ENDOSCOPIC ULTRASOUND PROCEDURE WITH NEEDLE BIOPSY
HARTFORD HOSPITAL
HARTFORD, CT
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00:00:09
ANNOUNCER: Welcome to Hartford Hospital. Over the next hour you'll see an endoscopic ultrasound performed live. Endoscopic ultrasound combines endoscopy and ultrasound in order to obtain images and information about the digestive tract and the surrounding tissue and organs.
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MICHAEL J. GOLIOTO, MD: With ultrasound, the closer you can get to something, the better picture you get and the more accurate vision of what the organ you're looking at is.
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ANNOUNCER: Doctors can obtain tissue samples by passing a special needle into enlarged lymph nodes or suspicious tumors. The tissue or cells obtained by the needle can be examined by a pathologist under a microscope.
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MICHAEL S. KARASIK, MD: We can biopsy lymph nodes, actually see smaller lymph nodes than most CAT scans can find, and in a non-invasive way within only about 15 minutes actually biopsy lymph nodes.
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ANNOUNCER: OR-Live makes it easy to learn more. Just click on the "request information" button on your webcast screen and open the door to informed medical care. Now let's go to Hartford Hospital.
00:01:10
Good evening and welcome to Hartford Hospital. Tonight you'll be seeing a live demonstration of endoscopic ultrasound with fine needle aspiration. My name is Dr. Michael Golioto. I'm a gastroenterologist here at Hartford Hospital. I'll be joined by Dr. Michael Karasik, who will be performing this procedure. We will be joined by Dr. Mark Ludwig, who is the director of anatomic pathology, and also Dr. Won Hae Ju, who is the director of anesthesia and will help in sedation of the patient. I want to have a couple reminders. First, as we join our broadcast, you will be able to participate in this broadcast tonight by emailing in questions by the following address: MDirectAccess button that's seen on your screen. An archive of this webcast will be available on both the hartfordhospital.org website in addition to the or-live.com website, and will permanently be available for viewing in the future. "See me" credits will also be available to any physicians or any healthcare providers that are – that are watching the broadcast live. Now I'd like to turn things over to Dr. Michael Karasik, who will introduce some of the team that will be helping to perform this endoscopic ultrasound procedure tonight.
00:02:13
MICHAEL S. KARASIK, MD: Good evening. I'm Dr. Michael Karasik, and this is our team. Our nurse specialists, Pat and Mary Lou. Our technicians, Val and Sean, and Mike in the department of cytology. This is Dr. Ju from the department of anesthesia. Now we're going to return to Mike.
00:02:32

MICHAEL J. GOLIOTO, MD: Great. Thanks for the introduction of the crew. It really helps to show that it's really a team effort to help get these complicated procedures performed and it's not just a one-person show; it involves a variety of healthcare levels. I'd like to run over briefly to take a look at some of the indications for endoscopic ultrasound. Endoscopic ultrasound is a very important procedure in the GI world. It can help change the treatment plan in up to 74% of the patients that require this. It helps in obtaining tissue for diagnosis in addition to helping stage malignancies of the gastrointestinal tract. Endoscopic ultrasound began as a test to look at submucosal masses of the stomach and of the esophagus, that is, tumor right under – directly under the layer of the esophagus and stomach. It had a limited role in GI staging and was used originally to look for gall stones in the gall bladder and bowel duct systems. It has now involved into a procedure looking, again, at submucosal masses, and have extensive staging of different gastrointestinal malignancies, in addition to lung lesions, mediastinal diseases, pancreatic cysts, and pancreatitis.
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Endoscopic ultrasound is a great technique because it allows a higher frequency ultrasound probe than a traditional transcutaneous ultrasound approach. What you will see is that with a higher frequency, you will have a great – a somewhat limited depth of penetration but a lot higher definition view, so you will see things in greater detail. By seeing things in greater detail, you'll be able to assess tumors of smaller size than can be picked up by conventional radiologic techniques and also be able to obtain tissue, since that by placing the ultrasound probe on the tip of an endoscope, we can place the ultrasound probe in close proximity to the organ of interest. So we are a lot closer to things. In addition, we have reduced interference between bowel, gas, or bone. The two scoops – the two scopes that we use, one is called the radial and one is called the linear. The radial scope evaluates an ultrasound plane that is perpendicular to the shaft of the scope and allows us to obtain images much like you're seeing – as you're seeing on the screen. But it allows us to obtain images that are similar to CAT scan procedures, which a lot of physicians are accustomed to evaluating and using. The linear echo endoscope allows us to use an ultrasound beam in the plane with – parallel to the shaft of the endoscope and allows us to use a needle placed through an accessory channel to obtain tissue and to allow us to do our biopsies under direct visualization by avoiding blood vessels and going directly through the gastrointestinal wall.
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Endoscopic ultrasound is very commonly used in cancer staging, or staging of masses above the esophagus, stomach, pancreas, rectum, and the lung, in addition to mediastinal masses or other retroperitoneal or pelvic masses. The key is that there's this high-resolution anatomic imaging in addition to targeted tissue collection. When you first place the radial echo endoscope into the esophagus, you get an orientation that shows the aorta, the heart, and the major blood vessels in the chest cavity. As we advance down to the – for the procedure today, we will be concentrating on a gentleman who is an 82-year-old who had a question of a pancreatic mass. The gentleman had abdominal pain and presented with some small amounts of weight loss. Since he had had a contrast reaction, he had a contra—a CAT scan performed without the use of intravenous contrast, which does obscure the views somewhat and doesn't provide the detail that we would like to obtain. Therefore, endoscopic ultrasound would be a perfect procedure for this to further delineate the abnormalities seen on the CAT scan and to give us a different modality to look – ultrasound, which does not use contrast, or does not use any MRI-type signal. If you look at the slide, you can see when we have the probe placed through the duodenum, you can get views of the – very good views of the gall bladder, the bioduct, the cystic duct, which drains the gall bladder, in addition to the pancreatic duct, where it enters into the intestinal tract.
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On this next slide you'll also see, too, that you can get very good pictures of the pancreatic head, some of the surrounding arteries, such as the superior mesenteric artery, the renal vein, the superior mesenteric vein, and the portal vein. The pancreas will lie between the

