OHSU DEPARTMENT OF SURGERY
Vol. 6, No. 1 Spring 2021

The Research Issue

On The Cutting Edge

OHSU

Message from the Chair

Kenneth Azarow, M.D., F.A.C.S., F.A.A.P.

Helen B. Tracy Professor in Pediatric Surgery

Mackenzie Professor and Chair

Ushering in a New Era of Surgical Discovery

AS WE ALL EMERGE FROM 2020, we continue to understand more about COVID-19 and its variants. Strategies to manage this virus have transpired and 2021 promises to be a year for the Department of Surgery to look to the future. A positive that has materialized from this crisis has been the weekly communication from the department as we remind folks of changes that the University and School of Medicine employ to keep us safe and continue the mission of our public institution. *On the Cutting Edge*, a quarterly publication to update faculty, staff, and alumni of the ongoing activities within the department, will make a slight adjustment and dedicate each edition to a separate mission. This current edition highlights the research initiatives and ongoing efforts surrounding the research mission.

Two years ago when I was named the Mackenzie Professor and Chair, I laid out a plan to re-energize the research efforts of the Department. Initiatives that are well underway are the hiring of designated surgical scientists, partnering our clinical faculty with basic science researchers to foster collaborative innovative efforts, and the hiring of a vice-chair of research (**Jonathan Brody, Ph.D.**) who crosses disciplines to support the innovative work occurring in all 9 of our divisions.

This edition of *On the Cutting Edge* will highlight just a few specific examples of how the department is developing its research line and recognize those individuals and programs who will take us into a new era of surgical discovery.

As you read ahead, I think many of you will be surprised at our new programs and the transformation of existing ones.

In 2014, then-Chair **John Hunter, M.D.**, invited interested faculty to a lunch where innovative ideas were shared. The "innovation lunch" eventually became an after hours extracurricular innovation internship and has now led to dedicated research fellowship for residents and the sponsorship of a national "Hack-a-Thon" (symposium to foster collaborations and innovations).

The Department is now home to its own research institute. With **Martin Schreiber, M.D.**, as director, The Donald D. Trunkey Research Center for Civilian and Combat Casualty Care was launched in 2020 and serves as a University-wide repository for all those interested in trauma related research.

Mackenzie Hall in Springtime

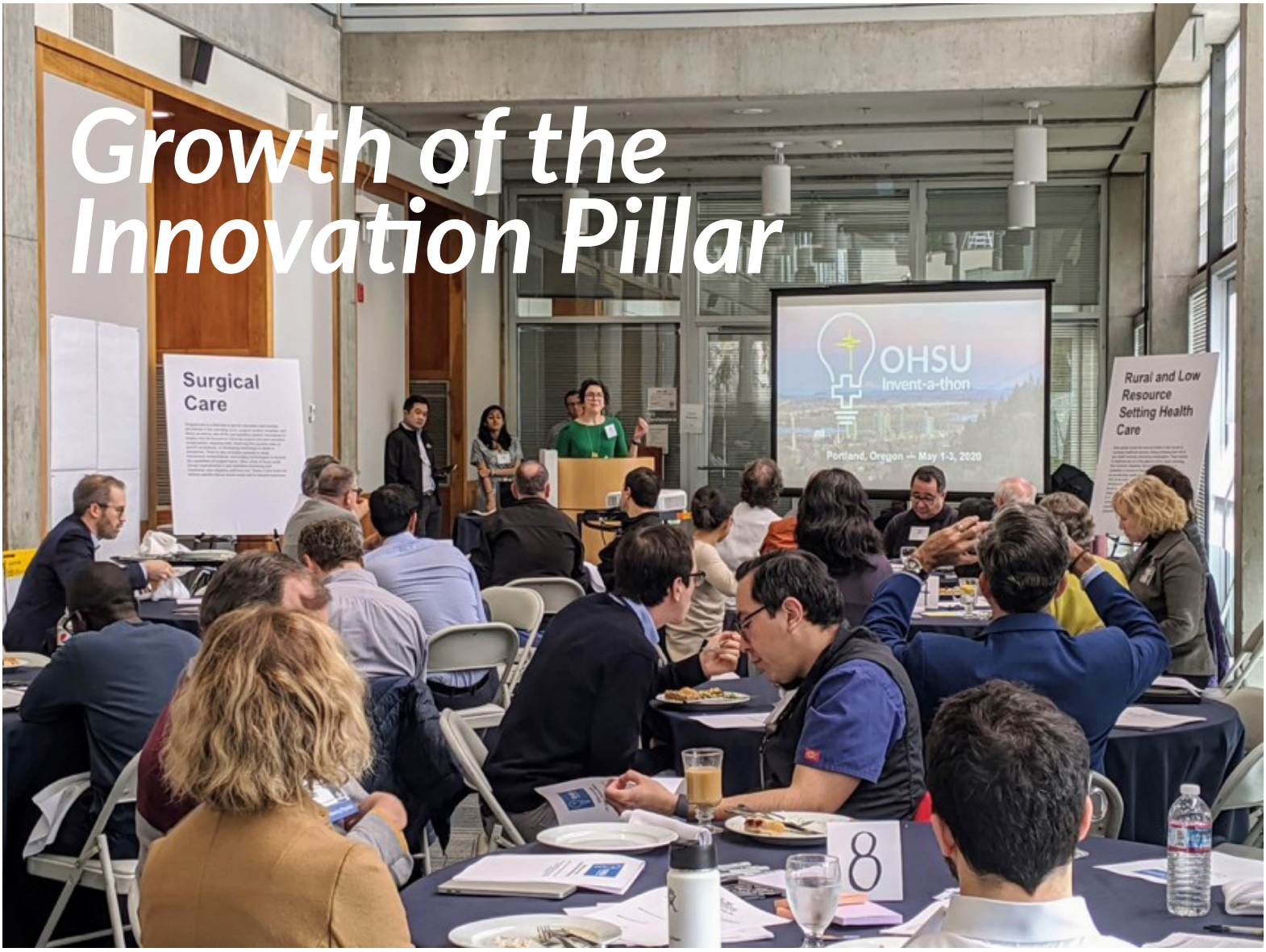
Pediatric Surgery is taking advantage of Doernbecher's renowned status as a quality-focused institution dedicated to the care of children to standardize and study dozens of pediatric clinical problems.

