DR. JAMES WALDRON: I'm pretty aggressive with this talk. So I try to get two topics in actually. I'm going to follow up Carol's excellent talk with the next kind of-- or one of the big frontiers for acute stroke therapy, which is the interventional treatment of stroke.

And then after that, I also want to talk about one of the main causes of hemorrhagic stroke, which is the brain aneurysm, and go over how we treat them? And just as importantly, which aneurysms do we treat? Just in terms of disclosures, I don't take money from anyone, don't have a bias other than my own personal opinions, which can be fairly strong sometimes.

As Carol told us, basically-- her numbers are more recent than mine. There's about 800,000 acute strokes in the US every year. 87% are ischemic, and 13% are hemorrhagic. It's a very big number.

She didn't show us this slide, but this shows the stroke belt for the United States. And guess where Texas is, right?

[INTERPOSING VOICES]

DR. JAMES WALDRON: This is-- although Central Austin might look a little different than this, this is definitely-- impacts the communities that this hospital serves and where we get patients from. And if you look at this, this is 55 to 65 death-- not just strokes, but deaths per 100,000 people. And so this means this is a very, very major problem.

I think one of the most important things to understand is the IV tPA trial that came out in 1995 was truly a big deal. Prior to that, we basically had nothing for strokes. I like this slide. I'm a neurosurgeon that likes clipping aneurysm and doing a lot of vascular procedures. I've never done this procedure for surgically taking out an acute clot for an acute stroke.

I was-- I actually include this slide, because I was just happy I actually found it in a textbook somewhere. I've never even heard of anyone doing it. Mainly because it takes too long and it doesn't work. In terms of-- let's start of with initial case. And in this case, this is kind of a standard story.

A 49-year-old contractor was hospitalized after having an episode of V-tach. Got a defibrillator for his arrhythmia. Two hours after, he started developing some left side weakness and had trouble talking.

What turns out, he basically ended up having what's called a right MCA syndrome, which is left arm weakness and other symptoms. He had a stroke score of 17. We did a head CT, like we do in all these cases. He had no hypodensity, no evidence of hemorrhage. But he's not a candidate for tPA, because he just had a procedure.

He was taken to the cath lab. And the cath lab looked like this. From Caro's slide, you can tell, this is not what you want your angiogram to look like. This region here is the carotid artery coming up. And right in here, there's a big clot. And it's blocking the MCA going out to the entire right side of the brain.

He was taken to the cath lab, and then we did intervention on him. This up here is one of the earlier Merci devices and has a clot that was pulled out in this case. And as you can see, this is the finishing angiogram, which demonstrates reperfusion.

And so similar to what IV tPA does, these mechanical methodologies are essentially just newer, more aggressive ways to reopen a blood vessel. All right, And another thing, I think it's important to understand about stroke therapy. Although we want everyone to be perfectly safe, not lose any brain at all, that's not realistic. Half of these therapies we're doing is we're decreasing the amount of brain that is lost during a stroke.

So if you look at the before and after CT scan here, you see this region of hypodensity here. This is stroke. And the patient still has some deficit. This is much better than having this entire area infarct. This is-- someone's recovery is going to be much better than a larger infarct.

There's been a lot of trials that have been done. The ones on the top are the ones that are truly gold standard trials. They're randomized and controlled. And they're mainly around IV tPA. They take IV tPA up to 4 and 1/2 hours. The PROACT II trial did look at interventional delivery of a drug called urokinase. The ones on the bottom of course are the ones from my specialty.

They have-- in general, they're small studies. The results look favorable, but they're not conclusive studies. They're not studies that have proved that the technology works.

Just to briefly go over the IV tPA trial-- again, great drug. 12% of people have a very, very good benefit. And just as importantly, a larger number of those patients are moved down to that modified Rankin of zero or one.

The tPA group had an issue with symptomatic hemorrhages, but it wasn't that high. It was 6.4%. And as like Carol said, the mortality rate was improved.

IV tPA has limitations-- 1, 3, now out to 4 and 1/2 hour window. Lots of people don't get here in time. There's lots of exclusions, like we were just talking about and I was kind of pestering her about a little bit.