duodenum and the portal vein when you're in the duodenum. Older modalities we have which serve a similar interest to evaluate the pancreas and the bile duct system would be an endoscop—an ERCP, or an endoscopic retrograde cholangiopancreatography, where dye is directly injected into the biliary system. This is a more invasive test and has extra risks that the endoscopic ultrasound does not have but gives different information looking at the duct work or the tubing or plumbing that drains both the liver and the pancreas. A nice view is to look at what the ERCP would give you and what the ultrasound would give you. On the right you'll see a picture where the ducts are injected with dye. You'll see what the duct work looks like. But you're really not seeing anything of the underlying tissue. In the next slide you'll see that you could have abnormal tissue surrounding the central pancreatic duct, which is hidden to view on the ERCP screen. We'd like to progress now to see – to Dr. Karasik in the room and see where we're progressing with the exam. As you can tell from the screen, we will see some ultrasound images of the radioscope in place as Dr. Karasik advances the scope to and fro to evaluate the different organs in both the mediastinum, the chest cavity, and the abdomen as well. And he will help describe some of the things that he's seeing.
00:07:59
MICHAEL S. KARASIK, MD: Thank you. We're going to start at the top of the stomach. What you can see is the nice folds around the center of the – which is the scope. Those wavy lines. We're going to pass further down the stomach.
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MICHAEL J. GOLIOTO, MD: I might add that endoscopic ultrasound does take additional training than most gastroenterologists have. A lot of people who – a lot of trained professionals who look at it think it looks like a bunch of fuzzy gray things next to a bunch of fuzzy dark things, so it actually takes an expert eye to look at these things and to in real-time analyze what you're looking at both endoscopically and by ultrasound.
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MICHAEL S. KARASIK, MD: All right, here we see the pancreatic neck, pancreatic body, and the tail is going to be running up this way. This is the splenic vein. Here's the celiac plexus. So this is an area that we see lymph adenopathy, abnormal lymph nodes, and oftentimes in people who have pancreatic cancer; we don't see any here. We're just going to continue to take a good look at the pancreatic tissue. Here you see the duct in the pancreas, this little tube right here, which is normal in caliber.
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MICHAEL J. GOLIOTO, MD: Just a little brief anatomy lesson here. The pancreas is a digestive organ which is responsible for the production of insulin and production of digestive enzymes and lays at the back of the abdominal cavity underneath the stomach. So it's traditionally very hard to get to or see with any other technique because you have overlying bowel gas or stomach gas, so by placing the endoscope directly into the stomach itself, you will see that by placing the probe against the back wall of the stomach, you're in very close proximity to it. You'll see at the center of the screen the ultrasound probe is there. And if Dr. Karasik were to measure things, he'd be within a centimeter or two, or about an inch or so away from the whole pancreatic tissue.
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MICHAEL S. KARASIK, MD: That's right. Here's the pancreatic neck. You can see a curve around to the body and towards the tail. So you get a very good look at the pancreas from inside the stomach. We can't see the pancreatic head from the inside of the stomach; we're going to look at that in just a minute. Now we pass further down in the stomach. We're going to go into the small intestine. And the first thing that you can readily see is the gall bladder filled with stones. All those areas are stones.
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MICHAEL J. GOLIOTO, MD: Again, a little anatomical note. As we proceed through the duodenum like that, you will see that the – that the scope in the middle of the screen is in

very close proximity to a lot of different organs, including the liver, the gall bladder, the bile ducts, the pancreas, the pancreatic head, and it's a very complicated area. There's a lot of very important vascular structures that go through this area and a lot of very important tubing and drainage systems that go through this area, so it's a lot of things going on in a very small space.
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MICHAEL S. KARASIK, MD: All right. Now we're seeing the pancreatic head, all this area over here. This vessel is the superior mesenteric artery, a very important artery when we're trying to determine whether there's a tumor that might be potentially unresectable, inoperable. We're just going to examine the pancreatic head in a little more detail.
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MICHAEL J. GOLIOTO, MD: You'll see why the superior mesenteric artery is so important. It's a major blood vessel that comes off the aorta and it provides the intestines with a majority of its blood supply in the upper intestinal tract. If anything were to involve this – this major blood vessel, you could not go around or bypass through this artery, so if anything is involved with it, it really limits any further treatment options.
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MICHAEL S. KARASIK, MD: Here's the inferior vena cava. Cross-section of the renal vein.
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MICHAEL J. GOLIOTO, MD: Okay.
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MICHAEL S. KARASIK, MD: I think we're going to need to rotate him a little more towards his stomach.
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MICHAEL J. GOLIOTO, MD: Occasionally you'll hear Dr. Karasik depo—will ask to reposition the patient. Sometimes by lying the patient in a little bit of a different position, it'll allow the scope to fall into a different position and get a different angle. The scope that he's using now is the radial scope, which takes a perpendicular view to the shaft. If you were to see an x-ray of the endoscope itself, you'd find that the shaft is curved and the end is very flexible and can contort itself. And the operator has full control over this. By maneuvering the scope, by twisting and turning the shaft, by inserting it and pulling it back, you get very—you can scan through different things, get a very different view of the organs of interest.
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MICHAEL S. KARASIK, MD: Okay. Here we see a focus and may be the abnormality that was suggested on the CAT scan. See a darkened area right over here.
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MICHAEL J. GOLIOTO, MD: So right now Dr. Karasik is measuring the lesion, which is a very accurate way of measuring the size, in addition to noting the location of things.
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MICHAEL S. KARASIK, MD: So that's 1.4 cm. That's a very small area. I'll have to see if we see that again on – with the linear scope. Here you can see the insertion of the pancreatic duct, which drains right into the intestine right over here.
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MICHAEL J. GOLIOTO, MD: So Dr. Karasik is referring to the duct which drains the pancreas, which runs like a spine down parallel to the entire length of the pancreas. This is about the size of a flounder and lies in back of the stomach. And the spine is very important to find and see. If there's any pancreatic duct dilatation or it's larger than it should be, that could be evidence that there's a disease process going on that would somehow block the drainage of the pancreas. If the duct is bigger than it should be -- tubes of the body are not like piping; if they are blocked, they will get bigger.
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MICHAEL S. KARASIK, MD: We saw the common bile duct for just a second. We're going to go back and see if we can find that again.

