

CENTER FOR INTERVENTIONAL ENDOSCOPY

C **2019** **E**

REPORT CARD

The AdventHealth Center for Interventional Endoscopy (CIE) is a state-of-the-art unit providing tertiary level endoscopic services for patients with complex digestive diseases.

The endoscopists at CIE are well-rounded and trained in cutting-edge techniques and latest technologies available for the endoscopic management of digestive disorders. Our team advances collaborative research not only within the AdventHealth System but globally to further the treatment and knowledge of digestive diseases.

2019 FACTS AND FIGURES

10,135

TOTAL ADVANCED PROCEDURES



4,356 EUS

Top 3 in the World | **#1** in the Americas

1,851 ERCP | **#1** in the Southern United States

1,089 Tissue Resection Procedures

38 Publications | **5** Published
Randomized Trials

#1 Most Attended EUS Symposium
in the Americas



"Orange County is fortunate to be home to AdventHealth CIE, which is recognized as a leader in the field of interventional endoscopy.

The fact CIE is ranked in the top three endoscopy units in the world is a testament to its excellence in specialized treatment and clinical research.

This cutting-edge health care center draws patients from around the country and the world to Orange County. Congratulations!"

- Jerry L. Demings
Orange County Mayor



2019 REPORT CARD

AdventHealth Center for Interventional Endoscopy

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Overview from Physicians

Dear Colleagues,

I am pleased to present the annual report card of the AdventHealth Center for Interventional Endoscopy. This report outlines our procedural volume, treatment outcomes, research investigations, educational endeavors, scientific presentations and other significant milestones achieved in 2019.

In 2019, we performed more than 10,000 complex endoscopic procedures which included 4,356 endoscopic ultrasound (EUS) examinations, thereby ranking CIE amongst the top three large volume EUS units in the world. Furthermore, CIE is retaining its status as the largest volume EUS program in the Americas. Our ERCP volume surpassed 1,850 and we performed more than 1,000 endoscopic mucosal resection procedures. Our third space endoscopy and submucosal dissection programs continue to expand with the performance of more than 100 procedures in 2019.

We concluded five published randomized trials and the CIE faculty authored 38 peer-reviewed publications and seven textbook chapters in 2019. The Orlando Live EUS Symposium drew more than 300 delegates, making it the most well attended EUS symposium in the Americas.

As our program continues to expand and grow, I invite you to visit CIE in person and give us the opportunity to share our vision with you.

Sincerely,



Shyam Varadarajulu
Medical Director
AdventHealth Orlando
Center for Interventional Endoscopy



Ji Young
Bang, MD



Muhammad
Hasan, MD



Robert
Hawes, MD



Udayakumar
Navaneethan, MD



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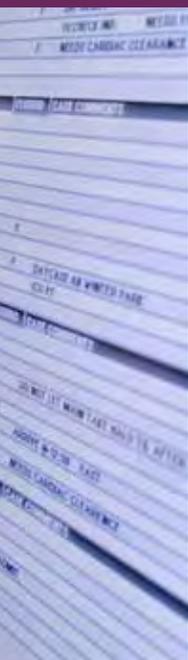
AdventHealth
CENTER FOR
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ENDOSCOPY



**AdventHealth
Center for
Interventional
Endoscopy**

STAFF





"I have been to CIE thrice in 2019 with a major illness. The physicians and staff not only got me through very difficult and painful times but also became very dear friends. They made me feel safe, sane and healthy. I love the CIE team very dearly."

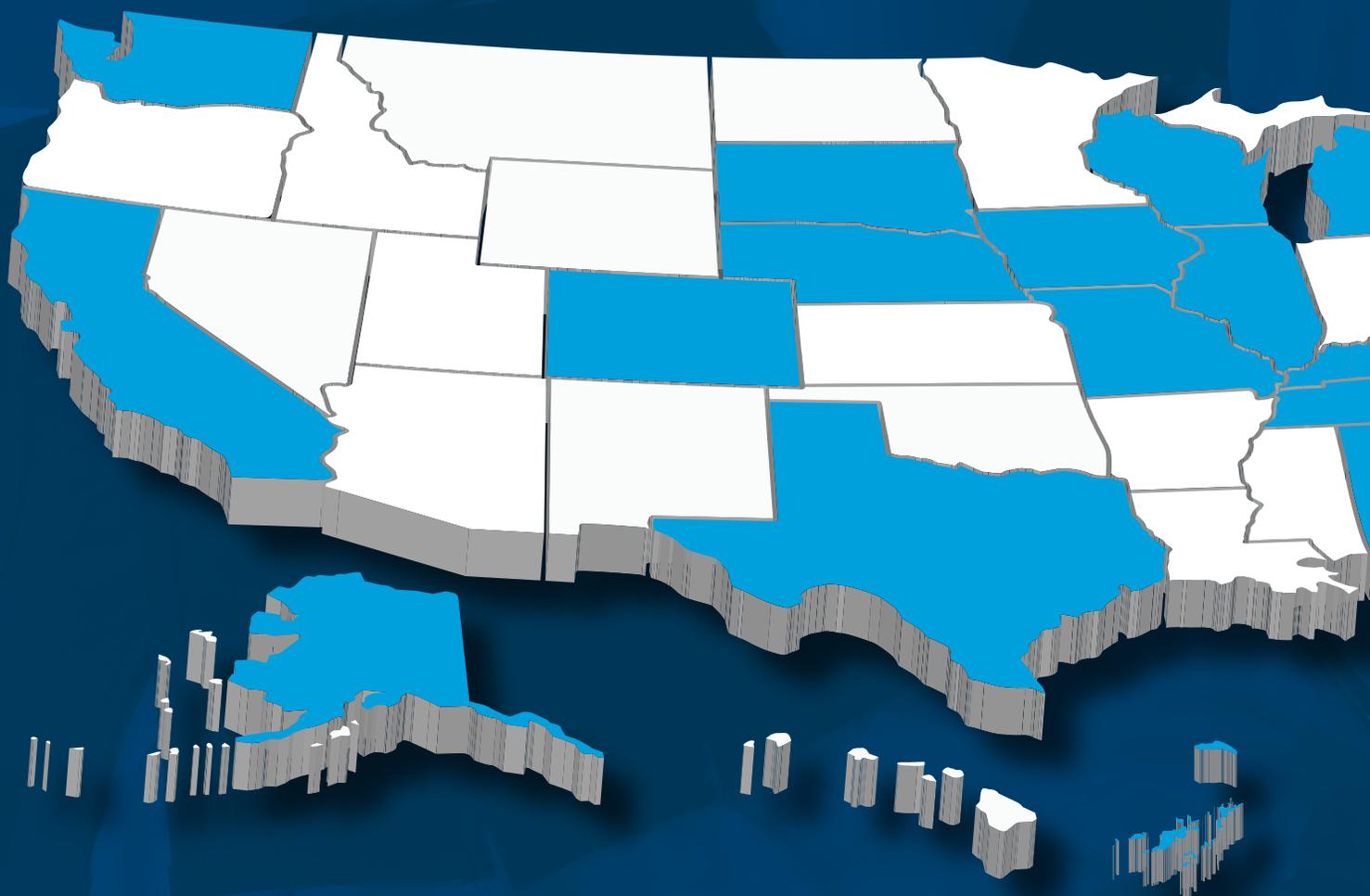
- Joan Taylor | Mount Dora, Florida

Patient Referral Statistics

Patients are referred to CIE for tertiary-level endoscopic care from across the United States as well as internationally. In 2019, patients were referred from 10 countries and nationally from 28 states. More than 50% of treated patients originated from outside the Tri-County area.

50%

of patients treated at CIE originated from outside the Tri-County area.



For more information or to refer a patient, call 855-341-3411.