And although it does help, there's a lot of room for improvement. It only helped by 12%. This slide here, although it's somewhat cluttered, I'm going to actually-- you're actually going to see it several times during my talk. And this is kind of what was already touched upon a little bit.

It matters where your clot is. And IV tPA is good for small clots and small vessels. The bigger the vessel, the bigger the clot, the less it works.

If you look down this very first column, if you have a blood clot in your internal carotid artery, even up in the brain, IV tPA only work 6 or 8% of the time. So you go a little further out, you get better numbers like 30%. But that's still a large number of patients you're not helping.

You see this same issue with large vessel occlusions in terms of mortality. Having a large vessel occlusion means you're more likely to die. And it means your outcomes are also worse, OK?

And so a lot of what I do and a lot of the work that's been done with imaging is focused on, how do we get to better outcomes in the context of a large vessel occlusion? And right now there are two big strategies being pursued. The first is improved patient selection.

Right now, so much of what we do for therapy is based on time windows. Time windows are great if you don't have any other options. But if you take two patients with a high stroke score at 2 and a 1/2 hours into their stroke, one of those patients could have a completely completed stroke, that there's no chance that you're going to help. And one could be a patient that you're going to completely reverse. Time windows don't tell you that.

And so there's a lot of studies going on now looking at MR and MR perfusion, with the goal of basically getting us a better filter. So when I take someone to the cath lab, I know that I have the potential to help them. And that justifies the risk of the procedure.

The other thing that we're going to talk a little bit about is the main goal of using all these interarterial techniques is just to increase the time-- or decrease the times to recanalization

and increase the rates of recanalization. This is a little bit of what was already touched upon about the ischemic number. In this image, the purple section's dead brain. The yellow section around it is brain that's being starved of oxygen but is still viable and can be saved.

All this kind of lead to what's called the mismatch hypothesis. And similar, if you look at the two circles on the top, the red region is the brain that can be saved. And the black region's the brain that's already dead.

It doesn't matter if you open that blood vessel. You're not going to change anything. If you look at the bottom with all that red, if you open that up, you're giving them a smaller stroke, and they're going to improve.

Here is another example of this. And this was just an IV tPA patient, where on the left you see a MRI with a small diffusion region, meaning a very small stroke that's completed. The perfusion shows a much larger region of starved brain tissue. And you can even see the occlusion in the left M1 on the MRA.

IV tPA was given. Stroke score went from 16 down to 5. Stroke got a little bit bigger. But look, on the perfusion section, that area's been completely reperfused. And you can see on the MRA, that vessel's now open, OK?

Actually, a very important study came out this past summer called the DEFUSE 2 study. And the reason I mention this is it actually went out and looked at doing an MRI on every stroke patient that came on the door. They got their MRI time down to about 15 minutes-- and basically figuring out who had this mismatch.

And if you had this mismatch, or even if you didn't, it was up to the people that were treating. This is actually a trial that came out of Stanford, so we did a bunch of these patients while we were there. We used this information to determine who would go to the cath lab.

And then we would open up their blood vessels, and basically using this data, would track to see how they did. And the top-- based on the sequences they used for the study, the top panel here is someone with what we would call a large mismatch. You see a little bit of purple. You see a lot of green.

The green is salvageable brain. The purple is not. Very big mismatch. This is someone we want to treat.

You look at the lower window. They're the same size. The chances of us helping this patient are very, very small.

And basically, that's what the study showed. It showed that if you had a mismatch, and we opened up your blood vessel, 70% of people had a good outcome, which was at least an 8-point drop in your stroke score. If we didn't open up, didn't help. And if you didn't have a mismatch, it didn't matter.

And that also correlated with a modified Rakin score at 90 days, which meant we were helping people with these studies. And although this isn't the grandfather study for this yet, this is very good solid data-- that we actually can improve stroke care by actually figuring out who we're going to help. The big issue with this is it's MRI based. And not many medical centers have emergent MRI capability or the volumes that justify doing that. And so for this to be a widely distributed technology, we need to get to CT perfusion.