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MICHAEL J. GOLIOTO, MD: So one of the portals of view he's using – he's going back and forth between the stomach and the duodenum and trying to obtain different images from different locations in the GI tract. You can sometimes see – you'll see different organs or you'll see them in different perspectives or a different angle.
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MICHAEL S. KARASIK, MD: And this is the common bile duct right there, which looks normal in size.
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MICHAEL J. GOLIOTO, MD: Okay, we have our first question from – from the or-live.com website. And someone asked who was here in Connecticut, "Why are the people in the procedure wearing a plastic welding mask?" What they're doing is they're wearing a shi—a face shield, which is the current recommendation for infectious disease control. Sometimes these procedures can involve body fluids or blood, and if the needle or any of the bio…you can have some droplets of body secretions that can come out from the endoscope. This protects the nursing staff, the doctors, and the healthcare professionals from exposure to different people, and it's the current recommendation for universal precautions. In addition, you'll see everyone wearing gloves and a gown, which is disposable. This is not a sterile procedure like you'll see in an emergency room, so you will not see hair nets or masks involved because it doesn't need to be. The gastrointestinal tract by its definition is a dirty place. It has bacteria in it, so it's not a sterile procedure where you'll see them cleaning the abdominal wall or making an incision, much as you would see for a surgery. That's an excellent question.
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MICHAEL S. KARASIK, MD: Okay, one additional finding here. Pancreatic head is demonstrating a number of abnormalities suggestive of some chronic inflammation. These white flecks here, and there's a little bit of lobularity to the gland. Sometimes that can make it look like a tumor that's actually not there.
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MICHAEL J. GOLIOTO, MD: Typically when you do an ultrasound exam of the pancreas, you'll get a salt and pepper type appearance to the gland. It'll be a very fine granulation. And what Dr. Karasik is describing is some of the scar-type changing you can get in a – He can share with us some of the other criteria that you can have for this chronic pancreatitis, or chronic inflammation.
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MICHAEL S. KARASIK, MD: Surely. There are a number of tissue abnormalities. They include the lobularity that we talked about, white flecks, a bright border of the pancreas, small cysts within the pancreas. If a duct is enlarged or strictured, or in particular, if the small ducts that branch off are dilated, enlarged, those are all markers suggestive of chronic pancreatitis. No one marker makes the diagnosis, but usually several are seen. We're going to take a minute now to change scopes.
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MICHAEL J. GOLIOTO, MD: Okay. And that's the interesting within this kind of ultrasound. It is a field of gray – there are really no black and whites a lot of the time, as – with no pun intended. You will see things that could potentially look like just scar tissue or inflammation. It will be very hard to differentiate between scar tissue or inflammation in a tumor itself. Oftentimes in that instance we need to do a needle biopsy. We would like the physician to obtain – to place a needle down the second scope that we're going to use to obtain tissue, and then it will be looked at under the microscope. That is the gold standard and the only known way to know if there is a major problem, such as a tumor or a growth, or if there is – if there is just simple inflammatory cells. If we can go to one of the – some of the slides here. In evaluating someone with a potential neoplasm or growth of the gastrointestinal tract, you'll see the CAT scan, as this gentleman had, is usually the first line of therapy. It's

available in the majority of hospitals. It's very commonly available. And this will see if this mass is resectable or unresectable.
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This would entail – this is a major decision point in the treatment of any pancreatic tumors. If it's unresectable, it means that there's distant disease, that cutting out the major part, the initial place where it started, would not help because it's already spread to other locations. Or if there's any obvious extension to any adjacent structure, as we looked at during some of the pictures that Dr. Karasik provided, we saw that there are major blood vessels intervening there. If there are any involvement of the portal vein or the superior mesenteric artery, then that could not be resectable. If you had an answer on your CAT scan like this, you would not do an endoscopic ultrasound; you would go into what they call palliative-type therapies, or therapies that help with symptom control. If the CAT scan doesn't show any of these definite, very advanced signs, we do refer people to endoscopic ultrasound. And again, that involves a major decision point. By getting a closer view of the tissue in question and seeing its relationship to the major structure of the abdomen, in addition to getting some cytology, or cellular sample or it, we are both able to diagnose, and secondarily, stage this tumor to see if it's potentially resectable or unresectable, and refer people to surgery, which is the definitive treatment for growths in the pancreas.
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Endoscopic ultrasound will avoid overtreatment and hopefully avoid undertreatment by providing the most accurate cancer staging of the local area. CAT scan and endoscopic ultrasound are very complementary procedures. CAT scan is better than endoscopic ultrasound at looking at areas of distant disease – looking in the liver for evidence of obvious metastasis, looking in the lungs, looking in the mediastinum – but in local area, if you're looking to see if it has any continuative within any of the local blood vessels, endoscopic ultrasound is superior and will help guide what therapy we need to go to. Some of the – just a couple pictures of some of the films that were taken in this hospital look at some of the endoscopic ultrasounds with the radial scope in place. And you'll see that occasionally, as you'll see in the – between 7 and 8 o'clock, they'll have a tumor that does involve that portal vein, that there's a loss of the border there. And on the right side of the picture, you'll see that there's an area of growth that starts in the pancreas and grows through the abdominal wall and into the stomach wall itself.
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Again, on the second – on the second side you'll see there's an area of tumor in the superior mesenteric venous area, and there's a very close proximity, and there's actually a loss of the border between the two. Once that vein is involved, it is very difficult to treat surgically and would change things. In Dr. Karasik's next slide, you'll see that there's evidence of a liver biopsy being performed through the endoscopic ultrasound of a very small liver lesion, which is approximately a centimeter in size, which can be very hard to detect with other modalities. In looking at [clears throat] – Now Dr. Karasik will be switching to the EUS-guided FNA scope. It's a linear – it's the linear scope which evaluates a whole focal plane parallel to the shaft of the endoscope. As you'll see in the middle picture, there's a needle that can be placed through this therapeutic channel, and through this needle we will obtain any tissue that we need to if there's an area of abnormality that needs further investigation. In the endoscopic ultrasound you'll see some of the pictures of a luminal view, or what the actual inside of the esophagus and stomach looks like. In addition, you will see the ultrasound image of what he's looking at behind the esophagus and stomach wall.
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For tissue sampling, the pancreas has been traditionally a very hard area of the body to obtain tissue from. You can perform a CAT scan-guided biopsy and you can perform through ERCP. We showed a picture of the ERCP, which is the injection of dye into the bile ducts in the biliary system. When there is a narrowing of the bile duct, it is typically caused from a growth in the pancreas. And if we were to sample through ERCP, the yield is somewhere

