REPLAY IN ADVANCES IN PANCREATIC CANCER CARE
PYLORUS-PRESERVING PANCREATICODUODENECTOMY
(MINI-WHIPPLE PROCEDURE)
THOMAS JEFFERSON UNIVERSITY HOSPITAL
PHILADELPHIA, PENNSYLVANIA
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ANNOUNCER: Welcome to Thomas Jefferson University Hospital in Philadelphia, Pennsylvania. Over the next hour, you'll see a pylorus-preserving pancreaticoduodenectomy, also known as a mini-Whipple Procedure. You'll also learn about the latest advances in pancreatic cancer care at Jefferson. During a classic Whipple procedure to treat pancreatic cancer, the gallbladder, common bile duct, lower part of the stomach, all of the duodenum, and the head of the pancreas are removed. The mini-Whipple preserves the entire stomach, the pylorus, and several centimeters of the upper duodenum. The procedure has many advantages including reduced hospital stay and fewer complications. Physicians may take a post-assessment survey at the end of the program for CME credit. Now let's join the doctors.
00:01:07
CHARLES YEO, MD: Good afternoon, and welcome to the Thomas Jefferson University Hospital. I'm Dr. Charles Yeo, the Samuel D. Gross Professor and Chair of Surgery here at Jefferson Hospital. Today we're going to be discussing advances in pancreatic cancer care and feature surgical footage from a recent pylorus-preserving pancreaticoduodenectomy which we commonly call the mini Whipple procedure. Joining me for today's discussion are several faculty members here at Jefferson. First, Dr. Thomas Kowalski, Assistant Professor and Director of Gastrointestinal Endoscopy here at Jefferson. Next, Dr. Jonathan Brody, Assistant Professor and research investigator in the Department of Surgery at Jefferson. Next we have Dr. Don Mitchell, Professor and radiologist extraordinaire here at Jefferson. Lastly, Dr. Jeffrey Joseph, Associate Professor and a research device researcher who's also an anesthesiologist here at Jefferson. Additionally today as a special treat, in our production area we're joined by the leadership of PanCAN, the Pancreatic Cancer Action Network. And we want to welcome them to this webcast as well - particularly their CEO, Julie Fleischman. We're going to start right in on a patient with a pancreatic lesion, and I've asked Dr. Tom Kowalski to go ahead and begin with telling us the role of the gastroenterologist in the workup of a patient with the pancreatic lesion. Tom?
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THOMAS KOWALSKI, MD: Thank you, Charlie. The patient that we're going to discuss this surgical procedure on today is a patient who had an incidentally found pancreatic abnormality when he had radiographic imaging for symptoms unrelated to the pancreas. Abnormalities - small abnormalities of the pancreas - are increasingly recognized because our population has better access to medical technology with the increased use of screening laboratory panels and more liberal use of cross-sectional imaging. The cross-sectional imaging that are available to us today, most notably in

multidetector helical CT scans and MRI with MRSP, or magnetic resonance cholangiopancreatography, have greatly improved resolution over previous generation scanners, particularly when it has to do with the pancreas. The role of the gastroenterologist with an expertise in pancreatic disease is to help interpret the significance of radiographic abnormalities and to develop a diagnostic and therapeutic plan - including the need for invasive tests and surgical intervention. The tools that are available to the gastroenterologist include endoscopic ultrasound guided fine needle aspiration and endoscopic retrograde cholangiopancreatography known as ERCP. Endoscopic ultrasound is a tool that allows a gastroenterologist to put an ultrasound probe at the tip of an endoscope and pass that probe adjacent to the pancreas in the stomach or in the duodenum. In this way, we can obtain very high resolution images of the pancreas, the surrounding lymph nodes, and the surrounding vasculature. This images shows our endoscopic ultrasound probe in the stomach and the adjacent pancreatic tail labeled PT, the left kidney, the left renal vein, and the left splenic vein. Not only do we obtain high resolution images of the pancreas, but the endoscopic ultrasound scope allows us to pass a needle under direct ultrasound visualization into the abnormal areas of the pancreas. So here's an image of the pancreas with again our ultrasound probe being within the stomach showing an irregular cystic lesion within the pancreatic parenchyma. Even when these cystic lesions are very small - this lesion being less than one centimeter in size - we can see these lesions with great detail by ultrascopic ultrasound. We can also pass a needle directly into small lesions to obtain a sample for definitive diagnosis. Solid lesions seen here can also be seen in very good detail by ultrascopic ultrasound. And the relationship between these solid lesions to the surrounding vasculature can be delineated. Once again, by directly sampling these small lesions in the pancreas, the gastroenterologist has the ability to determine which lesion is benign, which lesion may be precancerous, and which lesions are early cancers and may benefit from surgical reception for a cure or to actually even prevent pancreatic cancer.
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CHARLES YEO, MD: Thanks very much, Tom. For today's case, you had the opportunity to actually sample the patient's lesion. And tell us what the results from that sampling were.
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THOMAS KOWALSKI, MD: The results from the sampling showed us that there was a low amylase, a high CEA, and some mucinous cells on cytology. Based upon these parameters, we determined the lesion to be precancerous and amenable to surgical reception.
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CHARLES YEO, MD: Thanks very much, Dr. Kowalski. Next we'll ask Dr. Don Mitchell to review for us some remarkable pancreatic images which are now possible. Dr. Mitchell?
