AtriCure Inc. (2025 Investor/Analyst Day)
March 26, 2025

Corporate Speakers:

- Marissa Bych; Gilmartin Group; Investor Relations Principal
- Michael Carrel; AtriCure Inc.; President and Chief Executive Officer
- Doug Seith; AtriCure Inc.; Chief Operating Officer
- Richard Whitlock; McMaster University; Professor of Surgery
- Vini Doraiswamy; AtriCure Inc.; Chief Scientific Officer
- Edward Soltesz; Cleveland Clinic; Cardiovascular and Thoracic Surgeon
- Kevin Makati; St. Joseph's Hospital; Director of the EP Program
- Nitesh Sood; Southcoast Health; Director, Atrial Fibrillation Wellness Program
- Justin Noznesky; AtriCure Inc.; Chief Marketing and Strategy Officer
- Sam Privitera; AtriCure Inc.; Chief Technical Officer
- Angela Wirick; AtriCure Inc.; Chief Financial Officer

Participants:

- Marie Thibault; BTIG; Analyst
- Michael Matson; Needham & Company; Analyst
- Suraj Kalia; Oppenheimer; Analyst
- Unidentified Participant; Unknown; Analyst
- William Plovanic; Canaccord; Analyst
- John McAulay; Stifel; Analyst
- Lilia-Celine Lozada; JPMorgan; Analyst

PRESENTATION

Marissa Bych^ Okay. Good afternoon. Thank you. Welcome. We really appreciate having you here for AtriCure's 2025 Analyst and Investor Day. I'm going to turn the mic over shortly to Mike Carrel, President and CEO. But before we do, I just wanted to make a quick note that we are being webcast today. (Operator Instructions)

And with that, I will turn over to Mike Carrel for an introduction and an overview of AtriCure's business.

Michael Carrel^ Thanks. Well hello. Welcome to AtriCure's headquarters. It's so nice to see everybody. I mean obviously I know so many faces in the room and also as Marissa talked about online. But before we kind of get going today I just wanted to thank the entire team for putting it together. You got an opportunity to see kind of, I think AtriCure at its best, looking at both the product, hopefully meeting some of our engineers and the team that are building the product behind the scene. You got a sense and a feel for the (inaudible) accord that we kind of try to create here at AtriCure.

I mean we are all in atrial fibrillation, postoperative pain. Every single person that you met today is all in on this mission and what we're doing. And hopefully you got a really

good sense of that as you kind of walked around the facility and you saw how the facility was designed to make it at a place that people really like to come to work every day. We're fortunate to recruit people from all over the world to come. So again thank you for making the trip to all of you. And thanks to the team for putting it all together.

Obviously the forward-looking statements, we've got to hit. I did my little welcome there. It goes a little slow, so I apologize. Many of you have seen kind of a version of this slide over time. As we've looked at kind of our vision of getting after kind of the complex forms and really eradicating Afib long term and postoperative pain.

This is what we do as a business. This is what we live every single day. Again as I mentioned, you saw that. It's built on really some of the four premises that you're going to hear about today that are up there. Number one is that many of you have been a part or know a lot about AtriCure and you think of us in the sense of a strong portfolio that we have. Maybe what you don't know is that we've got over 550 patents to our name.

We've got many different products and we have lots of iterations that you saw some of earlier on today that we continue to develop. That pipeline is only building. We've had four new products just in the last six months or so roll out that are going to kind of generate revenue and growth for us over the coming decade. On top of that, we've got more product coming to market, and you're going to hear a lot more about that throughout the day today.

One thing I'm going to highlight and talk about real briefly is our markets are about a $10 billion market. Maybe even larger because you're going to look at the math and say wait, Mike, that adds up to more than $10 billion. These are very large markets, and we are talking about the complex Afib, not competing against -- you're going to hear from electrophysiologists today not competing against the catheter market. That's another market in and of itself.

We are talking about the surgical treatment of Afib for all those patients. The complex forms of Afib when you're in it for over one year and for any postoperative pain that you might go through. That's what we focus on. And we want to be category leaders, number one in the world in each of the areas that we are and today we are. We are market creators to help patients that have unmet needs. You saw that on the previous slide. These patients have unmet needs we're going after. And we, as a company, that is exactly what we try to go after.

Inevitably, people are going to follow us into these markets. We're not going into markets or areas where there's already a treatment paradigm that exists that works well for these patients today. As I mentioned, we're a global leader, number one in our categories. We do have local roots. I mean today it's kind of -- in today's political environment, saying that you manufacture 100% of your product in the United States is a super positive. I was down in Washington, D.C. recently and a senator basically from Ohio, Senator Moreno was complementing us on the fact that we are kind of in line with what the current

administration is. We didn't do it for that reason, though. We did it because we think it's the right thing to do to build great, high-quality products.

You saw the manufacturing, we create a great work environment, really nice jobs in an area where they can work collaboratively with the engineering team, the regulatory team and the marketing team to make sure that we have the highest possible quality. That's why we did it. And during Covid, it helped us out because we were able to get to the market and when things broke down, we had our supply chain really close. And for a company our size to be able to react, we had no slowdown during that period of time. So it really created a really good redundancy to be really close to home and a really deep and strong relationships right here in Mason, Ohio.

And in addition to that, just a little bit more about some of our local roots, we have -- you saw in the building today about 600 people are still in the building. We have 450 scientists and engineers that work for AtriCure. You see the term innovating, like that is what we think about. We've got great people. We've also got 400 people in the field who are serving and working directly day-to-day with our customers.

Then finally, none of this kind of works unless you've got really good clinical evidence and we're making major investments in this area that we think are going to pay dividends, not just from now until the end of the decade, but actually into decades to come. I think that's pretty exciting to hear from a lot of the physicians about that today. We'll get this to work here momentarily. I won't spend a lot of time on this slide other than to really highlight a couple of things. We all know Afib is a really bad problem. You guys all follow all of the catheter companies. It's a massive market. It's the fastest-growing market in med device.