8,781 | Total Patients



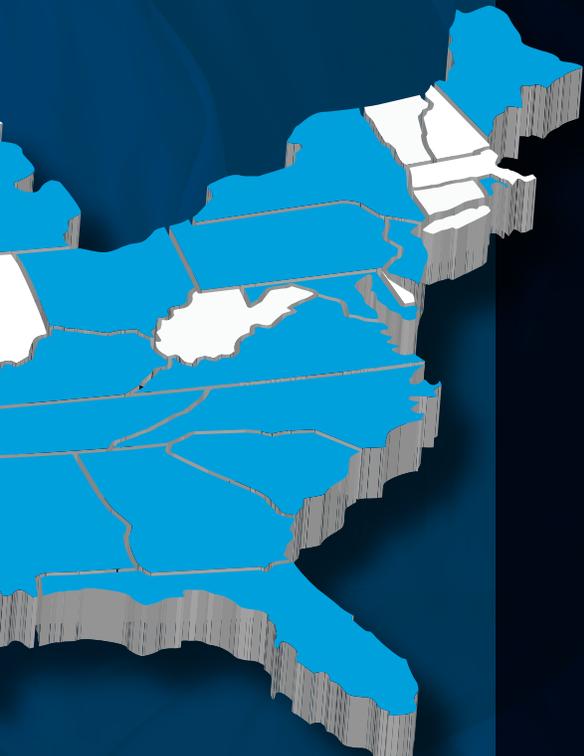
28 | **140**
States | Patients



8,612 | Florida Patients
Tri County 4,348 | Non-Tri County 4,264



29 | International Patients



“The endoscopists at CIE not only provide cutting-edge services in a timely and efficient manner but are also available at all times to answer my questions, accept a transfer or help develop a plan of care for my patients with complex clinical problems.

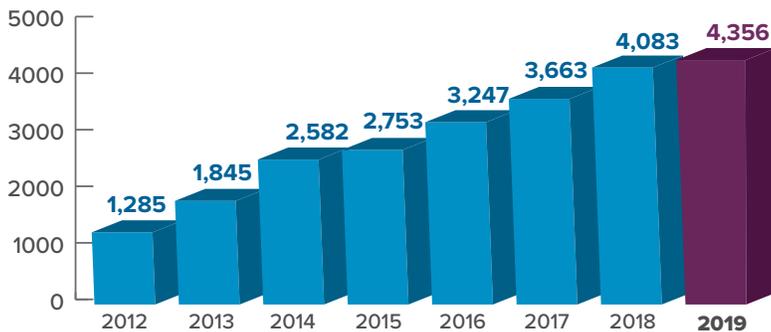
Every patient that I referred received world-class care and my patients had only the best of compliments for the CIE physicians and staff.”

–Dr. Rafael Ching Companioni | Gastroenterologist, Panama City, Florida

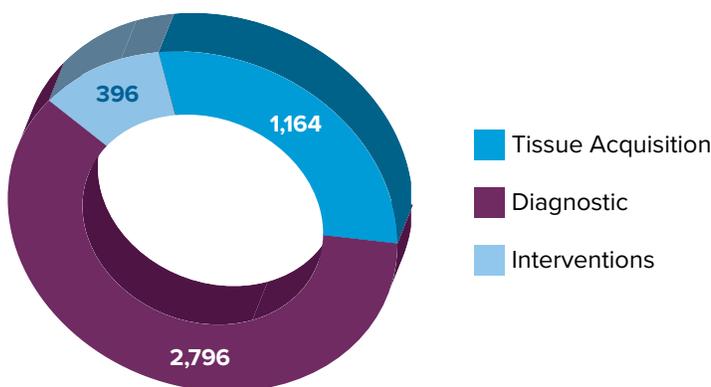
Endoscopic Ultrasound Program

The EUS volume at AdventHealth CIE stands at 4,356, ranking the program amongst the top three units in the World. Over the last six years the CIE investigators have successfully conducted eight randomized trials related to diagnostic and interventional EUS, more than any other center in the world.

EUS Volume



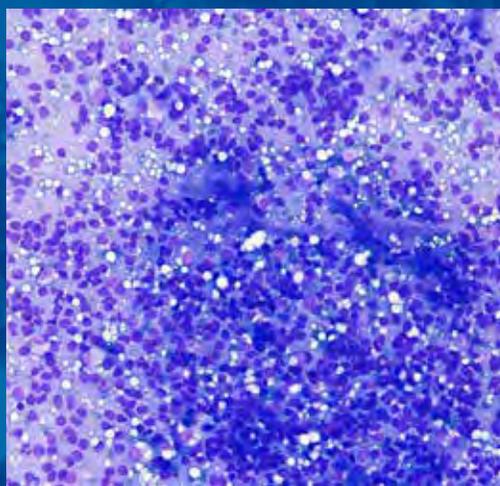
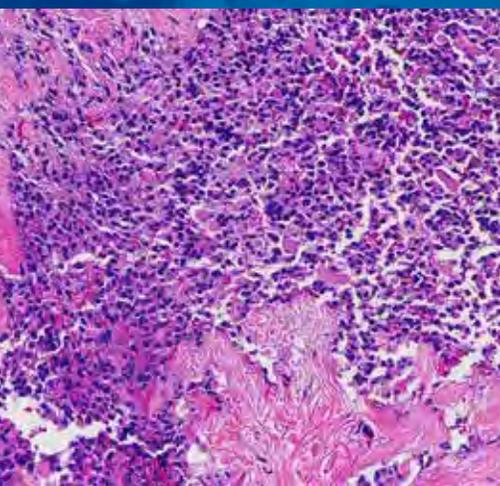
EUS Procedures



Diagnostic EUS

Clinical trials conducted at CIE have conclusively proven that fine needle biopsy (FNB) is superior to fine needle aspiration (FNA) for the sampling of solid mass lesions under EUS-guidance. When compared to FNA, the number of needle passes required to establish an onsite diagnosis is fewer, the yield at cell block is higher and molecular profiling and/or ancillary testing can be performed successfully when using the new generation FNB needles. The CIE investigators have also proven that performing tissue acquisition without the aid of suction or stylet yields high quality tissue. The 22G needle may be most ideal for sampling solid mass lesions.

Presently there are four FNB needle types that are commercially available with different needle tip geometries, three sampling techniques (suction, no suction and stylet-pull) commonly adapted for tissue procurement and two methods for specimen processing (rapid onsite evaluation and cell block). It is still unclear which technique is more suited for a specific needle and if there is a correlation to the method used for specimen processing.



Tissue acquisition at EUS-guided fine needle biopsy.

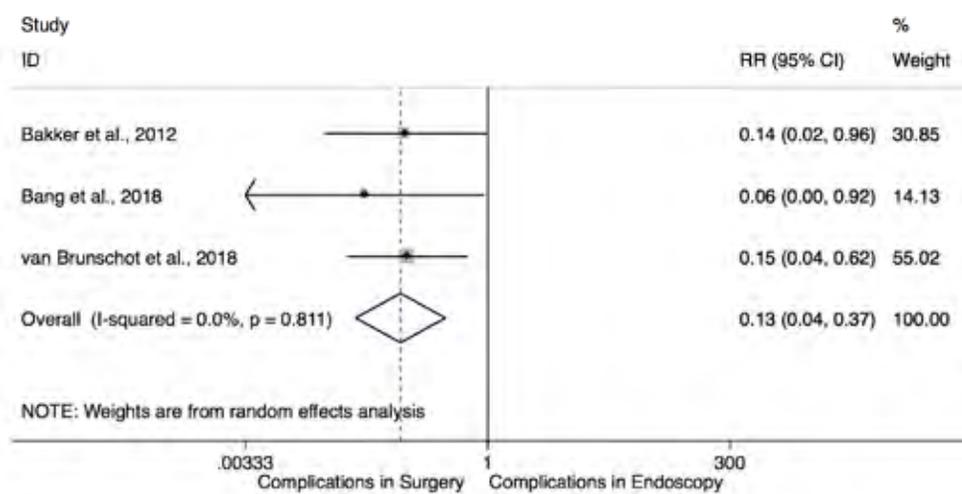
The CIE investigators have concluded a randomized trial that attempts to answer these questions using digital analysis to assess specimen quality (ClinicalTrials.gov Identifier: NCT04085055). The findings from this randomized clinical trial will be presented at the United European Gastroenterology Week 2020 in Amsterdam.

Although EUS-guided liver biopsies are being increasingly performed, it is unclear if the specimen quality is comparable to that of interventional radiology-guided liver biopsies. In an ongoing randomized trial conducted at CIE, patients with liver disease referred by transplant hepatologists undergo sampling using EUS-guidance or the percutaneous approach. A pathologist blinded to the technique of tissue acquisition will evaluate the specimen and grade the histological quality of the liver tissue.

