

STAVROS OK. Welcome back. 3:20. Hopefully, we can do this until 4:20. And then, we can do the colon ESD from 4:20 to
STAVROPOULOS: maybe before 6:30. If possible, get out a little early. So implementing ESD in the West. So I'm just going to speak about how you go about implementing ESD in the West, particularly with some focus on buttocks and colon, because frankly, these are the lesions that we have to-- in abundance in the West, compared to gastric ESDs or even squamous esophageal cancer, which are both easier than Barrett's and colon.

So implementing ESD in the West. So the standard nostrum is you fulfill your preconditions. It have to be an [INAUDIBLE] you can somehow get at least two ESDs a month, ideally one per week. And you have to have some experience in advanced endoscopy or at least EMR, and an endoscopy unit that is supportive to advanced/extreme endoscopy including the infrastructure, the staff, support from administration.

I train a lot of-- well, on ESD. And this often becomes an issue, the support of ESD in that institution. As somebody goes through their learning curve, some institutions are not willing to invest the time or money on that.

Now, phase I would be basic knowledge acquisition that can be found in tests, reviews, and courses, or even ESD videos on YouTube and whatnot, lesion assessment, knives, and electrosurgical generator settings. We cover some of that in the course today. ESD techniques, indications, limitations, risks, and outcomes. This is the basic fundal knowledge.

And then, you move to a preclinical training, training in ex-vivo animal models. You can often get support if you are promising from maybe Olympus and Boston to do some of that. But the course for ex-vivo models is pretty modest. We can probably get from [INAUDIBLE] a box for \$2,000 and then get a big stomach sent for \$150 to hook in there. And that-- one stomach could last you five, six hours at least, as a beginner at least.

Then, observe live ESDs by experts. Minimum of 10 to 20 cases, what is recommended the general. A trip to Japan would probably give you 40 cases over four weeks. But you can easily see the same amount if you visit my center or maybe other centers, Sergei's, Sergei Kantsevov. Although, he's very focused on colon. So the [INAUDIBLE] is not as essential anymore. I personally really developed it without going to Japan, but that was not popular back in 2000, in the early 2000s.

So some people like [INAUDIBLE] reported doing a big ex-vivo ESD and sending his videos to experts, friend of his in Japan, to-- for them to comment on what he should improve. That may help. And training in live animals, I don't think it's essential. But in live animals, where there is some bleeding control. And ESD in the stomach of pigs usually the ESGE recommends that you got to reach the speed of 30 minutes per 5 centimeter lesion as a sign of competence. And to be able to successfully marginalize any perforations or bleeding.

And then, you go to human experience. Phase III is training to competence, which may be achieved possibly, depending on what cases you have in maybe 40, 50 cases. I think in the West it takes longer than that. 20 could be the test cases, where you are trying to reach the competence. And the last 20, 30 you have to prove competence. So basically, that would mean at least 20 consecutive ESDs with en bloc resections over 80%, en bloc, not R0. And adverse event rates of less than 10% is the competence.

Then, you can move from competence to proficiency, more than 80 cases for sure where mainly you do self training now to achieve proficiency. And the idea is to reach those benchmarks-- en bloc more than 90%, R0 80%, dissection speeds of at least 9 square centimeters per hour-- some people use square millimeters per minute-- and significant adverse event rates of less than 5%.

So here, some master classes, watching expert cases may help. But there's a lot of effort put by the operator themselves. And finally, mastery is in the hundreds of cases. Curative resection rate more than 80%, ESD center of excellence, involved in training others.

So this is really the basic approach. And then in terms of the clinical experience, there is two rough approaches. The standard one that is recommended is the step-up approach. That is also proposed by European guidelines and most Asian experts, which is to start with easy areas and then go to difficult. The idea is start distal stomach, rectum, and then esophagus before you do any colonic lesions. And this has been followed by many EUS-- and many US and European adopters.

Now, a maverick approach but potentially more applicable to the West and useful is the prevalence based approach. It refers to just include the colon lesions early in the experience as they come in, which obviously are much more prevalent than gastric lesions. And then, you could be able to get your once per week ESD volume at a more appropriate rate to learn fast and avoid any injuries to patients. So the prevalence based approach may get you to competence much faster, which is also good for patients.

Now, this was proposed by Ogama-- Oyama as far as I think initially. And it was pursued by some early US operatives including myself and also some Northern European ESD adopters. And it has gained traction more recently in the US and has triggered development of ESD devices focusing specifically in the colorectum in the West.

Despite the fact that it's considered the most difficult organ to do it and our early phase adoption in the US, still companies are doing a lot of stuff for the colon-- ORISE-TRS for the left colon mainly, the DiLumen for the right colon mainly, and then we have another Medrobotics robotic platform mainly for the rectosigmoid, et cetera. So this is the step-up approach. Distal stomach, rectum, esophagus, proximal stomach, and then the colon, and then small bowel. It's a pretty esoteric domain that should be left to people with ESD mastery, mainly duodenal but also potentially jejunal lesions.

So ESD guidelines in the West make it difficult to follow a prevalence based approach. These are the ESGE ones and then the recent AGA Practice Update, which follows them pretty closely. So that allow ESD for basically any gastric neoplasia. They consider it the standard of care, as per the Japanese data and criteria. Then for Barrett's esophagus, the bottom line is that ESD is not shown superior to EMR. Therefore, EMR should be preferred. And I'm quoting the guidelines. There are some exceptions, bigger tumors, poorly lifting tumors, tumors with risk of submucosal invasion, et cetera.

Colon adenoma, same thing. Most can be effectively removed by standard polypectomy or EMR. But then, again, you have the high suspicion for submucosal invasion, particularly if larger than 20, and then, lesions that cannot be optimally and radically removed by snare techniques. Obviously, trying to learn ESD in these kind of lesions, without having access to the easier lesions, is turning things on to their head.

Now, what's the problem with the step-up approach? There's just no stomach lesions. So there goes that. The SEER database, of the 43,700 cases of gastric cancer, 1,828 were early, or 203 per year for this period. And that's not enough gastric ESD to go around.

This was also identified by mere attendees of hands-on courses on ESD that were polled in this study, that-- and this of an ESD course. They would ask about what they perceived as a barrier to ESD implementation in a Western practice. And the surveyed 34 ESD hands-on course participants. And really, by far, the number one reason, lack of lesions.