Some would say with all the PFA angle and everything happening out there, we know the bad effects that it basically causes in so many different ways, and many of us have loved ones that have suffered through it. But what I need to remind people is that 45% of the patients that have Afib, have been in Afib for more than one year. The catheter companies do incredibly good work on the patients that have been in Afib for less than one year.

You're going to hear from our physicians today that while we're under pressure on PFA in one part of our business, this is a massive market opportunity, and we are the only company in the world with a solution for that 45%. And not only that, nobody has got trials going on within that area either. Nobody is running an IDE trial today that's going to read out in the next two to three years.

On top of that, we got into the pain business several years ago. We kind of got into it by action because we were experts in ablation. And people thought some of the surgeries we were involved with were hurting people, and they were coming out of it with pain. That led to us to opening of a new market and becoming experts in this area and becoming the first and only company to really use cryo and actually prove it through clinical evidence and then build specific products to treat that pain. You're going to learn about that from

some of our leaders today. And we all know about the opioid epidemic. But it's really clear.

Obviously pain after surgery slows recovery, think about anybody that has to kind of get up and breathe after having gone to a thoracotomy, very difficult, very painful. Think about the amputation that you have to go through and having phantom limb pain and trying to actually get back on to that leg, very painful when you come out of surgery. Cryo Nerve Block helps solve that problem.

That slow recovery increases healthcare costs and obviously the quality of life. And we're not new with this at AtriCure. AtriCure has been around for 25 years. You probably saw it all over the walls here. That wasn't just done for all of you that have come out to come visit us today. We're celebrating it throughout the company, the 25 years.

We almost all wore all of our 25th anniversary sweatshirts, which I've got like eight of them, and my family thinks that's all I want to talk about nowadays. But what you -- you can see that over that time we have always been an innovator and at the base of that, the foundation has been that we innovate, we create clinical evidence to support that. Then we support that clinical evidence and the innovation with education and awareness so that we can change guidelines and then guidelines change reimbursement.

Over the last several years, you can see the acceleration for those investments and what's happened. The first FDA-approved product, changing guidelines in 2017. The change in the guidelines in 2017, for example, in open cardiac cases led to reimbursement changes. And I'm going to show you in a couple of slides what that looks like in terms of how reimbursement has changed as a result of the evidence that's led the guideline changes, that's led to that.

We've continued to innovate on the AtriClip franchise. We always here and talk about competition coming into the space. What does that mean? I welcome competition as I've talked about before. We think it's good for the market and represents the fact that we're creating a market that matters. And we have a vision for how we're going to go attack it and we've never stopped in going after and innovating in that particular space. Even in an area where we're really strong, many of you who are here today and had a chance to go to our engineering saw our new EnCompass Clamp that came out.

This is revolutionary. I don't use that word softly. I really mean this. We took a procedure that can take over 50 minutes to bring it down to 10 minutes or so by improving the way they can do it and getting better ablations and a better results also.

So the EnCompass Clamp is really kind of a foundational piece for us going forward and to access the market. I know it's an overused term. I was using it earlier. We've democratized kind of ablation. It went from a 10% up to now 35% of the patients are now getting treated, and that number is growing day by day as we get more and more surgeons to treat these patients.

You're going to hear a lot about our LeAAPS trial. We kicked it off. I'm not going to go into much detail there. But up until now we've helped 1 million patients, and you can see the innovation engine is continuing with cryoSPHERE+, MAX, FLEX-Mini launches that have just begun to occur. And it's shown in our growth.

If you look over the last decade, I came on board in around the 2012 timeframe, you can start to see that we had -- we got into double-digit growth, and we would be proud of hitting double-digit growth. We talked to investors about starting to see an acceleration on that growth rate.

What have you seen is that this year, we'll be over $500 million. If you just look at it over the last four years, we took that kind of mid-double-digit organic growth rate. And with bigger numbers and with those investments accelerated over the last four years, we're proud of the fact that we were able to kind of see that acceleration in that growth. And we continue to see strong growth within this business. When you look at the growth overall, we've also done that while starting to hit profitability.

We know that's important overall for a business like ours. You've got to begin to generate bottom line numbers. We've started to generate that. And you can see we've overexceeded expectation in '23 and '24. Obviously this year, we gave guidance in the $42 million to $44 million range for what we're going to drop to the bottom line. You're going to continue to see that expansion, and I'm not going to tease you, but Angie is going to give you some good numbers for our long term here in a little bit.

The way we've done that is those investments in research and development. You saw some of those milestones we had on the previous slide. It's the new products that we've rolled out. It's the investment in clinical evidence that has supported the guideline changes and reimbursement changes. Just to give you a visual of what that looks like on the guidelines, let's take a look at this slide real quickly. I think you're going to see it in one of our doctor slides as well. What this slide represents is, if you go back to 2014, nothing was in that Class I range.

Since then, across concomitant surgical ablation, surgical left atrial appendage occlusion and hybrid ablation, all of them are moving up to the top right to be high-level recommended guidelines. How does that happen? Clinical evidence. That clinical evidence was supported by AtriCure. Those are the kinds of investments that we've made to kind of accelerate and to get us to where we are. And as we go forward, you're going to hear about some of those trials. And from a reimbursement standpoint, what's the next phase after guidelines? Convincing CMS. So you see, it's actually a shorter timeline because that went back to 2014 when data started to be gathered.

Now you're looking at 2021. Since then, these are incredibly important. In 2021, CABG went up that this is CMS telling people, the data is so compelling that you should treat, they've actually increased, let me repeat that, increased reimbursement. If you have a CABG, you add ablation, you get almost $10,000 more. CMS is saying, it benefits the

healthcare system. They've looked at all the longitudinal data with us. They added -- they want you to manage the appendage.