Moving over to the endovascular side of things. Endovascular treatment basically got a kickstart from this PROACT II trial. Came out four years after the IV tPA trial.

And basically in this trial, people stuck a microcatheter up into the blood vessels. If you have a blood clot in the M1 segment, they injected a drug called prourokinase. Basically a similar effect as IV tPA, although it's just no longer available on the market.

Similar to the IV tPA trial, they had a good result. You had a statistically significant improvement in people's modified Rankin scores at 90 days. So 40% of patients improved versus the 25% that only received placebo. The other good thing about this trial is it went out to six hours. It wasn't just to 4 and 1/2 hours or 3 hours, OK?

When you looked at recanalization rates, the people that got the drug had close to a 70% recanalization rate, while the people who didn't basically had 18%. And that's just your body breaking down the clot on its own. Symptomatic hemorrhage rates, much higher with interarterial drugs. They're at 10%, versus people that didn't get anything at a 2% rate.

This is a little bit more than the 6.4% we saw with IV tPA, but it's still a consideration. I But even with that increased symptomatic hemorrhage rate, it improved mortality. And it improved outcome.

All right, and that was kind of the initial look at interventional therapy. Since then, we've

basically moved on to mechanical devices-- so things that we go up there, beat on the clot, suck on the clot, pull it out. And the reason is, we think these are faster. They work better in those large vessel occlusions that we were talking about, where you have a very big clot burden. And it allows us to potentially lower the dose of thrombolytic agent.

Again, it's a busy slide, but the most important thing here-- this is a slide that tries to justify that recanalization is a good surrogate for outcome. And basically what it shows-- they did a meta-analysis on all these studies that had evidence of vessel recanalization and how the patient did. And basically what it shows is if you've got your vessel opened up, you're in the green. And if you didn't, you're in the orange.

If you had-- if you got your vessel opened up, your odds of a good outcome are much higher. Your odds of dying were much less. And you didn't really have a bigger rate of hemorrhaging. So you would think you'd want to open your vessel. This is that same slide I showed you earlier, where it showed that if you had your clot in the internal carotid artery, you had a 6% rate of recanalization with IV tPA-- 30% in M1, 44% in M2, and 33% in the posterior circulation.

The Merci retriever was the first mechanical device on the scene. And this came out in the early to mid 2000s. These show the different versions of the Merci devices as they've added more features, trying to improve their clot-pulling rates.

And basically, the best study for this is this multi-Merci trial, which ended up showing if you use the Merci device, which is a corkscrew device, and you use adjunctive therapy as well, you can get recanalization rates up to the high 60% range. It takes about an 1 and a 1/2 or a little bit more to do. So it's not that fast.

But if you look at this chart, this is that last chart I showed you that had the 6% with carotid opening with IV tPA. This is with the Merci device. You're actually getting the blood vessels open with this device when-- in a patient population that IV tPA was not working for.

Again, the IV-- or excuse me, the symptomatic hemorrhage rates were high. There were no different than the PROACT II. And here's an example of the Merci device in action.

So a 64-year-old right-handed woman-- or, excuse me, man-- atrial fibrillation, not on Coumadin, shows up to the ER with a sudden onset of expressive aphasia, low stroke score four. Basically was not doing anything, because low stroke score are getting better. Here's his scan.

Maybe you can say he's got a little hypodensity up here in this region here, which can correspond with a small stroke. 4 and a 1/2 hours after his initial symptoms came into play, he got a lot worse. His stroke score went up to 18, and he's now having a major stroke.

CT angiogram was performed. If you look in the red circles there, it's hard to see, but a lot of clot in his left internal carotid artery and a lot of clot in the left M1 segment. Here's his initial angiogram. And this is actually down the neck.

He had this extremely large clot burden down here. We went in there, and just with suction actually, sucked this out with the catheter. So we were able to open that up very well. We actually-- and this is the stuff we got out.

So this is the nastiness you can sometimes see. Especially patients with atrial fibrillation, they get these really hard, dense chronic clots that are basically very resistant to IV tPA and hard to pull out. And so this is what it looked like afterwards.