So what does the step-up approach look like? This is from an expert in Europe, maybe one of the most prolific experts in Europe. These are old study publications, 2009, '12, '15, and '17. And if you put them in a grade, it shows you the slow progression of an-- of a step-up approach until the reasonable R0 resections of more than 80% are reached in various cases.

And these are span different periods. This is all ESDs that were done up to 2007. And you see the R0 rate at the end of that period was still 72%. These are all rectal ESDs from 2004 to 2011. The R0 proficiency rate of over 80%. Even the easier rectal lesions was reached in the 2000 to '11 period.

If you look at the esophageal cases by Probst, 2007 to '14, you can see again it took until 2010 to '14 to reach 86% R0. And the esophagus is definitely easier than some parts of the stomach. And then, in the stomach, 191 lesions over 11 years. By the way, don't steal my slides, please. So 191-- or at least not without attribution.

So this is the-- In this case, you see R0 resection in the first 96 cases in the stomach, 59%, and the last 100 or so cases, 93%, in the stomach, which is not the easiest of places. So he started doing ESDs in 2003, but he didn't achieve proficiency by R0 until 2010, '11. So it's really a eight to nine year period. As I showed you on our prevalence based approach data, it took us three to four years, less than half that to reach. And we are training in the same period approximately. I started in 2005, '06, '07, and then really started doing it in bigger numbers in 2009.

Now, this is a US multicenter agglomeration of cases from DDW in 2016 that shows mostly that these groups were dependent on a step-up approach. Seven endoscopies, did 304 ESDs. Mean of 51 per center. There were six centers. And you can see that 84% were stomach, esophagus, and rectum. And only 8% were colon.

And nevertheless, even after these 51 cases per center, the en bloc resection was 78, far below 90. And there R0 rate was 56%, far below 80%, with median ESD procedure of two hours. And at three months, half of them had the follow-up endoscopy, which showed 11.6% residual disease. And that doesn't really happen in ESD. So this is residual disease. So the step-up approach, slow going.

So what other issues have been identified for this type of approach? This is from Probst from his latest big gastric series in 2017, maybe the biggest one in Europe, where he said that their data on this gastric series were still lower compared to large Asian studies with R0 of 88 versus 94 in Asia. And he attributes that-- attributes that to the very low number of suitable gastric lesions in Europe. You can extrapolate this to the US.

And in their study, he says they needed 10 years to get 189 patients or 18.9 per year. In a similar study, he says by Pimentel, 162 patients over 10 years. That's 16 per year. Repici, 42 patients over four years, 10 per year. So very low numbers. And that is the issue.

There's another problem with the step-up approach. The step-up approach says that beginners should focus on the stomach and the esophagus. The problem with that compared to the colon is over 50% of lesions in the stomach and the esophagus end up being some form of carcinoma of T1a-- T1b nature, which means you have beginners now doing incomplete resections or margin positive resections on people that in a big number will have early cancers. And a positive margin may make the difference between a curative resection and referring them to do salvage gastrectomy or esophagectomy. It's a big impact.

In the colon, the vast majorities of adenomas are advanced adenomas. You get a positive margin. Usually, it's a lateral margin that can be dealt with with another ESD or ablation. And in any case, nobody is going to send for colectomy because a lateral margin of an adenoma was positive, unlike a lateral or deep margin of a Barrett's carcinoma or a gastric carcinoma. So these are the problems with the step-up approach.

So what about the prevalence based approach? As it was proposed by Oyama-- and he put it very nicely, so I'm quoting him verbatim-- early gastric cancer is too rare in the West to achieve a useful caseload of at least two ESDs per month. That will be 24 a year. And as I showed you from the Probst data, none of the European centers got above 18 per year. So none of them got two gastric ESDs per month. This recommendation of the step-up approach would impede the establishment of ESD for decades to the disadvantage of GI cancer patients.

Alternatively, a prevalence based approach allows for a reasonable caseload, but requires learning ESD mainly in the colon and early on in difficult locations. So Westerners must be, however, prepared for a longer learning curve than the one reported by Japanese studies, because of this need to include colonic lesions and particularly manipulated colonic lesions.

And Japanese studies have reported low learning thresholds for gastric and colon ESDs of 30 to 40 and 80 to 100 cases respectively for gastric and colon. These are likely only achievable in a Japanese training model with continuous tutoring by onsite experts and an abundance of gastric lesions, which allows allocation of easier gastric lesions to trainee cases during the early learning phase.

The highly manipulated Western colon polyps that represent a large proportion of the lesions encountered in the prevalence based approach in the US would result in substantially longer learning curves, as is the case I'll show you with our data. Now, there is data that support this contentions.

For example, this is a great piece of data, because it involves Dr. Nishimura, a very experienced ESD practitioner from Japan who moved to the-- to New York two years ago, or three years ago, and then reported his data in the US on ESD compared to his data in Japan. And he showed that in Japan, for example, less than half of his ESDs were colorectal. In the US, two thirds of his ESDs were colorectal-- again, prevalence based approach-- in the first year in the US

But however, what was really disturbing to him was that his en bloc resection rate for colorectal ESDs in Japan, 288, was 96.5%. But in the US, on those 44 first cases he did in the US, it dropped to 72%. And this is from his slide at DDW. Did my ESDs get-- skills get worse after moving to New York? He says, fancifully. But the answer is obviously not. Western patients are bigger with more redundant colons, difficult to move, mostly under general anesthesia, and most importantly highly manipulated.

You can see here in previously treated lesions, meaning attempted EMRs, bad tattoos. He had then a 46% en bloc rate. And without previous treatment, 83.8%, still below the 96.5. But again, no previous treatment in the US could mean a lot of biopsies. When in Japan, they don't even biopsy those polyps. And obviously, it means big patients with big colons that make scope operability difficult.

So we are arguing that the case mix in the West is what makes this prevalence approach harder. A way to prove that would be to do the following mental experiment and see what would be the ESD learning curve of a US advanced fellow versus a Japanese GI fellow. If both were tutored by an expert, a Japanese expert, but the US fellow had to deal with the Western case mix and the Japanese fellow with the Japanese case mix, what would the results do? And obviously, we could predict that the US fellow will have a much harder time reaching competence than the Japanese fellow. And this is supported by this data.