So they actually added a CPT code for the surgeon to get paid separately when they're doing that, separate, all this is based on clinical data and clinical evidence. Recently, in 2023, DRG 212 is when you've got a double valve procedure, they're going to pay almost $24,000 more. They don't just do that. Normally, CMS is trying to cut the different rates they're paying. They're saying, if you treat this, we know that patient is going to do better long term.

Then finally, you've seen recently DRG 317, which many of you are very well aware of, primarily because of the catheter ablation, putting WATCHMAN in or a occluder at the same time that they might be doing an ablation. It also benefits us. It's not specific to the endocardial. It actually -- when you do the combined left atrial appendage and you're going to do the ablation, you get paid more.

By the way that just increased the hospitals pay on that by almost $20,000. Another kind of tailwind for us as we kind of go forward, which leads us to Vision 2030, which is our goal is really to create and deliver standards of care. We are creating standards of care in all these new therapies that we're going after in these most complex arrhythmias and pain after surgery. We're doing that by expanding patient impact.

I'm going to show you a little bit about the market here momentarily in areas that we are the current market leader. Again in the markets we go after, we are very focused on being number one and leading the charge on that so that others will eventually follow as we create these multibillion-dollar markets. Combine that, the way that you deliver it is with new products and an engine that is able to deliver that with clinical evidence and growing revenue by 2030 to $1 billion. And again Angie is going to get into a little bit more details on what that revenue and profitability is going to look like at the end of the decade.

So quickly, back in 2010, if I were standing in front of you, I was talking and excited about $1 billion market. That's what AtriCure went public on in 2005. It might have even been a $500 million market.

I think I looked at a slide recently from -- around the IPO time. Since then, today that's expanded to a $5 billion global opportunity with what we have sitting today our current opportunity, which is concomitant surgery where there are 600,000 patients globally that have Afib when they undergo surgery globally. We are 35% penetrated in the United States, 20% penetrated OUS. Those numbers now have guidelines and reimbursement. And now you've got the EnCompass Clamp to make it even easier to do the ablation.

We anticipate great growth within that market. On top of that, you've got pain management for thoracotomies, of which there are about 150,000 in the United States, and there are about 500,000 of those globally. Big market opportunity that exists there. We're only 20% penetrated in the U.S. and just starting on our OUS expansion.

Then hybrid therapy, that actually looks even too big. There are 600,000 patients that undergo cardiac ablations for endocardial solutions today. That's what they're predicting. You guys hear it from all the big players. We did 3,000 patients last year. We are but a small portion of that. Yet of those 600,000; 60,000 of them have long-term Afib over one year, 60,000.

So we are just scratching the surface of the opportunity that exists there. And as they get bigger in terms of growth for the big companies and they go after those earlier-stage patients, they're not going to know what to do with it, and you're going to hear from our physicians on that. And we're expanding our markets, and you're going to hear a lot more about this, to a $10 billion total market opportunity.

The way that you get there is you take what I just talked about and you now start to do prophylactic treatment, which you're going to hear from two of our physicians here momentarily, you add extremities, and you get into sternotomy, and you've now got a very large $10 billion market opportunity for AtriCure, which leads us to concluding or very close to concluding on what is our vision for our standards of care when I think about it.

Our vision is that in cardiac surgery, the 2 million patients globally that undergo cardiac surgery, every single one of them benefit from an ablation and an AtriClip. Let me repeat that, every single one of them can benefit. Today we're treating just over 100,000 patients in that category. We have product with EnCompass and AtriClip. We've got knowledgeable people in the field. We've got guidelines and reimbursement that I just talked about. We've got robust education that we've been developing over the years, and we've got future trials to go after the entire market to actually prove with new clinical evidence. Combine that with our pain management business, which is to reduce pain after surgery, we started with thoracotomy. Our goal is to expand to other areas.

Our next area to go in a big way is extremities with a new product specifically built for amputations in patients that suffer dramatically with that. That is a $2 billion market opportunity globally. We have product in place, cryoSPHERE MAX, cryoSPHERE XT coming out later on this year. We've got a new platform that's going to be developed that they're going to talk about here later on. We've got trials and economic studies that prove that it actually benefits the healthcare system. So we've got a foundation to build on that.

On hybrid, it is to increase that treatment, to take those 3,000 patients. We know we're not going to get to true standard of care by the end of the decade. It'd be great if I could say that we were going to get there. But we are going to be well on our way to making progress towards that. So we go from 3,000 to 8,000 by the end of the decade. By then, you're still going to be less than 1% of the total population of patients that get treated with an ablation.

This is what AtriCure is going after. We think these are big market opportunities and some of the things that you're going to see over the next couple of years from us. You're

going to see AtriClip PRO Mini for a hybrid franchise, cryoXT PROBE for the extremity business. The LeAAPS is going to be fully enrolled later on this year. We'll get an update on that. We're going to initiate this new BoxX-NoAF trial that you're going to get a lot of really robust detail from Dr. Soltesz, and we will have our first in-human PFA devices in 2025. These are some of the milestones that you should look forward to us talking about on our calls, et cetera, as we kind of go forward, and you'll get more detail about it.

As we get into '26 and '27, we anticipate having a new cryo platform that's simpler and easier to use. We'll have finished our BoxX-NoAF enrollment. Initiating an EnCompass PFA trial, so taking that first in-human. And now actually moving into a true IDE, both for EnCompass and eventually on our MIS and EPi-Sense device as well. I'm going to talk about that a little bit later on today. And as we usually do, we will continue to invest in expanding our AtriClip franchise. And I think it's important in an Investor Day to really begin to think longer term as well.

So as you start to think at 2028 and beyond and the impact that all these investments are going to have on our growth and our trajectory going forward, we will have a new EnCompass Clamp at that point in time. Again we're not sitting still with what we've got today. You're going to have an indication by the end of the decade for post-op atrial fibrillation. That gets after that 2 million overall patients that we're talking about.

