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Annals of Pancreatic Cancer

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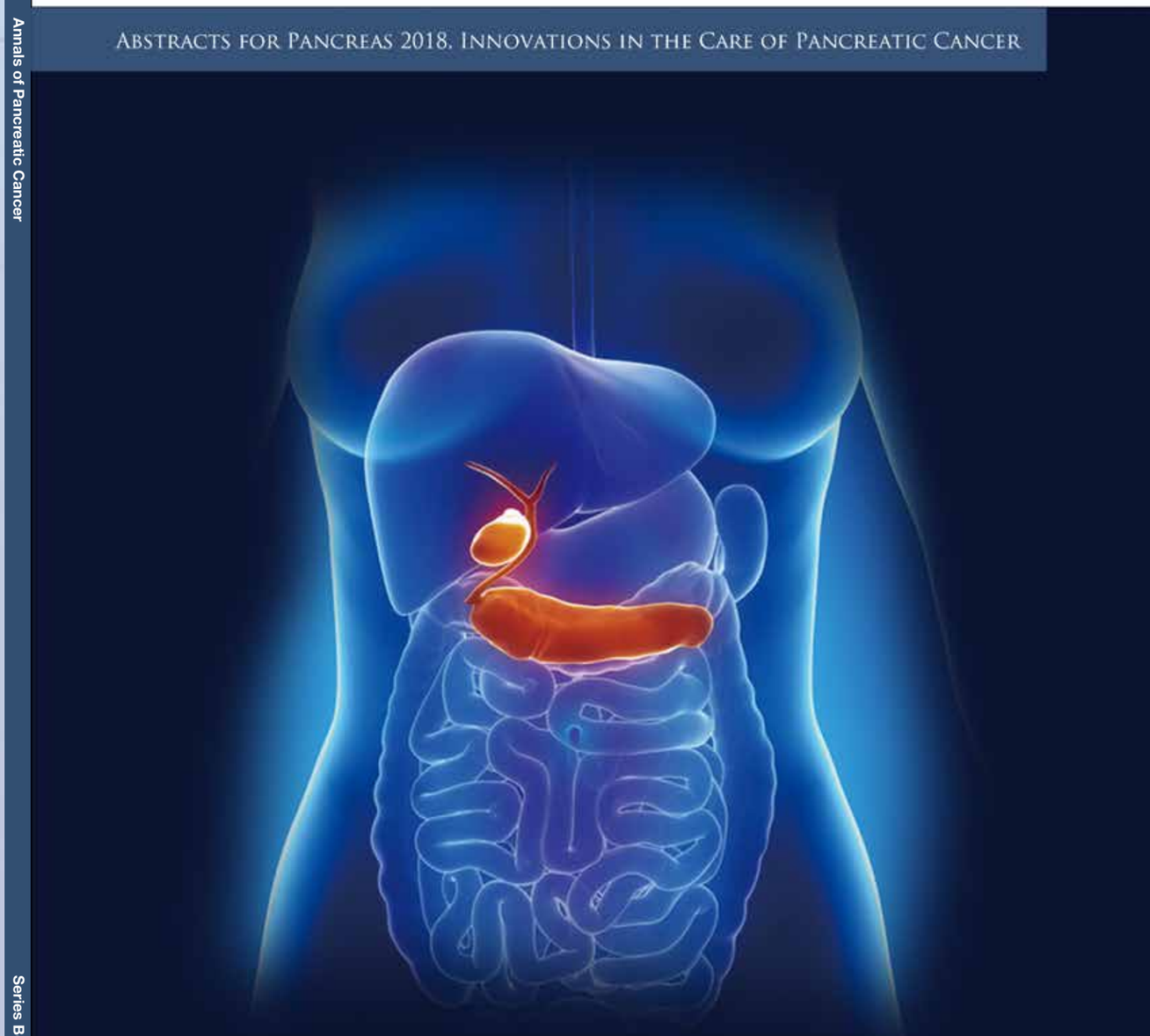
APC Annals of Pancreatic Cancer

An open access, peer-reviewed journal solely focused on the malignant diseases of the pancreas

Abstracts for Pancreas 2018. Innovations in the Care of Pancreatic Cancer



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Pancreas 2018

Innovations in the Care of Pancreatic Cancer

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Aim and Scope

Annals of Pancreatic Cancer (Ann Pancreat Cancer; ISSN 2616-2741) is a journal for all researchers in the field of pancreatic cancer and for all health care providers who manage the care of pancreatic cancer patients. The journal will cover topics from all aspects of pancreatic cancer including basic biology and immunology, epidemiology, prevention, diagnosis, treatment, and supportive care. We will use this journal to bring together all scientists and clinicians under the same ceiling to discuss how we can better understand and treat pancreatic cancer. The main goal of the journal is to make our clinicians incorporate the knowledge from basic science research into their routine management and clinical investigation of pancreatic cancer and also to inspire our scientists to have the translational intuitiveness in their epidemiology and laboratory researches.

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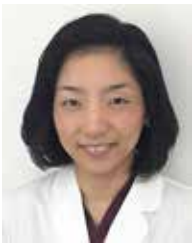
Peter Allen

Dr. Peter J. Allen is the Vice Chair of Surgical Services, and Murray F Brennan Professor of Surgery, at Memorial Sloan Kettering Cancer Center. He also serves as the Associate Director of Clinical Programs within the David Rubenstein Center for Pancreatic Cancer Research. He is originally from the state of Maine, received his undergraduate degree at Harvard University, and his medical degree from Dartmouth. Dr Allen performed his general surgical residency at Walter Reed Army Medical Center in Washington D.C. During this time he performed a research fellowship in the laboratory of Murray Brennan at Memorial Sloan-Kettering Cancer Center. Following residency, Dr. Allen performed a clinical fellowship at Memorial Sloan-Kettering Center and then returned to Walter Reed where he was an attending surgeon on the surgical oncology service. During his time as a surgical attending at Walter Reed, Dr. Allen was deployed to Iraq where he spent one year as a surgeon on a forward surgical team. Dr. Allen returned to Memorial Sloan-Kettering Cancer Center in 2005, and since that time he has lead the surgical efforts in the treatment of neoplastic diseases of the pancreas. His clinical and research efforts have been focused on the development of novel diagnostic and therapeutic approaches to invasive and pre-invasive lesions of the pancreas. He has led multiple prospective clinical trials, and his research has been funded by numerous organizations including the SSO and the NIH.

Nita Ahuja

Nita Ahuja, MD, MBA is the William H. Carmalt Professor of Surgery and Chair of the Department of Surgery, Yale School of Medicine and Surgeon-in-Chief at Yale New Haven Hospital. She is a national and international surgical leader and surgeon scientist with specializations in gastrointestinal cancers, including gastric, colorectal, and pancreatic cancers. She has an international reputation for the management of peritoneal cancer metastases with cytoreduction and heated intraperitoneal chemotherapy. Dr. Ahuja, a board-certified surgeon, obtained her medical education at Duke University, School of Medicine. She received her training in general surgery at Johns Hopkins where she also completed a fellowship in surgical oncology that focused on hepatobiliary malignancies. Dr. Ahuja obtained an Executive MBA from Johns Hopkins Carey School of Business. In 2003, she joined the faculty at Johns Hopkins. While there, she directed the multidisciplinary programs in soft tissue sarcoma and gastric cancers and lead the integration and expansion of surgical oncology programs across the Johns Hopkins health system. During her time there, she became one of their most accomplished faculty members. Her positions at Johns Hopkins included serving as Division Chief of Surgical Oncology and Vice Chair of Academic Affairs for the Department of Surgery. Dr. Ahuja also served as the Director of the Peritoneal Surface Malignancy Program, Director of Soft Tissue Sarcomas and Co-Director of Gastric Multidisciplinary Clinic. She also served as the Associate Director of Surgical Oncology for the Sidney Kimmel Comprehensive Cancer at Johns Hopkins.



Reiko Ashida

Reiko Ashida is currently Co-Director of Departments of Cancer Survey and Gastrointestinal Oncology at Osaka International Cancer Institute, Osaka, Japan. She graduated medical school in 1998 and obtained PhD in 2005 from the Graduate School of Medicine, Osaka City University. She started EUS since 1999 and trained EUS-FNA in 2002 at Aich Cancer Center and had the advanced fellowship program of Interventional EUS at University of California Irvine, Medical Center between 2007-2009. Her research interests include early detection and treatment of pancreatic cancer, Interventional EUS, and development of EUS-guided high intensity focused ultrasound (EUS-HIFU) with novel phase change nanodroplets as a sensitizer. She has received several awards and grants related to ultrasound technology from Japan Society of Ultrasonics in Medicine.

Claudio Bassi

Prof. Claudio Bassi is Full Professor and Chairman of General and Hepato-Bilio-Pancreatic Surgery Department. Professor in several degree courses, he directs the School of Specialization in General Surgery at the University of Verona and is responsible for the Translational Surgery Laboratory for Medical Research (LURM). Prof. Bassi's experience covers all surgical pathologies of the pancreas and the scientific activity was entirely dedicated to pancreatic diseases. Prof. Bassi has an **H-Index: 75** (updated at 21/02/2018 (Source SCOPUS)) and he's author of more than 350 publications up to date, was Invited Speaker in over 300 national and international congresses and performed more than 2000 pancreatic resections and more than 8000 major surgery interventions.

Angela Belcher

Angela Belcher is a biological and materials engineer with expertise in the fields of biomaterials, biomolecular materials, organic-inorganic interfaces and solid-state chemistry and devices. Her primary research focus is evolving new materials for energy, electronics, the environment, and medicine. She received her B.S. in Creative Studies with an emphasis in biology from The University of California, Santa Barbara. She earned a Ph.D. in inorganic chemistry at UCSB in 1997. Following her postdoctoral research in electrical engineering at UCSB, she joined the faculty at The University of Texas at Austin in the Department of Chemistry in 1999. She joined the faculty at MIT in 2002. Some recent awards include 2018 NAE (National Academy of Engineers) Fellow, 2015 NAI (National Academy of Inventors) Fellow, the 2013 $500,000 Lemelson-MIT Prize for her Inventions, 2010 Eni Prize for Renewable and Non-conventional Energy, in 2009 Rolling Stone Magazine listed her as one of the top 100 people changing the country.

Andrew Biankin

Professor Andrew Biankin is the Regius Chair of Surgery at the University of Glasgow a Cancer Research UK Clinician Scientist, a Wellcome Trust Senior Investigator, a Fellow of the Royal Society of Edinburgh and The Academy of Medical Sciences. He is the Director of the Wolfson Wohl Cancer Research Centre which is focused on precision oncology. He plays leadership roles in national and international consortia in cancer therapeutic development. He has authored over 150 articles in major journals including seminal works on pancreatic cancer, genomics and precision medicine. He works closely with industry and biotech companies to develop innovative interventions for pancreatic cancer.

Jonathan Brody

Dr. Jonathan Brody is currently the Director of Surgical Research and Co-director of the Jefferson Pancreatic, Biliary, and Related Cancer Center. He is also a member of the Kimmel Cancer Center (with a leadership role in GI Program) and a Professor within the departments of Surgery and Pathology. Dr. Brody received his Ph.D. from The Johns Hopkins University School of Medicine, and his thesis specialized in studying the molecular aspects of cancer and cancer genetics. He patented, with Dr. Scott Kern, novel buffers for DNA identification (DNA electrophoresis buffer), that have changed the format of this molecular biology technique used to detect DNA. He was elected Chair of the Cancer Research Program (PRCRP), Department of Defense council and serves on many international study sections, including currently being the Chair of the Tumor Biology and Genomics study section for the American Cancer Society and NCI study section panels. He has published over 100 peer review publications in many top tier scientific and cancer journals. Additionally, he was an American Cancer Society Research Scholar, is NIH (NCI, R01) funded, and won the American Association of Cancer Research, Pancreatic Cancer Career Development Award in 2010. His lab focuses on many molecular aspects of pancreatic cancer, including developing ways to target a novel pro-survival network in pancreatic cancer cells and optimizing current therapies used in the clinic. His also has an interest in personalizing therapy for pancreatic cancer patients (PanCAN, RAN grant PI).

Marco Bruno

Prof. dr. Marco J. Bruno (1963) is a full professor of Gastroenterology & Hepatology and chief of the department of Gastroenterology & Hepatology at the Erasmus Medical Centre in Rotterdam. He received his training at the Academic Medical Centre in Amsterdam under the supervision of Prof. dr. Guido Tytgat and Prof. dr. Kees Huibregtse. His clinical and research activities focus on gastrointestinal oncology, hepato-pancreato-biliary diseases and interventional endoscopy, including endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS). He (co)-author of numerous peer reviewed articles in high ranking journals including the New England Journal of Medicine, Gastroenterology, Gut, Endoscopy and Gastrointestinal Endoscopy. He is a recognized international authority on the diagnosis and treatment of biliary and pancreatic diseases and has served as invited faculty at many international conferences and live endoscopy workshops. He is council member end treasurer of the European Association of Gastroenterology, Endoscopy & Nutrition (EAGEN); past council member of United European Gastroenterology (UEG); and past chairman of the Education Committee of United European Gastroenterology (UEG) and the Dutch Pancreatitis Study Group.

Richard Burkhart

Richard Burkhart is an assistant professor of surgery at Johns Hopkins Hospital with a focus on cancers of the pancreas, liver and bile ducts. Dr. Burkhart received his medical degree from Boston University, completed his surgical residency at Thomas Jefferson University Hospital, and completed a fellowship in surgical oncology at Johns Hopkins. His research training has focused on pancreatic cancer biomarkers, tumor modeling, and therapeutic testing and includes fellowships at Thomas Jefferson University hospital and the Cold Spring Harbor Laboratory. His clinical focus is on complex minimally-invasive approaches to treat oncologic diseases of the pancreas, liver, and biliary tree. His current research focuses on precision medicine initiatives in pancreatic cancer care. He has a particular interest in using personalized models of pancreas cancer, made from a tumor after surgical resection, to select optimal adjuvant chemotherapeutics for each patient.

Mimi Canto

Marcia (aka Mimi) was born and raised in Manila, Philippines. After graduating summa cum laude at the University of the Philippines Medical School in 1985, she completed fellowship training in Gastroenterology at Johns Hopkins. After advanced endoscopic training in Cleveland, she returned to Johns Hopkins Hospital in 1996 as the first woman director of therapeutic endoscopy and endoscopic ultrasonography, quickly achieving international recognition as a multi-talented academic endoscopist in a male-dominated subspecialty. She was promoted to professor of medicine and oncology in 2011 as a clinical investigator, program builder, mentor, and clinician. Her research involves therapeutic endoscopy, advanced endoscopic imaging, and endoscopic ultrasonography. She is a world authority on screening and early detection of pancreatic cancer in high risk individuals. She organized and co-directs (with Michael Goggins) the Johns Hopkins Cancer of the Pancreas Screening (CAPS) clinical and translational research program and the multidisciplinary International CAPS Consortium for worldwide collaboration on pancreatic cancer screening and early detection. With a group of international experts, she organized the first CAPS Consortium Summit in Baltimore and co-authored the first CAPS Consensus paper in 2012.

David Chang

Dr David Chang is a surgeon scientist who specialises in the treatment of malignant pancreatic diseases. His research interest is on the development and implementation of novel therapeutic strategies for pancreatic cancer utilising molecular biomarkers of prognosis and therapeutic responsiveness. He is the co-lead of Precision-Panc, a pan-UK initiative to deliver personalized cancer care for pancreatic cancer, and is the chief investigator of its Master Protocol. He is also involved in Precision Promise, a Pancreatic Cancer Action Network (USA) initiative dedicated in delivering personalized treatment for patients with pancreatic cancer. In addition, he serves on the scientific planning committee of ICGC for Medicine (ICGCmed), to shaping the goals and the future of the next generation International Cancer Genome Consortium (ICGCmed) projects to realize the goals and promises of precision medicine.

Roberto Coppola

Dr. Roberto Coppola is Full Professor of Surgery at the Campus Bio-Medico University School of Medicine in Rome. Chief of the Department of General Surgery and Director of the Residency School in General Surgery at the same University. He is Member of The Ethical Committee of the Catholic University of Rome since 1999. The main field of research and clinical activity is surgery of the pancreas. Dr. Coppola became Fellow of the American College of Surgeons in 1996, and is Fellow of the Italian Society of Surgery since the beginning of his carrier. He was the Director of several international meetings on Pancreas Cancer in Italy. Recent fields of research are the standardization of the resection margins in pancreatic surgery, the impact of nosocomial infections in pancreatic surgery and the new applications of nanotechnology to pancreas cancer. Dr. Coppola is in the editorial board of International Journal of Surgery, and Pancreatology.

Marco Del Chiaro

Professor Marco Del Chiaro is Associate Professor and head of the Pancreatic Surgery Unit at Division of Surgery (CLINTEC), Karolinska Institutet. He is revisor of the European Pancreatic Club, member of the UEG General Assembly, member of the council of the International Association of Pancreatology, member of the EU Pancreas study group. Marco Del Chiaro is also the founder of the Italian Registry for Familial Pancreatic Cancer, of the European Study Group on Cystic Tumors of the Pancreas and of the Nordic Study Group on Cystic Tumors of the Pancreas. He is a member of editorial boards of International scientific journals (i.e., *JAMA Surgery*) and author of more than 600 scientific publications including 124 peer review papers.

Luis Diaz Jr

Dr. Luis Diaz is a leading authority in oncology who has pioneered several genomic diagnostic and therapeutic approaches for cancer. He is head of the Division of Solid Tumor Oncology at the Memorial Sloan Kettering Cancer Center where he specializes in the treatment of advanced pancreatic and colorectal cancers. Prior to his role at MSKCC, he was a member of the Ludwig Center for Cancer Genetics and Therapeutics at Johns Hopkins and also directed the Swim Across America Lab. He is also founder of several entities that focus on genomic analyses of cancers including Inostics, PapGene and Personal Genome Diagnostics (PGDx). Dr. Diaz has undergraduate and medical degrees from the University of Michigan, and completed residency training at the Osler Medical Service at Johns Hopkins and medical oncology training at the Sidney Kimmel Cancer Center at Johns Hopkins.

Michael Erdek

Dr. Michael Erdek is Associate Professor of Anesthesiology and Critical Care Medicine and Oncology at The Johns Hopkins University School of Medicine and Adjunct Associate Professor at the Berman Institute of Bioethics. Dr. Erdek received his undergraduate medical education at the University of Pennsylvania, where he was a Walter Lewis Croll Scholar. He trained in Surgery and in Anesthesiology prior to completing his subspecialty training in Pain Medicine and Critical Care Medicine at The Johns Hopkins University. Dr. Erdek has published and lectured extensively in the field of Pain Medicine, and has been appointed to the Polyanalgesic Consensus Panel and has received the National Pancreas Foundation Compassionate Care Award. He is a member of the editorial boards for several journals in the field of Pain Medicine. His interests center on interventional pain management of cancer pain, intrathecal therapy for spasticity, and spinal cord stimulation for neuropathic pain and vascular disease.

James Eshleman

Dr. Eshleman received his MD and PhD (cell biology) degrees from the University of Pennsylvania in 1988. He completed an internship in Internal Medicine and residency in Clinical Pathology. He joined the laboratory of Dr. Sandy Markowitz at Case Western Reserve University where he demonstrated that colon cancers with microsatellite had highly elevated mutation frequencies. He joined the faculty at Hopkins in 1997 where he has focused his work on the genetics of pancreatic cancer. His interests include early detection, minimal residual disease monitoring and pancreatic cancer predisposition genes. He also contributes to the Molecular Pathology clinical service.

Massimo Falconi

Dr. Massimo Falconi is currently Full Professor of Surgery and Chairman of the Pancreatic Unit at the University Vita e Salute, San Raffaele Hospital IRCCS, in Milan, Italy. He studied medicine at the University of Verona, specializing in general surgery, gastroenterology and endoscopy. He has participated in international medical research projects in such diverse places as Germany, Spain, Ecuador, and Japan. A member of many medical societies, including IAP, EPC, ENETS and I and EAHPBA. Prof Falconi is currently on the executive committees of both ENETS and IAP. He has written more than 300 peer-reviewed articles and currently reviews articles for the following publications: Annals of Oncology, British Journal of Surgery, Cochrane, Gut, Lancet, Neuroendocrinology, Nutrition, Pancreas, Pancreatology, Journal of Endocrinological Investigation (JEI), Journal Of the Pancreas (JOP), Surgery, Annals of Surgery. Dr. Falconi serves as Associate Editor for the section of the pancreas and neuroendocrine tumors for Digestive and Liver Disease, official journal of the Italian and French Gastroenterological societies. He is also editorial member of the following journals: World Journal of Gastroenterology, subject Area Editor of The International Journal of Biological Markers and of International Journal of Endocrine Oncology. He has an impact factor calculated on the basis of JCR 2014 of more than 1,500 and his h index on Scopus is 61.

Carlos Fernandez del Castillo

Dr. Carlos Fernandez-del Castillo was born in grew up in Mexico City, attended medical school at the National Autonomous University of Mexico, and then did a residency in internal medicine and surgery at the Instituto Nacional de la Nutricion. In 1989 he came to the Massachusetts General Hospital as a Research Fellow in the Pancreatic Research Laboratory of Dr. Andrew Warshaw, and in 1991 joined the staff in the Division of General/GI Surgery. He is currently the director of the Pancreas and Biliary Surgery Program, co-director of the GI Cancer Center, and the Jorge and Darlene Perez Endowed Chair in Surgery at the MGH, as well as a Professor of Surgery at Harvard Medical School. For several years he has performed the largest number of pancreatic resections in the state of Massachusetts.

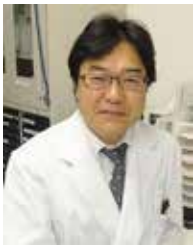
He has authored over 230 original articles and 100 book chapters and reviews, mostly on topics related to surgical diseases of the pancreas. He currently holds NIH funding for the study of the fluid of cystic neoplasms of the pancreas. Dr. Fernandez-del Castillo has been recipient of multiple teaching awards, and in 2016 was recognized with the Andrew L. Warshaw Master Educator Award given by the SSAT. He was also recipient of the 2011 Brian McGovern award for Clinical Excellence, given by the MGPO, and is currently a member of its board of trustees. He is member of many medical associations, and a former president of the American Pancreatic Association.

Elliot Fishman

Dr. Elliot K. Fishman is Director of Diagnostic Imaging and Body CT at Johns Hopkins Hospital, where he is Professor of Radiology, Surgery, Urology and Oncology. Dr. Fishman's clinical and research interests have focused on advanced medical imaging with specific emphasis on CT and 3-Dimensional imaging. Recent emphasis has also been focused on Deep Learning in Medical Imaging as Co-PI of the Felix Project for Early Detection of Pancreatic Cancer. Dr. Fishman's work in CT has resulted in over 1200 peer reviewed publications, and he has been the co-author of 10 textbooks. Dr. Fishman's research team has been one of the leading groups in developing new techniques and technologies, whether in visualization or post processing or in education. Dr. Fishman has expertise in computer and web-based education, developing the website, www.ctisus.com, which currently has over 300,000 users, as well as its Facebook version which has over a million followers from over 190 countries. Dr. Fishman and his team have also developed 14 iPad programs for the Apple store.

Toru Furukawa

Dr. Furukawa is currently Professor and Chairman of Department of Histopathology, Tohoku University Graduate School of Medicine, Sendai, Japan. He graduated Faculty of Medicine, Akita University, Akita, Japan, in 1986. He conducted his doctoral research at Department of Pathology, Research Institute for Tuberculosis and Cancer, Tohoku University, Sendai, Japan, and received PhD degree from Tohoku University in 1993. He did his postdoctoral research at Montreal General Hospital Research Institute, Montreal, PQ, Canada, from 1993-95. He had been an assistant professor of Department of Molecular Pathology, Tohoku University Graduate School of Medicine in 1996-2005, an associate professor of International Research and Educational Institute for Integrated Medical Sciences, Tokyo Women's Medical University, Tokyo, Japan, in 2005-2008, and a professor of Institute for Integrated Medical Sciences, Tokyo Women's Medical University in 2008-2017. He has been appointed to the current position from 2017. He received a number of awards including Government of Canada Award (1994), Pathology Research Award of the Japanese Society of Pathology (2002), and the Hirshberg Award for Pancreatic Cancer Research (2009). His research interests include the molecular pathobiology of pancreatobiliary neoplasms. His publications can be found at the following URL: http://scholar.google.com/citations?user=aQRfR_QAAAAJ&hl=ja&oi=ao.



Junji Furuse

Dr. Junji Furuse currently works as a professor, Department of Medical Oncology, Kyorin University Faculty of Medicine, Japan.

Occupation

In 1984, graduated from Chiba University of Medical School and then attended the First Department of Internal Medicine, Chiba University.

In July, 1992- February, 2008: Division of Hepatobiliary Pancreatic Medical Oncology, National Cancer Center Hospital East.

March, 2008-present: Professor, Department of Medical Oncology, Kyorin University School of Medicine.

Activities

Japanese Clinical Oncology Group (JCOG): Chair of Hepatobiliary and Pancreatic Oncology Group

Japan Pancreas Society (JPS): Director, Chair of health insurance committee

International Association of Pancreatology Council Member

ASCO	Active member
ESMO	Active member

Specialty

Gastrointestinal Medical Oncology, especially hepatobiliary and pancreatic cancer.

Steven Gallinger

Dr Steven Gallinger is an Hepatobiliary/pancreatic (HPB) surgical oncologist and member of the GI Site Cancer Program at Princess Margaret Cancer Centre. He is Professor of Surgery at the University of Toronto, and Head of the HPB Surgical Oncology Program at UHN and MSH. His research interests are primarily in the area of GI cancer genetics and he is co-Director of the Centre for Cancer Genetics at the Samuel Lunenfeld Research Institute, and co-PI of the Zane Cohen Familial Gastrointestinal Cancer Registry at MSH. He is also PI of the Ontario Pancreas Cancer Study, a member of the NIH funded Pancreas Cancer Genetic Epidemiology consortium, a population-based registry of pancreas cancer cases and their families which is now integrated with the International Cancer Genome Consortium at the OICR where he is Head of the Translational Research Initiative in pancreas cancer, termed PanCuRx. Dr. Gallinger also co-leads (with Dr. Jennifer Knox) the McCain Centre for Pancreas Cancer which supports the rapid diagnostic and treatment program at UHN.

Michael Goggins

Dr. Goggins is a Professor of Pathology, Medicine and Oncology at The Johns Hopkins University School of Medicine where he directs the Pancreatic Cancer Early Detection Research Laboratory. He is the Sol Goldman Professor of Pancreatic Cancer Research. He is an Attending Physician and Gastroenterologist at Johns Hopkins Hospital. His early detection research focuses on evaluating the potential clinical utility of measuring markers of early pancreatic cancer in pancreatic fluids and blood. He is the principal investigator of the multicenter Cancer of the Pancreas Screening-5, (CAPS5) study. He is supported by R01 and U01 grants from the National Cancer Institute. As a member of the pancreatic cancer research team at Johns Hopkins University, he was awarded the 2012 AACR Team Science award.

Thomas Gress

Thomas Gress completed his medical degree at the Philipps-University of Marburg in Germany, where he started his training in Internal Medicine and his basic research on pancreatic diseases. He performed a postdoctoral fellowship at the Genome Analysis laboratory at CR-UK in London (UK). Thereafter he moved to the University of Ulm in Germany where he completed his training in Internal Medicine and Gastroenterology and founded his research group working on translational and functional genome analyses in pancreatic cancer. Later he was appointed Professor of Gastroenterology at the University of Ulm and in 2006 Chair of Gastroenterology and Director of the clinical department of gastroenterology, endocrinology, metabolism and infectiology at the Philipps University of Marburg. His research covers translational and clinical aspects in pancreatology and gastrointestinal oncology, his department being a major referral center for GI-tumours and in particular pancreatic cancer and neuroendocrine tumours. He is the gastroenterologists of the Familial Pancreatic Cancer Registry (FaPaCa), one of the biggest European registries for familial pancreatic cancer, and coordinator of the Marburg ENETS-center of excellence for neuroendocrine tumours. He is associate editor for pancreatic diseases of the Journal "GUT".

Robert Grutzmann

Robert Grützmann is currently full Professor of surgery and Chairman of the Department of Surgery, University Hospital Erlangen, Germany. His main interest clinically as well as scientifically is pancreatic cancer, cystic and neuroendocrine tumors of the pancreas as well as chronic pancreatitis. He has published over 150 peer-reviewed papers.

Jin He

Jin He, M.D., Ph.D., is an assistant professor of surgery at the Johns Hopkins University School of Medicine. He is a surgical oncologist specializing in tumors from the Hepato-Pancreato-Biliary organs. He performs open as well as minimally invasive (robotic and laparoscopic) surgery, including the Whipple procedure. Dr. He received his medical degree from Beijing Medical University and a Ph.D. in oncology from Fudan University Shanghai Medical College. He completed the Halsted general surgery residency training at Johns Hopkins, followed by a ACGME accredited fellowship in complex general surgical oncology at Johns Hopkins. Dr. He's research focuses on personalized treatment through stratifying pancreatic tumors on their genetic features. He holds several patents in anti-cancer vascular targeting agents and has published extensively in peer-reviewed journals and lectured internationally. He serves on several national committees including the NCCN panel on neuroendocrine tumors and the Alliance for Clinical Trials in Oncology.

Joseph Herman

Dr. Herman is currently a Professor and Division Head ad-interim in the Department of Radiation Oncology at The University of Texas MD Anderson Cancer Center. He specializes in the treatment of pancreatic and hepatobiliary malignancies. Dr. Herman has been a writing member for the NCCN and ACR, AJCC guidelines committees and is currently on the medical advisory board for the pancreatic cancer action network and member of the NIH neuroendocrine and pancreas task forces. He serves as principal investigator for several institutional gastrointestinal protocols and a co-investigator (radiation oncology lead) for the Alliance borderline resectable cancer trial which is evaluating the role of SBRT. His major areas of clinical and basic research involve identification of novel biomarkers and integration of stereotactic body radiation therapy (SBRT) with immunotherapy and targeted therapies.

Ralph Hruban

Dr. Ralph Hruban is a Professor of Pathology and Oncology, the Director of The Sol Goldman Pancreatic Cancer Research Center, and the Baxley Professor and Director of the Department of Pathology at the Johns Hopkins University School of Medicine. He received his undergraduate degree from the University of Chicago and is a 1985 Johns Hopkins School of Medicine alumnus. He completed his residency training at Hopkins and he spent one year as a Fellow at Memorial Sloan-Kettering Cancer Center in New York. After completing his fellowship, Dr. Hruban returned to Johns Hopkins in 1990 to join the faculty. Dr. Hruban has received numerous awards including the Team Science Award from the American Association for Cancer Research (2013 and 2017). He is a member of the German National Academy of Sciences Leopoldina. In addition to his research efforts, Dr. Hruban created the Johns Hopkins Pancreatic Cancer Web Page (http://pathology.jhu.edu/pc).

Matthew Katz

Dr. Matthew HG Katz is currently Associate Professor, Chief of the Pancreatic Surgery Service and Vice Chair for Research in the department of Surgical Oncology at the University of Texas MD Anderson Cancer Center. His clinical and research interests focus on patients with pancreatic cancer. He has extensive experience in the design and conduct of clinical trials has led two national cooperative group studies of the effects of preoperative therapy on patients with advanced pancreatic cancer. He has published over 130 original articles that have described novel multi modality treatment approaches for patients with this disease. He has a thriving pancreatic surgery clinical practice.

Michael Kendrick

Dr. Michael Kendrick is Professor of Surgery at the Mayo Clinic in Rochester, Minnesota. He received his M.D. degree from George Washington University in Washington, DC. Doctor Kendrick completed his general surgery residency at the Mayo Clinic College of Medicine in Rochester, Minnesota. After residency, he received additional training as a Mayo Foundation Scholar in hepatobiliary surgery at the Mayo Clinic and in minimally invasive surgery at Mount Sinai in New York. His surgical interests include laparoscopic and open management of pancreatic and hepatobiliary diseases. Doctor Kendrick has published 20 book chapters and 151 peer-reviewed articles in the literature. He was named "Teacher of the Year in Surgery" for several years. He serves on multiple society and institutional committees and is the Chair of the Mayo Surgical Facilities Subcommittee. Doctor Kendrick is currently Chair of the Division of Hepatobiliary and Pancreas Surgery, and Director of the Advanced GI Minimally Invasive Surgery Fellowship Program at Mayo Clinic Rochester.

Masayuki Kitano

Dr. Masayuki Kitano graduated Tottori University School of Medicine, got medical degree in Japan in 1990 and earned PhD in 1994. From 2000, he began to work at Kinki University, and studied in the field of pancreatobiliary diseases, particularly endoscopic diagnosis and treatment. In 2016, he became a chairman and professor of Second Department of Internal Medicine (Gastroenterology), Wakayama Medical University. He and his colleagues made a novel EUS system equipped with contrast harmonic imaging which allowed visualization of tissue microcirculation, and reported role of EUS for diagnoses of pancreatobiliary and gastrointestinal diseases, particularly of small pancreatic cancers. By these works, he received the Ito Award from Japan Society of Ultrasonics in Medicine. He works as a faculty of the Japanese Society of Gastroenterology, of the Japan Gastroenterological Endoscopy Society, of the Japan Pancreas Society and of Japan Society of Ultrasonics in Medicine. He has authored / co-authored 172 peer reviewed English publications.

Richard Kozarek

Dr. Kozarek completed his gastroenterology fellowship at the University of Arizona-Phoenix VA Medical Center in 1978. He has been a member of the Section of Gastroenterology at Virginia Mason Medical Center since 1983, serving as Chief of GI for 15 years and currently as the Executive Director of the Digestive Disease Institute at Virginia Mason, as well as Clinical Professor of Medicine at the University of Washington. In a career spanning more than 40 years, Dr. Kozarek has contributed over 500 scientific papers, invited reviews, editorials, book chapters, as well as 12 medical texts to the medical literature on topics ranging from therapeutic endoscopy, inflammatory bowel diseases and practice economics. He is a past president of the American Society of Gastrointestinal Endoscopy (ASGE), and was the 2005 recipient of the ASGE's highest honor, the Schindler Award. Dr. Kozarek has served as the President of the Society for Gastrointestinal Intervention (SGI) and is a past president of the World Gastroenterology Organization (WGO).

Dung Le

Dr. Dung Le is an associate professor at the Sidney Kimmel Comprehensive Cancer Center at the Johns Hopkins University in Baltimore, Maryland. She is a member of the Gastrointestinal Malignancies Division of Medical Oncology.

Dr. Le received her undergraduate degree at Yale University and underwent internal medicine and oncology fellowship training at Johns Hopkins University. Her research interests include novel approaches to patients with gastrointestinal malignancies. Her main research focuses are on combination immunotherapy strategies or the use of predictive biomarkers to improve responses to immunotherapy. She has helped lead the development of programmed death-1 (PD-1) blockade in tumors with mismatch repair deficiency across disease types which led to the first biomarker selection tissue agnostic FDA approval. She is also testing multiple combinations with immune checkpoint blockade in the hopes of improving responses to immunotherapy in gastrointestinal malignancies.

Lindsey Manos

Lindsey Manos, DHSC, PA-C is a Lead Physician Assistant for the Hepatobiliary and Pancreas Surgery and Surgical Oncology Divisions at The Johns Hopkins Hospital. Lindsey is the Clinical Coordinator of The Johns Hopkins Multidisciplinary Pancreatic Cyst Program. Lindsey is certified by the National Commission on Certification of Physician Assistants and has a Doctor of Health Science degree, with a concentration in Organizational Behavior.

Yi Miao

Dr. Miao Yi, obtained his PhD from University of Leuven, Belgium (K.U.Leuven). He is Professor of Surgery, Chief Physician and Doctoral Tutor, and he enjoyed special government allowances from the State Council. He is the Chair of Department of Surgery, Nanjing Medical University. He is also Director of both Pancreas Center of The First Affiliated Hospital with Nanjing Medical University and the Institute of Pancreas of Nanjing Medical University. He is the Vice President of Chinese Pancreatic Surgery Association. He is also the Fellow of American College of Surgeons (FACS), the Fellow of Royal College of Surgeons in England (FRCS) and honorary Fellow of the International College of Surgeons (FICS(Hon)). He is the Standing Deputy Chief of Editor of "Chinese Journal of Digestive Surgery" and "China Journal of Practical Surgery". Besides, He is the Editor of "Chinese Journal of Surgical Journal", "Annals of Surgery Chinese Edition" and "Langenbeck's ARCHIVES OF SURGERY".

Quintus Molenaar

Quintus Molenaar is a professor of Hepato-Pancreato-Biliary Surgery at the Regional Academic Cancer Center Utrecht and the University Medical Center Utrecht, the Netherlands and is leading the HPB program performing approximately 200 HPB operations per year.

He is Co-founder and Board Member of the Dutch Pancreatic Cancer Group, Co-founder and Board Member of the Dutch Pancreatic Biobank, Board Member of the Dutch Hepato-Pancreato-Biliary Association and Member of the Research Commission of the Dutch Steering Group Liver Surgery. He is Principal Investigator of several national studies on the treatment of patients with resectable, locally advanced and recurrent pancreatic cancer. He is (co-) author of over 100 peer-reviewed papers and chapters in textbooks.

Masafumi Nakamura

Dr. Masafumi Nakamura is Professor at the Department of Surgery and Oncology of the Kyushu University, Fukuoka, Japan. He trained in Kyushu University, National Cancer Center, and Harvard University, and was appointed as the Chairman and Professor of Kawasaki Medical School before returning to Kyushu University. He is the President of Japanese Society for Endoscopic Pancreatic Surgery, Director of Japanese Society of Hepato-Biliary-Pancreatic Surgery, Japan Society for Endoscopic Surgery. He has organized the international difficulty score meeting for minimally invasive pancreatic resection in APHPBA 2017, and its fruits are preparing for publishing. His research interest is pancreatic cancer and pancreatic surgery. He has published more than 100 original papers in international journals about cancer biology and clinical studies focusing on pancreatic cancer and pancreatic surgery. His current topics are multidisciplinary therapy for advanced pancreatic cancer, minimally invasive pancreatic surgery and IPMN. He is a fellow of the American College of Surgeons, a Councilor of Asian Surgical Association, and a Councilor of Japanese several surgical and oncological societies including Japan Surgical Society. He is the Vice Editor-in-Chief of Journal of Japan Society for Endoscopic Surgery, an Editorial board of JHBPS, JLAST and IJCO.

Takao Ohtsuka

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Career

1994 MD, Kyushu University.
1999 Research Fellow, Department of Surgery and Oncology, Kyushu University.
2001 Research Fellow, Cancer Biology Program, Harvard University, MA, USA.
2004 PhD, Kyushu University
2009 Assistant Professor, Department of Surgery and Oncology, Kyushu University

Recent Publications

1. Tanaka M, Fernández-del Castillo C, Ohtsuka T, et al. Revisions of international consensus Fukuoka guidelines for the management of IPMN of the pancreas. ***Pancreatology*** 17; 738-753, 2017.
2. Date K, Ohtsuka T, et al. Molecular evidence for monoclonal skip progression in MD-IPMNs of the pancreas. ***Ann Surg*** 265; 969-977, 2017.
3. Segersvard R, Ohtsuka T, Rangelova E, Tanaka M. Comparison between IAP and European guidelines for the management of cystic lesions of the pancreas. In: Chiaro MD, et al (ed): ***Cystic Tumors of the Pancreas*** 171-175, Springer, Switzerland, 2016.

Eileen O'Reilly

Dr. Eileen M. O'Reilly serves as the Associate Director for Clinical Research for the David M. Rubenstein Center for Pancreas Cancer and is an Attending Physician and Member at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York and Professor of Medicine at Weill Cornell Medical College. Dr. O'Reilly has pancreatic and hepatobiliary malignancies as the major focus of her research and clinical activities. Research initiatives include integration of molecular and genetic-based therapies for the treatment of pancreas cancer along with identification of biomarkers that maybe used to select therapy. Dr. O'Reilly is the Principal Investigator of multiple phase I, II and III trials in pancreas cancer and has authored many articles, editorials and book chapters. Dr. O'Reilly's institutional responsibilities include Associate Chairpersonship of MSKCC's Institutional Review & Privacy Board (IRB), Chair of the Data and Safety Monitoring Committee (DSMC) and Chair of the Continuing Medical Education (CME) committee. Nationally, Dr. O'Reilly is the Co-Chair of the Alliance Co-Operative Group Gastrointestinal Cancers Committee, and serves on the Gastrointestinal Cancers Steering Committee (GISC), Scientific Advisory Board of the Pancreatic Cancer Action Network, NCCN Pancreas panel and the Board of the National Pancreas Foundation.

Nick Papadopoulos

Dr. Nickolas Papadopoulos is internationally known as a co-discoverer of the genetic basis of the predisposition to hereditary nonpolyposis colon cancer (HNPCC), one of the most common hereditary forms of cancer, earlier in his career. He is known for the development of diagnostic tests and he is considered an expert in cancer genetics and diagnostics. He was part of the interdisciplinary team that was first to sequence all of the protein coding genes, determine genetic alterations and construct expression profiles in multiple tumors of different cancer types. Currently, he is focused on translating the genetic information derived from cancer genome analyses to clinical applications in early detection, diagnosis and monitoring of cancer. He is a co-developer of sensitive methods for the detection of tumor DNA in liquid biopsy. He is also the co-founder of two companies that develop diagnostics for cancer.

Walter Park

Dr. Park is an Assistant Professor of Medicine at Stanford University, where he is Medical Director of the Pancreas Clinic within the Stanford Digestive Health Center. As a pancreatologist, he focuses on the diagnosis and management of a spectrum of pancreatic conditions including acute and chronic pancreatitis to pre-malignant pancreatic cysts. His research focuses on developing and validating novel biomarkers for early diagnosis of advanced cystic neoplasms and early pancreas cancer. He is a Principal Investigator within the NIH Consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreas Cancer (CPDPC), and Pancreatic Cancer Detection Consortium (PCDC).

Vincent Picozzi

Dr. Vincent J Picozzi, MD MMM directs the Pancreas Center of Excellence at Virginia Mason. A Yale University graduate (*summa cum laude, Phi Beta Kappa*), Dr. Picozzi trained at Stanford and Harvard University (Brigham and Women's Hospital), and holds a MMM degree, *Delta Omega*, (Tulane University). Dr. Picozzi has one of the largest US pancreaticobiliary oncology practices . He has received numerous clinician accolades, directs an active clinical research program, has published over 100 papers and abstracts, and has been a featured speaker at virtually every major national clinical oncology meeting. Dr. Picozzi has recently held national leadership positions including Educational Chair for Non-Colorectal Cancers (ASCO and the GI Oncology Symposium 2016), the Executive Committees of the Pancreas Cancer Research Team (PCRT) and Pancreatic Cancer Action Network (PANCAN) (Past Chairman and current Clinical Initiatives Committee Chair). He is co-principal investigator and Clinical Trials Consortium Chairman for the Precision Promise project.

Michelle Reid

Dr. Michelle Reid is a cytopathologist and surgical pathologist with subspecialty expertise in pancreatobiliary tract pathology who has been in practice for more than 10 years. After completing a cytopathology fellowship at Memorial Sloan Kettering Cancer Center in 2005, she joined the faculty at Medical College of Georgia and later Emory University Hospital in 2010. She is currently Professor of Pathology, Director of Cytopathology and Director of the Cytopathology Fellowship at Emory University Hospital. Dr. Reid has numerous peered-reviewed journal publications and book chapters on pancreatobiliary tract pathology. She has given courses, workshops and invited lectures on pancreatobiliary pathology at various national and international venues including the USCAP, CAP, ASCP, ASC, ECP and the IAP. Her experience and expertise as a cytopathologist and surgical pathologist with research interest in pancreatobiliary pathology give her a unique perspective on the challenges faced by pathologists who routinely interpret these specimens, as well as the importance of accurate diagnosis of lesions involving these sites, through the identification of key discerning cyto-histomorphologic features that will allow for better classification and prognostication of tumors.

Flavio Rocha

Dr. Rocha is a surgical oncologist and hepatopancreatobiliary surgeon in the Section of General, Thoracic and Vascular Surgery and Director of Research in the Digestive Disease Institute at Virginia Mason Medical Center. He also holds an appointment as a Clinical Assistant Professor of Surgery at the University of Washington. He attended the Pritzker School of Medicine at the University of Chicago. He then completed a residency in general surgery and postdoctoral fellowship in tissue engineering at the Brigham and Women's Hospital. After residency, he pursued a surgical oncology and hepatopancreatobiliary surgery fellowship at Memorial Sloan-Kettering Cancer Center in New York City. His clinical practice involves benign and malignant disease of the liver, bile ducts and pancreas. As an investigator at the Benaroya Research Institute, his research is focused on biomarker discovery and novel therapeutics in pancreaticobiliary cancer. He has been funded by ASCO and the Cholangiocarcinoma Foundation. He currently serves on the editorial boards of HPB, Journal of Surgical Oncology and PLoS ONE. He is also a member of several surgical societies including the SSO, AHPBA, and SSAT. He serves on the Pancreas Task Force at the NCI and sits on the executive committee of the International Cholangiocarcinoma Research Network.