Twenty-five patients have been enrolled to-date in this important ongoing clinical investigation (ClinicalTrials.gov Identifier: NCT04003766).

Interventional EUS

In a recent meta-analysis, the CIE group has demonstrated that an endoscopy-based approach is superior to minimally invasive surgery for the management of patients with infective necrotizing pancreatitis. Patients undergoing an endoscopy-based treatment approach have less organ failure, fewer enterocutaneous/pancreatic fistulae and a shorter length of hospital stay. Now that the endoscopy-based approach has been proven to be superior to surgery, it is important to refine the procedural steps and the endoscopic techniques to achieve superior clinical outcomes.



Forest plot comparing pancreatic fistula between endoscopy and surgery.

Endoscopic Ultrasound Program Continued



Walled-off necrosis CT.



Necrotic collection - EUS.



Direct endoscopic necrosectomy.

Endoscopic treatment approach in infective necrotizing pancreatitis involves two critical steps: transluminal drainage and direct endoscopic necrosectomy. It is unclear if performing an endoscopic necrosectomy at index intervention yields better clinical outcomes as opposed to a step-up approach that incorporates transluminal drainage, followed by necrosectomy on an as required basis. To investigate this question, the CIE team has commissioned the Direct Endoscopic Randomized Trial vs. Step-up Transluminal Interventions in Necrotizing Pancreatitis (DESTIN). This AdventHealth-led randomized trial includes an impressive team of international centers in Asia and the United States (ClinicalTrials.gov Identifier: NCT04113499).

High-quality databases which allow the capture of multiple variables that include long-term follow-up is needed for meaningful clinical research. At CIE, our interventional EUS database for diseases such as necrotizing pancreatitis prospectively captures almost 400 variables over a 60-month period. Institutional review board approved databases are hypothesis driven and registered in *ClinicalTrials.gov*.

A burning question in the mind of every academic endosonographer is, where is interventional EUS headed in the next decade? We, at CIE, believe the future of interventional EUS is intertwined tightly with tumor ablation and palliation. More innovation in terms of energy platforms for tumor ablation, such as radiofrequency and microwave, will be seen in this new decade. Technical innovations that enable palliation of tumor-related symptoms, such as obstructive jaundice via dedicated biliary drainage platforms and management of luminal obstruction, by means of EUS-guided anastomosis, will soon be developed. The CIE investigators in collaboration with industry partners are at the forefront of these technological innovations that hopefully will positively impact patient survival and quality of life.

Upcoming Study

Prospective validation of a tailored treatment strategy taking into consideration the type of fluid collection, degree of necrosis, pancreatic duct integrity, extension to the lower abdomen and the presence or absence of ongoing infection.

Luminal Interventions Program

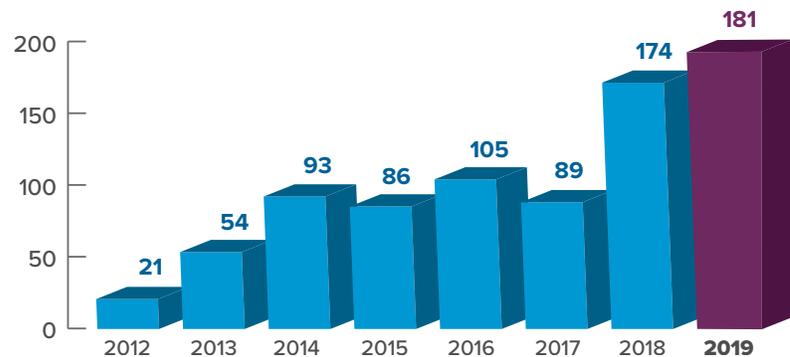
Value-Based Research

Peptic ulcer disease is the most common cause of non-variceal upper gastrointestinal bleeding, which is a common medical emergency requiring hospitalization. Despite improvement in endoscopic and pharmacologic therapies, bleeding continues or recurs in more than 10% of patients after initial endoscopic hemostasis. The clinical and cost implications of failed endoscopic hemostasis in this patient population are unclear. In an ongoing audit we aim to determine the clinical and financial implications of failed endoscopic hemostasis in

the AdventHealth Central Florida acute care hospitals. Based on this retrospective data and utilizing the latest endoscopic technology, we will develop a 'step-up' treatment protocol which will be applied prospectively to all patients presenting with peptic ulcer bleeding. We believe that this endeavor will not only fill much needed knowledge gaps in the literature but also positively impact the clinical outcomes, length of hospitalization and financial costs.

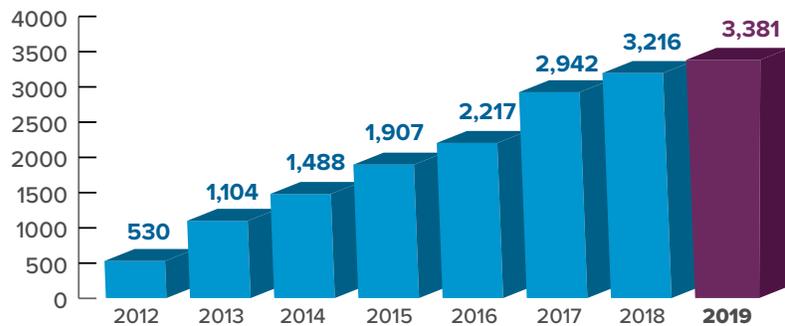
Radiofrequency Ablation

Clinical trials evaluating the utility of Optical Coherence Tomography for identifying neoplasia in Barrett's esophagus, inflammatory bowel disease and indeterminate biliary strictures are in progress.



Other Interventions

- EGD
- Colonoscopy
- Enteral Feeding Tubes
- Luminal Stenting
- Glue Injection
- Zenker's Diverticulectomy
- Fistula Closure (suturing clips)



Double Balloon Enteroscopy

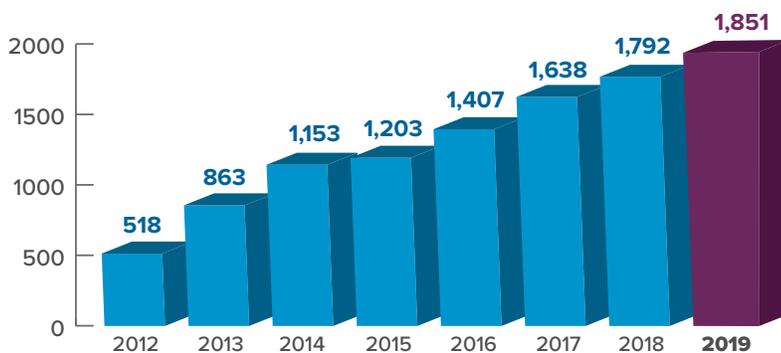
- CIE provides a wide range of diagnostic and therapeutic services that include management of small bowel bleeding, evaluation of inflammatory bowel disease, and treatment of small bowel strictures and polyps.
- Clinical trials evaluating the utility of motorized spiral enteroscope will commence in the near future.



ERCP Program

Our ERCP volume has steadily increased over the past six years to reach 1,851, which ranks CIE as the No. 1 unit by volume in the Southern United States. During this period, we have conducted three randomized trials and three other principle clinical trials are currently underway.

ERCP Volume



Research

Indeterminate biliary strictures can be challenging to evaluate and oftentimes patients may need to undergo multiple endoscopic, radiological or sometimes even minimally invasive surgical procedures to establish diagnosis. Biomarkers are being actively investigated in many disciplines of medicine as a noninvasive method for diagnosing cancer. We are presently conducting a prospective cohort study examining the role of lipidomics in differentiating benign from malignant biliary strictures. The findings of the study may be particularly relevant to patients with biliary strictures deemed indeterminate, such as, in the setting of primary sclerosing cholangitis or autoimmune cholangiopathy.

