DR. STAVROS N. STAVROPOULOS: This lecture will conclude our talk. Now, Isa is the most ethical and conflict-resistant physician I met. He invented the dual knife, which is probably the most popular knife in the United States. But he gives such an objective presentation of the merits of all the other knives. Just use dual. And I have no conflicts regarding the dual knife. And I also use a lot of hybrid.

But interestingly, he helped Erbe develop that hybrid knife. Right? Back 10 years ago, by doing the first colon study in Japan.

AUDIENCE: No. In Germany.

DR. STAVROS N. STAVROPOULOS: Oh, in Germany. In Japan, they wouldn't allow you to re-enter if I did that. So anyways, so I'm going to give you a Westerner's perspective, a much more sedate one because we have, obviously, a lot of regulators, lawyers, and others that want us to stay within the safe zone. So I'll talk to you-- Sergey will give you, also, that view-- giving this talk about how to put DSD in your practice, which can be devastating in terms of time reimbursement, back pain, and other reasons. So he's got folks on that in the afternoon.

And the other afternoon talk is by two Chinese physicians that have made innovations in the area of the EFTR and STER. We'll talk thus about variations in technique with 10 minute worth of videos in the afternoon. That will be the afternoon lectures.

So let's start. These are my disclosures. I'm consultant for Boston Olympus, and I've received honorarium from Erbe. So POEM-- it has become a prototypical, iconic procedure. It just revolutionized surgery with the endoscope. Not only did it do full thickness resection techniques, all the POEMS-- the Z-POEM for Zenker's, that's from Professor [INAUDIBLE] rectal POEM and G-POEM. You'll see POEMS and Z-POEMS today.

I'm not going to discuss the POEM. I did that last year. There hasn't been much progress. Their success is in the 70% rate. I also discussed Z-POEM. I'm going to focus on POEM this year in the interest of time. And I'm also going to focus a little bit on our view of full-thickness resection. And I'll talk about ESD a little bit, because maybe the most significant effect of POEM in the United States. Because let's be honest, there's not much achalasia to do POEM on. The most significant effect is really creating a whole wave of adoption for ESD due to the coolness of POEM. It's like, really, a reverse situation. We went backwards from how Asia went from ESD to POEM. So now, the ESD is expanding rapidly in the United States, and I think that's, to the large degree, a benefit from POEM.

Now, how do you adopt ESD in the West? So we have this conundrum. This is from, for example, the European guidelines. They accept ESD for gastric neoplasia, the traditional application and the reason ESD was invented for. But they don't do so for the legions we have a lot of in the West. Barrett's, early carcinomas and colon adenomas. Where EMR, they say, remains the standard because ESD has not proven its benefit, at least not in the West.

So basically, they ask you to learn ESD on gastric lesions. There are very few of. This is also supported those people advocating the step-up approach in terms of difficulty. You should really start in the stomach because it's easier. It's thicker, harder to perforate, easier to close, et cetera. And then move to the dreaded colon, which is thinner. The scope is looping. Perforations can be devastating. Leaks can be devastating, et cetera.

The problem with this approach in the West is there are a lot of gastric legions. So incidents of early gastric cancer is probably eight to 10 times less than in Japan. Do you see those numbers here versus the US? If you look at the SEER database over this nine-year period, 43,700 cases of gastric cancer, but only 1,828, or 203 per year, were early, so not enough material for the step-up approach.

This is a survey that was done on 40 ESD, hands-on participants of what they think is the most important obstacle to adopting ESD in their practice. And you can see here, by far, lack of available adequate number of lesions for appropriate ESD. 36% thought so. Everything else must lower. And reimbursement is touted as an impediment to adoption, not for these committed souls. Lack of reimbursement, 6% said that it's a significant obstacle. They're willing to do it for free if necessary.

So lesions, hard to find them. I don't know why this is self-advancing. I probably forgot some timings on the slides. But what is another problem with the step-up approach? When you are learning, one of the big problems is getting an R0 resection. You get scared. You make the perimeter too small, very close to the lesion. You burn the lesion a little. There's your pathologist saying you in the terminate margin, over even worse, positive margin. So that is not good.

