**DR. SHYAM VARADARAJULU:** I think this is a real exciting area. And I think that it'll be very informal and very-- get straight to the point. There's been a lot of things talked about fine needle biopsy. Most things did not live up to the expectations of what we wanted to see.

But the bottom line is there are a few things in tissue acquisition. Is it core issue, or is it all about more tissue? And will acquiring more tissue-- what is it going to do? Is it going to improve that diagnostic algorithm of how we manage our patients? And what outcome does it have on treating our patient and treating of patients? And when it comes to diagnosis, just because you got more tissue, does more tissue mean that you're going to have better diagnostic accuracy? Does getting more tissue make the procedure shorter and more efficient? And finally, the most important question, if you get more tissue, do you need a pathologist in the room?

I think if we can answer these three critical questions, it's going to be very important because now I think EUS is the gold standard for aspirational pancreatic masses, perilesional lymph nodes, sub-mucous lesions, and so on. And everything's about tissue and the pathologist making a diagnosis with what we do.

And this is an introduction slide, and this is all manuscripts published in 2016. And pretty much the message is quite the same. It really does not depend on the type of needle. Whether it is a FNA needle or a biopsy needle, it looks like our diagnostic accuracy is about 85% to 87%. Or it can be the newly designed side-port needle compared to the FNA needle. It's pretty much still the same. It's statistically insignificant.

So you can take the needle out of the equation, and let's look at the techniques. This is the study that came from Japan-- published I think this month or last month in *GI Endoscopy*-- where they describe this door knocking technique where you go back and forth into the mass multiple times compared to your standard FNA technique. And still there's no statistical significance. So all of these that the studies are telling you is well, you can get as much tissue as you want, but the diagnostic accuracy is not getting any better than 85% to 90%.

So Dr. Brugge the first question for you. We're going to find the biopsies that were developed. These needles have been in the market for about three to five years now. How has it really changed the algorithm in tissue acquisition? Have you seen a change? And what has been the impact?

**DR. BILL BRUGGE:** You're talking about the core biopsies, ProCore needles. So I think there's two possible approaches to the ProCore needles. One is to use them primarily to enhance your tissue acquisition rates upfront so that you can do fewer passes, and the procedure takes less time. That's one approach.

The other approach is that it's a salvage procedure. So you do FNA, you do three, four, five, six passes by the cytologist in the room who's helping you. They're telling you you don't have diagnostic tissue, then you turn to the ProCore. Personally, I favor the latter situation because often, it's quality and not quantity. What we want is very, very high quality, very, very cellular tissue. We don't want blood and guts, we want diagnostic epithelium.

**DR. SHYAM VARADARAJULU:** Dr. Chen, do you have a needle that you prefer? I mean, if you got a particular lesion where you say "I'm going to go with an FNA needle for this one, and a FNB needle for this particular lesion to sample?"

**DR. ANN CHEN:** Yes, definitely I individualize it to the patient. Typically for patients with suspected lymphoma, I will go straight to a core or try to get an FNB needle because there's a lot of subtle nuances in lymphoma where the histology is important. Just lesion is another example where I will try to get as big a piece of tissue as possible. Occasionally, our pathologist will ask for larger or more specimen for a special immunohistochemical staining. So that's when I'll reach for the FNB as well.

**DR. SHYAM VARADARAJULU:** There have been-- a couple of randomized trials have been published quite recently, and this is a metanalysis done by one of our wonderful former residents. And it clearly shows that when you-- in all the studies that compared the FNA and the FNB needle, there was no difference at all with the exception that when you use the biopsy needles, it appeared to be made a diagnosis with fewer passes. I mean, I think the mean number of passes were just two to three, and we were able to make a diagnosis.

At least if you look at the pathology literature that correlates with EUS, the recommendation has been if you do not have a pathologist in the room, you must perform seven passes for the pancreas and three on the lymph nodes to get a diagnosis in more than 90% of the patients. These are some of the people that came from Birmingham and by a very notable pathologist, Dr. [INAUDIBLE]. So Dr. Brugge, what do you think? You think because if you have a core biopsy needle, you do not have to perform seven passes if you don't have a pathologist? And is that a recommendation that you would make?