Our senior faculty will discuss their scientific collaborations with basic science research partners; and our junior faculty will discuss their research plans for the future. Lastly, we wanted to spotlight our department statistician, **Elizabeth Dewey**. As we have continued success at national and international presentations, publishing scholarly works that help determine standard of care across many disciplines, and reform education in surgery, Ms. Dewey has been a vital resource and a common thread tying our projects together.

I hope you enjoy this edition of *On the Cutting Edge*.

-Ken Azarow

Growth of the Innovation Pillar



Revamping the Surgical Innovation Program

SARAH BIBER, PH.D., is in the business of innovation. Under her leadership over the past two years, the Surgical Innovation Program has been significantly reimagined and expanded. Surgeons are natural innovators and a primary focus of SIP is on fully harnessing the department's considerable talent and problem-solving potential to accelerate and advance innovation and transform surgical care. Dr. Biber's work includes providing support and strategic guidance to individual innovators, helping to secure resources through grants and partnerships, facilitating adoption of impactful new technologies, and developing and implementing programs to expand the department's innovation capacity and footprint.

Building Innovation Capacity through Needs-Based Innovation and by Engaging the Broader Innovation Ecosystem

ON FEBRUARY 6, 2020, 40 thought-leaders from across OHSU came together for a workshop focused on developing impactful problem statements in advance of the planned in-person spring Invent-a-thon.

While gathering restrictions delayed the original event, the inaugural OHSU Invent-a-thon went virtual last October and brought together 12 departments at OHSU, 50 academic and industry partners, and more than 600 clinicians, entrepreneurs, designers, engineers, and business experts for a 48-hour healthcare hackathon (the recap is available at bit.ly/InventathonRecap). The focus of the event was on leveraging design-thinking and interdisciplinary teamwork to brainstorm and build med-tech and digital health solutions to pressing health care challenges, including surgical care. Forty-nine teams emerged from the event, were awarded $28,000 in prizes, and blew away the investor judges with the quality of the solutions they had launched.

The Invent-a-thon continues to make an impact. Five months later, half of these teams are continuing to advance their solutions, many through partnering incubator and accelerator programs, and 9 teams have incorporated. Seven of the new ventures are focused on advancing surgical care including one co-led by **Greg Landry, M.D., M.C.R.,** On April 21, the top teams will return to the virtual stage for the Invent-a-thon Post-Hack to compete for more than $40,000 in funding and support from partnering investment groups. Learn more and register for the Post-Hack at inventathon.org to cheer on rising stars and catch a glimpse of the future of med-tech and digital health.

Programs like the Invent-a-thon are critical to expanding our innovation capacity in both the short and long-term.

They empower budding entrepreneurs to flourish and provide them with the tools, inter-disciplinary connections, and support to launch successful new ventures. The Invent-a-thon team is in the process of publishing a study on the Invent-a-thon model in partnership with MIT Hacking Medicine and Portland State University.

An Exciting Era

In collaboration with the Knight Cancer Institute

Total Neoadjuvant Treatment Trials for Rectal Cancer

The Department of Surgery clinical teams are in close collaboration with the OHSU Knight Cancer Institute, currently supporting three trials for rectal cancer treatment.

INNATE

1

The most recent "**INNATE**" trial is a phase II randomized multicenter trial that examines the addition of a humanized monoclonal antibody (APX005M anti-CD40 maB) in the neoadjuvant chemotherapy regimen. Led by OHSU principal investigator **Adel Kardosh, M.D.**, of the Hematology Oncology Division, the addition of immunotherapy is designed to stimulate the anti-tumor immune response and shorten the course of radiation in rectal cancer treatment. It is thought that combining hypofractionated radiation and chemotherapy APX005M may generate a productive adaptive immune response to improve the pathologic complete response and improve long-term outcomes in treatment of rectal cancer patients with advanced local disease.

FIERCE

2

The second trial is a Phase 1b study known as "**FIERCE**," assessing the safety of neoadjuvant TAS-102 (tri**F**luridine/t**I**piracil) with concurr**E**nt **R**adiation in previously untreated resectable stage II and stage III re**C**tal canc**E**r. The trial is ongoing and accrued patients through this past year despite the pandemic, led by site PI and hematology/oncology faculty **Charles Lopez, M.D.** In particular, TAS-102, also known as Lonsurf, was shown in a clinical trial with patients with metastatic stomach and colorectal cancer to have improved survival outcomes. Primary endpoints similar to the INNATE trial are improved overall and disease-free survival and achievement of complete clinical response.

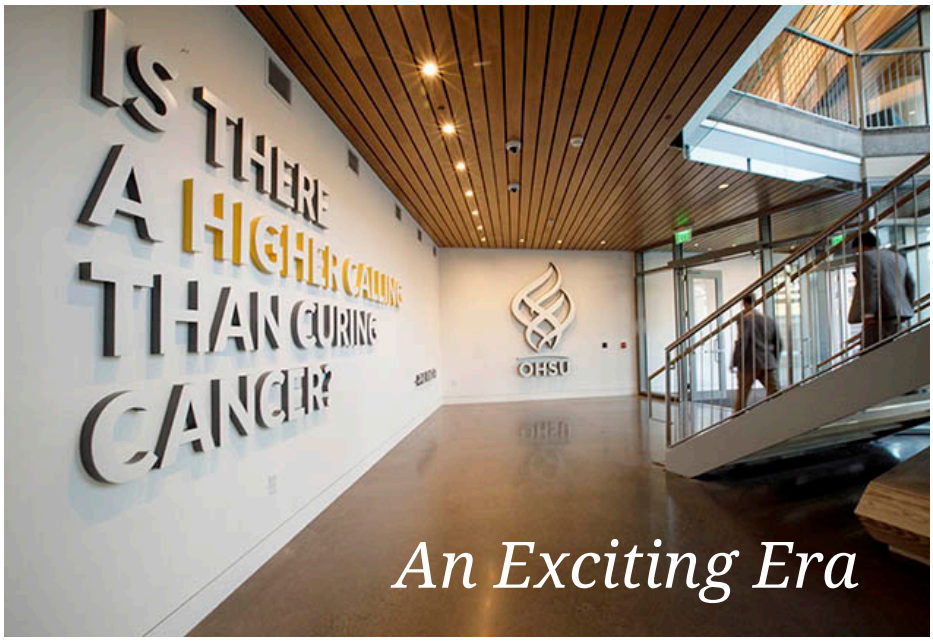
OPRA

3

Surgery faculty and site PI **Daniel Herzig, M.D.**, leads the NCI-sponsored Organ Preservation in Rectal Adenocarcinoma (**OPRA**) trial at OHSU. Dr. Herzig together with the multidisciplinary colorectal oncology team have established OHSU as a leading site in the study. OPRA compares total neoadjuvant treatment (TNT) protocols and evaluates the possibility of avoiding surgery in patients with stage 2 or 3 rectal cancer who have a complete response to TNT. The recently reported results demonstrate that over half of patients can safely omit surgery as part of their rectal cancer treatment.

