So today I'm talking about an update on tissue acquisition. There's a little bit of disclaimer here. OK, so the take home-- I always like to start with the take home-- is that the goals and capabilities of EUS-guided tissue acquisition appeared to be really, truly changing. We know Fine Needle Aspiration, FNA, works and can be sufficient in many cases. If you need a core, now you can really, truly get a core. For the purposes of this talk, I would define a core as any tissue sample that can be processed by histology. I think we do need to work on a better definition, but at this time I think that's what we can go with, and we'll get into some details a little later. Fine needle biopsy, FNB, can be truly helpful for both malignant and benign disease management.

So how good should we be? I've always felt that we should divide EUS-FNA cases into two different types of cases. There's the easy cases and the hard cases. So the easy cases are the obvious cancers. You know the patient has cancer, usually an epithelial cancer, and you just need to prove it. So a large, obvious pancreatic mass, large, clearly malignant nodes, things like large submucosal tumors that are obviously aggressive GISTs. I think in these cases, if you have good technique you should have a sensitivity of more than 95%.

This compares to the harder cases. These are the cases where you have smaller pancreatic masses in difficult places, certain types of lesions like just smaller something submucosal tumors, lesions that are in difficult positions, or, for example, when you have things like metal stents that are causing problems accessing the lesions. I think the sensitivity here probably goes down to 50% or 60%, and that's why the average sensitivities often are around 80%. But I think if you separate these into two different classes, the sensitivity in the harder cases is normally really much lower.

So what type of information can you get with FNA versus FNB? Basically, if you do FNA and you use a cell block, you're getting essentially the same information on everything except tissue structure. So a cell block does not give you structure, whereas a true core biopsy does give you structure.

The one other thing that I think is important to consider now in this era of personalized medicine is that I think you may get more tissue volume with a core biopsy, and I'll show you some data that corroborates that. This may be important because now if we're going to be looking at doing specific genetic testing, we may need more tissue volume and certain parts of tissue, such as the DNA or the stroma, for example, in pancreatic cancers. So this is a variable that may become more important in future studies.

So should we be doing FNA or FNB? My usual practice was that most FNA I found that we do certainly is for the diagnosis of epithelial cancers and that ancillary tests, such as immunochemistry, is really needed in only a minority of cases.

Believe it or not if you look at all the data there are really no convincing evidence that getting a core increases the diagnostic yield for epithelial cancers. OK? So the sensitivity for malignancy for epithelial cancer is not better if you get a core. Some people think it is, but there's really no data to support that. However FNB may reduce the number of passes required to get a diagnosis.

So my question is that instead of using an FNB needle or-- this was my attitude-- there was more expensive, why not just do an FNA and do an extra pass and maybe do a cell block if you need it? And as they say, I think in my mind things are changing and hopefully I'll show you why I think maybe FNB may be the way to go going forward.

Just a few words on FNA and FNB studies. There can often really be a lot of problems with these studies. I think you need to be aware of retrospective studies where a group has been doing something for a few years then gets a new device, usually offered by a device company, and then suddenly they get much better. So clearly in these retrospective studies, there's so many variables that can influence an FNA that can't be controlled for that I think most of the time they're really, really unreliable, unless there's some major difference. But even in those cases, I think a lot of the time the differences can be attributed to bias in the way the procedures were performed.

When it comes to randomized controlled trials, I think it's really important to look at the control group first. So what I've found is that most of the time when a group starts working with a new device, what happens when they publish a study is that the new device gets basically the results they were getting before but the old device, the control group, starts getting basically worse results. So the new device appears better, but it's not because it's better. It's because the control group is worse.

There is also inevitably I think this consultant bias. So if you look at DDW, there's inevitably tons of abstracts comparing different needles of DDW. If you look at what device turns out the best and you look at the bottom of the abstract, there is always a strong correlation between which device is best and what company they're consulting for.

And then again I think that in studies, you really have to separate out the easy cases, so the pancreatic masses and the large metastatic lymph nodes, versus the more difficult cases that I outlined earlier. And if that's not done appropriately in the case mix, it can bias studies in one sense or the other.

