EVAR surveillance.

Da-Vinci-assistierte pyloruserhaltende Pankreatikoduodenektomie bei chronisch-rezidivierender Pankreatitis: Operationstechnik und perioperatives Outcome

Dr. Maximilian Dölling
 Dr. Victor-Radu Negrini
 Dr. Seong Jeong
 Dr. Mirhasan Rahimli
 Dr. Roland Siegfried Croner
 Dr. Sara Al-Madhi

Hintergrund

Die chronische Pankreatitis ist eine progrediente entzündliche Erkrankung des Pankreas, die zu rezidivierenden Schüben einer akuten Pankreatitis, chronischen Oberbauchschmerzen, biliärer oder pankreatischer Abflussstörung sowie einer erheblichen Einschränkung der Lebensqualität führen kann. Eine operative Therapie ist bei ausgewählten Patienten mit persistierenden Beschwerden trotz konservativer Behandlung, entzündlich bedingten Komplikationen oder bei nicht sicher auszuschließender Malignität indiziert. Die Resektion des Pankreaskopfes bei chronischer Pankreatitis stellt aufgrund ausgeprägter Fibrose, veränderter anatomischer Strukturen und der engen Beziehung zu zentralen Gefäßstrukturen eine besondere chirurgische Herausforderung dar. Robotisch assistierte Verfahren bieten durch die hochauflösende dreidimensionale Visualisierung, die präzise Instrumentenführung und die verbesserte Beweglichkeit der Instrumente potenzielle Vorteile bei komplexen Resektionen und Rekonstruktionen. Ziel dieses Videoabstracts ist die Darstellung der wesentlichen Operationsschritte einer Da-Vinci-assistierten pyloruserhaltenden Pankreatikoduodenektomie bei chronisch-rezidivierender Pankreatitis.

Methoden

Fallbericht mit schrittweiser Darstellung des operativen Vorgehens anhand eines Operationsvideos.

Ergebnisse

Wir präsentieren den Fall einer 33-jährigen kachektischen Patientin mit progredienten chronischen Oberbauchschmerzen, unklarem Gewichtsverlust sowie rezidivierenden Schüben einer akuten Pankreatitis bei a. e. Nikotinabusus. In der präoperativen CT Abdomen zeigte sich eine entzündliche Raumforderung im Bereich des Pankreaskopfes mit Abbruch des Ductus pancreaticus sowie Erweiterung des Ductus choledochus auf über 10 mm. Aufgrund der symptomatischen chronisch-rezidivierenden Pankreatitis und des präoperativ nicht sicher auszuschließenden malignen Prozesses wurde im interdisziplinären Tumorboard die Indikation zur operativen Resektion gestellt. Die präoperative dreiphasige Computertomographie zeigte eine aberrante Arteria hepatica dextra mit Ursprung aus der Arteria mesenterica superior. Bei fehlendem Nachweis einer Gefäßinfiltration erfolgte die Planung einer Da-Vinci-assistierten pyloruserhaltenden Pankreatikoduodenektomie. Das Video demonstriert die wesentlichen Operationsschritte einschließlich der Präparation der zentralen Gefäßstrukturen, der Identifikation und Schonung der aberranten Arteria hepatica dextra, der Resektionsphase sowie der Rekonstruktion mittels Pankreatikojejunostomie, Hepatikojejunostomie und Duodenojejunostomie.

Diskussion

Die chirurgische Behandlung der chronischen Pankreatitis ist aufgrund ausgeprägter entzündlicher Veränderungen und fibrotischer Veränderungen technisch

anspruchsvoll. Insbesondere die Präparation im Bereich der mesenteriko-portalen Achse sowie die sichere Rekonstruktion der gastrointestinalen Kontinuität erfordern ein hohes Maß an chirurgischer Expertise. Das robotisch assistierte Vorgehen kann durch eine verbesserte Visualisierung und Instrumentenmanövrierbarkeit die Präzision der Resektion und Rekonstruktion unterstützen. Eine sorgfältige Patientenselektion bleibt jedoch entscheidend und sollte insbesondere das Fehlen einer relevanten Gefäßinfiltration sowie günstige anatomische Voraussetzungen berücksichtigen.