Grace Saunders

Grace Saunders is the President of the Joseph C. Monastra (JCM) Foundation for Pancreatic Cancer Research as well as a member and advocate of the World Pancreatic Cancer Coalition (WPCC). Grace has been the President of the JCM Foundation for the past 10 years. In the last meeting with the WPCC in Montreal, Grace participated in extensive discussions with many pancreatic cancer advocacy organizations. Over the 15 years with the JCM Foundation, she has worked with pathologists and scientists at John Hopkins Health Institutes and Emory University to continue to increase funding for pancreatic cancer research. She has worked at a local level in multiple different cities and is currently establishing new fundraisers in Chicago. The World Pancreatic Cancer Coalition was started in 2013 and has more than 70 foundations organizing activities in patient advocacy, services, education, and research. WPCC's goal is to bring together pancreatic cancer patient advocacy organizations from around the world to discuss working together to raise global pancreatic cancer awareness and work collaboratively to support each other's effort.

Tyler Saunders

Tyler Saunders is a 4th year medical student, grandson of Joseph C. Monastra, and advocate for the Joseph C. Monastra (JCM) Foundation for Pancreatic Cancer Research. Tyler is concluding his medical school education and going to start residency in July in Internal Medicine in Chicago. His career goals currently are focused on lifestyle as the staple of medical care and prevention of disease. Before starting medical school, Tyler worked at Johns Hopkins in the lab of Christine Iacobuzio MD, PhD and Christopher Wolfgang MD, PhD. When Tyler was eleven his grandfather, Joseph C. Monastra, was diagnosed with Stage 4 pancreatic cancer. His grandfather's influence continues to have tremendous impact on his life and career goals. Tyler's story describes how pancreatic cancer and the formation of this foundation have changed his life. The JCM Foundation was started fifteen years ago and continues to raise money for early detection and awareness of pancreatic cancer. The foundation has recently joined the World Pancreatic Cancer Coalition, the largest group of pancreatic cancer foundations in the world.

Aldo Scarpa

Prof. Scarpa is Chair of the Department of Pathology at Verona University and Director of the ARC-Net Centre for applied research on cancer at Verona University, Italy. He is leader of the Italian effort in the International Cancer Genome Consortium funded by the Italian Ministry of Research and Ministry of Health, Coordinator of the Italian National Consortium for innovative molecular diagnostics in pancreas cancer funded by the Associazione Italiana per la Ricerca sul Cancro (AIRC). The research focus of Prof. Scarpa is the translation into clinical practice of molecular subclassifications of cancers with prognostic-therapeutic relevance. He has published over 400 peer-reviewed papers. His interest in neuroendocrine neoplasms dates back to 1992 and ranges from histopathology and staging/grading to molecular characterisation.

Thomas Smith

Dr. Smith is an oncologist and palliative care specialist with a lifelong interest in better symptom management and improving access to high quality affordable care. He is the Director of Palliative Medicine for Johns Hopkins Medicine, charged with integrating palliative care into all the Johns Hopkins venues. The PC consult service sees over 1500 new patients a year, and a research agenda with "Scrambler Therapy" for pain, palliative care for patients on Phase I drug trials, topical gapabentin to prevent neuropathy (CIPN), and others. Dr. Smith has been recognized in "Best Doctors in America" for many years and is a Fellow in the American College of Physician, the American Society of Clinical Oncology and the American Academy of Hospice and Palliative Medicine. He received the ACS Trish Greene Award for "outstanding research that benefits cancer patients and their families" and was recognized as a "Visionary in Palliative Care" by AAHPM.

Kyoichi Takaori

Dr. Kyoichi Takaori is a pancreatic surgeon who has extensive experiences of open, laparoscopic, and robotic surgery. His academic career includes Professor of Surgery at Asahi University and Assistant Professor of Physiology and Biophysics at University of Arkansas for Medical Sciences. Throughout his career, he has struggled to improve the prognosis of pancreatic cancer, which is known as the worst malignancy. First, he has focused on early detection of pancreatic cancer and founded a Japanese Familial Pancreatic Cancer Registry in 2013. Second, he has endeavored to accelerate innovation in pancreatic surgery. In order to increase resectability and to improve local control, he has refined artery-first pancreatoduodenectomy by utilizing the "Tiger's Den approach" and developed new techniques of artery-first distal pancreatectomy and artery-first DP-CAR. Third, he is a great believer of multi-disciplinary approach and presently directing the multi-disciplinary team as the Head of Pancreatic Cancer Unit at Kyoto University Hospital.

David Ting

David Ting is currently a gastrointestinal medical oncologist at the Massachusetts General Hospital (MGH) Cancer Center and assistant professor of medicine at Harvard Medical School. After receiving his B.S. in chemical engineering and biology from MIT, he completed his medical degree at Harvard Medical School with *magna cum laude* honors. During his undergraduate and medical school studies, he trained with Dr. Robert Langer at MIT on drug delivery platforms and did a HHMI fellowship with Dr. George Daley formerly at the Whitehead Institute on hematopoietic stem cells. He completed internal medicine residency at the MGH and medical oncology fellowship in the combined Dana-Farber Cancer Institute and MGH Cancer Center program. He moved on to post-doctoral training with Daniel Haber's group at the MGH Cancer Center characterizing pancreatic circulating tumor cells (CTCs) and primary tumors with RNA-sequencing. His work revealed aberrant expression of non-coding satellite RNAs in pancreatic cancer as a potential novel cancer biomarker, and he has characterized the transcriptional programs in pancreatic CTCs with single cell RNA sequencing. He currently runs his own independent group at the MGH Cancer Center with a focus on CTCs and non-coding RNAs in gastrointestinal cancers as novel biomarkers and therapeutic targets.

William Traverso

William Traverso, MD, FACS is a graduate of the UCLA Medical School (1973), and Surgery Residency (UCLA, 1978). He has authored more than 250 articles on the treatment of pancreatic and biliary diseases.

He is past president of the Society for Surgery of the Alimentary Tract (SSAT), Society of the American Gastrointestinal Endoscopic Surgeons (SAGES), North Pacific Surgical Association (NPSA), and the American College of Surgeons, Washington Chapter. He was co-director of the Pancreas Club for 15 years.

Until his retirement in July 2015, Dr. Traverso served as the Director for the Center for Pancreatic Diseases for 5 years (St. Luke's Health Care System, Boise) following 25 years at the Virginia Mason Medical Center in Seattle. Since 2001 along with his Virginia Mason colleagues in gastroenterology and medical oncology, he has organized the Pancreas Cancer International Conferences in Seattle (2001), Pisa (2005), Rome (2009), Kyoto (2011), Verona (2014) and Glasgow (2016).

David Tuveson

David Tuveson is Director of the Cancer Center and the Roy J. Zuckerberg Professor of Cancer Research at Cold Spring Harbor Laboratory, and the Chief Scientist at the Lustgarten Foundation. Dr. Tuveson obtained a bachelors degree in chemistry at M.I.T., followed by M.D. and Ph.D. degrees at Johns Hopkins. Dr. Tuveson was a medical resident at Brigham and Women's Hospital and a medical oncology fellow at Dana-Farber/Harvard Cancer Center. During his post-doctoral years in Boston, Dr. Tuveson co-developed KIT inhibitors for gastrointestinal stromal tumors with George Demetri. Simultaneously, he generated several widely-used mouse cancer models with Tyler Jacks. As an independent investigator, his lab developed the first mouse models of ductal pancreatic cancer at the University of Pennsylvania. Subsequently, Dr. Tuveson was recruited to the University of Cambridge to develop preclinical and clinical therapeutic strategies for pancreatic cancer. In Cambridge, his lab identified a variety of parameters that limit therapeutic efficacy in pancreatic cancer, including poor drug delivery and survival factors in the microenvironment. Dr. Tuveson returned to the USA to direct the Cancer Therapeutics Initiative at CSHL and to serve as Director of Research for the Lustgarten Foundation. He continues to practice medical oncology with an adjunct appointment at MSKCC. His awards include the Rita Allen Scholarship and the Jan Waldenström Award, and the Hamdan Award.

Bert Voglestein

Dr. Bert Vogelstein attended the University of Pennsylvania, where he graduated with distinction in mathematics. He obtained his medical degree at the Johns Hopkins University School of Medicine and performed his residency in pediatrics at the Johns Hopkins Hospital. Following his clinical training, Dr. Vogelstein completed a post-doctoral fellowship at the National Cancer Institute, focusing on the development of new approaches to study human cancers. He is currently the Do-Director of the Ludwig Center for Cancer Genetics & Therapeutics at the Johns Hopkins Kimmel Cancer Center, a Lustgarten Foundation Distinguished Scholar, and an Investigator of the Howard Hughes Medical Institute.

Dr. Vogelstein's current research focuses on the genetic basis of human cancers and the use of this knowledge to improve diagnosis and management of patients with these diseases. He is a member of the American Academy of Arts & Sciences, the National Academy of Sciences, the American Philosophical Society, the National Academy of Medicine and the European Molecular Biology Organization (EMBO). His advisory roles have included Chairmanships of the National Research Council Committee on the Biological and Biomedical Applications of Stem Cell Research and the Board of Scientific Counselors of the National Human Genome Research Institute.

Matthew Weiss

Matthew Weiss, MD, FACS is an Associate Professor of Surgery at the Johns Hopkins University School of Medicine. He is board-certified in general surgery and dual fellowship-trained in both complex surgical oncology and hepatopancreatobiliary (liver, pancreas and bile ducts) surgery. He trained in general surgery at the Johns Hopkins Hospital and completed a research fellowship at the Massachusetts General Hospital in immunology. He completed clinical fellowships at Memorial Sloan-Kettering Cancer Center in both surgical oncology and hepatopancreatobiliary surgery. His clinical interests include both benign and malignant tumors of the pancreas, liver, bile ducts, and gallbladder.

Jordan Winter

Dr. Jordan M. Winter received his undergraduate degree in Chemistry from Princeton University and attended the Weill Medical College of Cornell University. He trained in General Surgery at Johns Hopkins, and spent additional years as a post-doctoral research fellow in Oncology. Dr. Winter received specialty fellowship training in Surgical Oncology at the Memorial Sloan-Kettering Cancer Center. In 2011, Dr. Winter was recruited as an Assistant Professor of Surgery at Thomas Jefferson University and was promoted to Associate Professor in 2014. He serves as a Co-Director of the Jefferson Pancreas, Biliary and Related Cancer Center, the GI Multidisciplinary Group in the Sidney Kimmel Cancer Center, and the Multidisciplinary Pancreas Cancer Clinic. Dr. Winter's clinical interest is in the management of pancreatic and related cancers. He has led clinical oncology trials, and maintains a basic science lab, funded by the NIH, American Cancer Society, and industry.

Christopher Wolfgang

Christopher L. Wolfgang, MD, PhD is the Chief of the Division of Hepatobiliary and Pancreas Surgery and the Vice Chair for Surgical Oncology at Johns Hopkins. He is the John L. Cameron Professor of Surgery and holds secondary appointments as a Professor of Pathology and Oncology. Dr. Wolfgang graduated from Temple School of Medicine in 1998 with a combined MD/PhD degree (biochemistry) and completed his residency in 2004 at Penn State. He went on to complete an Assistant Chief of Service fellowship in advanced gastrointestinal surgery in 2005. He has remained at Johns Hopkins ever since and spends the majority of his time as a clinical surgeon with a focus on pancreatic neoplasms. In addition, he leads a research group focused on understanding the biology of pancreatic cancer and cystic neoplasms of the pancreas.

Brian Wolpin

Dr. Wolpin is a medical oncologist and translational cancer researcher at Dana-Farber Cancer Institute and Harvard Medical School (Boston, MA). He obtained his M.D. from Harvard Medical School and completed a residency in internal medicine at Brigham and Women's Hospital. He completed fellowship training in medical oncology at Dana-Farber Cancer Institute (DFCI) and returned to Brigham and Women's hospital to serve as chief medical resident. Subsequently, he received a M.P.H. from Harvard School of Public Health. His research program is focused on understanding the factors that promote initiation and progression of pancreatic ductal adenocarcinoma. These studies involve evaluation of blood-based circulating markers, germline alterations, and somatic alterations in hundreds to thousands of subjects. Dr. Wolpin is Director of the Gastrointestinal Cancer Center and Director of the Hale Center for Pancreatic Cancer Research at DFCI, and an Associate Professor of Medicine at Harvard Medical School. He also serves as co-Principal Investigator for the Pancreatic Cancer Cohort Consortium, director of a large pancreatic cancer biospecimen bank at DFCI, and Director of the Pancreas and Biliary Tumor Center at Dana-Farber/Brigham and Women's Cancer Center. His research has been funded by the National Cancer Institute, Howard Hughes Medical Institute, Lustgarten Foundation, ASCO Conquer Cancer Foundation, Pancreatic Cancer Action Network, and U.S. Department of Defense. Dr. Wolpin's clinical practice involves the care of patients with gastrointestinal cancers, with a particular focus on pancreatic cancer. He has held several leadership positions related to clinical expertise, including membership on the Alliance/CALGB Gastrointestinal Cancer Committee, NCCN Guidelines Committee for Pancreatic Adenocarcinoma, and National Cancer Institute Pancreas Cancer Task Force.

Laura Wood

Laura D. Wood, MD, PhD is an Assistant Professor in the Department of Pathology, Division of Gastrointestinal and Liver Pathology at the Johns Hopkins University School of Medicine. Dr. Wood received her BS in Biology from the College of William & Mary, graduating Summa Cum Laude with membership in Phi Beta Kappa. She then went on to earn both her MD and PhD from The Johns Hopkins University School of Medicine, with membership in Alpha Omega Alpha. She completed her PhD research in the laboratory of Dr. Bert Vogelstein, where she led the first whole exome sequencing studies in human cancers. Dr. Wood then went on to complete residency in Anatomic Pathology (serving as Chief Resident in her final year) and fellowship in Gastrointestinal and Liver Pathology at The Johns Hopkins Hospital. Now, she leads her own basic science laboratory focused on molecular characterization of pancreatobiliary cancers and their precursor lesions. In addition, she signs out clinical specimens on the Gastrointestinal and Liver Pathology services.

Hiroki Yamaue

Dr. Hiroki Yamaue graduated Wakayama Medical University in 1981. He received PhD degree in 1989 from Wakayama Medical University. After graduation, he trained HBP surgery, especially pancreatic surgery. In 2001, he was appointed as Professor of Second Department of Surgery. From 2014 to 2017, He has been additionally appointed the Director of Education and Research of the Wakayama Medical University. He is currently Professor of Second Department of Surgery, Division of Digestive surgery, Wakayama Medical University School of Medicine in Wakayama, Japan, Where he is also the Director of Wakayama Medical University Hospital from 2017. He has been actively involved in the basic and clinical research of pancreatic cancer. His major interest of research is treatment of pancreatic cancer. He has been interested not only in surgery but also in Cancer Immunology. He has contributed extensively in professional activities in his area of expertise. He has published more than 400 papers in peer-reviewed journals including Annals of surgery and has conducted many clinical trials.

Jun Yu

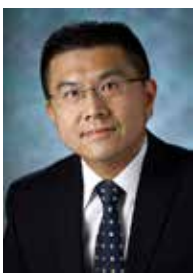
Jun Yu, MD, PhD is an Assistant Professor in the Department of Surgery, Division of Hepatobiliary and Pancreas Surgery at the Johns Hopkins University School of Medicine. He is the Chief Scientist of Division of Hepatobiliary and Pancreas Surgery at Johns Hopkins. Dr. Yu received his medical degree from Gannan Medical University and a PhD in Surgery and Oncology from Kyushu University School of Medicine. His research focuses on understanding the biology of pancreatic cancer and cystic neoplasms of the pancreas, and on detecting the actionable mutations/pathways for the patients with pancreatic cancer in a personalized therapeutic strategy. He developed several novel sequencing technologies, including digital Next-Generation Sequencing (dNGS) and Single-cell Next-Generation Sequencing (scNGS). He is the Principle Investigator of the Pancreatic Cancer Precision Medicine Center of Excellence (PMCoE) at Johns Hopkins. In addition, he serves as a Committee Member of the Clinical Research Review Committee at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins.

Herbert Zeh

Herbert J. Zeh III, MD, is chief of the Division of Gastrointestinal (GI) Surgical Oncology at UPMC CancerCenter, Associate Director of UPMC Hillman Cancer Center, Senior Director of UPMC Surgical Services and Watson Family Professor of Surgery. Dr. Zeh specializes in cancers and diseases of the stomach, liver, pancreas, and duodenum, and practices state-of-the-art robotic technology.

Board-certified in surgery, Dr. Zeh received a medical degree from the University of Pittsburgh School of Medicine. He completed post-graduate training in advanced GI surgery and surgical oncology at The Johns Hopkins Hospital in Baltimore, where he served as senior and chief resident, as well as the Society of Surgical Oncology fellow. Dr. Zeh served as a surgical oncology medical staff fellow at the National Cancer Institute - Surgery Branch in Bethesda, MD.

Dr. Zeh is a member of several professional organizations, including the American Surgical Association (ASA), Society of Surgical Oncology (SSO), American Society of Clinical Oncology (ASCO), the Society of University Surgeons (SUS), and the Pancreas Club. Dr. Zeh had authored over 110 peer reviewed articles and book chapters. He directs a translational research laboratory examining Damage Associated Molecular Pattern molecules (DAMP) in the setting of pancreatic cancer. In addition, Dr. Zeh is principle investigator on several Phase I and II clinical trials in pancreatic cancer. Dr. Zeh, together with his team at UPMC, has accumulated one of the world's largest experiences with robotic assisted pancreatic resections.



Lei Zheng

Lei Zheng, M.D., Ph.D. is an associate professor of Oncology and Surgery in the Gastrointestinal Oncology Program at the Johns Hopkins University School of Medicine and lead a large translational program that focuses on the preclinical and clinical development of novel vaccine- and antibody-based rational combination immunotherapy for gastrointestinal cancers at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins. He is Co-director of the Pancreatic Cancer Precision Medicine Program, a Pancreatic Cancer Center of Excellence (PMCoE) program at Johns Hopkins and also leads a personalized immunotherapy/relational database program at the Bloomberg-Kimmel Institute for Cancer Immunotherapy. His clinical work is focused on multidisciplinary management for pancreatic cancer, bile duct cancer, liver metastases, and gastric cancer. He is the founding Editor-in-Chief of Annals of Pancreatic Cancer.

Steven Gallinger: Familial pancreatic cancer/germline mutation carriers

Much has been revealed about the germline genetic basis of pancreatic ductal adenocarcinoma (PDAC), including the nature of low penetrant predisposition alleles discovered by genome-wide association study (GWAS), and important higher penetrant tumor suppressors including *BRCA1/2*, *p16*, *PALB2*, *ATM*, DNA mismatch repair (MMR) genes, and others. A fairly unified, and generally conservative, definition of familial pancreas cancer (FPC) has fostered attempts to identify PDAC-specific causative genes, with limited success, likely due to genetic heterogeneity, misclassification of cases, and challenges associated with linkage studies (i.e., lack of biospecimens) due to the rapidly fatal nature of the disease.

Recent efforts in 'personalised medicine' and the widespread availability of germline and somatic panel testing, have triggered much interest in 'routine' testing of PDAC to identify carriers of predisposition genes. Identifying PDAC cases with germline (and somatic) *BRCA/PALB2* and MMR mutations is relevant for selection of specific therapies in advanced disease, testing unaffected at-risk family members, and enrollment in screening programs.

Laura Wood: Genetic progression of pancreatic neoplasia

Pancreatic cancer is caused by the accumulation of somatic mutations in oncogenes and tumor suppressor genes, and it arises through non-invasive precursor lesions, including pancreatic intraepithelial neoplasia (PanIN) and intraductal papillary mucinous neoplasm (IPMN). Examination of genetic alterations in these precursor lesions can determine the timing of somatic mutations in pancreatic tumorigenesis and provide insights into clonal evolution in pancreatic neoplasia. This presentation will discuss genetic analysis of pancreatic cancer precursor lesions, including analyses of progression to high-risk lesions and intratumoral genetic heterogeneity.

Ralph Hruban: Using clearing to define the three-dimensional anatomy & pathology of the pancreas

Pathologists study diseases in two dimensions. The standard microscope slide frames our view and narrows our imagination and our understanding of multi-dimensional diseases. Three-dimensional visualization of diseases will increase our comprehension of the biology of human diseases. It will allow us to accurately measure three-dimensional lesions, and to define more accurately the relationships of cells and tissues.

We present a method to immunolabel and then clear intact thick sections of normal and diseased surgically resected human pancreatic parenchyma. Dibenzyl ether (DBE) is used to clear stroma-rich human tissues, and the penetration of antibodies (rabbit anti-human CK19) into dense pancreatic tissue is facilitated using centrifugation and by gradually increasing antibody concentrations.

This methodology was used to define the branching patterns of normal pancreatic ducts, to measure the volume of small pancreatic intraepithelial neoplasia (PanIN) lesions, to validate distinct patterns of invasion (mesenchymal and tubular), to demonstrate cancerization of the ducts, and to reveal that invasive cancer tends to grow in the stroma immediately parallel to muscularized vessels.

The addition of multiple markers using multi-color immunofluorescence will open the door to a diverse array of processes, from the mechanisms underlying vascular invasion, to the three-dimensional relationships of neoplastic cells to immune responses.

David Tuveson: Models of human pancreatic cancer biology and medicine

Pancreatic ductal adenocarcinoma (PDAC) is almost uniformly lethal, and surgical resection of localized tumors followed by adjuvant chemotherapy is currently the only curative regimen. Unfortunately, most patients are diagnosed with advanced and surgically unresectable PDAC, due to a lack of early detection methods. Furthermore, such patients oftentimes have a rapid disease course due to the ineffectiveness of therapies. We developed mouse and organoid models of PDAC to explore the biological aggressiveness of PDAC and to address these clinical challenges. Organoids generated from primary tumors and paired metastases revealed chromatin alterations that controlled the expression of genes involved in foregut and neural development. Mechanistically, these changes were

linked to the increased expression of a suite of developmental transcription factors during metastasis, and reveal new therapeutic opportunities for preventing or treating PDAC metastasis.

To investigate improved clinical approaches for pancreatic cancer, we have assembled a large collection of patient derived PDAC organoids. We find that the combination of therapeutic testing and transcriptional analyses identifies groups of patients who are more prone to respond to available therapeutics. Furthermore, our signatures predict clinical outcomes in PDAC patients who were retrospectively assessed, prompting a further investigation of organoid profiling as a means to prospectively increase survival in patients.

Lei Zheng: Dissect the tumor microenvironment for a precision immunotherapy of pancreatic cancer

Pancreatic cancer is characterized as an immune-quiescent tumor or a "cold" tumor. The tumor microenvironment (TME) of pancreatic cancer becomes pro-cancerous and also becomes immunosuppressive. Thus, it has been a challenge to treat pancreatic cancer with immunotherapy such as the checkpoint inhibitors. Science-driven clinical trials have helped further dissecting the TME and showed that vaccine therapy may reprogram the "cold" TME of pancreatic cancer by converting it into a lymphoid inflamed TME. However, a lymphoid inflamed TME does not appear to be sufficient to arouse a strong anti-tumor immune response, which succumbs to the immunosuppressive myeloid cells. Precisely dissecting the TME may hold the key to a success in treating pancreatic cancer with precision immunotherapy.

Michelle Reid: Pathologic subtypes of PDAC

Pancreatic cancer is the third leading cause of cancer-related deaths in the US. The vast majority of these are pancreatic ductal adenocarcinomas (PDAC), which is morphologically "pancreatobiliary type" and tubule-forming and arise *de novo*. Molecular profiling studies have recently identified several distinctive subtypes of PDAC such as cribriform, papillary and foamy-gland. Adenosquamous and osteoclastic/sarcomatoid carcinomas are close relatives of PDAC (and often coexist with ordinary PDAC), however they are classified separately because of their divergent behavior, prognosis and therapeutic targets. The highly aggressive adenosquamous carcinomas are of "basal" type by molecular profiling. These morphologic tumor types will be discussed. Additionally, while some pancreatic carcinomas are of ductal origin they have vastly different characteristics from conventional PDAC including a more protracted clinical outcome. These include colloid carcinoma which shows characteristic intestinal differentiation (diffuse MUC2 and CDX2 expression), and medullary carcinoma which is driven by microsatellite instability. A small percentage (~5%) of PDACs arise in association with tumoral intraepithelial neoplasms including intraductal papillary mucinous neoplasm (IPMN), mucinous cystic neoplasm (MCN) and intraductal tubulopapillary neoplasm (ITPN). These tumors have different biology and prognosis. Non-ductal pancreatic cancers including acinar, neuroendocrine, solid-pseudopapillary, pancreatoblastoma, and secondary tumors must all be carefully distinguished from PDACs, as they show entirely different biology.

David Ting: Impact of stromal microenvironment on pancreatic cancer cell heterogeneity

Single cell technologies have described heterogeneity across tissues, but the spatial distribution and forces that drive single cell phenotypes has not been well defined. We integrated different single cell technologies to investigate tumor heterogeneity of human pancreatic cancer (PDAC). Patient-derived PDAC cells co-cultured at different ratios with cancer associated fibroblasts (CAFs) were found to heterogeneously acquire proliferative (PRO) and invasive (EMT) phenotypes. Single cell RNA-seq enabled the identification of a novel cell phenotype with upregulation of both PRO and EMT programs, a double positive (DP) phenotype. Combined mass spectrometry-based phosphoproteomics and single cell mass cytometry (CyTOF) demonstrated enrichment of MAPK and STAT3 signaling pathways in driving different PRO and EMT phenotypes with dual activation in DP cells. Functional studies in mouse models confirmed the heterogeneous activation of PRO and EMT programs with different patterns of tumor growth and metastasis in mice orthotopically xenografted with distinct PDAC:CAF ratios. To evaluate the generalizability of these cell subpopulations, we performed RNA-ISH for EMT (FN1) and PRO (MKI67) across 195 human PDAC primary tumors and

scored 319,626 cancer cells revealing significant heterogeneity of PRO, EMT, and DP cells between patients. Single-cell analysis within the context of tissue architecture revealed these cells were grouped together in discrete tumor glands. We classified 8 distinct types of tumor glands in these primary tumors, which revealed significant inter and intra-tumor heterogeneity that was linked with patient survival. Altogether, this study has revealed the importance of variation of stromal content in driving PDAC heterogeneity.

Toru Furukawa: Pathobiology of intraductal neoplasms of the pancreas

Macroscopic intraductal neoplasms are classified into intraductal papillary mucinous neoplasms (IPMNs) and intraductal tubulopapillary neoplasms (ITPNs). IPMNs are characterized by dilated ducts filled with mucin and lined with dysplastic papillary epithelia. ITPNs are characterized by dilated ducts with a clogged solid tumor that is composed of tubulopapillary neoplastic glands. These neoplasms are clinically well described; however, their molecular pathology has not been uncovered until recently. We investigated genetic alterations in these neoplasms by means of the next-generation sequencing technology and found distinct molecular phenotypes between them. Exome sequencing uncovered frequent mutations in *GNAS*, *KRAS*, and *RNF43* in IPMNs. *GNAS* mutations were found in 48% (82/172) of IPMNs, mostly R201H or R201C and rarely R201S. *KRAS* mutations were found in 56% (96/172), mostly G12D or G12V and rarely Q61H. *RNF43* mutations were found in 14% (8/57) of IPMNs, mostly truncating mutations (frameshift or nonsense mutations) and rarely missense mutations. Interestingly, the *RNF43* mutations were associated with *GNAS* mutations, in which both mutations were overlapped. We proved that expression of the mutant *GNAS* was associated with hypersecretion of mucin in human cells and generation of IPMN in a genetically engineered mouse model. In ITPNs, we uncovered recurrent mutations in genes associated with pathways of PI3K (*PIK3CA*, *PIK3CB*, and *PTEN*), chromatin remodeling (*MLL1*, *MLL2*, *MLL3*, *BAP1*, *PBRM1*, *EED*, and *ATRX*), WNT (*CTNNB1*, *APC*, and *AXIN1*), GAS6-AXL (*AXL*), Rho (*ARHGAP26*, *ARHGAP35*, *ROR2*, and *KALRN*), tyrosine kinase (*KDR*, *FLT4*, *NTRK*, and *RET*), and ephrin (*EPHA2* and *EPHB3*). These results indicated distinct molecular features between IPMN and ITPN.

Aldo Scarpa: The genomic landscape of PanNETs

Pancreatic NETs (PanNETs) are characterized by recurrent features, as inactivation of genes *MEN1*, *ATRX*/*DAXX*, and hyperactivation of the PI3K/mTOR pathway. The International Cancer Genome Consortium effort on PanNETs provide a first snapshot of how heterogeneous is the combination of genetic alterations that drive this tumour type, yet converging into four pathways whose alteration has been enriched by newly discovered mechanisms. Whole-genome sequencing of 102 primary PanNETs and validation on additional 62 cases defined the genomic events that characterize their pathogenesis. The mutational signatures PanNET harbour include a deficiency in G:C > T:A base excision repair due to inactivation of MUTYH, which encodes a DNA glycosylase. Clinically sporadic PanNETs contain a larger-than-expected proportion of germline mutations, including previously unreported mutations in the DNA repair genes *MUTYH*, *CHEK2* and *BRCA2*. Together with mutations in MEN1 and VHL, these mutations occur in 17% of patients. Somatic mutations, including point mutations and gene fusions, are commonly found in genes involved in four main pathways: chromatin remodelling, DNA damage repair, activation of mTOR signalling (including previously undescribed *EWSR1* gene fusions), and telomere maintenance. In addition, gene expression analyses identified a subgroup of tumours associated with hypoxia and HIF signalling. While calling for further integration of genetic and epigenetic analyses, these data allow to reconcile previous findings in a defined frame, and may provide clinical research with markers for patients stratification and to guide targeted therapy decisions.

Jin He: Workup of PNET

In this talk, we review the epidemiology and diagnosis of PNET. We will discuss the role of endoscopic ultrasound (EUS)/fine needle aspiration (FNA) in the diagnosis. We will discuss the role of octreotide scan and Ga66 DOTATATE scan in the staging workup. Indications of genetic workup.

Elliot Fishman: MDCT, 3D rendering and computer learning

CT imaging has always been the study of choice for the detection of pancreatic cancer. Advances over the years have increased our capability for earlier lesion detection as well as lesion classification. However, we are now reaching an era where our capabilities for lesion detection, lesion classification and patient management is increasing. In this talk, I will present three major developments that are changing how we look at pancreatic tumors from an imaging perspective as well as how these advances may truly impact on patient management on ways we never thought possible.

Multidetector CT has allowed for the routine acquisition of isotropic datasets in both the arterial and venous phase which provides higher spatial resolution than previously available. These datasets can be used for 3D imaging which has a clinical impact on 20–30% of cases. While classic 3D has been volume rendering and MIP the recent introduction of cinematic rendering has proven to be both valuable in lesion detection and classification with texture mapping but also by providing higher quality images for patient planning. While once the Radiologists interpretation were the final uses of the CT data we are now looking at computer assisted analysis using radiomics and deep learning. Deep learning may help us detect lessons which are commonly missed and then provide a better insight into lesion discrimination. The opportunities for deep learning will be addressed.

Masayuki Kitano: EUS follow-up in patients with cysts

Pancreatic ductal adenocarcinomas (PDACs) arise in some patients with intraductal papillary mucinous neoplasms (IPMNs). The incidence of pancreatic cysts increases with age and the overall risk of malignancy is very low for an incidental pancreatic cyst. However, cyst size ≥3 cm, a dilated main pancreatic duct, and the presence of a mural nodule are factors associated with increased risk of malignancy. Therefore, IPMN patients with such findings are recommended to undergo intensive examinations and follow-ups. Because endoscopic ultrasound (EUS) has higher spatial resolution than the other imaging modalities and can be available for obtaining cystic fluid, it plays an important role for identification of mural nodules and/or cytology. In case of inconclusive EUS results at the first examination, EUS follow-up is also recommended for surveillance of malignancy alternating it with MRI in IAP guideline.

There are two types of IPMN-related PDACs, namely, IPMN-derived PDAC and IPMN-concomitant PDAC. Several studies revealed branch duct IPMNs (BD-IPMNs) without mural nodules has a very indolent course and rarely progress to IPMN-derived PDAC over short periods of follow-up. On the other hand, cumulative 5-year incidence of the development of IPMN-concomitant PDACs ranges from 2.2% to 8.8%. In a study using semi-annual EUS follow-up of BD-IPMNs without mural nodules/symptoms, seven IPMN-concomitant PDACs and no IPMN-derived PDACs were detected during follow-up. EUS depicted all the IPMN-concomitant PDACs, while the other imaging modalities depicted less than 50% of them, suggesting EUS follow-up in the management of IPMNs allows the early detection of IPMN-concomitant PDACs.

Angela Belcher: Developing new technologies for finding tiny tumors

We aim to detect tumor recurrence earlier than is currently possible to ultimately enhance survivorship. We want to see how early we can image pancreatic cancer tumors in a mouse model towards the goal of noninvasive early detection and treatment of pancreatic cancer. Fluorescence-guided imaging systems provide the capability of identifying sub-millimeter disease, and near-infrared (NIR) imaging technologies are already in clinical practice. The advantage of imaging tumors in the NIR domain is due to: (I) use of non-radioactive molecular probes, and (II) reasonably low cost. Second-window NIR light (NIR-II: 950 to 1,600 nm) penetrates biological tissues more efficiently than visible or NIR-I light, having a theoretical penetration depth of 10 cm, and a signal-to-noise ratio that may be 100-fold higher than that for NIR-I light. With NIR-II imaging, we can identify sub-millimeter sized tumors and plan surgical resection accordingly, in an ovarian cancer mouse model. Additionally, NIR-II fluorescence-guided surgical debulking resulted in a 40% improvement in median survival over naked-eye surgery in a mouse model of ovarian cancer. We can detect 1 mm-sized probes through up to 6 cm of tissue or through a whole living rat, or 0.1 mm-sized probes through up to 4 cm

of tissue phantom or 2 through a whole living mouse (compared with the 3.2 cm maximum reported by traditional optical imaging techniques). Optical imaging for noninvasive assessment is an unmet opportunity for interfacing biomolecular recognition, materials design, and instrument development to address current challenges in cancer detection and treatment.

Takao Ohtsuka: Indication of surgery; branch duct

There are 3 major guidelines (GL) for the management of the pancreatic cysts including intraductal papillary mucinous neoplasms (IPMNs): IAP consensus, European consensus, and AGA. IAP-GL focus only on IPMN, while the other two GL tackles various cysts which includes IPMN, mucinous cystic neoplasm (MCN), SCN, etc. "High risk stigmata" (HRS) and "worrisome features" (WSF) are well known factors, proposed by IAP, to determine the surgical indications for branch duct IPMN (BD-IPMN), which can also be applicable to main duct IPMN, wherein high grade dysplasia (carcinoma in situ) and invasive carcinoma are considered to be indication for resection. Many reports have validated the adequacy of IAP-GL 2012 in viewpoints of surgical indication of BD-IPMN. Revised IAP-GL 2017 set the cut-off value of mural nodule $\geqslant$ 5 mm in HRS and added two factors such as increased serum CA19-9 level and cystic growth rate $\geqslant$ 5 mm/2 years to WSF. European-GL also have two categories for surgical indications such as "absolute indications" and "relative indications", which are equivalent to "HRS" and "WSF", respectively. IAP-GL and European-GL obtained the same evaluation with regards to the adequacy of surgical indication for IPMN, however, there are still a lot of patients undergoing "unnecessary surgery". On the other hand, AGA-GL can reduce such "overtreatment", but have higher risk to miss high grade dysplasia or invasive carcinoma than the other two GL. To improve accuracy of surgical indication, many efforts have been carried out to establish a nomogram using multiple predictors and to assess molecular makers in addition to cytology using cystic fluid obtained by endoscopic ultrasound-fine needle aspiration (EUS-FNA).

Dung Le: Novel immunotherapy approaches for pancreas cancer

Immunotherapy is quickly becoming the fourth pillar of the therapeutic armamentarium for the treatment of cancer. While surgery, radiation, and chemotherapy have been used for decades in treatment of cancer, the modern day immunotherapy agents such as the cytotoxic T-lymphocyte associated-4 (CTLA-4) antibodies and programmed death (PD)-1/PD-L1 inhibitors have only become FDA approved over the last few years with the approval of ipilimumab in 2011 and the first PD-1 inhibitor, pembrolizumab, in 2014.

Despite the major advances of immunotherapy in the treatment of solid tumor malignancies, application of these approaches to an immune tolerant cancer such as pancreatic cancer remains a formidable challenge. Pancreatic cancers have few endogenous effector T cells in the microenvironment to be targeted by some of the newer therapies such as anti-CTLA4 or anti-PD-1 that target immune inhibitory molecules. Vaccine strategies and combination strategies try to induce antigen specific T cells and target other inhibitory signals. These vaccine strategies can then be combined with these checkpoint blockers to unleash the T cells activated by these vaccine strategies. CRS-207 is an attenuated *Listeria* modified to express the tumor associated antigen mesothelin. CRS-207 is able to induce both adaptive and innate immunity. Preclinical and clinical studies suggest synergy when CRS-207 is used as a boosting vaccine to allogeneic pancreatic tumor cells transfected with a *GM-CSF* gene (GVAX). There are hundreds of studies combining agents that will induce immune cell infiltration, improve antigen recognition, target inhibitory immune cells and molecules systemically and in the tumor microenvironment. Over the next few years, we will watch as these stories unfold and hopefully bring immunotherapy to more of our patients.

Luis Diaz Jr: Novel multiagent therapy for metastatic adenocarcinoma of the pancreas

Multiagent therapy for pancreatic cancer has shown initial promise in the treatment of pancreatic cancer. We will discuss new combination therapies that my improve outcomes in patients with metastatic disease.

Eileen O'Reilly: PARP inhibitors/BRCA mutated cancers and other immunotherapy

Germline BRCA mutations, in particular BRCA2 incur an increased risk of developing pancreas adenocarcinoma. BRCA mutations occur in 5–7% of an unselected pancreas adenocarcinoma population. In patients with Ashkenazi Jewish heritage and pancreas adenocarcinoma the frequency of BRCA mutations may be significantly higher at 12–15%. PALB2 (partner and localizer to BRCA2) mutations occur in a smaller fraction of patients with pancreas adenocarcinoma (approx. 1%).

Preclinical data has demonstrated hypersensitivity of BRCA 2 deficient pancreatic cell lines to DNA cross-linking agents mitomycin and cisplatin and more recently to the novel agents, poly ADP-ribose polymerases (PARP) inhibitors. We and others have reported increased sensitivity to DNA damaging agents in patients with pancreas adenocarcinoma arising on a background of a BRCA 1 or 2 germline mutation. PARP are a family of enzymes, two of which, PARP1 and 2, are key components of the DNA repair mechanism for cells with single-strand breaks and nucleoside base damage. PARP inhibition has particular application in tumors with pre-existing defects in homologous recombination, such as BRCA 1 or 2 deficient cells. This talk will focus on the emerging role of PARP inhibitors and other DNA-damaging strategies in pancreas adenocarcinoma reviewing combination and single agent PARP inhibitor approaches and identifying opportunities beyond germline BRCA based on germline and somatic profiling for therapeutic gain.

Vincent Picozzi: Transforming outcomes in pancreatic cancer: the precision promise initiative

Improving survival in pancreatic cancer depends on effective systemic therapy. The rate of progress of systemic therapy, and with that, overall survival in this disease has been unacceptably slow.

In this 15 minutes talk, fundamental causes for this deficiency will be identified using pertinent recent therapeutic trials as examples.

Additionally, then new Precision Promise Clinical Initiative for pancreatic cancer sponsored by the Pancreatic Cancer Action Network (PANCAN) will be described, illustrating how it attempts to "reengineer" the entire process of drug development in pancreatic cancer and by so doing, hope to transform the rate of therapeutic progress in this disease.

Junji Furuse: Adjuvant therapy experience (including S1)

In order to improve the survival in patients with pancreatic cancer, systemic chemotherapy has been applied not only for unresectable disease, but also as postoperative adjuvant therapy. Phase III studies of gemcitabine (GEM) as postoperative adjuvant therapy for resectable pancreatic cancer have been conducted, and the CONKO-001, JSAP-01 and ESPAC-3 trials demonstrated the beneficial effect on the overall survival (OS). GEM has been recognized as a standard of adjuvant therapy. In Japan, a phase III trial comparing S-1 with GEM as postoperative adjuvant therapy was conducted (JASPAC-01), and S-1 was demonstrated to yield statistically significantly better OS as compared with GEM; the median OS (S-1 *vs.* GEM) were 25.5 *vs.* 46.5 months. Based on these results, S-1 has been applied as the postoperative adjuvant therapy of first choice for patients with pancreatic cancer in Japan.

However, despite the establishment of a standard postoperative adjuvant therapy, the survival of patients with pancreatic cancer still remains poor. There are some limitations of postoperative adjuvant therapy, and neoadjuvant therapy using a combination chemotherapy regimen, namely, GEM plus S-1, was investigated in a phase III trial (UMIN000009634). Since FOLFIRINOX and GEM plus nab-paclitaxel are approved for unresectable pancreatic cancer, these regimens have been applied for neoadjuvant and postoperative adjuvant therapy in patients with resectable pancreatic cancer, including borderline resectable cancer.

I would like to show some experiences and clinical trials of chemotherapy including S-1 as adjuvant therapy prior to or after surgical resection in Japan.

David Chang: Precision-Panc: precision medicine platform for pancreatic cancer

A major challenge inherent to lower incidence cancer types (ranking 5th and lower) is that a network approach is required to make

significant advances through exposure to greater capacity and patient numbers. This is particularly the case for pancreatic cancer which although being the tenth in incidence, is the fourth, and soon to be the second leading cause of cancer death. Our increasing appreciation for the molecular diversity of cancer further exemplifies the need for a networked platform approach. To address this, we established Precision-Panc in the UK. Precision-Panc is a synergistic and dynamic therapeutic development platform aligning "discovery", "pre-clinical" and "clinical" therapeutic development to form a continuous loop of discovery, learning, refinement, and implementation through efficient forward and backward translation. In this presentation, the initial experience of Precision-Panc will be presented, including the early progress of initial suites of clinical trials. We will also discuss the trials in design.

Jonathan Brody: "Druggable" non-moving and moving targets in pancreatic cancer

To date, genome-wide sequencing and high throughput technologies have yet to translate new therapeutic targets to the clinic. Recently, data have emerged demonstrating the significant role post-transcriptional gene regulation has in regulating multiple core signaling pathways involved in pancreatic tumorigenesis. A key protein involved in this mode of gene regulation is the RNA-binding protein HuR (ELAVL1). HuR is overexpressed in pancreatic cancer cells and translocates to the cytoplasm in response to cancer-associated stressors (e.g., chemotherapeutic exposure and hypoxia) where it promotes gene expression of specific mRNAs that are functionally linked to pancreatic tumor progression and cancer cell survival. *In vivo* studies indicate that the efficacy of clinically relevant therapies [i.e., poly ADP-ribose polymerases (PARP) inhibitor] is enhanced by HuR inhibition, supporting the notion that HuR plays a role in pancreatic cancer cell survival. Therefore, we demonstrate that HuR is a unique and promising target in pancreatic cancer. We will present emerging, novel therapeutic strategies (one of which has been proven to be safe in humans) to target this pathway for the treatment of pancreatic cancer.

Flavio Rocha: Clinical trials on personalized medicine

Personalized or precision medicine in oncology is the application of tumoral genomic and/or proteomic information to tailor a specific therapy to the patient's cancer. With the advent of rapid, reproducible, and reliable sequencing, mutational analysis has revealed potentially actionable targets that may provide a more effective and potentially less toxic treatment for a particular malignancy. While conventional cytotoxic chemotherapy continues to be the backbone and mainstay of therapy, novel therapeutics have been designed to exploit these exposed genetic flaws. The majority of these developments have been applied to patients with advanced disease after the failure of multiple lines of therapy. However, recent basket trials have attempted to match genetic information to intended treatment in the first-line setting. This strategy has been employed regardless of tumor type in the hopes of identifying common pathways. In pancreas cancer, the implementation of combination chemotherapies and targeted agents has resulted in a renewed interest in applying these principles not only in the metastatic but also adjuvant and neoadjuvant space. The latter approach is particularly attractive as it affords the opportunity to measure radiographic, pathologic and genetic response to therapy and optimize postsurgical care. As new discoveries are made, it is imperative that they be studied through clinical trials mechanisms to validate their effects in order to continue to improve outcomes for our patients.