And then we went up looking for the remainder of the clot. And as you can see up here, there's actually two regions of clot. The left M1 segment is occluded here. And there's actually some clot in the ACA territory, although this is getting somewhat reperfused.

We actually gave this patient interarterial tPA and used the Merci device. This is us showing that we've pushed our catheter out beyond where the clot is, shooting contrast die out there to show that the vessels are still open. This corkscrew device, this is the Merci device having been stretched out through the clot. And this is what you do. You slowly pull this back, and you hope the entire clot comes with it.

One pull didn't work. A couple pulls later, we got partial reperfusions-- so not perfect. You still see, there's some thinner blood vessels here.

And over here, there should be more blood vessels in this region. But it was progress. And that's all we were able to achieve in terms of reperfusion on this patient, OK? The MRI afterwards showed a fair reason of stroke, but not nearly as big as you would have had otherwise. And again, a lot times what we're aiming at is not curing the stroke but making it a lot smaller than it would otherwise be.

After that device, the next player on the scene is this Penumbra device. And the Penumbra device is-- let me get this playing for you-- different technology. Instead of a corkscrew you pull

out, it's a suction catheter with a separator that you basically put up next to the clot. You beat on it, and provide a lot of suction and suck the clot back out.

And as you can see in this video, it works really, really good on jello, OK?

[LAUGHTER]

And-- but this is basically what the technology does. And the good thing about the Penumbra is it's very versatile. And you can keep at it. They make them in all the different sizes. And you can stick them in most places in the brain.

Penumbra trial showed improvement over the Merci. Rate of recanalization was 82%-- so higher than that 68% we saw before. Mean time to revascularization was faster-- to 45 minutes. Didn't change the rate of hemorrhage.

But if you notice down here, the good outcome rate in the study wasn't very good. And it gets back to that patient selection problem. If you're opening blood vessels on patients that have acute stroke, you're not really doing much for them, OK?

So here's another example of a stroke patient. A 52-year-old man, lots of risk factors, went to sleep at night-- so last seen normal at 11:00 PM-- was found 11:00 AM with stroke symptoms. Not an IV tPA candidate. No one knows when he was last normal.

It could have been at 11 o'clock last night. It could've been 10:00 AM. But we don't know that, so he's not going to get IV tPA. Has a high stroke score.

Did a CT-CT perfusion. This is actually another very good use for these scans. We don't see a big stroke on his CT scan. We look at the cerebral blood flow, which is a, to a certain extent, an indicator of the starved brain region.

And we look at the CBV here, which is an indicator of dead brain. And the only region on the CBV map that looks really bad is this region right here. When we look at the perfusion area, this entire area is down.

So based on this, we took him to the cath lab, OK? This is what we saw-- another clot in the right M1. First used the Merci device. Here's the corkscrew out. OK, got some opening there.

But if you look closely, he's still got additional blockage further out. So we went up with the Penumbra device. And this is what the Penumbra device looks like.

Spent some time trying to open that up and got even more reperfusion for him. His MRI at 24 hours just showed that initial region we saw in that CBV that was down. So this is-- we basically did a good job of preserving a large portion of his right hemisphere.

The latest technology that has come out, just actually got approved this past spring, is the retrievable stent. And this is something that we all like to use, because, for one thing, they're a lot less annoying and a lot quicker to use than the Penumbra or the Merci device. And essentially, the idea behind a retrievable stent is you go out, you put a stent in the clot, you give it some time to sit in the clot, then you pull the entire thing, because it's still attached to a wire. You pull it all the way down into your suction catheter and just pull the entire clot out.

And all the early data says this works really good. This past summer, they published the Swift trial, which is a trial that actually compared the Solitaire stent, which is the first of these stents to hit the market with a Merci device. And basically, as I'll show you on these things, it did much better than Merci. It opened blood vessels up at a much higher rate and had much better outcomes.

So right now my current paradigm is typically I'll start with a stent. If that doesn't work, I'll typically go to Penumbra. And then Merci, to be honest, I don't use much anymore, because it's similar to a stent. And the stent works better.