between 30% and 70%, with a risk of irritating the pancreas gland of about 5% to 10%. Endoscopic ultrasound – the tissue yield when we place the needle inside the abnormal area of the pancreas, 85% of the time we will have an 85% yield with a less than 1% risk of pancreatitis, probably a 1 in 500 to 1 in 1,000 is the recently quoted literature. So endoscopic advances in pancreatic disease. There are some limitations: pancreatitis of the ERCP, less so with the EUS. The learning curve: with ERCP, there's a moderate learning curve; in EUS, there's an extremely long learning curve. And as any physician will tell you, you never stop learning throughout your career. You always see something different and have a different techniques.
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Endoscopic ultra started and is currently with evaluation of submucosal masses, GI cancer staging, intraductal or biliary-type tumors, lung cancer staging, mediastinal diseases, pancreatitis, pancreatic… Where we'd like to go is by helping not only diagnose and stage diseases but also then perform therapy, which is brachytherapy, or the injection of radioactive materials into pancreatic tumor directly to minimize any risk of toxicity to surrounding tissue by delivering the most potent doses there, or biologic therapies with antibody therapies that are becoming available. We can now return to Dr. Karasik, who has now placed the linear echo endoscope into the esophagus, stomach, and through the duodenum. And we will obtain views of the pancreatic head, which looked abnormal on both the CAT scan and showed some changes on the radial echo endoscope.
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MICHAEL S. KARASIK, MD: Okay, so what you can see is, again, the pancreas is looking very splotchy here. This is fairly typical of chronic pancreatitis, that lobular pattern that we talked about earlier. And I'm just trying to sift through and see if there's anything in particular that looks like a mass. In the setting of chronic pancreatitis, it can be very difficult to differentiate the two, and a biopsy is often required to be able to tell the difference. Here I can get a sense of a more circular area that's a little darker, and it's a little bit more suspicious. That may be what it is that we saw before.
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MICHAEL J. GOLIOTO, MD: So we live in a world of shadows, and we're trying to determine what looks more abnormal. We're looking in a field that is abnormal, so we're looking for – we're not looking for a needle in a haystack, we're looking for a bent piece of straw in a haystack occasionally, so it can be very difficult when you have some degree of fibrosis, as this gentleman would appear to have, to see what is – if there's anything hiding in that.
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MICHAEL S. KARASIK, MD: I think this is the area that we're going to biopsy. Just going to make sure there's no vascular structures. The needle will be coming down through here.
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MICHAEL J. GOLIOTO, MD: So you'll see a little trapezoidal-shaped object that's on the screen, and what that is is a Doppler flow. As you see with the – with the weather forecast of Doppler, it's a very similar technology. What it allows you to do is see fluid motion to and fro – to and from the probe. And as he puts that in place again, you will see if he puts it over a blood vessel, you'll have a pulsating red or blue signal of if the flow is toward or away. When we're doing biopsies, we really don't care if it's to or fro; we don't want to go through any vessel, so it involves a great degree of safety that this technique allows us to avoid any major blood vessels. You'll see on the screen Dr. Karasik putting the needle and attaching it into the scope, and then he'll talk us through the procedure of what he's doing. So he's just attached the needle to the endoscope, and this needle will then go through – toward – through the therapeutic shaft, through this scope that this long needle goes through, to the tip of this endoscope. You'll see from his hand movements that the to and fro movement – and he's going to advance the needle under direct ultrasound guidance and under direct view, both endoscopically and ultrasound-wise, of where the path of this needle will go while avoiding any of the major structures in between.