So let's look at the Japanese side first. That's easy. There are plenty of studies that published results of Japanese trainees. This is one from 2017. Seven trainees train in ESD in this period. 45 to 50 gastric ESDs cases portrayed. And obviously, big abundance in Japan, and not only that. They're probably the easier lesions that that institution was getting.

But you can see phase I, their first 15 cases, phase II, the next 15 cases, and phase III, the last 15 to 20 cases. You can see on the resection speed, they met the proficiency benchmark even on the first 15, more than 9 square centimeters per hour. If you look at self completion, 86%, 96%, 98% completed completely by the trainee with no assistance from the mentor, zero assistance by the mentor.

En bloc resection, 100% across the board. Complete resection R0 96%, 94%, 94%. So they actually met most of the proficiency benchmarks on the first 15 cases, which means expert mentor along with appropriate easy cases in the distal antrum, and whatnot, maybe not too big, et cetera. So very quick accumulation of knowledge that are due to the appropriate cases.

Now, this is an example of the US advanced fellow, Dr. Ge, the advanced fellow for Dr. Aihara and Chris Thompson at Brigrman, two, three years back. We're doing great things now down in Texas. He did ESD training with Aihara. Now, Aihara is somebody who trained in ESD in Japan, which considered pretty much an ESD master in that.

He did one year-- in one year 72 ESDs. Nine had no trainee involvement. 19 had trainee observation assistants, 18 partially performed by the trainee. And 26 mainly performed by the trainee, but not defined in the Japanese way, meaning the trainee did almost the entire case, defined that the trainee-- as the trainee doing at least 50% of the case.

And look at the mix, very unfriendly mix for an ESD trainee. 54% colon, mostly right colon. 25% rectum. That's not bad. 14% stomach. That's minuscule. And then, even three cases in the duodenum, two in the esophagus. And in terms of previous manipulation, 33% were tattooed and 43% had previous EMR. Terribly manipulated stuff. In Japan, these numbers are close to zero.

If you look at what happened with no involvement, ESDs with no trainee involvement, partially performed, mainly performed by the trainee, you can see here en bloc resection, 85.7%, 77%, 88%. So none of the groups reached 90% in en bloc resection. If you look at complete R0 resection, 77.8%, a 76%, 88%. None of them reached 90% benchmark. And recall the Japanese trainee data, which were quite different.

And then, conversion to hybrid ESD, meaning EMR/ESD, big conversions in these cases, and in these cases, none. But the main benchmarks would be speed en bloc and complete resection. So difficult long learning curve with this prevalence based approach, because of the [INAUDIBLE] case mix.

This is a prevalence based approach from Europe from 2014. In the first 50 cases of this operator, 40 out of the 50 were colorectum. So you see very few stomach, esophagus, duodenum, mostly colorectum. And in fact, mostly rectum. Six out of the 40 colorectals were in the rectum. Everything else was colon, ascending cecum, sigmoid, transverse. So prevalence based approach with a lot of difficult colon.

And you can see here the progression. The case mix initially had some stomach and duodenum. But in the later phase, it was essentially all colon. And you can see how difficult it is to reach the en bloc rate-- 75%, 67%, 58%, 83%. It still hasn't reached 90% at the end of the 50 cases. R0, 75%. Hasn't reached 80%. Dissection speed plateaued after 50 cases at 3.3 square centimeters, one third of the benchmark speed of 9.

Now, let me show you our prevalence based approach, which after much effort to beat down the naysayers was published in CDH in March. Mind you, the naysayers were saying that we-- our threshold for proficiency was too high. I'll show you why that's not the case. So these are the volumes that we had in 2009 to 2018, ever increasing. The green is colon. The dark green is rectum.

You can see initially, we had a lot of subepithelial tumors. But then, as we started in 2012 [INAUDIBLE] there and EFTR, this dropped a little. And right about 2013, the prevalence based approach blew up the colon, as you see here, with now maybe two thirds of the cases being colon. And this is for 3egut up here. And this is subepithelial tumors.

And this is how long it took. So as I said, it took Probst about 10, 11 years with a step-up approach. But here, it's-- From 2009, you can see the very large-- zero en bloc on our first block of 50 cases. It went rapidly to 80% R0 and 90% en bloc at about four years or so, four, four and a half years, until the benchmarks were met.

Now, if you look at the blocks of 50 here, it's numbers another block of 50 cases. You can see the average rate for that block of 50, it goes up. You can see here the en bloc resection rising, the R0 resection rising, and again, the en bloc was achieved faster. 90% en bloc was achieved at about 200 cases. And then, the R0 is a little harder. It needed another 50 cases, at 250 until we could reliably stay over. Now, you can see at a very high level now.

And then, the adverse events is not an issue, if you are careful. I didn't show you that on the Berr study, but they're also, they're achieving a reasonable adverse event rate of less than 5% or so. It can be achieved fairly fast for careful operators.

What about the ESD speed of 9 square centimeters per hour? That also, this is a moving average of 50 cases. It took somewhere between 250 and 300, because again, these are 50 case moving average to achieve the-- So every-- So all the signals point to 200 to 250 for series that I have on colon. I didn't show you here. That's the consistency of our series. 52% colon. 88% in the right colon of these. Rectum, 8%. All of the foregut, including duodenum, is about less than a quarter and about a fifth subepithelial tumors. So very heavy on colon.

Now, why does colon make things difficult in the learning phase? This is the median speed in the different organs for this series of 540 ESDs. So you can see duodenum, very slow, 3 square centimeters per hour. But the next worst thing is the colon, with 6, in the 6's. Now, the rectum is 10.4 and is the easiest. The next easiest is esophagus and stomach that are about 8, 9 square centimeters per hour for the median for the whole series.

We'd look at this through a CUSUM graph, asking, how many ESDs does it take until in a particular program-- in a particular organ? You get to an ESD that is faster than 9 square centimeters per hour. So in the esophagus, it took 170 ESDs to reach that speed in esophageal lesions. It took 160 ESDs to reach that speed in stomach lesions.