In collaboration with the Knight Cancer Institute

Peri-operative and Innovative Surgical Trials in Hepatobiliary Oncology



An Exciting Era

*Two unique clinical trials in hepatobiliary oncology are underway with the Knight Cancer Institute and **Drs. Flavio Rocha** and **Skye Mayo***

OPT-IN

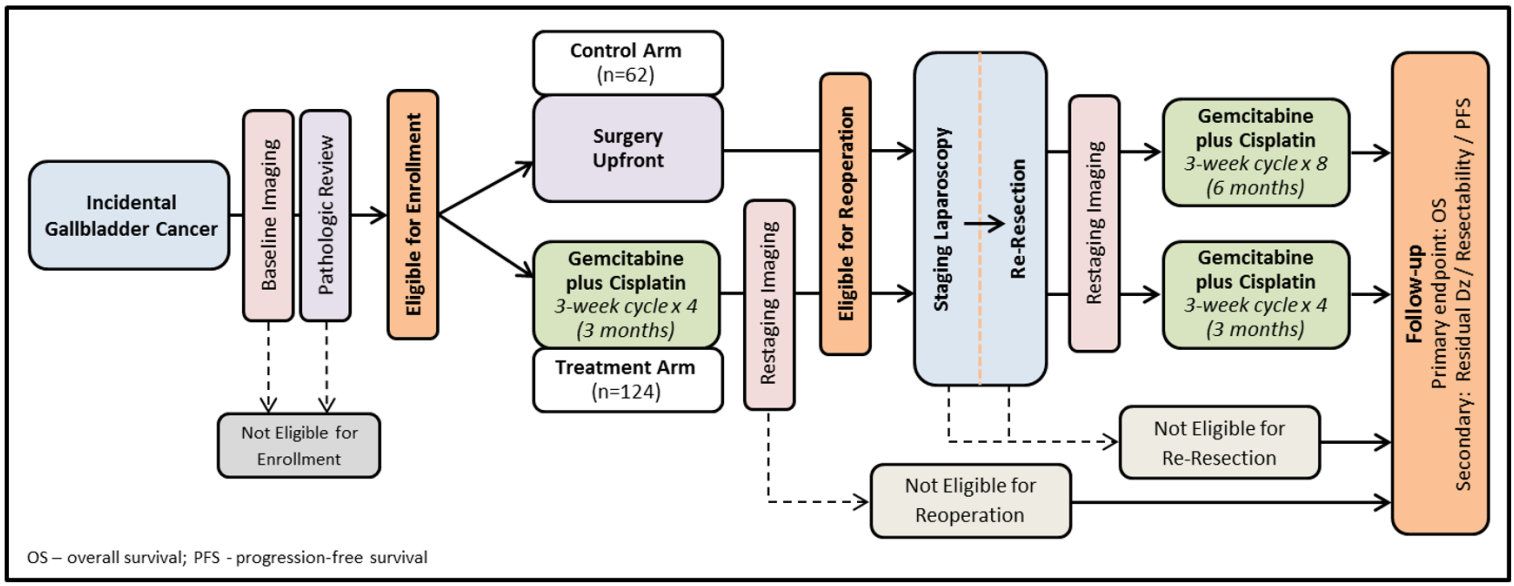
1

Gallbladder cancer (GBC) is the most common cancer of the biliary tract with 90 percent of patients having unresectable or metastatic disease at diagnosis. Patients often have advanced disease at diagnosis contributing to a 5-year overall survival (OS) of less than 5 percent. Globally, approximately 30 percent of all patients with GBC are diagnosed incidentally following cholecystectomy, with the proportion approaching 60 percent in the United States. Given the high risk of residual disease found at re-resection for patients with incidentally-diagnosed T2 and T3 GBC along with the upwards of 40 percent recurrent disease at 1 year after re-resection, there has been growing interest in the role of neoadjuvant treatment for these patients.

The **OPT-IN trial** (EA2197; ClinicalTrials.gov Identifier: NCT04559139) has recently been activated to compare peri-operative (neoadjuvant) gemcitabine plus cisplatin compared to post-operative (adjuvant) treatment with the same regimen.

This trial is sponsored by Eastern Cooperative Oncology Group (ECOG-ACRIN Cancer Research Group) and is being conducted as a collaborative effort through the National Clinical Trials Network (NCTN). It is led at the OHSU Knight Cancer Institute by **Flavio Rocha, M.D.**, Division Head of Surgical Oncology and Physician-in-Chief of the Knight Cancer Institute.

Figure 1. OPT-IN EA2197 trial schema



Patients must have undergone initial cholecystectomy with incidentally-discovered T2 or T3 GBC within 12 weeks prior to randomization. Patients will be randomized to either upfront re-resection followed by 6 months of adjuvant gemcitabine plus cisplatin or to 3 months of pre-operative gemcitabine-cisplatin followed by restaging and re-resection followed by 3 months of post-operative gemcitabine-cisplatin. (**Figure 1**). Importantly, this will be the first randomized trial done specifically for patients with incidentally-discovered GBC and will help to establish the standard of care for patients with this challenging disease.

For more information on the OPT-IN trial, contact OHSU Site Principal Investigator **Flavio Rocha, M.D., F.A.C.S.**, at rochaf@ohsu.edu.

In collaboration with the Knight Cancer Institute

Peri-operative and Innovative Surgical Trials in Hepatobiliary Oncology

HELIX ICC

2

Skye Mayo, M.D., M.P.H., from the OHSU Division of Surgical Oncology and Director of the Hepatic Arterial Infusion program, is opening up two trials for patients with advanced intrahepatic cholangiocarcinoma (ICC). This is a rare and deadly primary liver cancer that is increasing in incidence along with nonalcoholic fatty liver disease and steatohepatitis.