And here's a case of us using the Solitaire stent. And a young lady, mechanical heart, had basically a clot, a stroke score of 18. Here, this-- it probably looks like I'm showing the same angiogram over and over. Just clots always tend to go to the same place.

Here's a right MCA occlusion. You can see here, I've got my catheter past the MCA clot. And so I'm injecting contrast into the MCA vessels beyond the clot.

It's hard to see here, but you see these-- let me get my cursor here-- you see these three dots here? This is the end of the stent, OK? I've now deployed a stent all the way through this region here. And it's attached to this catheter here, OK?

And after deploying the stent, you can see the clot here. But the stent, just because-- by the active opening, has actually increased blood flow past it. It's created a little channel here along the wall. You let that stent sit in the clot for a while, and then you pull it out.

And this is what we got. We got a great result-- wide opening and the vessel will look great.

And here is actually a little video. It's hard to see, but you can see us pulling down the stent.

This is actually a different case, but this is simply what you do. And when it works, it works great. When it doesn't work, it's very frustrating. And there it goes.

All right, and again, we only like to show cases that work out very well. And so a stroke score of 18 now a stroke score of 3. Great outcome, great result.

And so this is that busy chart I showed you up front, which still shows that all these studies that justify what I do are down on the bottom. And they're not the big randomized controlled study. And that's kind of what's the big unanswered question out there.

Because right now, we know that we are getting better at vessel recanalization. We've got really good information, that we can choose our patients better now using this MR perfusion. But there are no trials showing that what I do compared to IV tPA actually improves patients.

And there's even a recent trial, the TIMI 3, that actually got stopped-- and was basically looking at a time-based window versus IV tPA, because the data wasn't supporting endovascular therapy. We believe you can do better based on the MRI data I was showing you. But this is still an emerging field that there's a lot of work to do in.

All right, so let's move on and take a look at brain aneurysms. This is a basilar apex aneurysm that I treated about two or three weeks ago. And it's a good illustration for showing you what a brain aneurysm is.

So basically, you have large blood vessels. They come up, and they divide into smaller blood vessels. The classic saccular brain aneurysm likes to form at these bifurcation points, where all that blood force is hitting the wall. We don't know why some people get them and some people don't, but this is the classic location where they do.

There are other types of aneurysms. By far, the most common are the saccular berry. And these are the ones that, for the most part, cause most subarachnoid hemorrhages.

You can get them from dissections-- old people with really bad atherosclerotic disease. You can get them from just all the calcifications and the changes in their blood vessel walls. And you can also get them from other rare causes.

Prevalence is about 6%, when you look at people perspectively on serial angiograms-- just the

general population. And these are the other types of studies. So they're fairly common overall. So it's reasonable to think 3 to 6% of the people in this room have an aneurysm-- just to make you feel--

But that said, that's not necessarily a bad thing. And you'll see at the end of the talk, most aneurysms don't actually even need to be treated, OK? And so you actually will see a lot of patients that show up in the emergency room because they had an MRI for a headache, and the radiologist saw a two millimeter aneurysm. They show up in the emergency room. That patient just had a lot of worry for no good reason, basically. And you send them out. You don't ever do anything about it.

Risk factors-- most are sporadic. There are some rare genetic things. But in general, they're not things we have a of control over.

This slide shows us the various locations. Most are in the anterior circulation, coming off the internal carotid arteries. 10 to 15% are in the posterior circulation coming off the basilar or the vertebral arteries.

The main way we find them are incidentally doing an MRI for a headache or someone presents with a subarachnoid hemorrhage. You can get other symptoms. But in general, they're big aneurysms. They either have clot in them or are pushing on critical structures, so they're not a common method of presentation.

The subarachnoid space actually, because you guys hear that term a lot and probably don't have a clear understanding of where that is-- so this is a cross section of the skull. Here's the skin. Here's the bone.

Here's a leathery layer of the brain called the dura. Below that is the subdural space. You have a thin, willowy layer called the arachnoid.