Schlussfolgerung

Der vorliegende Fall demonstriert die technische Durchführbarkeit einer Da-Vinci-assistierten pyloruserhaltenden Pankreatikoduodenektomie bei einer jungen Patientin mit chronisch-rezidivierender Pankreatitis und entzündlicher Raumforderung des Pankreaskopfes. Das robotisch assistierte Vorgehen ermöglichte eine präzise Präparation und Rekonstruktion trotz komplexer entzündlicher Anatomie und vaskulärer Variante. Es stellt somit eine sichere und effektive minimalinvasive Therapieoption für sorgfältig ausgewählte Patienten dar.

Preisträgersitzung der Sektion Chirurgische Forschung zum Hans-Jürgen-Bretschneider-Preis (1.500 EUR)

Activated CD4+ conventional T cells lead to a disruption of the gut barrier

Jessica Kümmel, Constanze Binder, Dr. rer. nat. Natalie Burkard, Univ.-Prof. Dr. med. Nicolas Schlegel, Dr. med. Johanna C. Wagner

The pathogenesis of inflammatory bowel diseases (IBD), manifesting predominantly as ulcerative colitis and Crohn's disease, is incompletely understood. It is known that genetic predisposition, environmental factors, imbalanced immune reactions, and loss of intestinal epithelial barrier function contribute to the onset of IBD. Mechanisms of the direct interaction between epithelial cells and the immune system remain to be resolved. Here we established a reductive in vitro model as a basis to assess these mechanisms.

The HT29/B6 intestinal epithelial cell line was used. Cells were seeded onto ThinCert® cell culture inserts and grown to confluence in RPMI 1640 medium for 7 days. The inserts were transferred to an ECIS 8-well Transfilter Array (8wTFA) to assess changes in intestinal epithelial barrier properties in transepithelial electrical resistance (TEER) measurements using an ECIS® Z-Theta device. Differentiated monolayers were then exposed to pro-inflammatory cytokines (IL-1 β , TNF- α , IFN- γ) or co-cultured with activated CD4+ conventional T cells. Continuous TEER measurements were then applied to assess the dynamics of intestinal epithelial barrier changes.

Under control conditions over 48 hours, TEER remained stable compared to baseline. Application of pro-inflammatory cytokines resulted in a loss of TEER to $71 \pm 3\%$ of baseline, which was sustained until the end of measurements. Conventional CD4+ T cells were activated using Dynabeads® human T-Activator CD3/CD28 and then co-cultured with the HT29/B6 monolayers. Preliminary results show a loss of TEER to $71 \pm 6\%$ of baseline with T cells on the apical side and loss of TEER to $73 \pm 5\%$ of baseline with T cells co-cultured on the basolateral side.

In summary, we established an in vitro model that successfully reproduces the effects of pro-inflammatory cytokines and co-cultured immune cells. This model provides a valuable tool for investigating in detail the mechanisms of the interaction between activated CD4+ T cells and intestinal epithelial cells.

Development of a model-specific, consensus-based score sheet for postoperative assessment following orthotopic single-lung transplantation in the mouse

Dr.med.-Birte-Ohm

-Institute for Laboratory Animal Science and Experimental Surgery, Faculty of Medicine, RWTH Aachen University, Aachen, Germany; Department of Thoracic Surgery, Faculty of Medicine, RWTH Aachen University, Aachen, Germany

Prof.Dr.med.-René H.-Tolba

-Institute for Laboratory Animal Science and Experimental Surgery, Faculty of Medicine, RWTH Aachen University, Aachen, Germany

on behalf of the study group

Introduction

Orthotopic single-lung transplantation in the mouse is a complex microsurgical model that is performed by only a limited number of specialized groups worldwide. It carries a relevant postoperative burden, yet monitoring and supportive measures have so far been described inconsistently, and standardized score sheets have not been established. Consistent monitoring and an objective application of humane endpoints are central elements of refinement within the 3R principle.