Adverse Events

Death.....	1
Perforation.....	0
Bleeding.....	3
Cholangitis.....	13
Pancreatitis.....	44

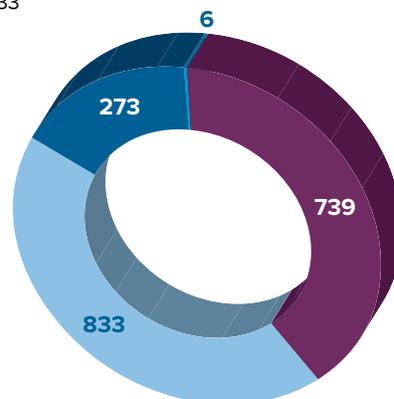
Treatment Outcomes

Technical Success.....	1,829
Technical Failures.....	22
Altered Anatomy.....	7
Failed Cannulation.....	15

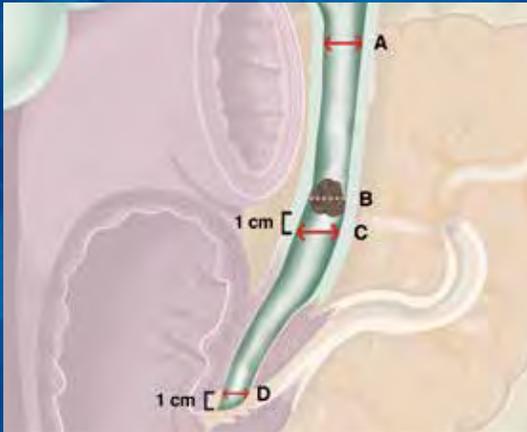
Procedures by ASGE Complexity Level

Single-operator
Cholangioscopy = 133

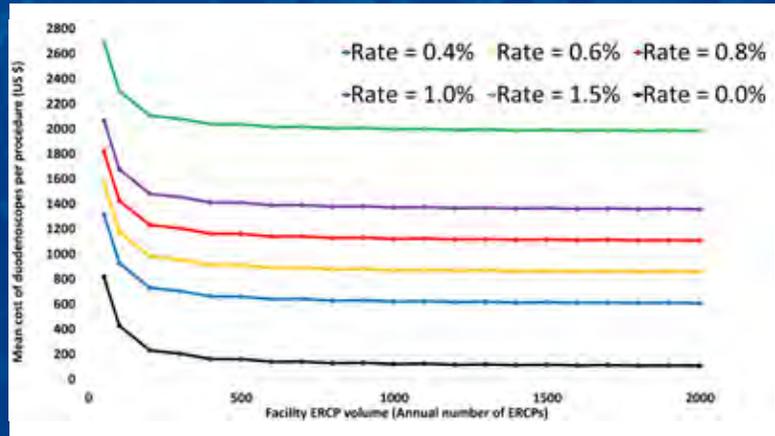
- Grade 1
- Grade 2
- Grade 3
- Grade 4



Although ERCP is commonly used for treating bile duct stones, there is no established road map to managing difficult stones which cannot be extracted using standard retrieval techniques. In a randomized trial of 66 patients with difficult bile duct stones in whom standard maneuvers at ERCP were ineffective, we identified factors predictive of the need for adjunctive measures such as single-operator cholangioscopy-guided laser lithotripsy and large balloon sphincteroplasty. Our study demonstrated that when the ratio



Treatment predictors for bile duct stones.



Cost analysis of single-use duodenoscopes.

of stone to bile duct size exceeds 1, the use of laser lithotripsy was predictive of successful outcome. Likewise, when the ratio of distal bile duct to widest area in the common bile duct was less than 0.5, sphincteroplasty alone was ineffective and adjunctive measures such as lithotripsy were required to achieve optimal outcomes. The findings of the study were presented at the United European Gastroenterology Week and published in *Clinical Gastroenterology and Hepatology*. These findings are presently being validated prospectively in a multicenter trial.

Although most post-ERCP biliary tract infections are attributed to suboptimal ductal drainage, transmission of infection, including carbapenem-resistant *Enterobacteriaceae* (CRE) by contaminated reusable duodenoscopes has been reported. To overcome this limitation, a single-use duodenoscope has recently been developed. However, given the widespread use and large volume of ERCPs being performed worldwide, the financial viability of this concept is unclear. Utilizing an activity-based costing and financial model, we estimated that the per-procedure cost of a single-use duodenoscope in the United States can vary from \$797 to \$1,547 for centers performing at the 75th percentile of ERCP procedure volume and from \$1,318 to \$2,068 for centers performing at the 25th percentile of procedure volume, based on infection rates of 0.4% to 1%, respectively. As a natural evolution of this analysis, a randomized trial has been commenced at CIE to compare the functionality and safety of the newly developed single-use versus reusable duodenoscopes. In order to facilitate an objective evaluation, recently, the CIE team developed a dedicated duodenoscope assessment form that was validated at seven tertiary academic medical centers. This validated assessment form will be used for objective comparison of both duodenoscopes. We expect

to present the findings of this study, supported by a grant from the AdventHealth Cancer Institute, at the United European Gastroenterology Week 2020 in Amsterdam.

Exposure to ionizing radiation remains a hazard for patients and health care providers. Therefore, we evaluated the utility of an artificial intelligence (AI) enabled fluoroscopy system to minimize radiation exposure during image-guided endoscopic procedures. In a prospective study of 100 consecutive patients who underwent fluoroscopy-guided endoscopic procedures utilizing either a conventional or artificial intelligence enabled fluoroscopy system (that utilizes ultra-fast collimation to limit radiation exposure only to the region of interest) we observed that radiation exposure to patients was significantly lower and scatter effect to endoscopy personnel was less by 60% for AI enabled fluoroscopy as compared to conventional system. The findings of the study were presented at the American College of Gastroenterology plenary session in San Antonio and published in the *American Journal of Gastroenterology*.

Other randomized trials currently in progress examine the role of pancreatic duct stent placement in patients with ductal disruption due to acute necrotizing pancreatitis, and the role of radiofrequency ablation in patients with cholangiocarcinoma.

What new developments will we see in ERCP in the next decade? The CIE investigators opine that there will be serious attempts by both endoscopists and industry to minimize, if not eliminate, the risk of duodenoscope-related infections. Additionally, new technology and techniques will evolve to ablate biliary tract tumors that are currently a challenge to treat.

Tissue Resection and Third Space Endoscopy Program



Endoscopic mucosal resection & submucosal dissection.

Tissue Resection Program

We performed 1,089 endoscopic mucosal resection (EMR) procedures in 2019 of which 69% involved lesions in the lower gastrointestinal tract. Although the upper gastrointestinal tract EMR procedures comprised only 31%, the number of procedures performed for treatment of laterally spreading duodenal lesions has increased significantly in recent years. Additionally, we have a robust esophageal program where patients with early-stage neoplasia are treated using multimodality techniques such as radiofrequency ablation and submucosal dissection.

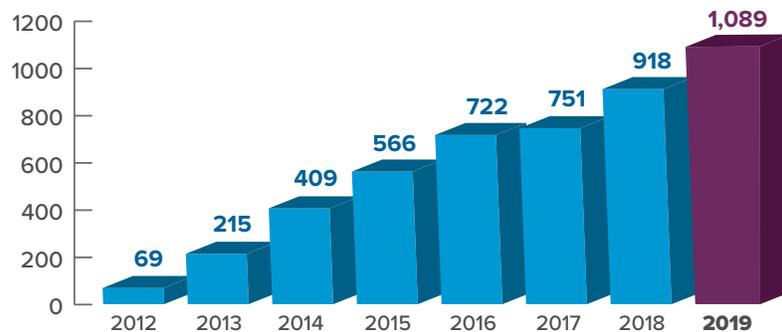
Our endoscopic submucosal dissection (ESD) program continues to evolve with the performance of

over 50 procedures in 2019. With the support of the AdventHealth Cancer Institute, we plan to establish a Visiting Professorship in 2020 whereby overseas experts in tissue resection will spend two weeks at CIE on a bi-annual basis to mentor, share their expertise and collaborate in research with the CIE faculty.

Research

CIE was part of a multi-center United States trial that compared prophylactic clip placement versus conservative management, after removal of large colon polyps in more than 900 patients. The study demonstrated that prophylactic clips were particularly beneficial when placed after removal of large, right sided colon polyps as they decreased the rates of post-procedure gastrointestinal bleeding. Randomized trials aimed at decreasing post-procedure adverse events and polyp recurrence after EMR of large colon polyps are currently in progress.

