Oral Sessions

PRESENTER: Katheryn Wilkinson (Surgical Oncology Resident)

PRESENTER: Peter Yu (Ohio State University)

PRESENTER: Claude Nganzeu (Colorectal Surgery Medical Student)

PRESENTER: Benjamin Stultz (Trauma Medical Student)

PRESENTER: Stefan Buettner (Erasmus MC University Medical Center, Rotterdam, ZUID-HOLLAND, Netherlands)
Oral Sessions

Patterns of Disease Recurrence Following Neoadjuvant Therapy for Localized Pancreatic Cancer: C. Barnes, M. Aldakkak, K. Christians, C. Clarke, P. Ritch, B. George, M. Aburajab, M. Griffin, B. Erickson, W. Hall, D. Evans, S. Tsai
PRESENTER: Chad Barnes (Surgical Oncology Research Resident)

PRESENTER: Lindsey Clark (General Surgery Research Resident)

Risk Factors for Revision Following Lower Extremity Amputations: M. T. Cain, M. Wohlauer, P. Rossi, B. Lewis, K. Brown, G. Seabrook, C. J. Lee
PRESENTER: Michael Cain (General Surgery Resident)

The Endocannabinoid System: A Biomarker for Pain in the Traumatically Injured” : C. M. Trevino, S. Chesney, C. Hillard, T. DeRoon-Cassini
PRESENTER: Colleen Trevino (Division of Trauma Assistant Professor)

Non-Invasive Neuromuscular Ventilator Assist after Congenital Diaphragmatic Hernia Repair: R. Amin, M. Arca
PRESENTER: Ruchi Amin(Pediatric General Surgery Fellow)
Breast Cancer in Women over 80: An Analysis of Treatment Patterns and Disease Outcomes: E. N. Ferrigni, C. Bergom, Z. Yin, A. Kong,
PRESENTER: Erin Ferrigni (Medical Student)

The Impact of Increasing Surgical Capacity at a Tertiary Hospital in Southern Haiti: L. E. Ward, M. M. Padovany, A. N. Bowder, T. Jean-Baptiste, R. Patterson, C. M. Dodgion
PRESENTER: Michelson Padovany (Saint Boniface Hospital, Dond Des Blancs, Haiti)

PRESENTER: Rita Shelby (Ohio State University)

PRESENTER: Zoe Morgan (Surgical Oncology Medical Student)

PRESENTER: Claude Nganzeu (Colorectal Surgery Medical Student)

Effect of HO-3867, a novel curcumin analog, on cholangiocarcinoma: H. Kazikh, S. Kunnimalaiyaan, T. Gamblin, M. Kunnimalaiyaan
PRESENTER: Haily Kazikh (CTSI Medical Student)

PRESENTER: Rachel Morris (General Surgery Instructor)

PRESENTER: Jacqueline Blank (Research Resident)
Quick Shots

Blood Transfusions Increase Risk of Venous Thromboembolism Following Ventral Hernia Repair: J. H. Helm, M. C. Helm, J. C. Gould
PRESENTER: Joseph Helm (Division of General Surgery Resident)

PRESENTER: Daniel Roadman (General Surgery Medical Student)

Preoperative Antibiotic Timing and Postoperative Duration in Ruptured Appendicitis: R. Amin, S. Walker, K. Somers, M. Arca
PRESENTER: Ruchi Amin (Pediatric General Surgery Fellow)

Epidurals are Associated with Increased Morbidity and Length of Stay in Open Ventral Hernia Repairs: S. L. Zhou, M. C. Helm, J. H. Helm, M. I. Goldblatt
PRESENTER: Steven Zhou (Division of General Surgery Medical Student)

PRESENTER: Neil Jariwalla (Division of Surgical Oncology Medical Student)

Liver Transplantation and Staged Biliary Reconstruction Improves Outcomes in Pediatric Recipients: J. Kim, M. A. Zimmerman, S. M. Lerret, B. Vitola, J. P. Scott, G. W. Telega, J. C. Hong
PRESENTER: Joohyun Kim (Division of Transplant Assistant Professor)

There is No Routine Gallbladder: A Call to Enhance the “Culture of Safety in Cholecystectomy”: T. T. Jayakrishnan, M. Chimukangara, T. P. Webb, C. S. Davis
PRESENTER: Christopher Davis (Division of Trauma Assistant Professor)
2018 Cores Fair

Weds, Feb. 28 | 11:30 a.m. - 1:30 p.m. | MCW Alumni Center

Learn more about the wide variety of cores and shared research resources here at MCW, ask questions, share information, and network with other researchers.

Office of Research
(414) 955-8495
research@mcw.edu
Colon Cancer and Colonoscopies - January 13, 2018
Focusing primarily on Colon Cancer and screening techniques
Dr. Carrie Peterson, Dr. Tim Ridolfi, Dr. Peter Eichenseer, Dr. William Hall, Dr. James Thomas and Janice Erbe

Pediatric Surgery and Related Medical Concerns in Babies and Children - January 20, 2018
Focusing on diagnosing surgical conditions in fetuses, team collaboration in caring for a prenatal child with a surgical condition, what happens after the baby is born, advantages of being cared for at a Pediatric Hospital, and the family’s perspective whose children have been cared for at the Children’s Hospital of Wisconsin.
Dr. Marjorie Arca, Dr. Steve Leuthner, Dr. Casey Calkins, Dr. Susan Staudt, Dr. Chris Spahr and Dr. Kevin Boyd
The Research Affairs Committee presents: New Faculty (Pilot) Grant

Eligibility

- Applicants must have primary faculty appointment at MCW.
- Apply within 4 years of first faculty appointment.
- Established MCW faculty or post-doctoral fellows are not eligible.
- It is inappropriate to receive funds for similar projects from more than one funding source (i.e. CTSI, Cancer Center, Digestive Diseases, CVC, AHW, NIH, American Heart Association etc.).
- Faculty may receive funding in this category one time only.

Overview

- Primary goal - help applicants obtain preliminary results to compete successfully for extramural funding (foundation, clinical trials, etc.).
- Application should contain explanation of how the pilot project relates to plans for future research.
- Applicants encouraged to seek mentorship from senior and successfully funded faculty members when writing the application.
- Maximum award is $25,000 for one year.

Key Dates

- Request for Applications (RFA) Release Date: February 19, 2018
- Letter of Intent: March 12, 2018
- Application submitted to the Office of Grants & Contracts: April 16, 2018
- Application Receipt Date: April 23, 2018 (5 pm) (e-mailed to Office of Research-Lynne Prost)
- Research Affairs Committee Review: May 2018
- Anticipated Start Date: June 1, 2018