LeAAPS data will likely be out by the end of the decade. We may not have an approval, maybe we do, but we will definitely have data at the rate that we're enrolling in that. So exciting opportunities that are sitting in front of us as we kind of get through, and you're going to hear much more about this.

So as you think about AtriCure, number one in the markets that we serve. We've got a robust pipeline of product and clinical evidence coming out over the next several years that are going to drive our growth in vastly underpenetrated markets, and we are going to do it profitably and growing that profits in an area where I think you guys are going to really like it when Angie gets up and talks later on today.

So with that, I'm a couple of minutes over, my apologies to the team on that. But I think it's important information for all of you to have to understand kind of where we're going, where we've been, where we're going and the foundation here. Part of today is you're going to get a chance to meet some of the executive team as well in addition to meeting some of our physician partners that have come to talk to you today.

So we're going to start with Dr. Whitlock and Dr. Soltesz, who are going to talk about the two trials I mentioned. We're then going to move into Dr. Makati and Dr. Sood to give you a perspective about hybrid and why, yes, PFA is in front of us. It is a headwind that we face today but why there is light at the end of this tunnel that is actually very bright and is going to help a lot of patients longer term.

I'll give an overview of our PFA platform that many of you may have seen some of it already. Then we're going to have two of our team members on the management team

talk about Cryo Nerve Block and some of the exciting opportunities there. We are going to close with Angie talking about some of the both short- and long-term financials.

So with that, I'm going to turn it over to our Chief Operating Officer, Doug Seith, who's going to introduce some of our speakers. Thank you.

Doug Seith^ All right. Thanks, Mike. So I'm going to kick off the afternoon with focus on our two landmark trials, LeAAPS and BoxX-NoAF. So for those that aren't familiar, both of these trials are focused on prophylactic treatment of patients already undergoing cardiac surgery. So if you think back to what Mike said, talked about earlier, these are landmark trials because it doesn't just help us only expand the market. This is an opportunity to dip into a much larger market.

So as Mike mentioned, there's 2 million people roughly in the world that have cardiac surgery every year. That open -- that market opens up for these patients because now you can look at patients that are undergoing everyday cardiac surgery and have an opportunity for a procedure. So that is a huge expansive market for us. And it also allows us to stay the premier leader in this space. With these two trials and the expansion of the market, we'll be a leader in this area of cardiovascular surgery with left atrial appendage and surgical ablation for the next decade easily.

So before I talk about our speakers, our physician scientist, I just kind of wanted to talk about these studies in kind of lay terms. So our physician scientists will get deep into the science and why this makes sense. But if you look at this from a high level, what is the opportunity?

So for the last 10 years, our understanding of Afib has changed tremendously. We used to think of Afib as a symptomology disease, a quality of life disease. So if you add Afib, take some drugs, take some anticoagulants, get used to it, you'll get used to it over time you will feel better. And really, we only intervene with patients who are very symptomatic. But that's changing. We now know that Afib is a malignant chronic disease that has serious consequences and can even shorten your life. That's a huge change in just a decade. So later on, you're going to hear from Dr. Whitlock about how the atrium is sick and diseased long before patients present clinically with Afib.

We're just learning about the science, and that's what LeAAPS is based on. You also know from many studies in the last five years that if you intervene on AF early, and if you get patients back in the normal sinus rhythm, what happens? You significantly reduce morbidity, such as stroke, heart failure, cardiac dev, and we're learning more and more now how much dementia is associated with Afib.

So again from a quality of life disease, symptomology disease to now something that impacts the length of your life and severe quality of life. So think about the current state of Afib. Right now if you have Afib, everything is reactive. It's reactive to get thrombosis protection with drugs or a device. You get rhythm protection with drugs. You get rhythm,

you get a rate protection with drugs, maybe you get ablation. But everything is reactive. Nothing is proactive.

The only thing proactive today is changing your life style or life modification so you can stop smoking, right? You can lower the alcohol consumption, you can lose weight, you can address hypertension, you can address your sleep apnea. Those are the only proactive things you can do right now which brings me to my final point.

Proactive and prophylactic treatment of Afib and left atrial appendage management has a unique and singular opportunity to stave off the pathophysiological process that brings on and creates Afib and also causes patients to have life-changing altering events like stroke. That's kind of the simple story in a nutshell. That's where all the science is taking us and that's how Afib has changed a lot in the last 10 years.

So our two science physicians that will be speaking, first will be Dr. Whitlock. Dr. Whitlock has done a talk on LeAAPS. LeAAPS was a very instrumental, obviously development by the company. But Dr. Whitlock's help there can't be understated. So for those don't know Dr. Whitlock was the primary investigator and the lead author for the LAAOS trial. The LAAOS trial proved that there's a significant stroke reduction in patients who have Afib and are getting left atrial appendage management while undergoing cardiac surgery.

So Dr. Whitlock is Professor of Surgery at McMaster University in Hamilton, Ontario, Canada. He is also the Associate Chair of Research, Chief and Division Head for Cardiac Surgery. Along with LAAOS III, he's been a leader in other multinational trials like SIRS, TRICS III, Cardiac Vision, STAR-T, SAFE, have I missed anything?

And I think he's got a few more -- he's got a few more he's thinking about. The bottom line is he's very steep in this area, and it's going to give us a great talk. BoxX-NoAF, that discussion will be headed up by Dr. Edward Soltesz.

For those that don't know Dr. Soltesz, he's a practicing Cardiothoracic Surgeon and Heart Transplant Surgeon in the Cleveland Clinic. He's also the Surgical Director of the Kaufman Center for Heart Failure and Recovery. He oversees all transplants and mechanical support device therapies at the Cleveland Clinic. He's been an author in multiple publications having to do with minimally invasive cardiac surgery, of course heart failure, optical imaging, long-term cardiac outcomes.