Endoscopic Mucosal Resection Procedures



Third Space Endoscopy Program

The Third Space Endoscopy Program was started in late 2017 with performance of the first per-oral endoscopic myotomy (POEM) procedure for the treatment of achalasia cardia. Subsequently, G-POEM for refractory gastroparesis and later the submucosal tunneling endoscopic resection (STER) procedure for gastric spindle cell neoplasms were performed.

Our Third Space Program is still in evolution with the combined procedural numbers being 76 over a two-year period. The CIE physician tasked with developing this program,

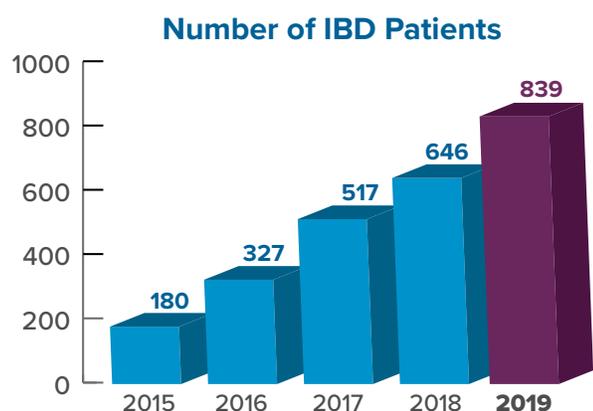
Dr. Ji Young Bang, is collaborating with industry partners and other investigators to develop novel tools and techniques to pioneer and advance this growing discipline.



Third space procedural steps.

Inflammatory Bowel Disease Program

The mission of the program is to provide state-of-the-art comprehensive care for patients with complex inflammatory bowel disease (IBD), to be at the forefront of research and foster cutting-edge clinical trials of the latest treatment options.



The program is designed to provide multidisciplinary clinical care and to rapidly translate research breakthroughs into treatments. The program brings together many specialists – medical gastroenterologists specializing in IBD, colorectal surgeons, radiologists, nutritionists, pathologists, psychologists, wound care (stoma) specialists, researchers, nurses, and others—with the shared goal of implementing a comprehensive, evidence-based approach to care for our patients.

Our clinical trial developmental program enables us to improve existing therapies and provide novel treatment for patients with ulcerative colitis and Crohn’s disease.

Additionally, at CIE, we place special emphasis on the endoscopic management of IBD complications that include strictures, fistulae and leaks. We utilize chromoendoscopy and confocal imaging to investigate early-stage neoplasia and offer endoscopic mucosal resection as a treatment option.

New Initiatives

- **Global Interventional IBD Group:** CIE is part of an international subspecialty group that coordinates clinical, educational, and investigational endoscopy based research trials for patients with IBD.

- **Clinical Trials:** Our research team comprises four study coordinators and one IBD specialist who is the principal investigator. The team coordinates 20 studies that include both investigator-initiated and pharmaceutical-sponsored (Phase II to IV) investigations.
- **IBD Board:** Modeled on functioning of the tumor board, the IBD program conducts periodic review of challenging cases with input from the IBD specialist, colorectal surgeons, radiologists and pathologists to coordinate medical, endoscopic and surgical management. The IBD board facilitates excellence in patient management via multidisciplinary evaluations.
- Endoscopic stricturotomy and stent placement is being offered as a treatment option for patients with refractory luminal strictures.
- Endoscopic fistula closure with over the scope clips is being offered for fistula treatment.

Annual Symposium in Inflammatory Bowel Disease

CIE hosts a nationally recognized annual symposium devoted to IBD in the month of April. The symposium draws experts from around the United States and Europe who share their expertise and explore the latest advances in the treatment of IBD.

Scientific Presentations



Digestive Diseases Week | San Diego, CA

- Ji Young Bang, Udayakumar Navaneethan, Muhammad Hasan, Bryce Sutton, Robert Hawes, Shyam Varadarajulu. Optimizing outcomes of single operator cholangioscopy (SOC)-guided biopsies: results of a randomized trial.

Pancreas Club 2019 | San Diego, CA

- Ji Young Bang, Udayakumar Navaneethan, Muhammad Hasan, Bryce Sutton, Robert Hawes, Shyam Varadarajulu. Endoscopic ultrasound-guided celiac ganglion radiofrequency ablation versus celiac plexus neurolysis for palliation of pain in pancreatic cancer: a randomized controlled trial.
- Ji Young Bang, C. Mel Wilcox, Juan Pablo Arnoletti, Shyam Varadarajulu. Superiority of endoscopic interventions over minimally invasive surgery for infected necrotizing pancreatitis: a meta-analysis of randomized trials.

United European Gastroenterology Week | Barcelona, Spain

- Ji Young Bang, C. Mel Wilcox, Juan Pablo Arnoletti, Shyam Varadarajulu. Superiority of endoscopic interventions over minimally invasive surgery for infected necrotizing pancreatitis: a meta-analysis of randomized trials.
- Ji Young Bang, Udayakumar Navaneethan, Muhammad Hasan, Bryce Sutton, Robert Hawes, Shyam Varadarajulu. Endoscopic management of difficult bile duct stones: results of a randomized trial.

Honors and Awards

The study “Endoscopic management of difficult bile duct stones: results of a randomized trial” was honored at the United European Gastroenterology Week 2019 with a Special Recognition Award.

Research in 2019

EUS

Registry for EUS evaluation of pancreatic cysts

Primary Aim: Prospective database to study the natural history of pancreatic cyst lesions.

EUS-guided pancreatic cyst ablation

Primary Aim: To maintain data on all patients undergoing EUS-guided ablation of pancreatic cysts using paclitaxel and gemcitabine and to assess its treatment efficacy.

Randomized trial comparing endoscopic ultrasound-guided liver biopsy vs. percutaneous liver biopsy

Primary Aim: Compare diagnostic adequacy and histological characteristics between techniques.

Randomized trial comparing biopsy needles and different sample techniques for endoscopic-guided fine needle biopsy of solid pancreatic mass lesions

Primary Aim: Compare the histopathological quality of the tissue samples and diagnostic yield between FNB needles using the different sampling techniques.

Registry of endoscopic management of pancreatic fluid collections (PFCs)

Primary Aim: Prospective database to study the algorithm-based management of pancreatic fluid collections.

Multicenter randomized trial comparing direct endoscopic necrosectomy vs. step-up transluminal endoscopic interventions in infected necrotizing pancreatitis (DESTIN)

Primary Aim: Compare rate of reinterventions between treatment groups.

Prospective registry of radiation exposure measurement in procedures utilizing fluoroscopy

Primary Aim: Evaluate the radiation exposure when an additional radiation exposure reduction component is added to a pre-existing fluoroscopy machine used during endoscopic procedures.

The Orange County Bleeding Consortium (OCBC): Registry of patients undergoing endoscopic procedures for upper gastrointestinal bleeding in AdventHealth hospitals in Central Florida

Primary Aim: Evaluate the outcome on all patients undergoing endoscopic therapy for upper gastrointestinal bleeding and patient outcomes.

Registry to evaluate the outcomes following algorithmic approach in the endoscopic treatment of bile duct stones

Primary Aim: Evaluate the clinical outcomes following an algorithmic approach for endoscopic treatment of bile duct stones.

ERCP

Stent vs. indomethacin for preventing post-ERCP pancreatitis: The SVI Trial – a multicenter randomized non-inferiority clinical trial of rectal indomethacin alone vs. indomethacin & prophylactic pancreatic stent placement for preventing post-ERCP pancreatitis in high-risk cases

Primary Aim: To compare the rate of post-ERCP pancreatitis between indomethacin versus pancreatic duct stenting and indomethacin.

Duodenoscope Assessment

Primary Aim: Develop and validate a tool for assessment of duodenoscope functionality.

Results of ERCP in Sphincter of Oddi Dysfunction (RESPOND)

Primary Aim: Assessment of symptom response following ERCP in sphincter of Oddi dysfunction.