*Please email the Division of Research if you are considering applying for this funding opportunity.
<table>
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<tr>
<th>SUNDAY</th>
<th>MONDAY</th>
<th>TUESDAY</th>
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<tr>
<td>American Pediatric Surgical Association (APSA) Annual Meeting</td>
<td>Eastern Association for the Surgery of Trauma (EAST) early Bird Deadline</td>
<td>Implementing Change and New Standard of Care in Surgery Early Bird Deadline</td>
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<td>AHPBA Research Fellowship Grant</td>
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<td>Early Bird Deadline</td>
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<td>Mayo Clinic Interactive Surgery Symposium Early Bird Deadline</td>
<td>Society of Surgical Oncology (SSO) Annual Cancer Symposium Early Bird Deadline</td>
<td>AACR Grant Neuroendocrine Tumor Research Foundation</td>
<td>Vascular Research Initiatives Conference (VRIC) Abstract Due</td>
<td>MCW Vitality Award Due Moore Inventor Award</td>
<td>GTSC Registration Deadline</td>
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<td>PCAN Translational Research Grant</td>
<td>ENDO 2018 Registration Deadline</td>
<td>Critical Care Congress Registration Deadline</td>
<td>Gastrointestinal Cancers Symposium 1/18-1/20 in CA</td>
<td>Central Surgical Association Foundation Grant</td>
<td>STS 54th Annual Meeting Early Bird Deadline</td>
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<td>VAM (SVS) Abstract Deadline</td>
<td>Society for Surgery of the Alimentary Tract (SSAT) Early Bird Deadline</td>
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<td>International Stroke Conference 1/23-1/26 Las Vegas</td>
<td>Cardiovascular Center Community Engaged Research (CEnR) Second Request for Proposals (RFP),</td>
<td>American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) Abstract Due</td>
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<td>Society of Thoracic Surgeons 54th Annual Meeting</td>
<td>Shock Society Conference Abstracts Due</td>
<td>Sarcoma Foundation of America Grants</td>
<td>WACEP Abstracts Due</td>
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**ACCR** - American Association for Cancer Research, $250,000/2 years

**Vitality Award** - full time or full professional effort service to MCW at the rank of Assistant Professor or higher are eligible, intended to promote academic vitality, career development, and clinical and/or research productivity

**PCAN Grant** - Pancreatic Cancer Action Network, $500,000/2 years

**CSAF Grant** - members in the rank of Assistant and Associate level Professors awarded $20,000, to support surgical scholarship and research and advance the science of surgery

**AHPBA** - The Americas Hepato-Pancreato-Biliary Association, $30,000

**VAM/SVS** - Vascular Annual Meeting/Society for Vascular Surgery

**STS** - Society for Thoracic Surgeons

**SCCM** - Society of Critical Care Medicine 47th Annual

**GTSC** - General Thoracic Surgeons Club

**WACEP** - Wisconsin Chapter American College of Emergency Physicians
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<td>ACS Health Policy Scholarships</td>
<td>Minimally Invasive Surgery Symposium (MISS) Registration Deadline</td>
<td>MCW Pancreatic Cancer Clinical Symposium Harley Davidson Museum</td>
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<td>American Society of Clinical Oncology (ASCO) Annual Meeting Abstracts Due SCVS Symposium Early Bird Deadline</td>
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<td>American Venous Forum (AVF) 2/20-2/23 Tucson, AZ</td>
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<td>Society of Surgical Oncology (SSO) Annual Cancer Symposium Registration Deadline</td>
<td>American Association of Endocrine Surgeons (AAES) Early Bird Deadline</td>
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Next Meeting: February 14, 2018
Cancer Center Conference Room M

Pediatric Surgery Research Updates

David Gourlay, MD
Surgical Oncology Research Update

Susan Tsai, MD, MHS
Amanda Kong, MD, MS
Tracy Wang, MD, MHS
MCW GI Oncology and Mixed Tumors

Kathleen Christians, MD
Callisia Clarke, MD
T. Clark Gamblin, MD, MS, MBA
Michael James, PhD
Muthusamy Kunnimalaiyaan, PhD
Harveshp Mogal, MD
Susan Tsai, MD, MHS

Medical College of Wisconsin
01/10/18
Neuroendocrine Tumors

- Pilot study to examine epigenetic changes using whole genome methylation studies
- Examine outcomes after surgical therapy of locally advanced and metastatic PNET.
- Develop best practices for treatment sequencing for locally advanced and metastatic PNET
Regional Therapy

Prospective Database – presentation, management and outcomes

- All patients undergoing CRS/HIPEC at MCW
- Established in 2015 initially as a research database
- Updated and converted to a clinical database in 2016
- ~330 patients (appendix, colorectal, gastric, mesothelioma)
- ~ 1300 datafields can be collected
- Maintained in RedCap (secure, password protected) by database manager
- Updated when new patients are added and on a monthly basis
Clinicopathologic correlation and outcomes of patients with Low-grade appendiceal mucinous neoplasms/ “Mucoceles”

Investigators:
- Harveshp Mogal, MD – Dept. of Surgery
- Volkan Adsay, MD – Dept. of Pathology

Background:
- Natural history of patients with mucoceles is unknown

Aims:
- To study the clinical and demographic characteristics
- To study the pathological characteristics and correlate these to outcomes in patients with LAMNs
- To determine the rate of progression to psudomyxoma peritonei
- ?Genetic markers that drive progression

Methods:
- Use i2b2 (CTSI Clinical Data Warehouse) to determine the number of patients in the database that have a diagnosis of LAMN
- After IRB approval, obtain identified data using the honest broker tool
- Perform a retrospective chart review and use the regional therapies database to abstract data (demographic, survival data)
- Pathology to pull available slides to review path characteristics
- ? Use tissue bank data (if available) to determine genetic markers of progression to PMP
Morbidity and mortality of patients with disseminated Appendiceal cancer and correlation with outcomes

Investigators
Harveshp Mogal – Dept. of Surgery

Background
CRS/HIPEC is associated with significant morbidity including delayed (60- and 90-day M and M)
Association of delayed Morbidity with outcome has not been well studied

Aims
- Review 30-, 60- and 90- day morbidity/mortality
- Correlate clinicopathological factors with morbidity/mortality
- Study survival in relation to major morbidity

Methods
- Query the Regional Therapies database for patients with appendiceal cancers
- Multivariable analysis of factors affecting survival including development of major morbidity
Can MRI predict unresectability in disseminated mucinous appendiceal cancers?

Investigators:
- Harveshp Mogal – Dept of Surgery
- Charlie Marn, MD and Stacy o’Connor – Dept of Radiology

Background:
- No specific MR characteristics identified to predict unresectability in disseminated mucinous appendiceal cancers

Aims:
- To determine MRI characteristics of tumor vs mucin in patients with disseminated mucinous appendiceal neoplasms
- Can a prospective protocol be developed for MRI in patients with moderate to high volume disease to determine resectability and avoid surgery?

Methods:
- Query HIPEC database for patients with resectable and unresectable disseminated appendiceal mucinous neoplasms
- Retrospective review of MR characteristics
Liver

- Banking of Hepatobiliary Tumors

- Research Collaborative with Life Technology – NC Research Triangle

- Prospective Database for Hepatobiliary
  - Presentation, Management and Outcomes
2018 Liver Outcomes Projects

4 Publications pending in 2018

• Overall Survival after Ablation for HCC at Academic Centers vs Community Cancer Centers
  • National Cancer Database

• Laparoscopic vs Open Ablation of Primary Liver Tumors
  • SEER Database

• Overall Survival and Margins after Hepatectomy for ICC and HCC at Academic Centers vs Community Cancer Centers
  • National Cancer Database

• Two-stage Liver Resections for Colorectal Liver Metastases a Multicenter Retrospective Review
  • MDACC, MSKCC, Hopkins, MCW
Liver Translational Work

- Cholangiocarcinoma and Hepatoma
  Cell lines, Small Animal Model, Phase 1
- Xanthohumol – natural product in hops; first to examine role in hepatobiliary cancer
  - Phase I Study of Xanthohumol in Adults With Refractory Malignancies
- Mitochondrial Targeted drugs – developed within MCW Biophysics Department
  - Supported by 2017 We Care grant

Antiproliferative and apoptotic effects of xanthohumol in Cholangiocarcinoma

Daniel Walden¹, Selvi Kunnimalaiyaan¹, Kevin Sokolowski¹, T Clark Gamblin¹ and Muthusamy Kunnimalaiyaan¹