Research Question

The project aims to establish a model-specific, consensus-based score sheet for standardized postoperative assessment following orthotopic single-lung transplantation in the mouse, developed through a structured expert consensus process.

Methods

Based on a literature review and the study group's practical experience with the model, a model-specific score sheet comprising seven domains (respiratory rate, breathing pattern, circulation, body weight, Mouse Grimace Scale, fur condition, provoked activity; 0-3 points each) and an associated intervention algorithm were developed. The score sheet is being evaluated in a modified Delphi process, with international experts in microsurgery and laboratory animal science from Germany, Belgium, the USA, Canada, and Japan.

Statistics

In round 1, ratings were obtained on a nine-point Likert scale. Consensus was predefined as a median of 7-9, an interquartile range ≤ 2 , and at least 70 % of ratings within the range of 7-9. A subsequent round is ongoing.

Results

Round 1 achieved consensus on the general suitability of the score sheet for standardized assessment and decision-making, on the four-level severity grading, the central role of respiratory parameters, and the definition of humane endpoints as a combination of score and critical individual criteria. No consensus was initially reached on domain weighting, operationalization of peripheral perfusion, and relevance of fur condition.

Discussion

The first round confirmed broad agreement on the overall structure of the proposed score sheet and identified the aspects requiring further revision, which are being addressed in

the ongoing rounds. The areas without initial consensus indicate where parameter definitions need to be operationalized more precisely to ensure their reliable application.

Conclusion

A modified Delphi process is a suitable approach to develop a model-specific score sheet for postoperative assessment following murine lung transplantation. To our knowledge, this is the first score sheet for a laboratory animal transplantation model developed through a formal expert consensus process. Once completed, the consensus-based score sheet is intended to enable early detection of characteristic complications, support the objective application of humane endpoints, and promote more consistent postoperative care.

Targeting Metabolic Dependencies to Reverse Chemoradiotherapy Resistance in Locally Advanced Rectal Cancer

Maximilian Hellkamp

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Simon Gertken

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Jonas Buchloh

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Julius-Leonard Hellwig

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Lukas Ben Kowitzke

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

PD Dr. Michael Linnebacher

Molecular Oncology and Immunotherapy, Clinic of General Surgery, University Medical Center
Rostock, Rostock, Germany

PD Dr. Matthias Wirth

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Department of Hematology, Oncology and Cancer Immunology, Campus Benjamin
Franklin, Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin
and Humboldt-Universität zu Berlin, Berlin, Germany

Univ.-Prof. Dr. Stefan Rieken

Department of Radiotherapy and Radiooncology, University Medical Center
Göttingen, Göttingen, Germany

Prof. Dr. Jochen Gaedcke

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Clinic for General and Visceral Surgery, Städtisches Klinikum Karlsruhe, Karlsruhe, Germany

Prof. Dr. Michael Ghadimi

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Prof. Dr. Jürgen Wienands

Institute of Cellular and Molecular Immunology, University Medical Center Göttingen,
Göttingen, Germany

Prof. Dr. Günter Schneider

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Institute for Translational Cancer Research and Experimental Cancer Therapy, Technical
University Munich, Munich, Germany

Dr. Melanie Spitzner

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Prof. Dr. Marian Grade

Department of General, Visceral and Pediatric Surgery, University Medical Center
Göttingen, Göttingen, Germany

Introduction

Neoadjuvant chemoradiotherapy (CRT) followed by total mesorectal excision is the standard of care for locally advanced rectal cancer (LARC). Pathological complete response rates of 20% to 30% remain low because many tumors exhibit intrinsic resistance to radiation and chemotherapy, exposing patients to unnecessary toxicity and a high risk of recurrence. Resistance to CRT is a multifactorial phenomenon driven by the interplay of tumor-intrinsic aberrations, the tumor microenvironment (TME), and metabolic adaptation.