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DONALD MITCHELL, MD: Thank you, Dr. Yeo. It's a pleasure to be here. I'll be first showing two examples of patients with cystic masses seen by MRI with MR cholangiopancreatography, or MRCP, showing how MRI can help evaluate and characterize these masses. Then we'll see the high-resolution CT scan with 3D reconstructive techniques in the patient in question. So let's look at the first slide. In this example, you're going to see somebody with an intraductal papillary mucinous neoplasm, or IPMN. We see that here in the coronal thin-slice, a complex cystic mass connected to a slightly dilated draining pancreatic duct confirming that this is indeed an intraductal papillary mucinous neoplasm. Here in the 3D projection, we see the entire ductal anatomy and again the connection of the cystic mass with

pancreatic duct. On the contrast-enhanced transverse image, we see no solid tissue enhancement within the mass. In this next example - in a different patient - we have a unilocular cystic lesion which is not connected to either bile duct or pancreatic duct. Again we see no internal enhancements at all because there are no septations but some slight thickening of the wall indicating that indeed this is a cystic neoplasm - not a simple cyst - and is therefore premalignant. In the next example here, the patient that we're discussing today is again a unilocular cystic mass with a slight wall thickening. And next we're going to see the video which will show similar slices to this as we pan up and down. The 3D data set of these multiple thin, rapidly-obtained, contiguous images can be post-processed to show projections - vascular anatomy related to the relevant surgical anatomy. Here is an example of the 3D data set with shading of vessels and their relationship to the surrounding soft tissues - invaluable for determining the best surgical approach. And the final example here is a rotating surface rendering of the relevant vessels showing no vascular encasement of any of them because indeed, although premalignant, this is an non-invasive mass and will not involve extensive dissection of involved encased vessels. So thank you for your attention. Dr. Yeo?
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CHARLES YEO, MD: Don, thank you very much for showing us these remarkable images. Now the patient that we're going to show the video on now is a middle-aged individual who presented with an asymptomatic, incidentally-discovered lesion that was nicely shown by Doctors Kowalski and Mitchell. And we're going to run now the first segment of the video. The main issue here and the worry is that this patient harbored either a malignancy or a premalignancy. And the beauty here that we'll see in this particular video is that we're able to do an operation and render the patient free of any neoplasia. So in a sense, the opportunity here is that one can deliver great news to the patient and provide for a cure. We're going to show now the mini-Whipple operation. The schematics will begin by showing from the incision through the Kocher Maneuver. We typically use a vertical midline incision. And in all the images you're going to see, the patient's head is to the right, and the patient's feet are to the left. We place the mechanical retractor, and initially here, the operating surgeons are exploring the abdomen. The colon has been lifted up and mobilized to the right showing a bit of diverticular disease. And now we're running the small bowel from the Ligament of Treitz towards the ileocecal valve. We've already assessed the liver. There's no evidence of dissemination. And thus we can tell from the initial exploration that this patient appears to have a resectable lesion without evidence of dissemination. So getting right down to the aspects of the mini-Whipple procedure, called medically the pylorus preserving pancreaticoduodenectomy, we typically commence the resection with a straightforward removal of the gallbladder or colosesectomy. Initially we've taken down the attachment of the gallbladder to the liver. Here we're skeletonizing the cystic duct - clamping the duct proximally and distally. And then we'll divide the cystic duct with the Metzenbaum scissors. The gallbladder is passed off the table as a specimen. And the cystic duct here is shown being secured. Let me credit one of our talented surgical residents, Dr. Candace McGuire here, who's actually tying this specific knot down. This is very much a team approach. The operation cannot be done by one or two human beings. The second part of the procedure we wanted to depict is incision through kocherization. The Kocher Maneuver is done to elevate the duodenum and head of the pancreas up out of the retroperitenium. Here we're using the electrocautery. The surgeon's hand is rotating the duodenum downwards towards the bottom of the screen. And we're completing the Kocher Maneuver. Next we're showing here the division of the structures of the hepatoduodenal ligament - that is, these are the superficial structures. In this particular piece of

tissue would, of course, be the right gastric artery. Here we're tying it in continuity, clamping it, and securing the right gastric artery. This allows us to mobilize the duodenum further caudally. The next aspect that we're going to show is GDA-controlled. This is the gastroduodenal artery, the largest artery that is typically tied and controlled during the mini-Whipple procedure. Here we've identified the gastroduodenal artery in its aspect just cephalad to the duodenum. And a suture ligature is being placed in order to secure the right side of this artery. This is the cephalad aspect of the artery that's going to remain in place. The left side of this artery that's soon to be divided comes out with the specimen. So here we're passing the suture ligature around. As I said, this is the largest artery that is typically taken. Once must always be certain that this artery is test-clamped before it is ligated in order to be sure that you're not dealing with a barren arterial anatomy up into the liver because it would be a mistake, for example, to divide the proper hepatic artery that could lead to hepatic arterial devascularization. Right here now, we're showing the very normal-sized, very tiny common bile duct which has been encircled with the clamp. Here a vessel loop is being passed around the bile duct, and the bile duct is being elevated. Just posterior to this bile duct, of course, will be the portal vein which we'll do our very best to preserve and not injure. Here the bile duct is being partially transected so we can harvest bile. This is part of our tumor and bile, blood and pancreatic juice harvesting which is used for research purposes. And we're very proud of the research done on these specimens here at Jefferson. This will be further discussed by Dr. Brody. You can see the bile slowly