XN treatment inhibits tumor growth in both CCLP-1 and SG-231 cells injected in a mice xenograft model.
Sarcoma Multi-Institutional Projects
Medical College of Wisconsin, Emory, Stanford, Ohio State, University Chicago, Wake Forest, Washington University, University of Wisconsin

16 Oral presentations in 2018 and accompanying manuscripts – ASC, SSO, ASA

• A Novel, Simplified, Externally-Validated Staging System for Truncal/Extremity Soft Tissue Sarcomas: An Analysis of the US Sarcoma Collaborative Database
• Perioperative Chemotherapy May Not Improve Survival in High Grade Truncal Sarcoma: A Multi-Institutional Analysis
• Outcomes of Elderly Patients undergoing curative resection for retroperitoneal sarcomas: Analysis from the US Sarcoma Collaborative.
• Management of Recurrent Retroperitoneal Liposarcoma Favors Surgical Resection for First but Not Subsequent Recurrences
• Timing of Radiation Improves Margin Status but Not Limb-Salvage Rates in Deep Extremity Sarcoma
• Resection Status Does Not Impact Recurrence in Well-Differentiated Liposarcoma of the Extremity
• The Effect of Margin Status on Multivisceral Resection of Retroperitoneal Sarcoma: Results from a 598 Patient Cohort from the U.S. Sarcoma Collaborative
• Studying Rare Diseases Using Multi-institutional Research Collaborations vs Big Data: Where Lies the Truth?
• Clinical Score Predicting Survival Following Resection of Sarcoma Liver Metastases
• Natural History of Undifferentiated Pleomorphic Sarcoma: Experience from the US Sarcoma Collaborative
• Eighth Edition of the AJCC Staging System for Retroperitoneal Sarcoma: Validation Using the US Sarcoma Collaborative and Recommendations for Refinement
• Presence, But Not Degree, of Tumor Necrosis is associated with Decreased Survival in Patients with Truncal and Extremity Soft Tissue Sarcomas: Results from the U.S. Sarcoma Collaborative
• Predictors of Early vs. Late Death in Resected Retroperitoneal Sarcoma (RPS): An 8-Institution Study from the U.S. Sarcoma Collaborative
• Margin Status and Postoperative Complications Influence Long-Term Oncologic Outcomes after Multivisceral Resection for Retroperitoneal Sarcoma: Results from a 598 Patient Cohort from the U.S. Sarcoma Collaborative
• Perioperative Outcomes After Extremity Sarcoma Resection— Results of a Contemporary Multi-institutional Experience
• Predictors of Disease Free and Overall Survival in Retroperitoneal Sarcomas: A modern 16 year multi-institutional study from the United States Sarcoma Collaboration (USSC)
Pancreatic Cancer

CRR9 – Mike James
PET Avidity - Barnes

Molecular Profiling Trial
Adaptive Neoadjuvant Trial
Metakaryote Trial - MIT

Sarcopenia
Immunologic response

Tumor
Host
Treatment

Precision therapies
Pharmacogenomic response

Biomarker Development
cfDNA (Kras) Tsai
CA19-9 Tsai
miRNA Goel

Germline Sequencing of Sporadic PC – Urrutia/Lomberk/Tsai
Dr. Michael James: WeCare Award Project and Ongoing Research Update

- “CLPTM1L/CRR9 Ectodomain Interaction with GRP78 at the Cell Surface Signals for Survival and Chemoresistance upon ER Stress in Pancreatic Adenocarcinoma Cells.”
  (under review Can. Research, 2018)

- Validation of novel therapeutic and chemosensitizing antibody inhibitors of CRR9/CLPTM1L (ESS102) using patient-derived PDAC organoid cultures.

Therapeutics in development described in:

“Novel Anti-CRR9/CLPTM1L Antibodies with Antitumorigenic Activity Inhibit Cell Surface Accumulation, PI3K Interaction, and Survival Signaling.”


- Development of patient-derived PDAC biomimetic models:
  “Development of Primary Human Pancreatic Tumor Organoids, Matched Stromal and Immune Cells and 3D Tumor Microenvironment Models”, Tsai, .. James et al. BMC Cancer
Directions and Collaborative Opportunities:

- PDAC Organoid Models: Multiple patient-derived lines, with matched blood and some with matched fibroblasts (proposed core for Pancreas PPG(P01))
- CRR9/CLPTM1L expression/function in therapy resistant PDAC and other solid tumors
- Exosomal CRR9/CLPTM1L as a circulating marker and effector of tumor survival at a distance
- Translational and preclinical studies using ESS102 experimental therapeutics / antibodies
  - Correlation with disease/outcome
  - Tissue cross-reactivity
  - In vivo models
  - Affinity, specificity
  - Dose saturation, PK, PD, biodistribution
Germline Sequencing of Sporadic Pancreatic Cancer

Hypothesis:
The combination of next generation sequencing, molecular modeling, and functional assays for transformation and growth will discover new genomic variants with oncogenic potential.

Project:
Perform germline sequencing of a panel of known hereditary cancer genes in 500 patients and further characterize the oncogenic potential of variants of uncertain significance.
Goal: To discover miRNA biomarkers for the detection of the earliest stages of invasive PC
Specific Aims

**Specific Aim 1:** Discover candidate cell-free and exosomal-miRNA biomarkers using small RNA-Seq in matched tissue and plasma from patients with PDAC, precancerous neoplasms (PNs), pancreatitis and normal pancreas.

**Specific Aim 2:** Develop a cell-free and exosomal-miRNA biomarker panel that distinguishes patients with PDAC from those with PNs or pancreatitis.

**Specific Aim 3:** Clinically validate the optimized panel of non-invasive miRNA biomarkers in prospective cohorts of patients with PDAC and PNs.

PCDC U01 Kickoff Meeting, 2017
Hypothesis:
Quantitative changes in cfDNA will correlate with changes in clinical disease status among patients with localized pancreatic cancer.

Crowley et al. Nat Rev Clin Onc 2013
Clinical Stage and cfDNA concentration

Reconstruction Experiment

Total cfDNA by Clinical Stage

Total cfDNA by stage of treatment

G12D

G12V

G12R

G13D

G61H
Clinical Research Projects

• Benefit of adjuvant therapy after neoadjuvant
  – Limited to Node Positive patients (MCW and NCDB)
• Value of PET in PC
  – Pretreatment PET predicts overall survival
  – Posttreatment PET predicts disease free survival
• Patterns of recurrence after neoadjuvant therapy
  – Survival after first recurrence is double that of patients who underwent a surgery first approach
• Conditional Survival after Neoadjuvant Therapy
Overall Survival by Pre-Treatment PET SUV

All Patients (n= 100)

Completed all NeoTx and Surgery (n = 81)

Median Overall Survival

**SUV < 7.2:** not reached

**SUV > 7.2:** 25.0 mo

**SUV < 7.2:** not reached

**SUV > 7.2:** 39.0 mo
Surgery-First vs. Neoadjuvant Treatment Sequencing

**SURGERY-FIRST**
Johns Hopkins (2017)

**NEoadjuvant**
Medical College of Wisconsin (2017)

Similar disease-free survival and patterns of recurrence.
### Surgery-First vs. Neoadjuvant Treatment Sequencing