Now, if you get this on an early Barrett's cancer, that's a problem, having an R1 resection, because this could commit a patient to a esophagectomy. Getting it into the stomach also could commit them to gastrectomy, because those lesions are usually cancers. In the colon, for those of us that do colon ESD, including Sergey, the vast majorities are adenomas. You get the R1 margin [INAUDIBLE] adenomas, it's not really the end of the world. They, or more people, do it on every case.

That [INAUDIBLE] is by definition an R1 resection. They go back, they fix it. They burn it. They cut it. And they tell us that 90% of the time they're able to get rid of it. So no big deal. That's another good reason to maybe consider starting early in the colon. Getting an R1 resection is not as devastating to the patient as getting an R1 resection in a cancer in the upper GI tract where the lesions are usually early cancers.

This shows you our path of adoption. Unfortunately, we didn't include colon early. We followed the traditional upper approach. We did do something a little bit fancy. We used those submucosal lesions that we were sent for EUS early. This orange stuff is subepithelial tumors. This is actually three years here. I don't have the data from Columbia. I did about 20 or 30 at Columbia from 2004 to 2008 before I came to Winthrop. But I lost this data.

So 2008 to 2011, these are the cases. You can see here a lot of subepithelial tumors and upper lesions. The colon is that little purple line here, minimal. But then the colon, by 2013-14, took over. Now, over half of the lesions are colon. Not rectum. Rectum is really this dark blue, which is also considered an easy beginning area. So we are mostly right-sided colon lesions.

So you need these to really proceed with the learning curve. And you can see, we didn't get to the competence benchmark, which is 9 square centimeters per hour speed, or 80% R0 resection. We reached the speed after about 150 cases, after we did quite a few colonic lesions. And we reached the 80% R0 resection rate somewhere after 200 cases. And you can see, colon now is really a mainstay in the last year. This is only half a year, where this year we did about 140. So the graph is continuing to increase in our ESD volume.

The problem with colon is that you have a lot of resistance from venerable thought leaders in the West, for example, Greg Ginsberg. ESD over EMR for the vast majority of colorectal neoplasms-- i.e. adenomas cannot be reconciled with increased risk and procedure duration. And then you have Doug Rex, recent editorial. Colorectal ESD and en bloc resection, in general, are powerful concepts that currently come with a high price tag for most American colonoscopies. However, we acknowledge that, as with many evolving technologies, deciding whether to learn colorectal ESD is a gray, not a black and white area.

He says in the same editorial that he figured that the number needed to treat for ESD to avoid surgery at least seven. And he comments that this is a lot of work to prevent surgery. But I would say many patients would disagree regarding this point. You should really put some effort to avoiding surgery for them.

Now, if you look at the final point here, how he calculated this number needed to treat-- of seven is mainly lesions that have superficial submucosal invasion. Where if you do EMR, you don't know how deep it is. You commit a patient to surgery. But if you do ESD, and you show that this very superficial invasion, then the patient is cured and avoid surgery. But there are the areas where ESD helps. Aborted EMRs due to fibrosis, non-lifting, difficulty in snare positioning. Sorry.

There is also another one, intractable recurrence. You do an EMR. The lesion comes back. It is impossible to get rid of. That's 2%, and it requires results in surgery. ESD, my experts, can deal with these lesions, as you'll see from now-- it's today, we have some good lesions, and from Sergey. Including these scenarios, the number needed to treat is probably five. I think that's a worthwhile effort, a number needed to treat five to avoid surgery. I mean treat five patients with ESD to avoid one surgery.

And this is what the power of ESD. So this is a large lesion in the ascending colon, 8 centimeters length, right on the turn, 70% of luminal circumference. And you can see here, retroflexion of the scope showing like a big granular lesion there, no particular evidence of invasive cancer with big perimeter. And then that's the completed resection four hours later. 90% of the circumference removed on a turn. But R0 resection and closure with OverStitch circumferentially. And this is the lesion.

So this guy's done. He's never going to need any reservalence or any concerns about recurrence. This was a complete R0 resection. Now, compared to piecemeal EMR, you get the pieces like that. And you get the recurrence. These are the recent data from the Australian Consortium from 2017, looking at the recurrence of adenomas at 18 months. And not all people had reached 18 months. 2,000 lesions over two centimeters. You can see that the normal recurrence-- this is serrated adenomas, so let's forget that. But typical adenomas, 20% to 30% recurrence at 18 months. But most people haven't reached that follow-up. If you look at lesions bigger than 35 millimeters, 30% to 40% recurrence at 18 months. And let me tell you, recurrence occur also way after 18 months.