David Ting: Pancreatic circulating tumor cells: the liquid biopsy

Circulating tumor cells (CTCs) provide a means for a "liquid biopsy" that evaluates the genotypic and phenotypic characteristics of a patient's cancer. Studies in pancreatic cancer (PDAC) mouse models indicate that CTCs may disseminate into circulation at an early point in pancreatic cancer development through epithelial-to-mesenchymal transition (EMT), which has significant implications for early detection. We have developed a novel microfluidic isolation device called the CTC-iChip to capture CTCs in an antigen agnostic manner. This device achieves high efficiency negative depletion of normal blood cells providing an enriched population of CTCs in solution that are not biased by a particular extracellular epitope and are captured without any antibody interactions that could affect expression profiles or cell viability. We have utilized this platform to fully characterize the heterogeneity of CTCs using

single cell RNA-sequencing. In the genetically engineered PDAC mouse model, we demonstrated significant heterogeneity of CTCs including: (I) non-viable CTCs; (II) classical CTCs (CTC-c) defined by established keratin expression, biphenotypic EMT markers, and enrichment of stem cell markers; (III) platelet adhered CTCs (CTC-plt); (IV) proliferative CTCs (CTC-pro); and (V) CTC clusters. Altogether, this not only indicates that there are multiple paths for metastasis, but also that entry into circulation is not a rate limiting step in the metastatic cascade. Consistent with this, we find detectable CTCs in patients with IPMN and resectable PDAC indicating CTC generation is likely a passive process and can be utilized as an early detection biomarker.

David Chang: Clinical utility of molecular profiling using EUS-guided biopsies in pancreatic cancer: The PRECISION-Panc experience

Introduction: Next-generation sequencing is enabling molecularly guided therapy for many cancer types, yet failure rates remain relatively high in pancreatic cancer (PC). The aim of this study is to investigate the feasibility of genomic profiling using endoscopic ultrasound (EUS) biopsy samples to facilitate personalised therapy in PC.

Methods: Ninety-five patients underwent additional research biopsies at the time of diagnostic EUS. Diagnostic formalin-fixed (FFPE) and fresh frozen EUS samples underwent DNA extraction, quantification and targeted gene sequencing. Matching resected specimens underwent genomic profiling for comparison. Whole genome (WGS) and RNA sequencing was performed in selected patients.

Results: Only 2 patients (2%) with a diagnosis of PC had insufficient material for targeted sequencing in both FFPE and frozen specimens. Targeted panel sequencing (n=54) revealed mutations in PC genes (*KRAS*, *GNAS*, *TP53*, *CDKN2A*, *SMAD4*) in patients with histological evidence of PC, including potentially actionable mutations (*BRCA1*, *BRCA2*, *ATM*, *BRAF*). WGS (n=5) of EUS samples revealed mutational signatures that are potential biomarkers of therapeutic responsiveness. RNA sequencing (n=53) segregated patients into clinically relevant molecular subtypes based on transcriptome; and reveals novel molecular differences between metastatic, locally advanced and resectable PC.

Conclusions: We demonstrate integrated multi-omic analysis of all stages of PC using standard EUS guided biopsies. This offers clinical utility to guide personalized therapy and study the molecular pathology in all patients with PC. Identifying gene signatures associated with pro-metastatic phenotype and poor prognosis may better select patients for therapy.

Nita Ahuja: Methylation biomarkers

This talk will discuss development of a point of care based test for early detection of pancreas cancer. Dr. Ahuja is a leader in the field of translational epigenetics. She identified the concept of CpG Island Methylator phenotype in cancers as well as the contributions of aging and chronic inflammation on cancer development. She has led the identification of epigenomic changes in multiple solid cancers including pancreas, colorectal, breast and ovarian cancers and then published the first studies identifying biomarkers for early detection of cancer using epigenetic changes. Her group has also been led the testing of combinatorial epigenetic therapies in multiple national trials including colorectal and pancreas cancer. Dr. Ahuja's group was one of the first to describe the use of epigenetic modifications as a biomarker for detection of pancreas cancer using liquid biopsies. Her laboratory is now working to develop a point of care test for detection of pancreas cancer in high risk patients.

James Eshleman: Pancreatic cancer liquid biopsy

We have monitored a series of surgically resected pancreatic cancer patients for plasma levels of mutated KRAS molecules. Using the specific KRAS mutation identified in the patients' surgically resected sample, we used digital droplet PCR (ddPCR) to measure the levels of the cancer specific mutation in circulating tumor DNA (ctDNA) in the peripheral blood, a so-called "liquid biopsy". Patients with detectable levels of ctDNA in their pre-incision sample, and those with increasing levels post-operatively correlated

with poor clinical outcome. In some patients, levels of ctDNA tracked closely to the protein tumor marker CA19-9. In other patients, increases in ctDNA in liquid biopsy predated cancer recurrence detected radiographically.

Richard Burkhart: Organoids as measures of response

Pancreatic cancer (PC) will soon become the second leading cause of cancer-related death. Even when surgery can offer hope for cure, adjuvant chemotherapy is recommended as disease recurrence is common. Despite recognizing several different subtypes of PC, current guidelines recommend the same type of chemotherapy for all patients. In other cancer types, such as breast and colon, molecular heterogeneity has led to biomarker-directed therapeutic selection and improved survival. We believe that a contemporary approach to PC, in which clinicians leverage molecular heterogeneity to personalize therapy, will lead to improved outcomes. While many predictive biomarkers have been proposed in PC, none are used in the clinic. This work evaluates patient-derived organoid cultures as a method to generate clinically-actionable data. We demonstrate that organoids can be generated quickly from fresh surgical specimens. Propagation in culture to a biomass sufficient for molecular analyses can be completed prior to initiation of adjuvant therapy in a surgical population. Organoids can be used as a tool to identify low-frequency mutations present in individual tumors and to subtype tumors according to gene expression data. Organoid culture can also be used *in vitro* to test for unique therapeutic sensitivities to the current standards used for systemic therapy. This testing may also hold promise for testing an expanded panel of chemotherapeutics in individuals who have failed the standard of care. These data suggest that rapid organoid generation with molecular characterization and *in vitro* drug sensitivity analyses is a tractable approach to precision medicine for PC.

Lei Zheng: Predict the responses to immunotherapy

It has been well recognized that immune checkpoint inhibitors as a single agent are not effective in the pancreatic cancer patients due to low mutation burdens or T cell excluded tumor microenvironment. Rational strategies of combination immunotherapy are being developed to overcome the resistance of pancreatic cancer to immunotherapy. It has also been a challenge to predict the responses to the immunotherapy. Potential genomic and immunologic biomarkers have been evaluated and a comprehensive relational database may ultimately be needed to better predict the response of pancreatic cancer to combination immunotherapy.

Kyoichi Takaori: Innovation in pancreatic surgery

Surgery alone is not good enough to cure pancreatic cancer because 90% of patients are complicated by metastatic disease. In fact, several randomized trials have demonstrated that extended resection does not improve survival of the patients. Nevertheless, surgery still plays a significant role in multidisciplinary approaches to the treatment of pancreatic cancer. Accordingly, innovation in pancreatic surgery may benefit patients. Owing to better selection of patients especially by neoadjuvant chemo-radiation therapy (NACRT), we now operate on patients with locally advanced disease more often than ever and have to deal with firm fibrotic tissues which remain around the tumor even after effective neo-adjuvant treatments. Furthermore, there is a demand for minimally access surgery by laparoscopic and robotic approaches. These situations have urged us to technological innovation such as artery-first approaches to pancreaticoduodenectomy. Although there are many methods of artery-first approaches, our preference is "Tiger's Den approach", which is useful particularly in obese patients and in those after NACRT. Distal pancreatectomy with celiac artery resection (DP-CAR) is an operation of choice for locally-advanced tumors located in the pancreatic body. We developed surgical techniques of artery first DP-CAR using the same Tiger's Den approach. These artery-first approaches are suitable and practicable in laparoscopic and robotic surgery as well. To further improve the safety of pancreatic surgery, ICG fluorescence technology has been utilized in evaluating blood flows to the remnant pancreas, stomach, colon, etc. In conclusion, innovation in pancreatic surgery is one of the keys to successful managements in the era of multi-disciplinary treatment.

Matthew Katz: Rationale for neoadjuvant therapy

Recent practice guidelines have recognized the administration of chemotherapy and/or radiation therapy prior to pancreatectomy for localized pancreatic ductal adenocarcinoma (PDAC) as the preferred treatment strategy for patients with borderline resectable cancer and an acceptable treatment option for patients with potentially resectable cancer. Purported benefits of this approach include the selection of patients with favorable tumor biology and a physiologic profile appropriate for major surgery, early treatment of micrometastatic disease, facilitation of a margin-negative resection, and guaranteed delivery of all components of multimodality therapy. During the past 3 decades, refinement of the therapeutic regimens administered in the preoperative setting has permitted the rational use of potentially curative surgery in patients with anatomically advanced cancer and has contributed to a significant increase in overall survival duration following pancreatectomy. In this talk, the rationale for this treatment strategy will be discussed in detail.

Jin He: Robotic surgery of PDAC

Since the first robotic whipple described by Giulianotti in 2003, and there has been significant technology evolvement and a surge of interest. In this talk, we will review the current indications of robotic pancreatectomy for pancreatic ductal adenocarcinoma (PDAC). We will review the postoperative outcomes and complications such as pancreatic fistula, postpancreatectomy hemorrhage, delayed gastric emptying, and re-explorations, length of hospital stay and 30-day mortality. We recommend the robotic pancreatectomy to be done only in high volume centers with expertise.

Masafumi Nakamura: Difficulty score in laparoscopic pancreatic resections

Laparoscopic pancreatic resection (LPR) is gradually spreading globally. However, LPR is still a challenging technique in the field of HPB surgery. According to the study of Kantor *et al.* (*Am J Surg* 2017), the 30-day mortality of laparoscopic pancreaticoduodenectomy (LPD) was significantly higher in low volume centers compared with high volume centers. Developing safe steps for learning LPR is urgently needed.

Currently, we are trying to construct a "Difficulty Score" (DS). Our aim is to pre-operatively evaluate and predict the difficulty of LPR. This can help identify which surgeon is suitable for a certain degree of difficulty (e.g., lower DS can be performed by surgeons still under the learning curve/less experience). At the same time, it can improve surgical outcomes of LPR.

Creation of DS for LPR is far more complicated compared with DS for laparoscopic hepatectomy. First, several different approaches can be done in a same tumor location (e.g., distal pancreatic tumor: vessel-preserving laparoscopic distal pancreatectomy (LDP), Warshaw method, or LDP with radical LN dissection). Second, resection portion can be easy, but the reconstruction can be difficult, and vice versa. Thus, DS was subdivided into LDP and LPD (resection portion only at this time). We expect that DS for LPR will provide a safer approach by properly matching the degree of difficulty to a surgeon's skill.

Hiroki Yamaue: surgery for stage III PDAC–arterial resection in pancreatic head resection and DP-CAR

R0 surgery is an essential requirement for long survival in patients with pancreatic cancer, however, pancreatic cancer should be considered as a systemic disease in the view point of its tumor biology. Therefore, one should consider that R0 surgery is an only issue for the impact of survival in patients with advanced pancreatic cancer (*Pancreas* 2016). The overall survival (OS) of borderline resectable (BR)-artery (A) patients with upfront surgery was significantly shorter than that of the patients with BR pancreatic cancer with portal vein involvement and resectable pancreatic cancer (median OS: 13.6 *vs.* 20.6 months, P<0.001). Therefore, NAT is strongly needed for longer survival (*Cancer Chemother Pharmacol* 2016, *Anticancer Res* 2017).

The indications for distal pancreatectomy with en-bloc celiac axis resection (DP-CAR) were extended to increase the R0 rate for

advanced pancreatic body/tail carcinoma (*Surgery* 2013). Another problem of DP-CAR is a delayed gastric emptying (DGE) due to the ischemic gastropathy after resection of left gastric artery (LGA). We have attempted preservation of LGA (modified DP-CAR) if the patients have a tumor situated more than 10 mm away from LGA, and we conclude that modified DP-CAR significantly reduced the incidence of DGE (*World J Surg* 2014).

Moreover, we have proposed the following strategy with anastomosis of LGA and middle colic artery (*Gastrointest Tumors* 2017) and the incidence of DGE decreased by arterial anastomosis.

The treatment strategy for patients with stage III pancreatic cancer has been still controversial, and further studies will be needed to confirm the appropriate treatment.

Yi Miao: Technical modification in pancreatic surgery

As highly technique-demanding procedures, pancreatic resections remain the most challenging ones in the field of abdominal surgery, with substantial postoperative morbidity world-widely. Furthermore, clinical outcomes after pancreatectomies varied from high-volume centers to low-volume centers, from experienced hands to young surgeons. In this presentation, we would like to demonstrate some representative technical modifications in pancreatic resections from our center, including: (I) one-layer modified duct-to-mucosa pancreaticojejunostomy (P-J) to simplify the anastomotic technique with satisfied postoperative pancreatic fistula (POPF); (II) one-layer duodenojejunostomy (D-J) with margin-sealing technique; (III) afferent loop decompression technique (ALDT) to reduce POPF after the construction of P-J; (IV) artery divestment technique for T4 pancreatic cancer to increase R0 resection; (V) artery-first approach distal pancreatectomy for left-sided pancreatic cancer with vessel invasion; (VI) uncinate-first approach total pancreatectomy. With all the reported surgical techniques, mortalities and morbidities had been significantly reduced during recent decades in our center. Our technical modifications are worthy for advocacy of its routine application in the clinics.

Matthew Weiss: If and when it's appropriate to operate on stage IV disease

Pancreatic cancer (PC) is a highly aggressive disease and has the worst prognosis amongst all gastrointestinal tumors. The most effective treatment for PC is surgical resection, however >50% of patients have metastatic disease on presentation and are not classically, considered for surgery. Hepatectomy or pulmonary metastasectomy are now well-established treatments for colorectal cancer with isolated hepatic or pulmonary disease due to the development of improved systemic therapies. Chemotherapy regimens for pancreas cancer have improved dramatically over the past decade. However, whether metastatic PC is ever operable and the indications for such resections are not clearly defined. We will review the current literatures on the surgical management of metastatic PC, specifically focusing on surgical resection for isolated hepatic and pulmonary metastasis.

Claudio Bassi: IRE/ablation

Most of patients with pancreatic cancer are diagnosed with an advanced disease, locally advanced or metastatic. The standard of care of locally advanced pancreatic cancer (LAPC) is chemotherapy, in order to increase the probability to reach the surgical treatment with a radical resection of the tumor. However, the majority of such tumors will never receive a surgical treatment. A part of this subgroup will show a prevalent local tumor growth. Ablative techniques emerged as palliative therapies for LAPC not further responsible to medical oncological treatments and not showing progression. They are applied to obtain a local control of the disease. Radiofrequency ablation (RFA) uses heat to destroy the tumor cells. The amount of necrosis produced varies greatly according to the settings. Irreversible electroporation (IRE) applies locally electric fields, capable to alter, almost selectively, the transmembrane potential of tumor cells, causing their death through apoptosis. Both techniques can be applied percutaneously, with a minimally invasive approach. Apart from their undisputed cytoreductive action, a presumed immune stimulation might be co-responsible of their clinical effects. So far, oncological results are far from being conclusive, since almost all studies published are biased by the retrospective nature or by their study design. However, some encouraging results authorize to investigate deeply their role within

the multimodality treatment approach to LAPC. RFA and IRE are not free from complications, thus their use should be deserved to high-volume centers of pancreatology, after a multidisciplinary decision and with a precise preoperative plan.

Michael Erdek: Pain assessment and treatment in pancreatic cancer

Patients with pancreatic cancer frequently present with pain as the initial symptom of their disease, with nearly 75% of patients suffering from pain at the time of diagnosis. Consultation with a physician with specific expertise in pain medicine is often helpful both in the outpatient clinic and multidisciplinary clinic settings.

Opioids are the mainstay of pharmacologic therapy for pancreatic cancer pain. Common side effects of opioids include sedation, constipation, pruritis, nausea, and testosterone suppression in those on long-term therapy.

The most common and effective procedural intervention for pancreatic cancer pain is celiac plexus block. Patients who may benefit most from a celiac plexus block are those who have pain refractory to escalating doses of opioids or those who suffer debilitating opioid-mediated side effects. Patients whose pain is relieved by diagnostic celiac plexus block may undergo subsequent celiac plexus neurolysis.

Intrathecal delivery of analgesic agents is helpful in patients whose pain is poorly controlled by less invasive means. Randomized, controlled studies have delineated the benefit of this modality, not only for pain control but particularly in minimizing the toxicities of systemically administered opioids.

Ongoing consultation with a pain specialist is advised to optimize an integrated approach to pharmacologic, procedural, and surgical pain care for the patient with pancreatic cancer. Reassurance given to the patient that his or her pain care is paramount during their care, regardless of the stage and severity of their disease, is essential in a process where the emphasis is often more focused on palliation rather than cure.

Jordan Winter: Depression and pancreatic cancer

Depression is more common in cancer patients than the general population, and amongst cancer patients, depression is most common in those with pancreatic cancer. Prevalence estimates range between 30–50%. Data across multiple cancer types reveal that depression is widely underdiagnosed and undertreated, and there is a high incidence of depression in caregivers of patients with cancer-associated depression. For pancreatic cancer patients, population-level data indicate that depressed patients have a worse survival, and that treatment compliance is adversely affected. Depressed patients with resectable pancreatic cancer are less likely to undergo surgery, and depressed patients with advanced pancreatic cancer are less likely to receive chemotherapy. Therefore, depression has a major impact on pancreatic cancer survivorship, and potentially impacts pancreatic cancer survival. Pancreatic cancer-associated depression is also unique because neuropsychiatric symptoms precede the cancer diagnosis in half of the cases. This observation is validated, suggests that depression may be more than a consequence of the complex psychosocial elements of the diagnosis and treatment. Instead, depression may be attributable to intrinsic pancreatic cancer biology. Emerging evidence implicates abnormal tryptophan metabolism, caused by increased IDO expression. These enzymes have been the focus of immunotherapeutic strategies, but also may divert tryptophan away from serotonin synthesis, and towards metabolites with antagonistic effects on patient mood and cognitive function. A prior randomized trial in head and neck cancer suggests that routine prophylactic antidepressant used can prevent depression. A similar study is in development to test the same hypothesis in patients with pancreatic cancer.

Richard Kozarek: Interventional endoscopic palliation in patients with pancreatic cancer

Historically, the primary endoscopic interaction in pancreatic cancer was endoscopic ultrasound (EUS) diagnosis by fine needle aspiration (FNA) and the placement of plastic prostheses in non-resectable malignant obstructive jaundice (MOJ). The latter has morphed into insertion of self-expandable metal stents (SEMS) because of prolonged patency; moreover, while multiple series suggest neither operative nor survival advantage in jaundiced pancreatic cancer patients undergoing pre-operative decompression,

current practice has evolved into SEMS placement in virtually all patients with borderline resectability undergoing neo-adjuvant therapy in hopes of ultimate resection. Finally, endoscopy has been used to palliate gastric outlet obstruction in non-resectable patients with pancreatic malignancy, and randomized controlled trials have demonstrated shorter hospitalization time, more rapid refeeding, and comparable survival when compared to palliative gastrojejunostomy.

What is new in 2018? On the one hand, EUS-facilitated celiac or neural ganglion block for refractory pain has virtually replaced CT-guided neurolysis. On the other hand, therapeutic EUS has provided multiple additional palliative maneuvers for obstructive cholecystitis and the palliation of MOJ. In the latter setting, placement of a SEMS from the proximal stomach to the left lobe of the liver has been utilized when there is poor access to the papilla as has utilization of a lumen-apposing stent (LAS) to perform a choledochoduodenostomy. A comparable anastomosis can be made to perform a cholecystoduodenal anastomosis and may preclude the need for a percutaneous cholecystectomy, a situation in which a drainage tube is often required indefinitely.

LAS can also be used to perform an endoscopic gastrojejunostomy, precluding the need for a palliative surgery or endoscopic placement of an enteral prosthesis. Currently, a randomized trial comparing the latter two procedures is planned with outcome measures including success, complication rate, long-term patency, and survival, all remaining to be defined.

Finally, although the majority of pancreatic malignancy is not amenable to direct endoscopic therapy, a percentage of patients with cystic or neuroendocrine neoplasms may be amenable to EUS injection of chemotherapeutic agents or direct ablation with RFA. The latter therapies currently have no curative or palliative role with conventional ductal pancreatic adenocarcinomas.

Thomas Smith: Concurrent palliative care for the pancreas cancer patient including transitions to end of life

Palliative care (PC) benefits include better quality of life (QOL), symptoms, depression, distress, care at the end of life, equal or lower cost, and equal or improved survival—proven in 13+ randomized clinical trials including one in pancreas cancer (*Maltoni Eur J Ca* 2016; Ferrell Smith *JCO* 2017). Concurrent PC can help pancreas cancer patients if we use the methods in the RCTs, and only if PC is available in the clinic when the patients are seen and can see patients several times. Some special considerations in pancreas cancer include the suddenness of the catastrophe, potential of cure or prolonged life in the minority, and the difficulty of discussing advance care planning (ACP). Use the TEAM approach (*Bakitas Smith JOP* 2017). T-time-an extra hour each month assessing symptoms, coping, spirituality, prognostic awareness, ACP. If the surgeon cannot do this, call PC. E-education about realistic options and prognosis. A-formal assessments of symptoms. M-management by a team.

Suggestions: establish a close working relationship with PC partners, and refer early. Yourself, ask "How are you and your family coping?" At each scan or assessment, ask "Would you like to discuss what this means?" Set up a hospice information visit when you think the person might have 6 months to live. Ask "What is your understanding of your situation?" on a regular basis. Automatically refer to PC with recurrence or advanced disease, or for symptoms. I will illustrate how to use the TEAM method to integrate PC into our care.

Abstract

AB001. S001. Defining DDR deficiency and replication stress in pancreatic cancer

Stephan B. Dreyer, Viola Paulus-Hock, Eirini Lampraki, Rosie Upstill-Goddard, Giuseppina Caligiuri, Holly Brunton, Bryan Serrels, Richard Cunningham, Nigel B. Jamieson, Colin J. McKay, Andrew V. Biankin, Peter J. Bailey, David K. Chang

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Background: Integrated multi-omic analyses revealed 24% of pancreatic cancer (PC) harbor defects in DNA damage response (DDR) and a subgroup demonstrate upregulation in replication stress pathways. DDR defective tumors preferentially respond to DNA damaging agents, and clinical responses to cell cycle inhibitors are seen in undefined subgroups, representing novel therapeutic strategies for PC. The aim of this study is to define and refine therapeutic segments for agents targeting DDR and replication stress in PC.

Methods: We performed whole genome and RNA sequencing (RNAseq) on 48 patient-derived cell lines (PDCL) generated and characterized as part of the International Cancer Genome Initiative (ICGC). This identified increased replication stress in a sub-group of tumours, correlating with previously defined molecular subtypes of PC, irrespective of DDR status. Cytotoxic viability assays were performed using agents targeting the DDR pathway and cell cycle checkpoints, including Cisplatin, and inhibitors of PARP, ATR, WEE1, CHK1, CDK4/6 and PLK4. Subcutaneous patient derived xenografts (PDX) were generated to test therapeutic regimens *in vivo*.

Results: DDR defective PDCLs, as defined by signatures of homologous recombination deficiency (HRD) were highly sensitive to Cisplatin and PARP inhibitors. A novel transcriptional signature of replication stress predicted differential responses to cell cycle inhibitors of ATR, WEE1, CHK1, CDK4/6 and PLK4. Response to cell cycle checkpoint inhibitors were independent of DDR status, but strongly associated with replication stress. A *BRCA1* mutant PDX model responded exceptionally to Cisplatin and PARP inhibitor monotherapy.

Conclusions: This proof of concept data demonstrates DDR deficiency and increased Replication Stress to be attractive targets in PC. Therapeutic vulnerabilities extend beyond platinum chemotherapy and can be targeted with novel small molecule inhibitors, with independent biomarkers that predict response to agents targeting either DDR or cell cycle checkpoints. This has led to the design and development of several personalized medicine trials in PC via the Precision Panc platform targeting DDR and Replication stress, and will allow clinical testing of signatures of HRD and replication stress in relation to therapeutic response. The parallel collection of molecular and clinical outcome data in these trials will allow biomarkers of response to be further refined in PC.

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AB002. S002. Wild-type *KRAS* allele exerts its tumor-suppressive function through decreased Yap1 activation in pancreatic cancer

Han Yan, Chih-Chieh Yu, Stuart A. Fine, Ayman Lee Youssorf, Dario Garcia-Carracedo, Dillon C. Carg, Edwin Cheung, Wei-Yann Tsai, Ji Luo, Yi Miao, Wanglong Qiu, Gloria H. Su

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Abstract: *KRAS* is the most frequently mutated oncogene (about 95%) in pancreatic ductal adenocarcinoma (PDAC) and it has been shown to be essential for pancreatic tumor initiation and maintenance in both humans and mice. We have previously reported that the wild-type *KRAS* allele was selectively lost in both primary pancreatic tumors and metastases developed in a mouse model of PDAC, and the frequency of the wild-type loss increased from primary tumors to metastases in this mouse model and human pancreatic cancer cells. To interrogate the wild-type *KRAS* functions and its underlying mechanisms in pancreatic tumorigenesis, we restored the wild-type *KRAS* allele in a doxycycline (Dox) inducible manner in two pancreatic cancer cell lines that have undergone loss of the wild-type allele. We observed that the re-expression of the wild-type *KRAS* significantly reverse the proliferation, motility, and colony formation capabilities of these cancer cells *in vitro*. Furthermore, *in vivo* xenograft studies also demonstrated stalled tumor growth upon wild-type *KRAS* restoration. In contrast, overexpression of wild-type *KRAS* exerted no impact on pancreatic cancer cells that have retained the wild-type *KRAS* allele, suggesting that it's the presence of the wild-type *KRAS* allele, not the dosage of total *KRAS* or the ratio of wild-type and mutant *KRAS*, that is vital in regulating tumor growth and metastasis. Lastly we examined several downstream signaling pathways associated with the regulation of *KRAS* and observed decreased Yap1 expression and nuclear translocation were induced by the restoration of the wild-type *KRAS* allele. Together these results ascribe the wild-type *KRAS* allele a tumor-suppressive role in the context of the mutant KRAS allele in pancreatic tumorigenesis via the inhibition of Yap1 activation.

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AB003. S003. *BRCA1/BRCA2* germline mutation carriers and sporadic pancreatic adenocarcinoma

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Background: The outcomes of sporadic pancreatic ductal adenocarcinoma (PDAC) patients with germline mutations of *BRCA1/BRCA2* remain unclear. The prognostic significance of *BRCA1/BRCA2* mutations on survival is not well established.

Methods: We performed targeted next-generation sequencing (NGS) to identify *BRCA1/BRCA2* germline mutations in resected sporadic PDAC cases from 2000 to 2015. Germline *BRCA* mutation-carriers were matched by age and tumor location to those with *BRCA1/BRCA2* wild-type genes from our institutional database. Demographics, clinicopathologic features, overall survival (OS) and disease-free survival (DFS) were abstracted from medical records and compared between the two cohorts.

Results: Twenty-two patients with sporadic cancer and *BRCA1* (n=4) or *BRCA2* (n=18) germline mutations and 105 wild-type patients were identified for this case-control study. *BRCA1/BRCA2* mutations were associated with inferior median OS (20.2 *vs.* 27.8 months, P=0.034) and DFS (8.4 *vs.* 16.7 months, P<0.001) when compared with the matched wild-type controls. On multivariable analyses a *BRCA1/BRCA2* mutation [hazard ratio (HR) =2.10, P<0.001], positive margin status (HR =1.72, P=0.021) and lack of adjuvant therapy (HR =2.38, P<0.001), were all independently associated with worse survival. Within the *BRCA1/BRCA2* mutated group, having had platinum-based adjuvant chemotherapy (n=10) was associated with better survival than alternative chemotherapy (n=8) or no adjuvant therapy (n=4) (31.0 *vs.* 17.8 *vs.* 9.3 months, P<0.001).

Conclusions: Carriers of *BRCA1/BRCA2* mutation with sporadic PDAC had a worse survival after pancreatectomy than their *BRCA* wild-type counterparts. However, platinum-based chemotherapy regimens were associated with markedly improved survival in patients with *BRCA1/BRCA2* mutations, with survival differences no longer appreciated with wild-type patients.

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AB004. S004. Differences in cancer metabolism between subtypes of pancreatic ductal adenocarcinoma (PDAC) are associated with survival and offer therapeutic opportunities

Frederike Dijk, Eline C. Soer, Johannes B. Halfwerk, Gerrit K. Hooijer, Veronique L. Veenstra, Lan Zhao, Olivier R. Busch, Marc C. Besselink, Lennart B. van Rijssen, Hanneke W. Wilmink, Hanneke W. van Laarhoven, Jan Koster, Xin Wang, Maarten F. Bijlsma, Joanne Verheij, Marc J. van de Vijver

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Background: Overall survival (OS) of patients with pancreatic ductal adenocarcinoma (PDAC) is extremely poor. Of patients eligible for surgery (20%), around 15% present with a recurrence within 6 months, while 10% survive over 5 years after diagnosis. Detailed clinicopathological and molecular knowledge of factors influencing survival will lead to better prognosticators and preselection of individual patients for specific treatment strategies.

Methods: Fresh frozen PDAC resection specimens from Academic Medical Centre Amsterdam (1993–2015) were histopathologically revised, and clinicopathological details were collected. From samples with a tumor cellularity of ≥30% (n=90), mRNA, miRNA, and DNA were used for next generation sequencing at multiple levels. Corresponding formalin-fixed paraffin-embedded (FFPE) blocks were selected for tissue microarrays.

Results: Unsupervised consensus clustering of gene expression profiles of 90 PDAC cases revealed four subgroups with divergent survival rates: secretory, epithelial, compound pancreatic, and mesenchymal subtypes, which remained after correction for potential confounders (a.o. LNM, differentiation grade, radical resection; multivariate Cox regression analysis). Supervised clustering demonstrated 10,041 genes to be differentially expressed between the subgroups, with prominent over-representation of ribosomal genes and oxidative phosphorylation (OXPHOS), dividing tumors in two major classes: secretory and epithelial vs. compound pancreatic and mesenchymal subgroups. These classes do not correspond in terms of median OS: secretory and mesenchymal with 14.7 and 14.0 m ('short') and epithelial and compound pancreatic with 31.8 and 21.5 m ('long'). Between 'short' and 'long' survivors, 683 genes were differentially expressed, associated with biosynthesis of macromolecules. Nutrients from extracellular space (Val, Leu, Ile) are converted into intermediates for the TCA cycle, creating increased metabolic flexibility in tumors of patients with shorter OS. To determine clinical relevance and identify biomarkers, we are currently characterizing the subtypes at the miRNA, mutational, copy number, and immunohistochemical level.

Conclusions: In our well-defined single-center set of 90 PDAC, we identified four transcriptomics-based subgroups with different survival outcomes that show a correlation with altered metabolic features. Complete characterization of metabolic liabilities will help to further identify prognosticators, f.i. measurement of elevated plasma levels of specific amino acids, and provide leads for targeted therapies, like mTOR inhibitors and anti-diabetic drugs.

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AB005. S005. A multi-institutional postoperative nomogram for disease recurrence following resection of localized G1/G2 pancreatic neuroendocrine tumors

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Background: Operative resection is the treatment of choice for the majority of patients with localized pancreatic neuroendocrine tumors (PanNET). Although resection is curative in most cases, approximately 17% of patients will experience disease recurrence. The purpose of this study was to develop a nomogram to predict time to recurrence (TTR) for patients with localized G1/G2 PanNET following surgical resection of the primary tumor.
Methods: A prospectively maintained database from Verona University Hospital and Memorial Sloan Kettering Cancer Center was queried to identify patients who underwent resection for G1/G2 PanNET between 2000 and 2016. Exclusion criteria were: the presence of a hereditary syndrome, treatment with neoadjuvant or adjuvant therapy, postoperative mortality and unknown ki67 on pathological report. Time to recurrence was calculated from the date of resection to date of recurrence and estimated using Kaplan-Meier methods. The selection of predictors of recurrence was based on the univariate analysis. The nomogram was constructed to predict the rate of freedom from recurrence at 5 years after surgery, and validated using bootstrap resampling method. Bias corrected c-index was used to evaluate the discriminative power of this prediction tool.
Results: Within the study period, 632 patients met the inclusion criteria. The median age was 57 [18–85] years, and 429 patients (68%) had a G1 tumor. The tumor was functional in 90 patients (14%), and within this group, 77 patients (12%) presented with an insulinoma syndrome. The median tumor size was 2 (0.4–13.5) cm with a median ki67 of 2% (0.3–20%). According to the AJCC 8th staging system, 463 patients (73.3%) had stage I disease, 142 (22.5%) stage II and 54 (8.5%) stage III disease. The median follow-up was 51 months, with 74 patients (12%) having a recurrence. Upon univariate analysis, the number of positive lymph nodes (P<0.001), ki67 (P<0.001), tumor size (P<0.001), R status (P<0.001), vascular invasion (P<0.001), and perineural invasion (P<0.001) were predictors of time to recurrence. Based on these variables a nomogram was created to predict the probability of recurrence free at 5 years after surgery. The nomogram was internally validated using bootstrap resampling with 100 repetitions, and the bias-corrected c-index was 0.86.
Conclusions: Although further external validation is needed, this nomogram accurately predicts disease recurrence after localized primary G1/G2 PanNET resection, and it may serve as a basis for surveillance recommendations following resection.

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AB006. S006. Variation in long-term oncologic outcomes by types of cancer center accreditation: an analysis of a SEER-Medicare population with pancreatic cancer

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Background: Cancer center-accreditation is designed to identify centers that provide high-quality cancer care. We sought to examine if accreditation is associated with long-term oncologic outcomes.

Methods: Using the SEER-Medicare database, we identified patients who underwent pancreatectomy for pancreatic adenocarcinoma from 1996–2013. Hospitals were categorized into three groups: Commission on Cancer-accredited (CoC) centers, National Cancer Institute-designated (NCI) centers, and "non-accredited" (NA) centers. Adjusted examined lymph nodes, disease-specific survival (DSS), and overall survival (OS) were calculated.

Results: We identified 5,118 patients who underwent pancreatectomy at 632 hospitals (41.0% NA, 49.6% CoC, 9.4% NCI). NCI had a higher median number of lymph nodes examined compared with CoC or NA centers (14 *vs.* 10 *vs.* 11.0 nodes, respectively; P<0.001). Patients treated at NCI centers had a higher 5-year DSS compared to those treated at CoC or NA centers (31.2% *vs.* 23.6% *vs.* 23.0%, respectively; P<0.001). Finally, patients treated at NCI centers had a higher 5-year OS compared to those treated at CoC or NA centers (23.5% *vs.* 18.9% *vs.* 17.9%, respectively; P<0.001). The associations held true when adjusted analysis was performed.

Conclusions: Patients with resected pancreatic cancer at NCI-designated centers are associated with higher number of lymph nodes examined, as well as improved OS and DSS. This effect was not observed with CoC-accredited centers. Further research is needed to elucidate the relationship between cancer center-accreditation and oncologic outcomes.

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AB007. S007. Survival in locally advanced pancreatic cancer: impact of surgical resection after neoadjuvant therapy

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Background: Current guidelines recommend systemic chemotherapy for locally advanced pancreatic cancer (LAPC). An increasing number of patients who respond favorably to neoadjuvant therapy undergo surgical resection of the primary tumor. The impact of surgery on patient survival is largely unknown.

Methods: This is a single institution retrospective cohort study that included all LAPC patients who presented to the institutional Pancreatic Multidisciplinary Clinic (PMDC) of a high-volume pancreatic cancer center from January 1st, 2013 to September 30th, 2017. Demographics and clinical data on neoadjuvant treatment and surgical resection were documented. Patients were stratified into two cohorts: surgical resection post neoadjuvant therapy, and systemic therapy only. Tumor resection rates and overall survival (OS) were the primary study endpoints.

Results: Overall, 415 patients were included in the study. Significant heterogeneity was identified in neoadjuvant treatment. Stratification in FOLFIRINOX-based therapy, gemcitabine-based therapy, and combination of the two and subsequent outcome comparison did not demonstrate significant differences in OS of 331 non-resected LAPC patients (17.4 *vs.* 16 *vs.* 17.2 months, respectively, P=0.134). Eighty-four patients underwent resection of the primary tumor (20%), after a median time of 5 months of neoadjuvant therapy. FOLFIRINOX-based therapy and stereotactic body radiation therapy (SBRT) correlated with increased probability of resection (P=0.006). Resected patients had better performance status, smaller mean tumor size (35 *vs.* 39 mm, P=0.029), and lower median CA19-9 values (72 *vs.* 206 U/mL, P<0.001) at PMDC. A significant improvement in OS was identified in resected patients, compared to non-resected (35.3 *vs.* 16.3 months, P<0.001). The difference remained significant when non-resected patients were matched for time of neoadjuvant therapy (19.9 months, P<0.001). Positive nodal status (P=0.026) and positive margin resection (P=0.032) correlated with shorter post-resection survival in the resected cohort.

Conclusions: Surgical resection of the primary tumor after neoadjuvant therapy is feasible in 20% of LAPC patients and results to significantly higher OS, reaching a median time of 35 months from diagnosis.

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AB008. S008. Diagnostic yield of intraoperative pancreatoscopy for the investigation of pancreatic IPMN

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Background: Intraoperative pancreatoscopy in a very promising tool that might, in the future, guide surgical resection during surgery for intraductal papillary mucinous neoplasm (IPMN). Nevertheless data about diagnostic yield are still lacking. The aim is to assess the diagnostic yield of intraoperative pancreatoscopy.

Methods: Retrospective cohort analysis in histologically proved main duct (MD)-involving IPMN patients. Sensitivity, specificity, positive predictive value and negative predictive value were calculated. Characteristics of patients and on definitive histology were recorded. Data about endoscopic features such as the presence/absence of mucus, pathological vessels, and intraductal exophytic growth were also recorded. Assessment about the presence or the absence of IPMN was expressed by the operator. Categorical variables were compared by fisher test.

Results: From 2015 to 2017, 22 patients, 10 (45.45%) male, median age 67 (45–82) years underwent intraoperative pancreatoscopy during surgical resection for MD-involving IPMN. 10 patients (45.45%) displayed endoscopic characteristics consistent with the presence of IPMN. Hundred percent of cases were confirmed at definitive histology to have high grade dysplasia-cancer. Twelve patients (54.54%) displayed negative endoscopic finding. Among those, definitive histology confirmed the absence of high grade dysplasia-cancer in 7 (58.33%). The overall sensitivity was therefore 66.67% (33.38–88.18%), specificity 100% (59.04–100%). PPV was 100% (69.15–100%) and NPV was 58.33 (27.67–84.83%). Pathological vessels were more prevalent in high grade dysplasia-cancer patients (53.33% *vs.* 0%, P=0.02) as well as intraductal exophytic growth (60% *vs.* 14.28%, P=0.07).

Conclusions: Intraoperative pancreatoscopy is an accurate tool that might guide the extension of the surgical margins and therefore improve radicality during surgery for pancreatic MD-involving IPMN.

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AB009. S009. Effect of endoscopic iodine 125 seeds brachytherapy on advanced pancreatic cancer: experience of single center

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Background: Pancreatic cancer (PC) is a highly lethal malignancy of digestive system, and nearly 80 percent of PC patients have lost the chance of surgery due to the lack of early diagnosis. For these patients, the only effective treatment (chemotherapy) is largely limited by drug resistance. Therefore, it is urgent to develop new therapy for PC. Endoscopic ultrasound (EUS) guided Iodine 125 (I^{125}) seeds brachytherapy is a novel way of radiotherapy, and its role in the treatment of advanced malignant tumors is not fully explored. This study is to explore the efficacy of I^{125} brachytherapy on advanced pancreatic cancer.
Methods: Log-rank test was used to analyze the difference of overall survival between different groups from one pancreas center.
Results: The overall survival (OS) of PC patients treated with I^{125} (n=27) was significantly longer than patients received palliative treatment (n=46). Subgroup analytic results suggested that the OS of patients with $I1^{25}$ alone (n=15) was similar to patients with palliative treatment; however, patients with I^{125} followed by chemotherapy (n=12) markedly survived longer than patients with palliative treatment. To further assess the association between I^{125} brachytherapy and chemotherapy, we analyzed the OS difference between I^{125} followed by chemotherapy group and chemotherapy group (n=19). The data revealed that patients in $I1^{125}$ followed by chemotherapy group obtained long-term survival than patients in chemotherapy group. The I^{125} brachytherapy combined with chemotherapy group got more satisfactory result than chemotherapy group.
Conclusions: The EUS guided I^{125} seeds implantation followed by chemotherapy may be an important therapeutic approach to advanced pancreatic cancer. However, more related large-sample, multi-center randomized controlled trial (RCT) studies should be conducted for further evaluating the value of this therapy.

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AB010. S010. Pancreatic cystic lesions' follow-up with abdominal ultrasound scan: could it play an alternative role to the routine use of MRI?

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Background: Pancreatic cystic lesions (PCL) without "worrisome features" (WFs) at the time of diagnosis, usually necessitate a lifetime surveillance. The routine follow-up in these cases comprises a magnetic resonance imaging (MRI) scan every 6 months in the 1st year, then annually for the next 5 years. Since these parameters can also be evaluated with an abdominal ultrasound scan (AUS), we studied the safety, feasibility and economic impact of AUS follow-up, with a delayed use of MRI.

Methods: We retrospectively evaluated all patients who had been followed-up with AUS for the presence of "low risk" PCL. All of patients underwent to an AUS every 6 months for the 1st year and then, in case of stable disease, annually from the 2nd to the 5th year. A surveillance MRI scan was routinely executed every 2 years, or according to the presence of considerable modifications at AUS. We compared the two methods regarding sensitivity and specificity in identifying cysts variations. We also focused on a costs-analysis between the theoretical application of the international guidelines follow-up with MRI, and our follow-up strategy with AUS and delayed MRI.

Results: Two hundred patients were followed-up with AUS between January 2012 and January 2016 for PCL. Mean follow-up period was 25.1±18.2 months. Surgery was required for 2 patients (1%), due to the appearance of WF at imaging [with concordance among ultrasonography (US) and MRI]. During the follow-up, AUS showed "low grade" modifications in 28 patients (14%), comprising main pancreatic duct dilatation <6 mm and increasing of the main cyst of about 0.5 cm, compared to previous examinations. In all of these cases MRI confirmed AUS findings, without adding more prognostic information. In only 11 patients (5.5%) a routine MRI identified an evolution of the lesions, not showed at AUS, but only related to an increased number of the PCL (P=0.14). Nevertheless, a MRI every 6 months would not have changed in any case the decisional process. The mean cost of surveillance for each patient, in a theoretical application of international guidelines with MRI at our group of patients, should have been 402€±273.7€, while according to our follow-up strategy it was 215.4€±212.6€ (P<0.0001).

Conclusions: In patients with PCL without WF, AUS, could be a safe alternative to MRI, reducing the numbers of 2nd level examinations and therefore reducing costs. Long term safety of this approach should be validated on a longer follow-up period, with a larger series of patients and prospective studies.

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AB011. S011. Mesenchymal pancreatic cancer cells inhibit pancreatic stellate cell activation

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Abstract: Pancreatic ductal adenocarcinoma (PDAC) is a malignancy with a poor prognosis. Resection is the only curative option and even then, reported 5-year survival rates are less than 10%. Most patients present with advanced disease and these rarely respond to chemotherapy. This lack of response is thought to be, at least in part, related to the abundant stromal tissue surrounding the tumor cells but tumor-restraining aspects have been attributed to the stroma as well. Pancreatic stellate cells (PSCs) are the main constituent of the PDAC stroma and are involved in remodelling the extracellular matrix. The crosstalk between tumor cells and PSCs has been studied extensively, but this has focused on PSC activation. Surprisingly, we now find that conditioned medium from mesenchymal but not from epithelial pancreatic tumor cell lines inactivates PSCs. This effect is stronger than that of known inhibitors such as retinoic acid and vitamin D, as determined by cell number and stromal activation marker expression. By differential filtration of the tumor cell conditioned medium, we find that the unknown protein should be between 30 and 50 kDa and using gene expression data a small selection of candidate proteins has been established. Validation experiments to identify the candidate protein are ongoing. Identification of this molecule can be used to devise novel therapeutics that act specifically on activated stroma and provide a more specific anticancer treatment.

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AB012. S012. Immunophenotypes of pancreatic ductal adenocarcinoma

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Abstract: Pancreatic ductal adenocarcinoma (PDAC) is the most common malignancy of the pancreas and has one of the highest mortality rates of any cancer type with a 5-year survival rate of <5% and median overall survival of typically 6 months from diagnosis. PDAC has not had much success with any of the known checkpoint therapies so far but there are other immunotherapies currently under investigation. Here we use known expression signatures of immune cells on two independent cohorts to postulate three immunophenotypes for PDAC. We define these as "adaptive", "innate" and "immune-exclusion" immunologic signatures, which are prognostic across independent cohorts. We subsequently looked at our immunophenotypes across previously published sub-type studies (Collisson *et al.* 2011, Moffitt *et al.* 2015, Bailey *et al.* 2016, Sivakumar *et al.* 2017). The immunophenotypes are present within sub-types described across all these studies. Despite the fact that immunotherapies have yet to have an impact in treatment of PDAC, the gene expression signatures that stratify PDAC across studies are immunologic. An appreciation of the immune composition of PDAC with prognostic significance is an opportunity to understand distinct immune escape mechanisms in development of the disease and design novel immune-oncology therapeutic strategies to overcome current barriers.