Research question

We asked what actionable determinants drive CRT resistance in LARC and whether pharmacologic inhibition of identified targets can restore radiosensitivity of treatment-resistant cells.

Methods

We established a panel of fourteen patient-derived colorectal cancer cell lines (PDCLs) obtained directly from primary tumors, patient-derived xenografts, or patient-derived organoids. For mutational characterization, panel sequencing was performed and all lines were phenotypically profiled using live-cell imaging. Therapy response was determined by colony-formation assays and ATP-based viability after a 4 Gy irradiation dose with or without standard CRT (5-FU + oxaliplatin). RNA-sequencing was applied to elucidate molecular determinants of CRT resistance and a focused drug screen of 126 compounds identified agents with selective activity in (chemo)irradiation (IR)-resistant PDCLs. Seahorse XF ATP-Rate analyzes quantified glycolytic and mitochondrial activity.

Statistics

Differential expression was analyzed with DESeq2 (adjusted $p < 0.05$, $\log_2 FC \geq 1$). Gene-set enrichment (GSEA) used an $FDR < 0.025$. Metabolic read-outs were compared by two-tailed Student's *t*-tests ($p < 0.05$). Drug-response was expressed as area-under-the-curve (AUC); a $\Delta AUC > \pm 0.05$ defined selective hits. Correlations between gene expression and tumor-regression grade (TRG) were assessed with the Mann-Whitney *U* test.

Results

From 14 PDCLs, six cell lines were classified as IR-resistant. Transcriptomic profiling revealed enrichment of oxidative-phosphorylation and glycolysis pathways in IR-resistant PDCLs. The drug screen uncovered only two compounds with selective efficacy in the IR-resistant cohort: the MCT1 inhibitor AZD3965 and the GLUT1 inhibitor BAY-876. Both agents

produced positive irradiation-sensitization scores (ISS) in IR-resistant models, confirming a re-sensitization to therapy. Functionally, IR-resistant PDCLs displayed significantly higher basal oxygen consumption (OCR) and extracellular acidification rates (ECAR), leading to increased mitochondrial and glycolytic ATP production. Clinically, GLUT1 mRNA levels were significantly higher in non-responder patients (TRG 1) versus complete responder patients (TRG 4) in our retrospective Gottingen rectal cancer cohort, which association was confirmed across two independent rectal-cancer datasets (MSK, TCGA).

Discussion and Conclusion

The data indicate that a metabolic-hybrid phenotype, characterized by concurrent up-regulation of glycolysis, lactate export (MCT1) and glucose uptake (GLUT1), underlies intrinsic CRT resistance in LARC. Pharmacologic blockade of GLUT1, and to a lesser extent MCT1, re-sensitizes resistant tumor cells to irradiation, providing functional validation of the metabolic dependency. Therefore, metabolic reprogramming seems to be a key driver of CRT resistance in rectal cancer. Targeting the glycolytic-lactate axis offers a promising strategy to improve response rates, enable organ-preserving treatment, and may provide a basis for stratifying patients who could benefit from more intensive, metabolism-targeted therapeutic approaches in locally advanced rectal cancer.

Glia-derived GDNF Deficiency Destabilizes Neuronal and Epithelial Integrity and Promotes Colonic Neuroinflammation and Colorectal Tumorigenesis

Jonah E.Lunnebach,Akram Abdulkadyrov,Ebrahim Hamza,Marius Hoerner,Charlotte D.L-L.VonGruenberg,Linda Schneider,Joerg C.Kalff,Natalie Burkard,Nicolas Schlegel,Reiner Schneider¹,SvenWehner¹

Introduction:Enteric glia are increasingly recognized as regulators of intestinal homeostasis and peripheral neuroimmune signaling. Glial cell line-derived neurotrophic factor (GDNF), produced by several intestinal cell populations, including enteric glia, has been implicated in epithelial and neuronal protection. However, the specific contribution of Sox10-lineage glial-associated GDNF to intestinal inflammation, enteric nervous system integrity, and inflammation-associated tumorigenesis remains incompletely defined.