Have I missed anything, Dr. Soltesz? You've got a lot there. He's got multiple patents on innovative surgical technologies, some of those are patient safety devices. He's also heavy into machine learning for predictive tools to help us get smarter about how to predict illnesses in the future and how to address those. I don't think I've missed anything, Dr. Soltesz. I can probably go on for a half hour on what you've done. So anyway we're going to start off with Dr. Whitlock, who'll give us a presentation. We'll have a question and answer session, maybe 15 minutes or so. Then we'll move on to Dr. Soltesz's presentation.

All right, Dr. Whitlock.

Richard Whitlock^ Yes. That was an impressive list. I don't think I could have remembered all that stuff from my CV. But yes, so I am a cardiac surgeon. I love my job. I go around. I give talks on this topic at least once a week. So as a surgeon, and I'm a good surgeon. It's not bragging. I know I'm a good surgeon. I get to touch patients one at a time and I make a difference for their families, and it's very satisfying. But I'll tell you, when I started my research path, I didn't realize the amount of satisfaction that I would get from some of the work that my group has achieved.

So LAAOS III has proven that left atrial appendage management reduces the stroke for patients. I'll show you some really terrible images of outcomes for patients. So now when I walk around and I get to travel the world doing this, I see all the people on the street. These are individuals that I probably have touched and my team has touched their family members because we have -- many of you probably had family members who have heart surgery, right? And I think the work that we achieved and the results that we accomplished with LAAOS III have likely touched these individuals. These are people I will never meet. That is very impactful for me. It really is a huge population.

I used to title this slide, managing the left atrial appendage during cardiac surgery, but it's grown because atrial fibrillation and that pathway this is a cancer of the heart. When I was younger, I was interested in science and let's try to cure cancer. We've made huge strides. We will never cure cancer, but we have gotten better at treating. I'm telling you, we have a long way to go as yet in atrial fibrillation. There are a lot of possibilities. I'm going to talk to a few of those and then introduce the evidence, building into Dr. Soltesz's talk about how we can improve pathway for our patients, 2 million patients a year undergoing cardiac surgery. (inaudible) all published that because they recognize that we are actually underreporting how many patients actually undergo these procedures a year.

So they got together developed countries, developing countries, and they really did a thorough count, 60,000 heart surgeons, 2 million surgeries a year. Many of them have this disorganized rhythm or lack of rhythm in the upper chamber of the heart, atrial fibrillation. We knew since the '40s, it was hypothesized that a lot of the events, the stroke events were coming from this little sac on the top of the left chamber of the heart, the left atrium, they're flicking off.

These cartoons are -- they're cute. A friend of mine drew this. But this is the reality of an atrial fibrillation stroke. This is a CT scan. Half of this person's brain is gone. If this is your brother, your mother, your sister, you will never interact with them in the same way if they survive. This is an atrial fibrillation stroke. The smaller strokes often come from the aorta, the carotids, but these are devastating.

LAAOS III was actually -- it was 12 years of my life. I somewhat foolishly agreed to do a PhD because -- with (inaudible), I don't know who knows (inaudible), in the room, he's a big cardiovascular researcher, I would say probably the top five in the world. He's at my

center. He convinced me to do a PhD because he says, Whitlock, you're already doing the work. There's more work to do to PhD, but my PhD culminated in the LAAOS III trial.

Then in that trial, we said there's lots of patients coming in for heart surgery, who have atrial fibrillation. We could prove with very robust evidence that the appendage should stay with the patient or it should leave to the pathologist or be occluded and die, right? And there were questions about safety, could we increase heart failure and efficacy because it has never been proven before that this reduces ischemic stroke.

So we took the opportunity in patients coming in for heart surgery. It's called LAAOS III because we did other studies to look at effectiveness of certain techniques for occlusion. We took evidence from other centers like Cleveland and Mayo and stuff that they had done. We established we would allow three techniques for occluding the appendage in this trial of atrial fibrillation patients coming in for heart surgery for other indications who have elevated stroke risk. We said, for sure, we really like to cut and sew. The only device -- because the TigerPaw, if anybody remembers, that had been pulled from market, only device on the market was the AtriClip, and AtriClip had done a great job demonstrating that it's very effective and very safe. At least 95% of appendage are occluded successfully with this device.

The stapler occlusion, we tested that in LAAOS I, it has some issues in terms of residual stump, but we thought it's good enough. We took these patients. We randomized them on top of usual care. So these patients stayed on blood thinners. That means there was no competition for the procedure. If the surgeon has the patient in the room, they don't think Oh, you know what, I can -- this patient is tolerating blood thinner, I can continue that or not. There's no question, the appendage must be managed.

I put this up. So Doug mentioned my first big trial. It was 7,500 patients, methylprednisolone in cardiac surgery. And my team built this network in over -- now it's 27 countries for LAAOS III, it's now over 35 countries of collaborating surgeons in academic institutes that would recruit patients into these trials. What's important about this is in LAAOS III, we were in 105 centers, 27 countries. Look at all the healthcare systems that this includes. This is every continent that has heart surgery. It doesn't matter what type of blood thinner you use, how you treat these post op. The results of LAAOS III are generalizable across all these centers, all these healthcare systems. That is very important.

The other thing that I highlight in LAAOS III is we did not exclude valvular atrial fibrillation, two-thirds of the patients had valve surgery. Once again it increases the generalizability to those patients. The results when they were -- this trial was stopped at the second interim analysis. There's a data safety monitoring board, I sit on many of those for other trials.

I had one for this trial. They contacted me. They almost stopped this trial at the first interim analysis because they're already seeing benefit, but they wanted to be confident. Second interim analysis, 3-point years, 8 years of follow-up.