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Okay, so what we're seeing now is the ultrasound view. So again, we're looking in the plane of the endoscope, parallel to the shaft. And Dr. Karasik has advanced the needle into the area – into an area of interest in the pancreas, and now there's a negative suction. If you'd like to describe what we're doing – he's placing – there's a negative pressure, so through this very thin needle, which is a – which is about a millimeter in size, he's advancing the needle to and fro with negative pressure to obtain cells that will go on the inside bore of the shaft. After tissue is obtained, we'll talk a little bit more with our pathologist and with our pathology tech about the techniques that they use to look at the material that we are able to provide them in this minimally invasive manner.
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MARK LUDWIG, MD: What Dr. Karasik is doing is removing cells from the area in question. And cytology has been a tremendous advancement in diagnosis, but it also has limitations. As Dr. Golioto said, we're taking a sample with a 1-mm needle. Traditionally, surgical biopsy is done openly, gives sizable pieces of tissue. They also have the architecture of the background tissue to help assess what is going on. With cytology, there are tremendous benefits because a patient doesn't have to undergo a surgical procedure, but the key question is, has the abnormality been sampled. And obviously we're using an endoscope, we're using ultrasound images to try and find the most abnormal area. Surprisingly, even with a procedure like this, the success is quite good, in the 80% to 90% range. We certainly do end up sometimes with samples that do not lead to diagnosis. But in many cases, the diagnosis is readily obtainable, and then one can go ahead and plan accordingly. So what -- what our cytotech is doing here is taking the cellular material and placing it on the slides. He will then fix that quickly and then stain it with a variety of stains which make the cells visible under the microscope. Then what I'll do is -- is take a look and try and get a sense of whether an abnormality has been sampled or not. That's not always as easy as it sounds. As has been described, there appears to be chronic inflammation or chronic pancreatitis, and with inflammation of the pancreas, one may see a variety of cellular changes that could be worrisome and yet are totally benign. Most of the time, however, even if there is pancreatitis, if there's a tumor that has produced it, we can make that separation on the slides. Now, sometimes we may get as many as 20 slides on a given case, and obviously, we want to give a quick answer because the patient is under anesthesia, but obviously we need a reliable answer, and sometimes that's not possible at the time of the procedure. We'll take several slides and stain them and review them. If it's obvious, we can make a diagnosis at the time of the procedure. If it is equivocal or there are confounding factors such as inflammation, we may have to go back to the laboratory, stain all the slides up, and look at them very carefully to come up with a final answer. So we'll have a look in just a minute at the cells that are present on this slide and see if we can, number one, identify an abnormality that would be causing the changes that are being seen by the ultrasound and CAT scan. Number two, if we can give a specific diagnosis, so we'll have that very shortly.
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MICHAEL J. GOLIOTO, MD: And we're very fortunate to have pathology -- a pathology tech in the room with us. The endoscopic literature will let -- will tell you that the -- the fact of having a person looking at the slides at the time you're doing a procedure will reduce the number of needle passes he needs to make because he will know if he has adequate tissue or not adequate tissue and will cut down on the number of repeat or unnecessary procedures by knowing how adequate your sample is. You'll see now, he's taking a second sample. We're dealing with such small quantities of material that more is always better, but you don't -- you don't want to do too many, obviously. If you can minimize -- every needle pass you make has a risk of irritating the pancreas or causing any bleeding, so if you can minimize the number of punctures that you need to make, that is by far better. And we're lucky to have such full support here and to have such a team approach to have in this. We do have another Internet question that comes in, says: what kind of anesthesia are you

using? That's an excellent question as well. It's a very hot topic in the gastroenterology community of what type of sedation is appropriate. Our goal is to have patient comfort primary and to do the test safely and to do the test well. By having him sedated with -- he's being sedated with propefol anesthesia under the guidance of an anesthesiologist. That allows us to give a moderate level of sedation, or a deeper level of sedation than would typically be conscious sedation, in which the patient may move or have -- or -- or be uncomfortable during the -- during the procedure itself. So we're lucky, again, to have full support of anesthesia in helping make complicated procedures easier. As you can tell from the webcast, this is -- this gentleman undergoing this test is having a endoscope about the width of your index finger placed down through his mouth into his esophagus for approximately 30 to 45 minutes, which is the typical time an endoscopical will perform. As you might imagine, even with -- with lesser levels of sedation, that can be uncomfortable, and we're lucky to have deeper levels of sedation.

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MARK LUDWIG, MD: If I can just make a comment here, the -- what I have here are slides that are placed in an alcohol fixative. The material has been placed directly on the slide and stains have been made. And so what I will do is try not to knock this over. And looking with the microscope, see what we can see. The red material that you see in the black-- in the background is blood. Obviously, if you're sticking a needle into a tissue, it's -- it's common to get blood, but usually it doesn't affect our ability to see what is going on. Now, here in the center of the field, there are some cells that are -- are dark blue. And it's a cohesive group, but they're fairly small cells, so I think we're looking at normal pancreatic tissue. One of the most important things as we look at aspirates is the cellularity. And in a normal -- a normal organ, we generally don't get a lot of material. When there's a -- a tumor or inflammatory process, sometimes we get quite a bit. So you can see that there are little nests of cells here that are forming little gland-like structures, and actually, I think what we're looking at is pancreatic acinar tissue. This would be the normal tissue that produces digestive enzymes. So at least as we've scanned around here, what I'm seeing, I think, is just normal tissue. Obviously, the slide is big and we're only looking at representative areas, but -- but generally on these, the material is fairly evenly distributed, so I don't see anything that makes me suspicious that we're dealing with a tumor. And as I said at the beginning, the key issue here is sampling and has the area with the greatest abnormality been -- been sampled? And so Dr. Karasik's approach will be to sample one area, and then while we're taking a quick look at this, he'll sample another area. And we'll -- we'll continue until he gets to the point where he's comfortable that he's sampled a good representation of the area that looks abnormal by ultrasound. What we'll then do is we'll look at representative slides from each pass. If we only see what we think are normal or reactive tissues, we'll say that that's the case as a provisional diagnosis. We then go back and carefully screen all of the -- the slides. Now this field right in the center, you can see, has kind of a geographic look to it, and I believe these are ductal cells. The ducts that line the tube, as Dr. Golioto said, that runs the course of the -- length of the pancreas. And this has a very regular quality about it, so again, I think these are benign ductal cells. So we've seen two of the major components of the pancreas, acinar cells and ductal cells, and I don't see anything that has the sort of irregularities in size and shape that would make me be suspicious that I'm dealing with a tumor.