**DR. BILL BRUGGE:** I think many of us have gotten very dependent on ROSE, rapid on-site cytology. It provides great comfort for us because we can limit the number of passes and limit the number of needles that we're using, and we can come up with a diagnosis, and we can tell the patient, and we can call the oncologist. It's a very uncomfortable situation. This happens to me after 5 o'clock. Our cytologists often are not available after 5 o'clock. It's a very uncomfortable time for us because then we have to determine when we have enough.

I think with a ProCore, certainly we get more tissue. Whether it's a higher quality tissue I think remains to be seen. Personally, I do five or six passes. I speak to our nurses. They're very good judges of the quality of the tissue. If they tell me it's clear fluid, if they tell me it's a bloody specimen, or it's a linear clot, then I know I don't have good tissue, and they're free to tell me that.

**DR. SHYAM VARADARAJULU:** And you will collect all the-- this is when you don't have a pathologist in the room?

**DR. BILL BRUGGE:** Correct.

**DR. SHYAM VARADARAJULU:** And Dr. Chen, what is your recommendation? You don't have a pathologist. You go to your hospital somewhere in California. You don't have a pathologist.

**DR. ANN CHEN:** [LAUGHS] That's rare.

**DR. SHYAM VARADARAJULU:** It's rare. What would your recommendation be? Would do you say those centers should use only FNB needles?

**DR. ANN CHEN:** Yeah. So actually, when I was in Irvine, we did not have a cytologist on site. We would process a specimen in a room. A nurse would run the specimen over to another building. But a pathologist was available to read it rapidly. So we got to preparing our own slides, but we'd be on the phone right away with the pathologist over the phone.

If it was after hours and I didn't have anyone, a couple of things that you can do. One is to prepare a smear, place it in isopropyl alcohol. Typically, that does preserve the specimen for later processing. If you have a pathologist that is not on site, but is able to process a specimen fairly quickly, you could just put it in the air dry saline slide, and they could actually process that right away.

I would say definitely I agree with Bill. Do a couple of passes to be sure. In fact, maybe even varying the technique. Some fanning, some suction, some wet suction. And also get used to looking at the expel specimen on the slide because after a while, you'll pick up which samples are cellular, which are serosanguineous. You get a pretty good idea of your yield.

**DR. SHYAM VARADARAJULU:** So you would not recommend centers that don't have rules to automatically convert to FNB needles, and just say-- why not just do an FNB on those patients? If you don't have a pathologist, what is there to lose? You get more tissue with the FNB needle. Just use FNB needles.

**DR. ANN CHEN:** I think if it's proven that you get clear cut samples, I'm in favor of it, actually. I think it's better to do fewer passes. It's safer for the patient, higher yield. Why not?

**DR. SHYAM VARADARAJULU:** What are the technical tips to improve their diagnostic performance?

**DR. BILL BRUGGE:** Well, all of us know, obviously, that our reputation, our abilities, are highly dependent upon a cytologist. So I always tell my trainees and my colleagues, "The person you need to make friends with first and make sure they're on your Christmas card list is the cytologist because we're highly dependent upon it. And your reputation is dependent upon the ability of the cytologist to come up with a definitive diagnosis." And if your diagnostic grade is 50%, you are looking bad. And whether it's your fault or not, it is your reputation.

So you have to have a very good cytologist. They must understand explicitly what you're doing, and they must understand exactly what are the questions you're asking them. So in my hospital, we have a very dedicated, very detailed form that we submit with each specimen. So they know very precisely what we did, what needles we used, how many passes we did, and what is the question. And we also have copies of it, so we have a copy and they have a copy.

So this all may change with fine needle biopsy. It is possible that fine needle biopsy will be able to bypass cytology. We may be able to go directly to pathology. We may not have it on site in the room, but we may have higher yields and more definitive diagnoses. But we don't have that yet.

**DR. SHYAM VARADARAJULU:** So when you communicate with the-- when a new person is going to practice, and they're going to communicate with the pathology department in the hospital that made up four or five people, who should be the person they are talking to among the pathologists?

**DR. ANN CHEN:** Well, ideally, somebody who has a cytology background, definitely. But I've also found that there are slight different preferences even among pathologists. Some prefer-- I actually have a pathologist that prefers all the specimen clumped in one little group, another that prefers it all smeared out, one that wants it completely wet right-- I mean, I can't even start the biopsy until she's in the room. Another that wants it completely dried. So I think definitely talk to the pathologist, see what-- yeah. Well, at least in my experience, it's what they--

**DR. BILL BRUGGE:** Also, I think a pancreatic pathologist is very useful. A vast majority of our FNAs are pancreatic. And you start talking about a wide spectrum of diseases of the pancreas, benign and malignant. So it's often very useful to have a pancreatic pathologist because they know the diseases that we're encountering, and they're pretty comfortable with that diagnosis.