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AB013. S013. Towards early detection of pancreatic cancer: applying NGS in the clinical setup

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Background: Pancreatic cancer (PC) is the third leading cause of cancer death in the US, with a lifetime risk of 1.5%. The 5-year survival rate is 7.2%, the poorest survival rate of any common malignancy. At early stages, surgical treatment is most beneficial, however, early diagnosis is rare, and most PC cases are confirmed as being locally invasive or metastatic. Inherited predisposition to pancreatic cancer is prevalent in 10% of PC cases. However, about 80% of PC cases with strong family history are still uncharacterized therefore making it hard to identify high-risk individuals. It was shown that PC development from a small precancerous lesion into a tumor is a relatively slow process, emphasizing the importance of screening in high-risk individuals. The concept of a dedicated high-risk pancreatic cancer clinic is relatively new and there are only a few such clinics worldwide. We established a high-risk pancreatic cancer clinic with the aims of (I) improving survival of individuals at high-risk for pancreatic cancer; (II) identifying genetic alterations and molecular pathways associated with familial pancreatic cancer risk.

Methods: We have recruited 135 high-risk PC individuals for genetic screening and clinical surveillance. Forty individuals fulfilled criteria for familial pancreatic cancer and 70% of the cohort have undergone genetic testing. We applied whole exom sequencing (WES) technique to screen families with high prevalence to PC for pathogenic germline mutations.

Results: Forty individuals (45% of those who were tested) were found to carry a pathogenic mutation. *BRCA2* mutation was found most frequently (20%), followed by *BRCA1* (14%), *PALB2*, *STK11* and *ATM* mutations. WES revealed a wide variety of genetic changes (*KLLN*, *HMMR*, *GATA5*, *MSR1* and *KDR* genes), that would not have been detected, if testing was limited to multi-gene panels.

Conclusions: Identifying high-risk PC individuals is crucial for surveillance and early detection that may lead to improved survival. WES is currently the test of choice for genetic evaluation of these high-risk individuals.

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AB014. S014. Fractional uptake of circulating tumor cells across liver-lung compartments during resections of periampullary cancer aimed at cure

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Background: Circulating tumor cells (CTCs) are prognostic for outcome in breast, colon, and prostate cancer and seem to represent promising biomarkers of pancreatic carcinoma as well. The aim of the present study was to demonstrate a statistically significant portal-arterial difference of CTC during resection of periampullary cancer aimed at cure in a limited number of patients.

Methods: A commercially available instrument (Isoflux®) was used to quantify blood content of CTC in ten patients with periampullary cancer according to preoperative diagnostics. Portal and arterial blood (each 8–10 mL) were simultaneously collected intra-operatively after surgical dissection before division of the pancreas for tumor removal. Quantitative CTC analyses were performed according to standardized protocols for immune-magnetic enrichment of CTC. Flow cytometry was applied for qualitative evaluations of various CTC markers in seven patients.

Results: There was a statistically significant difference in numbers of CTC collected in portal blood [58±43 cells per 100 mL, (±SD)] versus arterial blood (24±22 cells per 100 mL, $P<0.025$). A fractional uptake at 40% across liver and lung compartments of assumed malignant CTC was estimated to correspond to the appearance of approximately 400 tumor cells per minute during pancreatic resections based on estimated hepatic blood flow, measured tumor cell mass and tumor cell proliferation activity. Complications to collection of portal blood were not observed.

Conclusions: A significant uptake across liver or lung compartments of potentially malignant CTCs from periampullary carcinoma may represent a model to capture, define and characterize cell clones with high metastatic potential in liver and lung tissues following surgical resections.

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AB015. S015. Circulating tumor cells dynamics in pancreatic adenocarcinoma correlate with disease status: data from a prospective trial

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Background: Previous retrospective studies demonstrated that circulating tumor cells (CTCs) subtypes in patients with pancreatic ductal adenocarcinoma (PDAC) correlate with disease-specific survival. Herein, we report results of a prospective observational trial on CTC dynamics to assess their clinical significance.

Methods: The CLUSTER trial is a prospective longitudinal study on PDAC CTC dynamics (NCT02974764). Multiple peripheral blood samples are collected from 160 consecutively enrolled patients with PDAC diagnosis. CTCs are enriched using an isolation-by-size assay, and their phenotype is characterized by immunofluorescence.

Results: Two major CTC subtypes are identified in all patients: epithelial CTCs (eCTCs) and mesenchymal CTCs (mCTCs). Patients who previously received neoadjuvant chemotherapy have significantly lower total CTCs (tCTCs) and mCTCs, compared to untreated patients eligible for upfront resection (P<0.001). In multivariable logistic regression analysis, preoperative numbers of tCTCs and mCTCs are the only predictors of early recurrence and disease-associated mortality, within 12 months from surgery (P=0.03). Surgical resection of the primary tumor results in significant reduction in CTC burden across all cell subtypes (P<0.001). Longitudinal monitoring of CTCs postoperatively shows an increase in CTC numbers within a median time of 2 months, prior to radiological evidence of disease recurrence.

Conclusions: We report novel findings regarding CTCs from a large prospective trial in patients undergoing PDAC resection. CTC dynamics reflect response to treatment and progression of disease, providing important information on clinical outcomes, not available by current tumor markers and imaging.

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AB016. S016. Lymphadenectomy in resected node-negative pancreatic cancer: are some patients being understaged?

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Background: Validated benchmarks for adequate lymphadenectomy (LAD) are well established for gastric and colon cancers to avoid stage-migration. Although a harvest of 15 nodes has been proposed for pancreas cancer, this number has not been confirmed in a large, multi-institutional setting. We examined the relationship between LAD and survival in node-negative patients having undergone pancreatectomy for pancreatic adenocarcinoma to identify whether some patients with low lymph node counts are understaged.

Methods: We identified all node-negative patients undergoing pancreaticoduodenectomy (PD) and distal pancreatectomy (DP) for pancreatic adenocarcinoma within the National Cancer Database (NCDB) between 2004 and 2014. We excluded patients with clinical or pathologic M1 disease, as well as patients that died within 90 days from surgery and those with no data on lymph node harvest. Univariate and multivariate quantile regression were used to identify the effect of lymph node harvests and other patient and tumor-specific variables on survival.

Results: We identified 7,329 and 2,071 patients undergoing PD and DP respectively staged as pN0 and meeting inclusion criteria. Median survival was 21.5 (95% CI, 21.1–21.9) and 21.2 (95% CI, 20.1–22.1) months in the PD and DP groups, respectively. In the PD group, LAD ≥15 was not associated with a higher median survival [21.6 (95% CI, 20.9–22.4) and 21.3 (95% CI, 20.7–21.9) months in the <15 and ≥15 LN, respectively, P=0.223]. In the DP group, median survival was 20.2 (95% CI, 19.2–21.6) and 22.6 (95% CI, 20.9–24.4) in the LAD <15 and LAD ≥15 groups (P=0.068). On univariate quantile regression, age, higher tumor grade, lymphovascular invasion, higher T stage, positive margin and not receiving chemotherapy or radiation were associated with decreased survival and retained that association on multivariate regression whereas LAD was not associated with a change in survival in the PD group.

Conclusions: We did not identify a group of patients that were understaged as a function of low lymph nodes harvests. A benchmark of 15 lymph nodes for pancreas cancer cannot be recommended as a quality measure.

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AB017. S017. Is main pancreatic duct dilation really an independent risk factor for malignancy in main-duct and combined-IPMNs?

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Background: In main duct (MD) or combined main duct (CMD) intraductal papillary mucinous neoplasm (IPMN) pancreatic duct (MPD) diameter between 5–9 mm is identified by International Association of Pancreatology (IAP) guidelines as a worrisome feature (WF) requiring close follow-up. However, some authors argue that the risk of degeneration in these patients is already high enough to recommend surgery. The aim is to evaluate the significance of the MPD diameter at preoperative imaging as an independent predictor of high-grade dysplasia (HGD)/adenocarcinoma (ADK) in MD-/CMD-IPMN.

Methods: Prospectively collected data was analyzed of patients undergoing pancreatic resection for IPMN at three high-volume pancreatic centers between 2009 and September 2017. MPD diameter was measured preoperatively with magnetic resonance imaging (MRI), computed tomography (CT) or endoscopic ultrasound (EUS).

Results: Two hundred and sixty-three pts underwent pancreatic resection for either a MD (14.8%) or CMD-IPMN (71.7%). Of these, 179 (68.1%) had HGD/ADK (77.8% in MD-IPMNs; 66.4% in CMD-IPMNs). Among the pts with HGD/ADK, 88.8% had at least one high-risk stigmata (HRS). Of the 98 patients with MPD >10 mm, 77.6% had degenerated IPMNs. A HGD/ADK was found in 81/122 (66.4%) patients with MPD 5–9 mm. However, 69 (85.2%) of these had at least one HRS and 10 had at least one other WF. Of the remaining two pts, one had elevated preoperative Ca19.9 and the other had only micro-foci of carcinoma at pathology. Thus, most patients with HGD/ADK would have had other indications for surgery beyond MPD 5–9 mm according to IAP guidelines. ROC curve analysis identified 8.5 mm as the optimal cut-off to distinguish low grade and high grade/invasive IPMNs [area under the curve (AUC) 0.66)]. This cut-off was used in univariate analysis (OR =3.06, P<0.01) with jaundice (OR =7.9, P<0.01), the presence of nodules as an ordinal variable comprising non-enhancing (OR =1.1, P=0.81), enhancing (OR =4.2, P<0.01) and macroscopic solid component (OR =5.8, P<0.01), positive cytology (OR =14.8, P<0.01), elevated Ca19.9 (OR =5.2, P<0.01) and pancreatitis, cyst ≥3 cm, thickened wall, abrupt MPD change and altered glucose tolerance which were not statistically significant. Multivariate analysis identified MPD ≥8.5 mm (OR =7.8, P<0.01), enhancing nodules (OR =8.7, P=0.01), positive cytology (OR =12.2, P<0.01) and elevated Ca19.9 (OR =3.37, P=0.01) as independent predictors of malignancy.

Conclusions: Our study confirms that, while for diameters ≥1 cm the risk of degeneration is high and surgical treatment must be recommended, smaller MPD diameters without other HRS do not appear to be as strongly linked to malignancy. A diameter of 8.5 mm was identified as the optimal cut-off with significant correlation to IPMN degeneration at multivariate analysis.

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AB018. S018. The prognostic impact of primary tumor resection in pancreatic neuroendocrine tumors with synchronous multifocal liver metastases

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Background: Whether primary tumor resection benefits patients with synchronous multifocal liver metastases from pancreatic neuroendocrine tumors remains controversial. We investigated whether primary tumor resection significantly affects survival in this study.
Methods: A retrospective study of patients with synchronous multifocal liver metastases from pancreatic neuroendocrine tumors between 1998 and 2016 was performed. Patient demographics, operation details, adjuvant treatment, and pathological and survival information were collected, and relevant clinical-pathological parameters were assessed in univariate and multivariate survival analyses.
Results: Sixty-four patients were included in this study, including 35 patients who underwent primary tumor resection. For the patients who did not undergo primary tumor resection, treatment consisted of observation, octreotide administration, and/or systemic chemotherapy. The median survival time and 5-year survival rate of this cohort were 50 months and 45.8%, respectively. Median survival time in the resected group was significantly longer at 72 months than that of 32 months in the non-resected group (P=0.021). Multivariate analysis showed that primary tumor surgery was a significant independent prognostic factor (HR =0.368; 95% CI: 0.142–0.949; P=0.039).
Conclusions: Primary tumor resection significantly benefits patients with synchronous multifocal liver metastases from pancreatic neuroendocrine tumors. However, this treatment option should be individually evaluated for each patient and should become a part of the integrated therapeutic strategy according to the clinician's judgement.

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AB019. S019. Pancreatectomy plus arterial resection is superior to palliation in patients with locally advanced PDAC

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Background: Pancreatectomy plus arterial resection (PAR) for locally advanced pancreatic ductal adenocarcinoma (PDAC) (LAPC) might potentially offer additional therapeutic option and a better prognosis in patients traditionally addressed to palliation. Being a technically high skill demanding surgery, has been postulated that it could be hampered by higher rates of morbidity and mortality. Anyway few, small studies have specifically investigated its feasibility and data on short and long-term outcomes currently lack. To analyze complications and outcomes of patients underwent PAR.

Methods: Retrospective analysis of prospectively collected cohort of operated LAPC patients. Short and long term outcome were analyzed and compared in Group 1 (PAR) and Group 2 (palliative surgery).

Results: Seventy-three patients (T4M0) underwent surgical exploration with intent of resection, 46.6% (Group 1), 53.4% (Group 2). No differences were found for neo/adjuvant chemotherapy. Twenty-three patients (67.7%) in Group 1 received a combined artery-vein resection (AVR). Operation time and blood loss were superior in Group 1 compared to Group 2, respectively (425.7±14.3 *vs.* 171.4±10.67 minutes, P<0.0001) and (613.2±71.69 *vs.* 188.3±20.64 mL, P<0.0001) while no differences were found in post-operative mortality (2.9% *vs.* 2.6%, P=0.9) and post-operative surgical complications (38.2% *vs.* 25.6%, P=0.2). The 1, 3 and 5 years survival in Group 1 was superior to Group 2 (63.7%, 23.4% and 23.4% *vs.* 41.7%, 3.2% and 0%, P=0.003).

Conclusions: PAR seems to be safe and feasible in well selected patients and associated with an advantage of survival compared to palliations, in patients affected by LAPC.

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AB020. S020. Importance of adjuvant hepatic arterial infusion chemotherapy using high-dose 5-fluorouracil with systemic gemcitabine for resectable pancreatic cancer

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Background: Despite recent advances in cancer treatment, postoperative recurrence remains an unsolved issue for resectable pancreatic cancer. To prevent hepatic recurrence and prolong postoperative survival, we introduced postoperative adjuvant chemotherapy of high-dose 5-fluorouracil (5-FU) hepatic arterial infusion (HAI) with systemic chemotherapy using gemcitabine in 2006. We retrospectively evaluated the clinical impact of HAI.

Methods: A total of 251 patients who underwent pancreatic resection for pancreatic cancer (PC) were analyzed. Patients received weekly high-dose 5-FU through the hepatic artery using a port-catheter system (1,000 mg/m^2 for 5 h) plus concurrent systemic gemcitabine (1,000 mg/m^2) followed by systemic 3 cycles of gemcitabine or 4 cycles of S-1. Patients were divided into two groups. The patients who completed planned adjuvant chemotherapy of HAI were classified as the completion group (HAI), and the patients who failed to complete HAI or received systemic adjuvant chemotherapy other than HAI were classified as the control group.

Results: One hundred thirty-eight patients (55%) completed planned adjuvant chemotherapy of HAI. On the other hand, 28 patients (11%) failed to complete HAI and 85 patients (34%) received systemic adjuvant chemotherapy alone. The reasons for incompletion of HAI were as follows: any recurrence during HAI treatment in 8, poor general condition of patients in 4, hepatic arterial stenosis in 4 and catheter trouble in 3. Initial hepatic metastasis rate was significantly lower in the HAI group than the control group (15.2% *vs.* 26.3%, P=0.029), and liver metastasis free survival was significantly better in the HAI group than the control group (P=0.001). The HAI group had a better prognosis than the control group (58.1 *vs.* 26.9 M, P<0.001). Prognostic factor analysis indicated that failure to complete HAI (P<0.001, HR =1.95), borderline resectable tumor (P=0.028, HR =1.63), and lymph node metastasis (P=0.018, HR =1.59) were the independent adverse prognostic factors.

Conclusions: Our data demonstrate that HAI can significantly prevent hepatic recurrence and also improve the postoperative prognosis in pancreatic cancer.

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AB021. S021. Expression patterns and clinical implications of immunotherapy targets PD-1, PD-L1 and CD163 in undifferentiated carcinoma of the pancreas with osteoclast-like giant cells

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Abstract: One of the variants of pancreatic ductal adenocarcinoma (PDAC), the undifferentiated carcinoma with osteoclast-like giant cells (UCOGCs), has been recently studied with whole-exome sequencing. Despite striking similarities of somatic mutations with PDAC, the clinical course of UCOGC is very different from PDAC. Considering the relevance of immunotherapy markers in solid tumors, we investigated the expression of PD-1, PD-L1 and CD163 in a series of UCOGC. To this aim, 23 pancreatic UCOGC (10 pure and 13 PDAC-associated) and 5 extra-pancreatic tumors with osteoclast-like giant cells were immunostained using antibodies against PD-1, PD-L1 and CD163. In pancreatic UCOGC, PD-L1 was expressed in neoplastic cells of 15/23 (65%) cases, more often in cases with an associated PDAC (11/13) (P=0.039). This marker showed a poor prognostic value, confirmed at multivariable analysis: patients with PD-L1 positive UCOGC had a risk of all-cause mortality of more than 3 times fold than those with PD-L1 negative tumors (HR: 3.340; 95% CI: 1.062–17.999; P=0.036). PD-1 was expressed on rare lymphocytes in 10 UCOGC (43.5%), mainly located at the tumor periphery. CD163 was expressed on histiocytes, with a diffuse and strong staining pattern in all UCOGCs. Extra-pancreatic cases showed very similar staining patterns for the same biomarkers. Concluding, we report the expression of PD-L1, PD-1 and CD163 in a significant number of UCOGC, and show that PD-L1 has prognostic significance. Our results may have important implications for the immunotherapeutic strategies in this tumor type, and possibly for tumors with osteoclast-like giant cells of other organs.

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AB022. S022. A continuous clonal labeling method to reveal growth dynamics in developing, adult and injured pancreas

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Background: Although a wealth of knowledge has been gathered on normal pancreatic tissue maintenance and repair following injury, some fundamental questions remain. These pertain for instance to the existence and contributions of stem-like cells, and the plasticity of cell fates. Lineage tracing studies from predefined cell populations have been performed but these are invariably plagued by a priori assumptions on the cell of origin.

Methods: Using quantitative analyses of a marker-free and stochastic lineage tracing mouse model in healthy pancreatic tissue, we can quantitatively describe the growth dynamics during development and homeostasis. In addition, we can quantify the contribution of purported stem-like cells to this process and whether transdifferentiation occurs. To define the clonal dynamics during regeneration we will induce pancreatitis in this same mouse model.

Results: In our preliminary analyses we found increasing clone sizes during ageing of the mice, next to a stable fraction of small clones. We also noticed that mainly the acinar cell type is labeled, suggesting a higher turn-over rate in this compartment. Other pancreatic cell types, like duct and islet cells were also labeled but showed less dynamics. We established that this marker-free lineage tracing method is applicable to study the fundamental pancreatic growth dynamics.

Conclusions: Our incomplete understanding of the clonal dynamics in the healthy pancreas is an important hurdle to fully understand the growth and biology of the injured pancreas and eventually of pancreatic cancer. More knowledge about the growth dynamics during homeostasis and regeneration can give valuable insights to improve treatment of pancreatic cancer.

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AB023. S023. Identification and targeting of a poor-prognosis subgroup of pancreatic cancer

Veronique Veenstra, Frederike Dijk, Eline Soer, Lan Zhao, Johannes Halfwerk, Gerrit Hooijer, Naomi Donner, Helene Damhofer, Marco Marzano, Anne Steins, Cynthia Waasdorp, Olivier Busch, Marc Besselink, Johanna Tol, Lieke Welling, L. Bengt van Rijssen, Hanneke Wilmink, Hanneke van Laarhoven, Jan Paul Medema, Louis Vermeulen, Sander van Hooff, Jan Koster, Joanne Verheij, Marc van de Vijver, Xin Wang, Maarten Bijlsma

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Abstract: Pancreatic ductal adenocarcinoma (PDAC) has the worst prognosis of all common cancers, but strongly divergent outcomes are apparent between patients. To reveal and address the intertumor heterogeneity that contributes to this, we have performed RNA-Seq gene expression analysis on a large number of resected PDAC samples (n=90). Unsupervised class discovery in this single-center PDAC-only dataset identified four subgroups with distinct clinical manifestations. Biological interpretation and network analysis comparisons to existing classification systems revealed a poor-prognosis subgroup characterized by mesenchymal features. Species-specific transcript analysis on matching patient-derived xenograft (PDX) models allowed assembly of an epithelium-tailored classifier for use on cell lines and primary cultures. Experimental validation in models for PDAC subtyped using the modified classifier confirmed mesenchymal features and a highly invasive growth pattern for the poor-prognosis subtype in contrast to more epithelial (non-mesenchymal) subtypes. To identify specific therapeutic vulnerabilities of this poor-prognosis subgroup, drug sensitivity screen data were queried. This revealed that cell lines and primary cultures of the mesenchymal subtype are particularly sensitive to the one of a kind drug elesclomol. We found that elesclomol perturbs mitochondrial functioning, and that this specifically affects mesenchymal PDAC cells. These effects were independent of reactive oxygen species levels, previously reported as the effector of treatment with elesclomol. Concluding, we have identified and functionally addressed the mechanisms responsible for poor-prognosis PDAC and propose that perturbation of mitochondrial function is a promising therapeutic strategy to improve outcome of those PDAC patients that are in most dire need of improved therapies.

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AB024. S024. Drug responses of patient-derived cell lines *in vitro* that match drug responses of patient PDAc tumors *in situ*

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Abstract: Pancreatic ductal adenocarcinoma (PDAC) is a devastating disease for which the incidence and mortality rates are nearly equivalent. Only 2% of patients with metastatic disease survive 5 years after diagnosis. Even in rare cases of partial response to systemic chemotherapy, disease typically recurs and the National Comprehensive Cancer Network (NCCN) guidelines recommend clinical trials as the next best option. Outcomes are more promising if tumors are confined to the pancreas and can be surgically resected; yet only 20% of patients treated surgically are disease free after 5 years. Approximately 30% of patients diagnosed with metastatic PDAC have partial responses to modern standard-of-care (SOC) chemotherapy regimens, though these responses are typically short-lived. However, exceptional cases of durable response to chemotherapy do exist and understanding the nature of these chemo-sensitive tumors may reveal biomarkers of tumor susceptibility to chemotherapy. Moreover, no biomarker exists to guide selection of SOC FOLFIRINOX or gemcitabine + Abraxane regimens, and chance dictates response even though one regimen may be significantly more effective. Clinical trials using biomarker-guided, targeted therapeutics have not typically demonstrated efficacy over SOC chemotherapy. Given these findings it is important to identify which SOC chemotherapy regimen will be most effective against PDAC. We have identified PDAC tumors which were exceptionally sensitive to SOC chemotherapy *in situ* and used biopsied or resected tumor tissue to generate low-passage, continuously-regenerating cell lines (CRCs). We collected over 100 treatment-naïve tumor specimens and then tracked future responses to SOC chemotherapy to identify exceptionally chemo-sensitive CRCs. We found strong concordance between the *in situ* tumor response and the *in vitro* CRC responses to SOC agents. We performed a real-time, multimetric in vitro drug-response assay designed to measure growth rate, time and concentration required for drug-induced cell death, and the ability of CRCs to proliferate after drug withdrawal. Results from the multimetric, drug-response assay identified parameters other than conventional endpoint metrics (e.g., IC50) that best matched the known *in situ* response. By understanding the *in vitro* cell behaviors that reflect *in situ* tumor sensitivity we hope to identify biomarkers that can be used to guide drug selection in patients diagnosed with PDAC.

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AB025. S025. Basement membrane destruction by pancreatic stellate cells leads to local invasion in pancreatic ductal adenocarcinoma

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Abstract: Stroma invasion is an important step in pancreatic cancer progression. However, how pancreatic ductal adenocarcinoma (PDAC) with ductal structure invades the surrounding stroma has not been clear. Here, we elucidated the mechanism of stromal invasion of PDAC, using organoids. From resected PDAC specimens, we established human PDAC organoids, which developed ductal and basement membrane (BM) structures. When the organoids were co-cultured with pancreatic stellate cells (PSCs) in a collagen matrix, organoids lost their BM and ductal structures, and invaded collagen matrix more frequently than did mono-cultured organoids. Interestingly, direct contact by PSCs to PDAC organoids was observed before BM destruction. Matrix metalloproteinase (MMP) 2 or membrane type-1 MMP (MT1MMP) knockdown in PSCs significantly attenuated BM destruction by PSCs, and retained the ductal structures in organoids. Our results imply that direct contact by PSCs induces BM destruction and stromal invasion of PDAC via MMP2 which binds to MT1MMP on PSCs.

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AB026. S026. What is the optimal surgical strategy for grade-C pancreatic fistula after pancreaticoduodenectomy? A large retrospective multicenter study

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Background: The optimal surgical strategy for grade-C postoperative pancreatic fistula (POPF) is controversial. We aim to identify the optimal surgical strategy for grade-C POPF following pancreaticoduodenectomy (PD).

Methods: This retrospective study involved nine high-volume Chinese institutions, in which, 5,115 patients underwent PD between January 1, 2012 and December 31, 2016. Of them, 53 (1.04%) underwent re-laparotomy for grade-C POPF. We retrospectively reviewed their clinical data. We compared the re-laparotomy techniques used in terms of their outcomes and evaluated risk factors for unfavorable outcomes by using multivariate regression analysis.

Results: The following surgical strategies for re-laparotomy were used in this cohort: external wirsungostomy (20 patients, 37.7%), re-pancreaticojejunostomy (15 patients, 28.3%), simple peritoneal drainage (15 patients, 28.3%), completion pancreatectomy (2 patients, 3.77%), and pancreatogastrostomy (1 patient, 1.89%). Postoperative hospital stay in the external wirsungostomy group was significantly shorter than that in the simple peritoneal drainage group (20 *vs.* 38 days, P=0.03), and tended to be lower than that in the re-pancreaticojejunostomy group (20 *vs.* 34.5 days, P=0.068). Mortality and morbidity were comparable among the above three groups. Multivariate regression analysis showed that the presence of biochemical leakage or grade-B POPF prior to the development of grade-C POPF (odds ratio: 0.20; 95% confidence interval: 0.05–0.82) was independently associated with unfavorable outcomes.

Conclusions: Pancreas-preserving approaches were preferred for grade-C POPF. External wirsungostomy was associated with shorter postoperative hospital stay. Patients with less severe POPF before progressing to grade-C POPF may have better outcomes after re-laparotomy.

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AB027. S027. Factors associated with invasive intraductal papillary mucinous carcinoma

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Background: Invasive intraductal papillary mucinous carcinoma (IPMC) may have distant or lymph node metastasis, and postoperative recurrence may occur, leading to poor survival even after resection. To identify the specific predictors of invasive IPMC for branch duct (BD), main duct (MD), and mixed types.

Methods: This study included 286 consecutive patients undergoing surgical resection for intraductal papillary mucinous neoplasm (IPMN). We compared clinical features between invasive IPMC and noninvasive IPMN for each morphological type.

Results: High mural nodule size measured by endoscopic ultrasonography was an independent predictor of invasive IPMC in all types of IPMN [BD-IPMN: P=0.01, odds ratio (OR), 1.992; mixed-IPMN: P=0.042, OR, 1.178; MD-IPMN: P=0.01, OR, 1.443]. Its cutoff values, determined by a receiver operating characteristic were 9 mm in BD-IPMN and 6 mm in mixed- and MD-IPMNs. A high carcinoembryonic antigen (CEA) level in the pancreatic juice was an independent predictive factor of mixed- and MD-invasive IPMCs (mixed-IPMN: P=0.011, OR, 1.002; MD-IPMN: P=0.048, OR, 1.002), and the cutoff values were determined to be 150 and 300 ng/mL, respectively. In addition, we found that being female (P=0.014, OR, 6.135) and having elevated serum carbohydrate antigen 19-9 (P=0.009, OR, 29.412) were also independent predictors of mixed-invasive IPMC, and using any two among four identified predictors yielded the highest accuracy (79.0%). For all types, the accuracy for these predictors was 86.0% for differentiation between invasive and noninvasive IPMN.

Conclusions: The measurement of mural nodule size in all types of IPMN and the CEA level in the pancreatic juice in mixed- and MD-IPMNs might play important roles in predicting invasive IPMC, but further large studies are needed to confirm these results (*JAMA Surg*, 2017).

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AB028. S028. Risk of the serous cystic neoplasms in pancreas results from no surgical intervention: a multi-center retrospective study

Ning Pu, Ji Li, Gang Li, Xin Wang, Gang Zhao, Lei Wang, Xiaodong Tian, Chunhui Yuan, Kuirong Jiang, Jun Cao, Xiaowu Xu, Xueli Bai, Yongsheng Yang, Fubao Liu, Xuewei Bai, Rui Kong, Zheng Wang, Wenhui Lou, Wenchuan Wu

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Background: Serous cystic neoplasms (SCN) of the pancreas are known as no malignant potential, so accurate diagnosis of SCN is significant for pancreatic cancer early detection and prevention as well as avoidance of unnecessary surgeries. However, the faults of preoperative diagnosis may highly increase the risk of carcinogenesis.
Methods: A total of 99 patients with exactly preoperative diagnostic SCN and 678 patients with pathologically confirmed SCN were retrieved from sixteen institutions from January 1st, 2006 to December 31st, 2016. Analyses were conducted to evaluate the exact risks of SCN with no surgical intervention.
Results: Of the 678 patients, 4 were pathologically verified as carcinogenesis, so the canceration rate was 0.6%, which was less than the risk of surgical interventions. However, among the 99 patients with exactly preoperative diagnostic SCN, 3 were verified as intraductal papillary mucinous neoplasms (IPMN), 9 as mucinous cystic neoplasms (MCN), 4 as solid pseudopapillary tumors (SPT). Thus the canceration rate through preoperative diagnosis had approximately elevated to 2.9%, which was obviously higher than the risks from surgeries.
Conclusions: The preoperative diagnostic SCN still has the potential suitability for surgical resection. Therefore, one more precise diagnostic model should be investigated to improve the clinical practice.

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AB029. S029. Neoadjuvant therapy offers longer survival than upfront surgery for poorly differentiated and higher stage pancreatic cancer

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Background: Neoadjuvant therapy for pancreatic cancer remains controversial. Our aim was to assess differences in survival, disease recurrence and histopathological tumour characteristics between patients treated with neoadjuvant therapy followed by subsequent surgery and patients undergoing upfront surgery.

Methods: Out of 399 consecutive pancreatic ductal adenocarcinoma (PDAC) patients operated at Helsinki University Hospital in 2000 to 2015, 75 borderline resectable patients were treated with neoadjuvant therapy. Resectable propensity scored patients (n=150) underwent upfront surgery. Neoadjuvant therapy consisted of FOLFIRINOX, single gemcitabine or combined with cisplatin, nab-paclitaxel or capecitabine with or without radiation. Survival was calculated with Kaplan-Meier and compared with the Breslow test. Survival was determined from the start of treatment, being the first day of treatment for patients treated with neoadjuvant therapy and the date of surgery for others.

Results: Between 2000 and 2015 median disease-specific survival (DSS) [34 (95% CI, 29–39) *vs.* 26 (95% CI, 20–32) months, P=0.016] and disease-free survival (DFS) [22 (95% CI, 17–27) *vs.* 13 (95% CI, 9–17) months, P=0.001] were longer in patients treated with neoadjuvant therapy than in those undergoing upfront surgery. Survival differences were not significant in the 2000s but were, in turn, among patients treated in the 2010s with better survival for patients treated with neoadjuvant therapy [DSS 35 (95% CI, 25–44) *vs.* 26 (95% CI, 20–31) months, P=0.008 and DFS 25 (95% CI, 13–36) *vs.* 13 (95% CI, 6–21) months, P=0.001]. Especially patients with poorly differentiated G3 tumours had longer survival [DSS 30 (95% CI, 17–42) *vs.* 11 (95% CI, 8–15) months, P=0.004 and DFS 21 (95% CI, 11–31) *vs.* 7 (95% CI, 5–8) months, P=0.001] and higher stage IIB-III [DSS 34 (95% CI, 29–40) *vs.* 20 (95% CI, 14–26) months, P=0.006 and DFS 21 (95% CI, 12–29) *vs.* 10 (95% CI, 7–13) months, P=0.001].

Conclusions: Neoadjuvant therapy offers PDAC patients longer DSS and DFS than upfront surgery. Neoadjuvant therapy benefits especially borderline resectable patients with higher stage and poorly differentiated tumours.

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AB030. S030. Defining and predicting early recurrence in 957 patients with resected pancreatic ductal adenocarcinoma

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Background: A clear definition of "early recurrence" after pancreatic ductal adenocarcinoma (PDAC) resection is currently lacking. The aim of this study was to establish an evidence-based cut-off to differentiate between early and late recurrence and to compare clinicopathologic risk factors between the two groups.

Methods: Patients undergoing pancreatectomy for PDAC between 2000–2013 were included. Exclusion criteria were neoadjuvant therapy and incomplete follow-up. A minimum P-value approach was used to evaluate the optimal cut-off value of recurrence-free survival to divide the patients into early and late recurrence cohorts based on subsequent prognosis. Potential risk factors for early recurrence were assessed with logistic regression models.

Results: Of 957 included patients, 204 (21.3%) were recurrence-free at last follow-up. The optimal length of recurrence-free survival to distinguish between early (n=388, 51.5%) and late recurrence (n=365, 48.5%) was 12 months (P<0.001). Patients with early recurrence had 1-, and 2-year post-recurrence survival rates of 20% and 6% compared to 45% and 22% for the late recurrence group (both P<0.001). Pre-operative risk factors for early recurrence included a Charlson age-comorbidity index ≥4 (OR 1.65), tumor size >3.0 cm on CT (OR 1.53) and CA 19-9 >210 U/mL (OR 2.30). Post-operative risk factors consisted of poor tumor differentiation grade (OR 1.66), microscopic lymphovascular invasion (OR 1.70), a lymph node ratio >0.2 (OR 2.49) and CA 19-9 >37 U/mL (OR 3.38). Adjuvant chemotherapy (OR 0.28) and chemoradiotherapy (OR 0.29) were associated with a reduced likelihood of early recurrence.

Conclusions: A recurrence-free interval of 12 months is the optimal threshold for differentiating between early and late recurrence, based on subsequent prognosis.

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AB031. P001. The value of infectious biomarkers for prediction of complication after pancreatic surgery

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Background: To assess the predictive value of biomarkers for early complication after pancreatic surgery.
Methods: It was a multi-central, observational, prospective study. With 950 cases recruited from seven centers of China, procalcitonin (PCT), C-reactive protein (CRP) and white blood count (WBC) were measured in 1st, 3rd and 5th postoperative day (POD). Chi-square test was for the complication risk factors. One-way ANOVA was for the comparison between the biomarkers in these 4 days. Receiver operating characteristic (ROC) curves were for the complication predictive value. The ClinicalTrials.gov ID was NCT02878668.
Results: (I) There were 590 malignant and 360 benign pancreatic tumors; (II) 502 with and 448 without complication, pancreatic fistula (380, 40%) had the highest morbidity, while the level A, B and C fistula were 278, 90 and 12. Clavien-Dindo classification I–V were 163, 259, 24, 10 and 4, respectively. Hypertension, benign tumor was the risk factors of complication. Age >60 years, diabetes mellitus (DM), liver enzyme elevation, transfusion, intraoperative bleeding >200 mL and benign tumor were the risk factors of pancreatic fistula; (III) in the non-complication subgroup, the mean baseline, POD1, POD3 and POD5 of PCT were 0.10, 0.81, 0.93 and 0.57 μg/L (P=0.118); CRP were 8.39, 70.81, 99.59 and 49.49 mg/L (P=0.000). In the complication subgroup, the mean baseline, POD1, POD3 and POD5 of PCT were 0.09, 0.93, 0.77, 0.37 (P=0.000), CRP were 9.30, 79.70, 153.01, 85.83 (P=0.000); (IV) there were significant differences in the subgroups classified by occurrence of infectious complication, abdominal infection and sepsis in POD3 and POD5 of PCT, and significant difference by occurrence of complication, pancreatic fistula in POD3 and POD5 of CRP, WBC and neutrophil%; (V) the area under the curve (AUC) of POD3 and POD5 of PCT were 0.8, 0.7 and 0.6 (P=0.000) for the prediction of sepsis, abdominal infection and infectious complication. AUC of POD3 and POD5 of CRP and WBC were 0.7 and 0.6 (P=0.000) for the prediction of complication and pancreatic fistula.
Conclusions: PCT is better in the prediction of infectious complication, abdominal infection and sepsis while CRP, WBC and Neutrophil percentage are better in the prediction of complication and pancreatic fistula.

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AB032. P002. Radiomics based classification of pancreatic cystic neoplasms

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Background: Pancreatic cystic masses are detected in greater than 2% of abdominal CTs, and they vary in malignant potential based on underlying pathologic diagnosis. Many of these cystic masses share overlapping imaging features and are difficult to confidently diagnose based on visual assessment of these imaging features. These imaging features, including intensity, shape, size or volume, and textural features can be extracted and quantified through radiomics. The purpose of this study is to use radiomics features to classify different types of pancreatic cystic masses.

Methods: This was an Institutional Review Board (IRB)-approved retrospective study. A total of 103 patients (age: 60.0±15.9 years, 42 males, 61 females) with pathologically proven pancreatic cystic masses with preoperative dual-phase pancreatic protocol CT were identified from the radiology and pathology database from 2003 to 2016. This included 60 intraductal papillary mucinous neoplasms (IPMNs), 8 mucinous cystic neoplasms (MCNs), 20 serous cystadenomas (SCNs), 10 solid pseudopapillary epithelial neoplasms (SPNs), and 5 pancreatic neuroendocrine tumors (PNETs). Primary cystic masses and whole pancreas were manually segmented using Medical Imaging Interaction Toolkit (MITK). The phenotype of each cyst was expressed by 478 radiomics features, including the first order statistics, shape, texture, and textures from wavelet and Laplacian of Gaussian. Additional ten statistics from the whole pancreas and two demographic features of age and gender were also used for the analysis of the types of cyst.

Results: Among the whole 490 features, 30 features were found for the binary classification of IPMN. Radiomics features were significantly different among different types of pancreatic cystic neoplasms. The model was 77.7% accurate in the classification of five types of pancreatic cystic neoplasms. The model achieved 80.6% accuracy in differentiating IPMN vs. non-IPMN pancreatic cystic neoplasms.

Conclusions: Radiomics features were significantly different among different types of pancreatic cystic neoplasms and were potentially helpful for the classification of pancreatic cystic neoplasms.

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AB033. P003. Identification of germline mutations in cancer predisposition genes in patients with a personal and/or family history of pancreatic cancer

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Background: Pancreatic cancer is estimated to have a familial background in 5–10%. Although the underlying genetic basis for most of the familial clustering remains elusive, multiple known hereditary syndromes and genes are associated with an increased risk of developing pancreatic cancer.

Methods: We performed a retrospective genetic evaluation of 80 cancer patients with a presumed genetic predisposition for pancreatic cancer. The probands were selected from seven strata based on personal or family history of pancreatic cancer, breast and/or ovarian cancer, colon cancer or melanoma. Germline DNA was analyzed using a custom designed HEAT-Seq target panel of 52 (pancreatic) cancer susceptibility genes (Roche) and sequencing was performed on a MiSeq instrument. Detected variants were confirmed with Sanger sequencing.

Results: Fifteen patients (18.75%) were heterozygous for at least one loss of function germline mutation in one of 52 (pancreatic) cancer susceptibility genes. We detected 18 class 5 variants in eleven genes: *BRCA1* (n=1), *BRCA2* (n=2), *ATM* (n=3), *FANCM* (n=2), *PMS2* (n=1), *MSH6* (n=1), *FANCE* (n=1), *FANCD2* (n=1), *CHEK2* (n=2), *MUTYH* (n=2) and *NTHL1* (n=2). In addition, eight missense variants were predicted to affect function by in silico prediction programs in eight patients: *ATM* (n=3), *ERCC4* (n=1), *FANCA* (n=1), *BRIP1* (n=1), *RAD51D* (n=1) and *POT1* (n=1).

Conclusions: These preliminary results obtained in a relatively small cohort of cancer patients eligible for genetic testing because of a personal history of breast/colon/pancreatic cancer or melanoma and at least one close relative with pancreatic cancer, revealed inactivating mutations in cancer predisposition genes in 18.75% of the patients and certainly warrant a further extension of the study cohort. These findings warrant further segregation analysis in the families to evaluate their link with the different cancers and highlight the need for recommendations governing germline multi-gene panel testing of cancer patients with a personal or family history of pancreatic cancer.

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AB034. P005. What is the role of central pancreatectomy in pancreatic surgery? —a systematic review and meta-analysis

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Abstract: Background: Central pancreatectomy (CP) is an alternative procedure for the benign or low-malignant lesions at the pancreatic neck and proximal body. The aim of this systematic review and meta-analysis was to compare the clinical outcomes of CP with distal pancreatectomy (DP) and pancreaticoduodenectomy (PD), and evaluate the current status of CP.

Methods: A systematic literature research in PubMed/Medline, Embase and Cochrane Library was performed to identify articles reporting of CP from January 1983 to November 2017. Intraoperative, postoperative and long-term outcomes were evaluated. Pooled odds ratios (ORs) and weighted mean differences (WMD) with 95% confidence intervals (95% CI) were calculated using fixed-effect or random-effects models.

Results: Fifty studies with 1,305 patients undergoing CP were identified. The overall morbidity, mortality, pancreatic fistula (PF) and reoperation rate were 50.7%, 0.5%, 35.0% and 4.1%, respectively. Endocrine and exocrine insufficiency were occurred in 3.6% and 5.1% of patients. Meta-analysis of CP versus DP favours CP in less blood loss (WMD =−143.38, 95% CI: −224.90 to −61.87, P=0.001), lower endocrine (OR, 0.13; 95% CI, 0.08 to 0.20; P<0.001) and exocrine insufficiency (OR, 0.38; 95% CI, 0.24 to 0.61; P<0.001). However, CP was associated with longer operative time (WMD =59.14, 95% CI: 27.07 to 91.21; P<0.001), higher morbidity (OR, 1.93; 95% CI: 1.49 to 2.48; P<0.001) and PF rate (OR, 1.90; 95% CI: 1.46 to 2.48; P<0.001), longer hospital stay (WMD =5.24; 95% CI: 1.17 to 9.32; P=0.012). In regard to CP versus PD, CP had a lower risk of endocrine and exocrine insufficiency, less blood loss, shorter operative time and hospital stay, but a higher PF rate.

Conclusions: CP has an obvious advantage of better pancreatic endocrine and exocrine function than DP and PD, but associated with a higher PF rate. However, more prospective, multicenter, randomized controlled trials are needed to further define the real role of CP in pancreatic surgery.

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AB035. P006. Activity of heat shock protein-90 (HSP90) inhibitors against pancreatic cancers grown in 3 dimensions

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Background: Pancreatic ductal adenocarcinoma (PDAC) is one of the most deadliest cancers for which few curative therapies are available to date. Heat shock protein (HSP) inhibitors have shown some activity in other cancers and accordingly offer great potential for the targeted treatment of this disease.

Methods: *In vitro* effects of HSP-90 inhibitors on cell growth were evaluated, using three representative low-passage pancreatic cell lines (Panc10.05, Panc215, A6L). We screened them with five commercially available HSP-90 inhibitors: allylamine, AT 13387, AUY-922, ganetespib, rifabutin and three experimental HSP inhibitors: ICPD 26, ICPD 47, ICPD 62. IC50s were calculated for each in 2D and 3D assays.

Results: In 3 dimensions rifabutin was profounding inhibiting in all three pancreatic cell lines (Panc10.05, Panc215, A6L) by 80%. IC50s of rifabutin in 3D were sufficiently low (Panc10.05: 71.48, Panc215: 20.04, A6L: 18.38) while other HSP inhibitors were significantly less active.

Conclusions: Our data suggest that rifabutin (HSP-90 inhibitor) is a promising candidate for the treatment of PDAC and needs further testing *in vivo*.

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AB036. P007. BM-derived cells differentiated into multilineage hematopoietic cells regulate invasion and proliferation of pancreatic cancer

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Background: Pancreatic adenocarcinoma is characterized by a desmoplastic reaction, which provokes treatment resistance. Tumor-stroma interactions promote cancer malignancy. Cytokines secreted by tumor cells differentiate activated macrophages into tumor-associated macrophages (TAMs), which produce angiogenesis factor and cell growth factor to form tumor microenvironment. In breast cancer, a subset of stromal cells was descended from bone marrow (BM)-derived cells. While BM-derived cells seem to be involved in remodeling of microenvironment and tumor progression in pancreatic cancer, this mechanism remains unknown. We aimed to investigate an association between pancreatic cancer progression and BM-derived cells.