00:38:25

MICHAEL J. GOLIOTO, MD: On that note, Dr. Ludwig, we do have some Internet questions as well, mainly pertaining to the biopsy, one of which being: what types of stains are used and how do the different stains help in the diagnosis? The second being -- which I can help answer a little bit -- is: is a core tissue biopsy an option, or does fine-needle aspiration for cytologic evaluation offer the best possibility for accurate sample collection? I'll answer this a little bit and I'll turn it to Dr. Ludwig. Core tissue biopsies involves using a larger-gauge needle and getting some histology or architecture. Unfortunately, the scope that we use,

the channel is just so large, and we cannot typically place a very large needle in, nor would you typically want to. If you -- if you were -- typically, when larger needles have been used through an endoscope, you have more complications of bleeding or more complications of pancreatitis and -- and you are often able to use the fine-needle aspiration, which is a twin 2-gauge needle for -- and get full information of this. Would you like to answer what types of stains are you using and...
00:39:22
MARK LUDWIG, MD: Various people use different stains. We have usually used the standard stain that one uses for tissue biopsies, and that is hematoxylin-eosin. Hematoxylin stains the nuclei of cellular material, and it's generally the nuclei that tell us whether we're dealing with tumor or not. The eosin is the pink that you see here, and that's -- stains the cytoplasm, and it gives us some clues, but it's really the nature of the nuclei that tell us whether we're dealing with a reactive or a neoplastic process. Again, as we look at this group, it has a very regular honeycomb quality about it. I don't see any mitotic figures which are -- which is evidence of cells dividing. I don't see the -- the size and shape variation that we typically associate with tumors and cancers, so at least -- I'm not seeing anything that is dramatically abnormal and would -- would make me think that we're dealing with a suspicious --
00:40:37
MICHAEL J. GOLIOTO, MD: Let's briefly return to Dr. Karasik and -- and get an update on what's -- what's going on.
00:40:43
MICHAEL S. KARASIK, MD: Well, I must say, my impression is very much like what Dr. Ludwig is saying. I think I would refer to this as likely to be a pseudotumor, giving us a false sense of there being a tumor, and probably this darkened area here is all due to chronic inflammation, so in fact, I'm not convinced that there is a tumor here. But that's the area we've been biopsying because sampling errors certainly are a consideration, so we want to make sure we have enough tissue.
00:41:09
MICHAEL J. GOLIOTO, MD: One of our other questions was why is a second pass being performed before the first pass has been analyzed, and a lot of times, we do want to maximize the amount of tissue. It's -- it's not unusual, but it's -- it's not rare, but definitely unusual to have adequate cytology sample on the very first pass. Oftentimes we do need to have more. If you think about the miniscule amount of tissue we're taking out of the pancreas in relation to the size mass we're using, you're maybe sampling 1/10,000th or 1/100,000th of what the -- what this -- what this growth or what this area is. So we're looking at very small samples. It's almost as if you're trying to predict who won the presidential election by asking 10 people you know, so oftentimes we do need to do more polling or more samples and then a collection of all the cytology specimens at the end will help provide an adequate -- an adequate answer.
00:42:03
MARK LUDWIG, MD: I would say, based on what we have here, I don't see anything suspicious. My experience has been when we do these adequacy assessments, there will be a small percentage of cases where the diagnostic cells are not on the slide that we chose to stain, and my guess is it probably runs around 5 or 10%, but I think we -- we can certainly say that Dr. Karasik has been in the pancreas, he's got a fair amount of cellular material, and -- and although a lot of cells often means tumor, with pancreatitis one may sometimes see a lot of cellular material. Now, one thing that I don't see here in the background is -- is a lot of acute inflammation. Sometimes people develop abscesses that we can diagnose. I don't see a lot of hemorrhage and old blood, which sometimes a mass lesion can be -- can result from pancreatitis in what gets called a pseudocyst, so there are some things that I don't see, but on the other hand, I -- I don't see anything at this point that -- that I'm very suspicious of.

00:43:23
MICHAEL J. GOLIOTO, MD: Okay, we have another question. Dr. Karasik, I don't know if you'd want to help with this. I've got a question -- another question from one of our Internet viewers: when you do take samples out of the body and it bleeds, what do you do with the bleeding?
00:43:35
MARK S. KARASIK, MD: Well, bleeding firstly is very rare because we have the ability of dopplering, so we know what vessels are in the way. I personally have not had anybody who had any bleeding, but the -- the general practice is to observe it because the bleeding would stop spontaneously in most cases. And if a little hematoma was shown here, we'd be able to see an expanding area to show us that there had been bleeding. There is -- there's nothing therapeutic short of surgery to fix bleeding that won't stop, but most bleeding stops spontaneously and bleeding is very unusual.
00:44:16
MICHAEL J. GOLIOTO, MD: So right now, are we -- let's go back to the room and see what we're looking at in terms of on the ultrasound screen.
00:44:23
MARK S. KARASIK, MD: Well, I've been trying to find some different areas to see if there's any other area that I'm missing, and I really think we're dealing here with a pseudotumor, something that looks like a tumor but is really not. I saw no lymphadenopathy, no abnormal lymph nodes on the way down. I see no lymph nodes around the pancreas, around the head, and I've not seen anything besides the areas that we've biopsied several times already.
00:44:50
MICHAEL J. GOLIOTO, MD: So it's very interesting. We went into this procedure with an abnormal CAT scan, an abnormal picture, so obviously the patient was very worried about a potentially underlying tumor or malignancy. And we now come to a time where we look at it with the ultrasound scope, and again, the tissue looks very scarred or irregular. And a lot of times in situations like this, the only way we will know what they have or do not have is by taking a sample out of it. So that -- if the person were not to have had this procedure, we would still be left in the dark and not have a very firm understanding of what -- of what has gone on. The other things that Dr. Karasik are looking for are little footprints. When there is a growth or a tumor in the pancreas, occasionally, you will have lymph nodes or areas that are enlarged or should be. Again, you will also see if the pancreatic duct or the bowel ducts are bigger than they should be, as if there is abnormal tissue that is in the pancreatic head, these ducts would be dilated. So if -- in addition to just seeing some -- some mildly abnormal tissue, we're not seeing any of the typical footprints of -- of great concern.
00:45:56
MARK S. KARASIK, MD: Dr. Ludwig, do you think you have enough tissue?
00:46:00
MARK LUDWIG, MD: Let me take a look at this third pass.
00:46:02
MICHAEL J. GOLIOTO, MD: So we've made -- so we've made a third pass, and Dr. Ludwig's going to evaluate that for us, but there's an ongoing dialogue between the pathologist and the endoscopist of when to stop doing the biopsies or when to know and typically if he has an adequate sample of tissue that he's obtained and looked at. And it sounds like, from the first two passes, at least we have some adequate pancreatic tissue. And we'll now look at this -- at this third pass to see if there's any -- anything different from the prior two.
00:46:27
MARK S. KARASIK, MD: I'm going to hold off on any more sampling until we have a better idea.
00:46:33
MARK LUDWIG, MD: I think, based on the first two aspirates, we have good material to look at, and I think if you feel comfortable that you've been in the most abnormal areas, I have