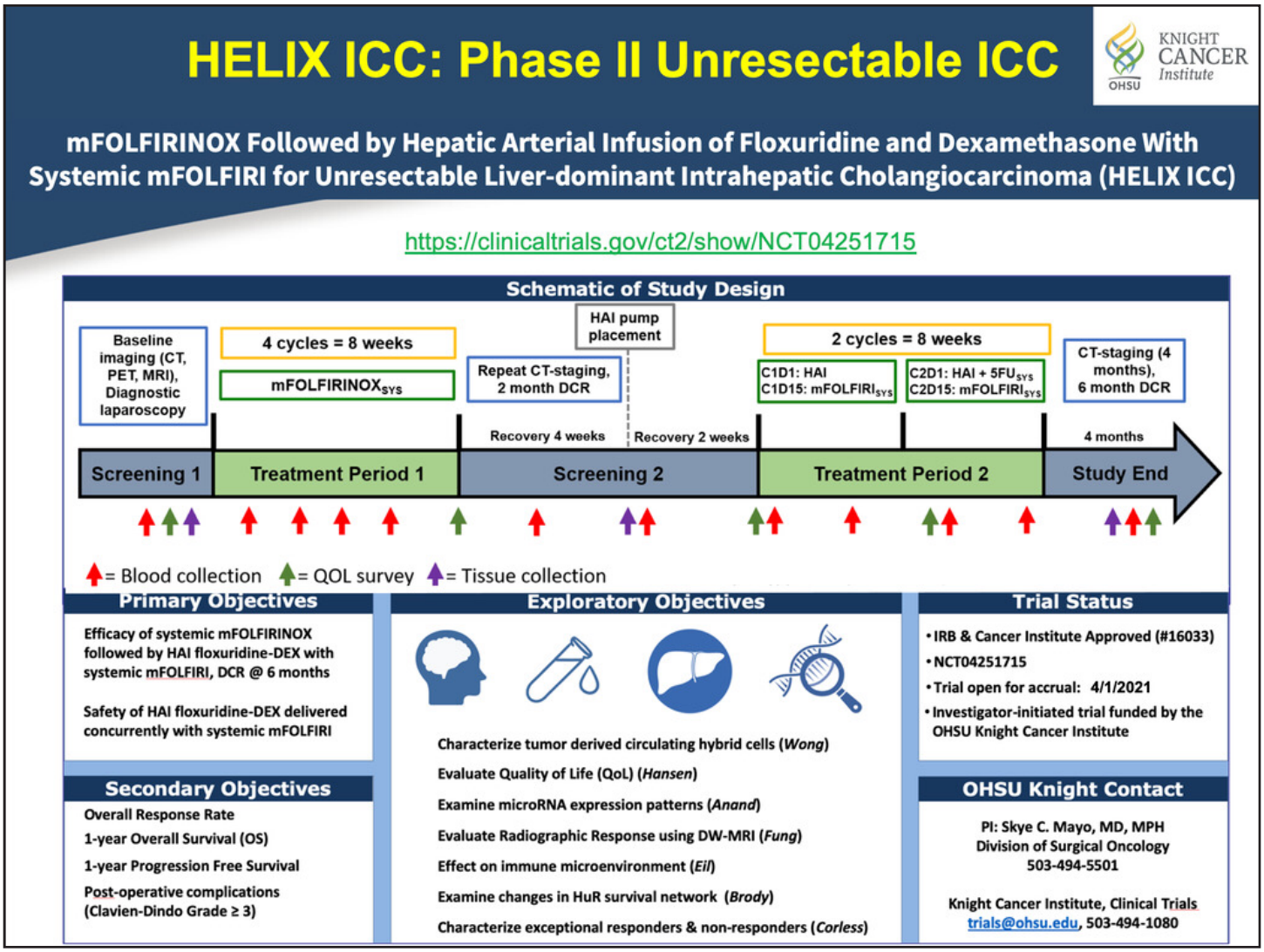
Similar to gallbladder cancer, patients are often discovered at an advanced stage of disease. For patients with liver-only disease, including multifocal intrahepatic lesions, or locally advanced disease making them unresectable, Dr. Mayo has developed an investigator-initiated Phase 2 trial funded by the Knight Cancer Institute (ClinicalTrials.gov Identifier: NCT04251715).

Patients with advanced liver-only ICC will be treated with 2 months of the triplet regimen FOLFIRINOX followed by placement of a hepatic arterial infusion (HAI) chemotherapy pump. Two weeks after the surgical pump placement patients will begin treatment with combined HAI chemotherapy along with systemic FOLFIRI (**Figure 1**). The primary endpoint is disease control rate at 6 months. As one of the only centers in the Western United States offering HAI, Dr. Mayo is pleased to be able to offer this treatment for patients with ICC that is showing increasing promise in other major cancer centers throughout the world. The trial opened for accrual in March 2021.

Dr. Mayo is also leading a single-arm trial as the OHSU site principal investigator for patients with patients with oncologically “high-risk” ICC ClinicalTrials.gov Identifier: NCT03579771). This includes patients without evidence of distant metastatic disease but with a >5 cm tumor, multifocal lesions in same segment, vascular invasion, or suspicious regional lymph nodes. Patients will be treated with the neoadjuvant regimen of gemcitabine, cisplatin, and nab-paclixel (“GAP”) for four 3-week cycles. The patients will then be restaged and taken for hepatic resection and portal lymphadenectomy. The primary objective is to assess the feasibility of neoadjuvant therapy with gemcitabine, cisplatin, and nab-paclitaxel. Secondary endpoints include resectability, recurrence-free survival, and overall survival.

For more information on these two trials for patients with cholangio-carcinoma, please contact **Skye Mayo, M.D., M.P.H.**, at mayos@ohsu.edu.

Figure 1. Schematic of advanced intrahepatic cholangiocarcinoma Phase 2 trial.



*This investigator-initiated trial includes many novel exploratory aims capitalizing on the innovative scientific expertise within our Department of Surgery and in the Knight Cancer Institute, including examining the effects of this treatment protocol on the immune microenvironment (**Robert Eil, M.D.**) and changes in the HuR survival network (**Jonathan Brody, Ph.D.**). Taken together, the objectives of this trial will help inform current treatment for this rare lethal cancer and importantly stimulate discovery of future options for these patients. This trial is endorsed and supported by the Cholangiocarcinoma Foundation (www.cholangiocarcinoma.org).*

Junior Faculty Gear Up for Bright Futures in Research

Casti Bhamidipati, D.O., Ph.D.,M.Sc.
Division of Cardiothoracic Surgery

Aortic Dissection and the TGFβ Pathway

Aortic dissection is a life threatening and serious medical complication where the inner layer of the aorta tears. The reported incidence of aortic dissection is 5 to 30 cases per 1 million people per year. However, the true incidence is unknown because many people die before a medical diagnosis.