In terms of just the data, there is a fairly recently published technical review by Sachin Wani, and if you want to look at most of the studies on FNA, up until to 2014 anyway, this is a very good review. I don't always agree with their conclusions, but it's really a well-done technical review.

So the take home in terms of FNA is that I think for the easy cases, the technique is probably more important than the device. So when you have an obvious cancer, I don't care what you do. As long as you have good technique, it doesn't really matter what type of needle you use, you're probably going to get very good results. Cytology is adequate in more than 95% of cases. And I think you should get a core, but only when it's really needed. I'm going to go into that a little later. And I think you should focus on a very simple technique, and I'm going to show you what I think is the best technique in a few seconds.

As for the hard cases, I think, one, before doing FNA in these difficult cases, I think you need to make sure that the FNA is really going to be helpful. For example, I really don't think needling small submucosal tumors is really going to change much. And that's one example where going to a more aggressive biopsy technique I think may not be worth it. But if you do think it's worth it, then you can bring out the big guns, and the big guns now are these new core biopsy needles.

So this is just a meta-analysis analysis of FNA of pancreatic masses just to show you that overall they've got an overall accuracy rate of about 90%. But again this is combining really easy pancreatic cases with harder cases, and I think if you tease out just the easy pancreatic cases, your sensitivity really should be higher than 90% to 95%.

So I just want to do a little review of just FNA technique and how to improve the yield of FNA. There are a few variables that do impact the field of FNA. Obviously the operator. If you're good at FNA, you're going to get better results as somebody who's bad at FNA, who doesn't have much experience. A really important variable is the cytologist. If you have a better cytologist you will definitely get better results. And you have to remember that a lot of pathologists don't really like doing cytology.

Lesion type, as I said, is really important. Some lesions are definitely easier or give up tissue more easily than others. Lesions that are hard to access, so you really have trouble getting the needle in or moving the needle adequately, will obviously cause problems. And then in certain situations-- for example in post-operative stomach where you don't have access to the lesion as well as you like or as close as you would like, if there's a large metal stent, or if they've had chemo or radiation-- these type of things can affect, I think, the yield of our cytology. And obviously the more likely it is to be a malignancy, the more likely it is for you to get a diagnosis. So the pretest probability also influences your results.

But I think one of the most important factors that people don't talk about too much is how we sample. When you're looking at a pancreatic mass, for example. If this is the pancreatic duct, this is a stricture, and this is the upstream dilation, and this is the mass you see on ultrasound. It's important to realize that within this mass, the actual cancer may be actually quite small. So if you sample in only one place then take the needle out and put the sample on the slide, you may actually miss the tumor. Whereas if you sample-- sorry. If you sample in many places before putting the sample on the slide, you increase your likelihood of actually going through some tumor. I would also point out that in cases where, for example, you actually don't see a mass very well or you just see a stricture, or the first pass is negative, focus on where the stricture is. That's usually where you'll find the diagnosis.

Shyam Varadarajulu showed in a nice comparative study that the fanning technique was better than a single pass technique. So fanning is when you put the needle into the lesion-- here's the GI wall, here's the needle tract, here's the lesion. Fanning means you put the needle into the lesion and then while you're in the lesion, you try and move your shoulders and move the needle around to get into different parts of the lesion. In my experience in hard lesions or lesions that are very deep, it's almost impossible to do fanning. So we favor what we call a multi-pass technique, where instead of staying in the lesion, we actually go in, move the needle around, and come out and move over and go somewhere else. OK? If you come out then you are actually, with the elevator, able to really completely move into a different part of the lesion.

So we actually did a study comparing fanning to a multi-pass technique where we limited it to 20 strokes, but we did one times 20 with a fanning versus 2 times 10, versus 4 times 5. And we actually found we got better results with this multi-pass technique. We've modified the technique since that time to really go through the wall only once, and then if there's some space between the wall and the lesion, we'll come out of the lesion but try and stay behind the wall, and then keep repeating this multi-pass technique. We believe this reduces the risk of contamination with wall cells, and it may also reduce the risk of tumor seeding, if that's a concern for you.