dripping out of the proximal bile duct. And a small, curved silver bulldog clamp being applied so as to prevent the bile from leaking into the operative field. Here we're dividing the loose connective tissue just anterior to the portal vein. We just got a nice view of the portal vein there. Now in the pylorus preserving operation, we do not do a gastric resection. In this particular aspect shows a Penrose drain which is a rubber drain being passed around the duodenum about four centimeters distal to the pylorus. And there we're showing the pylorus. What we're going to do now is complete the transaction of the loose connected tissue posteriorly. And here we're passing a gastrointestinal stapling device across the duodenum about four centimeters beyond the pylorus. This stapling device fires four rows of staples and a sharp knife in between, and it divides the tissue and controls each side with two rows of staples. The duodenum has been transected, and we'll transfix the duodenum here with the suture ligature to act as a retractor to help us hold the duodenum and the stomach out of the operative field. So at this point, we have divided the bile duct and the duodenum. Now this is a part of the operation that people can get lost in. This is a part for the occasional Whipplist [who] can have some trouble here. This is a magical plain that I like to talk about between the transverse mesocolon and the uncinate process. And by meticulously dissecting in this plain, one is able to expose the supramesenteric vein, the uncinate process, and, really, get nice separation of the specimen away from the structures that need to be retained. One nice way to think about the Whipple operation is one is separating the tumor and the structures of the head of the pancreas and duodenum away from the visceral vessels. And one must be very careful to avoid injury to the visceral vessels, namely the supramesenteric vein, the portal vein, and the supramesenteric artery. Here the downstream gastroduodenal artery - or what other people would term, "a branch of the inferior pancreaticoduodenal" - is divided. And now we're going to expose the inferior pancreatic neck and prepare to divide the pancreas harvesting pancreatic juice for subsequent molecular study. Here's a beautiful view now of the pancreatic neck being elevated in the cephalad direction that's to the right of the screen. You can see the SMV being bulated just inferior to the dissecting instrument. And here we are passing a clamp very cautiously through this tunnel that we've created. And we'll pass a Penrose drain completely around the pancreatic neck. This is a time in the Whipple operation where, if the tissue plains are well-preserved, this is a beautiful, fun part of the operation. If the cancer is invading into the SMV or portal vein, that can be a very, very dangerous part of the operation. Now here we're placing the fourth of four stay sutures on the inferior aspect of the pancreas, tying them down. And we place these stay sutures for hemostasis purposes. And what we've exposed now and will be showing is the pancreatic neck. This pancreatic neck then is one of the narrowest portions of the pancreas through which the pancreatic duct travels en route from the ampulla of Vater on the head portion all the way out to the pancreatic tail. There are many ways to divide the pancreatic parenchyma. We've chosen in the video to show the division with the electrocautery. Here we're slowly cauterizing across the pancreatic parenchyma. This provides reasonable hemostasis, although there's always a bit of blood loss here because the pancreas is a highly vascular organ. Soon we're going to show, as we get further and further through this parenchyma - this is typically about a centimeter and a half wide and about three to four centimeters in vertical dimension - as we go a little bit deeper here and towards the center of this particular transaction point, we'll be entering the pancreatic duct. And you'll see a little gush of pancreatic juice which will be clear, and then it will turn a bit white as the protein becomes denatured by the heat. We'll be sampling some of this pancreatic juice, banking it. And this is important for our early detection studies looking for markers of pancreatic cancer. We typically get less than a milliliter of pancreatic juice, but with our modern molecular techniques, that's more than sufficient to extract DNA, RNA, protein, and study. And here we're completing the transaction of the pancreas. We're exposing the SMV and portal vein. Now we're going to move down to the SMV exposure through actually getting the specimen out and marking the specimen. This shows division of small venous tributaries between the SMV and the uncinate process. Some of these can be divided with the electrocautery. Others need to be tied and secured for hemostasis purposes. Here we're completing the Kocher Maneuver - taking the thin connective tissue around the level of the second and third portions of the duodenum using the electrocautery to perform this delicate work. And now you can see beautifully exposed there the SMV and portal vein. Now the operation shifts, and the transverse mesocolon is mobilized towards the head. We'll place here a metallic retractor to hold the transverse colon and the mesocolon cephalad. And we'll work on the part of the operation that's a bit away from the pancreas. And this is the division and takedown of the Ligament of Treitz. Here we're working about 15 - 20 centimeters below the Ligament of Treitz and the proximal jejunum. And we're clamping the jejunal mesentery - tying it and then dividing it. And this will be done repetitively taking down all of these small vessels - each of which contains a vascular bundle with an artery and vein - making sure that the mesentery we leave behind had been properly secured for hemostatic purposes. We're tying these jejunal vessels. This can also be divided with various other instruments like the harmonic scalpel. Here's the second time in the case that we'll be using this GIA gastrointestinal stapler - again firing four rows of staples with a sharp knife in between. And now we've divided the proximal jejunum. The retained portion which is being held up here will have its stapled end oversewn using a series of 3-0 silk, what we call "pop-off" or detachable sutures. This just simply invaginates the staple line for security purposes to be sure that we have good serosa to serosa apposition at the site that we've transected the jejunum. We'll put in four or five sutures here and tie them all down in the fashion that's being depicted. There's the last of these sutures being placed. Now this part of the jejunum will be the part that will subsequently be brought up through the transverse mesocolon and will serve as our conduit for reconstruction after we've completed our resection. So here are the final sutures being tied down.