Now, this is all ESDs, because obviously, you learn from every single one. So it took 160 ESDs anywhere until you could do gastric lesions faster than 9 square centimeters per hour, because some people have trouble understanding what-- They think that we did 160 stomach lesions and 170 esophageal. That's not what this shows. It shows that we had to reach 160 ESDs before we could get that speed reliably in the stomach. Colon, 280 cases. And rectum is the easiest with 70 cases to basically start having decreased-- increasing speeds beyond 9 square centimeters per hour.

Now, we were accused of having too high thresholds. We had a reviewer that said, don't publish this, because the lawyers would use it. And it's too high a number. Well, the number is the number. And no lawyer cares about single retrospective studies. They care about guidelines. So that's irrelevant. If it's the truth, it's the truth. And it is the truth.

These are other thresholds from Western studies that do also prevalence based. I already showed you Berr, who after 50 ESDs was 10 percentage points below proficiency and at one third of the speed. The Sauer study, 182 colorectal ESDs. They had 15% technical failures. And in the 85%, where they succeeded in finishing the ESD, the R0 rate was 63% after 182.

In this study, they had 301 colorectal ESDs. Mind you, 57% rectal, so a fairly easy case mix, easier compared to in our series, you saw the rectal ones were like 8% or something, so-- 9%. So you can see with all these rectal lesions, still, the R0 of 80% was in the block between 240 and 301 cases. And a speed greater than 9 square centimeters per hour was in the block between 180 and 240 cases, smack down in the same number that we figured out.

And in the Mocker study, they did 381 colorectal ESDs that were prior to or concurrently with 39 foregut ESDs. So basically, these people studied the prevalence approach getting all colorectal ones. And once they became famous enough, they may have started getting some esophagogastric ESDs.

Even after all this training in colorectal and despite a total of 420 ESDs, the R0 rate in the easier foregut lesions was close to 80%, however. But still, after 381 colorectal ESDs, they were able to get to 77% on our-- on the foregut lesions. The experience is not completely interchangeable. But it helps. That's close enough to proficiency, even though they only had 39 foregut. But they were dependent on this vast experience in colorectal.

So I think based on that, it's important to avoid this, the world is falling, and Westerners cannot learn ESD mentality, and inferiority complex. Studies published in the West, the operator really should try to have done enough cases to reach proficiency before publishing data on ESDs. So the proficiency benchmarks, I believe, now are well-defined.

And using some arbitrary self-serving benchmarks-- which there are studies that look at the proficiency in that way, like looking at plateaus and learning thresholds based on arbitrary plateaus of things-- do not represent true proficiency. Unlike [INAUDIBLE] we don't have such clear benchmarks, we have very clear benchmarks on ESD that indicate when somebody has reached not just mere competence but proficiency.

And I think this should be used liberally. And it's a disservice, I think, to the field and to patients publishing studies without reaching proficiency as it propagates the myth that these benchmarks are not achievable in the West, or are too difficult to achieve, or whatnot.

This is one of these Westerners suck kind of meta-analysis. The Akintoye meta-analysis looked at Asian studies versus the Western world in colorectal ESD. And Fuccio looked at that, colorectal ESD, non-Asian, Asian. And you can see the problem.

En bloc resection, Asia, 87%, Western, 71%. Asia, above benchmark or close to benchmark, I should say. Western, well below benchmark. No, I'm sorry. That's R0. So they are above benchmark, below benchmark. Endoscopic en bloc, 94%, above 90%. Meet benchmark; Western world does not meet benchmark. But this is obviously publications that didn't meet the benchmark. Now, Fuccio, same thing. En bloc, 81%, 93%. R0, 71%, 86%, et cetera. So that's about the training.

Now, let's look at the other arguments, other than the-- that the ESD outcomes in the West versus East are inferior for some magical reason, which really, if you put the same effort the Asians put in learning ESD except in colon instead of stomachs-- so it's going to take longer-- you shouldn't have inferior outcomes. So that's one. But then, ESD has more severe adverse events that lead to surgery. ESD is not cost effective. I think these are arguments that we should really look at, particularly as it relates to lesions that Westerners would use on the prevalence approach, such as colon or Barrett.

So let's look at the colon, because as you saw, any prevalence based series may have a majority of such lesions. So this is one of the often quoted meta-analysis regarding complications. They looked at eight studies, six retrospective historical cohorts, and two case controls on EMR versus ESD. And they said, oh. Delayed bleeding was in fact more on the EMR group. But risk of perforation, 1.4% in the EMR, 5.7% in the ESD. But this is all correctable endoscopically.

There is a need for surgery difference of 5.8% to 9.9%. And the assumption might be-- and I've seen people make this assumption when they quote this meta-analysis-- is that the perforation led to the surgery. No. This is based only on two historical cohort studies, which means that the easy lesions may have been getting EMR, and the cancer lesions may have been getting ESD.

And you can see this here, the mean size on EMR, 21 to 32, the mean size on ESD, 27 to 39. And so on this historical-- these were not case control. They were retrospective cohort studies. So probably ESD included more difficult lesions. If you look surgery due to perforation, 0%, 0.9%. Most of this difference was due to surgery for submucosal invasion on histology, 4.4% versus 7.8%. It's not the side effects.

Now, if we look in more detail, this is the Michael Burke mega studies on EMR. They are probably among the best colon EMR people in the world. So if you look at their study on 803 EMRs, 3% had deep muscle injury or perforation that was dealt with conservatively. 2.2% of lesions amazingly had muscle serosa or fat in the path specimen. Seven muscle, two serosa, nine fat. Again, a lot of them were dealt with non-surgical, because only two people went to surgery. Same thing with ESD.

So if you look at the-- our series, 407 colon ESDs and 63 rectal. No surgery for perforation or any other type of adverse event. 4% inconsequential micro perforations, type III or IV with a Michael Burke classification. And one had the suspected delayed perforation. Two, three months later, the patient had a microabscess in the intersphincteric region that may have come from a rectal ESD two months before. We placed the-- a small drain in this 2 centimeter collection. So you can count probably this one as a 0.2%.