And below that arachnoid is where all your CSF is. And it's also where all the blood vessels run. And that's the subarachnoid space. So on this chart, that's space that's very adjacent to the surface.

When you see a patient in the emergency room with a subarachnoid hemorrhage, most common is because they got hit in the head. Take those patients out, the next 85 to 90% are due to a ruptured aneurysm. So it's fairly common.

There's about 30,000 cases in the US a year. It's very severe. 60% of people die or are left severely disabled. And then you look at the next stat. Other people that survive, half really have difficulty with their jobs or have long-term cognitive issues from it.

And again, this just summarizes that again. The classic grading scales, the Hunt-Hess Grading Scale, low being good, high being bad-- five is the person that's basically in a severe coma, almost brain dead. Grade one means you have a little bit of a headache.

Grade three is actually the most common. And that's the person that comes in, they've got a headache, they're confused, but they're still moving everything. In general, when an aneurysm ruptures, you see a huge spike in the pressures inside the skull from basically arterial blood being able to pump into the space around the brain. Incredibly irritating, horrible headache.

Depending on how much comes out before it stops determines how bad your grade is when you show up. If it doesn't stop, you die on the spot. If it's just a little leak, you have a headache and nothing else.

In general, if someone shows up in the emergency room with a concern for subarachnoid hemorrhage, they get a CT scan, just a plain one of the head. CT scans are very sensitive if done within the first six hours. I use 95% here. In the first six hours, it's probably higher than that.

Patients that you have a high clinical suspicion of subarachnoid hemorrhage but don't have a negative CT scan will go for a lumbar puncture, because sometimes you can detect either older subarachnoid hemorrhages or small amounts of blood. If someone has a subarachnoid hemorrhage, then they typically go for an angiogram for both treatment planning and also it's the gold standard for identifying and understanding the morphology of aneurysms. This is a classic subarachnoid CT scan. You can tell by the little bit of clot in the frontal lobe there that this is due to probably an interior communicating artery aneurysm.

This is the angiogram on that patient. This is one that was-- I took from a magazine, because they had a very well-- parallel pictures. And so on this one, on the left side, you see the digital subtraction angiogram, which are the routine pictures we get. On the right, you see the 3D reconstructions that we get that really allow us to really plan our planning.

3D angiographies have really come a long way. And this is an example of a Siemens biplane suite. This is what we have downstairs. We just got installed in the past year. So we've got a

very, very good equipment here.

So now you have an aneurysm that's ruptured. What do you do about it? Two ways to treat it.

One, surgery-- put a clip on it. Two, go to the cath lab-- put coils in it. Surgery's been around since probably the late '70s, early '80s. And it's kind of been the gold standard, because if you try hard enough, you can put clips on most aneurysms, OK? Some of the really big, giant ones are extremely difficult and dangerous, but you can do it.

Coiling, it's-- I won't say new now, because it basically came to its fore in the early to mid '90s. But it's a very good technology. Its one limitation is some aneurysms and some structures don't let you fill them with coils without blocking off normal blood vessels.

And here are some pictures just kind of showing you the standard neurosurgical approach. It's called a frontotemporal craniotomy. You go down there, you see the blood vessels, you split the Sylvian fissure. You don't go through brain. And you go down to where the aneurysm neck is.

And here's an example, minus the brain, of kind of what you're doing. I So you get an exposure. We don't take that orbital zygomatic piece off in all cases. That's somewhat one.

And boom. And it's always that easy. Here are some interoperative photos from clippings. In this case, this aneurysm was previously coiled.

It was a large mannerism. Coils on large aneurysms are at risk of having coil compaction. This view had a recurrence of the neck here.

And because the neck was very suitable for clipping, we went in and just put a clip around it. This is a patient that bled previously and so was at risk of having a repeat hemorrhage. Here's a second case of surgery.

And this is a case that the patient was in the cath lab. Some coils were put in the dome in the aneurysm. The aneurysm re-ruptured. If you look at the CT scan, that's blood. It's very, very white, because that's actually the contrast from the angiography procedure that makes it so bright.