Moreover, very little is known about the processes that cause aortic aneurysms to dissect and rupture. This gap in knowledge prevents the development of new medical therapies aimed at impeding the progression of aneurysm to dissection or rupture. Currently, the main aim of medical therapy is to reduce shear stress on the diseased aortic segment by reducing blood pressure and heart rate.

Aortic dissection arises from a tear in the aortic intima exposing the medial layer to the pulsatile blood flow. The intimal tear is frequently found in segments exposed to the greatest shear stress, namely the right lateral wall (opposite the main pulmonary artery) of the ascending aorta or in the proximal segment of the descending aorta. The progressive separation of the aortic wall layers results in the formation of a false lumen and its subsequent propagation can be followed either by aortic rupture in the case of adventitial disruption, or by re-entry back into the true lumen through another intimal tear. Aortic rupture quickly leads to exsanguination and death.

There is no good medical treatment that can prevent aortic dissection and rupture. The mainstay for management of ascending aortic dissection is open cardiac surgery. The role of medical therapy in the treatment of aortic dissection has been limited to prevention of blood pressure spikes through oral medications such as beta blockers, angiotensin receptor blockers, angiotensin converting enzyme inhibitors, and calcium channel blockers. However, these are very broad categories of medications with

limited specific application to aortic dissection.

Aortic degeneration in humans with Marfan Syndrome (MFS) is currently the most predictable model of aortic aneurysm formation. Autosomal dominant mutations in FBN1, the gene for fibrillin-1, cause MFS, whose major features include skeletal overgrowth, pectus deformities, scoliosis, lens dislocation, mitral valve prolapse, thoracic aortic aneurysm, and aortic dissection and rupture predominantly at the level of the ascending aorta and the sinuses of Valsalva. MFS results from an inherent structural weakness of tissues containing abnormal fibrillin-1 protein, hampering postnatal aortic homeostasis and leading to catastrophic aortic failure. Because of this, MFS is considered an aortopathy and is also considered a congenital heart disease.

In the general population, circulating fibrillin-1 fragments have been associated with aortic aneurysm — the highest levels of fibrillin-1 fragments were found in patients with acute ascending aortic dissection compared to those with chronic ascending aortic dissection. Therefore, even without a mutation in FBN1, pathogenic processes can lead to thoracic aortic aneurysm and dissection, resulting in the degeneration of the aortic wall and in the liberation of fragments of fibrillin-1 into the circulation. These findings support the use of FBN1 mutant mice as models of thoracic aortic aneurysm and dissection in the general population.

In vivo administration of TGFβ neutralizing antibodies in genetically modified Marfan mice restored the size of the aortic root and the architecture of the aortic wall, and losartan, an angiotensin II type 1 receptor (AT1R) blocker with presumed TGFβ neutralizing potential, prevented elastic fiber fragmentation, reduced TGFβ signaling, and reduced aortic root growth. Based on these observations, it was suggested that MFS-related aortic disease was driven by AT1R-dependent stimulation of TGFβ pathways. These findings propelled the idea of angiotensin II receptor blockers (ARBs), such as losartan, as a potential cure for MFS. Several clinical trials comparing the effects of ARBs and β-adrenergic blockers (BBs), however, showed no clear benefit of ARBs over BBs in respect to slowing the rate of aortic root dilatation in patients with MFS. Therefore, the role of TGFβ signaling in the pathogenesis of MFS remains controversial.

We accept that TGFβ likely plays an important role in aortic disease, but how TGFβ really works and how medical therapeutics could be targeted along the TGFβ pathway to intercept the cascade remain unclear. My research effort is aimed at using very unique FBN1 mutant mouse models that focus the aortic dissection and rupture in the ascending aorta in a predictable way, allowing for basic science investigations to evaluate the TGFβ pathway in aortic dissection and identify potential treatment targets. To this end, our research collaboration is submitting for extra-mural research funding in the upcoming cycle.

***Casti Bhamidipati, D.O, Ph.D., M.Sc.**, is Assistant Professor of Cardiothoracic Surgery, joining OHSU in 2017*

Andrea Stroud, M.D., M.S.
Division of Bariatric Surgery

Bariatric Surgery and Reduced Cancer Risk

Andrea Stroud, M.D., M.S., Assistant Professor in the Division of Bariatric Surgery, contends that obesity research is one of the most exciting and timely areas of biomedical inquiry. Obesity is a chronic disease that affects millions of individuals worldwide and continues to increase in prevalence. By 2030, more than half of American adults are expected to be affected by this disease. Thus, the potential for impact is high. As a bariatric surgeon, Dr. Stroud works directly with the individuals most seriously affected by this chronic disease. Her research program explores the association of obesity with certain types of cancer, with the goal of better understanding the underlying mechanisms that cause bariatric surgery patients to exhibit reduced cancer risk.

Dr. Stroud joined the Department of Surgery at OHSU in 2017, initially splitting her time between two clinical practices, including bariatric surgery on the main campus and general and emergency surgery at OHSU-affiliate hospital Portland Adventist. During this time she worked closely with her research mentor, Bruce Wolfe, M.D., developing and publishing a manuscript on incident cancer in the Longitudinal Assessment of Bariatric Surgery (LABS) cohort. She presented this work at the Top Scientific Paper session for the American Society for Metabolic and Bariatric Surgery at Obesity Week in 2019. In the fall of 2020, she transitioned to full-time practice at OHSU and is excited to be dedicating time to building upon the division's successful research track record.

Currently, Dr. Stroud is working on extramural funding to perform a focused analysis of stored blood samples from patients that developed breast cancer in the LABS cohort. Her interests include multiscale changes in metabolism and nutrition associated with bariatric surgery and significant weight loss, and their combined impact on obesity-associated diseases, including cancer. She will participate in the Nestle Clinical Nutrition fellowship this year and is a co-investigator on the division's NIH-funded grant investigating a novel essential amino acid supplement in post-bariatric surgery patients.

Groundbreaking Immune-Based Cancer Treatments

Robert Eil, M.D., is a surgeon-scientist focused on applying immunotherapy to cancers involving the liver, pancreas, and bile ducts. During his general surgery training at OHSU, Dr. Eil completed a research fellowship at the Surgery Branch of the National Cancer Institute, focusing on T cell biology and tumor immunology.

Following his clinical fellowship in surgical oncology at Memorial Sloan Kettering, Dr. Eil returned to OHSU in 2019 with appointments in the Departments of Surgery and Cellular, Developmental, and Cancer Biology. Dr. Eil's multidisciplinary expertise provides a unique perspective in alleviating suppression of T cell function in cancer to improve the lives and outcomes of patients.