#### ***PATIENTS WITH DISEASE RECURRENCE ONLY***

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Total Cohort</th>
<th>Patients with Recurrence N (%)</th>
<th>Disease-Free Survival (Months)</th>
<th>Survival after Recurrence (Months)</th>
<th>Overall Survival (Months)</th>
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<tr>
<td>MCW (2017)</td>
<td>271</td>
<td>153 (56)</td>
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<tr>
<td><strong>SURGERY FIRST</strong></td>
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<tr>
<td>Wangjam (2015)</td>
<td>209</td>
<td>174 (83)</td>
<td>10</td>
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<tr>
<td>Neoptolemos (2016)*</td>
<td>730</td>
<td>479 (66)</td>
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<td>Groot (2017)</td>
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<td>531 (77)</td>
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* The median OS of all patients enrolled in the ESPAC-4 trial (with and without recurrence) was 25-28 mos.
### Surgery-First vs. Neoadjuvant Treatment Sequencing

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<td>531 (77)</td>
<td>12</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

* The median OS of all patients enrolled in the ESPAC-4 trial (with and without recurrence) was 25-28 mos.
**Percentage of patients for whom drugs are ineffective**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>38%</td>
</tr>
<tr>
<td>Asthma</td>
<td>40%</td>
</tr>
<tr>
<td>Cardiac Arrhythmias</td>
<td>40%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>43%</td>
</tr>
<tr>
<td>Migraine</td>
<td>48%</td>
</tr>
<tr>
<td>Arthritis</td>
<td>50%</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>52%</td>
</tr>
<tr>
<td>Alzheimer's</td>
<td>70%</td>
</tr>
<tr>
<td>Cancer</td>
<td>75%</td>
</tr>
</tbody>
</table>

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**Precision Medicine for Advanced Pancreas Cancer: The Individualized Molecular Pancreatic Cancer Therapy (IMPaCT) Trial**

*Purpose:* Personalized medicine strategies using genomic profiling are particularly pertinent for pancreas cancer. The Individualized Molecular Pancreatic Cancer Therapy (IMPaCT) trial was initially designed to exploit results from genome sequencing of pancreatic cancer under the auspices of the International Cancer Genome Consortium (ICGC) in Australia. Sequencing revealed small subsets of patients with aberrations in their tumor genome that could be targeted with currently available therapies.

*Experimental Design:* The pilot stage of the IMPaCT trial assessed the feasibility of acquiring suitable tumor specimens for molecular analysis and returning high-quality actionable genomic data within a clinically acceptable timeframe. We screened for three molecular targets: HER2 amplification; KRAS wild-type; and mutations in DNA damage repair pathways (*BRCA1*, *BRCA2*, *PALB2*, *ATM*).

*Results:* Tumor biopsy and archived tumor samples were collected from 93 patients and 76 were screened. To date 22 candidate cases have been identified: 14 KRAS wild-type, 5 cases of HER2 amplification, 2 mutations in *BRCA2*, and 1 ATM mutation. Median time from consent to the return of validated results was 21.5 days. An inability to obtain a biopsy or insufficient tumor content in the available specimen were common reasons for patient exclusion from molecular analysis while deteriorating performance status prohibited a number of patients from proceeding to the study.

**Box 1. Practical recommendations for precision medicine trials**

- Formation of a cohesive, collaborative tissue acquisition team focused at key sites
- Consent for tissue acquisition and screening undertaken at time of biopsy
- Personal transport and processing by team members
- Consideration of incorporating newer “liquid biopsy” techniques instead of tissue analysis
- Effective channels of communicating results to clinicians in real time
- Design of studies that appeal to patients: nonrandomized studies of novel agents allowing standard treatment to start while analysis is undertaken
Rates of Completion of all intended Neoadjuvant therapy and Surgery

Preoperative Gemcitabine-Based Chemoradiation for Patients With Resectable Adenocarcinoma of the Pancreatic Head

Evans et al. JCO 2008

Preoperative Gemcitabine and Cisplatin Followed by Gemcitabine-Based Chemoradiation for Resectable Adenocarcinoma of the Pancreatic Head

Varadhachary et al. JCO 2008

Borderline Resectable Pancreatic Cancer: The Importance of This Emerging Stage of Disease

Katz JACS 2008

Majority of patients do not have surgery following neoadjuvant therapy due to metastatic disease progression

Hypothesis:
More effective systemic therapy may increase the proportion of patients who are able to complete all intended neoadjuvant therapy and surgery.

Molecular profiling based on the primary tumor may improve the efficacy of neoadjuvant therapy by identifying drugs to which tumors may be susceptible.
Primary Endpoint: To compare the proportion of patients who complete all intended neoadjuvant therapy and surgery among patients who received profile directed therapy as compared to historical controls.
Molecular Profiling Trial
(2012-2017)

130 Subjects Enrolled

60 (46%) Resectable

- 13 (21%) Inadequate FNA → ChemoXRT → 55 (92%) Resected
- 47 (78%) Adequate FNA → Profile Directed Therapy

70 (54%) Borderline Resectable

- 13 (21%) Inadequate FNA
- 48 (68%) Adequate FNA → Profile Directed Therapy + ChemoXRT

55 (92%) Resected

47 (78%) Adequate FNA → Profile Directed Therapy

51 (74%) Resected
Monitoring Treatment Response in Pancreatic Cancer

Response of Borderline Resectable Pancreatic Cancer to Neoadjuvant Therapy Is Not Reflected by Radiographic Indicators

Matthew H. G. Katz, MD; Jason B. Fleming, MD; Priya Bhosale, MD; Gauri Varadhachary, MD; Jeffrey E. Lee, MD; Robert Wolff, MD; Huamin Wang, MD; James Abbruzzese, MD; Peter W. T. Pisters, MD; Jean-Nicolas Vauthey, MD; Chuslip Charnsangavej, MD; Eric Tamm, MD; Christopher H. Crane, MD; and Aparna Balachandran, MD

Radiological and Surgical Implications of Neoadjuvant Treatment With FOLFIRINOX for Locally Advanced and Borderline Resectable Pancreatic Cancer

Katz et al. Cancer 2012
Hypothesis:
Adaptive modification of neoadjuvant chemotherapy (experimental approach) based on clinical treatment response elements, as measured by changes in CA19-9 levels, radiographic response, and performance status, will result in an increased rate of completion of all neoadjuvant therapy and surgery as compared to patients who received non-adaptive therapy (standard approach).
Targeting Pancreatic Cancer Stem Cells

- Cancer Stem Cells
  - Resistant to chemotherapy and radiotherapy
  - Low rate of division
  - Capable of symmetric and asymmetric division
  - May be responsible for cancer recurrence after "curative therapy"

Window of Opportunity Trial
Administer metakaryocidal drug prior to surgery and examine surgical specimens for metakaryotic death
NORMAL (UNAFFECTED METAKARYOTIC STEM CELL)

Disintegrating (pyknosis stage I) nucleus of metakaryotic cancer stem cells
MCW Pancreatic Cancer Group

Pancreatic Cancer Group
- Murad Abu Rajab, MD
- N. Volkan Adsay, MD
- Callisia Clarke, MD
- Kulwinder Dua, MD
- Beth Erickson, MD
- Douglas Evans, MD
- Katheline Christians, MD
- Jennifer Geurts, CGC
- Ben George, MD
- Katherine Hagen, MD
- William Hall, MD
- Brian Hunt, MD
- Abdul Khan, MD
- Jennifer Knight, MD
- Paul Ritch, MD
- James Thomas, MD, PhD
- Catherine Hagan, MD
- Parag Tolat, MD
- Susan Tsai, MD, MHS