Methods: To establish the allogeneic BM transplantation models, BM-derived GFP+ cells were intravenously transplanted into KPC mice after sublethal irradiation. The phenotypic characterization and distribution of engrafted GFP+ cells were analyzed by flow cytometry or immunohistochemical staining. To evaluate invasive capacity and proliferation activity of pancreatic cancer cells (PCCs) co-cultured with BM-derived cells, we performed cell invasion assay and cell viability assay.

Results: The engraftment of BM-derived GFP^+ cells was detected in recipients' peripheral blood, BM, pancreas, liver, and ascites. The engrafted GFP^+ cells expressed CD45 consisting of a few $CD4^+$/$CD8^+$ T cells, a few natural killer (NK) cells, or macrophages. In recipients' pancreas, GFP^+ cells, $F4/80^+$ macrophages, and $CD163^+$ TAMs were accumulated around acinar-ductal metaplasia/pancreatic intraepithelial neoplasia (ADM/PanIN) and at invasive front. Invasive capacity of PCCs co-cultured with BM-derived macrophages significantly increased compared to the control. BM-derived lymphocytes inhibited the proliferation of PCCs. BM-derived GFP^+ cells showed a distribution similar to $aSMA^+$ cells, and a few GFP^+aSMA^+ cells were detected.

Conclusions: BM-derived lymphocytes, macrophages, and TAMs were engrafted in recipients' pancreas, and their distribution was biased. The present data also suggest that BM-derived macrophages have an insignificant effect on the proliferation of PCCs, while are involved in infiltration of PCCs.

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AB037. P008. Intratumoral regulatory T cells (Tregs) reduced by neutralization TGF-β in murine pancreatic ductal adenocarcinoma model without promising functional change

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Abstract: Regulatory T cells (Treg) is a vital cell subset inducing immune tolerance in tumor microenvironment by secreting suppressive cytokines and inhibit innate immune cells. Transforming growth factor-β (TGF-β) plays an important role in this process because both the differentiation and functioning of Treg are relied on it. Elevated Tregs and TGF-β in pancreatic ductal adenocarcinoma (PDAC) microenvironment was previously explored with a protein expression array. In this study, we evaluated the quantity and quality change of Treg after neutralizing TGF-β with different doses of monoclonal antibody 1D11: the tumor volume was measured, the T cell subsets was assessed by flow cytometry in peripheral blood and spleen and was stained by immunohistochemistry in tumor, and main cytokines in tumor tissue were detected by enzyme linked immunosorbent assay in a murine PDAC model. As a result, only tumor infiltrating Tregs decreased significantly (high dose, low dose and control, 38.6±8.1, 38.6±1.8, 74.6±4.9/40× field, P=0.024) after 1D11 administration, the CD8+ T cells in the tumor microenvironment elevated in the low-dose group but remain almost the same level in the high-dose group (high dose, low dose and control, 3.1±11.9, 12.3±2.1, 5.4±0.5/40× field, P=0.016). The frequency of CD4+, CD8+ or Treg in peripheral blood and spleen showed no significant change and the typical cytokines TGF-β and inerleukin-10 secreted by Tregs and interferon-γ produced by T cells in tumor tissue also remained at the same level as untreated. In conclusion, this research indicated neutralizing TGF-β with monoclonal antibody can reduce Tregs in tumor niche, however, the functional alteration should still be evaluated in further studies.

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AB038. P009. Tyrosine kinases and their prognostic value in digestive tract cancers

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Background: Recent studies have revealed that excessive TK activity contributes to tumorigenesis. Consequently, the therapeutic efficacy of targeted TK-inhibitors is currently under investigation in the field of digestive tract cancers. However, a considerable number of TK family members have not been studied in relation to digestive tract cancers. This study aims to analyze the transcriptional expression levels and prognostic roles of tyrosine kinases (TKs) in digestive tract cancers based on data from The Cancer Genome Atlas and Gene Expression Omnibus.

Methods: Gene expression, DNA methylation, and clinical data on seven digestive tract cancers, and GSE62452 microarray data on pancreatic cancer, were downloaded and processed. The Student's t-test and Benjamini-Hochberg method for correcting P value were used to identify differentially expressed TKs. Cox proportional hazards analysis was utilized to perform a prognostic analysis, and the R package ggm was used to conduct a partial correlation analysis. Four factors—age, sex, histologic grade, and pathologic stage—were used to correct P value.

Results: Many TKs were differentially expressed in digestive tract cancers. Five genes—*erb-b2 receptor tyrosine kinase 4*, *platelet-derived growth factor receptor A*, *fibroblast growth factor receptor 1*, *protein tyrosine kinase* 7, and *BMX non-receptor tyrosine kinase*—were differentially expressed in the seven tumors. Moreover, the results of our analysis suggested that TK expression had a strong relationship with the outcomes of patients with gastric, hepatocellular, and pancreatic cancers, but not in those with other cancers. In addition, a wide range of significant relationships existed among TKs in different tumors. The maximum value of seven average correlation coefficients, equaling 0.88, was observed between *fms-related tyrosine kinase 4* and *tyrosine kinase with immunoglobulin-like and EGF-like domains 1*.

Conclusions: In conclusion, many TKs were differentially expressed in digestive tract cancers. TK expression demonstrated prognostic value in patients with gastric, hepatocellular, and pancreatic cancers. Our findings might have wider implications for treatment or drug development of digestive tract cancers.

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AB039. P010. Use GeCKO lentiviral pooled libraries screen to identify genes which contribute to chemoresistance of pancreatic cancer

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Abstract: Pancreatic cancer is one of the most lethal malignancies and 5-year survival rate is below 7%. It is known that pancreatic cancer is highly resistant to systemic therapy. The Genome-scale CRISPR Knock-Out (GeCKO) pooled libraries consist of specific single guide RNA (sgRNA) sequences for gene knock-out in either the human or mouse genome. In this study, we generate Cas9 positive mouse pancreatic cancer cell line TB32047 and human pancreatic cancer cell line PANC1. Then transduce the libraries into the cells by lentivirus with multiplicity of infection (MOI) =0.3 and select the positive cells by puromycin. After puromycin selection, we use gemcitabine and oxaliplatin to screen the chemoresistant cells and extract genomic DNA for deep sequencing to identify which gene deletion contribute chemoresistance of pancreatic cancer. This study can help us to identify the critical genes that determine treatment response.

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AB040. P011. Prognostic and diagnostic value of REG4 serum and tissue expression in pancreatic ductal adenocarcinoma

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Background: Expression of regenerating islet-derived protein 4 (REG4), a secretory protein involved in cell differentiation and proliferation, is upregulated in inflammatory bowel diseases and in many gastrointestinal malignancies. The prognostic significance of its expression in pancreatic ductal adenocarcinoma (PDAC) is unknown. Our aim was to investigate tumor tissue and serum REG4 expression in PDAC patients. We also evaluated as a control the diagnostic value of serum REG4 level in patients with chronic pancreatitis (CP).
Methods: Immunohistochemical expression of REG4 was evaluated in 154 surgical specimens and serum REG4 level in 130 samples from PDAC patients treated at Helsinki University Hospital, Finland, in 2000–2011. REG4 tissue and serum expression was assessed in relation to clinicopathological parameters and patient survival. A CP control group comprised 34 patients who underwent pancreatic resection because of suspicion of malignancy.
Results: Significant survival differences were detectable in subgroups: in tumor stages IA–IIA, high serum REG4 level predicted worse survival (P=0.046). In patients with grade I tumor, positive tissue REG4 expression predicted better survival (P=0.006). In multivariate analysis, neither tissue nor serum REG4 expression were independent prognostic factors. Serum REG4 levels were higher in PDAC than in CP (P=0.002), with diagnostic sensitivity of 45% and specificity of 91%. In logistic regression analysis, a multivariate model with REG4, CA 19-9, and age provided sensitivity of 82% and specificity of 79%.
Conclusions: REG4 tissue expression is a prognostic marker in subgroups of PDAC patients. Serum REG4 level might be useful in differential diagnosis between PDAC and CP.

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AB041. P012. The effect of pancreatic cancer patient derived serum on macrophage M1/M2 polarization

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Background: Monocytes differentiate into inflammatory M1 or anti-inflammatory (pro-tumorigenic) M2 macrophages in tissue. We set out to explore whether serum from pancreas cancer patients and healthy controls could alter the differentiation of monocytes into M1 or M2 macrophages.

Methods: Monocytes were left to mature into macrophages in media supplemented with pancreatic cancer patient or control serum (15%). Two different cancer cell line cells (MiaPaCa-1 and HPAF) were added to the cultures. After 2 days of co-culture, the macrophages were harvested and their expression of cluster of differentiation (CD) markers was measured by flow cytometry. Cytokine levels in serum were assessed by Q-Plex (Biosciences). Cancer cell migration rate was measured by microscopy.

Results: The pancreatic cancer patients (n=14) and control serums from healthy individuals (n=6) differed in levels of cytokines. Patient derived serum was significantly richer in IL-1b (P=0.041), IL-6 (P=0.041), IL-10 (P=0.020), TNFα (P=0.020) and had higher levels of RANTES (P=0.008). The expression of CD markers connected with macrophage differentiation changed depending on the culture conditions. Co-culture with MiaPaCa-1 and HPAF significantly increased the expression of CD209 (P=0.004) and CD86 (P<0.001). Interestingly, CD86 (M1 marker) expression increased more in the presence of control than patient serum when co-cultured with cancer cells (P=0.017). No difference was found in the initial expression of CD markers in patient derived monocytes and monocytes drawn from healthy controls (P=0.537). The presence of macrophages increased the migration of cancer cells in serum supplemented media (P<0.001). No difference was found between patient and control derived serum with respect to increased migration rate.

Conclusions: M1 polarization may be reduced in pancreatic cancer patient macrophages compared to healthy controls when cultured in autologous serum. Further studies need to be conducted to examine whether this effect is due to the altered cytokines in patient sera or due to intrinsic differences in patient-derived monocytes compared to monocytes from healthy individuals.

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AB042. P013. LncRNA-PTCHD3P1 enhances chemosensitivity of gemcitabine in pancreatic cancer and inhibits cancer cell proliferation and metastasis via inhibiting Warburg effect

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Abstract: Warburg effect is associated with cancer chemosensitivity, and gemcitabine can increase the level of Warburg effect in pancreatic cancer. However, whether lncRNAs has impact on Warburg effect and further affect the chemosensitivity of gemcitabine, the proliferation and metastasis of pancreatic cancer are still unknown. In our previous researches, we have demonstrated that the expression of lncRNA-PTCHD3P1 is decreased in pancreatic cancer, and this reduction significantly inhibits Warburg effect, enhances chemosensitivity of gemcitabine, and inhibits pancreatic cancer cell proliferation and metastasis. In addition, lncRNA-PTCHD3P1 also suppresses the expression of phosphofructokinase-1 (PFK-1), the key factor of glycolysis pathway. Therefore, we assume that lncRNA-PTCHD3P1 inhibits PFK-1 expression, and PFK-1 down-regulation inhibits the Warburg effect of pancreatic cancer, finally enhances chemosensitivity of gemcitabine and inhibits cancer cell proliferation and metastasis. In conclusion: lncRNA-PTCHD3P1 pathway regulating pancreatic cancer metabolism and provide metabolic prospective for treatment of pancreatic cancer.

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AB043. P014. Genomic characterization of pancreatic cancer in Chinese population

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Background: In pancreatic cancer (PC), pancreatic ductal adenocarcinoma (PDAC) is the most common type, accounting for >90% of all patients. PDAC is one of aggressive diseases that mostly presents at an advanced stage and have a poor prognosis with the 5-year survival rate is 8.2%. Researchers have identified a large number of mutations and copy number alterations (CNAs), including *KRAS*, *TP53*, *SMAD4*, and *CDKN2A*. But the genomic features of PC in Chinese population are still largely unknown. This study aims to expound the genomic characterization of PC in Chinese population by whole exome sequencing.

Methods: Patients of Han nation were recruited and consent obtained for researches from the Pancreas Biobank in Pancreas Centre of the First Affiliated Hospital of Nanjing Medical University. Whole exome sequencing (WES) was performed on 64 primary PDAC specimens with criteria of neoplastic cellularity over 50% to an average depth of 97×, and compared to the germline from the blood samples (an average depth of 102×). Mutations and indels were detected by qSNP and Genome Analysis Toolkit (GATK).

Results: The mean age of our patients was 66.0±9.4 and there were 35 males and 29 females in these patients. Surgical procedures for these patients included distal pancreatectomy [14], segmental resection [1], (pylorus-preserving) Whipple's procedure [46], total pancreatectomy [3]. The results of WES revealed recurrent somatic mutations in *KRAS* (72%), *TP53* (50%), *SMAD4* (22%), *RNF43* (8%), *MUC5B* (8%), *U2AF1* (6%), and *FLG* (6%). We next investigated the mutation spectrum of PC and the result showed that the predominant substitution in PC was C to T and C to A.

Conclusions: Our study updated the genomic features of PDAC to help us know more about the initiation and progression in this deadly disease.

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AB044. P015. Clinicopathological relevance of SMAD4 and RUNX3 in pancreatic cancer

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Abstract: *SMAD4/DPC4* is one of the "big four" genes, namely, *KRAS*, *SMAD4*, *CDKN2A*, and *TP53*, that are considered to play primary roles in tumorigenesis and progression of pancreatic cancer. Runt-related transcription factors (RUNX) are important regulators of lineage-specific gene expression in developmental pathways. RUNX3 was initially found to be a neurogenic TrkC neuron-specific transcription factor and also has critical functions in lineage specification and homeostasis of CD8-lineage T lymphocytes. Besides, *RUNX3* functions as a tumor suppressor in some kinds of cancers through TGF-beta, Wnt, and other signaling pathways. A published report has indicated that *RUNX3* and *SMAD4* coordinately regulate the balance between cancer cell proliferation and dissemination in genetically engineered mouse models. We examined the relevance of genetic and expression state of *SMAD4* and *RUNX3* as well as *KRAS* in clinicopathological features of 104 patients who received surgery for pancreatic cancer. We found that retain of the expression of SMAD4 in primary pancreatic cancer tissues was significantly associated with their metastatic recurrences. Moreover, the diffuse expression of RUNX3 and loss of SMAD4 was significantly associated although the association between RUNX3 and SMAD4 did not show any specific association with clinicopathological features. These results suggest that retain of SMAD4 may promote the metastatic recurrence in pancreatic cancer. Although there may be some specific associations between RUNX3 and SMAD4, we could not find any relevant association of them with clinicopathological features of pancreatic cancer.

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AB045. P016. Profile of neoepitopes on human pancreas tumor tissue by proteomics

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Abstract: Mutated peptide ligands could be attractive targets for cancer immunotherapy. For direct identification of clinically relevant neoepitopes, we have surveyed the pancreatic cancer-associated immunopeptidome by using advanced mass spectrometry (MS) analysis. Peptides are biochemically purified from human leucocyte antigens (HLA) class I and II binding peptides from pancreas tumors followed by sample clean using C18 columns. The purified peptides were analyzed by Q Exactive plus hybrid quadrupole-Orbitrap mass spectrometer, followed by bioinformatics analysis. Totally, we identified novel 34,247 peptide sequences from HLA class I binding peptides. The distribution of peptide length showed that 9-amino acid (AA) are the most abundant, followed by 10-AA and 8-AA, with a frequency of 3,580, 2,463, and 2,368 respectively. We will do genomic sequencing to verify the proteomic profile of these neoepitopes.

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AB046. P017. Identification of pathological ampullary adenocarcinomas subtypes and their prognosis using the immunohistochemical score of CDX2, CK7 and CK 20

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Background: Ampullary adenocarcinomas (AACs) are heterogeneous and numerous methods of categorization histological subtypes exist. Histology phenotype based on immunohistochemistry (IHC) of caudal-type homeodomain transcription factor 2 (CDX2) and Cytokeratins (CK7 and CK20) staining has been tested in order to identify three most important sub-classes: intestinal (INT), pancreato-biliary (PB) and mixed-type (MT). The identification of MT tumors is often difficult with conventional histology and its clinical outcome is unclear. We attempt to identify only two subtypes in AACs samples, using an IHC score based-on CDX2, CK7 and CK20 evaluation on AAC samples.

Methods: Tissue samples from 20 patients with resected AAC were arranged on tissue microarrays (TMA) platform and their classification was obtained by histology and IHC expression of CDX2, CK7 and CK 20. IHC score was obtained for each marker summing the number of positive cells (0: no stained cells; 1: <25%; 2: <50% and 3: >50%) and their intensity (1, weak; 2, middle and 3, strong). A global score (GS) for each tumor was obtained by the contribution of each marker. The MT tumor were located into INT or PB group on the basis of predominant immune-molecular phenotype. The overall survival values of INT and PB patients were obtained by Kaplan-Meyer methods.

Results: Histological parameters defined AAC subtype samples as follows: 15% INT, 45% PB and 40% MT. Using the IHC expression and the GS, 75% and 25% of MT samples were assigned to INT and PB, respectively. The mean value of GS was 9.5 (range, 4.0–16.0). All INT samples had a GS over the mean, while all PB sample had a global score under the mean (P=0.0011). In particular, the INT samples are identified by high expression of CDX2 and CK20, while PB samples showed high expression of CK7 and negative expression of CK20 (P=0.0008). The overall survival (OS) of molecular intestinal histomolecular phenotype (INT) *vs.* PB phenotype showed significant differences (85.7 *vs.* 20.3 months; HR, 8.39; 95% CI, 1.38–18.90; P=0.0152).

Conclusions: Histopathologic and molecular criteria combination define clinically relevant histomolecular phenotypes of AACs and potentially represent distinct diseases with significant implications for current therapeutic strategies.

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AB047. P018. A technical refinement of the pancreaticojejunostomy after pancreatoduodenectomy (PD): the pancreas encompassing jejunal anastomosis (PEJA)

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Background: Postoperative pancreatic fistula (POPF) is the factor most strongly implicated in life-threating complications and death in most pancreatoduodenectomy (PD) series. It's well demonstrated that the incidence of pancreatic leak following PD depends from surgeon's and center experience as well as from certain predisposing factors. In particular, the fistula is most likely to occur when anastomosis involve a normal and soft pancreas and a small pancreatic duct, with no significant difference in the different techniques. Nevertheless, the knowledge of these predisposing factors can lead to possible technical refinements to mitigate the risk of POPF.

Methods: We developed some changes in the standard pancreatojejunostomy (PJ) with the aim to minimize the weak points of the PJ in patients with high risk of POPF. This anastomosis is an invaginating anastomosis in which the jejunum is sutured end to side to the pancreas. The unique aspects of this procedure are the apposition of 8 not absorbable stitches in two rows encompassing the pancreatic gland. A stent in the Wirsung duct is left in place. We initially validated this technique on 15 consecutive patients (male =8, female =7) with different diseases involving the pancreatic head; 13/15 patients were older than 70 years (range, 60–83 years).

Results: A patient died due to ischemic perforation of the sigmoid colon, and two patients had an upper gastrointestinal (GI) bleeding treated conservatively. The risk of POPF was calculated according to the most recently published risk scores; 5/15 patients were at high risk to develop POPF. No patients in the whole series developed POPF of any degree. No patients developed abscesses and no patient were discharged with drains. No patients developed gastric delayed emptying.

Conclusions: After a thorough examination of the many different technique to perform the PJ, their advantage and disadvantages, we developed some changes to the standard PJ. This technique minimizes the tension on the anastomosis, the trauma of the knots on the pancreas, and preserve the vascularisation of the stump. The only weak point of the anastomosis seems to be the potential leak from the needle holes. In fact, six patients had a biochemical leak in the first days after the operation, related to the technique itself and the presence of encompassing stitches, but without any clinical consequence. This biochemical leak solves spontaneously in 3–5 days after the operation. Pancreas encompassing jejunal anastomosis (PEJA) is a reliable anastomotic procedure to minimize POPF even when the texture of the pancreas is soft and normal. Further validation of the technique is needed.

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AB048. P019. Middle segment pancreatectomy: the complications and safety

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Background: Middle segmental pancreatectomy (MSP) is designed for lesions in the neck and body of the pancreas. The peri-operative courses and outcomes of the procedure are conflicting.

Methods: A total of 115 consecutive patients underwent MSP from March, 2006 to April, 2015. Demographic variables, clinical data and pathological findings were retrospectively analyzed. Long-term endocrine and exocrine function and post-operative status outcomes were followed up.

Results: The median age of the patients was 52 years old (male:female =39:76). The top 3 indications for surgery were serous cystic neoplasms (33, 28.7%), pancreatic neuroendocrine tumors (23, 20.0%) and intraductal papillary mucinous neoplasms (16, 13.9%). The mean operative time was 214.9±91.7 minutes and the mean intraoperative estimated blood loss was 233.4±275.5 mL. The mean post-operative hospital stay was 21.5±10.2 days. The overall morbidity rate was 49.5%, with pancreatic fistula (43.5%) being the most common post-operative complication including 45 clinically related cases. Follow-up revealed that 14.8% experienced long-term complications (new-onset diabetes: 1.7%, pre-existing diabetes worsened: 4.3%, regarding exocrine pancreatic function: 11.3%).

Conclusions: MSP provides excellent long-term pancreatic function at the expense of a significant post-operative morbidity rate. MSP is best indicated for benign or low-grade lesions in well-selected patients who are able to sustain potential serious complications and could benefit from improved long-term results.

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AB049. P020. Robotic pancreatoduodenectomy: results of the first twenty procedures

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Background: Minimally invasive surgery is gaining momentum in pancreatoduodenectomy. Presumed benefits include fewer major complications, less blood loss and a shorter hospital stay. However, a conventional laparoscopic approach to pancreatoduodenectomy is hindered by the straight, non-articulating laparoscopic instrumentation. The robot was designed to overcome these technical restrictions. The aim of this study was to demonstrate safety and feasibility of a robotic approach to pancreatoduodenectomy.
Methods: Patients underwent robotic pancreatoduodenectomy in two centers in the Netherlands, performed by the same surgical team, between March 2016 and September 2017. Patients were selected for robotic pancreatoduodenectomy in a multidisciplinary meeting. Tumors with vascular involvement were excluded. Data were prospectively collected and postoperative outcomes were scored up to 90 days after resection.
Results: In total, 20 robotic pancreatoduodenectomies were performed. Two procedures were converted to an open procedure: one due to failure to progress during the resection phase and one due to a portal bleeding that could not be controlled robotically. Median operative time was 415 min. (IQR, 355–457 min). Median blood loss was 325 mL (IQR, 178–675 mL). Four patients had postoperative pancreatic fistula (ISGPS gr. B/C). Eight patients suffered from delayed gastric emptying (ISGPS gr. B/C). One patient had a bile leak (ISGLS gr. C). One patient suffered from post-pancreatectomy hemorrhage (ISGPS gr. C). In total, ten patients suffered from a major complication (≥ gr. III Clavien-Dindo). There were no grade IV postoperative complications and there was no mortality. Median length of hospital stay was 16 days (IQR, 9–24 days). Five patients had to be readmitted within 90 days for surgery-related complications.
Conclusions: Robotic pancreatoduodenectomy is a safe and feasible procedure in selected patients.

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AB050. P021. The impact of surgical experience and work routine on operative morbidity and mortality in pancreatic surgery

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Background: Annual surgeon volume has been inversely related to operative mortality in complex surgery (Birkmeyer *et al.* 2013). The importance of surgical experience and work routine of the operating surgeon, however, is uncertain. We aimed to determine the impact of surgical experience and work routine on operative morbidity and mortality in pancreatic surgery in a high-volume center with a pancreatic surgery training program.

Methods: Using information from a single center database, we examined surgical morbidity and mortality of 1,281 patients who underwent pancreatic resections from 1993 to 2013. All cases were stratified according to the surgeon's level of experience, which was defined as the total number of previously performed pancreatic resections (beginner: n<20, intermediate: n=21–90 and expert n>90). Additional stratification was based on the surgeon's work routine in pancreatic surgery (rare: 3 resections >6 weeks, frequent: 3 resections ≤6 weeks). Using logistic regression models, we examined the relations between operative outcomes and the surgeon's level of experience as well as his recent work routine in pancreatic surgery.

Results: The levels of beginner and expert experience was related to a decreased risk of postoperative pancreatic fistula s (OR, 0.46; 95% CI, 0.26–0.82 and OR, 0.54; 95% CI, 0.36–0.82, respectively) and in-hospital mortality (OR, 0.45; 95% CI, 0.17–1.16 and OR, 0.42; 95% CI, 0.21–0.83) compared to the level of intermediate experience. Independent from the level of experience, a frequent work routine was associated with a significantly lower risk of delayed gastric emptying (OR, 0.56; 95% CI, 0.38–0.83), postpancreatectomy hemorrhage (OR, 0.64; 95% CI, 0.42–0.98) and in-hospital mortality (OR, 0.45; 95% CI, 0.24–0.87).

Conclusions: Within a pancreatic surgery training program of a high-volume center, rates of operative morbidity and mortality of inexperienced surgeons supervised by expert surgeons are comparable to those of expert surgeons. However, with increasing experience and subsequent reduction of expert supervision the risk of operative morbidity and mortality increases.

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AB051. P022. Vein invasion in pancreatic adenocarcinoma is a topography: vein resection in pancreaticoduodenectomy is worthy while

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Background: Portomesenteric venous resection (PDVR) during pancreaticoduodenectomy (PD) was supported by view that venous invasion was triggered by tumor location but argued by view that venous invasion was indicating more aggressive tumor biology. This study analyzes venous invasion in pancreatic cancer meaning tumor topography or tumor biology by collecting clinical data.

Methods: Patients underwent curative surgical treatment were divided into two subgroups: those having PD procedure and those having PDVR procedure. The tumor location was subdivided histopathologically into head-neck region, main head region, and uncinated region.

Results: Of 225 studied patients, 146 patients underwent PD, and 79 underwent PDVR. The postoperative mortality rate was 4.8% (7/146) in PD group and 3.8% (3/79) in PDVR group (P>1.0). A total of 64 patients in PD group and 43 in PDVR group had complications after surgery (P=0.129). Of the 79 patients in PDVR group, 65 patients were confirmed positive venous invasion by histology. There was no statistical significance in the tumor location, perineural invasion, tumor grade and nodal status between PD and PDVR groups. The mean tumor diameter of uncinated region was significant greater in PDVR group than that in PD group (4.1 cm in PDVR group and 3.3 cm in PD group, P=0.039). The R1 resection was 43 cases in PD group, while 15 cases in PDVR group (P=0.516). There was no statistical difference in the model of recurrence between the two groups (P=0.802). The highest local recurrence occurred in head-neck region with significant difference to other two regions in both groups. No statistical difference of survival time was observed between two groups (P=0.124). Endogenous PRRX1A and PRRX1B expression was assessed in pathological specimens of 62 patients in PDVR group in the way of IHC. Patients with high degree of PRRX1A staining intensity (n=56) had longer overall survival (OS) than those with low degree of PRRX1A (n=6) (P<0.001). Using univariate analysis involving age, gender, tumor location, nodal status, perineural invasion, tumor grade and tumor size showed than only tumor size was an independent risk factor for PRRX1B expression.

Conclusions: PDVR is as safe as PD. The patients with venous invasion had comparable prognosis after PDVR to those without venous invasion after PD. Tumor infiltrating the vein was related to the location rather than aggressive tumor biology. However, single surgical treatment for PDAC could not bring satisfactory OS on account of high rate of dismal recurrence. Epithelial-mesenchymal transition (EMT) probably played an important role in dismal recurrence.

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AB052. P023. Diagnosis and management of postpancreatectomy hemorrhage: a systematic review and meta-analysis

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Background: Late postpancreatectomy hemorrhage (PPH) is a rare, yet potentially lethal complication after a pancreatic resection. The objective of this study was to compare clinical outcomes of different invasive interventions for late PPH.

Methods: A systematic search was conducted on the literature from February 2007 to June 2017 in PubMed, Embase and the Cochrane library. Included were clinical studies evaluating the success rate (i.e., discharge alive without need for additional invasive interventions) and mortality of the first invasive intervention for late PPH, defined according to the International Study Group of Pancreatic Surgery (ISGPS) definition as occurring at least 24 hours after pancreatic resection.

Results: A total of 14 studies on 464 patients with late PPH were included. Seventy-four patients underwent conservative treatment; 56 patients underwent primary endoscopic intervention; 82 patients underwent primary relaparotomy; 252 patients underwent primary angiographic intervention and three patients died before any intervention could be performed. Pooled success rates showed no significant difference between primary endoscopic intervention and primary interventional angiography (48% *vs.* 56% respectively; OR =1.11; 95% CI, 0.48–2.52, P=0.81), nor between the endoscopy and relaparotomy (48% *vs.* 44% respectively; OR =1.47; 95% CI, 0.47–4.56, P=0.50), nor between the interventional angiography and relaparotomy group (61% *vs.* 56% respectively; OR =1.34; 95% CI, 0.64–2.81; P=0.44). Mortality was significantly lower after primary interventional angiography as compared to primary relaparotomy (16% *vs.* 37% respectively; OR =0.34; 95% CI, 0.12–0.95; P=0.04).

Conclusions: Interventional angiography appears to be superior to relaparotomy as first intervention for late PPH in terms of mortality.

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AB053. P024. Ki-67 proliferative index in resectable pancreatic ductal adenocarcinoma: does it have a prognostic role?

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Background: Pancreatic ductal adenocarcinoma (PDAC) is a tumor with a complex biological behavior and a dismal prognosis. New targets to stage the disease correctly and manage treatment are needed. Ki-67 expression in tumor tissues is a well-known parameter representing the aggressiveness of neoplasms, but it is not used for PDAC. The aim of this study is to analyze the role of Ki-67 as a prognostic factor in a series of resected PDAC.

Methods: A total of 176 patients who underwent upfront pancreatic resection for histologically confirmed PDAC with Ki-67 immunohistochemical staining between August 2010 and October 2014 were included in this study. Disease specific survival (DSS) and disease-free survival (DFS) were calculated starting from the date of surgery.

Results: Median Ki-67 index was 30% (IQR, 10–40%). Ki-67 cut-off of 10% and 50% were the only values significantly discriminating for both DFS and DSS. The median DFS time was 24 *vs.* 19 *vs.* 8 months for patients with Ki-67 index ≤10%, 10–50% and >50% respectively (P=0.018). Furthermore, even DSS decreased significantly through the three categories (47 *vs.* 35 *vs.* 14 months, P=0.003). Ki-67 index [hazard ratio (HR), 1.570; P=0.013], grading (HR, 1.458; P=0.032), N status (HR, 2.137; P=0.003) and resection margins (HR, 1.778; P=0.004) were identified as independent predictors for DSS. Except for grade of tumor differentiation, these same factors were independently associated with DFS.

Conclusions: Ki-67 was an independent predictor of DSS and DFS in resected PDACs. Therefore, Ki-67 may play a valuable role as prognostic factor, to better characterize tumor behavior and treatment strategies.

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AB054. P025. Impact of pasireotide on post-operative pancreatic fistulas after pancreatic distal resections

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Background: Complications in pancreatic surgery are potentially life-threating. Post-operative pancreatic fistulas (POPF) can form in pancreatic tissue after surgery and can cause peripancreatic fluid collections and infections. In addition, pancreatic fluid is corrosive and can lead to post-operative bleeding in the operative area. Clinically significant class B and C fistulas increase post-operative morbidity and can lead to prolonged hospital stay. Delaying of adjuvant therapy due to fistula formation in cancer patients can affect their prognosis. Diagnosis of pancreatic fistula can be set according to international study group of pancreatic surgery (ISGPS) criteria (Bassi *et al.* 2016). Previously, the use of perioperative pasireotide decreased the number of clinically relevant pancreatic fistulas (Allen *et al.* N Engl J Med 2014). According to Seppänen *et al.* (abstr. 2016) the use of pasireotide after pancreaticoduodenectomy was seen beneficial in risk patients.

Methods: There were 235 distal pancreatic resections in HUCH 2005–4/2016 that were analyzed. Pasireotide (Signifor) was used in 7/2014–4/2016. Pasireotide treatment was started in patients on the morning of surgery and was continued until released from hospital or for a week. In one patient treatment was discontinued on day one because of side-effects. Patients who had octreotide (Sandostatin) treatment were analysed separately. Complications were analyzed 90 days post-operatively using the ISGPS POPF criteria and Clavien-Dindo I–V classification.

Results: There were 48 (20%) patients who received pasireotide, 21 (9%) octreotide and 166 (71%) did not receive either. There were 34 (14%) clinically relevant B/C POPF: 7 (15%) in pasireotide group, 3 (14%) sandostatin group and 23 (14%) in group without either, sandostatin or pasireotide (P= ns). Severe complications according to Clavien-Dindo grade III–IV were 61 (26%): in pasireotide-group 17 (35%), in the octreotide group 4 (19%) and 39 (23%) in the group who did not receive either (P= ns). During the 90-day follow-up period mortality was 0.

Conclusions: In this study, pasireotide did not reduce clinically relevant POPF or severe complications after pancreatic distal resection.

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AB055. P026. Prediction of clinically relevant pancreatic fistula in the early phase after distal pancreatectomy

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Background: Postoperative pancreatic fistula (PF) remains a major complication after distal pancreatectomy (DP). We aimed to investigate the predictors of clinically relevant PF (cPF) in the early phase after DP.

Methods: Between July 2009 and March 2017, 101 consecutive patients underwent DP at Hyogo College of Medicine. The postoperative data were collected, and the predictors for cPF after DP were identified.

Results: cPF were identified in 34 patients. In the multivariate analysis, two factors [serum C-reactive protein (CRP) ≥10 mg/dL and amylase value in drain (d-AMY) ≥1,200 U/L] were found to be independently the predictive factors of cPF on postoperative day (POD) 4 (odds ratio, 6.4; 95% confidence interval, 2.4–16.8, P<0.001 and odds ratio, 3.4; 95% confidence interval, 1.3–8.9, P=0.011, respectively). A scoring scale for the prediction of cPF was developed. Serum CRP ≥10 mg/dL (score: 2) and d-AMY ≥1,200 U/L (score: 1) were included in the scoring scale, and a score of 2 yielded the most optimal diagnosis value for cPF (AUC =0.780). Therefore, only one factor, the CRP ≥10 mg/dL was found to be independently predictive factors of cPF on POD4.

Conclusions: Serum CRP ≥10 mg/dL was predictive factor for cPF on POD4 after DP.

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AB056. P027. Preoperative chemotherapy for resectable pancreatic cancer improves prognosis of node positive pancreatic head cancer

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Abstract: Recently, preoperative chemotherapy or chemoradiotherapy has been tried to improve the prognosis of pancreatic cancer after resection. We retrospectively evaluate the efficacy of preoperative neoadjuvant chemotherapy (NAC) with gemcitabine (GEM) based regimen for resectable pancreatic cancer. Between 2006 and 2015, NAC with GEM was performed for 52 cases out of 86 resectable pancreatic cancer cases in our department. In the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines for the treatment effect, partial response (PR) in 5 cases, stable disease (SD) in 35 cases and progressive disease (PD) in 2 cases were respectively observed. However, standardized uptake value (SUVmax) values of fluorodeoxyglucose-positron emission tomography (FDG-PET) and cancer antigen 19-9 (CA19-9) values were significantly reduced after preoperative chemotherapy. The treatment effect was grade I in 31 patients, grade IIa in 8 and grade IIb in 3 cases, judged with the Evans grading system. There were not significant differences in overall 5-year survival rate between the NAC group (pancreatic head cancer 45.4% and pancreatic body and tail cancer 26.7%) and control (non-NAC) group (pancreatic head cancer 29.2% and body and tail cancer 47.1%). However, survival period of the NAC group was slightly extended compared with the control group in the patients with node positive [Union for International Cancer Control (UICC) stage IIB] pancreatic head cancer. On the other hand, in early recurrent cases within a year, significantly higher CA19-9 value of peripheral blood and higher lymph node metastasis and plexus invasion rates were observed. In conclusion, NAC with GEM prolong survival period of node positive pancreatic head cancer cases, and it is considered that PET-CT and tumor marker (CA19-9) is useful for judgment of preoperative treatment effect. Furthermore, high CA19-9 value, lymph node metastasis and plexus invasion would be the risk factors of early tumor recurrence after surgery.

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AB057. P029. Rescue ERCP with pancreatic stent replacement against post-ERCP pancreatitis following prophylactic pancreatic stent placement

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Background: Previous meta-analyses show that prophylactic pancreatic stent (PPS) placement reduces the rate and severity of post-ERCP pancreatitis (PEP) in both high-risk and low-risk patients; however, PPS do not eliminate the risk completely. Early PPS dislodgement and occlusion may occur prematurely and contribute to more frequent or severe PEP. The aim of this study was to assess the safety and efficacy of rescue ERCP with pancreatic stent replacement against PEP following PPS placement.

Methods: Between January 2005 and December 2017, out of 3,991 ERCPs, PPS placement was performed in 344 patients at our institution. Among them, PEP occurred in 15 patients (4.36%). Out of these 15 patients, 9 patients (4 men, 5 women; mean age: 74 years, range, 54–82 years) who underwent rescue ERCP with pancreatic stent replacement were analyzed. The cause of PEP following PPS placement was stent dislodgement (n=6) and occlusion (n=3). Timing of stent dislodgment was assessed radiographically. The mean serum amylase level before initial ERCP was 79±41 (range, 26–159) IU/L. Rescue ERCP after PPS placement was performed within 24 h in five patients, 48 h in 3, and 5 days later in one. The stent used in the present study was a straight, double-barbed, 5F in diameter and 3 cm in length pancreatic stent. PEP was defined based on the consensus criteria.

Results: Indications for initial ERCP were biliary stricture (n=5) and choledocholithiasis (n=4). The median risk score for PEP was 0.5 (range, 0.5–3.0). Pancreatic stent replacement was technically successful in all patients. The median bedside index for severity of acute pancreatitis was 2 (range, 0–2) and median CT severity index was 4 (range, 2–6), respectively. The mean serum amylase levels of the next day after replacement (965±926 IU/L, range, 111–2,293) were significantly decreased compared with those before replacement (1,692±1,431 IU/L, range, 116–4,186; P=0.0382). Pancreatic pain was promptly reduced after the procedure in eight patients. Two patients developed severe PEP. There were no procedure-related deaths.

Conclusions: Rescue ERCP with pancreatic stent replacement seems to be an effective procedure for the management of PEP due to stent dislodgement and occlusion following PPS placement. Factors other than ductal obstruction may contribute to PEP in high-risk patients undergoing ERCP and PPS placement. Additional studies are necessary to fully evaluate pancreatic stent replacement for this indication.

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AB058. P030. The 8th versus the 7th edition of the AJCC Cancer Staging Manual in predicting the prognosis of pancreatic ductal adenocarcinoma

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Background: The American Joint Committee on Cancer (AJCC) released the AJCC Cancer Staging Manual 8th edition with modifications mainly on the definitions of T3 and N2 stages pancreatic cancer. This study aims to assess its strengths and weaknesses related to the 7th edition AJCC staging system.

Methods: A clinicopathological data of 225 patients who underwent pancreaticoduodenectomy for pancreatic ductal adenocarcinoma (PDAC) between 2010 and 2016 were statistically analyzed.

Results: AJCC 8th edition (P=0.022) predicts survival more effectively than the 7th edition (P=0.180). On multivariate analysis, tumor grading (P=0.000), positive lymph nodes (P=0.028) and tumor location (P=0.022) are independent predictor s for survival, and among stage N0 patients, tumor grading (P=0.002), tumor locations (P=0.016) and level of preoperative serum cancer antigen 19-9 (CA19-9) (P=0.006) are independent predictors for survival.

Conclusions: This finding suggests that the 8th edition of the AJCC grading system achieves the higher predictive ability on pancreatic cancer than the previous edition. Further predictive ability can be achieved by combining the tumor differentiation grades and their locations.

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AB059. P031. Outcomes of pylorus-preserving versus conventional pancreaticoduodenectomy in the era of enhanced recovery: a single-institution experience

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Background: Recent randomized trials and meta-analysis have demonstrated an increased incidence of delayed gastric emptying (DGE) with pylorus preserving pancreaticoduodenectomy (PP) compared to conventional Whipple (CW). At our high-volume referral center, both techniques are performed according to individual surgeon preference, with perioperative care standardized by an enhanced recovery [Electronic Residency Application Service (ERAS)] protocol—a setup akin to an expertise-based trial. We therefore set out to compare the morbidity experience of patients undergoing PP and CW at our institution.

Methods: Following IRB approval, we accessed our prospectively collected complications database for patients undergoing PP and CW after the institution of our ERAS protocol. This protocol included routine use of epidural analgesia, limited opioids, early ambulation and no routine nasogastric tubes. We compared their preoperative characteristics and postoperative complications using student t-tests, chi-square tests, Wilcoxon rank-sum test, and univariate logistic regression to identify variables associated with DGE. We performed a multivariate logistic regression to adjust for confounding variables and isolate the effect of pylorus preservation on DGE.

Results: In total, 133 CW and 147 PP were identified during the study period. Their preoperative characteristics were similar, but more patients in the CW group underwent a portal vein resection (24.8% *vs.* 14.3% for CW and PP respectively, P=0.026). Moreover, 21.7% and 17.7% of patients developed DGE in the CW and PP groups respectively (P=0.457). DGE was associated with diabetes (OR, 2.9; 95% CI, 1.43–6.06; P=0.03) but not body mass index (BMI) (OR, 1.04; 95% CI, 0.98–1.11; P=0.177) at univariate logistic regression. Patients that developed a pancreatic fistula had higher odds of DGE (OR, 2.9; 95% CI, 1.58–5.46; P=0.001). At Multivariate Logistic Regression, there remained no association between PP and DGE.

Conclusions: The morbidity of patients undergoing CW and PP by expert surgeons under an ERAS protocol was similar at our institution.

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AB060. P032. 2,029 cases of Whipple's procedure: 12-year experience from a single center

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Background: Whipple's procedure is one of the most challenging operation in abdominal surgery. Better outcomes were reported in experienced hands and in high-volume centers. This study aims to investigate short- and long-term outcomes after Whipple's procedure.

Methods: From January 2006 to December 2017, 2,029 patients underwent Whipple's procedure in our hospital, which is a tertiary referral center in a developing country. Data were reviewed and analyzed in retrospective way, and missing data were not imputed or deleted.

Results: The male:female ratio in this group was 1.6:1, with a mean age of 60.5±11.6 years old. Near half of the patients reported comorbidities on their admission, while 23.1% were classified as American Society of Anesthesiologists (ASA) grade III/IV, 44.5% were pylorus-preserving Whipple, with extended resection and combined vascular resection accounting for 8.5% and 7.1%, respectively. The most common pathological diagnoses were pancreatic malignancies (46.0%), duodenal malignancies (14.2%), ampullary malignancies (10.4%) and lower bile duct malignancies (8.5%). Intraoperative data showed a median operation time of 255 (range, 210–315) min and a median estimated blood loss of 300 (range, 200–500) mL. Pancreatic fistula rate according to ISGPS2016 definition was 17.2%. Reoperation rate was 1.6%, while in-hospital mortality rate was 1.2%. Length of postoperative hospital stay and hospitalization cost were 16 (range, 12–22) days and 11,272 (range, 8,922–14,134) USD. Unadjusted median survival time was 15.3 months after resection for pancreatic adenocarcinomas in our cohort.

Conclusions: Though its mortality rate dropped to around 1%, Whipple's procedure remains a challenging procedure for surgeons. With limited healthcare resource allocation, measures should be taken to improve the long-term survival for cancer patients.

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AB061. P033. A comparison of delayed gastric emptying and nutritional status after pylorus-preserving versus stomach-preserving pancreaticoduodenectomy

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Background: This study was performed to compare the incidence of delayed gastric emptying (DGE), postoperative outcome and long-term nutritional status between pylorus-preserving pancreaticoduodenectomy (PPPD) and subtotal stomach-preserving pancreaticoduodenectomy (SSPPD).
Methods: We retrospectively analyzed 133 patients who undergoing PPPD (n=89) or SSPPD (n=44) between March 2011 and December 2015. All cases of duodenojejunostomy in PPPD and gastrojejunostomy in SSPPD were performed antecolically. The postoperative nutritional status was explored by changes ratio in the body weight, serum total protein and serum albumin for 1 year after surgery.
Results: The overall incidence of the DGE was 12%. The incidence of DGE was 13.5% (grade A: 5.6%, grade B: 4.5%, grade C: 3.4%) in PPPD group and 9.1% (grade A: 4.5%, grade B: 4.5%, grade C: 0%) in SSPPD group, and was no significant differences in both groups. The mean postoperative hospital stay was 42.8 days in the PPPD group and 37.2 days in the SSPPD group, and was no significant differences in both groups. The body weight ratio was decreased at 6 months after surgery in the SSPPD group, whereas it continued to decrease at 9 months after surgery in the PPPD group. It was gradually increased 9 months later after surgery in SSPPD group, and it was increased 12 months later after surgery in PPPD group. The serum total protein ratio and serum albumin ratio were decreased at 3 months after surgery and were gradually increased 6 months later after surgery in both groups. There were no significant differences with regard to postoperative body weight ratio, serum total protein ratio and serum albumin ratio in both groups for 1 year after surgery.
Conclusions: SSPPD is equivalent outcomes in incidence of DGE and in postoperative long-term nutritional status comparing PPPD.