They'll be divided. Now we're nearly through with our clearance at the Ligament of Treitz. The ligament is now completely freed up. Here is the jejunum that is attached to the duodenum. That is swung through, and that's what we call "the flip" - where the proximal jejunum is flipped behind the mesenteric vessels over to the patient's right side. A small pack is put there for hemostasis purposes. And now the only thing left as regards the final resection is the final separation. Here we're showing the cystic lesion in the uncinate process of the pancreas. And we're meticulously dissecting the tumor and the uncinate process away from the right lateral aspect of the portal vein and SMV and away from the right lateral aspect of the superior mesenteric artery. Much of this material can be divided with the electrocautery. However, there are small branches that need to be tied. This is the last pedicle that needs to be tied. This is the final "bite," if you will, that is holding this particular tumor in place. The tumor and then the specimen can then be resected. The operative bed you can see is nicely hemostatic. Here we're showing the SMV portal vein of the [unintelligible] cell placed down just for packing. So there we've completed the resection. And what's left for us now is to deliver this specimen to pathology. This is a picture of the specimen. This shows the gallbladder still attached. Here is the specimen "alive," if you will, with the head, neck, and uncinate process of the pancreas, the duodenum beyond the duodenum bulb. This patient has a little duodenum diverticulum that we're showing right there. So now at this point, the resection is complete, and the specimen is delivered to pathology for routine pathologic assessment. But in addition here at Jefferson, these specimens are fully studied by molecular techniques. So we can learn more and more about pancreatic cancer in an effort to provide a cure. So I wanted to turn the discussion over now to Dr. Jonathan Brody to talk about the role of the pathologist and the role of the molecular geneticist in the assessment of these specimens.

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JONATHAN BRODY, PhD: Well thank you, Dr. Yeo. This is a really exciting time in pancreatic cancer research. And I'm excited to be apart of this panel and be here at Thomas Jefferson. I'm going to give you a small snippet, a small vision on the first slide, if you will, of where we're at with pancreatic cancer and what we study here at Thomas Jefferson. So just a little quick overview: pancreatic cancer is, in part, a genetic disorder. And what do we mean when we say, "pancreatic cancer?" Other diseases are a genetic disorder. What I mean is if you think about the genetics or the DNA of a "house" or cell if you will, the genetics in DNA as a metaphor are the blueprint for that cell or that "house." And when you have a genetic disorder such as pancreatic cancer, there's defects in the blue prints of making that house. That is, there's a defect of the blueprint making of that cell that is cancer. In this instance, if I get 100 resected pancreatic cancers - ductular carcinomas - from Dr. Yeo, I can tell you that basically 95 or 97 out of those 100 will have a specific defect in the blueprint of the making of those cells. Furthermore if you look at what I like to show here as an example, so on the blue patient on the left here if you will, there's a T mutation, a misspelling or defect in the blueprint of this pancreas cell's DNA or genetics blueprint again. And then there's the normal C here mutation, so there's not a misspelling. This is a misspelling, let's say, in a sentence in the book here. And if I'm telling you that 95 out of 100 pancreatic ductular carcinomas have this mutation, we believe this is an advantage that the tumor is using. And what we want to do at Thomas Jefferson through multiple fronts is actually take advantage of that. So the tumor's using this mutation to their advantage to form the tumor - to do something that we call in the molecular biology lingo, "pancreatic tumor genesis." We want to reverse that and view that as the Achilles ' heel in the tumor. And let me give you an example. So here are some experiment models that we actually use in the laboratory. And we use experimental models that are basically isogenic cells.

So these are cells, let's say the top R is a model, normal cells. And these are tumor cells. Now the only difference between these cells is one genetic mutation. And what we've done is tested a number of chemotherapeutics. And in this example, we're using an anti-cancer drug that's used commonly in the adjuvant setting for pancreatic cancer. And we can find by just changing by this one mutation that happens - this one misspelling in the blueprint of the DNA of tumor cells versus the normal cells - these cells become hypersensitive. These are cell survival assays that we like to use. We like to expand this at Thomas Jefferson, and we are actually doing that. Here you can see it all really starts with Dr. Yeo and his colleagues' surgery on a patient's tumor. And then as he discussed, we bring this to my laboratory. And through pathology, we isolate the DNA, the RNA, the protein of the tissue. I'm actually leaving out a number of hours here of a number of different studies that are ongoing here. We look at different targets. We look at different biomarkers. WE look at different disruptive pathways including different defects in the blueprints again of these cells. And that ultimate idea is again to document this and actually look at this in the adjuvant setting so that we can actually look at a patient's tumor and say they should be on "cocktail Y" of chemotherapy. Let me give you a small example before we move forward of something that's ongoing in my laboratory. So here again Dr. Yeo and I work very closely together. And we talked about a young woman who we knew the family history about. And in this case, what we were able to do is: I actually went up to the OR floor, received the tumor myself, brought it to the lab, personally isolated the DNA, RNA, and protein, created a cell line to get pure DNA, and we've now subsequently in just a couple of months gone through about a half a dozen genes. Again, (we are) looking for defects in the DNA. And we've found here that, in this one gene here - and we're calling it "Repair Gene Y" - there's a loss compared to these other patients' tumors. There's a loss of this gene. And what does this mean? Well, the implications are huge - not just for this patient but for other family members of this patient. And there's much relevance for other patients with pancreatic cancer and their families. So basically the bottom line is these defects and these disruptions in pathways for cancers are selective for and in a Darwinian sense for the tumor cell. And they take advantage of it. What we'd like to do is reverse that strategy and do it as an Achilles ' heel and attack it so we can study it postoperatively.