Lipidomics, proteomics, micro RNAs and volatile organic compounds biomarkers in bile and serum in the diagnosis of malignant biliary strictures

Primary Aim: To identify and evaluate proteomics, lipidomics, micro-RNAs and VOCs changes in blood and bile that may provide specific indications of malignant cell metabolism in cancer. By extensive characterization of these tumor-specific changes, we aim to determine their usefulness as biomarkers in the early diagnosis of cancer.

A prospective multicenter cohort study evaluating the association between competency in trainees and clinical outcomes in ERCP: The Act-ERCP study

Primary Aim: To assess the relationship between trainee skills (overall, technical and cognitive) and clinical outcomes (technical success and adverse events).

Randomized trial examining the impact of pancreatic duct stent placement in patients with acute necrotizing pancreatitis in the prevention of walled-off necrosis

Primary Aim: To compare the incidence of walled off necrosis between the pancreatic duct stent and no stent groups at 4-6 weeks post-index ERCP.

Research in 2019 Continued

Bariatrics

Randomized, double-blind, sham-controlled, prospective, multi-center pilot study to evaluate the safety and effectiveness of duodenal mucosal resurfacing using the revita™ system in the treatment of type 2 diabetes

Primary Aim: To assess the safety of the Fractyl Revita™ System for the treatment of subjects with T2D suboptimally controlled on 2 oral antidiabetic medications; to assess the effect of DMR versus Sham procedures on glycemic endpoints 24 weeks after the procedure; to assess the effect of DMR on glycemic endpoints 48 weeks after the randomized procedure for durability of effect determination.

Colon

Safety of endoscopic resection of large colorectal polyps: A randomized trial

Primary Aim: Examine whether clip closure of the mucosal defect after endoscopic mucosal resection of large polyps (≥20mm) will reduce the risk of delayed bleeding

Endoscopic resection of large colorectal polyps: An observational cohort study (Large Polyp Study group, study III)

Primary Aim: Examine the rate of complications, complete polyp resection, and polyp recurrence during 5 years of follow-up

Flexible endoscopic septal myotomy: a prospective registry of endoscopically treated symptomatic zenker's diverticulum

Primary Aim: Evaluate the beneficial effect of endoscopic treatment of Zenker's diverticulum

Prospective randomized controlled trial describing the recurrence rate of adenomas in sessile or flat colonic lesions 15mm or larger, receiving post-resection site treatment with snare tip soft coagulation or argon plasma coagulation

Primary Aim: Recurrence rate of adenomas at the site of any qualifying, previously resected lesions at the 6-month follow-up colonoscopy

IBD

Entyvio (vedolizumab) long-term safety study: An international observational prospective cohort study comparing vedolizumab to other biologic agents in patients with Ulcerative Colitis (UC) or Crohn's Disease (CD)

Primary Aim: To assess the long-term safety of vedolizumab versus other biologic agents in patients with UC or CD.

Vedolizumab 4006 (EXPLORER): An Open Label, Phase IV study to evaluate the efficacy and safety of triple combination therapy with vedolizumab, IV, adalimumab
Primary Aim: To determine the effect of triple combination therapy with an anti-integrin (vedolizumab IV), a TNF antagonist (adalimumab SC), and an immunomodulator (oral methotrexate) on endoscopic remission at Week 26.

A Phase IIb, randomized, double-blind, placebo controlled, parallel-group, multicenter protocol to evaluate the safety and efficacy of JNJ-64304500 in subjects with moderately to severely active Crohn's disease
Primary Aim: To evaluate the efficacy of JNJ-64304500 to reduce the CDAI score from baseline. To evaluate the safety of JNJ-64304500.

GS-US-419-3895: A Phase III, double-blind, randomized, placebo-controlled study evaluating the efficacy and safety of filgotinib in the induction and maintenance of remission in subjects with moderately to severely active Crohn's disease

Primary Aim: To evaluate the efficacy of filgotinib as compared to placebo in establishing clinical remission by PRO2 at Week 10.

GS-US-418-3898: A combined Phase IIb/III, double-blind, randomized, placebo-controlled study evaluating the safety and efficacy of filgotinib in the induction and maintenance of remission in subjects with moderately to severely active ulcerative colitis

Primary Aim: To evaluate the efficacy of filgotinib as compared to placebo in establishing EBS remission at Week 10.

A Phase II/III, randomized, double-blind, placebo- and active-controlled, parallel-group, multicenter protocol to evaluate the efficacy and safety of guselkumab in subject with moderately to severely active Crohn's disease

Primary Aim: Evaluate the clinical efficacy of guselkumab in participants with Crohn's disease; Evaluate the safety of guselkumab.

A Phase II, double-blind, randomized, placebo-controlled study evaluating the efficacy and safety of filgotinib in the treatment of perianal fistulizing Crohn's disease

Primary Aim: Evaluate the efficacy of filgotinib as compared to placebo in establishing combined fistula response at Week 24.

M16-067 - A multicenter, randomized, double-blind, placebo-controlled induction study to evaluate the efficacy and safety of risankizumab in subjects with moderately to severely active ulcerative colitis who have failed prior biologic therapy

Primary Aims: Characterize the efficacy, safety, and pharmacokinetics of risankizumab as induction treatment in subjects with moderately to severely active ulcerative colitis; Identify the appropriate induction dose of risankizumab.

16T-MC-AMAN: A Phase III, multicenter, randomized, double-blind, parallel, placebo-controlled induction study of mirikizumab in conventional-failed and biologic-failed patients with moderately to severely active ulcerative colitis

Primary Aim: Evaluate if mirikizumab is superior to placebo in inducing clinical remission at Week 12 in patients with moderately to severely active ulcerative colitis.

POWER - A Phase IIIb, randomized, double-blind, multicenter study to evaluate the safety and efficacy of intravenous re-induction therapy with ustekinumab in patients with moderately to severely active Crohn's disease - CANTO1275CRD3008

Primary Aim: Evaluate the achievement of clinical response at Week 16 following a single IV re-induction dose of -6 mg/kg ustekinumab, compared with continuing regular SC q8w 90 mg ustekinumab administration, in participants with secondary loss of response (LoR) to SC q8w 90 mg ustekinumab maintenance therapy.

A Long Term Non-Interventional Registry to assess safety and effectiveness of HUMIRA® (adalimumab) in patients with moderately to severely active ulcerative colitis (UC)

Primary Aim: To evaluate the long-term safety of HUMIRA® in moderately to severely active UC adult patients (18 years of age or older) who are treated per routine clinical practice.

GS-US-419-3896 - A long term extension study to evaluate the safety of filgotinib in subjects with Crohn's disease

Primary Aim: To observe the long-term safety of filgotinib in subjects who have completed or met protocol specified efficacy discontinuation criteria in a prior Gilead-sponsored filgotinib treatment.

GS-US-418-3899 - A long term extension study to evaluate the safety of filgotinib in subjects with ulcerative colitis

Primary Aim: To observe the long-term safety of filgotinib in subjects who have completed or met protocol specified efficacy discontinuation criteria in a prior Gilead-sponsored filgotinib treatment.

An open label, long term safety trial of BI 655130 treatment in patients with moderate to severely active ulcerative colitis who have completed previous BI 655130 trials

Primary Aim: To evaluate the long-term safety and efficacy of BI 655130 in patients with moderate to severely active ulcerative colitis, who have completed treatment in previous trials.

A Phase II/III, randomized, double-blind, placebo controlled, multicenter study to evaluate the safety and efficacy of bi 655130 induction therapy in patients with moderate-to-severely active ulcerative colitis who have failed previous biologics therapy

Primary Aim: To prove the concept of clinical activity of BI 655130 in patients with moderate to severely active ulcerative colitis who have failed previous biologic treatments and to identify efficacious and safe dose regimens in Part 1 (Phase II); To confirm efficacy and safety of BI 655130 in patients with moderate-to-severely active ulcerative colitis who have failed previous biologic treatments in Part 2 (Phase III).

Phase II, double-blind, randomized, placebo-controlled study evaluating the efficacy and safety of filgotinib in the treatment of small bowel Crohn's disease (SBCD)

Primary Aim: Evaluate the efficacy of filgotinib, when compared to placebo, in establishing clinical remission at Week 24.