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AB062. P034. Prior cholecystectomy and the survival of resected pancreatic cancer: a single-center retrospective cohort in Chinese population

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Background: Cholecystectomy is carried out as one of the most extensive abdominal surgery. Patients with a long-term history of cholecystectomy may have an increased risk of pancreatic cancer. However, it's uncertain whether prior cholecystectomy is associated with the outcome of patients with pancreatic cancer.

Methods: Retrospective study comprising 390 consecutive patients with pathological diagnosis of pancreatic adenocarcinoma in Pancreas Center of the First Affiliated Hospital of Nanjing Medical University (January 2010 to December 2014) was conducted. Analyses were carried out to assess the association between clinical characteristics and prior cholecystectomy on overall survival.

Results: A total of 31 patients (7.9%) had prior cholecystectomies. Univariate analysis showed that differentiation degree (P<0.05), tumor size (P=0.014), perineural invasion (P=0.008), vascular invasion (P<0.05), lymphatic metastasis (P<0.05), TNM stage (P<0.05), adjuvant chemotherapy (P<0.05) and tumor location (P=0.011) were associated with overall survival while prior cholecystectomy showed no significant value of prognosis (P=0.510). Multivariate analysis revealed that prior cholecystectomy was not an independent prognostic factor (P=0.266) for resected pancreatic cancer while vascular invasion (P<0.05), differentiation degree (P<0.05) and adjuvant chemotherapy (P<0.05) were significantly associated with the outcome.

Conclusions: Prior cholecystectomy may not be an independent prognostic factor for pancreatic cancer, although patients with prior cholecystectomy seem to have worse outcome.

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AB063. P035. Radiofrequency ablation and irreversible electroporation in locally advanced pancreatic cancer: competitive or complementary treatment modalities?

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Background: Radiofrequency ablation (RFA) and irreversible electroporation (IRE) are both local ablative strategies for the treatment of locally advanced pancreatic cancer (LAPC). It remains unclear to what extent IRE and RFA are competitive or complementary modalities. This study aims to assess the degree of overlap and exclusiveness in treatment eligibility for both techniques in a consecutive cohort of patients with LAPC.

Methods: A post-hoc analysis of patients with Response Evaluation Criteria in Solid Tumors (RECIST)-stable LAPC after 2 months induction chemotherapy previously registered in the prospective IMPALA cohort from September 2013 to March 2015 was performed. A literature search was done in order to identify original articles reporting on eligibility criteria for RFA and IRE. These criteria were used to reassess the treatment eligibility for both techniques.

Results: A total of 58 patients were included of which 53 (91%) were considered eligible for local ablative therapy. Of these, 36 patients (62%) were eligible for RFA and 44 (76%) for IRE with 27 patients (47%) eligible for both techniques and thus 26 patients (45%) eligible for one of both strategies. The main reason for ineligibility for RFA was perivascular tumor growth in 13/22 ineligible patients (59%) and tumors too large for IRE in 9/14 IRE ineligible patients (64%). Mean tumor diameter was significantly different between groups eligible for solely RFA, eligible for both and eligible for solely IRE [58 mm, standard deviation (SD) =8 mm; 43 mm, SD =12 mm and 33 mm, SD =15 mm respectively; $P<0.001$].

Conclusions: The vast majority of patients with LAPC are eligible for either IRE or RFA. IRE and RFA are equally complementary as they are competitive for LAPC. For larger tumors RFA appears to be more suitable, where for smaller perivascular tumors IRE seems more appropriate.

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AB064. P036. Fat tissue and pancreatic parenchyma play different roles in pancreatic cancer invasion

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Background: Although the formation of desmoplasia in the local invasion of pancreatic cancer is one of the important common histological changes during invasion to surrounding tissues including adipose tissues and pancreatic parenchyma. However, the differences and the underlying mechanism in surrounding tissue-specific invasion remain unclear. This study aims to investigate the differences in the mechanisms of local invasion to peripancreatic adipose tissues and pancreatic parenchyma.

Methods: We used organotypic fat invasion model and visceral fat transplantation model to investigate the local invasion to peripancreatic adipose tissues. We also analyzed pancreatic tissues from patients and KPC mice with pancreatic cancer and used orthotopic transplantation model to investigate the mechanism of the local invasion to pancreatic parenchyma.

Results: In organotypic model, we found that GFP positive adipose tissue-derived stromal cells (ASCs) infiltrated toward cancer cells. In visceral fat transplantation model with cancer cells, the weight of tumors with visceral fat was significantly heavier than the groups without visceral fat ($P<0.001$). In the analyses of resected samples, we found that cancer-associated atrophy (CAA) area was significantly associated with acinar-to-ductal metaplasia (ADM)-like lesion ($P<0.01$). KC mouse orthotopic models formed ADM-like lesion around tumors and induced desmoplasia in the invasive front and the progression of the tumors was accelerated ($P<0.01$).

Conclusions: Our data provide the new insight that fat tissue and pancreatic parenchyma play different roles in pancreatic cancer invasion.

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AB065. P037. Prognostic role of the parenchymal frozen transection margin during pancreaticoduodenectomy (PD) for ductal pancreatic adenocarcinoma

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Background: During pancreatectomy for ductal adenocarcinoma (PDAC) an intra-operative frozen section analysis of the transection margin is usually performed to achieve an R0 resection. An extension of the resection is required for positive margins until a total pancreatectomy (TP). However, it is unclear whether an extended resection up to TP leads to a survival advantage. This study aims to evaluate disease-specific (DSS) and disease-free (DFS) survival in patients who underwent TP for PDAC compared to standard or extended pancreaticoduodenectomy (PD).

Methods: Patients with head PDAC were divided into three groups per type of resection: standard PD (SPD), extended PD (EPD) or TP because positive transection margin(s). Patients with intraductal papillary mucinous neoplasm (IPMN)-associated PDAC were excluded. Survival analysis as well as evaluation of pathological data and postop morbidity/mortality were performed.

Results: Between 2009 and 2016, 313 patients underwent SPD, 22 EPD group and in 36 TP was performed because of repeated positive margins. The three groups were homogenous for age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score and intra-operative variables. No differences were observed among the three groups regarding N+ rate, number of positive nodes and lymph node-ratio, perineural and microvascular invasion. In the TP group a statistically significant increase in peri-operative mortality [odds ratio (OR): 2.1, 95% CI: 0.03–0.50, P=0.04] was observed. Moreover, in TP group the rate of R1 resections was significantly higher than in SPD and EPD groups ($\chi 2$: 4.52, P=0.033). Compared to SPD and EPD patients, those who underwent TP had a significant decrease of DFS (median: 11 months in TP, 12 in EPD and 20 in SPD, P=0.002) and DSS (median: 16 months in TP, 17 in EPD and 27 in SPD, P=0.001).

Conclusions: In patients with head PDAC, TP performed to achieve a negative pancreatic resection margin is still associated with a significant rate of R1 resection (retroperitoneal margin), with higher postoperative mortality and worse both DFS and DSS, when compared to SPD or EPD. Therefore, in this setting, once after PD the transection margin is positive TP does not seem useful.

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AB066. P038. HHLA2 is overexpressed in pancreatic ductal adenocarcinoma and precancerous lesions

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Abstract: Although immune-based cancer therapies, such as immune checkpoint inhibitors, are showing promising potentials, current strategies remain unsatisfactory for treating pancreatic cancer. HHLA2 is a newly identified immune checkpoint as a member of the B7 protein family which contributes to regional tumor-related immune suppression by regulating T cells' proliferation and function. Approaches have been made in targeting HHLA2 alone or co-targeting with PD-1/PD-L1 for cancer immunotherapy. However, there are limited information about HHLA2 expression profile available in pancreatic cancer. In this study, we performed Immunohistochemistry (IHC) using tissue microarrays (TMAs, n=92) from surgical resection of pancreatic ductal adenocarcinoma (PDAC) with matched peritumoral tissues. Positive staining was seen in 77.17% (71/92) of PDAC tissues. Of the 20 cases of pancreatic intraepithelial neoplasia (PanIN) in variant stages captured from peritumoral tissues, 95% (19/20) were featured with HHLA2 positive staining, suggesting that HHLA2 expression and its induced immunosuppression has been induced from early PanIN lesions. We also examined HHLA2 expression in TMAs containing intraductal papillary mucinous neoplasm (IPMN) cohort (n=41). The overall HHLA2 positive staining rate of IPMNs is 70.73% (29/41), with low grade dysplasia at 67.65% (23/34) and high-grade dysplasia at 85.71% (6/7). Among the different morphological subtypes, HHLA2 positive staining rates of the intestinal type (92.86%, 13/14) and pancreaticobiliary type (83.33%, 5/6) are higher than the gastric type (52.38%, 11/21). In conclusion, HHLA2 is widely expressed from early pancreatic precancerous lesions (both PanINs and IPMNs) to the late stages of carcinoma in PDAC. HHLA2 is also highly overexpressed in all subtypes of IPMN. Our findings suggest that HHLA2 represents a novel immunosuppressive mechanism and an attractive target for checkpoint inhibitor therapies in pancreatic cancer.

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AB067. P039. Rab37 mediates exosomal osteopontin secretion to promote pancreatic cancer metastasis and stemness

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Abstract: Pancreatic cancer is one of the most formidable malignancies in the world. The poor prognosis associated with pancreatic cancer has been attributed to the high incidence of local invasion, distant metastasis, and chemoresistance. The cancer secretome has been linked to the hallmarks of cancer and may be the key to identifying novel therapeutic targets for cancers. Rab small GTPases are master regulators of secretory pathways. However, the role of Rab-controlled trafficking pathways in pancreatic cancer remains poorly defined. Using cell lines, *in vivo* experiments, and clinical analyses, we identified an oncogenic role of Rab37 in pancreatic cancer. Osteopontin (OPN) was identified as a major cargo of Rab37-associated vesicles, and Rab37 overexpression enhanced OPN release, mainly through the exosome pathway, to activate extracellular signal-regulated kinase (ERK) signaling, thereby promoting pancreatic cancer metastasis and stemness. Dysregulation of Rab37-mediated OPN secretion may result from KRAS mutation. Our findings have possible implications for prognosis evaluation and therapeutic strategies for pancreatic cancer.

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AB068. P040. Heterotopic ossification in abdominal surgery incisions as an independent predictor of prognosis of malignant abdominal tumors: a case-control study from a single institution

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Background: The development of heterotopic ossification in abdominal incisions is not as uncommon as previously reported. However, the relationship between heterotopic ossification in abdominal surgery incisions and the prognosis of malignant abdominal tumors is unclear. This study aims to evaluate heterotopic ossification in abdominal surgery incisions as an independent predictor of the prognosis of malignant abdominal tumors.

Methods: We analyzed data from a retrospectively recorded database on patients who underwent open abdominal surgery in a single center from January 1, 2012 to December 30, 2012 regarding the relationships between heterotopic ossifications and primary disease, and between ossification occurrence and the stage of disease; ossification and its characteristics were also evaluated.

Results: There were 182 patients who underwent open abdominal surgery and received postoperative computed tomographic scans. This included 121 patients in the malignant tumor group (42 pancreatic cancer, 79 gastric cancer), and 61 in the benign disease group. Heterotopic ossifications were found in 35 of 182 overall cases (19.2%). The earliest ossification was present at 21 days postoperatively, and most heterotopic ossification was in the upper abdominal region (82.9%, 29/35). Incision ossification was present significantly more frequently in the malignant group (33 of 121 cases, 27.3%) than in the benign group (2 of 44 cases, 4.5%). Furthermore, 21 of the 33 cases (63.6%) with ossification in the malignant group also had metastasis detected on CT.

Conclusions: Heterotopic ossification in abdominal incisions was more frequently encountered in patients with malignancy than in those with benign disease. Furthermore, heterotopic ossification manifestation was an independent predictor of tumor prognosis.

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AB069. P041. A nomogram based on postoperative neutrophil-to-lymphocyte rate and TNM stage to predict the prognostic value in pancreatic ductal adenocarcinoma with open distal pancreatosplenectomy

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Background: The prognosis of pancreatic ductal adenocarcinoma (PDAC) remains poor. Open distal pancreatosplenectomy (ODPS) is prevalent in the patients of early PDAC located in pancreatic body or tail. However, the models for relapse or survival prediction in those patients are still limited. Postoperative neutrophil-to-lymphocyte rate (poNLR), a novel inflammation-based score, has been formulated to analyze the prognostic significance in PDAC patients with ODPS. Therefore, this study aims to generate a valuable prognostic nomogram for PDAC following ODPS.

Methods: We retrospectively enrolled 97 patients of PDAC undergoing ODPS in this study. The Cox proportional hazards regression methodology was used in univariate and multivariate survival analyses to identify significant independent prognostic factors. The prognostic nomograms integrating poNLR into the American Joint Commission on Cancer (AJCC) staging system (8th edition) for predicting overall survival (OS) and relapse-free survival (RFS) were established to achieve superior discriminatory abilities. Further, these prognostic nomograms were verified according to concordance index (C-index), calibrations and decision curve analyses (DCA).

Results: The optimal cut-off value of poNLR for assessing OS determined by X-tile program was 14.1. Higher poNLR was associated with higher postoperative neutrophil (poNeutrophil), lower postoperative lymphocyte (poLymphocyte), lower preoperative lymphocyte-to-monocyte rate (preLMR) and higher △NLR (postoperative-preoperative NLR). In the univariate and multivariate analysis, poNLR was identified as an independent prognostic indicator for OS and RFS (P=0.044 and 0.028, respectively) and patients with higher poNLR level were probable to have shorter OS and RFS. Compared with the TNM staging system of the AJCC 8th edition, the nomogram comprising of poNLR and AJCC 8th edition exhibited superior predictive accuracy for OS and RFS.

Conclusions: poNLR can be a proven, inexpensive and novel survival predictor of PDAC patients with ODPS. One more advanced and accurate predictive model will be achieved to assist in risk stratification via the incorporation of poNLR into nomograms.

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AB070. P042. Serum protein profile in IPMN

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Background: The incidence of intraductal papillary mucinous neoplasm (IPMN) is increasing and thereby the number of patients under surveillance. There is a need for easily available serum biomarkers to distinguish patients with low or moderate grade dysplasia from those with high grade dysplasia or IPMN-associated cancer needing surgery.
Methods: In 45 patients operated for IPMN 2000–2015 had preoperative serum samples available. There were 13 patients with mild, 10 with severe dysplasia and 22 with IPMN associated cancer. The preoperative serum samples of the IPMN patients and of 11 healthy individuals were analyzed with mass spectrometry (Synapt-G2S, Waters Ltd). Two or more unique peptides were used to identify 436 proteins that were quantified. Statistical analysis was performed with principal component analysis, orthogonal partial least square discriminant analysis and receiver operating curve analysis.
Results: The proteomic signature separated IPMN patients and controls by C-reactive protein (CRP) (UniProt accession P02741), kininogen-1 (P0042), lipoprotein lipase (P06858), SPINK2 [kazal-2 type serine-protease-inhibitor (P20155)] and SPARCL1 (secreted protein acidic rich in cysteine like protein, Q14515). The proteomic signature between dysplastic IPMN and cancer differed less. Mild and severe dysplasia did not differ significantly.
Conclusions: The protein profile differed between IPMN-patients and healthy controls but not within IPMN groups.

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AB071. P043. TLR1 predicts favorable prognosis in young pancreatic cancer patients

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Background: The link between inflammation and carcinogenesis is irrefutable. Trying to pinpoint key factors at play, cancer research has found interest in Toll-like receptors (TLRs), through which pathological molecular patterns trigger immune cell response. TLRs appear to show prognostic value in adenocarcinomas of the mouth, colon and ovaries. We set out to investigate whether the expression of Toll-like receptors 1, 3, 5, 7 and 9 could be used for prognostic evaluation in pancreatic ductal adenocarcinoma (PDAC) patients.
Methods: We collected tumor biopsies from 154 stage I–III PDAC patients who were surgically treated at Helsinki University Hospital between 2000 and 2011. We used tissue microarray and immunohistochemistry to assess the expression of TLRs 1, 3, 5, 7, and 9 in PDAC tissue, and we matched staining results against clinicopathological parameters using Fischer's test. For survival analysis we used the Kaplan-Meier method and log-rank test, and the Cox regression proportional hazard model for univariate and multivariate analyses. Patients receiving neoadjuvant therapy were excluded from the study.
Results: High TLR1 expression was observed in 60 (39%), high TLR3 in 48 (31%), high TLR5 in 58 (38%), high TLR7 in 14 (9%), and high TLR9 in 22 (14%) patients. Overall, none of the markers associated directly with patient survival. However, univariate analysis showed high TLR1 expression to associate with better survival in patients who were under 65 years old (P=0.019). Also, we found noteworthy how poorly patients fared if they were scored negative in TLR1, TLR3, TLR7 and TLR9 expression.
Conclusions: We found high TLR1 expression to be of positive prognosis in patients under 65 years of age.

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AB072. P044. Analyses of aberrant methylation of tumor suppressive miRNAs in the patients with pancreaticobiliary diseases in bile juice

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Backgrounds: Dysregulation of miRNA is associated with carcinogenesis of various cancers. However, there have been no reports about epigenetic abnormalities of tumor suppressive miRNA using the samples other than pancreatic tissues in the patients with pancreatic cancer (PC). In this study, we tried to examine methylation of tumor suppressive miRNAs in the patients with pancreaticobiliary diseases in order to detect miRNAs specific for PC in bile juice.

Methods: Bile juice was collected by endoscopically or percutaneously in 26 patients with PC, nine patients with biliary tract cancer (BTC), and ten patients with benign pancreaticobiliary diseases (BD). DNA was extracted from bile juice, treated with sodium bisulfite, and amplified by PCR. Next, sequencing analyses were performed by next generation sequencer and methylation rate were evaluated in 16 tumor suppressive miRNAs.

Results: Moderate to high methylation was observed in eight miRNAs (miR-30a-3p, 34a, 34bc, 96, 126, 141, 200a, and 200bc). In miR-34a and 34bc, methylation rate of miRNA in the patients with BTC was significantly higher than that with PC and BD. On the other hand, in miR-126, methylation rate of miRNA in the patients with BD was significantly higher than that with PC and BTC. However, methylation rate of miRNA in the patients with PC was not significantly higher than that with other pancreaticobiliary diseases.

Conclusions: Methylation analyses of miRNAs in bile juice were supposed to be useful for differentiation of pancreaticobiliary diseases. Further investigation is necessary for detecting tumor suppressive miRNA specific for PC.

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AB073. P045. Mutant GNAS drives pancreatic tumorigenesis via PKA-SIK signaling and reprogramming lipid metabolism

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Abstract: G-protein α_s (GNAS) mediates receptor-stimulated cAMP signaling, a conserved pathway that integrates nutritional and hormonal cues with regulation of cellular metabolism. GNAS is mutationally activated in many human tumors, yet its oncogenic functions remain elusive. We investigated the functions of activated $GNAS^{R201C}$ in pancreatic tumorigenesis where concurrent *GNAS* and *KRAS* mutations define an important pancreatic ductal adenocarcinoma (PDA) subset arising from intraductal papillary mucinous neoplasms (IPMNs). By developing genetically engineered mouse models (GEMMs), we show that $GNAS^{R201C}$ cooperates with $KRAS^{G12D}$ to drive initiation of IPMN, which progress to invasive PDA following Tp53 loss. Moreover, continued expression of mutant GNAS remains critical for tumor maintenance in both GEMMs and human PDA cells. Additionally, we demonstrate that tumor maintenance requires $GNAS^{R201C}$-mediated activation of protein kinase A (PKA) and resulting inhibition of the salt-inducible kinases (SIK1-3). This pathway reprograms cellular metabolism, potentiating lipid remodeling and fatty acid oxidation. Furthermore, comparison of *KRAS* mutant pancreatic cancer cells with and without *GNAS* mutations reveals striking differences in the circuitry and functional impact of this network. Thus, our studies uncover GNAS-driven oncogenic mechanisms, identify SIK kinases as potent tumor suppressors, and demonstrate unanticipated metabolic heterogeneity among KRAS-mutant pancreatic neoplasms.

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AB074. P046. Comprehensive analysis of links between diabetes and pancreatic cancer: a bioinformatical approach

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Background: Long standing type 2 diabetes (T2DM) is a risk factor for pancreatic cancer, whereas new-onset diabetes could be seen as a result of pancreatic ductal adenocarcinoma (PDAC). Additionally, diabetes has also been suggested to be an adverse prognostic factor for PDAC. This study was to investigate shared genetic etiology underlying diabetes and pancreatic cancer, and molecular alterations in PDAC with/without diabetes from the TCGA cohort.

Methods: By integrating data from disease related microarray analysis, we carried out a dynamic biological network analysis on the overlapping differential genes in diabetes (GSE28735) and pancreatic cancer (GSE25724) with expression profiles downloaded from GEO database. Besides, differential molecular profiling for PDAC with/without diabetes from TCGA were performed by the differential gene expression and pathway analysis. Protein-protein interaction (PPI) and miRNA network were also constructed.

Results: The overlapping between diabetes and pancreatic cancer revealed 16 differentially expressed genes (DEGs). Gene ontology (GO) analyses revealed that most of the DEGs were significantly enriched in hormone metabolic process, organic hydroxy compound metabolic process and alcohol metabolic process. Highly relevant pathways include butanoate metabolism and propanoate metabolism. Comparative genomic analysis of TCGA data suggested that DEGs of PDAC with/without diabetes were mainly enriched in immunity-related pathways including T cell receptor signaling and natural killer cell mediated cytotoxicity.

Conclusions: The molecular connections between diabetes and pancreatic cancer are complicated. Glycometabolism and immunity alterations might hold the key to this riddle in terms of bioinformatics.

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AB075. P047. Human pancreatic stellate cells secreted fibronectin promote chemoresistance to gemcitabine in PDAC

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Abstract: The pancreatic stellate cell (PSC) is the primary cell type of the desmoplastic stroma of pancreatic ductal adenocarcinoma (PDAC). A prominent characteristic of PDAC that contributes to its malignant features is the presence of a dense stroma which is composed of various extracellular matrix (ECM) proteins such as fibronectin (FN) and collagens. PSCs interact with cancer cells and influence the progression of the disease through a complex network of signaling molecules involving ECM proteins. Gemcitabine remains a cornerstone of PDAC treatment in all stages of the disease despite suboptimal clinical effects partly linked to the development of chemoresistance within weeks of treatment initiation. We investigated PSC populations isolated from different human PDACs and examined the effects of PSC-conditioned medium (PSC-CM) on the chemosensitivity of different commercial human pancreatic cancer cell lines: AsPC-1, BxPC-3, Capan-2, HPAF-II, Mia PaCa-2, Panc-1 and SW-1990. The PSC-CM induced varying degree of resistance to cytotoxic activities of gemcitabine among the cancer cell lines examined. Secretome analysis of PSC-CM identified 5,245 peptides corresponding to 687 different proteins (532 of them with more than one peptide), including several ECM-related proteins with the highest number of peptides observed for FN. A FN inhibitor, synthetic Arg-Gly-Asp-Ser (RGDS) peptide, blocked the development of PSC-CM induced chemoresistance in cancer cells, suggesting that the use of FN blocking agents in addition to the gemcitabine-based chemotherapy could counteract chemoresistance and provide better clinical outcomes.

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AB076. P048. Microsatellite instability and tumor volume inversely affect early progression free survival in adjuvant setting of patients with pancreatic ductal adenocarcinoma: lights and shadows of molecular pathology and immunotherapy

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Background: Pancreatic ductal adenocarcinoma (PDAC) may present microsatellite instability (MSI), phenotype related to a damage of DNA mismatch repair (MMR) system. The MSI-driven cancer pathway leads to the synthesis of aberrant and potentially immunogenic neo-antigens by the tumor cells. Immunotherapy with ICK inhibitors has recently constituted a source of personalized treatment for MSI cancer patients and support the evaluation of MSI phenotype in PDAC. The aim of this study is to evaluate MSI in PDAC patients presenting metastatic pathology after pancreatic resection featuring first line of chemotherapy in order to evaluate a possible immunotherapy treatment.

Methods: Ten patients affected by metastatic PDAC after surgical resection and adjuvant chemotherapy with curative intent were selected for MSI analyses. Immunohistochemistry (IHC) evaluations for genes MLH1, MSH2, MSH6 and PMS2 were performed. We assessed MSI when at the least 30% of selected markers lost their protein expression. Pathological data of primary tumor were assessed consulting VIII edition of TNM and the size of tumor was evaluated as volume (cm^3). Clinical data, progression free survival (PFS) and overall survival (OS) were obtained by Long-Rank tests.

Results: The mean follow-up was 19.02 months and the living patients were 70% (7/10). The median PFS and OS were 7.51 and 23.02 months, respectively. All patients showed a microsatellite stability, in which no alteration of protein expression in MMR system was found. Indeed, nobody was treated with immunotherapy. We identified 2 different groups (5 patients each), based on their early (E) or late (L) metastatic pathology (less or more 6 months after surgery), respectively. Furthermore, we found a significant difference in terms of PFS between these 2 groups (E *vs.* L; 2.20 *vs.* 14.63; HR =4.644; 95% CI, 3.982–103.200; P=0.0018). Nevertheless, we found significant differences comparing E *vs.* L group in terms of mean tumor score (2.780 *vs.* 1.870; P=0.0067) and volume (88.68 *vs.* 8.30; P=0.0068). No significant difference in term of OS were observed.

Conclusions: Our results confirmed that MMR/MSI alterations are very rare or absent in PDAC patients. This fact represents a limit in order to submit the PDAC patients to immunotherapy clinical trials. It's not still clear whether MSI pathways might be involved in early metastatic process of PDAC. Nevertheless, we showed that both tumor scoring and volume could play a pivotal role in early recurrence of pathology.

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AB077. P049. Genetic relationship of pancreatic ductal adenocarcinoma and co-occurring IPMN

Matthaus Felsenstein, Michael Noe, David Masica, Waki Hosada, Peter Chianchiano, Cathy Guerra, Gemma Lionheart, Lodewijk Brosens, Antonio Pea, Jun Yu, Georgios Gemenetzis, Vincent Groot, Martin Makary, Jin He, Matthew Weiss, John Cameron, Christopher Wolfgang, Ralph Hruban, Nicholas Roberts, Rachel Karchin, Michael Goggins, Laura Wood

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Background: Cystic precursor lesions, in particular intraductal papillary mucinous neoplasms (IPMNs), have a significant potential to transform into invasive pancreatic ductal adenocarcinoma (PDAC). After resection, pathological examination of a sizable proportion of invasive PDACs reveal a co-occurring IPMN. Yet, it remains unclear whether the co-occurring IPMN represents a precursor to the invasive PDAC or an unrelated lesion.

Methods: Over a ten-year period, we analyzed lesions of individuals with invasive pancreatic carcinoma and co-occurring IPMN. Tissue of three separate areas (carcinoma, adjacent IPMN, distant IPMN) were laser capture micro-dissected and DNA subsequently extracted. Targeted next generation sequencing of a panel of pancreatic cancer driver genes was used to identify mutations in order to characterize the relatedness of the IPMNs and co-occurring carcinomas.

Results: Thirteen patients with IPMN/colloid carcinoma and 7 patients with IPMN/carcinoma of the ampullary region validated the reliability of our assay. Of the 61 patients with co-occurring IPMN and PDAC, 51% were likely related. Strikingly, 18% of the patients showed a genetically independent IPMN and co-occurring PDAC sharing no somatic mutations despite close anatomic proximity of the two lesions, suggesting that the two lesions may have developed from a distinct precursor. The relatedness of the remaining cases was indeterminate using our targeted assay. However, whole exome sequencing on three indeterminate cases revealed that they can be genetically independent, suggesting that an unexpected proportion of co-occurring IPMNs/PDACs arising independently. In addition, we report on extensive genetic heterogeneity within cystic lesions.

Conclusions: This study determined the genetic relationship between co-occurring PDACs and IPMNs in a large cohort. It revealed an unexpectedly high prevalence of likely independent co-occurring IPMNs and has important implications for molecular screening and patients risk stratification.

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AB078. P050. Efficacy of integrated immune ratio associated with tumor growth and prognosis in pancreatic cancer

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Background: The prognosis of pancreatic ductal adenocarcinoma (PDAC) remains poor owing to its difficulty in diagnosis and therapy. Immunotherapy has revealed its robust performance in several malignancies.
Methods: The tissue microarray was stained and analyzed associated with clinicopathological characteristics. The preclinical murine models administrated with various immunotherapies were analyzed by growth inhibitor, flow cytometry, ELISA and immunohistochemistry.
Results: The infiltrating FoxP3+ regulatory T cells (Tregs) and PD-1 expression in tumor tissues were associated with survival, while CD8+ infiltrating T cells (TILs) was lack of evidence. Then, CD8, FoxP3 and PD-1 expression were merged together to create a new estimated value—integrated immune ratio (IIR) comprehensively considering their drawbacks, which showed excellent distinction in risk stratification of survival. IIR was verified as an independent prognostic factor according to multivariate analysis, so did T and N classification. In the preclinical murine model, CD25 and TGF-β combinational blockade revealed higher tumor growth inhibitor value. Under overall consideration, the combinational therapy significantly depleted periphery and intratumoral FoxP3+ Tregs and enhanced intratumoral CD8+ T cells compared to control or anti-TGF-β monotherapy (all $P<0.05$). The intratumoral IL-10, TGF-β was notably lower associated with higher IFN-γ excretion with the combinational immunotherapy. Such combinational immunotherapy was further verified to synergize with anti-PD-1 monotherapy to promote the tumor growth inhibitor and cure rate.
Conclusions: The combination of CD25, TGF-β and PD-1 blockade has a potentially effective role in inhibiting tumor formation and progression and provides a strong rational strategy in clinical trials on the basis of IIR.

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AB079. P051. Blockage of CTR1-dependent copper absorption increases autophagy to resist apoptosis of pancreatic ductal carcinoma cells

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Abstract: Clinical observations have demonstrated that copper levels elevate in a number of cancer types, and copper deprivation is considered a prospective anti-cancer therapeutic strategy. However, the cellular mechanism underlying copper depletion in cancer therapy is still not fully understood. Here, we demonstrate that CTR1-dependent copper level is negatively correlated with the survival time of pancreatic ductal carcinoma patients and copper increase is important for pancreatic ductal adenocarcinoma progression. However, copper depletion via CTR1 knockdown or copper chelation did not induce pancreatic cancer cell apoptosis. We found that copper deprivation causes increased ROS and decreased ATP, which rendered cancer cells in a dormant state. Strikingly, copper deprivation caused an increase in autophagy to resist apoptosis of pancreatic cancer cells. Simultaneous treatment with copper chelator tetrathiomolybdate (TM) and autophagy inhibitor chloroquine diphosphate salt (CQ) increased apoptotic cancer cells in vitro and retarded cancer growth in xenotrans planted mice. These findings reveal that copper deprivation-caused cell dormancy and an increase in autophagy is a major reason for the poor clinical outcome obtained from copper depletion therapies for cancers. Therefore, the combination of autophagy inhibition and copper depletion is potentially a novel strategy for the treatment of pancreatic cancer and other copper-dependent malignant tumours.

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AB080. P052. Role of neutrophil extracellular traps (NETs) in pancreatic cancer liver metastasis

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Background: Liver metastasis is the major cause of pancreatic ductal adenocarcinoma (PDAC) related death and preventing liver metastases may improve the patient's survival. Neutrophil extracellular traps (NETs) were identified in 2004 and are extracellular networks that consist of DNA released from neutrophils together with antimicrobial peptides and proteases derived from neutrophil granules. Recently, it was shown that NETs promote various human pathology, such as cancer-associated thrombosis and auto-immune disease and cancer, but the role of NETs in pancreatic cancer progression is not well known. This study aims to investigate the role of NETs in pancreatic cancer liver metastasis using genetically engineered mice that spontaneously develop PDAC and tumor intrasplenic injection mouse model that forms experimental liver metastases.

Methods: Two mouse models, spontaneous pancreatic cancer mice KPCL (LSL-Kras G12D/+; LSL-Trp53 R172H/+; LSL-Luciferase; Pdx-1-Cre) mice and tumor splenic injection model were treated with DNase I, NETs inhibitor, and examined the influence of DNase I on invasion and metastasis of pancreatic cancer. Neutrophils isolated from bone marrow of C57BL/6 mouse were co-cultured with pancreatic cancer cells derived from KPC (LSL-Kras G12D/+; LSL-Trp53 R172H/+; Pdx-1-Cre) mouse.

Results: KPCL mice treated with DNase I from the 8 weeks of age had significantly longer survival time compared to the control group, and liver metastasis was suppressed. However, liver metastasis was suppressed in the group that started administration from the 13 weeks of age, the survival period was not extended. In the tumor intrasplenic injection model, neutrophils were recruited to the liver micrometastases, and liver metastasis formation was inhibited in the DNase I treated group. In vitro study revealed that cancer cells derived from KPC mice indirectly co-cultured with neutrophils promoted NETs formation.

Conclusions: DNase I, a NETs inhibitor, suppressed liver metastasis formation in KPCL mice and tumor intrasplenic injected model, suggesting that NETs promotes liver metastasis in pancreatic cancer.

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AB081. P053 Survival of unresectable pancreatic cancer patients after artery divestment combined pancreatectomy: a retrospective and propensity score-matched analysis

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Background: For non-metastatic pancreatic patients, artery involvement is the major obstacle of curative operation. Here we present the oncologic effect of artery divestment in unresectable pancreatic cancer patients.

Methods: Twenty-four artery-involved unresectable non-metastatic pancreatic patients were identified with contrast-enhanced CT received curative pancreatectomy with artery divestment (UR group). A total of 247 contemporary pT1-$^{3}N_xM^0$ pancreatic cancer patients receiving therapeutic surgery were enrolled as control. Univariate analysis of demographic and clinical data was performed to reveal risk factors of prognosis. Propensity scored matching (PSM) analysis was performed for independent risk factors to assess the median overall survival (MOS) of two groups of patients.

Results: For the primary survival analysis, the MOS of all 271 patients was 17.8 months (95% CI: 16.0 to 19.6 months). MOS of UR group and control group were 16.7 and 17.8 months respectively (P=0.481). Pre-operative CA19-9, pancreatectomy category, tumor grading, tumor size, lymph node metastasis, and post-operative chemotherapy were independent risk factors and introduced into PSM analysis. A 24 versus 24 PSM analysis revealed no statistical MOS difference between UR group and control group [MOS 16.7 months (95% CI: 5.7 to 27.7 months) for UR group, 17.3 months (8.2 to 26.4 months) for control group].

Conclusions: For UR pancreatic cancer patients, artery divestment combined pancreatectomy could offer similar prognosis comparing to earlier T staging patients.

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AB082. P054. Non-functional pancreatic neuroendocrine tumor (NF PNET) imaging and evaluation using ^{18}F-FDG and ^{68}Ga-DOTANOC-PET/CT: initial data of a prospective study

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Background: Predicting aggressive behavior of non-functional pancreatic neuroendocrine tumor (NF PNET) still remains controversial. It is known that lymph node metastases are rare but possible also on small (1–2 cm) NF-PNET. Positive ^{18}F-FDG-PET/CT avidity is associated with poor prognosis in NETs. This study aims to evaluate the possibility to enhance diagnostic accuracy by using dual trace functional imaging ^{18}F-FDG and ^{68}Ga-DOTANOC PET/CT in patients with NF PNET.

Methods: In this prospective study 29 patients underwent PET-imaging with two tracers, ^{18}F-FDG and ^{68}Ga-DOTANOC, followed by surgery or endoscopic ultrasonography biopsies (EUS-FNA) with follow-up. The imaging results were compared to a histology report.

Results: Average tumor size was 36 mm (range, 9–103 mm). Twenty-seven patients had a ^{68}Ga-DOTANOC positive (sensitivity 96%) and 10 had an ^{18}F-FDG positive tumor. One had a ^{18}F-FDG positive, ^{68}Ga-DOTANOC negative tumor with multiple lymph node metastases (LN+). Histology reports were available for 24 patients: 4 EUS-FNA (of which 2 are waiting for surgery) and 20 operated. Five patients are only followed-up (on average 5 months). Five out of 18 patients had LN+ tumor of which 2 were ^{18}F-FDG positive. There were WHO Gr1 tumors in 11 patients, WHO Gr2 in 7 patients, Gr3 in 1 patient and 1 MANEC. Tumors were 18F-FDG positive 5/11 Gr1 tumors (3 over Ø 9 cm, 1 LN+), 4/7 Gr2 tumors (2 LN, 1 only EUS-FNA) and 1/1 Gr3 tumor. MANEC was ^{18}F-FDG negative. 2 of 5 LN+ patients had ^{18}F-FDG positive tumor.

Conclusions: The high sensitivity of ^{68}Ga-DOTANOC-PET/CT in differential diagnosis of a hypervascular pancreatic lesion is known. Our initial findings suggest that ^{18}F-FDG-PET/CT can be used to discriminate tumor grades but not lymph node status of NF PNET.

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AB083. P055. Total pancreatectomy in radical pancreatectomy for pancreatic cancer

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Background: Total pancreatectomy (TP) may be required in locally advanced or centrally located pancreatic cancer to achieve curative resection (R0 resection). However, it remains a controversial approach, due to the potential short and long-term complication and uncertain survival benefits .The present study aimed to assess the outcome of TP for primary pancreatic cancer.

Methods: We reviewed all patients underwent TP between Jul. 2014 and Nov. 2017 in Pancreas Center of the First Affiliated Hospital of Nanjing Medical University.

Results: From Jul. 2014 to Nov. 2017, 24 patients underwent TP in our center. Median age was 66 (range, 43–86) years. Median operative time was 280 (range, 195–530) min with median estimated blood loss 350 (range, 100–1500) mL. Portal vein resections in 45.83% (11/24). Postoperative morbidity (41.67%, 10/24) included 2 cases grade B postpancreatectomy hemorrhage (PPH), 1 case of grade C PPH, 1 cases grade B Delayed gastric empty (DGE), 2 cases grade C DGE, 1 cases grade B chyle leak, 1 case hypoglycemic coma and 1 case fistula of colon. Median postoperative hospital stay was 12 (range, 7–86) d. "1 mm" R0 resection was achieved in 7 patients (29.17%, 7/24). Overall 30-day and in-hospital mortality rate were 4.17% (1/24) and 8.33% (2/24). Until the last time of follow-up (Oct 2017), 12 patients (50%, 12/24) are dead, with median survival time 8.8 months.

Conclusions: Total pancreatectomy, if needed, can be performed in high-volume pancreas center, but with high morbidity and acceptable mortality. Survival benefits of TP in patients with primary pancreatic cancer may needs further observation.

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AB084. P056. Intra-operative ultrasound to determine resectability during surgical exploration of primary non-resectable pancreatic cancer following induction chemotherapy

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Background: Determining the resectability of primary non-resectable pancreatic cancer after induction chemotherapy is complicated by under-estimation of tumor regression upon pre-operative imaging. Diagnostic modalities to accurately predict resectability are therefore highly needed. This study describes the initial results of intra-operative ultrasound (IOUS) as diagnostic tool during explorative laparotomy of primary non-resectable pancreatic cancer following induction chemotherapy.

Methods: Prospective multicenter study of patients who underwent surgical exploration following two months of induction chemotherapy because of primary non-resectable pancreatic cancer. Patients with RECIST non-progressive disease proceeded to explorative laparotomy with IOUS in the case of <180 arterial or reconstructable venous involvement [i.e., NCCN (borderline) resectable disease] or if they persisted unresectable and had been randomized for local ablative treatment within a clinical trial. IOUS outcomes were compared with pre-operative, post-chemotherapy CT-imaging and pathological examination only in case of a resection specimen.

Results: Twenty LAPC patients underwent explorative laparotomy of which 5 had RECIST partial response and 15 RECIST stable diseases. The majority had received FOLFIRINOX (n=18). CT-imaging classified 1 (5%) patient as NCCN resectable, 9 (45%) as borderline resectable and 10 (50%) as unresectable. Upon IOUS, 5 (25%) patients were deemed resectable, 6 (30%) borderline resectable and 9 (45%) unresectable. Consequently, IOUS deemed 4 NCCN borderline resectable patients to be primary NCCN resectable and 1 unresectable patient to be borderline resectable. Therefore the resectability status was changed in 5/20 (25%) patients. Ultimately, 12 patients underwent resection of which 50% had radical vascular resection margins.

Conclusions: IOUS is a promising tool for the surgeon to determine resectability during surgical exploration of primary non-resectable pancreatic cancer following induction chemotherapy. Future series to assess the diagnostic value, including pathology confirmation of IOUS findings are needed.

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AB085. P057. Early monocentric experience in EUS-FNA wet-technique for pancreatic lesions

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Background: A preoperative diagnosis of pancreatic adenocarcinoma is often indispensable to guide the right treatment. EUS-FNA is an established procedure for obtaining a pathological specimen and a correct diagnosis. The FNA wet suction technique relies on pre-flushing the needle with saline instead of the air column contemplated in the dry technique. The aim of this study was to evaluate the performance of wet EUS-FNA technique with 19 and 22 G needles.

Methods: Thirty-one consecutive patients underwent EUS-FNA for pancreatic lesions between 7/2016 and 1/2017 at our interventional endoscopy unit. The type and size (19 or 22 G) of needle were chosen at the discretion of the endosonographers. Macroscopic on- site quality evaluation (MOSE) was performed. Cellularity was assessed by using a 4-point scale (0: no cells to 3: high cellularity). Specimen adequacy was graded on a 2-point scale (0: unable to make a diagnosis; 1: adequate tissue). For patients who underwent surgery (8/31) the final diagnosis was based on the resected specimen. In the absence of surgical pathology the final diagnosis was based on a minimum follow up of 36 weeks (23/31).

Results: Patients median age was 63±11 years (15 males and 16 females). Lesions were located in: pancreatic head 17/31, body/tail 11/31, uncinate 3/31. The mean size of lesions was 4.3±1.6 cm. Results of FNA: adenocarcinoma 24 (77.4%), 1 GI stromal tumor, 6 negative for malignancy. In one case the procedure was repeated (successfully) for inadequate specimen. 22 G needles have been used in 10/32 procedures, 19 G in 22/32. Mean number of passes 3.4±0.1. Cellularity score (mean 2.29±0.78) results: score 1 in 19.4%, score 2 in 32.3%, score 3 in 48.4% cases. In 2 cases there was no accordance between FNA and the final diagnosis. Regarding the use of the two needles (19G and 22G), no significant differences were found in terms of number of passes (19G 3.3±0.1 *vs.* 20G 3.4±0.1; P=ns), adequacy (19G 90% *vs.* 22G 100%; P=ns) and cellularity of the sample (2.0±0.1 *vs.* 2.41±0.8; P=ns), as well as in ability to obtain a correct diagnosis (19G 90.0% *vs.* 22G 94.5%; ns). No adverse events occurred. Wet-FNA sensitivity and specificity were respectively 92.59% and 100%, positive and negative predictive values were respectively 100%, and 66.67% (accuracy 93.5%).

Conclusions: Wet EUS-FNA technique, performed with 19G and 22G needles, showed a high performance in terms of adequacy and cellularity of the sample as well as in obtaining a correct diagnosis.

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AB086. P058. Current status of pancreatic cystic neoplasm: diagnosis and treatment a multi-institution retrospective study in China

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Background: The aims of this study were to introduce our current situation of diagnosis and treatment of pancreatic cystic neoplasm (PCN) in China.

Methods: A total of 2,251 PCN patients who underwent surgical resection from January 2006 to December 2016 in 16 institutions were retrospectively analyzed.

Results: The male to female ratio was 1 to 2.4, and the age at diagnosis was 47.5 years (range, 8–89 years). The preoperative diagnostic coincidence rate of solid pseudo-papillary tumor (SPT) was 48.5%, serous cystic neoplasm (SCN) was 13.7%, intraductal papillary mucinous neoplasm (IPMN) was 49.7, mucinous cystic neoplasm (MCN) was 15.6% respectively and the PCN was 33%. SPT, SCN, IPMN, MCN were 713 cases, 678 cases, 495 cases, 365 cases respectively by pathologically diagnosed, and the malignant transformation rate was 12.3%,0.6%,32.1%,10.4% respectively. The rate of postoperative complications was 46%, the pancreatic fistula (PF) and delayed gastric emptying (DGE) were the main complications. The tumor marker, such as CEA, CA19-9, CA125, was significantly increased in the malignant group.

Conclusions: SPT maybe the most common tumor in all PCN in China. Improving the accuracy of subtype (especially the SCN and the MCN) diagnosis preoperatively can avoid unnecessary surgery.

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AB087. P059. Strategy for radical dissection of two anatomical difficult triangles for pancreatic head cancer—laparoscopic pancreaticoduodenectomy with left uncinate first approach

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Background: We describe a technique modification with emphasize a left lateral dissection of superior mesenteric artery (SMA) and uncinate process (UP) as a novel approach for laparoscopic pancreaticoduodenectomy (LPD). Local recurrence are quite high for pancreatic cancer and mostly are around celiac and SMA trunk. Here we suggest two anatomical triangles, which are difficult to dissect and easy for recurrence. If we take the root of SMA as radiation center, cranial triangle is surrounded by SMA root, PV, hepatic artery and aorta, caudal triangle or sectorial area is surround by SMA trunk, SMV trunk until its division, and aorta. We are proposing a new strategy aiming at improving R0 resection with focusing on both triangles.