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CHARLES YEO, MD: Dr. Brody, thank you so much for giving us just a little nutshell of the work being done on the molecular genetics of these pancreatic tumors. Now in the particular patient that we're going run (in) the second part of the video, the patient's tumor turned out to be a premalignant lesion. This patient did not fortunately have pancreatic cancer. And the patient was spared the need for postoperative therapy. Now we're going to go ahead and show the second aspect of the video. This video shows the reconstruction after the mini-Whipple procedure. And it really falls into three sections. The First is the reconstruction of the pancreas via a pancreaticojejunostomy. So at this point in the operation, we're preparing to open the transverse mesocolon and create a small window through which we can bring the retained jejunum. It's the retained jejunum that serves as the conduit for our reconstruction. So here the jejunum is being passed up through the transverse mesocolon. You can see that the jejunum looks quite healthy. It's the part of the jejunum that we had oversewn. And we're going to place it right adjacent to the pancreas. Now this pancreaticojejunostomy requires that the pancreatic remnant be cleared for about a distance of two sonimeters. And one has to be very careful when one dissects this loose connective tissue because there are small vessels here that need to be tied or controlled with the electrocautery. We're showing one here that will be divided. By clearing this pancreas up nicely off the splenic vein, it's quite

mobile. And it really allows the anastomosis to be accomplished much more successfully. Here are sutures being placed in the superior aspect of the pancreatic remnant. And we're preparing to perform an endocide pancreaticojejunostomy allowing the pancreatic juice to drain into the lumen of the jejunum. There are scores of different wants of performing this reconstruction. The way that we're showing here involves a horizontal mattress row of silk on the back. And then we'll perform an interlayer of running 3-0 vicryl or 3-0 absorbable suture. Here the posterior outer row has been completed. And we're opening the jejunum to allow the pancreas to be invaginated into the jejunum thereby avoiding the spillage of pancreatic enzymes into the abdomen. So here the jejunal mucosa is being opened. Small clamp (is) placed in. You don't want to open the serosa too far. So we've limited the serosal opening to about half of the length of the cut edge of the pancreas. And here we show the vicryl sutures being placed. This is the posterior inner layer. This will be a running, locking layer. First half of the suture (is) placed between the pancreas, and the second half of the suture (is) being placed full thickness jejunum. This is clearly one of the most technically challenging parts of the Whipple operation and the part that has really the most in the way of sequelae should the patient have a leak or failure of healing of this anastomosis. Here we're continuing with the running, locking posterior inner layer of sutures. We'll come around the corner here subsequently after placing one more suture here. This is the last suture, if you will, in the back wall (that is) running, locking. Pull that up. We're being very meticulous here not to in any way to incorporate the pancreatic duct. Here we're not around the anterior inner layer. We have a small probe in the pancreas duct that's coming out right there. And here the last stitch will be placed in the anterior inner layer. It's very important that one try to get all of the jejunal mucosa invaginated so as to get good jejunal serosa to pancreatic capsule apposition. Here now is the final stitch. Being careful not to get the pancreatic duct in this. (I) apologize for my head in the way there. There's the final stitch of the vicryl. And then that will be tied down. As I said there are many different ways of doing this particular part of the operation. And studies are ongoing. We have a nice prospective randomized trial that looks at two different ways of performing this anastomosis because there's quite a bit of controversy world-wide among pancreatophiles and experienced pancreatic surgeons about the right way to accomplish this anastomosis. This is the final layer. This is our outer anterior layer being done with 3-0 interrupted silk. And we make every effort to bring the jejunum down and allow the jejunum to roll over the anastomosis to protect the anastomosis. I personally think this is an important part of the technique here because the pancreas itself is immobile. But the jejunum can be brought down and sweep over the anastomosis and serve as a little protection against pancreatic juice leakage. So there we're just showing a couple of the sutures. Here's the completed endocide pancreaticojejunostomy which has been done here in two-layer technique. So that completes the first part of the reconstruction. We're showing it here as the pancreaticojejunostomy. That's going to be right behind the stomach. Now here we're moving on to the second part of the reconstruction. It's the bile duct reconstruction done as a patojejunostomy. We'll open a very tiny hole here in the jejunum. We'll open it full-thickness. Go ahead and excise a bit of the redundant mucosa there. And then this will be done as a single-layer anastomosis using very fine 5-0 PDS suture or other synthetic absorbable suture of your choice. This first stitch is placed in the nine o'clock position to get full thickness jejunal serosa and mucosa. And here we're putting the corner stitch in that tiny bile duct. That's the first stitch of our hepaticojejunostomy, and you can see pulsating right to the right of the screen there the hepatic artery. Here we're now putting in the middle stitch of the back row. This is such a tiny bile duct; not many sutures were required to perform this particular anastomosis. (We're) getting good full thickness bites of the jejunum and good thickness bites of this very tiny bile duct. These sutures are placed in interrupted fashion. They're all first placed - and then the anastomosis is parachuted down in position to keep tension off the anastomosis. And it's very important when you tie these sutures down to make sure they're tied down fully but that tension is avoided on the tying-down sutures. Here's the final suture being placed. You can see for this whole back row, we've only placed about five or six sutures because this was a normal-sized bile duct. This patient did not present with obstructive jaundice. And her bile