Phase II/III, randomized, double-blind, placebo and active-controlled, parallel-group, multicenter protocol to evaluate the efficacy and safety of guselkumab in subject with moderately to severely active Crohn's disease

Primary Aim: To evaluate the clinical efficacy of guselkumab in participants with Crohn's disease; To evaluate the safety of guselkumab.

A Phase IV open-label-study to evaluate vedolizumab iv dose optimization on treatment outcomes in non-responders with moderately to severely active ulcerative colitis

Primary Aim: To determine the effect of vedolizumab IV dose optimization on mucosal healing compared with the standard vedolizumab IV dosing regimen at Week 30 in subjects with UC and high vedolizumab clearance, based on a predefined Week 5 serum vedolizumab concentration threshold and who are Week 6 nonresponders.

Clinical Trials

INVESTIGATION	SPONSOR
Randomized trial comparing four fine needle biopsy needles and three different techniques for endoscopic ultrasound-guided fine needle biopsy of solid pancreatic mass lesions	AdventHealth
Multicenter randomized trial comparing direct endoscopic necrosectomy vs. step-up transluminal endoscopic interventions in infected necrotizing pancreatitis (DESTIN)	AdventHealth
Registry for endoscopic ultrasound (EUS) evaluation of pancreatic cysts	AdventHealth
Registry for EUS-guided pancreatic cyst ablation	AdventHealth
Stent vs. Indomethacin for preventing post-ERCP Pancreatitis: The SVI Trial – A multicenter randomized non-inferiority clinical trial of rectal indomethacin alone vs. indomethacin & prophylactic pancreatic stent placement for preventing post-ERCP pancreatitis in high-risk patients	NIH/NIDDK
Registry to evaluate outcomes adopting an algorithmic approach to endoscopic management of bile duct stones	AdventHealth
Registry of endoscopic management of pancreatic fluid collections	AdventHealth
Prospective registry of radiation exposure during fluoroscopy-aided endoscopic procedures	AdventHealth
Duodenoscope Assessment Tool	AdventHealth
Results of ERCP in Sphincter of Oddi Dysfunction (RESPOND)	NIDDK
Lipidomics, Proteomics, Micro RNAs and Volatile Organic Compounds Biomarkers in Bile and Serum in the Diagnosis of Malignant Biliary Strictures	AdventHealth
Randomized trial examining the impact of pancreatic duct stent placement in patients with acute necrotizing pancreatitis in the prevention of walled-off necrosis	AdventHealth
Randomized, double-blind, sham-controlled, prospective, multi-center pilot study to evaluate the safety and effectiveness of duodenal mucosal resurfacing (DMR) using the Revita™ System in the treatment of Type 2 diabetes	Fractyl
Safety of endoscopic resection of large colorectal polyps: A randomized trial	VA
Endoscopic resection of large colorectal polyps: An observational cohort study (Large Polyp Study Group, study III)	VA
Flexible Endoscopic Septal Myotomy: A Prospective Registry of Endoscopically Treated Symptomatic Zenker's Diverticulum	AdventHealth
Prospective randomized controlled trial examining the recurrence rate of adenomas in sessile or flat colonic lesions 15mm or larger receiving post-resection site treatment with snare tip soft coagulation or argon plasma coagulation	Indiana University
The Orange County Bleeding Consortium (OCBC): Registry of patients undergoing endoscopic procedures for upper gastrointestinal bleeding in AdventHealth System Hospitals in Central Florida	AdventHealth
Entyvio (vedolizumab) long-term safety study: An international observational prospective cohort study comparing vedolizumab to other biologic agents in patients with ulcerative colitis (UC) or Crohn's disease (CD)	Janssen
Vedolizumab 4006 (EXPLORER): An open-label, Phase IV study to evaluate the efficacy and safety of triple combination therapy with Vedolizumab, IV, Adalimumab	Takeda
A Phase IIb, randomized, double-blind, placebo controlled, parallel-group, multicenter protocol to evaluate the safety and efficacy of JNJ-64304500 in subjects with moderately to severely active Crohn's disease	Janssen
GS-US-419-3895: A Phase III, double-blind, randomized, placebo-controlled study evaluating the efficacy and safety of Filgotinib in the induction and maintenance of remission in subjects with moderately to severely active Crohn's disease	Gilead

Clinical Trials

INVESTIGATION	SPONSOR
GS-US-418-3898: A combined Phase IIb/III, double-blind, randomized, placebo-controlled study evaluating the safety and efficacy of Filgotinib in the induction and maintenance of remission in subjects with moderate to severe active ulcerative colitis	Gilead
A Phase II/III, randomized, double-blind, placebo- and active-controlled, parallel-group, multicenter protocol to evaluate the efficacy and safety of Guselkumab in subjects with moderate to severe active Crohn's Disease	Janssen
A Phase II, double-blind, randomized, placebo-controlled study evaluating the efficacy and safety of Filgotinib in the treatment of perianal fistulizing Crohn's disease	Gilead
M16-067 - A multicenter, randomized, double-blind, placebo-controlled Induction study to evaluate the efficacy and safety of Risankizumab in subjects with moderately to severely active ulcerative colitis who have failed prior biologic therapy	Abbvie
16T-MC-AMAN: A Phase III, multicenter, randomized, double-blind, parallel, placebo-controlled Induction study of Mirikizumab in conventional-failed and biologic-failed patients with moderately to severely active ulcerative colitis	Eli Lilly
POWER - A Phase IIIb, randomized, double-blind, multicenter study to evaluate the safety and efficacy of intravenous re-induction therapy with Ustekinumab in patients with moderately to severely active Crohn's disease - CNTO1275CRD3008	Janssen
A long-term non-interventional registry to assess safety and effectiveness of HUMIRA® (Adalimumab) in patients with moderately to severely active ulcerative colitis	Abbvie
GS-US-419-3896 - A long term extension study to evaluate the safety of Filgotinib in subjects with Crohn's disease	Gilead
GS-US-418-3899 - A long term extension study to evaluate the safety of Filgotinib in subjects with ulcerative colitis	Gilead
An open label, long term safety trial of BI 655130 treatment in patients with moderate to severely active ulcerative colitis who have completed previous BI 655130 trials	Boehringer Ingelheim
A Phase II/III randomized, double-blind, placebo controlled, multicenter study to evaluate the safety and efficacy of BI 655130 induction therapy in patients with moderate-to-severely active ulcerative colitis who have failed previous biologics therapy	Boehringer Ingelheim
Phase II, double-blind, randomized, placebo-controlled study evaluating the efficacy and safety of Filgotinib in the treatment of small bowel Crohn's disease	Gilead
Phase II/III, randomized, double-blind, placebo and active-controlled, parallel-group, multicenter protocol to evaluate the efficacy and safety of Guselkumab in subject with moderately to severely active Crohn's disease	Janssen
Phase IV open-label-study to evaluate Vedolizumab IV dose optimization on treatment outcomes in non-responders with moderately to severely active ulcerative colitis	Janssen

Upcoming Study

A randomized trial to evaluate the efficacy of radio frequency ablation in cholangiocarcinoma will commence in 2020.



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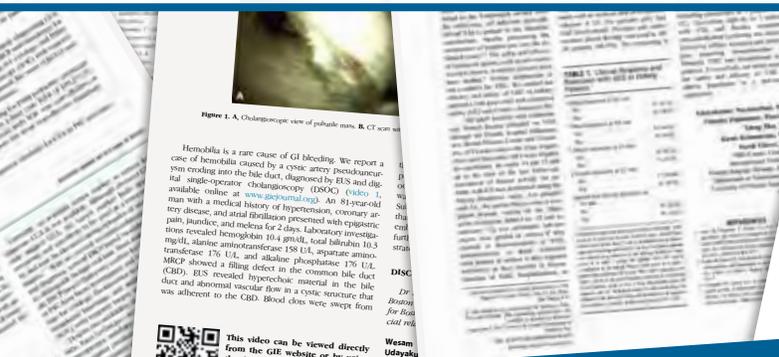
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We take pride in highlighting our rate of abstract-to-manuscript conversion which nears 100%. Publication of scientific findings in high-impact peer-reviewed clinical journals is one of our top priorities.