Methods: During LPD, the camera was transferred to left paraumbilical trocar, ventral part of hepatoduodenal ligament or ventral part of cranial triangle, are dissected from left view. Then in infra colic region, the Treitz ligament is incised, the SMA root was reached left posteriorly above left renal vein. By rotating mesentery root upward from left, the distal part of uncinate process (UP) are rotated to left side, so its connections with SMA and SMV jejunal branch are clearly exposed from left view. Dissection continued along SMA axis from its root until its crossing over duodenum and whole length of UP, after IPDA and IPDV are ligated and transected, the distal part of UP can be completely freed from SMA/SMV, and the caudal triangle is mostly cleared. Then the camera was transferred to right paraumbilical trocar, in right posterior view, the dorsal part of cranial triangle, are also cleared from behind to upward until the whole mesopancreas are freed. Resection was complete after transecting pancreas neck.

Results: Forty patients underwent the novel surgical procedure between April 2016 and December 2017 during laparoscopic PD. SMA root and distal UP was dissected via left approach in all patients.

Conclusions: The location of cancer in pancreatic head can be divided into 3 categories, with different infiltration and metastasis area, and should require different focus for dissection. Lateral posterior approach will provide a good exposure of major vessels, the approach here we proposed will provide a complete dissection of both anatomical triangle along SMA-CA axis with good visualization.

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AB088. P060. Safety assessment of standardized pancreatectomy in patients with solid pseudopapillary tumor and pancreatic ductal adenocarcinoma: retrospective case-control study in a single center

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Background: The aim of this study is to evaluate the surgical safety of standardized pancreatectomy for solid pseudopapillary tumor (SPT) and pancreatic ductal adenocarcinoma (PDAC).

Methods: Sixteen SPT cases and matched-pair 32 PDAC cases, that underwent standardized pancreatectomy between January 2015 and October 2016 in the pancreas center of Nanjing Medical University, were composed the cohorts. The demographic and pathologic dates were compared between two cohorts. The surgical safety index and clinical outcomes were evaluated.

Results: The mean age at diagnosis was 49.4±10.28 years (range, 41–83 years) in SPT group and 60.9±6.68 years (range, 49–73 years) in PDAC group respectively. There is no difference in age, sex, tumor location and surgical procedures between the two groups (P>0.05). The pancreatic remnant texture in SPT group was softer than PDAC group (0/16 *vs.* 10/22, P<0.001). The diameter of the pancreatic duct in SPT group (2.1±0.18 mm) was finer than PDAC group (2.6±1.26 mm) (P<0.05). SPT with standardized pancreatectomy was associated with lower overall postoperative complications (2/16 *vs.* 13/32, P<0.05), pancreatic fistula (4/16 *vs.* 19/32, P<0.05) and shorter hospitalization days (15.7±1.75 *vs.* 20.5±13.14, P<0.05) compared to PDAC. There was no significant difference between the two groups in operation time (243.4±86.30 *vs.* 231.1±98.59 min, P=0.63), bleeding loss (493.7±362.80 *vs.* 637.5±227.41 mL, P=0.10), reoperation rate (0 *vs.* 0, P=1.00) and postoperative mortality (0 *vs.* 0, P=1.00).

Conclusions: Standardized pancreatectomy is a safer and more effective treatment of SPT compare to PDAC.

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AB089. P061. Pancreatectomies associated to vein resection: a large single institution experience

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Background: Potential benefits of pancreatectomies associated to vein resection (PAVR) are still contradictory in literature. This study aims to analyze short and long term outcomes of PAVR.

Methods: A retrospective analysis of a consecutive series of patients underwent PAVR from 2008 to 2017 was performed.

Results: Of 258 patients underwent PAVR at Karolinska University Hospital, 194 with histologically proved PDAC were included. Severe post-operative complications were observed in 10.3%, and required reoperation in 7.7% of cases. Mortality was 2.6% and the median post-operative stay was 14 days. No differences in post-operative complication rates were observed comparing different surgical techniques. Patients with ASA score ≥3 experienced more surgical complications (27.2% *vs.* 13.8%; P=0.02). In multivariate analysis ASA score ≥3 and multivisceral resections were predictive factors for complications. The 1, 3 and 5 years survival rates were 64%, 21% and 12.6% respectively. The median survival of patients underwent lone vein resection was superior to patients underwent combined artery-vein resection (17 *vs.* 10 months; P=0.02). Patients who received adjuvant chemotherapy had also a longer median survival (23 *vs.* 12 months; P=0.0005) as well as patients with pre-operative levels of serum Ca 19-9 ≤200 U/mL (23 *vs.* 15 months; P=0.01).

Conclusions: PAVR are safe and feasible. The selection criteria for resection play a key role in the outcome. Post-operative chemotherapy is confirmed as one of the most important prognostic factors. Pre-operative levels of Ca 19-9 could maybe be used for selecting good candidates for neo-adjuvant treatment.

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AB090. P062. Strategy of postoperative follow-up for intraductal papillary mucinous neoplasms

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Background: This study aimed to evaluate the postoperative recurrence risk factors for intraductal papillary mucinous neoplasm (IPMN), and to suppose an appropriate surveillance after surgical resection.
Methods: This study included 257 consecutive IPMN patients undergoing surgery from 1999 to 2014. Pathological diagnosis showed low- or intermediate-grade dysplasia in 85 patients (33.1%), high-grade dysplasia in 87 patients (33.8%), and invasive intraductal papillary mucinous carcinoma (IPMC) in 85 patients (33.1%). The median postoperative follow-up period was 53.5 months.
Results: Fifty-six IPMN patients (21.8%) had recurrence after surgery, including those with remnant pancreatic recurrence (n=14) and extra-pancreatic recurrence (n=42). Remnant pancreatic recurrence had no influence on the overall survival (OS), whereas, patients with extra-pancreatic recurrence had significantly worse OS (P<0.001). Five patients (35.7%) experienced remnant pancreatic recurrence more than 5 years after surgery. All extra-pancreatic recurrences occurred within 5 years. The OS after recurrence in the remnant pancreas tended to be better among patients who underwent second resection than for those without (P=0.081). We found that the positive pancreatic transection margin was the only independent risk factor for remnant pancreatic recurrence (P<0.001; OR, 8.92), whereas the risk factors for extra-pancreatic recurrence were invasive IPMC (P<0.001; OR, 29.41), mixed-type (P=0.008; OR, 6.41), elevated serum CA19-9 (P=0.019; OR, 3.57), and intraoperative transfusion (P=0.025; OR, 3.33).
Conclusions: Our data suggest that continuous surveillance for more than 5 years after surgery is needed for all IPMN patients to evaluate the remnant pancreatic recurrence, and strict 5-year surveillance is necessary for IPMN patients at risk for extra-pancreatic recurrence.

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AB091. P063. Case report: stage 4 pancreatic cancer to remission using paricalcitol and hydroxychloroquine in addition to traditional chemotherapy

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Abstract: I am a physician specializing in Allergy and Asthma, who in July 2016, had tumors in the head and the tail of the pancreas with scattered peritoneal metastases and a CA19-9 of 11,575 U/mL. Working with physicians from Weill-Cornell and Johns Hopkins, I began treatment with gemcitabine and capecitabine, plus IV Paricalcitol (25 mcg 3x's/week) and hydroxychloroquine (600 mg BID). These are both safe and inexpensive treatment options that have shown success in pre-clinical models, phase 2 human trials, and are readily available. I have now enjoyed a complete response with my latest CA19-9 of just 15 U/mL and no evidence of active disease on my most recent CT scan. Paricalcitol is Vitamin D receptor agonist without the systemic toxicity of Vitamin D such as hypercalcemia. Evidence suggests that paricalcitol helps break though the pancreatic tumor's protective stroma produced by pancreatic satellite cells that are particularly activated in pancreatic cancer. These satellite cells have high levels of Vitamin D receptors and the blocking of these receptors by paricalcitol inactivates the stromal production. These satellite cells also produce cytokines and growth factors that enhance local tumor growth, contribute to angiogenesis, and enable metastasis. Vitamin D has also been shown to exert anti-proliferative effects secondary to the upregulation of the cell cycle inhibitors which control cell proliferation, differentiation, and division. Studies have shown a reduction of several pancreatic tumor lines in mice treated with paricalcitol correlating with the degree of cell cycle kinase inhibition. Hydroxychloroquine is a relatively inexpensive drug currently available for the treatment of malaria and autoimmune diseases. Hydroxychloroquine has been shown to inhibit autophagy. Autophagy is a process of self-cannibalization in which injured cancer cells ingest pieces of themselves, such as organelles and macromolecules, to conserve energy, and, therefore, thrive. Additionally, autophagy helps rid the cancer cells of toxic substances and free radicals, such as hydrogen peroxide and superoxide. The k-Ras genetic mutation, found in over 90% of pancreatic tumors, appears to upregulate the process of autophagy which and may be responsible for the extreme resilience of pancreatic cancer cells. When combining chemotherapy with autophagy inhibition, damaged cancer cells are unable to conserve the needed energy to survive.

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AB092. P064. The preliminary experience of total or proximal intestinal derotation procedure applied in pancreatoduodenectomy

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Background: At present, pancreaticoduodenectomy (PD) is the surgical treatment for patients with periampullary tumors. Masanori Sugiyama has reported an intestinal derotation procedure for facilitating mesopancreas excision. According to their research, this procedure simplifies the anatomic situation, decreased operative time, reduced blood loss and tended to increase the rate of R0 resection. In clinical practice, we designed proximal intestinal derotation on the basis of intestinal derotation procedure. To simplify the intestinal derotation process but maintain the benefits, we cut the Treitz ligament only to complete proximal intestinal derotation. The anatomic situation can be simplified like total intestinal derotation during the operation. The object of our study is to introduce the preliminary experience of total or proximal intestinal derotation procedure and reveal the merits and demerits of these methods through our retrospective analysis.

Methods: We investigated 29 malignant tumor cases underwent PD by the same pancreatic surgeon in last years. 14 cases are in the intestinal derotation procedure group (total: proximal =7:7) and 15 cases are in the conventional procedure group. Perioperative factors including patient characteristics, operation situation, the number of lymph nodes, and the volume of dally drainage and the time of removing the drainage were compared.

Results: The patient characteristics, operation time and intraoperative bleeding are not different between the two groups. But the intestinal derotation procedure significantly increased the number of lymph nodes dissection (12.43±3.55 *vs.* 8.33±5.80, P=0.031). However, the volume of drainage after POD2 increased significantly (POD2 R 232.43±352.42 *vs.* 168.00±192.74 mL, P=0.031; POD3 L 337.21±300.45 *vs.* 110.67±135.30 mL, P=0.019; POD4 L 307.86±227.08 *vs.* 103.20±116.52 mL, P=0.007; POD4 R 237.36±165.80 *vs.* 65.60±44.69 mL, P=0.002). Meanwhile, proximal intestinal derotation procedure still maintain the advantage of lymph nodes dissection (13.86±3.80 *vs.* 8.33±5.80, P=0.033) and make up for the defect of increasing the drainage.

Conclusions: The intestinal derotation procedure simplifies the anatomy of mesopancreas and obtains a good surgical field, which makes it easier to dissect more lymph nodes. But it has the demerit that increased the drainage which can be covered through proximal intestinal derotation procedure.

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AB093. P066. Pancreas-preserving management of grade-c pancreatic fistulas after pancreaticoduodenectomy: a single center's experience

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Background: Optimal surgical strategy for grade-C postoperative pancreatic fistula (POPF) after pancreaticoduodenectomy (PD) is not justified. External wirsungostomy is feasible. However, the subsequent repeat pancreaticojejunostomy (PJ) is challenging. This study aims to introduce our experience of external wirsungostomy for grade-C POPF and a novel technique to do the repeat PJ (re-PJ).
Methods: From January 1, 2012 to December 31, 2016, all consecutive patients who underwent pancreaticoduodenectomy (PD) with PJ were identified. The clinical data were retrospectively collected and analyzed.
Results: Out of 325 patients, 11 patients (3.38%) underwent salvage re-laparotomy for grade-C POPF. External wirsungostomy was performed in 10 patients (3.08%). Four patients died of severe complications within 90 days postoperatively or tumor progression before the scheduled re-PJ was performed. Three patients got their external pancreatic drainage tube pulled out accidentally without causing severe consequences. Three patients underwent planned re-PJ after external wirsungostomy, including one with duct-to-mucosa PJ and two with the novel bridging technique. The operative time of the two patients undergoing the novel bridging technique is 120, 135 min, respectively, and the length of post-operative hospital stay (LPHS) is 7, 5 d, respectively. The operative time and the LPHS of whom underwent duct-to-mucosa PJ is 315 min, 24 d, respectively. There was no major post-operative complication.
Conclusions: External wirsungostomy is an easy and safe way to preserve the pancreas remnant in grade-C POPF patients. The novel bridging technique may be a simpler alternative to traditional PJ with a comparable prognosis.

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AB094. P067. Therapeutic strategies and prognosis in patients with borderline resectable pancreatic adenocarcinoma: a multicenter retrospective study

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Background: In order to increase the rate of curative resection and improve the prognosis for borderline resectable pancreatic adenocarcinoma (BR-PDAC), neoadjuvant therapy (NAT) has been adopted. However, sufficient evidence has not been established and therapeutic strategies for BR-PDAC differ from institution to institution. Multicentre retrospective study was performed to reveal the therapeutic strategies and outcome in patients with BR-PDAC.

Methods: Patients with BR-PDAC treated in 10 institutions from January 2010 to December 2014 were included in the present study. BR-PV involved the portal vein (PV) or superior mesenteric vein (SMV). BR-A involved the superior mesenteric artery, celiac axis, or hepatic artery.

Results: The present study included 176 patients (BR-PV, 106; BR-A, 70). NAT was performed in 69 patients (39.2%). The patient number of NAT plus resection, upfront surgery, and no resection group was 25, 104, and 47, respectively. NAT involved 29 of chemotherapy (42.0%) and 40 of chemoradiotherapy (58.0%). The overall median survival time (MST) of patients in NAT plus resection, upfront surgery, and no resection group was 53.7, 17.8, and 15.0 months, respectively. NAT plus resection was independent prognostic factor (HR =0.447, P=0.007). In patients who underwent surgical resection, there was no significant difference in clinical factors at initial diagnosis. However, the rates of the SMV/PV involvement and lymph node metastasis were significantly lower in NAT plus resection group compared upfront surgery group (P<0.001). In multivariate analysis in patients who underwent surgical resection, NAT (HR =0.535, P=0.044) and postoperative adjuvant therapy (HR =0.423, P<0.001) were independent prognostic factors.

Conclusions: In treatment for BR-PDAC, NAT may lead to downstage of the tumor and improvement the prognosis.

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AB095. P069. Identification of therapeutic genomic alterations by investigating cancer-related genes and microsatellite instability: road to precision medicine for pancreatic ductal adenocarcinoma

Ding Ding, Ammar Javed, Dea Cunningham, Jonathan Teinor, Michael Wright, Chunhui Yuan, Cara Wilt, Amy Ryan, Carol Judkins, Keith McIntyre, Rachel Klein, Amy Hacker-Prietz, Eun Ji Shin, Atif Zaheer, Dung Le, Anne Marie Lennon, Mouen Kashab, Vikesh Singh, Jin He, Alex Blair, Vincent Groot, Jun Yu, Georgios Gemenetzis, Ross Donehower, Ana Jesus-Acosta, Adrian Murphy, John Cameron, Lindsey Manos, Christi Walsh, Lara Espin, Caitlin Brown, Tiffany Zavadsky, Matthew Weiss, Richard Burkhart, Nilo Azad, Amol Narang, Valerie Lee, Elizabeth Thompson, Elliot Fisherman, Robert Anders, Ralph Hruban, Elizabeth Jaffee, Christopher Wolfgang, Lei Zheng, Daniel Laheru; on behalf of Johns Hopkins Precision Medicine Program

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Background: Cancer-related gene mutations (CGMs), microsatellite instability (MSI), and tumor mutation burden (TMB) have been identified as potential targets for drugs and immunotherapeutics, providing an avenue for individual patient clinical decision-making. Data on CGMs, MSI, and TMB is limited.

Methods: All patients with pancreatic ductal adenocarcinoma (PDAC) who underwent next-generation sequencing (NGS), between 2009 and 2017, were included in the study. Tissue was obtained from either surgical specimens or biopsies. NGS was used to obtain data on over 300 cancer-related genes. Furthermore, data on general demographics, histopathological findings, clinical treatment, and outcomes were obtained from the institutional databases and analyzed.

Results: A total of 94 specimens from 93 patients were obtained and sequenced. The mean age was 61.9 years (95% CI: 34.3–80.9). The majority was male (N=48, 51.6%) and white (N=80, 86.0%) and underwent surgical resection (N=49, 52.7%). The samples were processed by FoundationOne (N=74, 78.7%), Perthera (N=15, 16.0%), and Personal Genome Diagnostics (N=5, 5.3%). The median time from tissue collection and ordering of test by clinicians was 11.3 months (IQR: 2.4-15.1), while the mean time to report genomic results was 12.4 days (95% CI: 8–23.7). The most commonly altered driver mutations were KRAS (N=86, 92.6%), TP53 (N=64, 68.1%), CDKN2A/B (N=47, 50%), and SMAD4 (N=27, 28.7%). Other common mutations included BRCA1/2 (N=20, 20.2%), LRP1B (N=16, 17.0%), ARID1A (N=15, 16.0%), and ARID1b (N=14, 15.0%). None of the sixty (64%) patients tested for MSI and 51 (54%) tested for TMB were found to have MSI or TMB.

Conclusions: This study further demonstrates that the rate of and clinically actionable CRMs, and MSI in patients with PDAC is low. However, in patients with presence of these clinically actionable CRMs, with appropriate management encouraging outcomes can be achieved. Furthermore, exploration of other avenues of assessing tumor biology could present more effective means of providing individualized care to these patients.

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AB096. P070. Feasibility and efficacy of an analysis using FFPE blocks of resected pancreas with micro CT

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Abstract: Recently, the importance of 3D imaging constructed by computed tomography (CT) data is increasing in clinical practice especially for preoperative usage. On the other hand, Micro-CT (inspeXio SMX-90CT, Kyoto, Shimadzu Corporation) can provide exceptionally high-resolution imaging with pixels in the dozens of micrometers range. When we use micro-CT for imaging of formalin fixed paraffin embedded pancreatic specimens, it gives us a chance to resolve clinical questions and discrepancy which may emerge perioperatively, particularly between preoperative diagnosis and pathological results. Pancreatic ductal adenocarcinoma is one of the lethal diseases, so it is important to detect and resect in the earlier stage. Intraductal papillary mucinous neoplasm (IPMN) is known as one of the precursor lesions of the pancreas, developing from low grade to high grade dysplasia that may further progress to invasive cancer. International Consensus Guideline for management of IPMN has been published in 2012. According to this guideline, indications of pancreatectomy are the presence of main and mixed duct IPMN, or branch duct IPMN with "high-risk stigmata of malignancy present". On the other hand, branch duct IPMN with "worrisome features" requires more thorough examination before deciding to do a surgical resection. Sometimes, it is not easy to identify such small features like mural nodules, or critical site of caliber change of pancreatic duct in resected specimen pathologically. Herein, we show the feasibility and efficacy of the usage of micro-CT in evaluating IPMN lesions to reveal the answer for these uncertainties.

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AB097. P071. Implications of the pattern of disease recurrence on survival following pancreatectomy for pancreatic ductal adenocarcinoma

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Background: After radical resection of pancreatic ductal adenocarcinoma (PDAC), approximately 80% of patients will develop disease recurrence. It remains unclear to what extent the location of recurrence carries prognostic significance. Additionally, stratifying the pattern of recurrence may lead to deeper understanding of the heterogeneous biological behavior of PDAC. The aim of this study was to characterize the association of recurrence patterns with survival in patients with resected PDAC.

Methods: This single-center cohort study included patients undergoing pancreatectomy between 2000–2013. Exclusion criteria were neoadjuvant therapy and <24 months follow-up. Sites of first recurrence were stratified into five groups and survival outcomes were estimated using Kaplan-Meier curves. The predictive values of specific recurrence locations on overall survival were analyzed using a Cox proportional-hazard regression model.

Results: Accurate follow-up data were available for 850 patients, 662 (77.9%) of whom had documented recurrence at last follow-up. The most common manifestation was "multiple-site" recurrence (n=227, 34.3%), followed by liver only (n=166, 25.1%), local only (n=158, 23.9%) and lung only (n=93, 14.0%) recurrence. "Other" recurrence sites (n=18, 2.7%) included osseous structures such as the spine and iliac crest, the brain, supraclavicular lymph nodes, the groin, thigh muscle and the skin. Patients with multiple-site (4.7 months) or liver only recurrence (7.2 months) had significantly worse median survival after recurrence when compared to lung or local only recurrence (15.4 and 9.7 months respectively). On multivariable analysis, the unique recurrence patterns had variable predictive values for overall survival, while both adjuvant chemotherapy and chemoradiotherapy were associated with prolonged overall survival.

Conclusions: This study demonstrates that specific patterns of PDAC recurrence result in different survival outcomes. Furthermore, distinct first recurrence locations have unique independent predictive values for overall survival, which could help with prognosis stratification and decisions regarding the treatment after diagnosis of recurrence.

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AB098. P072. Investigation of BRCAness in pancreatic cancer using patient-derived organoid models

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Background: Efforts to characterize the mutational landscape in pancreatic cancer have revealed almost ubiquitous activating mutation of KRAS, high incidence of inactivation of TP53, SMAD4, CDKN2A and KDM6A but a very low prevalence of currently actionable targets. However, patients with high genomic instability suggesting defective DNA maintenance (up to 20%) show high response rate to platinum agents with or without PARP inhibition. While no more than 5% of patients harbor germline BRCA1/2 inactivation, molecular alterations in other genes related to homologous recombination are also found in these pancreatic tumors. These observations support the concept of BRCAness in pancreatic cancer, where tumors showing traits of defective homologous recombination (HR) even in the absence of BRCA1/2 deficiency are associated with exquisite sensitivity to DNA-damaging agents. This study seeks to identify new molecular determinants of BRCAness in Pancreatic cancer and what assay constitutes the best predicator of a favorable response to therapeutic targeting HR defects.

Methods: Given the heterogeneous mechanisms that can drive BRCAness, we have performed a comprehensive analysis of a large repository of pancreatic cancer patient-derived organoids including molecular characterization by next-generation sequencing (exome and transcriptome) allowing quantification of genomic scars and mutational signatures concomitantly to an evaluation of HR proficiency by IRIF assay and drug sensitivity profiling including platinum-based agents and PARPi.

Results: Multidimensional characterization of 75 pancreatic cancer led to the identification of 9 tumors (12%) so far that showed clear evidence of BRCAness, featuring high HR deficiency score (elevated amount of genomic scars), sub-micromolar sensitivity to cisplatin and PARPi, low induction of rad51 foci following irradiation and a highly operative BRCA mutational signature. Interestingly, in the absence of alteration in BRCA1 and BRCA2 some of these specimens show enrichment in alterations of HR component genes (RAD51, PALB2) and in RecQ helicase family (BLM, WRM) or ATM.

Conclusions: This study identifies evidence of BRCAness in pancreatic cancer tumors without any deficiency in BRCA1 and BRCA2 and therefore broadens the scope of patients who may benefit from platinum and/or PARP therapy.

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AB099. P073. Clinicopathological analysis of cystic pancreatic carcinoma in 31 cases

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Background: To summarize the characteristics of cystic pancreatic adenocarcinoma, and to improve the general understanding of the imaging and pathologic features, and other pancreatic cystic diseases are compared for differential diagnosis.

Methods: This study included patients treated in the Department of General Surgery, Peking University Third Hospital, from Jan 2000 to Dec 2012 due to pancreatic neoplasm. The imaging data and diagnostic imaging reports showed that in the cases that were diagnosed as pancreatic carcinoma there were cystic performance and "cystic mass". The characteristics of these patients were collected, such as gender, age, major symptoms, tumor marker tests, imaging diagnosis, preoperative clinical diagnosis, surgical operation, gross specimen and pathological diagnosis. Further analyses were conducted to find out the common features of cystic pancreatic carcinoma. The imaging features were compared with gross specimen; and the causes of cystic imaging findings were analyzed; other pancreatic cystic diseases were also listed and discussed in our study to avoid misdiagnosis, differential ways among them were also explored.

Results: Among the 398 cases of pancreatic carcinoma, 31 patients had cystic characteristics, accounting for 7.8%. Imaging results found that there were low (no) echo, or low-density mass, but most of the reports for preoperative diagnosis were vague, with only 4 cases diagnosed as cystic pancreatic ductal adenocarcinoma. Thirty-one cases were all underwent surgical exploration. These cystic pancreatic carcinoma have a variety of performances, there is no uniform morphology. Based on preoperative imaging and gross pathological results, the cystic lesions were divided into the following three types: cystic-solid type (14 cases), cystic type (13 cases) and duct dilated type (4 cases). The cystic-solid lesions were primarily located in the head and body of pancreas, while the cystic lesions were commonly seen in the tail of pancreas. Pathological examination revealed that 24 cases were pancreatic ductal adenocarcinoma, which was moderately or poorly differentiated; and the other 7 cases were rare types of pancreatic carcinoma.

Conclusions: Pancreatic ductal adenocarcinoma and its variants may have cystic features. When analyzing preoperative imaging findings of pancreatic cystic mass, the characteristics of the cystic pancreatic ductal adenocarcinoma should be fully taken into account to make differential diagnosis.

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AB100. P074. Novel biomarkers for differential diagnosis of intraductal papillary mucinous neoplasms revealed by profiling microbial composition and translocation markers in liquid biopsies

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Abstract: Pancreatic ductal adenocarcinoma (PDAC) has a major impact on public health, being the fourth-leading cause of cancer-related death in Western countries with a low overall survival rate and rapid deterioration in quality of life. Intraductal papillary mucinous neoplasms (IPMNs) are neoplastic precursor lesions which are understood to evolve from lesions with low-grade dysplasia to high-grade dysplasia to PDAC. Currently, the accuracy of pre-surgery differential diagnosis of cystic lesions is merely 47–78%. However, only after surgical resection of the pancreas can the type of cystic neoplasms and degree of IPMN dysplasia accurately be determined. The discovery of novel biomarkers that improve timely and accurate diagnosis of IPMN and its grade of dysplasia, and thus assist the determination of health risk, are of great importance for better patient management and to minimize diagnostic errors and unnecessary surgical procedures. We hypothesize that gut microbiota may have a role on pancreatic tumorogenesis and progression, given the strong association of oral pathogens such as *P. gingivalis* and *F. nucleatum* with systemic inflammation and intestinal cancers. We aimed to (I) determine whether (oral) bacteria are present in pancreatic cystic lesions, and (II) whether cystic microbiota composition associates with IPMN disease severity. We have established a biobank of pancreatic cyst fluid and peripheral blood from patients with pancreatic cystic lesions (n=90, IPMN and benign neoplasms as control) with post-surgery validated diagnosis. The absolute bacterial 16S rRNA gene copy numbers were determined by TaqMan qPCR and microbial compositional profiling by 16S rRNA gene sequencing is being undertaken. Additionally, we measured the magnitude of microbial translocation (MT) inflammation markers in these samples. We found a statistically significant difference of bacterial 16S gene quantities as well as biomarkers of MT and inflammation between different types of pancreatic cystic lesions, as well as significant correlation with IPMN grade of dysplasia. Our finding that several novel biomarkers from liquid biopsies might be used to differentiate between benign and (pre-)malignant pancreatic cystic lesions is of important clinical relevance in diagnosis and treatment for IPMN-related morbidity and mortality, including PDAC.

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AB101. P75. Surgical management of pancreatic neuroendocrine neoplasms (PNENs) in a single center

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Background: To evaluate the clinical features and surgical results of pancreatic neuroendocrine neoplasms (PNENs) in a single institution. PNENs are a kind of rare, indolent, heterogeneous tumors with unknown natural history. Surgical resection is still the treatment of first choice regardless of liver metastasis.
Methods: From January 2012 to December 2016, the clinical data of 136 consecutive patients who underwent surgical resection for PNENs was analyzed.
Results: Of the 136 patients, females accounted for 58.9% and nonfunctional PNENs constituted 63.2% of all. The median age at diagnosis was 50.5 (range, 19–80) years. The median tumor diameter was 2.5 (range, 0.2–18.0) cm. 52.2% cases were located in head/neck of the pancreas, 37.5% in body/tail, while others were multifocal. All patients underwent surgical resections, including 29.4% cases of distal pancreatectomy, 27.2% of enucleation, 21.3% of pancreaticoduodenectomy, 13.2% of middle segment pancreatectomy and others. Postoperative complications included pancreatic fistula (53.7%), intraabdominal infection (9.6%), postoperative hemorrhage (4.4%), delayed gastric emptying (3.7%) and biliary leakage (1.5%). A total of 124 patients were followed up. Ten (7.4%) patients died of tumor progression during the follow-up.
Conclusions: PNENs are rare pancreatic neoplasms with low-malignant potential. Radical resections should always be attempted and may result in long-term survival.

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AB102. P076. Preoperative panel of CA 19-9, coagulation FVIII, fibrin turnover marker D-dimer and thrombin time predicts postoperative survival in pancreatic ductal adenocarcinoma

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Background: Pancreatic ductal adenocarcinoma (PDAC) is one of the leading causes of cancer-associated death worldwide. It is often diagnosed at a late stage, but even after surgery survival is poor. CA 19-9 is the most used tumor marker for PDAC, and it correlates with survival. PDAC associates with enhanced coagulation activity. The aim of this study was to explore whether a combination of CA 19-9, FVIII, D-dimer and thrombin time (TT) predicts outcome after surgery better than CA 19-9 alone.
Methods: Patients (n=124) were operated during 2010–2015 in Helsinki. Patients were divided into two groups: local (n=94) and metastasized (n=30) disease. Neoadjuvant treatments (NT) were recorded. The median (IQR) follow-up time was 1.9 (1.2–2.4) years for local and 0.82 (0.47–0.97) years for metastasized PDAC. The time and causes of death were checked. CA 19-9, FVIII, TT and D-dimer were analyzed preoperatively. The results were analyzed with a 10-point panel score. Kaplan-Meirer survival analysis was made.
Results: The median panel score was 7 (IQR, 6–8) for local and 8 (IQR, 8–9) for metastasized PDAC. Of the local PDAC, 73% had scores of 7 of more and 44 were alive at follow-up. All patients with metastasis were deceased. In local PDAC panel score of 7 or more predicted worse survival (P=0.001), regardless of NT. The panel did not predict survival in metastasized disease. CA 19-9 alone predicted worse survival only in local PDAC when over 340 kU/L (n=22).
Conclusions: Preoperative CA 19-9 combined with FVIII, D-dimer and TT can predict survival after PDAC surgery. Further studies are needed to determine whether patients with a high panel score could be benefit from prolonged postoperative anticoagulant medication.

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AB103. P077. Preoperative biomarker panel distinguishes PDAC from IPMN

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Background: Pancreatic ductal adenocarcinoma (PDAC) is one of the leading causes of cancer-associated deaths worldwide. It is associated with increased coagulation and venous thrombotic events (VTE). PDAC is often diagnosed late. CA 19-9 is the most used tumor marker for PDAC, but it is more useful in follow-up than diagnosis. Intraductal papillary mucinous neoplasm (IPMN) is a benign tumor of the pancreas, which can become malignant; however, pancreatic tumor surgery is extensive and should not be done needlessly. The aim of this study was to determine whether PDAC could be distinguished from IPMN preoperatively using coagulation biomarkers and whether combing them in a panel score aids diagnostics.

Methods: Patients (n=580) were operated during 2010–2015 in the Helsinki University Hospital. Of these patients 318 had preoperative coagulation variables available. Patients who had another tumor than PDAC or IPMN, had received neoadjuvant treatments or another active cancer in the previous five years were excluded. There were 80 patients with a confirmed PDAC and 18 with IPMN. Of the PDAC patients 67 had stage I–III and 13 stage IV diseases. Blood cell counts, coagulation, inflammation, liver and tumor markers were analyzed 1–3 days preoperatively.

Results: FVIII, fibrinogen, CA 19-9, albumin, alkaline phosphatase and bilirubin conjugates were higher in both stage I-III and IV PDAC *vs.* IPMN ($P<0.05$). FVIII was also higher in stage IV *vs.* stage I–III ($P<0.05$). Combining CA 19-9 with FVIII, fibrinogen, albumin and bilirubin conjugates in a panel score increased the sensitivity and specificity for PDAC compared to CA 19-9 alone, as in a ROC curve, the AUC for the panel was 0.952 (95% CI, 0.900–1.000) for the panel and 0.804 (95% CI, 0.713–0.896) for CA 19-9 alone.

Conclusions: PDAC is associated with increased coagulation activity, especially FVIII, even without VTE. A combined panel score of FVIII, fibrinogen, CA 19-9, albumin, and bilirubin conjugates may provide a useful tool for PDAC diagnostics in the future.

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AB104. P078. Exosomal microRNAs in pancreatic juice have possibility as biomarkers to detect pancreatic ductal adenocarcinoma

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Background: Because pancreatic ductal adenocarcinoma (PDAC) is a lethal neoplasm which is often diagnosed late due to difficult early detection, it is crucial to devise biomarkers to detect PDAC. Exosomes are small membrane vesicles secreted from various cells and identified in several body fluids. Recently, some studies have indicated exosomes have a potential to become novel biomarkers. This study aimed to prove the existence of exosomes in pancreatic juice (PJ) and investigate whether exosomal microRNAs (ex-miRs) could be used as biomarkers for PDAC.

Methods: PJ was collected by endoscopic retrograde pancreatography in patients with PDAC and chronic pancreatitis (CP). The ultracentrifuge method was applied to extract the exosomes. Relative expression levels of ex-miR21 and ex-miR155 were quantified and their expression levels were compared between PDAC and CP.

Results: A total of 35 PJ samples (27 PDACs and 8 CPs) were collected. Presence of exosomes in PJ was determined by electronic microscope and western blot using anti-CD63, CD81, and TSG101 antibody. Relative expression levels of ex-miR21 and ex-miR155 were significantly higher in PDAC than in CP ($P<0.0001$ and $P=0.008$, respectively). On the other hand, the whole PJ had no significant difference in the expression levels of miR21 and miR155 between PDAC and CP ($P=0.08$ and $P=0.61$, respectively). Ex-miR21 and ex-miR155 distinguished PDAC from CP with area under the curve values of 0.90 and 0.89, respectively. Accuracies of ex-miR21, ex-miR155, and PJ cytology were 87%, 83%, and 67%, respectively.

Conclusions: Ex-miR21 and ex-miR155 in PJ may be potential biomarkers for PDAC.

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AB105. P079. Impact of extravasated platelet activation surrounding cancer associated fibroblasts by neoadjuvant chemotherapy in pancreatic ductal adenocarcinoma

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Background: Extravasated platelet activation (EPA) associated with cancer-associated fibroblasts (CAFs) as well as pancreatic cancer cells were detected in our previous study. C-type lectin receptor (CLEC-2) has been identified as an endogenous receptor of podoplanin (PDPN) on platelets. The expression of PDPN by stromal CAFs has been reported to be a prognostic indicator in various types of cancer. We investigated the effect of neoadjuvant therapy on EPA and PDPN-expression by CAFs using immunohistochemical analysis.

Methods: A total of 56 patients were enrolled in this study. We evaluated the expression of platelet-specific marker (CD42b) and CAF marker (PDPN) using immunohistochemistry. Cases in which >10% of CD42b positive-CAFs were stained were defined as positive. Density of PDPN positive fibroblasts was determined by hybrid cell counting. This was compared to a group of untreated specimens, a group treated with conventional gemcitabine (GEM) alone, a group of GEM plus S-1 (GS) and a group of GEM plus Nab-paclitaxel (GnP).

Results: By immunohistochemistry CD42b expression was observed in 30 out of 56 (54%) patients surrounding CAFs. The expression of CD42b was observed in 10% of the GnP group. However, CD42b expression was detected in 64%, 63% and 63% in untreated, GEM alone and GS groups. There were significantly fewer CD42b expressions in the GnP than in the untreated, GEM alone and GS groups. PDPN expression was reduced in the GnP group, as revealed by markedly disorganized collagen and a low density of PDPN -positive fibroblasts. There were significantly fewer PDPN -positive fibroblasts in the GnP than in the untreated, GEM alone and GS groups, but there was no significant difference between the latter 3 groups.

Conclusions: This data suggests that the GnP regimen decreases EPA in the stroma through PDPN-positive CAF depletion.

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AB106. P080. Interferon gamma-inducible protein 10 in pancreatic cancer progression

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Abstract: CXCL10 or the Interferon gamma-inducible Protein 10 (IP10) belongs to the CXC subfamily of chemokines. Classically, chemokines are known to modulate leukocyte trafficking of cells expressing corresponding receptors. CXCL10 expression in pancreatic ductal adenocarcinoma (PDA) patient samples has been correlated with CXCR3 (receptor for CXCL10) positive regulatory T cell (T_{reg}) infiltration contributing to an immuno-suppressed tumor microenvironment. However, other studies suggest a more direct and non-classical role of CXCL10 in promoting acinar cell injury and apoptosis. Chronic pancreatitis patients have also been shown to express high levels of CXCL10 which is suggestive of its role in the pathogenesis of the disease. Clinically, there is a significant overlap between chronic pancreatitis and pancreatic cancer, but the role of CXCL10 specifically in the context of genetic mutations causing pancreatic cancer has not been fully explored. Our preliminary in situ hybridization data show that the cells in PanIN lesions of $p48^{Cre}$;LSL-$Kras^{G12D}$ mice express CXCL10 in contrast to no expression seen in normal adjacent acinar cells, whereas the receptor CXCR3 is highly expressed in the normal adjacent acinar cells as compared to that in the precursor lesion cells. Induction of CXCL10 expression in the PanIN cells and expression of CXCR3 in normal adjacent acinar cells suggests an important role of this chemokine in exacerbating the inflammatory pancreatic environment during the development of pancreatic cancer. This study aims to (I) delineate the mechanism of induction of CXCL10 expression in areas with precursor lesion; (II) determine the effect of CXCL10 on normal acinar cells; and (III) test if CXCL10 neutralization in the pancreas has an effect on the progression of the disease.

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AB107. P081. Metabolic oligosaccharide engineering of pancreatic cells: measurement of sialylation and identification of sialylated glycoproteins

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Abstract: Pancreatic cancer (PC) accounts for 7% of all cancer related deaths in the US. The 5-year survival rate is only 7%. This poor prognosis is attributed to the fact that the in over 80% of cases, PC is diagnosed at a stage of malignancy where surgical removal is not an option. In cases where the cancer is detected early enough that surgical removal is possible, the survival rates go up to 25%. Thus, it is imperative to identify selective biomarkers that can distinguish precancerous lesions or an early stage cancer from pancreatitis and other gastroenterological cancers. The currently used FDA approved serum biomarker CA19-9 [the tetrasaccharide sialyl Lewis a (sLe^a)] brings forth the importance of glycans as biomarkers, although it lacks the specificity to screen for pancreatic cancer and is currently used to monitor treatment response. Metabolic oligosaccharide engineering (MOE) has been used by our lab to supply patented 'high-flux' analogs of carbohydrates to intercept intracellular metabolic pathways and provide a means to track their incorporation on the cell surface. In this study, we utilize MOE to screen a non-neoplastic pancreatic cell line and a panel of pancreatic cancer cell lines with varying degrees of genetic complexity for the production of 'free' monosaccharide sialic acid when treated with the N-acetylmannosamine analog, 1,3,4-O-Bu_3-ManNAc, at different doses and time points. We also utilized this difference in the flux through the sialic acid biosynthetic pathway as a tool to screen the secretome of the non-neoplastic cell line against an early stage cancer cell line, as a means to identify serum glycoproteins for detecting early-stage pancreatic cancer.

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AB108. P082. Role of epigenetic modifying enzymes in the chemoresistance of pancreatic cancer

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Abstract: Gemcitabine (GEM) is a chemotherapeutic drug and the standard treatment option for pancreatic cancer patients. Although some patients respond well in the treatment firstly, development of resistance is commonly observed in clinic. To dissect the mechanism underlying GEM resistance, we screened for the epigenetic modifying enzymes that are increased in GEM-resistant pancreatic cancer cells and identified 21 upregulated enzymes in resistant cells. We first addressed the functional role of a H3K9 methyltransferase EHMT2 and found that ectopic expression of EHMT2 in pancreatic cancer cells increased GEM resistance while inactivation of EHMT2 in resistant cancer cells reduced it. Mechanistically, we showed that interleukin-8 (IL-8) is one of the downstream effectors of EHMT2 to increase GEM resistance. EHMT2-overexpressing cancer cells exhibited autocrine IL-8/CXCR1/2 stimulation to prevent GEM cytotoxicity which could be attenuated by anti-IL-8 antibody or chemical inhibitor. IL-8 released by cancer cells also activated pancreatic stellate cell (PSC) to increase GEM resistance. Combination of EHMT2 inhibitor and GEM significantly decreased tumor growth, metastasis, IL-8 expression and PSC activation in animals. Expanding from our previous study, we also found the upregulation of protein arginine methyltransferase 3 (PRMT3) in GEM-resistant pancreatic cancer cells. By using proteomics approach, we identified a number of PRMT3-interacting proteins. One candidate gene possibly involves in the chemoresistance is the transporter ATP binding cassette subfamily G member 2 (ABCG2). In this study, we will introduce how PRMT3 modulates the expression of ABCG2 via a novel post-transcriptional mechanism. Our results suggest that PRMT3 could be a potential target to overcome GEM resistance.

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AB109. P083. Low expression of KLF9 in pancreatic cancer and its correlation with tumor differentiations

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Background: To investigate the expression level of Kruppel-like factor 9 (KLF9) in pancreatic cancer and its correlation with tumor differentiations *in vitro*, which might provide potential diagnostic value for pancreatic cancer.
Methods: The expression level of *KLF9* in pancreatic cancer and adjacent non-cancer tissues as well as pancreatic cancer cell lines PANC-1 and BxPC-3 were measured by using immunohistochemistry and Western blot analyses. The correlation between expression level of *KLF9* and proliferation, cell cycle as well as cell apoptosis of pancreatic cancer were analyzed by using CCK-8 and flow cytometry analysis. Transwell assay was used to evaluate its effects on invasion and migration of tumor cells. The expression of target proteins that correlate with cell cycle distribution, apoptosis, migration and invasion were also evaluated by Western blot analyses.
Results: *KLF9* showed low expression in both samples of pancreatic cancer tissues and cell lines PANC-1 and BxPC-3, which was associated with the depth of vascular invasion (P=0.016) and tumor differentiation (P<0.001). *In vitro* studies confirmed that overexpression of KLF9 reduced the proliferation of pancreatic cancer cells, induced apoptosis, blocked S phase of cell cycle, and inhibited migration and invasion of the tumor cells. In addition, overexpression of KLF9 upregulated the levels of cyclin D1, *cdk4*, *p53*, *Bax* and *E-cadherin*, and down-regulated *cyclin B*, *Bcl-2*, *N-cadherin*, *MMP-2* and *MMP-9*, which suggested that overexpression of *KLF9* inhibit tumor cell epithelial-mesenchymal transition (EMT).
Conclusions: *KLF9* shows low expression in pancreatic cancer, which correlates with tumor differentiations. It maybe has potential diagnostic value in this kind of cancer.

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AB110. P084. OGDHL inhibits human pancreatic ductal adenocarcinoma progression and is regulated by microRNA-214/TWIST1 negative feedback pathway

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Abstract: Oxoglutarate dehydrogenase like (OGDHL) is involved in tricarboxylic acid cycle and was reported as a candidate tumor suppressor in some other tumors. We first explored the mechanisms of OGDHL in human pancreatic ductal adenocarcinoma (PDAC) progression. OGDHL is frequently down-regulated in human PDAC and predicted poor prognosis. OGDHL suppresses PDAC growth though G1 cell cycle arrest both *in vivo* and *in vitro* and OGDHL also inhibits migration and invasion ability of PDAC both in vivo and in vitro. Compared with non-tumor tissues, PDAC tissues showed down-regulation of OGDHL and up-regulation of miR-214 and TWIST1. The results showed that OGDHL is a target gene of miR-214 and always negatively regulated by miR-214 and the decrease expression level of OGDHL was on account of the increased expression level of miR-214 in PDAC. In addition, TWIST1 is frequently up-regulated in PDAC and induces miR-214 expression. However OGDHL could inhibit TWIST1 expression via both promoting ubiquitin-mediated proteasomal degradation of HIF1a and regulating AKT pathways. The effect of OGDHL/HIF1a/TWIST1/miR-214 signaling pathway in pancreatic carcinogenesis and metastasis were also determined both *in vivo* and *in vitro*. A combination of down-regulation OGDHL and over-expression miR-214 and TWIST1 predicts a poorer overall survival in PDAC patients. Finally, we demonstrated that the relationship of expression among OGDHL, miR-214 and TWIST1 may be a significant predictor of prognosis in PDAC patients. It is a novel pathway in OGDHL-regulated inhibition of PDAC tumorigenesis and metastasis. It may be a brand new targeted therapy in PDAC through OGDHL, TWIST1, miR-214, and HIF1a for prevention, treatment and prognosis.