This past January, Dr. Eil was one of three researchers across the U.S. awarded Transformative Cancer Research Grants from the AACR-MPM Oncology Charitable Foundations.

The awarded funding will support Dr. Eil's exploration of pathways to engineer the anti-tumor function of T cells, the cells that enact all effective immunotherapies for solid cancers. His research will test the hypothesis that cancer cell death suppresses T-cell function via potassium-sensitive signaling. His goal is to understand how cancer cell-death byproducts — specifically intracellular ions — influence T-cell activation in human cancers, and apply this knowledge to reprogram ion transport, an underappreciated aspect of T-cell biology.

Dr. Eil believes this exciting line of investigation has the potential to produce groundbreaking immune-based treatments to patients with treatment-resistant cancers.

Robert Eil, M.D.
Division of Surgical Oncology

Vahagn Nikolian, M.D.
Division of Gastrointestinal and General Surgery

Applying New Age Solutions to Age-Old Problems

From an academic perspective, my interests are broad but fall into three, and what I refer to as "Age Old," domains: Hernia Surgery, Surgical Education, and Improving Delivery of Care. Surgeon-scientists have focused on these problems for decades, but data elements and strategies for improvement are quickly evolving. My lab is focused on applying new age solutions for these age-old problems by maximizing technology and collaboration.

For hernia and abdominal core health, we have been using our unique data base at OHSU to provide answers to questions related to outcomes following traditional and more novel approaches to reconstruction. Along with **Robert Martindale, M.D., Ph.D.**, and **Sean Orenstein, M.D.**, we're proud to lead and contribute to multi-institutional projects aimed at improving hernia care. We have partnered with, and are actively contributing to the Abdominal Core Health Quality Collaborative, a group of more than 250 surgeons from around the country. The ACHQC allows for retrospective studies, with more than 75,000 cases abstracted over the last few years – kind of like NSQIP for hernia surgery.

Surgical education is similarly evolving. COVID has served as a natural experiment to the potential of telecommunications in education. We are exploring real-time teleproctoring for medical students, residents, and surgeons in practice. Beyond real-time proctoring, we are working to better understand what happens in the operating room and how to maximize education with assessment and feedback tools like OpTrust. Most recently, I'm happy to announce that we have set up the Surgical Telecoaching and Telementoring collaborative—STAT. This OHSU-led initiative has partnerships with multiple

institutions around the country and connects senior trainees and junior faculty with sub-specialty surgeons for video coaching sessions on commonly performed operations. Our STAT Collaboration allows surgeons to review their "game tape" and proactively improve during their transition to practice.

Finally, for delivery of care, our surgical telehealth analytics and research laboratory is working to understand and optimize telehealth solutions. Our lab is one of the first to be set up intentionally as a tele-lab. Our lab meetings are virtual and we have team members stationed all around the country. Through this approach, we are breaking down geographic barriers in academics and working to break them down for patients as well. The lab is actively working on projects centered on health care policy, implementation science, surgical outcomes, and experiences for the various stake holders involved in telehealth encounters. We have developed dozens of project templates that can be applied to any disease process or patient population. Through this approach, we're excited to help identify potential projects and work together to deliver high-impact work.

***Vahagn Nikolian, M.D.**, is Assistant Professor of Gastrointestinal and General Surgery, joining OHSU in 2019*

JONATHAN BRODY, PH.D., WAS NAMED VICE CHAIR OF RESEARCH FOR THE DEPARTMENT OF SURGERY IN 2019 and is the Associate Director of Translational Research for the Brenden Colson Center for Pancreatic Care. He is a member of the Knight Cancer Institute and the Department of Cell, Developmental & Cancer Biology Cell.

Dr. Brody's lab focuses on many molecular aspects of pancreatic cancer, including developing ways to target a pro-survival network his team has identified in pancreatic cancer cells, and optimizing current targeted therapies used in the clinic. Dr. Brody came to OHSU with an additional focus on elements of the tumor microenvironment, taking advantage of his lab's innovative models and techniques to further explore an understudied mechanism of gene regulation. Finally, Dr. Brody, who won awards for education and mentoring at his previous institution, has a passion for mentoring not only his students in the lab, but helping surgery faculty and residents successfully navigate their research portfolios and interests. He has hit the ground running since joining OHSU and is working hard to continue to grow a strong research infrastructure for the Department of Surgery.

Initiation and Growth of the Donald D. Trunkey Center

Building an Interdisciplinary Research Consortium Across the Pacific Northwest to Advance Trauma Care

Launched in April 2020 in honor of the late emeritus OHSU chair of surgery **Dr. Donald D. Trunkey,** the **Donald D. Trunkey Center for Civilian and Combat Casualty Care** is on a mission to synergize and advance trauma research, innovation, and patient care across OHSU and the Pacific Northwest. To date, the Center, led by **Martin Schreiber, M.D.**, has created a research consortium that spans across 18 different departments and 3 schools at OHSU, regional research hubs like the Veterans Administration and Pacific Northwest National Laboratory, and numerous industry partners.

The **Trunkey Center Seminar Series** has served as a centerpiece of activity and helped catalyze the Center's growth. Each month the Seminar Series brings together around 100 researchers working across trauma-related disciplines, highlights cutting edge research in the field, and serves as a focal point for new collaborations. Speakers include basic scientists, clinicians, engineers, epidemiologists, and public health experts, many of whom were brought together for the first time by the Trunkey Center. The series has a central role to play as the Center continues to grow and amplify research in trauma by fostering interdisciplinary collaboration, increasing research funding, and accelerating bench to bedside discoveries.

Join the Trunkey Center mailing list to receive news updates and invitations to the Trunkey Center monthly seminar series.