Size does apparently matter. Smaller needles appear to be better. I think it's not just because smaller needles have a-- the smaller internal diameter gives you a stronger capillary effect, suction effect. But I think these needles are easier to move in the lesions. So it's easier to sample more deeply and more completely. They're easier to move with the elevator, so it's easier to sample in different areas. If you're using a fanning or multi-pass approach. They do seem to give you less blood, and then, therefore, better quality samples. And there are actually data showing that the 25 appears to be better than the 22.

So here's a meta-analysis, eight studies, almost 1,300 patients, showing that the 25 was better than 22. So I think if you do want to have an evidence-based approach, you should favor the 25 gauge needle for solid lesion FNA, which is what we do now. We never used the 22 gauge for FNA.

[12:39] concluded that on-site cytology was not necessarily the best thing to do, but I think if you speak to anybody who has access to a good quality cytologist who can get in the room quickly, and you ask them would you like to get rid of your cytologist or keep them, nobody will say they want to get rid of their cytologist. Everybody wants to keep their cytologist.

So I'm honestly not sure that it increases the yield if you use an aggressive, multi-pass technique, but this technique can take time to do two or three passes, two or three times going in and out through the lesion in many different areas. But if you do, I think probably the cytologist becomes a little redundant. However, if you want to simplify the technique, do less passes, I think having a cytologist is very helpful, particularly in pancreatic cases, because it can show you right away whether you have a good sample, whether you're actually in the tumor or not, and it can let you know right away whether you need to do extra passes to get special stains like immunochem for a neuroendocrine tumor. It can also help reduce the number of passes, again, if tumor seeding is a concern. However we tend to not use the cytologist in cases where we think that it's going to be a benign disease or we're just going to do benign appearing lymph nodes, where we're just going to do like a flow cytometry and a cell block and that's it.

Here are some studies looking at the benefits of cytology versus no cytology, of on-site cytology versus no on-site. Interestingly most of these studies show that there is a benefit, so I'm not quite sure why they concluded in the technical review that it wasn't really helpful.

Now as far as needle types, this was an interesting study comparing just a regular 22 gauge Expect needle versus a 22 gauge ProCore needle. And they showed no difference at all in terms of sample adequacy, yield from malignancy and even the yield for cores. OK?

And then these are a few studies looking at the ProCore needle for cytology. And, again, the problem with these studies is that if you look at the control groups, in all those studies where they show a benefit, the control groups had very, very poor results, in the 60s. So again I think in these studies, they show that this ProCore was better because they basically show that the control group was worse. So they appear to have tried harder with the ProCore than what their standard needle, and that's why they showed some benefit with the ProCore.

Since that time, there have been two multi-center randomized trials showing that there is no difference in the yield for cytology with a ProCore needle. The only thing is that it may reduce the number of passes by about one. In our experience, we've done our own randomized trial, which is being prepared for publication, we've shown that if you use an aggressive multi-pass technique, even then the one pass-- you still don't get-- you still don't need more passes with a standard needle as compared to the ProCore needle.

So in summary, how do we maximize the yield of FNA? I think you should use a multi-pass technique as opposed to the fanning technique. Use a 25 gauge needle. I really do think it's easier to use and gets better results. And, remember, I was a 22 guy, and I really switched to the 25 once we did our own randomized trial. Make slides and a cell block if you need ancillary testing. And get a cytologist in the room, a good cytologist, if you can.

So for me, FNB has traditionally been sort of a salvage procedure. But I hope to show you that my philosophy has been changing a bit. Actually, quite a lot.

So why would we get a core? Well, I think people who really just can't get a good cytologist have no choice but to get a core if you truly need structure. So these are cases-- for example lymphoma, autoimmune pancreatitis, liver biopsy-- and I would point out that I think liver biopsy could be one of the biggest potential indications for EUS-guided sampling in the future.