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AB111. P085. The key factors related to the postoperative survival duration of patients with pancreatic ductal adenocarcinoma

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Abstract: Pancreatic ductal adenocarcinoma (PDAC) is a rarely highly malignant disease, with a poor prognosis and a low survival rate. PDAC with its characteristics of stealth clinical manifestation, rapid disease development and poor prognosis, is hard to be diagnosed at an early stage. Thus, the lethality of PDAC ranks top four in many countries. The 5-year survival rate of the patients with PDAC was only between 2-6%, which is the lowest in all kinds of cancer. Surgery is the main treatment method, but it is hard to stop the progress of the disease completely. As the technology of radical surgery becoming mature, and the adjuvant radiochemotherapy becoming common, the postoperative 5-year survival rate of the patients with PDAC in our hospital was up to about 10%, and the median survival time was up to 30 months. According to our long-term follow-up results, some patients with the same pathological diagnosis did survive much longer than the others after the same radical operation. Therefore, we separated those patients into two groups (postoperative survival duration <1 year, and ≥5 years), and detected their cancer samples through whole genome sequencing. In the aspect of clinical situation, the level of CA19-9, as a good predictor, was much higher in the short-survival group than that in the long-survival group before surgical treatments (P<0.001). Positive lymph nodes rate was also much higher in the short-survival group than that in the long-survival group (P<0.001), which indicated the capability of potential metastasis of the tumor mass. In the aspect of basic medicine, *Lamp2*, *Tmem219*, *TTI2*, *Rdm1*, *Ppp2ca*, *Ezr*, *Serpini2*, and *Cep85*, were detected to have the most important mutations between these 2 groups, as well as T*wist1*, *Ywhaz*, *Sqstm1*, *Gna13*, *Lrig1*, and *Myc*, were proved to have the most significant changes in their expression levels. Experiments *in vitro* and *vivo* had confirmed these findings, and the most crucial genes related to the postoperative survival of patients with PDAC emerged.

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AB112. P086. MicroRNA miR-141/200c inhibit proliferation, invasion and metastasis of human pancreatic cancer cells by targeting WIPF1-YAP/TAZ pathway

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Abstract: MicroRNA-200 gene family (miR-200, including miR-200a, miR-200b, miR-200c, miR-429 and miR-141) is downregulated in some malignancies by heavy CpG island hypermethylation. Its methylation status and function in pancreatic cancer have not been well understood. We have found that miR-200c and miR-141 were hypermethylated in human pancreatic ductal adenocarcinoma compared to the surrounding non-cancerous tissues and this hypermethylation resulted in their silencing, whereas miR-200a, miR-200b and miR-429 were hypomethylated instead. Overexpression of miR-141 inhibited the proliferation of pancreatic cancer cells. In addition, overexpression of miR-141 or miR-200c suppressed invasion and metastasis of pancreatic cancer cells both in vitro and in mouse model. To understand the mechanism of tumor-suppressive effect of miR-141 or miR-200c, we searched for target genes and identified WIPF1 gene as a direct target of miR-141 and miR-200c. miR-141 and miR-200c bind to the 3'-untranslated region of WIPF1, a gene that binds to the untranslated region of Wiskott-Aldrich syndrome protein that is frequently mutated in Wiskott-Aldrich syndrome, an X-linked recessive disorder. This indicates that WIPF1 may be involved in the oncogenesis of pancreatic ductal adenocarcinoma. We further showed that miR-141 and miR-200c mediated the downregulation of WIPF1 which led to the inactivation of the YAP/TAZ complex. YAP/TAZ complex mediates signal transduction of Wnt/beta-catenin and other key pathways. Taken together, our study shows that miR-141 and miR-200c inhibit the proliferation, invasion and metastasis of pancreatic ductal adenocarcinoma by targeting WIPF1-YAP/TAZ pathway.

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AB113. P087. Single-cell sequencing defines genetic heterogeneity in pancreatic cancer precursor lesions

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Abstract: Intraductal papillary mucinous neoplasms (IPMNs) are precursors to pancreatic cancer; however, little is known about genetic heterogeneity in these lesions. We report the first characterization of genetic heterogeneity in IPMNs at the single-cell level. We isolated single cells from fresh tissue from ten IPMNs, followed by whole genome amplification and targeted next generation sequencing of pancreatic driver genes. We then determined single-cell genotypes using a novel multi-sample mutation calling algorithm. Our analyses revealed that different mutations in the same driver gene frequently occur in the same IPMN. Two IPMNs had multiple mutations in the initiating driver gene KRAS that occurred in unique tumor clones, suggesting the possibility of polyclonal origin or an unidentified initiating even preceding this critical mutation. Multiple mutations in later-occurring driver genes were also common and were frequently localized to unique tumor clones, raising the possibility of convergent evolution of these genetic events in pancreatic tumorigenesis.

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AB114. P088. Comparison between robotic assisted and the 'gold standard' open approach for left sided cystic tumors of the pancreas: results from a single center

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Background: Pancreatic cystic lesions are increasingly found incidentally and those located in the body/tail of pancreas, can benefit from spleen preserving left side pancreatectomy (LSP) with laparoscopic surgical approach increasingly considered an appropriate surgical option. On the other hand, laparoscopic LSP remains a challenging operation, with a steep learning curve, high unplanned splenectomy and conversion rates, even when performed in high volume centers. For these reasons, open LSP is still considered the 'gold standard' by many pancreatic surgeons. The advent of the robotically-assisted surgery (RAS) with the da Vinci surgical System may, by facilitating the execution of LSP, address these issues of direct manual laparoscopic surgery, thereby reversing the situation. The present study compares RAS with the open approach, for surgical management of cystic lesions of the body and tail of pancreas, with a view to documenting benefits from the more expensive robotic approach.

Methods: From April 2010 to April 2017, 37 robotic-assisted LSP for lesion of the body/tail of the pancreas were performed, of which 27 were patients with cystic tumors (RAS-group). Baseline features, surgical outcomes and histopathological examination were compared retrospectively with a group of 27 consecutive patients treated with open surgery for the same indication from May 2005 to April 2010, obtained from the institutional prospectively collected database (OS-Group).

Results: The spleen-preserving rate was significantly higher in the RAS group (63% vs. 33.3% in the OS-Group, P<0.05). No difference in the post-operative pancreatic fistula and morbidity was found between the two groups. The median postoperative length of hospital stay was significantly shorter in the RAS-group: 8 (range, 3–25) *vs.* 12 (range, 7–26) days in the OS-Group (P<0.01). No conversion to open approach was reported in the RAS-group.

Conclusions: The robot-assisted LSP is a safe and effective procedure. The robotic approach significantly increases the spleen preservation rate and reduces the post-operative hospital stay. By reducing the trauma of access, it results in smoother post-operative course and faster recovery, particularly important in patients harbouring cystic pancreatic tumors, in increasing their acceptance for surgery when recommended. Prospective studies are necessary to validate the clinical benefits of robotic approach for LSP.

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AB115. P089. Comparison of prognostic prediction between nomogram based on lymph node ratio and AJCC 8th staging system for patients with resected pancreatic head carcinoma: a SEER analysis

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Background: The prognosis of pancreatic carcinoma (PC) remains poor and the AJCC 8th staging system for survival prediction in PC patients after curative resection is still limited. Thus, we aim to refine a valuable prognostic model and novel staging system for PC with curative resection.

Methods: The data of 3,458 patients used in this study were retrieved from the Surveillance, Epidemiology, and End Results (SEER) database registry of National Cancer Institute. The prognostic value of lymph node ratio (LNR) was analyzed in the primary cohort and prognostic nomogram based LNR was established to create a novel staging system. Then, analyses were conducted to evaluate the application of the formulated nomogram staging system and AJCC 8th staging system. The predictive performance of model was further validated in the internal validation cohort.

Results: Significant positive correlations were found between LNR and all factors except for surgical procedures. The results of univariate and multivariate analysis showed, LNR was identified as an independent prognostic indicator for OS in both primary and validation cohorts (all P<0.001). A prognostic nomogram based on LNR was formulated to obtain superior discriminatory abilities. Compared with the AJCC 8th staging system, the formulated nomogram staying system showed higher HRs of stage II, III and IV disease (reference to stage I disease) that was 1.637, 2.300 and 3.521 respectively by univariate analyses in the primary cohort and the distinction between stage I, II and III disease at the beginning or end of the survival curves was more apparent. All these results were further verified in the validation cohort.

Conclusions: LNR can be considered as a useful independent prognostic indicator for PC patients following curative resection regardless of the surgical procedures. Compared with the AJCC 8th staging system, the formulated nomogram showed superior predictive accuracy for OS and its novel staging system revealed better risk stratification.

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AB116. P090. Preliminary results with laparoscopic pancreatoduodenectomy: a comparative series with open procedure in a single center

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Background: Laparoscopic pancreaticoduodenectomy (LPD) has been demonstrated to be feasible and may have several potential advantages over open pancreaticoduodenectomy (OPD), including lower blood loss and shorter hospital stay. However, the safety and oncologic performance have not yet been conclusively determined. This study aims to directly compare the 90 days outcomes of laparoscopic pancreatoduodenectomy (LPD) and open pancreatoduodenectomy (OPD) in in a single institutional with periampullary neoplasia.

Methods: We reviewed data for all patients undergoing LPD (N=8) or OPD (N=16) in *intention* to treat settings for periampullary lessons at our institution between January 2015 and July 2017.

Results: The median duration of postoperative hospital stay was longer for OPD than for laparoscopy 11.6 (range, 5–35) *vs.* 15.8 (range, 6–39) days respectively. Duration of operation was longer in the laparoscopy group (352.5 *vs.* 331.8 min, P=0.943). Blood loss was greater in the open group mean. Number of nodes retrieved and R0 rate were similar in the two groups. There was no difference between the open and laparoscopic groups in delayed gastric emptying, pancreatic fistula, or post-pancreatectomy haemorrhage. Overall complications (according to the Clavien-Dindo classification) were worst em OPD. There were 3 deaths in OPD.

Conclusions: Minimally invasive pancreaticoduodenectomy are feasible, safe, and oncologically equivalent alternatives to open pancreaticoduodenectomy. Minimally invasive operations have the advantage of the less blood loss, but totally laparoscopic procedures last longer than open procedures.

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AB117. P092. Safety of intraoperative pancreatoscopy for the investigation of main pancreatic duct involvement and assessment of skip lesions in operated main duct (MD) involving IPMNs: a feasibility study

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Background: Current management of main duct (MD)-involving intraductal papillary mucinous neoplasm (IPMN) is driven by intra-operative frozen section. However, data regarding the clinical utility of this approach are discordant. In fact, frozen section of pancreatic resection margin can't detect skip lesions within MPD and this might imply incomplete resections and short term recurrences after resection. Peroral pancreatoscopy is a promising tool to investigate the MPD but is technically highly skill demanding and therefore difficult to use on a large scale. The application of intraoperative pancreatoscopy might be able to bypass this problem but data about its safety are currently lacking. This study aims to assess the safety of intraoperative pancreatoscopy.

Methods: Retrospective cohort analysis of patients undergoing surgical resection for MD-involving IPMN. All indications for surgery were decided according to the European Guidelines for the management of pancreatic cystic tumors. Data about characteristics of patients, type of surgery, mortality and length of hospital stay, overall complications and procedure related preoperative complications (pancreatitis, perforations) were recorded.

Results: From 2015 to 2016 22 patients, 10 (45%) male, median age 67 (45–82 years) underwent surgical resection for MD-involving IPMN and intraoperative pancreatoscopy. Overall complications were reported in 9 (40%) of patients. 1 patient (4.5%) underwent reoperation for incisional hernia, 1 (4.5%) developed pancreatic fistula, 2 (9%) had GI bleeding requiring endoscopy. None of the patients developed procedure related morbidity and mortality. The mean length of hospital stay was 15.36 days.

Conclusions: Intraoperative pancreatoscopy in the investigation of IPMN patients with dilated MPD is a feasible and safe procedure.

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AB118. P093. Impact of neoadjuvant chemoradiotherapy using full-dose gemcitabine and concurrent radiation for resectable pancreatic cancer

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Background: Although much attention has been paid to neoadjuvant treatment for pancreatic cancer (PC), its efficacy remains to be established. In this study, we have retrospectively evaluated the impact of neoadjuvant chemoradiotherapy (NACRT) on perioperative and long-term clinical outcome in PC.

Methods: One hundred sixty patients who preoperatively received full-dose gemcitabine (1,000 mg/m^2) with concurrent radiation of 54 Gy between 2006 and 2016 were analyzed. One hundred thirty patients who underwent upfront surgery were served as control.

Results: Among the 160 patients treated with NACRT, 153 patients (96%) completed the protocol treatment. The reasons of failure to complete NACRT were drug-induced pneumonia, acute mucosal injury, severe cholangitis and poor performance status (PS). Furthermore 21 (13%) couldn't undergo pancreatic resection after NACRT because of distant metastasis in 9 patients, tumor progression in 7 and poor PS in 5. The rate of pancreatic fistula was lower and hospital stay was shorter in the NACRT group compared to the control group (P=0.033, P=0.002). Furthermore, the rate of lymph node metastasis, R0 resection and pathological stage were favorable in the NACRT group (P<0.0001, P=0.006, P<0.0001). The completion rate of adjuvant chemotherapy was also higher in the NACRT group (P=0.015). Importantly, patients treated with NACRT had a better prognosis than those without (median survival time: 60.2 *vs.* 28.5 months, P=0.008). In addition, according to tumor resectability status, patients were classified as R (resectable), BR-P (borderline resectable with venous involvement) and BR-A (borderline resectable with arterial involvement) groups. As a result, patients treated with NACRT had a better prognosis than those without in the R and BR-P groups (58.6 *vs.* 34.2 months, P=0.013; 62.4 *vs.* 18.8 months, P=0.015), while NACRT had no significant impact on prognosis in the BR-A group.

Conclusions: Neoadjuvant chemoradiotherapy may have a variety of favorable impact in pancreatic cancer treatment. Furthermore, NACRT may improve the prognosis especially in resectable and borderline resectable pancreatic cancer with venous involvement.

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AB119. P095. Organ preserving pancreatectomy for pancreatic benign or low-grade malignant tumor: a report of 66 cases in a single institution

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Background: To explore the clinical value of organ preserving pancreatectomy in the treatment of benign or low-grade malignant pancreatic tumor.
Methods: The clinical data of 66 patients with pancreatic benign or low-grade malignant tumor underwent organ preserving pancreatectomy from January 2009 to December 2016 were retrospectively analyzed, including 34 tumor enucleation, 10 middle segmental pancreatectomy, 13 spleen-preserving distal pancreatectomy, 6 pylorus preserving pancreaticoduodenectomy and 3 duodenum-preserving pancreatic head resection.
Results: The mean operative time was (163.6±77.4) min. The mean intraoperative blood loss was (234.4±242.7) mL, and the mean postoperative hospital stay was (11.3±8.1) d. The incidence of overall complications, pancreatic fistula, bleeding, abdominal infection and delayed gastric emptying were 36.3%, 25.8%, 1.5%, 6.1% and 3.0%, respectively. There had no reoperation and death. Excluding patients with insulinoma, the incidence of postoperative new-onset diabetes mellitus was 3.1%. The incidence of requiring pancreatic enzyme replacement therapy was 1.5%. All patients had no recurrence or metastasis with the mean follow-up period of 47.2 months.
Conclusions: Organ preserving pancreatectomy can maximally preserve the pancreatic parenchymal and adjacent organs, avoid the excessive loss of pancreatic endocrine and exocrine functions, and preserve the function of spleen. It should be considered as the first option in the treatment of benign or low-grade malignant pancreatic tumor.

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AB120. P096. A new pancreatojejunostomy of duct-to-mucosa combining "back-to-back" cross horizontal mattress anastomosis reduce postoperative pancreatic fistula

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Background: Postoperative pancreatic fistula (POPF), the main complication after pancreaticoduodenectomy (PD), is always related to the morbidity and mortality. Too large potential clearance of anastomotic stoma (needle stitch clearance and peripheral suture clearance), destruction of suture shear force to pancreatic tissue upon knotting and delayed healing of the PA are possible factors resulting in the POPF. Aiming at above factors, we design a duct-to-mucosa combining "back-back" cross horizontal mattress anastomosis. In this method, we take the way of pancreas—jejunum end-to-side anastomosis, and suture by cross horizontal mattress way at the anterior and posterior walls of the pancreas and the jejunum, to eliminate the needle stitch clearance; as the pancreas has a large thrust face which is inappropriate to be incised, apply the interrupted suture way for the pancreas mucosa to jejunum mucosa; after anastomosis, the pancreas remnant will get into the jejunum serosa about 1cm, making the pancreas—jejunum in "back-to-back". The objective of our study was to evaluate the safety and efficiency of the novel anastomotic method that termed duct-to-mucosa combining with "back-to-back" cross horizontal mattress inserting pancreatojejunostomy.

Methods: We investigated the postoperative recovery and complications of 102 patients who underwent pancreaticoduodenectomy from October 2015 to October 2017 retrospectively. The new technique was used in 52 patients, and was compared with the classical method of invagination anastomosis technique in 50 patients as controls. We collected the general characteristics of patients, the postoperative complications, hospital stays and hospitalization expenses, etc. We use the statistical software SPSS19.0 to analyze the data. We chose the methods of Chi-square test, independent sample t-test, rank-sum test depend on the data type.

Results: The duct-to-mucosa combining "back-to-back" cross horizontal mattress method significantly reduced the postoperative pancreatic fistula rate (9.6% *vs.* 30%, P=0.010). The mean drainage amylase level of "back-to-back" group is lower than invagination group at POD3. However, the operation time in "back to back" group is longer than in the invagination group (327.69±90.49 *vs.* 217.80±41.47 min, P=0.000).

Conclusions: Duct-to-mucosa combining with "back-to-back" cross horizontal mattress inserting pancreatojejunostomy reduced the incidence of POPF effectively in our study.

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AB121. P097. Retrospective comparison analysis between pathology and the fukuoka consensus in resected IPMN in a single center

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Background: We retrospectively review 112 resected intraductal papillary mucinous neoplasms (IPMNs) to assess the validity of the Fukuoka consensus guidelines for predication of advanced neoplasia (AN). The management of IPMN continues to evolve. According to the 2017 Fukuoka consensus guidelines, IPMNs including branch duct IPMN (BD-IPMN), main-duct IPMN (MD-IPMN) and mixed-type IPMN (MT-IPMN). If with high-risk features, it should be resected. Here we assess its validity for predication of AN, by comparing it with pathology in resected IPMNs.

Methods: One hundred and twelve patients who underwent resections and pathological were identified as IPMN pathologically from 2010 to 2017 in the First Affiliated Hospital of Nanjing Medical University were retrospectively reviewed. Forty-three patients of the overall were selected to retrospectively review the imaging findings and the Fukuoka consensus guidelines were applied to predict the malignancy of IPMNs.

Results: In the all one hundred and twelve patients, there are 73 males and 39 females, which the average age is 63.87±9.17. There are 57 patients' pancreatic cystic lesions were ≥3 cm and the other 65 patients' <3 cm. Nevertheless, AN was 33.93% (38/112). According to the worrisome features and high-risk stigmata of the Fukuoka consensus, the 43 patients were divided into BD-IPMN, MD-IPMN, MT-IPMN, 16, 8 and 19, respectively. There are 13 patients (30.23%) with worrisome features, 6 patients (13.95%) with high-risk stigmata, 16 patients (37.21%) without worrisome features and high-risk stigmata, and 8 patients (18.61%) with both worrisome features and high-risk stigmata. AN was 12.50% (2/16) and lesions with atypical hyperplasia were 93.75% (15/16) for patients without worrisome features and high-risk stigmata. Moreover, for the patients with worrisome features and high-risk stigmata or both, AN was 25.93% (7/27) and lesions with atypical hyperplasia were 100% (27/27).

Conclusions: There are still limitations of guidelines between surgery and surveillance for IPMNs. Radical surgery or close surveillance is important to the patients with IPMNs, especially BD-IPMN with worrisome features or high-risk stigmata or both. However, the practical safety remains uncertain because of invasive carcinoma cases and unresected cases.

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AB122. P098. The effect of somatostatin analogues on postoperative outcomes following pancreatic surgery: a meta-analysis

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Abstract: Leakage from the pancreatic stump is a leading cause of morbidity following pancreatic surgery. It is essential to evaluate the effect of somatostatin analogues (SAs) following pancreatic surgery by analyzing all recent clinical trials. We performed a literature search in the Medline, EMBASE, Cochrane Central Register of Controlled Trials and Web of Science databases up to May 29, 2016. Publication bias was assessed with Egger's test. Study quality was assessed using the Jadad Composite Scale. Twelve clinical trials involving 1,703 patients from Jan 1st, 2000 to May 29th, 2016 were included in the study. With improvements in surgical management and peri-operative patient care, prophylactic use of somatostatin and its analogues reduced the overall incidence of pancreatic fistulas (RR =0.72; 95% CI, 0.55–0.94; P=0.02) and decreased the post-operative hospital stay after pancreatic surgery (The weighted mean difference was –1.06; 95% CI, –1.88–-0.23; P=0.01). Other post-operative outcomes did not change significantly with the use of somatostatin analogues.

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AB123. P099. Type 2 diabetes mellitus, a vital and independent risk factor for acute pancreatitis in patients with severe hypertriglyceridemia

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Background: The incidence of hypertriglyceridemia-induced acute pancreatitis (HIAP) is increasing worldwide, and now is the third leading cause of acute pancreatitis in the United States. There are 5% of patients with severe hypertriglyceridemia (>1,000 mg/dL) which might generate acute pancreatitis. A case-control study was performed by us to evaluate the influence of type 2 diabetes mellitus on acute pancreatitis in patients with severe hypertriglyceridemia.

Methods: We identified a case-control study of severe hypertriglyceridemia patients without AP (HNAP) and HIAP with a fasting triglyceride level >1000 mg/dL from The First Affiliated Hospital of Nanjing Medical University during January 1, 2014 to December 31, 2016. Baseline patient characteristics, comorbidities, and risk factors were recorded and evaluated by univariate and multivariate logistic regression analysis between HIAP and HNAP.

Results: A total of 124 patients with severe hypertriglyceridemia were included in this study, 62 patients were in HIAP group. Univariate logistic regression analysis shows that there was no gender difference in both groups, however younger in the HNAP group *vs.* HIAP group (P<0.001), and the HIAP group had low level high density lipoprotein **vs**. HNAP group (P<0.05). Meanwhile, the presence of pancreatitis was associated with higher glycemia and a history of type 2 diabetes mellitus (P<0.05). Multivariate logistic regression analysis indicated that a history of type 2 diabetes mellitus was an independent risk factor for acute pancreatitis in patients with severe hypertriglyceridemia.

Conclusions: Patients with uncontrolled diabetes mellitus is a potential risk factor in patients with severe hypertriglyceridemia to develop into acute pancreatitis.

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Cite this abstract as: Zhu X, Hou C, Peng Y, Shi C, Zhang K, Li Q, Miao Y. Type 2 diabetes mellitus, a vital and independent risk factor for acute pancreatitis in patients with severe hypertriglyceridemia. Ann Pancreat Cancer 2018;1:AB123. doi: 10.21037/apc.2018.AB123

AB124. P100. The prevalence and characteristics of pancreatic solid pseudopapillary tumor associate with malignance: a multicenter retrospective study in China

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Background: The main aim of this study was to seek the clinical risk factors for malignance of pancreatic for solid pseudopapillary tumors (SPTs) in China.

Methods: Seven hundred five-four patients' information included preoperative or postoperative for diagnostic SPTs were collected from the standardized reports from January 2008 to December 2015 in the 16 institutions. And 685 cases with complete information relatively which have preoperative diagnosis concurrently.

Results: Of the 754 patients, 88 (12.3%) cases were pathologically proved as malignant tumor. Of the 685 patients, 314 (45.8%) cases were diagnosed SPTs correctly before operation and 644 (94.0%) cases confirmed as SPTs by the pathological diagnosis. The mean age at diagnosis was 33.1 years and the tumor longest diameter greater than 3cm appear in 74.5% patients. 210 patients were subjected to postoperative pancreatic fistula (PF), and 4 cases experienced grade C PF. The clinical factors, such as sex (P=0.97), age (P=0.38), tumor location (P=0.45) and size (P=0.21), CA 19-9 lever (P=0.71), mural nodule (P=1), solid component (P=0.84), wall enhancement (P=0.66), calcification (P=0.18), were meaningless to judge the malignant SPTs before operation.

Conclusions: Maybe the regional discrepancy in distribution existed through the percentage of SPTs. There's some room for improvement to make the right judgment for SPTs diagnosis in the preoperative. Evaluating the risk of the malignancy of SPTs still requires more accurate diagnostic criteria.

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AB125. P101. Recurrence and survival after surgery for pancreatic cancer with or without acute pancreatitis

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Background: In pancreatic cancer, acute pancreatitis is a serious morbidity, but its negative effect on long-term outcome remains to be elucidated. The aim of this study is to determine the impact of acute pancreatitis on recurrence pattern and long-term survival after surgery for pancreatic ductal adenocarcinoma.

Methods: The medical records of 219 patients with curative pancreatectomy for pancreatic cancer were reviewed. The severity of acute pancreatitis was classified according to the Atlanta classification of acute pancreatitis. Early recurrence was defined as relapse within 12 months after surgery. Overall and disease-free survivals and recurrence patterns were analyzed. Mild acute pancreatitis was excluded because the negative effects can be negligible.

Results: Moderate or severe acute pancreatitis was an independent risk factor for early recurrence (odds ratio =4.13; 95% confidence interval, 1.41–12.10; P=0.001). According to the analysis of disease-free survival in patients with recurrence, Median time to recurrence was shorter in patients with acute pancreatitis than in those without (8.4 *vs.* 12.8 months; P=0.003). Multivariate analysis identified acute pancreatitis as an independent prognostic factor for Overall survival (hazard ratio 2.33; 95% confidence interval, 1.44–3.79) and disease-free survivals (hazard ratio =2.43; 95% confidence interval, 1.46–4.07) in patients with pancreatic ductal adenocarcinoma.

Conclusions: Patients with moderate or severe acute pancreatitis developed recurrence earlier than those without. Moderate or severe acute pancreatitis adversely affects the overall and relapse-free survival of patients with pancreatic ductal adenocarcinoma.

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AB126. P102. Clinicopathological feature of early-stage pancreatic cancer—tumor size was less than 10 mm

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Abstract: The remarkable progress of diagnostic imaging modality has made it possible to detect small pancreatic tumor, but has not lead to improvement of poor prognosis of pancreatic adenocarcinoma. Even in small pancreatic cancer, invasive nature is apparent and mostly it is "advanced" cancer. To improve its prognosis, it is necessary to detect pancreatic cancer in "earlier" stage, high grade PanIN (pancreatic intraepithelial carcinoma) or minute invasion (MI) to stroma before forming mass. The aim of this study was to investigate clinicopathological features of high grade PanIN (PanIN-H; n=14) and MI (n=6) in our institute. In 7 of the 20 patients tumor was located in the head of pancreas. Nine patients were asymptomatic and suspected pancreatic disease during the follow-up of other diseases (n=8), on routine medical check-up (n=4). Six of 14 PanIN-H and all of MI patients had dilatation of branch pancreatic duct, which was detectable with imaging modality. Microscopic examination revealed that stromal fibrosis existed around carcinoma, even in PanIN-H. Fatty change of the pancreatic parenchyma was detected around minute pancreatic cancer. Only Five patients were diagnosed as having pancreatic cancer at first attempt of cytological examination, whereas the remaining patients required repeated cytological examination. In conclusion, pancreatography combined with cytological examination is advised for patients with minute abnormal findings on imaging modalities to detect carcinoma in situ. And a fatty change of the pancreatic parenchyma may be associated to "early pancreatic cancer".

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AB127. P103. Evaluation of new stent for EUS-guided pancreatic duct drainage: long-term follow-up outcome

Yukitoshi Matsunami, Atsushi Sofuni, Takayoshi Tsuchiya, Reina Tanaka, Ryosuke Tonozuka, Shuntaro Mukai, Mitsuru Fujita, Kenjiro Yamamoto, Yasutsugu Asai, Takashi Kurosawa, Takao Itoi

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Background: EUS-guided pancreatic duct drainage (EUS-PD) has been reported as an alternative for failed conventional endoscopic retrograde cholangiopancreatography (ERCP). However, there are few dedicated devices for EUS-PD. Recently, we have developed a new plastic stent dedicated for EUS-PD and have conducted a feasibility study to evaluate its efficacy. In the present study, we evaluated the long-term efficacy of this new plastic stent.

Methods: Thirty-two patients (62±15.2 years old, 16 men) with acute recurrent pancreatitis were treated at our institution using our recently developed 7Fr plastic stent between Aug. 2013 and Jan. 2018.

Results: The stent was placed successfully in all the patients (32/32) and clinical success was achieved in all the patients. Early adverse events occurred in 7 patients (21.8%). Two died of primary disease and 3 were lost to follow-up. The remaining 27 patients were followed up after initial EUS-PD for a median of 23 months (range, 1–43 months). Twenty-one patients required regular stent exchange (3 times; range, 1–12 times). Spontaneous stent dislodgement was observed in 6 patients without any symptoms. Four patients wanted the stent removed after 1 year of the initial intervention. Twelve (44%) patients had regular stent exchange even after 1 year of the initial intervention. Three patients converted to standard transpapillary pancreatic duct stenting by conventional ERCP. Nine (33%) patients had complete stent removal either intentionally or by spontaneous dislodgement without any symptoms.

Conclusions: The new plastic stent for EUS-PD allows not only short-term technical success but also long-term clinical success in the majority of patients evaluated in this study.

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Cite this abstract as: Matsunami Y, Sofuni A, Tsuchiya T, Tanaka R, Tonozuka R, Mukai S, Fujita M, Yamamoto K, Asai Y, Kurosawa T, Itoi T. Evaluation of new stent for EUS-guided pancreatic duct drainage: long-term follow-up outcome. Ann Pancreat Cancer 2018;1:AB127. doi: 10.21037/apc.2018.AB127

AB128. P104. Gemcitabine/taxane adjuvant therapy with chemoradiation in resected pancreatic cancer: a novel strategy for improved survival?

Zaheer Kanji, Alicia Edwards, Margaret Mandelson, Nadav Sahar, Bruce Lin, Kasra Badiozamani, Guobin Song, Adnan Alseidi, Thomas Biehl, Richard Kozarek, Scott Helton, Vincent Picozzi, Favio Rocha

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Background: Gemcitabine-taxane combination chemotherapy has demonstrated a survival benefit, clinically, in metastatic PC. We present our experience with gemcitabine/docetaxel (gem/tax) based adjuvant treatment (Rx) following curative intent surgery.

Methods: Patients with de-novo resectable PC from January 2010 to December 2015 were identified from our institutional database and registry. We only included those patients who received gem/tax as initial Rx administered exclusively at our institution ± chemoradiation (CRTx). Survival analysis was performed by Kaplan-Meier methods and prognostic factors were investigated by Cox proportional hazard modeling.

Results: Of 102 patients identified, 58 met study criteria. Median age of diagnosis was 65 years with 55% of patients undergoing an R1 resection (margin ≤1 mm). Tumor characteristics included: median tumor size 28 mm, poor differentiation 54% and lymph node positivity 67%. Ninety percent of patients (52/58) completed ≥80% of 24-week Rx. Of those, 71% received post gem/tax CRTx Rx. Grade 3/4 toxicity was observed in 52% of patients. Median length of follow-up was 51.2 months and the observed median overall survival (OS) was 52 months (95%CI: 27.4-NR). Actuarial 5-year OS was 49% (95%CI: 33.7-63.4). On multivariate analysis, an R1 resection and AJCC stage 2 *vs.* stage 1 were negatively associated with OS whereas administration of CRTx was positively associated with OS.

Conclusions: Adjuvant gem/tax ± CRTx is feasible with favorable OS. Future prospective studies of gem/taxane-based adjuvant Rx in PC are warranted.

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AB129. P105. A comparative study of the totally one-layer and stratified pancreaticojejunostomy in pancreaticoduodenectomy

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Background: Pancreatoduodenectomy (PD) is used to treat diseases of the pancreatic head, the duodenum and ampullar region. The most common disease treated includes cancer, traumatic lesions and chronic pancreatitis. Pancreatojejunostomy (PJ) is surgical procedure commonly used to reconstruct the pancreatic stump after pancreatoduodenectomy, which means the pancreatic stump must be connected with the small bowel where pancreatic juice can play its role in food digestion. There are dozens of different ways about Pancreatojejunostomy. All of these procedures have a non-negligible rate of postoperative complications. Since it is unclear which procedure is better, there are currently no international guidelines on how to reconstruct the pancreatic stump after pancreatoduodenectomy, and the choice is based on the surgeon's personal preference. The aim of this study was to compare the safety and efficacy of a new technology, totally one-layer pancreaticojejunostomy, with conventional stratified pancreaticojejunostomy after pancreaticoduodenectomy in preventing post-operative pancreatic fistula (POPF).

Methods: In this retrospective observational study, the clinical data of 79 patients who received pancreaticoduodenectomy from January 2015 to February 2017 were collected, which included 43 patients in the observation group who underwent totally one-layer end-to-side pancreaticojejunostomy, the control group of 36 cases, who underwent stratified Pancreaticojejunostomy. The time of anastomosis, bleeding volume, postoperative hospital stay and postoperative complications were observed.

Results: All 79 pancreaticoduodenectomy were performed successfully. The mean pancreatic anastomosis time in the totally one-layer end-to-side pancreaticojejunostomy was significantly shorter in the stratified Pancreaticojejunostomy [(26.65±1.84) *vs.* (34.47±2.29) min, P<0.05]. In addition, the mean postoperative hospital stay was not statistically significant between the two groups [(19.93±8.29) *vs.* (22.28±13.46) d, P>0.05]. There were no deaths in 79 patients, and there was no significant difference in the incidence of postoperative complications between the two groups (P>0.05). Among them, there were 8 cases of postoperative pancreatic fistula (Pancreatic fistula), the total incidence of PF was 10.1%. The incidence of pancreatic fistula in the totally one-layer end-to-side pancreaticojejunostomy was 7.0% (3/43), which was 13.8% (5/36) in the stratified Pancreaticojejunostomy. The total incidence of abdominal infection was 13.9% (11/79), which was 9.3% (4/43) in the observation group and 19.4% (7/36) in the control group. The total incidence of pulmonary infection was 18.9%, which was 14.0% (6/43) in the observation group and 25.0% (9/36) in the control group. The total incidence of gastric emptying was 3.80%. There were 2 cases (4.7%) in the observation group and 1 case (2.8%) in the control group.

Conclusions: The results of this study show that the totally one-layer end-to-side pancreaticojejunostomy has the advantages of being more easily to operate, shorter operative time, and effectively reducing the morbidity of pancreatic fistula. It is a simple, convenient and safe way of pancreatic anastomosis, which is worthy of clinical promotion.

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AB130. P106. Three-dimensional visualization technology used in pancreatic surgery: a valuable tool for surgical trainees

Chen Lin, Junyi Gao, Hua Zheng, Jun Zhao, Hua Yang, Yue Zheng, Yihan Cao, Yufei Chen, Guoliang Wu, Guole Lin, Jianchun Yu, Hanzhong Li, Hui Pan, Quan Liao, Yupei Zhao

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Background: Pancreatic cancer is one of the most aggressive malignancies, and currently surgical resection is the only curative approach. The success of the surgery depends on the precise evaluation of the tumor resectability, which requires detailed assessment of tumor invasion, vessel involvement and anatomical variation. Therefore, we conducted a randomized study to explore the value of three-dimensional (3D) visualized pancreatic model in surgery planning for surgical trainees.

Methods: Three cases with pancreatic cancer were used in this study. Fourteen questions in the respect of anatomy, diagnosis, tumor staging and surgery planning were developed by a group of pancreas surgeons in each case. Eighty-eight surgical residents participated in this study. The participants were randomly assigned into two groups. Both groups began with training on how to evaluate the resectability of pancreatic tumor, which was based on the NCCN clinical practice guidelines and then a clinical case was taken as sample and practiced. After the training, the 3D group learned the sample case on the 3D real-time reconstruction multi-touch visualization table by themselves; meanwhile, the 2D group studied the same case through the conventional cross sectional computed tomography (CT) images. Finally, both groups completed the same test consisting of two pancreatic cases with CT images. After the test, all the participants completed a questionnaire.

Results: Differences in the scores between the groups were tested with the unpaired *t* test. No differences was found in the scores of anatomy part, however, the mean scores for questions, associated with diagnosis, tumor staging and preoperative planning, were consistently and significantly higher in the 3D group compared with the 2D group. Year of training, sex and previous pancreatic surgery experience had no effect on the scores. In addition, participants in 3D group agreed that the 3D visualized pancreatic model was more beneficial for trainees in understanding and making pancreatic surgery planning.

Conclusions: The 3D visualization table may have the potential to be a valuable supplemental learning tool in building anatomy-image-surgery knowledge system and thus making surgery planning for surgeon trainees, as it provided a better 3D understanding of the tumor and its surroundings, and demonstrated advantages for interacting with cross sectional images.

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AB131. P107. Prognostic value of preoperative nutritional and immunological factors in patients with pancreatic ductal adenocarcinoma

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Background: Preoperative nutritional and immunological patient factors have been found to be associated with prognostic outcomes of malignant tumors; however, the clinical significance of these factors in pancreatic ductal adenocarcinoma (PDAC) remains controversial. The aim of this study is to evaluate the prognostic value of nutritional and immunological factors in predicting survival of patients with PDAC.

Methods: Retrospective studies of 329 patients who underwent surgical resection for PDAC and 95 patients who underwent palliative surgery were separately conducted to investigate the prognostic impact of tumor-related factors and patient-related factors including Glasgow Prognostic Score (GPS), modified GPS, prognostic nutritional index (PNI), neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio, and lymphocyte/monocyte ratio.

Results: In multivariate analysis for patients with surgical resection for PDAC, PNI was an independent factor for overall survival (OS) and disease-free survival. The median OS of patients with PNI ≤45 was significantly shorter than that of patients with PNI >45 (17.5 and 36.2 months, respectively; P<0.001). In multivariate analysis for patients undergoing palliative surgery for PDAC, only NLR was an independent prognosis factor. The median OS of patients with NLR >5 was significantly shorter than that of patients with NLR ≤5 (2.7 and 8.9 months, respectively; P<0.001).

Conclusions: PNI in patients with surgical resection and NLR in patients with palliative surgery for PDAC may be useful as prognostic factors.

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Cite this abstract as: Abe T, Nakata K, Kibe S, Mori Y, Miyasaka Y, Ohuchida K, Ohtsuka T, Oda Y, Nakamura M. Prognostic value of preoperative nutritional and immunological factors in patients with pancreatic ductal adenocarcinoma. Ann Pancreat Cancer 2018;1:AB131. doi: 10.21037/apc.2018.AB131

AB132. P108. Intraoperative radiotherapy (IORT) followed by concurrent chemotherapy (CCRT) or stereotactic radiotherapy (SBRT) for locally advanced pancreatic cancer

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Background: Pancreatic cancer is the fourth leading cause of cancer-related deaths worldwide. Approximately 30% of pancreatic cancer patients present with locally advanced, unresectable nonmetastatic disease, with median overall survival (OS) ranging from 5 to 11 months. Currently, no standard treatment has been established for these patients. In our previous study (Chen *et al.*, Medicine 2016), we retrospectively reviewed a large cohort in China. Two hundred and forty-seven consecutive patients with nonmetastatic locally advanced pancreatic cancer (LAPC) who underwent intraoperative radiotherapy (IORT) between January 2008 and May 2015 were identified and included in the study. The 1-, 2-, and 3-year actuarial survival rates were 40%, 14%, and 7.2%, respectively, with a median OS of 9.0 months. On multivariate analysis, an IORT applicator diameter <6 cm [hazards ratio (HR), 0.67; 95% confidence interval (CI), 0.47–0.97], no intraoperative interstitial sustained release 5- fluorouracil chemotherapy (HR, 0.46; 95% CI, 0.32–0.66), and receipt of postoperative chemoradiotherapy followed by chemotherapy (HR, 0.11; 95% CI, 0.04–0.25) were significantly associated with improved OS,1-, 2-, and 3-year OS rates of 70.5% , 25.1% , and 18.4%, respectively. We finally concluded that chemoradiotherapy followed by chemotherapy might be a recommended adjuvant treatment strategy for well-selected cases. The optimal treatment strategy followed IORT has not been clearly defined. We conducted a study to find the best model of combination of IORT and postoperative radiochemotherapy for pancreatic cancer.

Methods: We did a comparative (2 arms), single-center, randomized controlled trial in China National Cancer Center/Cancer Hospital. The trail started from January 1, 2016. Eligible participants were previously untreated patients with LAPC, and were confirmed by cytology. Patients had at least an Eastern Cooperative Oncology Group (ECOG) performance status of 2 or less. During the surgical procedure, IORT was delivered using the Mobetron linear accelerator (Intraop Medical Corporation, Sunnyvale, CA, USA). The electron energy was 9 MeV. The surgeon and radiation oncologist assessed the extent of disease at operation and a cylindric applicator of appropriate size was selected to cover the tumor comfortably within the field, usually with a 1-cm margin around the pancreatic mass. Cone sizes were selected to deliver a dose of about 15 Gy (range, 10–20 Gy, which was confirmed by calculation) to a field that included the primary tumor and a margin of 1 to 2 cm covering the regional lymph nodes. After IORT, we randomly assigned participants (1:1) to two groups. Participants in the stereotactic radiotherapy (SBRT) Group received SBRT (total dose: 45 Gy; single dose: 3 Gy; frequency: 15) followed by taking S-1 orally (40 mg/m^2, bid on day 1–28 in 42-day circles), while participants in the concurrent chemoradiotherapy (CCRT) Group received CCRT [total dose: 46 Gy; single dose: 2 Gy; frequency: 23; with an intravenous infusion of gemcitabine (300 mg/m^2 weekly)] followed by taking S-1 orally as the SBRT Group. Patients continued treatment until unacceptable toxicity, disease progression, or patient withdrawal. The primary endpoint was overall survival. Kaplan-Meier method was used to analyze the difference of survival time between the two groups. Statistical analyses was performed by using IBM SPSS Statistics (version 20; IBM, Chicago, USA). The study protocol was approved by the Ethics Committee of China National Cancer Center. This trail is registered at Clinical Trials.gov, number NCT02981641. This trial is in progress and we report the interim analysis here.

Results: Between January 1, 2016, and January 1, 2018, we randomly assigned 64 LAPC patients to treatment: 33 patients (51.6%) to the SBRT Group and 31 patients (48.4%) to the CCRT Group. There was no significant difference between the two groups in terms of gender, age, lifestyle factors, tumor locations, and tumor sizes. Median follow-up time was 8.10 (range, 0.3–25.3) months. Till the last follow up, 37 patients (57.8%) had died: 19 patients (57.6%) in the SBRT Group and 18 patients (58.1%) in the CCRT Group. The 1-year survival rate was 38.2% in the whole patients: 36.0% in the SBRT Group and

40.6% in the CCRT Group, respectively. Median OS was 10.6 (95% CI, 7.8–13.4) months for the whole patients: 10.4 (95% CI, 6.1–14.5) months for the SBRT Group and 11.0 (95% CI, 7.6–14.3) months for the CCRT Group (log-rank test, P=0.604). No treatment-related death or fatal complications occurred till now.

Conclusions: IORT is an effective and safe strategy for LAPC. The median OS in LAPC patients who received CCRT after IORT was slightly longer than patients who received SBRT after IORT. However, the study need more patients to be included and a longer time to follow up.

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Andrea	Pietrabissa
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Camilla	Pilati
Giovanni	Pirozzolo
Roberta	Pisano
Justin	Poling
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Nicholas	Roberts
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Toon	Rosseel
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Salvatore	Russo
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Kapo	Saukkonen
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Xiaoshan	Shao
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Toshihiro	Tanaka
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Tianhong	Teng
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Jiabei	Wang
Lei	Wang
Peng	Wang
Xianze	Wang

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Jishu	Wei
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Guoliang	Wu
Heshui	Wu
Junli	Wu
Linquan	Wu
Mingming	Wu
Pengfei	Wu
Wenchuan	Wu
Wenming	Wu
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Chunhua	Xi
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Ping	Xiong
Dianrong	Xiu
Peiran	Xu

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Ye-Ran	Yang
Yinmo	Yang
Yongsheng	Yang
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Kevin	Yarema
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Jie	Yin
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Xiangbao	Yin
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Tonglin	Zhang
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