So what you get with EMR-- the meta-analysis by Fujiya, on colon ESD versus EMR, six retrospective cohort comparisons, two case-control shows it. Even though the lesions were larger in ESD en block resection better-- sorry, curative resection better, 80% versus 42% local recurrence-- much, much, much lower. Delayed bleeding, similar. But it was longer, about four times longer, to do the ESD. And these were experts. And risk of perforation was higher. But this is irrelevant. Perforations of ESD are closed by experienced operators with clips. It may result in an extra day, or two, or three in the hospital, but it never results in emergency surgery or severe morbidity.

Westerners may not be quite as good yet. These are meta-analysis that compared non-Asian countries with colorectal ESD in Asian countries. You can see that on block resection 81 versus 93, R0, 71%, versus 86%. Not quite as good but decent data given how early we are in our experience. And then, obviously, can you EMR this? ESD helps with fibrotic lesions, helps with recurrent lesions, helps with lesions that [INAUDIBLE]. But it also helps with ridiculously difficult lesions.

This is a 4-to-5-centimeter circumferential adenomas, so this also in my last year's talk. But it's really impressive. I felt I should show it again. So this would commit this patient to, most centers, to have a colectomy, because the big lesion that is partially involving that TI. There's no way to kill this thing with the MR. It's going to come back. It's going to recur. Then it's going to develop high-grade displays. Everybody was getting scared. It's like, oh, they will throw in the towel, and you'll get surgery. Or some of them will just send you straight to surgery.

So ESD takes four hours for something like that. But it saves the patient from having a colectomy and completely eradicates the lesion. Then you make an incision in the ilium, completely around it, with negative margins. Then in this case, we put [INAUDIBLE] to keep the orientation during the dissection to avoid damaging the specimen. Then you do an incision in the cecum. Now, you can see the muscular rim of the valve. You can tell what the plane is because there's the stance, so the plain to cut is right here, to jump from the proximal lip valve to the distal lip valve. And then you'd complete the resection. That's a [INAUDIBLE] and negative [INAUDIBLE] margin, negative sickle margin. Looks good. Basically, it's done. We have done five or six. None of them has recurred. And this was the data from the DDW, at two-four months. Now we have data up to about a year.

But it's difficult to learn. This is our learning curve. You have Japanese studies with expert mentors, lots of easy lesions or whatnot. I'd say 40 cases. Well, 40 cases in the stomach. In the West, it can be a little harder. This is the work of Xiaocen Zhang right there in the audience, who worked for a year with [INAUDIBLE] in Shanghai and us. He's a resident at [INAUDIBLE]. So he did this fantastic work using the CUSUM analysis on our 600 DSDs. And this is by Oregon. It so far goes about 160 cases on the CUSUM graph. Stomach also about 150, 160 cases. That's the easy ones. But colon, 200, then 70-- 260 or 80. I can't tell-- well above 200 to get over the competence speak on the CUSUM graph.

Rectum, fewer lesions. That's why it's a bit choppy, but 70 cases. Our rectum is the easiest, followed by the upper ESDs. And finally, the colon is the hardest, but we know this. If I can take significant numbers to read, say, reasonable procedure time, we may be held now, in this learning curve, by these newly-available devices. The Lumendi, FDA approved about a year or two ago. We did the first pilot trial in the US at Winthrop. And this just came out. We're happy to do the first human case in the US. This is a previous luminal device.

Let me say here, please give Sergey the credit and financial [INAUDIBLE] he deserves for helping develop this device. Right, Sergey? So he was a pioneer in developing the early version. Boston bought it, and they made this beautiful ORISE device. We use it on the first case. Here we are. Like at 10:00 at night at Winthrop with a lot of Boston friends. And this is the lesion-- big, difficult rectal lesion resected very nicely with the traction that-- these are two traction forces that come through the cage. They stabilize the scope. So these may help. Probably these in the right colon and these in the left colon. So they are complimentary devices interestingly.