[Mark Howell from Ottawa] called me. He said, Rich, we have to talk. You need to report this. This is going to change the field. It has changed the field. This is a (inaudible) curve.

I think everybody in the room is familiar with it, but just in case, the X axis in time since surgery in months, Y-axis is [cumulative] incidence of strokes. The blue line are the patients who had their occlusion. The red line is no occlusion. There is an early and ongoing divergence of these curves.

Now we were talking with (inaudible) earlier about number needed to treat, right? By 5 years, 5 years, 30 patients need to be treated with this. I will tell you, when you look at the literature, this competes with any medication out there for cardiovascular disease. This is a onetime intervention that the patients don't have to be compliant with, right?

So I say to the surgeon, 30 at 5 years, 15 at 10 years and it keeps getting -- I hope my patients live 10 years. It keeps getting -- fewer and fewer numbers needed to treat for -- prevent one event to the patient. So I say to surgeons when I give this talk. If you, people, don't do this, you should walk out to the ICU, explain why you didn't manage the appendage. If you do it systematically, just stop prescribing medications because it doesn't make sense because this outperforms them.

So New England Journal covered this. A good friend of mine, (inaudible), is the editor whose (inaudible) passed away. (inaudible) summarized 12 years of my life in 2-minute New England Journal video, wow, it was like, wow, 12 years in two minutes. But 33% reduction in the risk of stroke. This has had huge impact. Every guideline that reports on atrial fibrillation has made this a Class I recommendation. It is now becoming a quality marker across the U.S. (inaudible) is one of the very few quality markers cardiac surgeons have. This is now a quality marker in three states thus far, and there is a push by various bodies that get this across the U.S. So surgeons better be doing this. If they're not doing it, the cardiologist need to start thinking about their referral lines. Now I'll tell you, the trial showed this is very safe to do. You have a single chance to do this very safe procedure that's very effective to prevent stroke in people with atrial fibrillation.

So a question I get is, why don't we just do this in everybody? Everybody has an appendage, 99.9999% of patients have appendage. There's some weird congenital cases. But the answer is, should we do it, and everybody, no. You must be sick of seeing this slide, but this is my best -- one of my best friends. This is (inaudible), he represented my country twice in the Olympic Marathon. I like marathons. I run a lot of marathons. We run together, he shows me up, embarrasses me, but that's okay. I'm a decent marathoner. Some of you in here, I mean you're all pretty darn young and active.

I'll tell you, our expectations of our hearts are quite different than the 72-year-old patient with atrial fibrillation. I don't know what it's going to do. If I get someone like [Reed] or even myself on the table and I suddenly -- I occlude their appendage, the appendage does contribute to cardiac output, there's hormones in the (inaudible). In sinus rhythm, we

don't know the long-term effects. We need to make sure it's safe, but also if we're putting cost into it, we need to make sure it's effective.

So atrial fibrillation, as Doug mentioned, this is not like a light switch that something goes on and you suddenly have atrial fibrillation. We now recognize that it's on a spectrum of disease, where at first, you start getting some inflammation in the left atrium and right atrium. You start getting some fibrose, your atrium starts to enlarge, you start getting premature atrial contractions. You start getting subclinical atrial fibrillation. You get studied by my friend, Jeff Healey at McMaster. You start getting paroxysmal atrial fibrillation, you get short persistent, you get permanent. It's a spectrum. We can identify patients who are on that pathway. This is a consensus document by all of the heart rhythm societies across the world. They've got together, and they've talked about this entity now that's well established called atrial cardiomyopathy.

I'll tell you, the risk factors for developing atrial cardiomyopathy are very similar, if not exactly the same as the risk factors that create the disease that we are operating on in the operating room, people with coronary disease have hypertension, diabetes, advanced stage valvular disease, same thing, aortopathy, same thing. They all feed into a sick heart. It is yet another manifestation of those comorbidities, atrial cardiomyopathy. And at least half of our patients coming for heart surgery, because they carry these comorbidities, have this.

I've already told you, there's a single chance to do this as a concomitant procedure that is very safe and highly effective. So we have a LAAOS III like design in atrial cardiomyopathy patients or patients who are enriched, they have sick atria that we know are on the pathway to atrial fibrillation. But in fact, they're probably having the disease manifestations even before they get there. The trials, you guys have maybe have looked at the PFO closure trials, closure 1, closure 2, other things. looking at stroke of unknown origin.

I'll tell you, some of this is coming from this. These patients are having events from the atrium before they even manifest electrically the disease because it's a prothrombotic environment. So we are now performing LeAAPS. It was highlighted that this started in 2023. We started working on it in 2022 in terms of FDA meetings, et cetera. This is a 6,500 patient study. It is a new era in cardiac surgery.

The level of evidence that are being generated now in cardiac surgery studies far exceed anything from a decade ago, 6,500 patient trial. We've enriched this with patients who have advanced age elevated chadsvasc, and they basically have a large atria. They have sick atria. They randomized 1:1 to AtriClip or no AtriClip and otherwise, they're treated exactly as they should be treated, according to guidelines, standard of care. We follow these patients every six months, and we want to prove that early management or prophylactic management reduces the risk of stroke or systemic thromboembolism.

Now this trial has done extremely well. We thought the trial would take about four years to recruit. It's recruiting -- recruited nearly at 200% the rate that we expected. The reason

surgeons have bought into this concept, people are already performing prophylactic management of left atrial appendage. They believe the trial is going to be positive. They want to be a part of that. The patients are very common. Last week, my center put in nine subjects, nine subjects, right? They -- it's like 60% of our patients. We have enrolled 5,100 patients so far.