Partnering with the Community to Mitigate the Impacts of Urban Violence and Trauma

THIS PAST JANUARY the Trunkey Center was honored to host a panel discussion on **"Urban Violence. This is Our Lane."** The event brought together researchers, community members, and a group of incredible panelists to explore urban violence, its impact, and mitigation strategies from the public health, public policy, and healthcare provider perspectives. The discussion was moderated by trauma head and Trunkey Center Director, **Martin Schreiber, M.D.**, who was joined by the following:

Andre Campbell, M.D., Professor of Surgery at the University of California, San Francisco, School of Medicine and an attending trauma surgeon at Zuckerberg San Francisco General Hospital and Trauma Center

Kathleen Carlson, Ph.D., Associate Professor at the OHSU School of Public Health and a core investigator with the Health Services Research Center of Excellence and the VA Portland Health Care System

Nike Greene, Director of Office of Violence Prevention under the Portland Mayor's Office

Roy Moore, Outreach Coordinator at Healing Hurt People

Martin Schreiber, M.D., Professor and Head of the Division of Trauma, Critical Care and Acute Care Surgery and the Director of the Donald D. Trunkey Center for Civilian and Combat Casualty Care, OHSU

The panel event drew more than 125 attendees and highlighted the importance of addressing trauma patient needs across the continuum of care and in partnership with the community. As a follow up to this event, the Trunkey Center will be partnering with the Office of Violence Prevention at the Portland Mayor's Office to implement Healing Hurt People at OHSU. Healing Hurt People is a hospital-based, trauma-informed, community-focused violence intervention and prevention program that supports young people of color who have experienced violence and traumatic injury. It is dedicated to decreasing violence and trauma through public health policy, research, and training. We hope that this initiative will serve as a jumping off point for research collaborations with the city and the OHSU School of Public Health aimed at addressing and mitigating the impact of urban violence.

Innovation in the Time of COVID-19

Over the past year, the pandemic has created an unprecedented need for new solutions and spurred an explosion of creativity, resourcefulness, and innovation within the department. Some highlights of COVID-19 related innovation initiatives supported by Surgical Innovation Program include:

CRISIS Vent

PI: Albert Chi, M.D.

Dr. Chi and team have developed a low-cost 3D printable ventilator that is optimized for low-resource settings. The team was awarded a Biomedical Innovation Award to further refine the vent through bovine testing and is now in the process of completing FDA clearance and licensing the technology to several developing countries.

Remote Critical Care Management Program

PI: David Zonies, M.D., M.P.H., M.B.A.

Dr. Zonies and team received funding from Medical Technology Enterprise Consortium to develop and implement a versatile tele-critical care platform to extend urgently needed critical care expertise from centers of excellence like OHSU to underserved areas.

Proximie

PI: Cherrie Abraham, M.D.

Dr. Abraham has helped pioneer the Proximie technology at OHSU and beyond. The Proximie augmented reality platform enables remote proctoring of surgeries and sharing of expertise while simultaneously reducing exposure during COVID and saving money. It is currently being used for a clinical trial at OHSU focused on advancing resident training and is being actively explored for other valuable applications.

SureFlo

PIs: David Warner, M.D., and Albert Lwin, M.D.

Drs. Warner and Lwin are the inaugural Surgical Innovation Fellows and are being mentored by Dr. Biber over the course of their research year to turn a problem into a product. The team was awarded a Biomedical Innovation Award to develop SureFlo, a novel connected wearable blood flow monitoring system. A prototype is currently being built in partnership with two engineering faculty at Oregon State University.

SureFlo

We expect digital health and telemedicine to be a growing focus of innovation efforts within the department. The pandemic has underscored the immediate and ongoing need for advances in these technologies. Additionally, recent faculty recruits **Rushi Thanawala, M.D.**, and **Vahagn Nikolian, M.D.**, have active and expanding research programs in this area.

Pediatric Surgery

Transforming Clinical Practice with Outcomes-Based Research

Randall Children's Hospital

In the **Division of Pediatric General Surgery**, there are nine faculty across two tertiary children's hospitals with diverse research interests and expertise. We partner with faculty in other departments – including neonatology, pediatric gastroenterology and the biomedical sciences – to collaborate on clinical and translational research. Our group currently has more than 70 active studies, at various stages of development, enrollment and publication. Many of these are multi-institutional prospective and retrospective studies within three national research consortia.

Doernbecher Children's Hospital

Clinical outcomes research represents a large focus of our effort.

For example, our "**Minimizing Variance in Pediatric Surgery**" program investigates the effectiveness of evidence-based protocols for the management of common pediatric surgical diseases ranging from perianal abscesses to gastroschisis. Additional studies include those investigating congenital anomalies, pediatric solid tumors, and global health.

Pediatric trauma research results from work at the two Level 1 Pediatric Trauma Centers in Oregon including 15 current studies.

Basic science efforts include building a biobank of patient serum, stool and surgical tissue specimens – with **Brian Scottoline, M.D.**, Neonatology – and we are now conducting microbiome-based and stem-cell-based experimental research into pediatric inflammatory intestinal diseases such as necrotizing enterocolitis.

Additionally, grant-funded research includes large national clinical studies related to congenital diaphragmatic hernia (**DHREAMS**), pediatric inflammatory bowel disease (**ENRICH-US**), and pediatric disaster management (**WRAP-EM**) as well as institutional studies focused on hypercoagulability in injured children.

"Our faculty are proud to mentor students, residents and pediatric surgery fellows during their clinical and/or dedicated research time. We offer a pediatric surgery research fellowship to interested residents, for one or two years. As our division's director of research, I lead our effort and welcome new ideas for collaboration. The breadth of pediatric surgery offers limitless research opportunities, and we strive to make a meaningful difference in the care of our patients."

-Elizabeth Fialkowski, M.D., Pediatric Surgery Assistant Professor and Research Director

Shining Examples of Setting up a Surgery-Based Registry

Nancy Puzziferri, M.D., M.S.C.S., Bariatric Surgery

Daniel O. Herzig, M.D., M.B.A., Colorectal Surgery

Bruce M. Wolfe, M.D., Bariatric Surgery

Sur·ger·y Reg·is·try
/sərj(ə)rē rejəstrē/
noun

A surgery-based clinical registry is simply a record of patient variables – baseline and outcome – organized in a database.[1] The uniformity of data collected is aided by following traditional observational study methods. Registries are usually disease-based. Their intent is to provide a mechanism to evaluate and improve outcomes for patients.

Historically, registries were created by researchers, funders, or institutions for scientific purpose. In the last decade, novel patient-powered registries and/or networks have been developed. Patient-powered registries shift the focus from outcomes deemed meaningful by traditional healthcare stakeholders to outcomes defined by patients as mattering to them.[2]

Quality Assurance

Registry quality improves with establishing a priori questions prior to database creation, standardizing outcome measures, implementing strategies to minimize missing data, and attaining external funding to support its mission. Quality of clinical research questions guiding a registry are enhanced with collaboration of multidisciplinary nonsurgical specialties. Sources for data can be electronic medical records, clinician or patient report, collected bio-specimens, survey results, and others. The over-arching benefits of a registry are the opportunity to answer many yet unanswered questions about treatment comparative effectiveness, disease natural history, intervention safety, or quality of medical care.