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- Ajay Goel, PhD
- Brian Haab, PhD
- Bryon Johnson, PhD
- Gwen Lomberk, PhD
- Matt Riese, MD, PhD
- Raul Urrutia, MD
- Lily Wang, PhD

Funding
- Advancing Healthier Wisconsin
- Ronald Burklund Eich PC Research Fund
- Research Affair Committee Grant
- WeCare Fund
- American Cancer Society Pilot Grant
- Dept of Veterans Affairs
- Karl Storz VA Surgeons Award
- Society of Black Surgeon’s Resident Research Award
- Batterman Foundation
# Symposium Schedule

<table>
<thead>
<tr>
<th>Time</th>
<th>Topic</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00 AM</td>
<td>Registration and Breakfast</td>
<td></td>
</tr>
<tr>
<td>9:30 - 10:00 AM</td>
<td>Neoadjuvant Therapy Localized Pancreatic Cancer</td>
<td>Douglas Evans, MD</td>
</tr>
<tr>
<td>10:00-10:30 AM</td>
<td>Endoscopic Techniques for the Management of Pancreatic Cancer</td>
<td>Kulwinder Dua, MD</td>
</tr>
<tr>
<td>10:30-11:00 AM</td>
<td>The Importance of Accurate Radiographic Staging for Pancreatic Cancer</td>
<td>Naveen Kulkarni, MD</td>
</tr>
<tr>
<td>11:00-11:15 AM</td>
<td>Break</td>
<td></td>
</tr>
<tr>
<td>11:15-12:00 PM</td>
<td>Pancreatic Surgery – Five Decades of Progress</td>
<td>O. Joe Hines, MD</td>
</tr>
<tr>
<td>12:00-1:00 PM</td>
<td>Lunch</td>
<td></td>
</tr>
<tr>
<td>12:30-1:00 PM</td>
<td>Prognostic value of CA19-9 monitoring in Pancreatic Cancer</td>
<td>Susan Tsai, MD, MHS</td>
</tr>
<tr>
<td>1:00-1:45 PM</td>
<td>GI ASCO Updates</td>
<td>Daniel Laheru, MD</td>
</tr>
<tr>
<td>1:45-2:05 PM</td>
<td>Pre-operative Radiation Therapy for Pancreatic Adenocarcinoma: When, Where, and How?</td>
<td>William Hall, MD</td>
</tr>
<tr>
<td>2:05-2:30 PM</td>
<td>Novel Treatment Strategies in Metastatic Pancreatic Cancer</td>
<td>Paul Ritch, MD</td>
</tr>
<tr>
<td>2:30-2:40 PM</td>
<td>Break</td>
<td></td>
</tr>
<tr>
<td>2:40-3:00 PM</td>
<td>Complex Vascular Resection and Reconstruction for Pancreatic Cancer</td>
<td>Kathleen Christians, MD</td>
</tr>
<tr>
<td>3:00-3:20 PM</td>
<td>Locally Advanced Pancreatic Cancer: Is there a Role for Radiation?</td>
<td>Beth Erickson, MD</td>
</tr>
<tr>
<td>3:20-4:00 PM</td>
<td>Mock Tumor Board</td>
<td>Beth Erickson, MD, Douglas Evans, MD, Ben George, MD, Naveen Kulkarni, MD, Paul Ritch, MD, Susan Tsai, MD, MHS</td>
</tr>
<tr>
<td>4:00 PM</td>
<td>Concluding Remarks</td>
<td></td>
</tr>
</tbody>
</table>

Register at: ocpe.mcw.edu/surgery  
CME 4.75 AMA PRA Category 1  
Contact: Heidi Brittnacher (955-1831)
Endocrine Surgery

- Primary hyperparathyroidism
- Secondary hyperparathyroidism
- Familial hyperparathyroidism
  - MEN1
  - MEN2
- Parathyroid cancer

- Hyperparathyroidism
  - Graves’ Disease
  - Toxic nodules
  - Thyroid nodules
  - Multinodular goiters
- Thyroid cancer
  - Differentiated
  - Medullary
  - Anaplastic

- Adrenal nodules
- Primary aldosteronism
- Hypercortisolism
  - ACTH-independent
  - ACTH-dependent
- Pheochromocytomas and paragangliomas
- Adrenal cancer

- Pancreatic neuroendocrine tumors
- Gastrointestinal neuroendocrine tumors
- Inherited syndromes
  - MEN1
  - MEN2
  - Familial HPT
  - Others
Endocrine Surgery Faculty

Douglas B. Evans, MD
Chair, Department of Surgery

Tracy S. Wang, MD, MPH
Chief, Section of Endocrine Surgery

Tina W. Yen, MD, MS

Azadeh A. Carr, MD

Stuart D. Wilson, MD
Professor Emeritus
Clinical Databases

- Maintenance of 3 prospectively-collected databases
  - Parathyroid (1999 – present)
    - 2310 patients
  - Thyroid (2009 – present)
    - 1828 patients
  - Adrenal (2001 – present)
    - 344 patients
    - Housed in RedCap, with Vanderbilt University Endocrine Surgery
Clinical Databases

• Foundation of retrospective and prospective studies
  – Institutional, investigator-initiated prospective studies
    • Multiple studies that have changed institutional protocols
  – Multi-institutional collaborations
    • The Cancer Genome Atlas
    • A5 (Australian-American-Asian Adrenal Alliance)
    • U.S. Adrenocortical Carcinoma Study Group
    • Vanderbilt University, Columbia University, University of Calgary, Massachusetts General Hospital, University of Pittsburgh
  – Collaboration with scientists at MCW
    • Jong-in Park, PhD – mouse model for medullary thyroid cancer
• Collaborative Endocrine Surgery Quality Improvement Program
  – Established in 2012 as a joint venture with the American Association of Endocrine Surgeons (AAES)
  – Patient-centered data collection with goal of ongoing performance feedback to clinicians
  – Is now a Qualified Clinical Data Registry by the Centers for Medicare and Medicaid Services (CMS)
    • Fulfill requirements of the Merit-based Incentive Payment System
    • Utilized by American Board of Surgery for Maintenance of Certification
  – First MCW patient: 2014
    • Registered for FMLH for all Surgical Oncologists and Head and Neck Surgery
    • Thyroid, Parathyroid, Adrenal, Gastrointestinal Neuroendocrine Tumors
Research in Progress (1)

• Submitted manuscripts
  – Oncocytic variant papillary thyroid cancer has similar prognosis to matched classical papillary thyroid cancer controls.
    • Carr AA, Yen TW, Ortiz DI, Hunt BC, Fareau GG, Massey BL, Campbell BH, Doffek KL, Evans DB, Wang TS.