Now I do a lot of trials. I run currently 11 randomized trials. This is my trial. It's a lot of work, but this is my trial that is on track, like really. Our hypothesized event rate, we are -- the aggregate data, when I look at it, and I have the DSMB, the Data Safety Monitoring Board meeting tomorrow. It is exactly as we thought it would be. It is following the profile of the LAAOS III aggregate data to "T", which is very good news. Events are accruing. The patients are high risk. They have a chadsvasc score showed of 4.4. This is all very good news because I want this to work because I want to save tens of thousands of strokes a year because if there's 2 million patients who have heart surgery globally and 60% get this done, there'll probably be more. That will be immense impact.

So first site activated January 23, Pam Simons from AtriCure's birthday actually recruited on her birthday. These are things I remember. (inaudible) surpassed expectations, right? 5,000 patients, 5,100 patients, the 5,100 patient was recruited today I get this text constantly. So it's been an amazing momentum, but a few important things is that, again in terms of geography, we are touching healthcare systems across the world. We have 14 -- over 14 centers in Canada. We're in Europe, Germany opened today. We're in Asia Pacific, Australia is about to open, we're in the U.S. Representation and generalizability, incredibly, incredibly important.

Next, are we executing the trial well? Well I've already shown you, the data has been coming in faster than we expected, but we just hired more people and said, we've got to be on top of this. 99% of the data forms collected are without queries and clean. We have ongoing adjudication of every event that goes on so that we always have at least 95% of the events adjudicated. The DSMB has me met twice, the meeting tomorrow.

So far, they've said keep going, great job. High-risk patients, events are accruing. Chadsvasc score 4.4, a very high-risk group. Generally, these people are coming in because of advanced stage in left atrial enlargement. And as evidence emerges from when we first developed this protocol, those are some of the strongest predictors, NT-proBNP, we included an inclusion criteria, very few patients included based on that criteria. It's shown now to be a weaker predictor. So I'm happy about that.

Generalizability, we're in every -- many, many continents that do heart surgery. But what about -- does it represent the population? Because we want this for all cardiac surgery population. Does it represent that population? Here's a comparison of some of the characteristics in LeAAPS to STS data. STS data around 699,000 patients in the U.S. and Canada. LeAAPS data, this is based on 4,700 patients, female representation, we are doing better than the STS, 29% of our patients are female versus 24%, nonwhite, again as a society, there's some discussion here because this 42% of the U.S. is nonwhite.

In Canada, only 16% are getting heart surgery, under representation, but we're doing well 11% in LeAAPS. Black patients are about the same, 5% versus 5.8%. Isolate CABG, so procedure type, 63% versus 72%, very close. We're enriched. So we are -- in terms of some criteria, we want enlarged atria, so we have a lot of valvular disease, right? So we're seeing isolated AVR, 6% versus 8%. Combined valve and CABG are very, very close. Aortic surgery, 9% versus 7%. This represents well the patients who are having cardiac surgery.

Now during LAAOS III, as I was doing the trial, publications started popping up, you can mimic trials by using administrative databases throughout the world, but here's some stuff from the U.S. Pat McCarthy is a good friend of mine. He's the Head of Northwestern in Chicago, contact me and he said, let's mimic the LeAAPS trial. And let's get a sense if we're on the right track because I told you, some people are already prophylactically managing the appendage.

So we did that. What did it show? This is looking very good. Just like in LAAOS III, when they started acquiring the administrative databases, they started some studies, if they didn't address confounders appropriately, it looks like it's going to be neutral, but most of the studies in the LAAOS III area done under administrated database suggested an effect size similar to what LAAOS found. The study that we did as well as a study by Derek Tam that he did in microvalve patients, both have found about a 30% reduction of stroke over 4 years.

So I think we're on the right track here. Every signal suggests that. We have high-risk patients. We're accumulating the event rates as expected. It's a well represented -- it's a study well represented in the population having heart surgery and there are signals from other data suggesting that we are going to have a positive result. And to be honest, we have patients on the pathway to atrial fibrillation. Eventually, they just become LAAOS III patients. That's what they become. They're AF patients.

So this should work, period. As I said, LAAOS III has had impact. It saves thousands of strokes a year globally, no question. As long as surgeons are doing it and they are doing it. But it only applies to 10% to 15% of patients. LeAAPS applies to 55% -- at least 55%. This will save tens of thousand strokes, this will shift management in the operating room of all of these patients globally.

So I've highlighted to you that the majority of patients having heart surgery, they have sick atria, they have sick hearts. It's not a surprise. We have proven therapies that are established by surgeons and arrhythmia docs to reduce the burden of atrial fibrillation once they use this and therefore, the risk of adverse events. But imagine if we can alter the pathway before patients even get there. Certainly, I think we will do this in LeAAPS.

We will reduce the stroke risk of these patients as the disease progresses. But Dr. Soltesz is here to talk about the study now next. Imagine if you identify that pathway the patient is on and you say you know what, not only do I want to prevent their stroke. I'll manage their appendage. But I'm actually going to attenuate the disease.

We have lesion sets with radio frequency energy, with PFA that are known to reduce the burden of atrial fibrillation. If we apply these lesion sets to these patients, maybe we can stop them from going into atrial fibrillation. That's a whole new game. Because right now the guidelines debate if you have AF ablation, should we stop anticoagulation, how long to give antiarrhythmics? Imagine if they never have to start anticoagulation or antiarrhythmics. Or imagine if it's delayed for 10 years and the risk of exposure to the disease and exposure to the medications is put off for 10 years. That is a big deal in a 65-year-old, I'll tell you, because once you go on to an anticoagulant, no matter if it's DOAC or VKA.

You've got a bleed risk of 1.5% to 2% per year, you get older, you start having falls, you have bad adverse effects of the Class I antiarrhythmic. This will be magical for our patients, really. The legacy of evidence, and I've become a strong academic partner to AtriCure. This is a company that invests into high-level data. This sets the bar for the field. This will not be a class effect. All the devices behave differently.