**DR. SHYAM VARADARAJULU:** So I'm going to ask both Dr. Chen and Dr. Brugge. And let me start with you, Dr. Brugge. Solid pancreatic mass intersecting of chronic pancreatitis. What are your tips for best diagnostic yield?

**DR. BILL BRUGGE:** Well, before we jump in and make a conclusion that this is a malignancy, of course, one of those little evil diseases that is always in the back of our mind is, "Could this patient have autoimmune pancreatitis?" So the patient has recurring pancreatitis, they have an abnormal gland, they have a focal mass before, concluding that the patient has a malignancy. It would be very nice to have a biopsy, a core, histology, to make a diagnosis of autoimmune pancreatitis. We want to try hard not to use cytology to make a diagnosis of AIP. So that's just one warning upfront.

The second one is when you have a very hard fibrous gland, you can have, of course, pseudo tumors, local inflammatory areas in the pancreas. But what we're really concerned about is that these masses may have intervening fibrous tissue and may make it very difficult to get the needle in there. Very difficult to aspirate the tissue. The fibrous tissue interferes with both. So sometimes, people advocate the use of very small needles under those situations to try to pick out those little tiny malignant cells.

**DR. SHYAM VARADARAJULU:** Dr. Chen, technical tips for endoscopers when they have in their sample masses and chronic pancreatitis. What are your principles? I'm very rigid in my thoughts. I brought up a couple of things. I'm not a good moderator because I'm always biased about what I'm going to tell you. So what are things that it's really, really about, and the sonographer should do and should not do?

**DR. ANN CHEN:** I think this is a case where fanning is really important because you're trying to sample as many different areas as possible. Also avoiding typically more necrotic areas, if you can pick those out typically more in the center, maybe perhaps the edges a little bit more. Also there's a cutoff at the duct. That's typically where I like to go to right at where the duct caliber changes-- pancreatic duct caliber change, for example.

**DR. SHYAM VARADARAJULU:** I think that's very important. I mean, I think I have a lot of respect for Dr. Sahaj. He was somewhere here, and he always told me, "No suction, no stylet." And I think that's really, really important. We did a randomized trial of 352 patients. We had four groups, 88 in each arm, 22 gauge with suction, without suction, 25 with suction, 25 without suction, and whatever [INAUDIBLE] told us was correct. Don't use suction. When you use suction, the yield was the lowest. And when we used styled, it was just bloody, and there was no yield.

So we don't use suction, we don't use stylet at all. The very first pass, we used suction-- I mean, the stylet. Subsequently, we don't put in the stylet, we don't use suction. We just fan the needle to get some tissues. Is there anything else that I'm missing, Dr. Brugge?

**DR. BILL BRUGGE:** Well, you also want to look for other target lesions for malignancy. So you always want to-- I take a quick look at the left lobe of the liver. You have a metastasis, you have some lymph nodes, you have ascites, or other areas of infiltration of vessels. These are great targets if you have chronic pancreatitis, and the primary lesion is difficult to access.

**DR. SHYAM VARADARAJULU:** What should an endosonographer who has only a cytologist or maybe no pathologist in the room do to get the best outcome on this patient?

**DR. ANN CHEN:** Well-- so a couple of things we talked about already. Fanning, perhaps different biopsy techniques. One of the things I like to do is try approaching the lesion at different angles. If you can approach it from both the duodenal bulb, as well as the second portion in duodenum. Sometimes I like to do that just to see if you get different angles. Do a lot of passes. [LAUGHS]

**DR. SHYAM VARADARAJULU:** Dr. Brugge, I could have done seven passes and still not had a diagnosis if I did not have a pathologist. Anything else that we can do to maximize the yield in this patient?

**DR. BILL BRUGGE:** Well, you want to be comfortable. You want to have a straight scope. You want to have straight access. You want to go for the dense hypoechoic tissue. You don't want to get distracted by necrosis, by fluid, by inflammatory areas.

Sometimes in pancreatic malignancy, the mask can obstruct the duct and can make the entire pancreas look very, very abnormal, and we get very distracted. We're sort of thinking that the entire pancreas is malignant. Try to find the most focal hypoechoic area that you can FNA.