not seen anything that would want me to push you to -- to get more material. We -- we do have another half-dozen slides or more that we'll have to look at, but I think as far as assessing that you have a reasonable sample, I think I can say yes on that.
00:47:07
MARK S. KARASIK, MD: That was the most abnormal area that I saw. I'm going to come back now and examine the pancreas again on the way out and make sure there's no other areas of concern.
00:47:16
MICHAEL J. GOLIOTO, MD: So we've focused a lot on the pancreatic head, since that's where the CAT scan pointed us, and now Dr. Karasik's going to look at the pancreatic body and tail, the remaining half to two-thirds of his pancreas, which is best viewed there through the stomach. Dr. Karasik, there's another question, it says: is the biopsy only taken if there's a region that looks suspect or would you sometimes take a biopsy in a general area of the pancreas to test for disease?
00:47:40
MARK S. KARASIK, MD: It's -- it's not adequate really, I think, in the setting of a -- of a nonmalignancy to be sticking a needle in. first of all, sampling is not going to really be adequate. I think Dr. Ludwig can attest to that more than I, but the size that we get is really not adequate for making just about any diagnosis with certainty other than tumor. And there is risk associated with passage of a needle, so we don't -- we don't do it lightly.
00:48:12
MICHAEL J. GOLIOTO, MD: Sometimes we can be fooled by abnormal-looking tissue, but if you get a good ultrasound view and it looks like the typical density that you're used to seeing with the ultrasound, you can -- with some pretty good weight -- tell people what is normal. If it does look abnormal, a lot of the times, like there is some scar tissue or fibrosis here, the only thing that will differentiate that is a piece of tissue to look at under the microscope. So no, we typically don't biopsy normal-appearing parts of the pancreas because, again, it's a -- the pancreas is a very delicate and soft tissue, and when you poke it with a needle, sometimes it gets angry at you.
00:48:46
MARK S. KARASIK, MD: Here's an interesting finding. I'm now in the stomach and I'm looking at the aorta. Over here, you'll see a branch -- a dark branch -- that's the celiac artery. In patients who have abdominal pain secondary to pancreatic cancers, we can inject medication right over here to dampen the sig-- kill the nerves and decrease the pain. It's one of the therapeutic things that we can do with endoscopic ultrasound, and in fact, right by the needle you'll see a little stripe go by, and that's the nerve plexus itself.
00:49:28
MICHAEL J. GOLIOTO, MD: When we do -- when we perform these needle -- as Dr. Karasik was saying, when we look at the celiac plexus, you can see there's a very large blood vessel, the aorta, which is the major blood vessel that goes through your abdominal cavity, and obviously placing a needle in close vicinity to this, you'd want the optimal imaging of this area to protect things. You're trying to help someone by decreasing pain by doing an injection there, and it's an area that you can cause a lot of potential harm, so if you're looking at the size and location, there's not a lot of organs in between the stomach and the aorta at that part, and you're looking at some -- a very dangerous area if you were to go from a -- from a needle from outside the body. So being close gives you a lot better view of things.
00:50:13
MARK S. KARASIK, MD: I think we're going to pull the scope out now. I don't think that there are any other abnormalities, thankfully. We're just going to examine as we come up into the chest to make sure there's no lymph nodes that we missed.
00:50:29

MICHAEL J. GOLIOTO, MD: I have a question that both Dr. Karasik and myself can answer because the next question is -- there's two questions: how long has this procedure been in place at Hartford Hospital? And: are you in a learning curve if the time has been short? That's an excellent question. Dr. Karasik has been at Hartford Hospital since 1997, I believe. Correct me if I'm wrong. He has performed approximately 300 procedures a year -- between 200 and 300 procedures a year -- so we're all still learning, but I'd say the learning curve is -- he's not on the steep part by any stretch of the imagination. I have been at Hartford Hospital for five years. I've performed approximately 150 to 200 per year. So that's -- in the realm of endoscopic ultrasound, that's not -- not exactly a short time. But these are excellent questions. many times patients do not ask their doctors how many of these procedures do they perform, how long they've been performing them. It's somewhat of a gray zone. We usually welcome questions like that when people ask. The other question is: can you explain about the post-op and how long the patients stay in the hospital. The patient -- this is an outpatient procedure. This gentleman will -- will be going home tonight after the sedation wears off. The type of sedation, which is propefol, that we're using would typically -- after the infusion is finished -- he will be awake within five to ten minutes and talking with his family. There are some amnestic effects to the medication, so he might not remember a lot of the events and will not remember the procedure at all, but typically this is done as an outp-- on an outpatient basis. As Dr. Karasik is now finished with the procedure, we can invite him to have any comments about this specific case. Dr. Ludwig, are there any points you'd like to make about...

00:52:17

MARK LUDWIG, MD: No, I think we've pretty well covered it. I think, as he -- it really is a team effort. And as I work with the gastroenterologists and other -- people who do the FNAs, I think things have to make sense. If they're seeing something that they're very concerned about and I'm not, then I think the working diagnosis has to be that there's a sampling error. If what I see matches their opinion, then I think we feel pretty comfortable about accepting that as the final diagnosis. That said, there's always the chance that we may not actually identify the underlying disorder, and so clinically, patients need to be followed. It's not just "go home, everything's fine," but followed just to make sure that things play out as one would expect.