If you look at the Fuccio meta-analysis on surgery for any ESD complication, Western studies, 3.1%, Asian studies, 0.8%. But it's not even about West or East. When they looked at these differences, they found that they were due to learning curve effect, because centers with more than two ESDs per month-- and that's a very permissive definition for high volume center-- 0.7% surgery for complications. If you look at centers with less than two ESDs per month, defined as low volume, about 2% surgery for complication. So that's what I have to say about complications.

Now, let's look at the cost effectiveness. And to look at cost effectiveness, I think it's important to discuss recurrence data, which is often overlooked with a focus being on other factors that may have to do with cost effectiveness. So this is from Michael Burke again. All adenoma recurrence, 28% at two months-- at two years.

If you go to adenomas more than 35 millimeters, 35% at 18 months. But you can see the graph is still-- you're still rising. And these were all data with only 84% having had the six months-- the four to six month surveillance, and only 33% of these 1,700 lesions having reached the second surveillance. And it's still rising here at the end of the study.

Their argument is that 90% of the recurrences can be dealt with endoscopically, as per their prior publications. Of course, that still leaves, if we say 30% recurrence, 10% of 30% is 3%. So the overall cohort, that would leave 3% still that may face the prospect of surgery after multiple colonoscopic attempts to EMR the lesion.

Now, if you look at the-- our recurrence after colorectal-- this actually looks at the Akintoye meta-analysis. Recurrence rates, Western studies, 6.5%, Asian studies, 0.4%, far lower than EMR even for us poor Westerners. But again, it has nothing to do with the West or East, because if you get an R0 resection, whether you are in the East or the West, the recurrence is zero. I think it was actually 0.04%.

Now, this is our data on the first half, the learning half of our cases, and the second half of our cases. We've been able to get follow-up on the 84% and 71% eligible patients at one year. And the recurrence on R0 lesions is zero. And the recurrence overall was 0.9%. But as you can see, our en bloc rate on the second half was 97%. And R0 resection was 92%.

So why does this recurrence happen? Well, because these piecemeal resections leave small residuals. And I know there's a whole debate about that, about people buzzing around the edges and all that. We can address this maybe in the Q&A. So piecemeal leaves this rough little something. It causes a little thing sticking out like this that could have microadenoma cells. You get these. But all of these, you can't get any margins on this. And the comparison with ESD is stark.

This is an 8 centimeter lesion, 70% of the circumference that we did on the turn of the hepatic flexure in the ascending colon. Very good markers for not having malignancy. So we did a ESD. You can see here retroflexion. Outlined the lesion, and then complete resection with 90% of the circumference [INAUDIBLE] of the muscle here. But we were able to actually circumferentially suture it.

Multihour procedure, but the patient got this, a lifetime guarantee of non-recurrence. This was all adenoma-- 9 by 11 centimeters specimen, 9 by 7 lesion. Lifetime guarantee of non-recurrence. You don't even really need to follow this any sooner than three months-- than-- sorry-- than three years. And with a suturing lifetime guarantee of no delayed bleeding at 0%.

Is this taken care of in the cost effectiveness analysis? Not really. I'll show you why. Most EMR experts focus, for unclear reasons to me, on the surgery sparing benefit of ESD in SM1 cancers. The idea is you have a cancer with more than 1,000 micrometer-- with less than 1,000 micrometer invasion in the submucosa, which the Japanese tell us has very low risk of lymph node metastases. If you get an EMR, the specimen is all screwed up. You don't know the exact depth. Automatically, submucosal invasion means surgery.

As you get an ESD, the pathologist measures less than 1,000 micrometers, curative resection, no surgery. And in this meta-analysis by Fuccio, they found from Japanese studies that SM1 cancers occur approximately 8% of polyps more than 2 centimeters in the colon. And therefore, you save 8% of patients potentially from colectomy. But I'm perplexed. Is that the only way ESD saves people from surgery? No, it's not.

What about aborted EMRs and technical failures due to non-lifting, difficult positioning of the snare, difficult location, or suspected but not known submucosal invasion? This is up to 10% in series by experts like Michael Burke. If you look at the 1,700 polyps in the Pellise study, when you look at the flow diagram of the study, I don't remember if it's 8% or 9% were taken off the top, because the EMR was intended but not even attempted because of reasons such as these.

Now, most ESD experts at the level of hundreds of cases, where I am and Sergei is, can remove most of these lesions that are impossible to remove by EMR. That could be another 10% of a series of lesions more than 2 centimeters. What about recurrence? I already showed you the issue with recurrence. And I told you that about 3% of the entire group may have recurrence that cannot be eradicated and end up with surgery. It could be 2% if it's 20% recurrence. It could be 3% if it's 30% recurrence.

But this [INAUDIBLE]. Let's say it's 2%. 2% plus 8%, 10% plus 10%, 20%. So basically, in 20% of patients that have SM1 cancer, or impossible lesions such as these for EMR, or have recurrences on EMR that would have led to surgery, ESD can largely save most of these patients from surgery, looking at number needed to treat of five to seven.

Now, if you think about that a colectomy costs something like \$50,000 to \$100,000 if there's no complication in the US. And on the [INAUDIBLE] study that colectomy for benign adenomas in the colon had 0.7% 30-day mortality and 14% severe adverse events, mainly leaks. You see how the picture is rapidly changing on the cost effectiveness there.

Moving on, now there is this cost effectiveness study from Michael Burke's group, ESD versus EMR for colon lesions of at least 2 centimeters. And I'll show you what the issues is with this that, again, majorly bias things in favor of EMR, in my opinion. So the problem is so they looked at 1,000 EMRs in the Australian registry and used their data on that. And then, they took ESD data from the literature, and created this model, and looked at cost effectiveness in Australia with Australian assumptions that are pretty-- non-replicable in the US.

So the submucosal invasive cancer assumptions, they had a very low SM1 rate. I told you that the meta-analysis by Fuccio showed 8% SM1 lesions. They had 3.4% lesions in their group, clearly favoring EMR, because then, you cannot save people from resection due to SM1.

Now, this may be because, as I said, 9% were removed off the top, maybe because there was suspicion of submucosal cancer. They said that their specificity of detecting submucosal invasion from endoscopic prediction was 98.4%. Whenever they said, look, this is invasive and needs surgery, they were 98.4% of the time correct, which is unusual.