Pros and Cons

There are pros and cons of registry development within or outside of a formal clinical trial. Databases generated within randomized controlled trials are usually well-funded, and suffer less cohort attrition. Well-designed self-standing registries, by definition, provide real-world and broader patient settings perhaps belying more realistic outcomes or enabling greater generalizability.

continued on next page

Creating a local registry as a first step to multicenter-funded research participation

Colorectal surgery exemplifies an excellent way to establish academic surgical research on a foundation of clinical care. In 2006, the Division of General and Gastrointestinal Surgery funded a research coordinator position to establish a novel registry for patients with or at risk for colorectal cancer, including hereditary syndromes. While commonplace now, this was the first OHSU clinical registry to also collect tissue and blood samples to create a biobank of specimens that can be tied to specific clinical scenarios. Since surgeons are involved in patient care at the time of tissue collection, surgeon involvement can lead to substantial enrollment in registries that include tissue.[3] The registry and biobank proved to be a valuable resource to coordinate translational research projects with OHSU basic science investigators.

These collaborative studies can provide a source of funding as the registries mature. The research infrastructure in place through building the registry can also support participation in multicenter clinical trials, as well as selected industry-sponsored trials that are aligned with the mission and vision of the institution. A key to being a site for high-profile multicenter trials is showing ability to recruit patients locally. Demonstrating patient accrual in a registry without early funding, and by collaborating with other subspecialists who have access to the required support, provides a solid foundation for building capacity for clinical trial participation.

Participation in these trials includes funding that can sustain the research infrastructure. Both local and multi-center collaborative research efforts result in long-standing access to rich databases for subsequent projects beyond inceptive aims.

Use that participation in multicenter-funded research to leverage its registry locally

The Division of Bariatric Surgery participated in and houses a 7-year database from the Longitudinal Assessment of Bariatric Surgery (LABS), a 10-year NIH-funded multicenter prospective study. At the start of the study many important, fundamental bariatric surgery questions were yet unanswered. Though well-funded, the feasibility of answering all bariatric surgery comparative treatment questions was limited. Feasibility constraints dictated thoughtful strategizing and deliberate focus on only the most important questions e.g. surgical effect on type 2 diabetes or quality-of-life. Standardized variables were created to answer questions comparing safety, weight-loss efficacy, obesity-comorbidity outcomes and mechanisms between different bariatric procedures.[4] Bio-specimens were included to analyze gut and fat hormones, genetics, and biomarkers. Behavioral, quality of life, and multiple other health-related data were collected by self-report. The LABS database is perhaps singular in its 93% retention of a >2400 patient bariatric cohort through 7 years.[5] Though LABS recruitment has concluded, data continues to be collected as further analyses of bio-specimens is done. The LABS registry is actively in use for addressing new questions and providing pilot data for new grant applications.

References:

1. Gliklich RE, Leavy MB, Karl J, Campion DM, Levy D, Berliner E. A framework for creating standardized outcome measures for patient registries. J Comp Eff Res. 2014;3(5):473-480.

2. Workman TA. Engaging Patients in Information Sharing and Data Collection: The Role of Patient-Powered Registries and Research Networks. Rockville (MD)2013.

3. Tsikitis VL, Lu KC, Douthit M, Herzig DO. Surgeon leadership enables development of a colorectal cancer biorepository. Am J Surg. 2013;205(5):563-565; discussion 565.

4. Belle SH, Berk PD, Courcoulas AP, et al. Safety and efficacy of bariatric surgery: Longitudinal Assessment of Bariatric Surgery. Surg Obes Relat Dis. 2007;3(2):116-126.

5. Courcoulas AP, King WC, Belle SH, et al. Seven-Year Weight Trajectories and Health Outcomes in the Longitudinal Assessment of Bariatric Surgery (LABS) Study. JAMA Surg. 2018;153(5):427-434.

By Any 'Counting' Method: a VERY Successful Year in Biostatistics

Department biostatistician Beth Dewey reports the numbers

It's been over 365 days since OHSU went into modified operations on March 16, 2020. Since then, at least 55 Principal Investigators in the Department of Surgery have requested statistical support on more than 60 total projects. In 2020, our department investigators published 21 manuscripts and submitted 31 abstracts.

- We examined the effects of bariatric surgery on diabetes remission.
- We evaluated our own resident interview process for bias.
- We identified differences in gene expression between early and late-onset colorectal cancer.
- We published multiple papers on the effects of tranexamic acid and traumatic brain injuries.

During my four-year tenure with OHSU, 2020 has been our most published year. And there's still so much more to come.

As the biostatistician in the Department of Surgery, I do my best to count all the things surgeon scientists want me to count. But if we're counting success, then I would say that working together to do good work during this particularly challenging time has been the best metric.

On The Cutting Edge

School of MEDICINE

OHSU Department of Surgery
Mail code: L223
3181 S.W. Sam Jackson Park Rd.
Portland, OR 97239
Tel: 503 494-7758
Fax: 503 494-5615

Non-Profit Organization
U.S. Postage
PAID
Permit No. 722
Portland, Oregon

[Address]

OHSU School of Medicine | Department of Surgery

Department Chair

Kenneth Azarow, M.D. 503 494-7758

Division Chiefs

Susan Orloff, M.D. 503 494-7810
Abdominal Organ Transplantation

Farah Husain, M.D. 503 494-2681
Bariatric Surgery

Howard Song, M.D., Ph.D. 503 494-7820
Cardiothoracic Surgery

V. Liana Tsikitis, M.D., M.C.R., M.B.A. 503 494-6900
Gastrointestinal and General Surgery

Mubeen Jafri, M.D. 503 494-7764
Pediatric Surgery

Juliana Hansen, M.D. 503 494-7824
Plastic and Reconstructive Surgery

Flavio Rocha, M.D. 503 494-5501
Surgical Oncology

Martin Schreiber, M.D. 503 494-5300
Trauma, Critical Care and Acute Care Surgery

Gregory Landry, M.D., M.C.R. 503 494-7593
Vascular Surgery

Questions or comments? Email *On the Cutting Edge* Editor Sara Szymanski at szymanss@ohsu.edu – we'd love to hear from you.

Oregon Health & Science University is a nationally prominent research university and Oregon's only public academic health center. It educates health professionals and scientists and provides leading-edge patient care, community service and biomedical research.

Change can't happen if we see things just one way. That's why diversity is so important to OHSU.