• Manuscripts in progress
  – Extent of elevation of serum aldosterone in patients with primary aldosteronism: Can we forgo adrenal venous sampling? (Coan et al.)
  – Techniques for intraoperative identification and confirmation of parathyroid tissue: results from a survey of the American Association of Endocrine Surgeons (Coan et al.)
  – Intrathyroidal and subcapsular parathyroid glands: an elusive etiology of primary hyperparathyroidism (Murphy et al.)
Research in Progress (2)

• A postoperative parathyroid hormone algorithm to reduce symptomatic hypocalcemia following completion/total thyroidectomy: a retrospective analysis of 591 patients (Mazotas I et al)
  – Accepted for oral (podium) presentation at the 2018 Central Surgical Association
  – Follow-up study of prospective-randomized trial of calcium supplementation following completion/total thyroidectomy (Cayo et al. Surgery 2012;152(6):1059-1067)

• Postoperative hypocalcemia secondary to hypoparathyroidism is one of the most common complications following total thyroidectomy
  – No standard protocol for postoperative management, issues surrounding costs of (unnecessary) lab testing, possible hypercalcemia with oversupplementation
• Initial study findings:
  – No predictors of PTH $\geq 10$ pg/mL
  – PPV of PTH $\geq 10$ not reporting symptoms: 91%
    PPV of PTH $\geq 10$ not requiring supplementation: 100%
  – Optimal protocol for patients with PTH $< 10$ remained unclear
• Patients who underwent completion/total thyroidectomy, 2012-2016
  – May be able to amend protocol for pts with PTH $< 10$, include calcitriol at the time of discharge to minimize symptomatic hypocalcemia
  – Initial univariate analysis: thyroid cancer, central compartment neck dissection, and parathyroid in specimen more likely in pts with PTH $< 10$
    • Multivariate analysis in progress, in conjunction with Dept of Biostatistics
Research in Progress (3)

- Time to recurrence in patients with primary hyperparathyroidism: does the number of glands resected at first surgery matter? (Mazotas et al.)
- Study evaluating trends in parathyroidectomy in elderly patients at MCW (O’Sullivan et al)
1. Outcomes from adrenal metastatectomy
   Primary institution: Massachusetts General Hospital (MGH)
2. Quality-of-life in patients with primary aldosteronism
   Joint project with colleagues at University of Michigan, MGH
3. CESQIP – both will be poster presentations at 2018 AAES
   1. Adrenalectomy Volume-Related Outcomes of CESQIP-participating Surgeons
   2. Practice Trends and Outcomes of Adrenal Surgeons: A comparison of data from CESQIP and NSQIP
      Kiernan CM, Solórzano CC, Miller BS, Perrier BD, Lee JE, Gauger P, Grubbs EG, Wang TS
Future projects

1. Molecular Testing to Direct Extent of Initial Thyroid Surgery
   – Clinical trial for patients with indeterminate thyroid nodules
   – Host institution: University of Pittsburgh (Linwah Yip, MD)

2. European Network for the Study of Adrenal Tumors (ENS@T)
   – Examining natural history of patients with mild hypercortisolism

3. A5: Australian-American-Asian Adrenal Alliance
Founding Institutions

- University of Michigan
- Brigham & Women’s Hospital / Harvard Medical School
- Boston Children’s Hospital
- Mayo Clinic, Rochester
- Medical College of Wisconsin
- University of Colorado
- University of Florida
- University of Texas Health Science Center at San Antonio
- University of Texas M.D. Anderson Cancer Center
- Centre Hospitalier de l’universite de Montreal
- Peter MacCallum Cancer Center, Melbourne
- Hospital das Clinicas de Faculdade de Medicina da Universidade de Sao Paolo
Introduction to A5

• **Regular exchange** platform for scientists/physician with an interest in adrenal and related diseases

• **Initiate common studies.**
  • Increase study population for (rare) adrenal diseases
  • Facilitate the regulated exchange of samples & patient data

• **Grant funding**
  • Increase chances of grant funding for rare diseases using an organized larger platform
  • Improve awareness at funding organizations, e.g. NIH study section representation

• **Improve adrenal-related research and patient care**
• Collaborate with European Network to Study Adrenal Tumors (ENS@T)
Adrenal Network

Member sites/individuals

- Patient data
- Patient samples
- Local repositories

Executive Committee

- Research ideas
- Approval: avoid double efforts, feasibility, resources

Core Registry

Network Project Manager
David Madrigal
- Works closely with sections & study coordinators/PI

Research studies

Working groups – rotating chairs

- Adrenal cancer
  T. Else/G. Hammer/M. Habra
- Primary aldosteronism
  A. Vaidya/B. Rainey
- Pheo/Para
  L. Fishbein/K. Pacak
- Congenital Adrenal Hyperplasia
  A. Turcu/T. Bachega
- Benign Adrenal Tumors
  I. Bancos/J. Findling/C. Fragoso/A. Lacroix

Add more over time
(e.g. Adrenal Insufficiency)
Endocrine Surgery Research Program

• Research meetings: Mondays at 4:00 PM
  – Room 6338 of the Hub

• Tracy S. Wang, MD, MPH
  – tswang@mcw.edu
  – 414-955-1459
Surgical Oncology Research Update

Section of Breast Surgery
Amanda L. Kong, MD, MS
Section Chief
Breast Surgery Team

Alonzo Walker, MD
Tina Yen MD, MS
Amanda Kong, MD, MS
Caitlin Patten, MD
Miraj Shah-Khan, MD
Breast Surgery Group

• Health Services Research
• Translational & Basic Science Research
• Investigator Initiated Trials
• Clinical Trials
• Systematic Review
• International collaboration
Breast Cancer Health Services Research Projects

• Understanding the use of advanced practice providers in breast cancer care
• State-wide intervention to reduce the use of unproven breast cancer interventions
Understanding the Use of Advanced Practice Providers in Breast Cancer Care

State of Wisconsin Tax Check-Off Program for Breast Cancer Research and MCW Cancer Center

Co-investigators: Nattinger, Pezzin, Laud
Oncology Workforce Shortages and Implications

• Increase demand for cancer services
  – Growth of an aging population
  – Increasing cancer burden and number of survivors

• Workforce issues
  – Aging and retiring workforce
  – Burnout

• Disparities in quality of care and access to care

• Longer wait times or travel distances
  – Rural and Underserved

• Impact on patient outcomes

Yang W. J Oncol Pract 2014
Shanafelt TD. J Clin Oncol 2012
ASCO. J Oncol Pract 2014
Strategies

• Leverage the existing oncology workforce
  – Collaborate with PCPs on coordination/transition of cancer care
  – Expand use of advanced practice providers (APPs)
  – Monitor and address burnout
• Leverage technology and innovative practice models to improve patient access
  – Telemedicine
  – Visiting consultants
• Increase the number of oncology fellowships
• Improve the efficiency of care delivery
  – NCI-ASCO Teams in Cancer Care Delivery Project
  – Survivorship clinics

IOM. 2009 Ensuring Quality Cancer Care Through the Oncology Workforce: Workshop Summary.
Specific aims

1. Determine the prevalence and longitudinal time trends of an APP-based practice model and variations in this care model related to demographic and patient characteristics and type of care (active treatment vs. surveillance)
   APP model more likely: healthier, rural areas, states with fewer restrictions, surveillance phase

2. Perform comparative effectiveness analysis of outcomes (ER visits, hospitalizations) of patients in an APP-based model vs. MD-based model
   APP care model will have slightly increased resource utilization

3. Explore the development of an EMR-based novel measure of APP involvement in cancer care
Aims 1 and 2: study cohorts and definitions

- **Medicare**
  - Incident breast cancer in 2008 with claims through 2012
- **Marketscan**
  - Employees and their dependents covered by employer-based private health insurances
  - Medical and drug data on over 50 million individuals annually
  - Incident breast cancer in 2012 with claims through 2015
- **Active treatment end date:**
  - Date of last bill for surgery, chemotherapy or radiation therapy OR
  - First year from diagnosis (whichever occurs first)
- **Surveillance phase:** period after active treatment ends
  - 12-month increments from start of surveillance date
2008 Medicare cohort

- 42,550 women with incident breast cancer in 2008
- Median age: 74 years (IQR 10.0)
- Race: 90% white, 7% black, 3% other
- Comorbidity: 53% healthy (score 0)
- 23% lived in a rural county
- NP scope of practice by state:
  - 10% independent practice
  - 17% reduced practice
  - 73% restricted practice
- 19% dead by end of 2012
- 15% had at least 1 breast cancer care APP claim during active treatment or surveillance phase
Logistic regression model with patient level random effect to predict likelihood of seeing an APP at each time point