Now, let's move to POEM quickly, and then to, finally, [INAUDIBLE]. So what's happening with POEM? You had a lot of talks, no need to belaboring. It's the endoscopic version of Heller. There is some learning curve data. From [INAUDIBLE] group in Shanghai, we have now a huge learning curve trial with 1,346 cases from seven operators. Fastest POEM in the world, 41 minutes. You can see the duration of the other learning studies. This is ours from 2015, 97 minutes.

41-minute POEMS. They did a fantastic analysis with the CUSUM graph that was risk adjusted and used failures and adverse events and the moving average and procedure time-- very comprehensive study that showed 70 to 100 cases. Now, this is the operator from all the studies with the largest is the experience and the fastest POEM. But found that you need the most prestigious learned POEM, which, obviously, is much closer to reality than this Hopkins study with 11 cases to learn POEM. If it takes you 180 cases to learn the ICP. It cannot take you 11 cases to learn POEM. Let's be serious here.

They used this inverse curve fit analysis, basically the plot asymptotic curve arbitrarily on the first 60 points. Then they estimate where this will plateau. They call this the ideal time achievable by this operator. And 90% of that is what they consider competent. And then they calculate when they reach that-- 11 cases. Why? Because this underestimates the plateau level, because you only have 60 cases. No time to belabor this, but you probably need more-- we said 40 to 60 cases. The Chinese group said 70 to 100. It starts somewhere in there, so you need quite a number of cases.

Now, what about outcomes? They remain fantastic now at midterm to long-term data. So two-year data from this Asian in gray, blue-- Western in blue studies, you can see 80 to 100%. These are two-year data. All these patients have reached two years. Not the mean two years. These are minimum two years. And then these are patients that have reached a minimum of three to five years. And you can see, 80% to 90% also. This is our study here.

You can see some of the big Asian studies. Unfortunately, Louis and Joe were missing a lot of follow-up data for the 2% of patients at three years here and 30-- so these are not real-- these are not direct estimates. These are Kaplan-Meier probability estimates, but still very good data. This is our data. Note five to eight years. [INAUDIBLE] did a fantastic job chasing these patients down. We only missed 8% follow-up on this patient. 90% success on these 50 patients that are now five to eight years, so very good results.

We recently published this article, that Xiaocen Zhang is lead author. So he did a lot of the work on that. We looked at consecutive Winthrop POEMS from 2009 to 2016 and compared those that had the previous Heller-- these are challenging patients-- to the 272 that did not have a previous Heller. This is the largest single center study in the world of POEM in failed Heller, just coming out today. I think this month or next month. It is online already.

So if you look at the results, this is a challenging group, the prior Heller, these 46 patients. Three times more of them had pneumatic dilation. Twice as many, 40%, had Botox. And the disease duration is 12 years versus two years. And also, half of them are end stage, more than 8 centimeter sigmoid, compared to 12% in the other groups. So a very challenging group. Nevertheless, procedure time only slightly longer in the prior Heller, mainly due to difficult tunneling. A lot of fibrosis, you can see here, didn't quite reach that discal significance.

And you can see, you can have people like this-- big, sigmoid, [INAUDIBLE]. It looks like an intrathoracic stomach here full of food. It's easy to lose your tunnel where a lot of fibrosis from food stays, et cetera. One of the tricks we described in 2013, and now we republished in the new publication-- these are the pictures from the recent publication, the upcoming publication-- we put the tape market, and that shows you the precise torque of the scope to avoid losing tunnel orientation. It helps orient. Another important trick that Hirohito mentioned is the trans illumination trick to make sure that you reach the cardia.

Success rate, 96% prior Heller, 94% in the other 272 patients. There was a study from Hopkins that put together cases from 10 different centers that showed 80% success rate in these patients. But these were small centers that probably did not properly select the patients and didn't have enough experience. We did our first failed Heller as case 38, very close to when we're competent in POEM. And we also rejected one quarter of the referrals, because they wouldn't benefit from POEM. They didn't really have residual [INAUDIBLE]. The failure was due to progression of disease, reflux. But you have to do Endoflip, endoscopy, barium. Pick those patients that would benefit from a POEM.