Research question:We investigated whether Sox10-lineage glial-associated GDNF protects against intestinal neuroinflammation, epithelial and neuronal injury, and inflammation-associated colorectal tumor development.

Methods:Mice with tamoxifen-inducible Sox10-dependent deletion of GDNF were generated and subjected to acute and chronic dextran sulfate sodium-induced colitis as well as azoxymethane/DSS-induced colorectal tumorigenesis. Disease severity and tissue remodeling were assessed by clinical scoring, colonoscopy, histology, immunofluorescence, transcriptomic, and proteomic profiling. Epithelial responses were studied in vivo and in colonoids, enteric neuronal alterations were analyzed in intestinal tissue, and macrophage responses were examined in bone marrow-derived macrophages.

Statistics:Data were analyzed using appropriate parametric or non-parametric tests depending on distribution and experimental design. Transcriptomic and proteomic datasets were analyzed using differential expression and pathway enrichment approaches. P values below 0.05 were considered statistically significant.

Results:Experimental colitis induced *Gdnf* expression in enteric glia and was accompanied by glial remodeling. Loss of Sox10-lineage glial-associated GDNF did not cause overt baseline abnormalities but aggravated acute and chronic DSS colitis, with increased disease activity, more severe endoscopic and histological injury, goblet cell loss, elevated inflammatory mediators, and reduced colonic GDNF levels. Proteomic profiling revealed enhanced innate immune activation, leukocyte- and macrophage-associated programs, migration, proliferation, and cell death-associated pathways in inflamed GDNF-deficient colon. GDNF deficiency impaired epithelial barrier integrity in vivo, whereas recombinant GDNF reshaped LPS-induced epithelial transcriptional responses, improved barrier properties, and reduced epithelial stress in colonoids. Loss of glial-associated GDNF also compromised enteric nervous system integrity, reflected by reduced neuronal abundance, altered synaptic and neurotransmitter-associated programs, and decreased dopaminergic and nitrergic marker expression. Immunoprofiling demonstrated increased leukocyte recruitment, MPO⁺ myeloid cell accumulation, and macrophage infiltration in GDNF-deficient mice. Bone marrow-derived macrophages expressed GFRα1 and responded functionally to GDNF. In the AOM/DSS model, GDNF deficiency increased tumor burden and tumor-associated macrophage accumulation.

Discussion: These findings identify Sox10-lineage glial-associated GDNF as a protective trophic signal within the inflamed enteric neuroimmune niche. The data suggest that GDNF contributes to epithelial barrier resilience, enteric neuronal preservation, and control of excessive myeloid inflammatory remodeling during colitis.

Conclusion: Sox10-lineage glial-associated GDNF limits intestinal neuroinflammation, colitis severity, and inflammation-associated colorectal tumor development by coordinating epithelial, neuronal, and immune protective mechanisms.

MSC adopt a Meflin-CAF-like phenotype and exert functional roles in early pancreatic carcinogenesis

Tina Seidel,

Medical Faculty of the Martin Luther University Halle-Wittenberg, Department of Internal Medicine, Hematology and Oncology, Halle (Saale), Deutschland

Dr.rer.nat.Jana Lützkendorf,

Medical Faculty of the Martin Luther University Halle-Wittenberg, Department of Internal Medicine, Hematology and Oncology, Halle (Saale), Deutschland

Jun.-Prof.Dr.rer.nat.Tony Gutschner,

Medical Faculty of the Martin Luther University Halle-Wittenberg, Institute for Molecular Medicine, Halle(Saale), Deutschland