Now, recurrence at 18 months, I don't understand at all. Most of the lesions were colon, 82% in the model. And they put as down as a recurrence at 18 months, 12%. Their study from their group by Moss had 20% at 16 months. And the study by Pellise later with 1,700 lesions had 23.4% at 18 months. So where does the 12% come from? I'm not sure, or even the 19% in the rectum.

Now, the ESD side, I showed you our recurrence rate of 0.9%. They put 2% to 3% recurrence on ESD. Now, if you look at that Akintoye meta-analysis, the recurrence was 1% at 19 months for every comer, all comers, and 0.04% if you got an R0 resection, which the majority did. In the Fujiya meta-analysis, the overall recurrence after colorectal ESD was 0.9%. So these numbers are 10 times-- I'm sorry-- are two to three times higher than or this meta-analysis. And obviously, the EMR recurrence data are extremely rosy.

Now, other assumptions are problematic. They assume that the EMR costs \$1,000, and ESD \$4,000, mainly caused by the fact that they are doing EMR under conscious sedation and not-- and assume that they don't admit anyone. And they do ESD with MAC anesthesia and automatically give it a two-day admission.

These are, again, biased over EMR, because and interestingly, the same authors from the same group, the Australian group, when they did a cost analysis comparing EMR to surgery, their assumption for admission, not the EMR, was that 12% of EMR patients are admitted for up to three days, and 1% more than three days. Why they assume zero admissions when they were comparing EMR to ESD? I'm not sure.

Now, if you look at surveillance colonoscopy at six and 18 months, at \$861 each-- I wish I was in Australia as a patient or as an insurer-- \$861 for a colonoscopy. So they assume it's a very low cost, which gets done-- again, you need a lot more recurrence checking with EMR than ESD. But if the colonoscopy is so cheap, you're looking good.

Even so, though, they assume the same surveillance after EMR and/or ESD. When you have an R0 ESD, they wanted you to get a colonoscopy at six months and at 18 months. This doesn't make any sense. As I said, the recurrence after an R0 ESD with 80% to 80% to 90% of resections by ESDR is 0.04%. These patients do not need a six month surveillance. It's debatable whether they even need a one year surveillance, or whether to go directly to the three year surveillance.

So all these assumptions-- and still, interestingly, the most cost effective of the-- of these approaches-- See, they had this imaginary 1,000 patients. And the four approaches is everybody gets EMR. Very few selected ones get ESD in this approach.

Only people with Paris 2c or Kudo V pattern, which basically guarantee cancer, so 43 out of the 1,000. Then, using Japanese criteria for colon ESD, a little more permissive, you could get 40% of the patients to get ESD, 400 out of the 1,000. And then, universal ESD, everybody gets ESD. Obviously, that's very expensive at 6.9 million. But look at the difference between these other three approaches. So the most cost effective was, in fact, selective ESD at 4.2 versus 4.3 million, but very similar.

Now, look at this. Using Japanese criteria, with 400 out of 1,000 ESDs, a great volume to learn ESD on, you get 5.2 million versus 4.3 in EMR, less than 20% difference, which means that for every surgery-- and here, the total surgeries for SM1 were 27 versus 11, for suspected submucosal cancer invasion, 12 versus 0.

So they don't even count the cost of the recurrences, because they assume everybody gets two surveillance colonoscopies in both groups, number one. And to treat the recurrence costs them \$157. I don't understand that. But that's probably because since both groups get the same surveillance, if you treat the recurrence during a surveillance colonoscopy, all you're counting is the snare and-- I don't know-- the clip, or whatever.

So very small difference, which means that for every of these surgeries that you-- for every this of this extra 20 patients that you saved surgery from, it cost \$34,000. That's a very nice number. Saving a surgery for \$34,000 extra, I think, is a very [INAUDIBLE] number. And this is all calculated with these assumptions that clearly favor, in my mind, EMR rather than ESD unfairly.

Now, I don't know if I should beat this down any further. I was a bit irritated by those assumptions. So I did my New York analysis on the back of a napkin. Looking at, let's say you get 100 patients with large adenomas more than two, and 100 are referred for EMR and [INAUDIBLE] to Michael Burke or somebody with exceptional quality, and 100-- or [INAUDIBLE] for that matter, and then 100 are sent to ESD. And then, what happens?

So as you saw, first of all, you have failed EMRs, deep submucosal invasion, 8% SM1, 2% failed eradication, you get 18% colectomies. You get 28% post EMR adenoma recurrence by two years. Again, Michael Burke data. Recurrence means at least three additional post EMR colonoscopies before going to routine surveillance. You do a colonoscopy. On the surveillance colonoscopy, you treated. And then, you get two more surveillances to make sure it's gone.

For non-recurrence, you still get two post EMR surveillance colonoscopies. And then, hospital days for observation after treatment colonoscopies 10% percent, two days, which is optimistic compared to the data Michael Burke used on EMR versus surgery. So the total tally, 15 colectomies, 192 post EMR colonoscopies before going to routine surveillance, and 30 days of hospital stay.

Now, if you look at the hundred patients sent for ESD, 5% will get colectomy-- 3% due to deep submucosal invasion, 1% due to perforation, 1% due to failure of the ESD. And then, 90% will have R0 resection. And then, our rate is 95%, 97%-- I'm being very charitable here-- which means negligible recurrence than can go to routine surveillance.

10% who are non-R0, I will assume similar to EMR. And usually, this non-R0 means you just went close. You didn't [INAUDIBLE]. So I'm going to assume that this is similar to EMR, with 20% recurrence and four post ESD surveillances, 80% no recurrence, and they get two post ESD surveillance colonoscopies.

And then, hospital days, let's assume-- which is not true in our current series, and I'll show you why-- 80% of treatment colonoscopies admitted for two days. Net result is 10 less colectomies in the ESD group, 159 less surveillance repeat colonoscopies to detect recurrence and treat recurrence, and-- but maybe 128 more hospital days for observation compared to EMR.

So at \$2,000 a day, \$5,000 per colonoscopy, and \$50,000 per colectomy-- and mind you, in New York, the colonoscopies can often be closer to \$10,000 than \$5,000-- you can see basically savings of a million dollars, or \$10,000 per patient. And these are realistic assumptions based on the literature. So that's my back of the napkin analogy.