And because of the large clot there, the patient was taken to the operating room. And you can see that this is the clipping of the aneurysm there. Endovascular coiling is pretty

straightforward. You go in most typically in the right common femoral artery, follow the great blood vessels up into the neck, and then use smaller coils to get up into the head, to where the aneurysm is.

Primary coiling basically means you get a microcatheter in the aneurysm, and then you put the coils out. In general, coils are these little platinum 3D structures. And they call them coils. They're actually not helices. Most of them either form 3D balls, or there's a bunch of other different shapes. They're designed to help fill an aneurysm.

Coiling really became the standard of care when the ISAT trial was published. And what this trial showed-- it was a big study that was done in Europe, where they compared directly coiling and clipping. If you have-- in this study, if you are able to choose between the two therapies, and you had your aneurysm, coil versus clipped, you had a risk reduction of 7 and 1/2%. So-- and that's the risk of death and dependency.

So if you had your-- in that study, if you had surgery, you had a 30% risk of death or dependency. And if you had your aneurysm coiled, it was 23%. And that kind of really pushed coiling to the floor.

There are some concerns about coiling. In general, a lot of aneurysms, in particular, bigger ones or ones with wide necks, you leave a little neck remnant. It's kind of accepted. But there is some concern that with a neck remnant, you could have the aneurysm recur and be a risk for additional bleeding.

Three main types of coiling we use. Primary treatment, which is the top block here-- that means you can stick a microcatheter in the aneurysm. The neck's small enough. You can fill the aneurysm with coils. Balloon-assisted, where you put a balloon over the neck, because the aneurysm's wider, and you don't want the coils to fall down to the underlying vessel. And stent-assisted, where the stent, and you see on the bottom there, acts as a strut and keeps the coils in.

Here is a-- some slides demonstrating a stent-assisted coiling. And as you can see, again, when we look at this middle panel here, these dots here represent the two ends of the stent that's coming around here. And here are the coils being put in. And here is the end result product after coiling.

This is just another example of a stent-assisted coiling. Again, stent-assisted coiling is very

important when you have an aneurysm like this, where the major blood vessels are actually involved in the neck of the aneurysm. The latest new thing in the coiling world or in the aneurysm treatment is something called flow diversion.

And there's a new stent system out called the pipeline flow diversion system, where essentially it's a stent. But it's got a lot more coverage to it. And as you can see it here, is-- you just lay it down over the neck of the aneurysm, and it redirects blood flow away from the aneurysm to keep in the artery.

If you down here, this is one of the stents we used for stent coiling. This is that flow diversion device. You see how much tighter the weave is there? And so this actually has about 30 to 35% coverage over the neck of the aneurysm. And so the goal is to let blood flow through the pipe, not going into the aneurysm or go in at such a slow rate that the aneurysm clots off-- but with this weave, still hopefully let blood go into small perforating vessels that come off the artery.

Here's the first pipeline case I was ever involved with. And this was a patient I treated at Stanford-- very tough aneurysm right in front of her brain stem. So you see this here? This is an aneurysm pushing into her brain stem. And she was having a lot of symptoms from this.

You do the angiogram. It's what we call a vertebro-basilar junction aneurysm. And you can see, it's very large and in a very dangerous place. It's not a good place for surgery.

Here again is a 3D view. And then here is us deploying our two pipeline stents. This is the first one. And again, it's very hard to see, and I apologize. These aren't nearly as radio-opaque as some of the other markers.

And the second comes out here. You can actually kind of see it. Yeah, here comes the second one down.

You can see the edges of the stent here and here. And the second one ends up finishing up here to give us very good coverage of the aneurysm. And there you go. And then-- actually, I'm going to go back here.

And here's another video showing-- so they went through and injected it from one of the vertebral arteries. So here, you still see a filling of the aneurysm. But this right here is that pipeline stent. You don't actually see much blood going to the stent. So we've already got good stasis in this aneurysm.

And because there was still an artery feeding directly into the aneurysm, we actually went ahead and blocked that artery off-- what's called a vessel occlusion. The reason we were able to do that-- I'm having trouble with this here-- is that you have two vertebral arteries, and the other one was widely open and was working well. So this is the other side. We've blocked off the one on the left side.