6TH ANNUAL ORLANDO LIVE EUS

AUGUST 28-30 | 2019

This three-day event was attended by 326 delegates from 33 countries. Seven international faculty from seven countries performed 44 procedures that were transmitted live. In addition to didactic lectures, a dedicated cytopathology symposium and a self-assessment program were conducted as part of the convention. The hands-on lab at our state-of-the-art Nicholson Center was attended by 128 delegates. The Robert Fulbright Memorial Lecture was delivered by Professor Nirag Jhala from Temple University in Philadelphia. The symposium received a delegate rating of 4.9 on a scale of 0 to 5.

326 delegates from 33 countries attended

7 international faculty from 7 countries performed 44 procedures that were transmitted live

128 delegates attended a hands-on lab





Breakfast session



ROBERT FULBRIGHT memorial lecture was delivered by Dr. Nirag Jhala

Delegate Countries Represented at Orlando Live EUS 2019

- Argentina
- Australia
- Bolivia
- Brazil
- Canada
- Chile
- China



Colombia

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Ecuador

Germany

Greece

India

Israel

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Kenya

Mexico

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Peru

Poland

Romania

Russia

South Africa

Spain

Taiwan

Thailand

Trinidad

Tobago

United Kingdom

USA

UAE (United Arab Emirates)



Educational Symposiums



Live Endoscopy Webinar

March 15, 2019 | Orlando, Florida

In order to make endoscopic education seamless and globally available we conducted a Live Endoscopy Webinar on March 15th 2019. Dr. Nageshwar Reddy from the Asian Institute of Gastroenterology in Hyderabad was the visiting faculty. Seven procedures were demonstrated live from CIE. 953 delegates from 53 countries viewed the event and texted questions on a chat box that was answered in real-time. We administered a questionnaire to which 75% of the audience responded stating that live webinars will replace live symposiums in the near future.

Update on Techniques and Tips in GI Endoscopy

March 16, 2019 | Palm Beach, Florida

This six-hour CME program was attended by 90 delegates from across the state of Florida. Guest speakers at this event included Dr. Gottumukkala Raju, Professor of Medicine at the MD Anderson Cancer Center in Houston, Dr. Nageshwar Reddy, Chairman of the Asian Institute of Gastroenterology in Hyderabad, India and Dr. Amrita Sethi, Associate Professor of Medicine at the Columbia University School of Medicine in New York.

5th Annual Clinical Update in Inflammatory Bowel Diseases

May 4, 2019 | Orlando, Florida

This one-day event had an attendance of 210 delegates. Invited faculty included Dr. Shazia Beg, Assistant Professor of Medicine at the University of Central Florida in Orlando, Dr. Yehuda Chowers, Professor of Medicine at Rambam Health Care Campus in Israel, Dr. Raymond



K. Cross, Director of the IBD Center at University of Maryland School of Medicine in Baltimore, Dr. Gary Lichtenstein, Director of the IBD Center at the University of Pennsylvania Hospitals in Philadelphia and Dr. David A. Schwartz, Director of the IBD Center at the Vanderbilt University Medical Center in Nashville.

The symposium provided participants a comprehensive education in inflammatory bowel disease evaluation and management. The program covered six major topics:

1. Assess treatment decisions for patients with moderate-to-severe inflammatory bowel disease (IBD) based on risk stratification and treatment history.
2. Discuss the safety and efficacy data for new and emerging therapeutic options for IBD, including unique mechanisms of action and potential place in therapy.
3. Determine the appropriate timing of surgery in patients with IBD.
4. Determine potential causes of treatment failure including therapeutic drug monitoring for patients on biologic treatment.
5. Explain the relationship of current treatment strategies to the underlying mechanisms of disease progression in IBD.
6. Select goals for treat-to-target strategies in IBD according to evidence and consensus-based recommendations.

Digestive Diseases Week Update

June 13, 2019 | Orlando, Florida

This two-hour event reviewed 40 key abstracts presented at DDW 2019. The event was attended by 42 regional delegates.

Orlando live endoscopy

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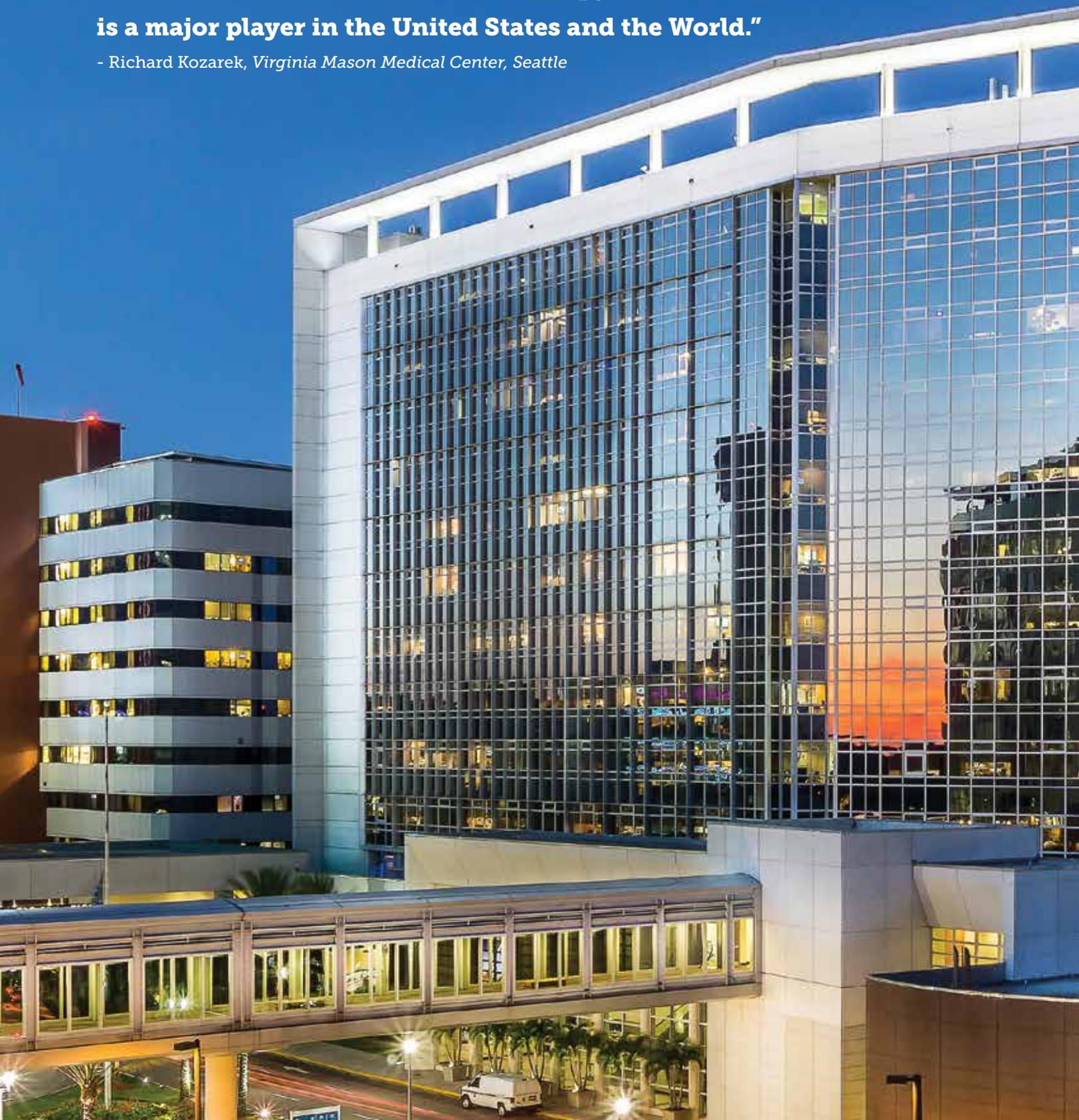
for Nurses and Technicians

AUGUST 26-27 | 2020

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Celebration, FL

“Whether it is caring for patients with complex pancreaticobiliary, liver or inflammatory bowel diseases, running controlled clinical trials, evaluating new technologies, techniques, or medical therapies, or organizing world-class educational symposiums, the Center for Interventional Endoscopy in Orlando is a major player in the United States and the World.”

- Richard Kozarek, *Virginia Mason Medical Center, Seattle*







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