No adverse events in the Heller group-- no mortals, no aborted POEMS, no surgery or IR interventions, no bleeds, no leaks, no prolonged states more than five days, and no re-admissions. Very good results, interestingly. On the no-prior Heller, we did have five prolonged stays and three re-admissions, but it was minor stuff that did not require surgery or other intervention.

Now, in terms of the [INAUDIBLE], the only thing I'm going to say-- because you are going to see a lot of POEM today-- we are now at the area of anterior versus posterior getting hot. We had the retrospective study in 2016 that showed-- because this still remains very hotly debated among expert centers. We showed that there were more mucosal injuries anteriorly because of the way the POEM turns into the cardia. We showed that it was faster posteriorly, easier access of the scope, particularly for the my myotomy part and the closure part. And we couldn't show it as we expected a difference in reflux.

But this is an India study. Their statistician calculated that they needed 341 patients per arm, clearly not a feasible study. So they decided to do 30 per arm as a pilot done by three different operators. Nevertheless, miraculously, they found huge differences. Closure time, eight minutes versus six minutes, like we found. Faster closure posteriorly, less clips posteriorly. It's easier to close a posterior POEM. Accidental mucosotomies, much more-- 20% versus 3%. Our data was like 30 versus 20.

And let's say abnormal DeMeester score in the 25 and 27 patients that got pH studies, 16% versus 37%. This is like, huge, and so discal significant. They got lucky. There is a huge difference to anterior with 30 patients per group. We have now 215 patients in the randomized study, which we were presenting as a [INAUDIBLE] on the Plenary at DDW. And we didn't really find a big difference on reflex. But we confirmed the difference in myotomy, speed, and closure time-- faster posteriorly-- would confirm the accidental mucosotomy is more anteriorly than posteriorly. The numbers are large because we count even simple burns.

And then we confirmed more pain posteriorly-- 50% versus 25%. This is the immediate post-operative pain in the first day, once they reach the floor-- so more pain posteriorly but faster. GERD I'm not going to belabor. Hirohito did a great job. Symptoms occur. These are the best studies from the West. The Asian studies all have less reflux, so they're not very relevant to our Western experience. Five studies from Oregon, Rome, Chicago, Prague, and Mineola that look at all dimensions.

So 12 to 28% symptoms, 20 to 48 esophagitis, 38 to 54 pH study positivity. We have the most data representing at DDW. 209 pH studies. Now, we are probably 250. 54%-- we have plateaued at 50%. So I think that's the real rate of GERD after POEM, if you do a complete, full thickness myotomy-- not as different to Heller as people believe.

These are high-quality Heller fundoplication studies-- 18 to 42% with door to bed, not very different. These are the acute measurements at one to two years. Fundoplication probably loosen with time, so it may get even higher later. These are metaanalysis very well done by Repici. There's also another surgical one that included everything. Repici did a very good job looking at the quality studies.

POEM, 39%. If you discard Shiwaku's Japanese study, which had very low rates as Asian studies tend to do, it goes to 47%. Laparoscopic, 16%. But if you remove three publications by our studies, 22%. So there's a 25% absolute difference. Not worth going and having POEM, Heller, and fundoplication on everyone. As [INAUDIBLE] said, you can have the Heller-- the door, two pairs of separate procedure if you don't want to take PPIs, which are very effective. As I said, [INAUDIBLE] can have POEM-F now.

Comparison with other studies, the retrospective studies with Heller, they show equivalents. This is the new, important stuff that was presented at DDW-- multi-center randomized trials from six centers in Europe, 64 patients randomized to POEM, 66 to pneumatic. At one year, 92% for POEM. 70% for pneumatic. Now look at type III achalasia. The balloon only treats the sphincter, but POEM treats the entire spastic segment. One year, 83% versus 33%. For type III, the POEM is incontestably the first-line approach.

Now, people think with balloon you don't get much reflux. This puts this to the lie because 24-hour pH study-- in the POEM, 49%-- in the balloon, 38.6%-- 39%. If you disrupt the sphincter, it doesn't matter how you disrupt it. You're going to get reflux. And you're going to get much really for the dysphagia, however.