Dr.rer.nat.Nico Hesselbarth,

Medical Faculty of the Martin Luther University Halle-Wittenberg, Department of Internal Medicine, Gastroenterology & Pneumology, Halle (Saale), Deutschland

Dipl.-Bioinf.Edith Willscher,

Medical Faculty of the Martin Luther University Halle-Wittenberg, Department of Internal Medicine, Hematology and Oncology, Halle(Saale), Deutschland

Katrin Nerger,

Medical Faculty of the Martin Luther University Halle-Wittenberg, Department of Internal Medicine, Hematology and Oncology, Halle(Saale), Deutschland

Amirhossein Nafari,

Medical Faculty of the Martin Luther University Halle-Wittenberg, Department of Internal Medicine, Hematology and Oncology, Halle(Saale), Deutschland

Tanvi Inamdar,

Medical Faculty of the Martin Luther University Halle-Wittenberg, Department of Internal Medicine, Gastroenterology & Pneumology, Halle (Saale), Deutschland

apl.Prof.Dr.med.Lutz Müller,

Medical Faculty of the Martin Luther University Halle-Wittenberg, Department of Internal Medicine, Hematology and Oncology, Halle (Saale), Deutschland

Introduction

The pancreatic stroma comprises diverse celltypes that influence the progression of pancreatic ductal adenocarcinoma(PDAC), including multipotent stromal cells(MSCs), which possess immunoregulatory properties and can differentiate into carcinoma-associated fibroblasts(CAFs)

We hypothesize that MSC-like cells act as modulators during pancreatic carcinogenesis and are activated by interactions with PDAC cells.

Material and Methods

In vitro, we co-cultured human MSCs with PDAC cell lines(PANC-1, MIA-PaCa-2, Capan-1) and analyzed RNA-sequencing, cytokine profiles, and phenotypic markers to identify PDAC-induced alterations in MSCs. To study stromal dynamics during early PDAC, we analyzed

KC,Cpa1,and KC-Cpa1 mouse models at 6 and 20 weeks.Pancreatic stroma content wasassessed histologically,the population of native stroma cells including potential MSC-like cellswas isolated by FACS and analyzed by single-cell RNA sequencing as wellas by in vitroassays.

Results

In co-culture,MSCs were activated by PDAC cells,showing upregulation of IL-6 and immuneregulation genes and reduced expression of differentiation and ECM genes.In addition,cellline-specific changes in cellproliferation,spheroid formation,CAF characteristics includingFAP expression and other cytokines were observed.Flow cytometry revealed an increasedproportion of MSC-like cells(CD45-MHC II⁻CD11b-CD105Sca-1+CD73+)in the pancreas ofmurine models of chronic pancreatitis and early PDAC carcinogenesis correlating to anincreasing degree of fibrosis.Differentiation analysis proved their MSC nature and single-cellRNA sequencing revealed that these MSC-like cells undergo a dynamic differentiation tospecific CAF-phenotypes during early PDAC carcinogenesis.Inparticular,MSC are present inearly PDAC as Meflin+CD105+Fap-cells,serving as progenitors for myCAF.

Conclusion

This study presents MSC-like cells as Meflin+cells in ealy pancreatic carcinogenesis PDACwhich increase in their number during PDAC development and undergo CAF-differentiationupon interaction with tumor cells.These findings support a dynamic and modulatory role forMSC-like cells n stromal remodeling and pancreatic tumor progression

Surgeomics at the Tumour Margin: ML-Enhanced Raman Lipidomics for Label-Free Detection of Tumor Stem Cells

Dr.med.-Lennard Merlin-Wurm

-Charité-Universitätsmedizin Berlin,Deutschland; Heinrich-Heine-Universität
Düsseldorf,Deutschland; Inselspital-Universitätsspital
Bern,Schweiz(presenting/corresponding)