So now, finally, I want to finish with a few slides on Barrett's, because that's another controversy. Again, the guidelines say you should do EMR. ESD is not indicated except in exceptional cases. But why? So there is a lot of esophageal. As I said, more than half the nodules in Barrett's will have at least Tis, T1a, T1b cancer.

If you look at these lesions in the SEER database, half of them are bigger than 15 centimeters. So EMR is going to be piecemeal. Medium size of esophageal EMR specimen, 13 by 18 in this study. And then, in terms of determining the depth of invasion on EMR, 26% of EMR specimens have minimal or no submucosa present based on this study. So you get very poor specimens.

So why the support of EMR as the standard of care? Well, the ESD publications from the West are horrendous. OK? So we start here back in 2012 with R0 rate of 39%. All right. Wow. 74%, 63%-- all these are below proficiency. Hobel reached proficiency, and Coman. The rest is below proficiency.

Now, Neuhaus' group did in 2017 this randomized study with 20 EMRs versus 20 ESDs, prospective randomized trial. The ESD R0 resection was 59%. That is not a rate that is ready for a randomized trial. In this digestive endoscopy study, cohort EMR compared to cohort ESD, R0 resection, 20% versus 81%. Now, we're talking.

And then, in this recent GIE from Mayo Clinic, case control of EMR versus ESD, 72 patients in each group matched. You get-- I don't know what they-- well, the R0 rate on EMR is irrelevant. It's never going to be more than 12% to 20%, as we know. But the R0 rate on ESD was 42%. 42% R0 rate for Barrett's early cancer.

This study used a scissor knife to do the ESD of the Barrett's. As I said, this is a knife that sends electricity everywhere and cooks everything around it. And it may be easy to use, but nothing that will give you crisp margins. These are really-- these studies, as I said, publishing studies like that gives ESD a bad name, really, and then create their own guidelines, which means you can remove cancers by chopping it up in pieces, something that is antithetical to oncologic and surgical principles.

This is our study that we submitted to DDW in 2017. Not surprisingly, a poster. 33 cancers-- high grade dysplasia, adenocarcinoma, and squamous carcinoma. That's cases we have completed until 2016, very early days. So most of [INAUDIBLE] adenocarcinoma shown here.

But you see R0 on the first 11 cases, 54%. But then, we got better. The next 11 cases, 91%. And the next 11 cases, 91%. Mind you, we didn't get better from here to here, because we did 11 ESDs. Between these and these, along with 11 Barrett's ESDs, there were many other ESDs in other organs. Hence, the prevalence based approach.

And then, you can see procedure time dropping rapidly within a year or two. But again, a year or two of doing other ESDs as well. So it's very doable if you follow the prevalence based approach to get to Asian levels of R0 resection, which would clearly show the superiority of ESD.

And some studies are beginning to show this even in the West. So this is a very interesting study from Stanford that retrospectively looked at their Barrett lesions for five years that were resected endoscopically, initially with EMR maybe the first 30 of the 50 lesions, and then ESD the next 20.

And they looked at the last cohort from the previous cohort. And they show what an ESD all nice, deep margin, lateral margin. A good EMR, it looks nice and not cooked. But this transition here could be right in the middle of the deepest part of the cancer. So the deep margin is affected. The lateral margin is undeterminable, indeterminate. And then, you can have a bad EMR. This is a cooked, completely through and through cooked specimen, where any depth of assessment becomes impossible.

So does this have an impact on patient care? Yes, it does. And that's the genius of this study, I think. So they looked what happened on this [INAUDIBLE] 31 EMRs and those 20 ESDs. R0 resection, 20% in the EMR, 81% in the ESD. So these people got to proficiency. Now, lesions containing carcinoma, 17 in this group, 10. About 54% here, 50%, as I said. And then, they were removing all nodules. Some of them had low grade. Some of them had high grade. Some of them had cancer. But about half of the nodules in Barrett's contained cancer, T1a or T1b.

Now, equivocal path-- meaning this notorious assessment by the pathologist that there is at least intramucosal cancer, clearly because they cannot assess the deep margin-- was evident in 65% of the 17 cancers in the EMR group and 0% of the 10 cancers in the ESD group, which of course, you can expect from this specimen versus this or this specimen. Now, if you look at the-- And that, obviously, has consequences. See, equivocal vertical deep margin in 77% of cancers here, and 0% of cancers there. This should be 10 here instead of 20. So big, big significance.

And that results in this problem. Total esophagectomy goes down in five people in this group and three people in this group. These were all appropriate, all three, because 100% were T1b or worse. And then, on this group, three out of the five, 60% were inappropriate, because they were done, unfortunately, for T1a or less, including some for high grade dysplasia because of the confusion, and only two out of the five due to T1b cancer or worse.

So in conclusion, the ESD learning curve is longer in the West where an untutored prevalence based approach is often inevitable and requires tackling challenging lesions, such as colon lesions and previously manipulated lesions. Once proficiency, however, is achieved, the outcomes are identical with the excellent outcomes achievable in Japan, including in the colon.

And the surgery sparing benefits of colon ESD over EMR include, in addition to the much doubted SM1 cancers, EMR failures in difficult locations, EMR recurrences that fail endoscopic treatment. Additional benefits include sparing patients the anxiety of cost, of multiple surveillance and treatment colonoscopies for recurrences. Finally, approximately 50% of Barrett lesions may contain carcinoma. ESD offers definitive resection and diagnostic certainty with negative and assessable deep and lateral margins, preventing unnecessary esophagectomies.

Now, I had some interesting cases since this came up. This is the final resection. This was shown at the video forum, which was virtual, a month ago and got the award on the ESD section for best video. So this was that case I was talking to you about, 74-year-old woman, not the cirrhotic from San Diego, the 23 hours, but this 74-year-old woman that took about, I think, six, seven, or eight hours.

74-year-old woman with alopecia, coronary disease on Plavix, non-Hodgkin's lymphoma, status post chemo and radiation in the upper abdomen, who underwent endoscopy to evaluate dysphagia. So had stenotic esophagus. It had been dilated multiple times with Bougie before. And then, enlarged 2a circumferential lesion from 1 centimeter proximal to the Z line to 4 to 5 after the Z line.