duct had not been obstructed by the space occupying lesion. So we'll go ahead and tie these all down. They've all been tied at this point. And here's a little trick I like to use. This takes a T tube - in this case, it's a 10 French T tube - passed down into our jejunal limbs so that the T tube is being forced down in the caudal direction downstream. And then we'll also pass this little T tube - which has been cut on a bias at the end you're going to see here soon - we're going to pass this T tube up into the bile duct. You'll see we struggle a little bit getting this T tube in the bile duct. But this serves as an internal stent. We don't leave this in permanently as you see. We take it out when we open our jejunotomy for the duodenojejunostomy. But by putting this little tube into the bile duct, I feel very comfortable that we're leaving a lumen and that we're not, when we do our anterior row, inadvertently hitting the back wall or somehow compromising the lumen of the bile duct. And I think particularly for these tiny bile ducts in patients who are not jaundiced, this is a nice technique that, once you learn how to do it, I think you'll love it because it prevents you from inadvertently sewing that bile duct closed. So here we're doing our anterior row of interrupted sutures - full thickness jejunum to full thickness of the bile duct. And again, we'll only use just a handful of sutures here, perhaps three or four for this very small bile duct. Here's the last one going in. You can see the T tube showing a bit. You want to make sure that you see each of these sutures very well and that you do not spike the T tube with the suture. We always check that T tube before we cut all of our sutures. Here all of the sutures are being tied down now. The anterior row of the hepaticojejunostomy has been completed. Again, this was a very small bile duct, well less than a centimeter in diameter. And I just feel very comfortable with that T tube in there that we've left a lumen. We'll cut the sutures now. There we've completed the hepaticojejunostomy. The last part of the reconstruction is the duodenojejunostomy - this restores GI tract continuity. And here we're showing the duodenum. Now look at this duodenum right here. This is a beautiful duodenum. It's well-vascularized even though we took the right gastric artery. It has no evidence of being compromised. It looks healthy, and it's clearly ready to be anastomose to the small bowel. We do the duodenojejunostomy. Here we're measuring the length of the duodenum. It's about four centimeters off the pylorus. We do this duodenojejunostomy about 15 centimeters or so downstream of the hepaticojejunostomy. There are many different techniques for doing this particular anastomosis. We're going to show you a two-layer technique using silk for the outer layer and vicryl for the inner layer. But clearly you could do it with one layer as well. Here this shows the duodenal margin, the final duodenal margin, being taken off - which means we're cutting off the previously placed staple line. In this particular case, this margin is irrelevant. But if you're operating for a duodenal cancer or you're operating for a large, bulky villas adenoma, for example, of the ampulla, you want to be sure that you don't have tumor at this site and that you're leaving the patient behind with a clean GI tract. So we've excised the duodenal margin. Here we're marking the small bowel, and we will open the small bowel with the electric cautery. And of course, right inside of this small bowel will be this T tube that we placed because we fed it downstream. And once we get this open, we then remove the T tube. Pull it out gently. If it comes

out with any resistance, we know that we've left a nice intact bile duct anastomosis. And we can sleep well at night knowing the patient's not going to have jaundice from a surgical mishap or bit of mischief. So here we're opening the jejunal mucosa completely. Here we're retrieving the T tube. Pass that off the table. You see it's coming out without any resistance. And then we're going to complete the duodenojejunostomy with an inner layer of - we use 3-0 vicryl suture running, locking on the back row here on the inner layer. Tying down the sutures, you can see the small val looks very healthy. The duodenum looks very healthy. Place another one of our vicryl sutures here - full thickness duodenum to full thickness jejunum. (A) great opportunity to practice surgical skills here - knot tying, etc… And then we'll use a running, locking suture to go from the left to right here to complete the inner layer. And now here we're switching around. We've already done the inner layer. Here we're to the anterior inner layer which is done with a cannel suture - it's a running mattress suture. The point of the cannel suture is to allow all of the small bowel, both duodenal and jejunal mucosal, to be invaginated. We recognize that serosa to serosa apposition is the critical aspect of healing of these GI tract mastomosis. And then as we wrap up our reconstruction here, finally we're showing the last layer of the duodenojejunostomy. This is done with 3-0 silk interrupted sutures placed in Limberg fashion. So these are basically vertical mattress sutures which again allow good serosa to serosa apposition. They've all been placed. They're tied down. They can be cut. We can check out…we can palpate at this point - the pyloric ring and palpate anastomosis - and be confident that it's wide open. Now at this point, we've shown the three bits of the reconstruction of pancreatic ojejunostomy, the hepaticojejunostomy, and the duodenojejunostomy. Here we're tacking the jejunum about ten centimeters downstream from the DJ. We're tacking it to the transverse mesocolon so that we don't leave behind an internal hernia. Several of these sutures are placed. Here now we're panning out. The operation is complete. So at this point, we've completed the mini-Whipple procedure. We would end the operation by irrigation and by closure of the abdomen - return the organs to their normal position. And the patient would go to an intensive care unit for careful postoperative monitoring. The Whipple operation is a big operation. It's a bit of a physiologic insult. Now one of the most important aspects of postoperative care would be the monitoring of the patient's glucose control because we're resecting islet cell mass. Now I'm going to turn the discussion over to Dr. Jeff Joseph who's going to discuss with us some of the innovative aspects of a glucose monitoring in both the intraoperative and postoperative setting. Dr. Joseph?