00:53:13

MICHAEL J. GOLIOTO, MD: Dr. Karasik, we have a question potentially about the future. It says: if 3-D ultrasound was available, would this help at really knowing your sample was in the tumor?

00:53:27

MARK S. KARASIK, MD: 3-D ultrasound is not available here, but I've seen many demonstrations of it, and my personal impression is that it probably would not help. What we do right now with two planes allows us to see the -- the area of interest, the tumor usually, and -- and the needle. And you can see the needle in it, so I don't think it'll help in that way. 3-D ultrasound may help with staging a little better. I don't have personal experience with it and I'm not totally convinced that it adds anything at the moment, but it's an evolution as well.

00:54:02

MICHAEL J. GOLIOTO, MD: Absolutely. I -- I believe it's pretty much a research tool right now, is not commonly clinically available. There wouldn't be a majority of hospitals that would have it available. I don't know what the -- what is involved with the equipment versus the typical equipment people will have is, but like we said, sometimes more is better and sometimes more is not better. Sometimes you can get things done pretty well with what you have. If we look at the slide I have here, in looking at tumors, endoscopic ultrasound was such an advance over CAT scanning and for both detection of tumors and detection of staging on the slide I have here. The sensitivity of a CAT scan for tumor staging, for getting the tumor accurate, knowing the size and location and what it connects to, is

about 44%. With regular ultrasound from the outside of the body would be about 35%, so lower. With endoscopic ultrasound, it's in excess of 80%. And in testing for lymph nodes, which typically will happen in the immediate or direct area, again, endoscopic ultrasound excels by having a sensitivity of 72% versus ultrasound from the outside of the body, which is 42% and CAT scan, which is 48%. Portal vein involvement: that major blood vessel Dr. Karasik was looking at in the pancreatic -- next to the pancreatic head, endoscopic ultrasound is the best modality to look at the portal vein, which is a major determinant over sectability or treatment, and that's at 85% versus 69% for CAT scan. Arterial involvement is somewhat lower in endoscopic ultrasound than CAT scan because it does involve some distance from the probe in how far it can go or not go. Dr. Karasik, do you have any closing comments about the case in particular or about the procedure or the technique or things that we do or should do differently?
00:55:45
MARK S. KARASIK, MD: I think that endoscopic ultrasound is something which is becoming very widespread right now, but most centers don't have a lot of experience, where I've been lucky in the past and have been able to get trained in it, as is Dr. Golioto, and our numbers are -- are still on the rise. When we first got here, there were five cases per week, and having demonstrated all of the advantages of EUS, we're now doing up to sixteen cases per week, and I -- I think that in the future, it will have many more uses. In this particular gentleman, I think it's very helpful, but because of the risk of sampling error, I wouldn't let a negative biopsy allow this to be the end of the story. I would recommend we repeat a CAT scan in three to four months and make sure there's been no change in the finding that we've seen previously. But I'm expecting that there won't be any evidence of tumor on that either.
00:56:39
MICHAEL J. GOLIOTO, MD: That's an excellent point. I don't think we can look at any test in isolation as a time point alone and by itself. We do need to look at things with time, and it does look normal at this point in time. The tissue sample looks normal as well, but we can't -- we can't always trust the normal. We have to keep on following and treat the patient for what the symptoms they have and what other kind of diseases or processes occur and go on. As you saw a little bit from the demonstration today, it is not a solo effort. There are many people in the room with Dr. Karasik. We had two endoscopic technicians with us helping with both setting up the endoscope and with obtaining the tissue and processing the tissue. We had a pathology technician who, on a typical day, provides us a lot of expert evaluation and preparation of the slides and letting us help and determine adequacy of the sample. We have an anesthesiologist who's extremely experienced in providing moderate levels of sedation. Not too much and not too little. It's like the three little bears: too big, too large, or just right. And she gets it right a lot of the times, and we're lucky to have help like that in performing complicated procedures. We have two very well trained endoscopic nurses in the room as well. They're accustomed to dealing with anything they need to during the procedure: in getting the sample, getting the needle, potentially with any complications. And we have a very experienced physician, Dr. Karasik, who's done many cases like this, in addition to the pathologists who help us as well. We get a lot of help from radiologists, both before and after the test, from telling us what we see during the CAT scans which set up these exams and in helping us figure out later what -- what is involved. As you'll see on this last slide, there's a lot of the resources that patients and healthcare professionals can look at. The -- not on this slide, the American Society of Gastrointestinal Endoscopy, ASGE.org, has a lot of very good information on this procedure, as does the SGNA, the Society of Gastrointestinal Nurses. The American Cancer Society is always an excellent reference on endoscopic ultrasound, on pancreatic cancer, on pancreatic masses, as is the National Cancer Institute at cancer.gov. There's the National Pancreas Foundation, pancreatica.org, and pancan.org, which is a patient-specific organization to help people with pancreatic cancer or pancreatic masses in finding the resources they need, in finding the

health care they need, and just support systems as well. I would like to thank everyone here. I would like to thank Olympus America for coming and helping with our technical feeds. They provide us excellent endoscopy equipment and excellent endoscopes, in addition to the nurses we have in prep and all the staff here at the GI unit which make this -- make our job a lot easier. I'd like to thank Dr. Ludwig for spending an hour with us and helping give his expertise for us, and finally go back to the room with Dr. Karasik for any final comment.
00:59:27
MARK S. KARASIK, MD: I'm also very appreciative of the -- of the staff. We really work as a team here in the endoscopy unit here at Hartford Hospital, and thank you for joining us.
00:59:52
ANNOUNCER: This has been an endoscopic ultrasound performed live from Hartford Hospital. OR-live makes it easier for you to learn more; just click the "request information" button on your webcast screen and open the door to informed medical care.
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