**DR. SHYAM VARADARAJULU:** So Dr. Brugge, in your clinical practice, if you perform an FNA, and your pathologist tells you, "Well, you've got diagnostic material," do you routinely perform passes for ancillary studies?

**DR. BILL BRUGGE:** Our pathologists-- our cytologists that I work with really expect that. They demand that because it's not known at the time, of course, what the definite diagnosis is, and what they can use the tissue for. So they like to have a dedicated pass for a cell block. So this is particularly important for neuroendocrine tumors where you want to do immunohistochemistry staining, just lymphomas. But it is part of our practice that you have a dedicated pass.

**DR. SHYAM VARADARAJULU:** So Dr. Chen, a rare cancers where you would say-- once your pathologist tells you, "It's cancer. That's it. I don't need anymore. No more cell block, nothing." Are there specific cases where you don't need nothing? Just cancer on the side is gone.

**DR. ANN CHEN:** No, I don't think so. I think it's always good to get an extra pass, because you just never know what the oncologists want, what the surgeons want. So always do that one extra pass. You just never know. Especially with this patient who had a prior history of malignancy, it's absolutely essential to do that.

**DR. SHYAM VARADARAJULU:** And what if the oncologist want more tissue?

**DR. ANN CHEN:** They always want more. [LAUGHS]

**DR. SHYAM VARADARAJULU:** So Dr. Chen, what is your take on these studies? Is personalized treatment for pancreatic cancer and other cancer going to be the norm now or in the next few years?

**DR. ANN CHEN:** I think so. I think so, definitely. It's a lot of excitement going on in this field. Actually, I had a patient with a history of rectal cancer, I recall. We didn't have the surgical specimen. It was done somewhere else. Later on, she was having recurrence of a perirectal lymph node.

The oncologists actually asked me to get a bigger sample so they could do an immunohistochemical staining. Apparently, 5% of colorectal cancer is actually expressed her to gene, which you can treat with Herceptin, which is a drug usually used to treat breast cancer. So that was very helpful to be able to get a bigger chunk of tissue from a recurrence of lymph node. That made a difference in this patient's treatment.

So I think this is-- absolutely, I think the way of the future. It's really exciting actually to potentially be part of this.

**DR. BILL BRUGGE:** I think another example's in colon cancer. Now it's a routine, at the very minimum, to determine whether they have a kras mutation or not. I mean, this has a huge impact on their treatment and on their prognosis. And it's extremely likely that this is going to happen in pancreatic cancer. Currently, now there's a company who will process the specimens and give us their next genome sequencing of 16 common mutations in pancreatic cancer. So it's very likely that this is going to be a routine.

**DR. SHYAM VARADARAJULU:** I think there's an NIH sponsored study on getting preoperative tissue for tailoring treatment. But surprisingly, the protocol has got [INAUDIBLE] biopsies. For some reason, some oncologists will still call the CT radiologist when it comes to getting your core tissue. And the indication is always that please, get us a CT graded biopsy of core tissue to perform molecular testing. Is this being-- and this is an NAH grant. Is this being done because of ignorance that we don't have EUS? Or are the oncologists replacing CT graded biopsies because we don't give them reliable core tissue?

**DR. BILL BRUGGE:** I think the pathologists and the oncologists are still fascinated by the technique by CT where they put a needle in-- a hollow needle-- and then multiple specimens can be taken with one pass of a needle.

**DR. SHYAM VARADARAJULU:** And are there any studies happening in your institutions on personalized treatment? Are you being requested specifically tissue for that purpose?

**DR. BILL BRUGGE:** For pancreatic cancer? They are actually specifically not asking right now.

**DR. SHYAM VARADARAJULU:** I think if you look at the studies, this is what they want. They want cancer cells. They want a lot of fibrosis. And they want a combination of normal and abnormal cells.

I think-- I once asked a pathologist, "What do you really want from us, and what would you be happy?" And this was exactly the picture he suggested. He said he wants a lot of stroma, he wants a few SNR and a few ductal cells. He wants malignant cells, and a couple of atypical cells. He said-- this was a picture he sent me-- and said, "This is exactly what a core tissue is."

I want to thank Bill and Ann for being here this late. And thank you so much for your presence. I'm so thankful. Thank you.

[APPLAUSE]