00:48:34
JEFFREY JOSEPH, DO: Thank you, Dr. Yeo. There is increasing evidence that tight glucose control during surgery and after surgery - and even after the patient leaves the hospital - improves outcome. And it is often difficult to achieve that glucose control with our current methods. So here at Jefferson, we are developing those tools to improve monitoring of glucose and improve the delivery of insulin to get tight glucose control. Here we see a landmark study by Van den Berghe, et al, and this shows in postoperative surgical patients requiring ICU care that the tighter the glucose control with intensive insulin therapy, when you could keep the average glucose control and the normal range at 110, the risk of dying greatly decreased. So with this information and other studies in mind, we are attempting to delivery insulin very aggressively. However, the downside of this insulin therapy is a greatly increased risk of hypoglycemia - and that's something we want to avoid. So the way to avoid that is with technology that possibly can monitor the patient in real-time. Instead of four or six glucoses per day, we have a glucose every minute to every five minutes. And the beauty of that is it gives us trend data. And so the nurse at the bedside can see the glucose rising slowly or falling slowly or, if it's falling quickly,

intervening to avoid hypoglycemia. The current method is open-loop where we get glucoses infrequently. The technology we're working on currently is a closed-loop system where you measure glucose minute by minute. It goes into a computer control algorithm. And the computer determines the appropriate dose of insulin and delivers that insulin. Several of the devices we're showing right now are investigational. However, in the next 12 to 18 months, we plan to be applying these clinically in all patients. This is a device that has a catheter in a vein, and it draws blood into the center which is on the patient's left arm. It samples blood. It measures glucose using an enzyme and a chemical technique. And then it delivers the blood back into the patient so there's no blood loss. It then gives the glucose measurement for the nurse. And we envision a flat panel display above the patient's bed which gives the glucose trend information, the insulin information, and any fluid that's been delivered. Here's an actual patient that we took care of, and preoperatively, you can see the glucose values that were four to six per day, or between 35 and 450 which is poor glucose control. And this shows the difficulty currently in managing people that have diabetes that require insulin. And the two things that we've shown is the average increase in glucose - the mean glucose being high is detrimental to the patient as well as glucose variability. So preoperatively, this person has a glucose 35 up to 450, and that's something you definitely would try to avoid. You now see in the read the patient is now attached to this continuous glucose monitor. And here we are able to measure glucose every ten minutes. And we're able to titrate insulin intravenously to those glucose measurements. And intraoperatively and postoperatively, we're able to keep this person's glucose level in the normal range. There are sensors that can go intravenously in the vena cava or a peripheral vein. These are sensors that go on the black device on the patient's abdomen on the patient's right. A little needle goes under the skin and measures glucose and interstitial fluid minute by minute. And on the other side of the patient's abdomen is an insulin delivery catheter. And for people that have insulin-requiring diabetes, this is the future of management where you sense glucose minute by minute - and you deliver insulin according to a computer algorithm. This is data in a surgical patient at Jefferson that shows the advantage of data every five minutes. And you can imagine if the nurse saw a glucose dropping at a fast rate, there would be an intervention of decreasing insulin giving additional glucose. And you eliminate the actual risk of hypoglycemia. And the last slide here shows actually our goal is artificial pancreas close-loop. On the top is glucose concentration, milligram per deciliter. And the patient is eating breakfast, lunch, dinner, snack. And it's excellent glucose control from 65 to 110 over a day and a half of monitoring. The middle graph shows insulin delivery - and that's rate of delivery. And as the sensor recognizes, after a meal, a rate of rise, the computer tells the pump to give additional insulin. And when the meal is being absorbed and the glucose plateaus and then starts to come down, the device turns off the insulin at the appropriate time to get a soft landing to avoid hypoglycemia. So this is the direction, this type of device research is heading. And it's very exciting because it works and we've demonstrated feasibility. And it has great potential to help patients. Back to you, Dr. Yeo.

00:54:45

CHARLES YEO, MD: Well Dr. Joseph, thank you very much. I think it's really exciting - the opportunities here for tighter glucose management in these patients - particularly in these patients who have lost islet cell mass and have had a pancreatectomy. Now while this concludes the formal part of our presentation, we have had a number of questions that have been emailed in to us. So I want to start first with Dr. Kowalski. Tom, someone has emailed in the question: "If, in the ideal world, when you sample one these cystic structures, what exactly should you send

that fluid for? What tests should be ordered so that you know that you're going to get the best information from the cyst fluid?"
00:55:25
THOMAS KOWALSKI, MD: Well Charlie, I think that that is an ongoing area of research. We currently send the pancreatic cyst fluid for chorionic embryonic antigen - CDA. And also we send it for amylase. And we also send it for Rhydian DNA studies. Some of these are research tools and some of these are used clinically. But right now we are using a variety of tests to come up with a formula to suggest what a pancreatic lesion is. We generally do not get one hundred percent accurate answer unless the cytologist - we also send material from the cell wall as well as the fluid to their cytologist - if the cytologist tells us there's a cancer cell in there or a dysplastic cell, then we can be very definitive in our answer. But otherwise it's a formula which gives us an estimate of what the lesion is. Many of these lesions are very similar in their origin, and so using these fluid analyses, we can make a suggestion of whether this is a benign, precancerous, or early cancer.
00:56:48
CHARLES YEO, MD: Great, Tom. Thank you. Another question that has come in has come for Dr. Mitchell. And Dr. Mitchell, the audience wanted to ask, in your opinion, which is the best imaging technology available to date. You showed an MR scan - a beautiful MR scan. And you showed a beautiful CT scan. So, in the limited environment where dollars are limited, which studies should be done to evaluate these patients, say with a cystic neoplasma of the pancreas? What's your best answer to that, Don?