And notice how long that contrast stays in the aneurysm. So now all the blood's run through the brain, run out the veins. And that's what we call stasis. And that's what we want, because that, to us, indicates that aneurysm's going to go on to clot off.

Three months later, came back for an angiogram. This is like a poster-child case. You don't see any aneurysm at all.

You see, this is an injection on the other side. You see that vessel that we closed off is still blocked. If you look at the MRIs, the only important pictures here are this right here. This entire space here was the preop aneurysm.

And if you come look all the way over here, it's actually shrunk in size now that it's clotted off. So she's had an improvement in her symptoms of her mass effect. Granted, she had horrible headaches for about three months and was on all sorts of painkillers as this aneurysm clotted off. But overall, given an aneurysm there wasn't really a good treatment for, this has been a really good thing for her.

And I think one of the most important things that I see now, because we do so much-- so many MRIs, we do CT scans for stroke, so you now find a lot aneurysms that weren't found, because they ruptured, just because someone took a picture of someone's head. And originally, we used to go around telling everyone that your aneurysm had a 1 to 2% chance a year to rupture. And that was the justification used to treat almost all brain aneurysms, because they are ticking time bombs.

There was a trial that came out called ISUIA. And this is actually the worst chart I've ever seen in a paper describing the outcomes and risks of aneurysm rupture. But it's the only one they put there.

And basically what it shows is that if you have a aneurysm that's under seven millimeters in size-- this is a five year rupture rate. The rupture rate in this trial was 0.5%. And this actually

took a lot of neurosurgeons back, because it's not what they believe. It's not what they saw in their clinic practice.

And the reason I say that is in this trial here, this is a group that looked back on-- over several hundred aneurysms that they treated for ruptured aneurysms. And if you look at the aneurysms in the first two columns, which are less than a centimeter in size, that accounted for 85% of the aneurysms they treated. So-- and particularly less than five millimeters was a fairly large number. So then how did these never rupture based on that trial? But this is what we see in clinical practice.

More recently, there was a Japanese cohort that came out actually this past summer-- and a very big study. And the way they did it, they had over 5,000 patients. You had to have an aneurysm greater than three millimeters.

And they basically followed you until your aneurysm was treated. And if it was a large aneurysm, people still got treatment. To be in this study didn't mean you didn't have your aneurysm treated. But they would follow for rupture until that aneurysm was treated.

Overall, when they're were looking at this, if the aneurysm was less than five millimeters, the rupture rate was 0.36% a year. That's a very low rupture rate. If it's bigger, it's a different ball game, OK?

And basically what the study showed is that five to six millimeter range is kind of the transition zone. If you're less than five millimeters, the rupture rate's really slow-- small. And it's pretty hard to justify treating your aneurysm.

When you get to the five to six millimeter range, most probably should still be watched unless someone's extremely young. Or there were two areas that were higher risk aneurysms. They were the ACom location and the PCom location. And what this red line on this chart means is these are that location.

A PCom location had a relative risk of 1.9 times. The ACom had two times risk. And so those were viewed as found to be higher risk locations in this trial.

So basically, my take, when I see someone in the office who had an aneurysm they just found, and it's less than five millimeters, I'm not going to treat them unless they have actual physical changes in the aneurysm or other warning signs like that. Five to seven or so, if it's in the range-- if it's in a PCom or an ACom. We'll talk about it.

If they're 30 years old, we might go ahead and do it. If they're 70 years old, I still don't think it makes sense. When you get larger than that, unless you have a lot of comorbidities or you're very old, then a lot of times it does make sense to treat those aneurysm.

So anyway, just in conclusion, again, with both stroke and aneurysm treatment, we've got a lot of technology coming out on the market. A lot of it's new and exciting. These retrievable stents are exciting. These pipeline embolization devices are exciting. They're both real new technologies.

Normally, you get two years, you find that these technologies have other problems with it, which is the standard issue. But that said, in general, these technologies still always represent another step forward. And that's kind of what we're aiming for.