Dr.rer.nat.-Björn-Fischer

-Institut für Pharmazeutik und Biopharmazeutik,Heinrich-Heine-
UniversitätDüsseldorf,Deutschland; RSS,Raman Spectroscopic
Services,Meerbusch,Deutschland

Prof.Dr.med.-Volker-Neuschmelting

-Klinik für Neurochirurgie,Universitätsklinikum Köln,Deutschland

Prof.Dr.med.-Roland-Goldbrunner

-Klinik für Neurochirurgie,Universitätsklinikum Köln,Deutschland

Prof. Dr. med. Dr. h. c. - Roland S. - Croner

- Klinik für Allgemein-, Viszeral-, Gefäß- und Transplantationschirurgie,Abteilung für
Molekulare und Experimentelle Chirurgie,UniversitätsklinikumMagdeburg,Otto-von-
Guericke-Universität,Deutschland

Prof.Dr.med.-Erol1.-Sandalcioğlu

-Klinik für Neurochirurgie,Otto-von-Guericke-UniversitätMagdeburg,Deutschland

Prof.Dr.med.-Katharina A.-Faust

-Klinik für Neurochirurgie,Universitätsklinikum Düsseldorf,Deutschland

Prof. Dr. rer. nat. - Michael C. – Hacker

- Institut für Pharmazeutik und Biopharmazeutik, Heinrich-Heine-Universität
Düsseldorf,Deutschland

Prof. Dr. rer. nat. - Jakub - Dybaś

- Jagiellonian Center for Experimental Therapeutics, Jagiellonian University,Krakau,Polen

Prof. Dr. rer. nat. - Ulf D. - Kahlert

- Klinik für Allgemein-, Viszeral-, Gefäß- und Transplantationschirurgie,Abteilung für
Molekulare und Experimentelle Chirurgie,Universitätsklinikum Magdeburg,Otto-von-
Guericke-Universität,Deutschland;Forschungscampus STIMULATE,Otto-von-Guericke-
UniversitätMagdeburg,Deutschland

Introduction.Across solid tumours,cancer stem cells(CSCs)drive therapy resistance and recurrence,and their intraoperative identification at the resection margin is a general unmet need in surgical oncology.Glioblastoma(GBM)serves here as a model of treatment-resistant tumour stem cells:it grows infiltrativelyand recurs,and glioblastoma stem-like cells(GSCs)evade standard fluorophores such as 5-ALA.Label-free Raman micro-spectroscopy provides a non-destructive molecular fingerprint and thus embodies the surgeomics idea of bringing molecular information directly into the surgical decision.

Research question.Is visible(532 nm)or near-infrared (785 nm)Raman excitation better suited for a generalizable,explainable classification of tumour stemness,and does restricting the features to protein-and lipid-specific spectral windows improve robustness?

Methods.Single-cell Raman spectra of human GBM cell lines(stem-like vs.BMP4-differentiated)were acquired(1,560 at 532 nm;203 at 785 nm).After a standardized preprocessing pipeline,classifiers(PLS-DA,SVM,gradient/histogram boosting,random forest)were trained on the fullfingerprint(700-1780cm⁻¹)and on protein-rich(1550-1730

cm^{-1}) and lipid-rich ($1260\text{--}1510\text{ cm}^{-1}$) regions. Explainable AI (SHAP/TreeExplainer) linked the features to a high-frequency C-H lipid proxy.

Statistics. For a clinically realistic evaluation, a strict leave-one-cell-line-out cross-validation (LOGO) was used: all spectra of a given cell line were entirely withheld from training and used only for testing, preventing cell-line and batch leakage. Primary metrics were balanced accuracy and pooled ROC-AUC.