And then cases where we have failed cytology. The famous dry pass, situations such as linitis plastica, sclerotic tumors, where the FNA is just not working, small SMTs, but again I would ask you to ask yourself, do you really need to sample small SMTs? because they never seem to grow anyway. And so just various lesions where your standard FNA is not working. Maybe a core will work.

If you don't have ROSE, there are some people now suggesting that getting a core biopsy may obviate the need for ROSE, because they're getting the same results as when they were using ROSE and also because, as I'll show you, you can actually look at the sample and you can see macroscopically whether you've got a good sample or not.

So how do you get a core? There have been several core devices. There was the original tray gun device, which was quite expensive and worked basically only at the Mayo Clinic, with Mike Levy. So we basically stopped using that a long time ago. Now there is these new core needles. I would point out that I think that the 25 gauge core needles are probably-- they get you micro-cores, but I don't think they're good enough to really be considered true core samples.

I think that also in future studies we do need to standardize what we mean by a core. We need to know if we're going to be using cores, for example, genetic testing or other special tests, how much tissue we really need, how big the core has to be, what type of maybe weight of DNA or weight of other parts of the tissue that we need, before we define what's the best way to get a core.

So this is the type of tissue we are getting with just our 19 gauge needle. Most of this is blood, but this white stuff here is presumably tissue. This is the 25 gauge needle, and you can imagine there's a few little micro-cores here, but it's but it's not great.

This is an interesting study, I think, comparing in liver biopsy the SharkCore 19 versus SharkCore 22 versus the ProCore 19 versus an Expect 19 versus percutaneous needles. What it shows is that if you look at the ability to get actual cores versus fragments, the SharkCore was getting true cores. The percutaneous needle was getting true cores. And the Expect 19 was getting true cores, but only about 50% of cases. So, my question after this study is, why not just do two passes with a 19 as opposed to one pass with a SharkCore.

What's also interesting is that the 19 gauge ProCore really was really rarely getting cores. So I think most people have realized that the ProCore really does not give you core samples. I think it's really just been bypassed by the new needle tip designs.

So these are the new designs we have this is the Acquire with its 3 tip design versus the SharkCore, which has this sort of, I guess, pitchfork more type design. And this is one of the first Acquire studies done by Shyam Varadarajulu's group showing basically excellent results, but again not really better than the FNA results they were getting. But really good size tissue samples in standard lesions.

And here's a study where they actually compared the Acquire needle to the standard FNA needle. Here clearly there were differences, though. The FNB needle, the Acquire needle was getting bigger samples, bigger tumor area, more of this desmoplastic fibrosis that they need, apparently, now for doing special testing in pancreatic cancer. And then for the cell block, they were getting better results in terms of cell block as compared to FNA. So clearly the Acquire seems to be getting bigger better samples than the FNA and the cellblocks obtainable by FNA.

This is a SharkCore study in GISTs, just basically showing that the frequency of an insufficient amount of tissue with FNA was higher than with the cores, and that they were getting better results for immunochemistry with the core needle versus the FNA needle.

This was the first study comparing, actually, the SharkCore to the Acquire needle, and this study showed actually a 20% benefit with the SharkCore. When I saw this study, I just couldn't believe it. It just didn't make any sense to me. And I think most people who've used both needles would agree with that.

Fortunately Shyam's group did a true randomized trial of SharkCore versus the Acquire, and they showed basically no difference between the two, which to me pretty much makes sense. I do tend to prefer the Acqire, because to me it's basically like a standard FNA needle. It can be used exactly like a standard FNA needle, so it's just a simpler needle to use. So these are just showing that basically all the results were the same with both types of needles.

I want to focus now on what I mentioned earlier were these harder cases, these cases were really we found that FNA is insufficient. So we prepared our first 125 cases for DDW this year. And here are our results.