And two more cancers. So these are probably lesions created by the chemoradiation in the upper abdomen. See now in surveillance, has developed yet another carcinoma in the antrum. So these were three ESDs at the same time, including the circumferentially one and then this one in the greater curvature and this one in the cardia, on the same session.

This is the circumferential involvement right at the Z line of this gastric carcinoma. And then, this is another lesion down there that you barely saw in the distance. So on retroflexion, you can see a circumferential lesion, and then a second lesion here can be seen, and another lesion here.

So basically, what we're doing is we are-- we start in the esophagus with a bit of a tunnel technique. That's the muscularis mucosa there, very thick. She had a lot of fibrosis, prior-- consistent with a previous radiation to the GE junction and upper abdomen from the-- for the lymphoma. So you can see the submucosa is not ideal. And you can see now we have anterior and posterior tunnels. And then, we're continuing the dissection.

Now we're trying to get between the two flaps of the anterior and posterior tunnels. You can see they are stuck together. We're using water to separate them and try to get through there to do the distal dissection. Distal dissection is very difficult due to scar tissue, as you see there. And obviously, the fundus is the most difficult area. As you can see, we have a perforation that happens in the fundus at some point. Now, the dissection of the esophagus is complete.

And now, we're going to work on this difficult fundic area, which fundus has extremely thin muscle. And you have to dissect perpendicular to that muscle, as you see there. Now, we're introducing our, again, reported [INAUDIBLE] 360 loop of the endoscope to facilitate dissection of the fundus. That's what you do when you don't have enough retroflexion.

And now, you can see we are dissecting here. Again, we're trying to be careful using a protected knife, an IT2. But nevertheless, there's a little perf there, I guess, with this knife. And what we do is, after finishing the dissection and getting farther from the perforation, we close the perforation. We don't close it yet. We leave the fat there, until we are away from it, because if we put any clips there now, they will interfere with the resection.

So after we complete a little more resection, we use the micro omental [INAUDIBLE] technique to close the micro perforation. So basically, what we do is we grab the fat and fix it there. And that closes the perforation securely. Because otherwise, it's very difficult to close. You have to put a clip on muscle, that doesn't hold clips well.

So this is the completed final resection. We bring out. And you see it was a bit of a-- took us 30 to 40 minutes to finish the pinning of the specimen. Oh, actually, sorry. No. What I'm doing here is I'm using a grasper external to the skull to create traction. When you do this tunnel technique for the anterior wall, you always need traction on the anterior wall tunneling.

So anyway, this is it. I know it took a while to pin with the help of the pathologist, because you see the esophagus. we made it hang through the cork. And we pinned the disk. I'm scoping now the specimen there. That's the gastric side we've pinned. And then, that's the closure. And you can see the big resection.

And then, there were two smaller resections of smaller carcinomas like that one. I'm not going to bore you with that, because that's far easier. So that's the other one, and then there is the third one. So these are the three resections of the three cancers, probably radiation induced, because there's a field effect clearly. And now she has a natural one. So that would be her fourth ESD now. ESDs in one, two, and three there. So that took a while, but definitely not 23 hours. Hold on. So these are-- the lesion one took 424 minutes, R0 resection. Lesion two, 5.5 by 3.5, 55 minutes, R0. And the last lesion, R0.

Oh, I think I had the follow-up video at the end showing that everything looks good. So that's the one year follow-up. Hold on. I'll show you. OK. That's the closure there. So that's a year later. And you can see a pretty good result with complete resection, nice GE junction. The clip with the omental fat is still there. And these are the results here.

Now, I have a circumferential doughnut resection for lesions that are around the ileocecal valve, with probably seven of those all with R0 resection in surgical endoscopy. So I think you can go. The video is there. You can look at it there, because I think we better get going with the colon ESD if we're going to finish at 6:30.

Basically, the doughnut ESD produces a specimen like that. That's illium margin. And that outer margin is cecum margin. And it's removed en bloc in one doughnut with ileocecal valve fat in between like that. So that is an R0 resection, saves the patient from a hemicolectomy. And that's the cecal side with the hole of the ileocecal valve.

And this is a case that I did in the Athens live symposium, which is a circumferential EFTR in the end, ESD turning into EFTR for a circumferential recurrent adenoma in a staple line after low anterior section of a cancer, and bouts of radiation, and chemo, and multiple EMRs. So that needed a start as an ESD, and then EFTR at the staple line to get the staples with the embedded adenoma into the scar, and then back to ESD to finish the resection, to get a complete specimen.

So these are marking one side of the lesion, the anal side. We did tunnel posteriorly using traction. Then, that's the posterior tunnel completed. This is a full thickness resection of muscle there. And that's adventitia. So this is the part of the posterior tunnel that had EFTR. And you can see the staples there.

And then, we went to do the anterior tunnel. You see that traction doesn't help. So what you can do is modify with a pulley. That's the posterior tunnel showing the complete resection. So you put an extra clip, change the vector a little, so we can work on the anterior tunnel as shown here. And then, see, we hold it there while pulling, because otherwise, you're going to tear. You can't deploy the clip and then form the pulley. You use the pulley and then deploy the clip, important tricks. And anyway, so you deploy this.

And then, we move on. You can see now we have very good access to the anterior tunnel. And we complete that. I think I have time to make a complete video here. But this is the start of the anterior tunnel, the anterior tunnel with all kinds of scar, and sutures, and clips that we had to dissect with a hook knife of the-- of the rectal fascia and fat, until it was complete. And then is there's the anal side all market. There's the oral side all removed en bloc with a staple line and muscle.

And this is the end result here. You can see a nice circumferential excision. And then, that comes also with a lifetime guarantee of non-recurrence. But this was full thickness. But we didn't penetrate the serosa. So this guy didn't need a stent or anything. He did need a bunch of dilations from what they told me, the Greek physicians that were following him. These are data on doughnut resection, which were seven cases, all R0 resection. Again, it's in surgical endoscopy.

Anyway, for more videos, you have seven years of Long Island lives with people like Yahagi, Inoue. Repici came one year. Zhou, Kantsevov, every year, and myself, doing really challenging cases. We don't hold back in stressing out the master operators. You have seven years to watch. And let's go do the colon ESD now with a DiLumen. So that's it for the lecture. And I'm going to answer questions, again, in the room.