<table>
<thead>
<tr>
<th></th>
<th>APP care during treatment or surveillance phase</th>
<th>APP care during surveillance phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>OR (95% CI)</td>
<td>P-value</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;75</td>
<td>1.00</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>≤ 75</td>
<td>1.40 (1.33-1.48)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Black</td>
<td>1.20 (1.08-1.34)</td>
<td>1.29 (1.15-1.45)</td>
</tr>
<tr>
<td>Other</td>
<td>0.86 (0.73-1.02)</td>
<td>0.96 (0.79-1.15)</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1</td>
<td>0.90 (0.84-0.96)</td>
<td>0.88 (0.82-0.94)</td>
</tr>
<tr>
<td>2+</td>
<td>0.84 (0.78-0.90)</td>
<td>0.82 (0.75-0.89)</td>
</tr>
<tr>
<td>Rural</td>
<td>1.37 (1.29-1.46)</td>
<td>1.41 (1.32-1.51)</td>
</tr>
<tr>
<td>NP scope of practice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restricted</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Reduced</td>
<td>1.04 (0.97-1.12)</td>
<td>1.09 (1.00-1.18)</td>
</tr>
<tr>
<td>Independent</td>
<td>1.36 (1.26-1.47)</td>
<td>1.36 (1.25-1.48)</td>
</tr>
<tr>
<td>APP care during treatment phase</td>
<td>---</td>
<td>11.88 (10.94-12.91)</td>
</tr>
</tbody>
</table>
Summary of findings

• 15% of cohort had at least one APP breast cancer care claim over 4 years
  – Majority during surveillance phase
• More likely to see APP if younger, healthier, black, live in NP independent practice state, rural county
  – Largest effect if see APP during treatment phase
• Overall proportion of visits with an APP increases as get farther out from treatment
• Seeing an APP one year does not translate to seeing an APP in future years
• No association between outpatient APP exposure during chemotherapy before adverse event and chemotherapy-related adverse events
Ongoing work/Future plans

• Marketscan younger cohort analyses
  – Similar data

• MCW Clinical Research Data Warehouse (i2b2): Aim 3
  – 100 patients with breast cancer in 2011
  – 1933 breast care clinic visits between 2011-2014
    • 24% billed by APP
    • Of MD billed visits, about 20% have evidence of APP involvement (orders, prescriptions, notes)

• R21 submission
  – SEER-CAHPS linked database
  – Patient care experience among cancer survivors
    • Pattern of APP involvement
    • Relationship of care model (APP vs. MD only) to patient care experience
    • Effect on disparities (urban-rural, SES, race)
A Statewide Intervention to Reduce the Use of Unproven Breast Cancer Care

- R01 NCI grant
- Research Answers to NCI’s Provocative Questions Initiative

What methods and approaches induce physicians and health systems to abandon ineffective interventions or discourage adoption of unproven interventions?

- Co-PIs: Ann Nattinger, MD, MPH
  Liliana Pezzin, PhD, JD

- Co-investigators:
  Tina Yen, MD, MS  John Charlson, MD
  Joan Neuner, MD, MPH  Prakash Laud, PhD
Background

• The Congressional Budget Office estimates that 30% of health care provided is unnecessary

• 2009 – Dr. Howard Brody challenged specialty societies to develop a Top Five list of relatively expensive procedures that do not provide meaningful benefit

• 2012 – The Choosing Wisely® campaign was launched by the ABIM Foundation
  – Over 70 specialty societies
Background

• The extent to which the development of these lists influence the behavior of physicians or patients is not known

• Need for supplemental methods to change the current US healthcare culture
  – Public reporting systems
    • Motivate quality improvement:
      – Selection
        » Consumers preferentially select higher performing providers
      – Change
        » Pressure to avoid stigmata of being identified as a poor quality provider
    • Uncertain effect on improving health outcomes
  – Mobile app
    • Potential to facilitate provider change
    • Scant evaluation

Tilburt JC. JAMA 2013
Ketelaar NA. Cochrane Database Syst Rev 2011
Wisconsin Collaborative for Healthcare Quality (WCHQ)

• A multi-stakeholder voluntary consortium of 38 organizations throughout Wisconsin, founded in 2003
  – Health systems, medical groups, hospitals and clinics

• Mission:
  Publically report and bring meaning to performance measurement information that improves the quality and affordability of healthcare in Wisconsin, in turn improving the health of individuals and communities

• Collects and publically reports 46 different quality metrics based on local system billing data
  – Ambulatory care
  – Specialty care
  – Patient experience (CG-CAHPS)
Research Design

• Two-phase, quasi-experimental, nested approach
• Two intervention strategies:
  – Phase I: *basic* practice-level public reporting on WCHQ’s website
  – Phase II: *enhanced* intervention
    Public reporting is augmented by a smart phone/web-based *app* that will provide just-in-time information, decision aid tools, patient education materials, and personalized benchmarking
• Outcomes: breast cancer metrics
• Data sources: Medicare claims data and Marketscan commercial database
# Breast cancer metrics

<table>
<thead>
<tr>
<th>Metric</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial diagnosis and treatment</strong></td>
<td></td>
</tr>
<tr>
<td>Needle biopsy done before surgery</td>
<td>Choosing Wisely® CoC; NCCN, ASBrS</td>
</tr>
<tr>
<td>Axillary lymph node dissection without attempted sentinel lymph node biopsy</td>
<td>Choosing Wisely® ACS</td>
</tr>
<tr>
<td>Contralateral prophylactic mastectomy (CPM)</td>
<td>NCCN, SSO, Choosing Wisely® ASBrS</td>
</tr>
<tr>
<td>Intensity modulated radiation therapy (IMRT) within 6 months of BCS</td>
<td>Choosing Wisely® ASTRO</td>
</tr>
<tr>
<td><strong>Surveillance (6 months after surgery to end of study)</strong></td>
<td></td>
</tr>
<tr>
<td>Tumor biomarker blood testing (CA 15-3, CA27.29)</td>
<td>Choosing Wisely® ASCO</td>
</tr>
<tr>
<td>PET scan or CT-PET scan</td>
<td>Choosing Wisely® ASCO</td>
</tr>
<tr>
<td>CT (chest/abdomen/pelvis) scan</td>
<td>Choosing Wisely® ASCO</td>
</tr>
<tr>
<td>Bone scan</td>
<td>Choosing Wisely® ASCO</td>
</tr>
<tr>
<td>Breast MRI</td>
<td>American Cancer Society, NCCN, ASBrS</td>
</tr>
<tr>
<td>Follow-up mammograms performed more frequently than annually among women with BCS and XRT</td>
<td>Choosing Wisely® ASTRO</td>
</tr>
</tbody>
</table>
SA1. Examine effectiveness of basic public reporting on reducing the use of targeted breast cancer practices in WI (pre- vs. post-intervention) and relative to usual care in comparison states.

SA2. Examine effectiveness of enhanced intervention relative to basic intervention in WI and relative to usual care in comparison states.