Finally, something that can help us with payers. In 2013, Richter and some others put out a review on American Journal of Gastro that killed us. Said something that POEM was investigation-- the most-quoted study on all payers denying POEM coverage. This now will help. That's Richter and [INAUDIBLE] saying-- yes-- POEM should be considered primary therapy for type III achalasia. Thank you. A little too late, really. If the expertise are available, POEM should be considered a treatment options comparable with Heller for any of the achalasia syndromes. Thank you. And POEM should be performed by experienced physicians in high-volume centers. Thank you, but I wish there were more than words behind this statement.

I'll finish with a brief, two-minute presentation of full-thickness resection. China is leading the way. You saw these amazing cases-- removing splenules-- I don't know-- gallbladder. Nothing is safe. Appendix. Now, in China, the peritoneum is being invaded on a daily basis. Now, we are a little more conservative over here. But both STER and POET, invented by Inoue and the Chinese group and EFTR, are thriving in China.

This is our attempt to follow. We have now 107 patients as of October of last year-- of EFDR, 81, STER, 26. Mean size of tumor, more 2.8, slightly larger than the literature in China. We do tumors all the way up to 6 centimeters. That requires some special techniques. We're going to a 4 centimeter one today. Complete en bloc resection, 96%. 80% of these tumors had malignant [INAUDIBLE] The other ones were a bunch of exotic things.

Length of stay, two days. We still have this one severe complication, pleural effusion requiring a pigtail drain and three or four weeks in the hospital with antibiotics. This is from 2014 from a large [INAUDIBLE]. Still remains the only severe complication. Everything else is really mild, moderate stuff, and less that you would get from the equivalent surgery to remove these tumors.

I'll finish with a case that I did in Mexico in September of 2016, on a live course. They said, we're going to give you a new [INAUDIBLE]. I'm like, oh, great. Then I found out the [INAUDIBLE] in the duodenum. At that point, I was-- September 2016-- I hadn't done EFDR in the duodenum. If you know anything about the duodenum, you should know that you should stay away from it.

So this is the major papilla. This is the tumor, 2.5 by 3. So I start cutting it. I tried to do it in ESC, endoscopic submucosal excavation, but it's really in the muscle. So the 20 surgeons in the room from Mexico say, well, that's no good. You're going to leave that in the muscle. I'm like, well, I can't [INAUDIBLE] don't worry. I bought it. We have duodenal stabbings all the time here in Mexico. That will be like an acute trauma of the duodenum. We can close it in a jiffy. I'm like, OK.

So I proceed to this full thickness now. We've got the entire wall thickness. There's the tumor. There's the retroperitoneal membrane there in this sweaty room with 30 people in there. So we are cutting-- oh, now Isa was in the next room doing a difficult ESD. So he's leaving for the faculty dinner two hours late at 9:00 PM. And he looks through the door at my room and immediately averts the eyes and proceeds. I don't know if you remember that day.

Anyway, so this is the resecting the tumor off the retroperitoneal fat and retroperitoneal membrane. And there it is finally. And this is the defect. 3 to 4 centimeter lateral wall defect opposite the papilla. You can see here the retroperitoneum. This is the defect. This is the area where the tumor was deepest, in the retroperitoneal membrane. And then we have to close. And then I find out the double [INAUDIBLE] that they ask is not 180. It's a 100, a 2T100. So we had to jerry-rig the [INAUDIBLE] there. It worked out, as you may want to know. So that's why the image is a little lo-def. So this is a 2T100 scope.

So we closed the hole. And then we put the nice gastroscope 190 to take pictures, complete closure. Probably it helped that it was on the lateral wall, and they sent me this picture of the patient on day 5. I was in New York by then. He's been discharged. It doesn't play, but he says, thank you, Dr. Stavros. I'm going home. I feel great.

In conclusion, POEM as the first successful NOTES procedure has revolutionized endoscopic surgery, spawning many other new NOTES procedure. It has also spurred ESD adoption in the US. But the adoption will require inclusion of colon lesions early in the operator's experience. POEM efficacy and safety remain excellent in emerging midterm data. Technique refinements continue with data now emerging on the optimal orientation, anterior versus posterior. GERD is modestly higher than after Heller but treatable with PPIs. And STER and EFTR, although technically challenging, achieve effective en bloc resection of small subepithelial tumors, less invasively than traditional surgery. Thank you.

[APPLAUSE]