We looked it at basically a selective use of the Acquire needle in what we consider difficult cases. These are cases where we had previous failed FNA, atypical masses where it could have been a different type of tumor or we wanted to differentiate a neuroendocrine tumor from an adenocarcinoma, suspected GISTs, suspected linitis plastica, suspected automimmune pancreatits, indeterminate lesions in chronic pancreatitis, and suspected lymphoma. We performed the EUS with a 22 gauge Acquire needle. And the samples were expressed into formalin just using air express technique. And we only did additional passes if we thought the sample was inadequate based on just visually looking at the sample. So there was no ROSE in this study.

So in this study which is over about a six month period, there were 615 lesions that were biopsied during the whole period. But about only 125, so about 20%, of these cases met our criteria for what we considered difficult lesions. And what we saw, the prevalence of malignancy was quite high, it was about 77%. What we found was that we got an adequate sample for histology in almost 93% of cases, and that the sensitivity for malignancy was 92%.

So remember, these are cases where FNA was getting us results in the 50% to 60% range. These were difficult cases, and we basically got our results up to the yield as we were getting with our regular, easy FNA cases. So we concluded that in summary, in selected difficult EUS tissue sampling cases, the 22 gauge Acquire provides adequate tissue for histology in 92% of cases, and the sensitivity for malignancy is 92% as well. And these results were obtainable without ROSE. So this needle may truly obviate the need for ROSE.

So we concluded then that the 22 gauge Acquire is an excellent choice in cases where traditional FNA results are inadequate. So it's kind of a salvage needle.

But I must say-- and this is the type of tissue we're getting here with the Acquire. So this is way too much tissue, actually, to do a smear for a cytological analysis. So what you have to do is there's so much tissue that you have to actually scrape this into the formalin and I just hope that you leave a bit of residual tissue on the slide. That then can be used to do ROSE if you have a cytologist. Available.

If you compared this to what we were getting with our 19 gauge technique, I think really this Acquire needle is getting much more tissue. It's just a huge, huge amount of tissue. And I would also say we've really been seeing some unforeseen benefits, and it's making me think now that I've been a little bit biased against the core needles because they're a little bit more expensive. For us, we do about 1,000 biopsies a year. So if we switch to using just a core needle all the time, it would really increase our budget. But what I'm seeing now with the results we're getting, they're so good that I'm thinking now that if you are in a center that's not doing nearly as many biopsies, maybe 50 to 100 a year, switching to a core needle, even if it's more expensive, probably in the end is going to be very cost effective because you're going to reduce the number of failed cases. And in the end it's really not going to increase your budget a whole lot.

And we've really found some unforeseen benefits with the core needle as well. What we've found, interestingly, is that compared to cytology-- when cytology is negative, it doesn't give you any more information. All it's telling you, basically, is that there's no cancer. But with a true biopsy result, when it's negative not only is it negative for cancer, we're finding that it's positive for a benign diagnosis, such as chronic pancreatitis, or in the lung cases, for example, silicosis. You're actually getting a true positive negative result, if you wish, which is usually enough to stop any further work up.

We've also had some surprise positives. In lesions that we've been sampling for years that were constantly negative but sort of suspicious, we were getting back, for example, low grade IPMNs. Cases that were really low grade malignancies that we were able to prove with a true core biopsy specimen.

We've also found that you're getting a true surgical, serious pathology report. So it's not just positive for malignancy or negative, we're getting a true path report with tissue volume, tissue structure, a number of tissue markers that they could just never normally do unless we did maybe a cell block with the cytology. So we're getting a true, serious path report, and I'm sure that our oncologists are very much appreciating this.

Finally as I pointed out, we're finding you can actually look at the sample and get a good visual macroscopic assessment of whether this sample is a good quality sample. If you have a long white core tissue, that can't just be gastric wall. That has to be tumor, pure tumor, and that's basically the type of tissue we're getting with this needle.

So the take home as far as FNB goes is that the goals and capabilities of EUS-guided tissue acquisition appear to be truly changing. We know FNA works and can be sufficient in many cases, but now we know that if you need a core you can truly get a core. These new core needles are really getting core samples. And we've found now that FNB can truly be helpful for the management of both malignant, but also benign disease, because you're actually getting a true diagnosis of a benign disease.