SA3. Simulate cost savings from nationwide implementation of both interventions (relative to each other and to usual care).
Project status

- 7 health systems recruited
  - About 70% of incident breast cancer cases in WI
- Breast cancer cohorts identified
- Metrics developed and validated
  - ICD-9 to ICD-10 coding changes
- Phase I: **basic** intervention
  - First public reporting – July 2016
  - Second public reporting – January 2017
- App development and testing completed
- Phase II: **enhanced** intervention began Winter 2017
  - Third public reporting – December 2017
- Analyses ongoing
The American Society of Clinical Oncology's Choosing Wisely® list recommends against performing a computerized tomography (CT or CAT) scan of the chest, abdomen or pelvis for routine breast cancer surveillance for recurrence in asymptomatic patients who have been treated with curative intent, citing their unproven effectiveness in improving survival. CT scans may be indicated if there is concern for disease recurrence (e.g., development of symptoms or lab abnormalities), to follow-up a prior abnormal CT scan finding, or for reasons that are not related to breast cancer.
Benign Breast Systematic Review

• Surgical management of benign papillomas

Caitlin Patten, MD
Benign Intraductal Papillomas of the Breast

- Surgical excision is recommended for intraductal papillomas with atypia
  - high rate of upstaging to in situ or invasive carcinoma (up to 30%)
- Treatment of intraductal papillomas without atypia remains controversial
  - Upstaging varies in the literature from 6-44%
  - The standard of care has been surgical excision of benign intraductal papillomas
  - New evidence suggests the upstaging of benign intraductal papillomas is lower than previously reported
  - Non operative management with imaging follow up is now being explored
PICO question

- Do benign intraductal papillomas of the breast still require surgical excision?
- Is conservative management with imaging follow-up a reasonable option compared to surgery in this group?

**P** - Patient, Population, or Problem
- How would you describe a group of patients similar to yours? What are the most important characteristics of the patient?

**I** - Intervention, Prognostic Factor, or Exposure
- Which main intervention, prognostic factor, or exposure are you considering? What do you want to do for the patient?

**C** - Comparison
- What is the main alternative to compare with the intervention?

**O** - Outcome
- What can you hope to accomplish, measure, improve or affect? What are you trying to do for the patient?
Systematic Review

• Methods
  – Database review yielded approximately 750 articles
    – Pub Med
    – Scopus
    – Cochrane

• Progress of the project
  – Currently reviewing the 750 articles to identify pertinent articles
Collaboration With Basic Scientists and Investigator-Initiated Trial

• Chemotherapy Induced Microvascular Dysfunction and the Role of Telomerase
• The Psychological Effects of Multi-gene Panel Testing on Breast Cancer Patients

Amanda L. Kong MD, MS
Mitochondrial Telomerase as Regulator of Mitochondrial Damage and Secondary Messengers in Chemotherapy Induced Microvascular Dysfunction

Co-PI: Andreas Beyer, PhD
The Problem

Cancer

1 in 2 American men
1 in 3 American women

- Hormone receptor blockage
- Growth factor inhibition
- DNA damage induction

Cardiovascular system

- Vascular Dysfunction
- Heart Failure
- Decreased Angiogenesis
- Metabolic defects
- Hypertension
- Atrial fibrillation

The Cardiovascular Disease Continuum
Medical Problem

Cancer Population + Chemotherapy

Cancer recurs
CV complication free

No PROBLEM (ULTIMATE CLINICAL GOAL)

Problem → Cancer death

Problem → CV related death

Problem → CV related and/or cancer related death
Microvascular endothelial dysfunction is an underlying cause of most Cardiovascular disease however few studies have directly linked microvascular defects to adverse cardiovascular events after cancer therapy.

Cancer therapy (chemo, Radiation or some immunotherapies) induces lasting impairments in endothelial dysfunction in human microvasculature that contribute to further advent events.
Effect of Doxorubicin on Microvascular Dilator Function

- Human Arterioles (coronary or adipose) (~150 µM ID)
- Doxorubicin - Widely used Chemotherapy with severe CV side effects including chronic HF

Ex vivo treatment

Endothelial dependent

Smooth Muscle dependent
Increased DNA damage and decreased Telomerase activity in Cancer patients

→ Is decreased telomerase activity responsible for chemotherapy-induced microvascular defects and can reactivation of telomerase overcome microvascular defects induced by anti-cancer therapy

Scuric et al 2017 doi:10.1038/s41523-017-0050-6
Mitochondrial Telomerase Activation Rescues Chemotherapy Induced Microvascular Defects
Evaluating the effects of genetic testing on patients' stress levels

Co-Investigators: Christianson, Geurts, Depas, Jacquart
Background

• Genetic screening has become increasingly important in treating breast cancer patients
  – 5-10% of breast cancers linked to mutations

• Field of genetic testing has rapidly expanded
  – Multigene panels are now available → positive, negative, VUS
  – Unclear what psychological consequences have resulted from the knowledge gained from these tests

• Evaluating the impact of genetic testing on stress levels will enable healthcare professionals to provide better care for patients both medically and psychologically through potential interventions to decrease stress
Hypothesis

• Hypothesis
  – Stress levels pre- and post-test will initially increase but then decrease in patients who test positive, will decrease in patients who test negative, and will remain elevated in patients with a genetic variant of uncertain significance (VUS)

• Prospective study
  – establish baseline stress levels, evaluate pre- and post- test stress levels at multiple time points, focus on the changes in stress levels for the different resulting subgroups
Study Design

• Patient population
  – currently diagnosed with breast cancer within the past 6 months or are classified as being at high risk for developing breast cancer
• Prior to genetics consultation
  – the State-Trait Anxiety Inventory (STAI) for Adults, baseline anxiety
  – the Health Anxiety Inventory (HAI, first 14 questions only)
  – the Cancer Worry Scale (CWS), baseline health anxiety
  – several additional demographic questions (Appendix IV)
• Subsequent testing with CWS and HAI after testing
  – 3 and 5 weeks, 3 and 6 months
Project Status

• Data Collection
  – Goal: 164 patients
  – Current accrual: 41
Investigator Initiated Trial

• Prospective Study Evaluating the Utility of Bioimpedence Spectroscopy in identifying Subclinical Lymphedema in Breast Cancer Patients

• Co-investigators: Verbeten, Gottschalk J
Project Status

- Upper extremity lymphedema is a risk of axillary surgery and adjuvant radiation in breast cancer patients.
- Current standard of care to objectively monitor lymphedema in the perioperative and surveillance settings
  - use of Gulick arm measurements
- Prospective study
  - evaluate the utility of an alternative method of identifying subclinical lymphedema by measuring extracellular fluid shifts with bioelectrical impedance spectroscopy as compared with standard circumferential tape.
- Study will focus on patients treated in the community setting at St Joseph Hospital, West Bend
International Collaboration

• Access to Cancer Care in a Resource-Constrained Country – Breast Cancer Treatment in Anambra State, Nigeria
  – Working in collaboration with Nnamdi Azikwe University Teaching Hospital (NAUTH) in Anambra State, Nigeria
  – Collecting data with respect to access to screening and treatment of breast cancer in this community
  – connecting with local officials for health care advocacy
Other

- **Alliance**
  - 11202: A Randomized Phase III Trial Evaluating the Role of Axillary Lymph Node Dissection in Breast Cancer Patients (cT1-3 N1) Who Have Positive Sentinel Lymph Node Disease After Neoadjuvant Chemotherapy
  - 11104: Effects of Preoperative Breast MRI on Surgical Outcomes, Costs, and Quality of Life of Women With Breast Cancer

- **COMET trial**
  - Comparison of Operative to Monitoring and Endocrine Therapy (COMET) Trial for Low Risk DCIS: A Phase III Prospective Randomized Trial

- **Prospective clinical database**
Pediatric Surgery Research Updates

David Gourlay, MD