Results. Under LOGO validation, NIR excitation (785 nm) generalized more robustly than 532 nm. Restricting features to protein- and lipid-specific windows improved the 785 nm models (PLS-DAROC-AUC 0.706 to 0.747; linear SVM balanced accuracy 0.667 at ROC-AUC 0.708). SHAP demonstrated a lipid-driven mechanism peaking at approximately 1440 cm^{-1} (CH_2 deformation) and reliably predicted the high-lipid state (pooled ROC-AUC approximately 0.95 at 532 nm and approximately 0.82 at 785 nm).

Discussion. Targeted, biologically motivated spectral windows outperform full-fingerprint analysis by discarding patient- and cell-line-specific nuisance variation; NIR is more favourable for translational, intraoperatively conceivable use. The classification is explainable and biophysically coherent (lipid bands) rather than a black box. Limitations are the in-vitro single-cell design and the smaller 785 nm sample.

Conclusion. Label-free Raman combined with explainable machine learning enables a lipid-based, interpretable discrimination of tumour stem cells and represents a methodological building block of surgeomics towards intraoperative tumour-margin diagnostics. Because it targets generic lipid and protein signatures of stemness rather than tumour-type-specific labels, the approach is in principle transferable to cancer stem cells in other solid tumours; translation to tissue remains to be established.

Zelluläre Therapien in der perioperativen Multimodaltherapie solider Tumoren

Development of a 3D hepatocyte model for the investigation of CAR-associated proliferative mechanisms relevant to hepatocarcinogenesis

Solveig Arndt(1,2)Dr.rer.nat.Andrea Scheffschick(1,2)Dr.rer.nat.Georg

Damm(1,2)Prof.Dr.med.Daniel Seehofer (2)

1 Saxonian Incubator for Clinical Translation,Leipzig

2 Department of Hepatobiliary Surgery and Visceral Transplantation,Leipzig University Hospital

Introduction:Preclinical assessment of hepatocarcinogenic risk is crucial in pharmaceutical development,as hepatotoxicity remains one of the most reported side effects.While the exact mechanisms of non-genotoxic carcinogens are not fully understood,the induction of cellular proliferation via nuclear receptors,like the Constitutive Androstane Receptor (CAR),plays a pivotal role.Upon activation,CAR promotes hepatocyte proliferation and rodent hepatocarcinogenesis,whereas comparable proliferative responses are largely absent in humans.

Previously,we established a 2D hepatocyte assay that successfully displayed CAR-mediated,species-specific proliferation,but was compromised by rapid cellular dedifferentiation,resulting in reduced cytochrome P450(CYP)activity over time.

Research question:We aimed to preserve metabolic competence by transferring the 2D assay into a 3D culture configuration.The 3D configuration enables the investigation of proliferative responses in metabolically active cells via extracellular matrix biomimicry and mirrors in vivo conditions more accurately.

Methods:Primary murine and human hepatocytes were maintained in a 3D configuration for 72 hours and treated with the CAR activator phenobarbital under controlled conditions.Proliferation was quantified via Ki67- and BrdU immunofluorescence staining.Metabolic competence was evaluated by measuring CYP enzyme activity(CYP-1A,-2B,-3A) via Alkoxyresorufin O-dealkylase (AROD) assay and expression patterns via qPCR over time.

Results:The 3D model successfully replicated species-specific responses:CAR activation through phenobarbital stimulated proliferation in murine hepatocytes,whereas human hepatocytes remained largely non-proliferative.Concurrently,CYP enzyme activity was preserved over 72 hours and exhibited donor- and treatment-dependent functional induction,indicating that the cells maintained their differentiated status in 3D culture.Additional experiments are currently performed to further validate these findings.

Discussion:This 3D hepatocyte model provides an in vivo-like microenvironment,that preserves metabolic competence and allows simultaneous evaluation of proliferative and functional responses after CAR activation.It offers a physiologically relevant alternative to conventional 2D cultures.

Conclusion:Ultimately,this 3D model represents a promising,translationally relevant screening tool for non-genotoxic proliferative events,contributing to the reduction of animal testing in preclinical safety assessments.