00:57:19
DONALD MITCHELL, MD: That's a very good question. And it does depend on a few things. Number one is the quality of equipment and radiological services available to suit the patient. Assuming that there is optimal technology and expertise available, for characterizing a cystic mass, MRI has exquisite ability to separate fluid from solid tissue and to define the morphology of the cystic mass. CT scanning - where it really excels at the present - is for delineating vascular anatomy for surgical planning. So for characterizing: when possible, I prefer MRI. But for surgical planning and vascular anatomy delineation, CT has the edge at the present time.
00:58:09
CHARLES YEO, MD: Great, Don. Thanks very much. Tom, I understand you've been passed some questions.
00:58:13
THOMAS KOWALSKI, MD: Yes, we have a couple questions from our audience. And this is directly for you, Dr. Yeo, in an area that you have a great deal of interest and have devoted much of your life to. And that is, what is the difference between the mini-Whipple and the classic Whipple? And why should we preserve the pylorus?
00:58:32
CHARLES YEO, MD: That's a great question, whoever asked that. Thank you very much for asking it. So the classic Whipple operation has been around for many, man years. It's actually very different than the operation Dr. Whipple described. But what we think of (as) the classic Whipple operation, it takes out about the lower third of the stomach and the pylorus and the entirety of the duodenum. Now the stomach is a large reservoir, and it helps be able to eat large meals. By preserving the pylorus and the entire stomach, they have a more normal GI tract physiology. They have a much more normal neuroendocrine milieu of the GI tract - that is, their hormones work normally. In addition, several studies now have shown that there's no cancer advantage - there's no oncologic advantage - to doing a bigger operation. So in this operation and in this disease - much like breast cancer - bigger is not better. It's not better to do a big resection. And as long as you can extricate the

tumor and the lymph nodal draining basin, that's what you should do. So the other key point is that the mini-Whipple operation takes a little bit less time so there's less anesthesia. Patients tend to recover more quickly following that. And here at Jefferson, we actually end up targeting about a six-day hospital stay following the mini-Whipple operation. Now that's in contrast to the classic Whipple operation of decades ago where people often stayed in the hospital two, three, (or) four weeks. So we've really made great progress, I think. And for most patients, the mini-Whipple operation would be the operation of choice. Dr. Brody, I wanted to ask you a question that came in from the audience. And that is: "Share with us in 30 seconds to a minute, Jon, where do you think we're going to go as far as this molecular genetics? What's on the forefront? What do you think is going to be the big breakthrough coming up here?"
01:00:25
JONATHAN BRODY, PhD: That's a great question. A number of my colleagues and mentors have made great strides over the last ten years in really depicting the molecular defects that cause that pancreatic cancer (to be) formed. I think what we're looking over the cliff right now is actually the same way that we treat bacterial infections. You know, you don't just get a classic dose of penicillin. Usually it's sent to a microbiology lab, and you describe whether it's gram-positive, gram-negative, what brand of bacteria it is - (and so) you get what brand of antibiotic. And I really think the forefront over the next five to ten years is we can actually tailor-make the antibiotic chemotherapy, if you will, as we find out more of these magic targets and describe some more of these more magic bullets. We'll be able to tailor-make, optimize, give a logical, rational therapy in the adjuvant setting.
01:01:21
CHARLES YEO, MD: Well great, Jonathan. I think we have time for one more quick question. And I think I'd like to direct it to Jeff. Somebody from the audience has asked, "how far away are we from a close-loop artificial pancreas?" Dr. Joseph, predict the future for us here.
01:01:37
JEFFREY JOSEPH, DO: Our lab and others have developed technologies to do it today in the laboratory. The sensors, however, are not as accurate and robust as they need to be in the ambulatory patient. So in the hospital setting, I envision an artificial pancreas being around in the next year to 18 months. It's that soon. In contrast in the outpatient setting, it'll be several more years.
01:02:09
CHARLES YEO, MD: Well great. I wanted to thank all of our panelists for participating in this webcast. And thank all of our viewers for logging on. I do want to mention that the patient that we showed today had a splendid recovery following the pylorus-preserving pancreaticoduodenectomy. The patient actually went home on postoperative day number six, has been seen in follow-up, and is doing quite well. For those of you who registered for CME credit, you may take the post-assessment survey by clicking the button on your webcast screen. You may also make an appointment or refer a patient by clicking that appropriate button also on your computer screen. If you by chance missed any of this webcast and would like to view it again, it will be archived and available for viewing later this evening. On behalf of all of our panelists, Thomas Jefferson University Hospital, thanks again for watching. And I'd encourage all the physicians out there who deal with this patient population to please take good care of the many pancreatic cancer patients that entrust their care to us. Good evening from Center City Philadelphia. I'd like to also comment that the beautiful illustrations you saw come from the surgical atlas of Dr. John Cameron. That's the *Atlas of Surgery, Volume One*. And the illustrations were actually drawn by Cory Sandone, one of the most talented watercolor illustrators that

I'm aware of. So thank you very much again. And thanks for joining us here at Thomas Jefferson University Hospital.
01:03:47
ANNOUNCER: This has been a pylorus-preserving pancreaticoduodenectomy performed from Thomas Jefferson University Hospital in Philadelphia, Pennsylvania. To make an appointment with a Thomas Jefferson University Hospital physician, call 1-800-JEFF-NOW or click the "make an appointment" button. Physicians may take a post-assessment survey for CME credit. Instructions are on the computer screen. This internet broadcast represents the hospital's ongoing efforts to bring the latest medical education to both patients and the healthcare community.
01:05:03
[end of webcast]