Suraj, as we talked, the WATCHMAN, its intracardiac events, other devices that occlude the appendage in different ways, you cannot extrapolate this data. This is not a class effect. And device has to reach this type of bar, this type of evidence to claim, show benefits. We are generating evidence between AtriCure and PHRI and myself that will live beyond any of us. We will leave a legacy in this field, and we will treat this like cancer because it is a cancer, and we will better the therapy for these patients. Thanks so much.

QUESTIONS AND ANSWERS

Operator^ Your questions now.

Marie Thibault^ We really appreciate it. Marie Thibault from BTIG. It's on. Oh, you got it. Okay. Thank you for your work and all the trial work you've done. Quick question. You said at least 55% of cardiac surgery patients could benefit from LeAAPS and this prophylactic use. I think you've mentioned 50% are on the path to having a sick atria, 60% in your case as you're showing up. What's kind of the right number? Shouldn't it be 100% of those folks without preop?

Richard Whitlock^ I think that's where we will get. So again we generate evidence. There is always evidence creep. I think once we've done LeAAPS, if this shows that in this huge proportion of patients that it's safe and that is effective. Ultimately, I do think the field will move towards if you're having heart surgery, your chest is open, the appendage is there, it's going to get managed. That's where the field will go.

Michael Matson^ Mike Matson, Needham & Company. So longer term, with WATCHMAN potentially getting used more and more with concomitant use and the CHAMPION study coming, how do you see this market kind of shaking out? Do you

think there's a point at which you could start to see these patients showing up and already having a WATCHMAN implanted?

Richard Whitlock^ I mean we do already see some patients coming in with WATCHMAN. It's a different device. First of all, their trials thus far have been demonstrating or designed to demonstrate non-inferiority compared to a blood thinner. They have never actually demonstrated. If you look at the patient level made analysis of the PROTECT AF and PREVAIL, the number went the wrong way for ischemic stroke. By getting the patients off of blood thinners, they reduce hemorrhagic stroke. It is a big driver for the neutrality or basically non-inferiority.

We are also -- have been talking to this today but we are also doing a trial called ATLAC. I supervised two PhDs in Denmark in my spare time and we will, I believe, show that we can pull these patients off the blood thinners, which this procedure has been shown to reduce ischemic stroke, right?

I think one of the Achilles heel right now in the intra cardiac devices is the fact that there's device-related thrombus and they still have some leaks. We don't have that, right? That's not meant to say a stand-alone, that shouldn't be in the armamentarium ever. I think the field will slowly adjust as we build evidence because I don't plan on stopping here. We have effective measures of occluding epicardial lead with stand-alone techniques in very safe ways. The devices are getting smaller and smaller, we're down to 5-millimeter port.

So -- and now our center, we've recognized that in the TAVR space, when we do a heart theme approach to patients, the population grows, they start coming out of the woodwork, right? For you, the market grows, we treat more and more. We have 1.5 years wait list for our atrial fibrillation catheter ablation. There's so many patients. We can't even treat stand-alone. So that's why we started saying, we're shifting. We're going to hybrids, sharing the burden of treating this disease. So there's just so much space and so many patients to be managed. I am not worried about stepping on toes. Ego’s amongst physicians create worry, but that's BS. There's so many patients.

Michael Matson^ Just as a follow-up, could you or would you ever put a clip on a patient that already had a WATCHMAN? Could you remove the WATCHMAN?

Richard Whitlock^ I've had -- I've been referred some patients who had severe (inaudible), they still had a significant WATCHMAN leak. I go in, and I've removed the WATCHMAN, you can put a clip on. It depends on how much of the appendage you have to cut out to get it out or whether it just pops out. There's other techniques. Again you can cut and sew in that, again that's on the clinical side. But yes, that happens. So yes.

Suraj?

Suraj Kalia^ So Richard, just a curiosity for LAAOS III, the fact the patient did not (inaudible)

Richard Whitlock^ 25%.

Suraj Kalia^ And it was a split (inaudible) curves be different? I guess I'm just trying to think through (inaudible) for something like (inaudible).

Richard Whitlock^ Yes. So with respect to LeAAPS, if I'm understanding your question right. Again LeAAPS is on top of usual care, right? So just like LAAOS III. So I think there will actually be a lower percentage of patients who are on blood thinners. When you entered into the LAAOS III trial, we really pushed sites to make sure they were discharged on the coagulation. About 90% were discharged, over 3.8 years, that fell down to 75% in each group.

Now LeAAPS is different because they don't have atrial fibrillation yet, and they kind of go up to the wild and they experience what things are like in kind of, I'll call it, the Wild West, right, because the level of care depends whether they present to their family doctor, to the emergency, to a cardiologist, right, as to whether they started.

If you look at GARFIELD registry or other registries, management of atrial fibrillation, we don't do a great job. This is why I think that in LeAAPS, we actually have a chance of seeing a greater effect size because the first presentation of their atrial fibrillation maybe while they're not on anticoagulant.

In the treatment arm, they have protection. In the control arm, their first presentation, they got nothing. So I think this is a positive thing for LeAAPS. Not a great thing for patients, I wish we did better for patients, but it's a positive thing for LeAAPS. I think we may see a bigger effect size.

Suraj Kalia^ (inaudible) one of the things that all of us are trying -- struggling (inaudible) symptomatic TAVR want to check (inaudible) so what is the right time (inaudible)? So if you look at something like LeAAPS, it is essentially [prophylactic], right? And let's say Suraj has cardiac surgery. (inaudible) you have the first episode of AF (inaudible) So the question I have is (inaudible) more predisposed to doing a concomitant and vascular. (inaudible)

Richard Whitlock^ So if I said to you, Suraj, you're coming for a heart surgery with me, you've got a bicuspid aortic valves, you need your AVR done. You have evidence on your echo that you're on the pathway to developing atrial fibrillation. Would you like me to do a procedure at the same time same time that is highly effective and it will prevent strokes once you develop atrial fibrillation? Or potentially even before you develop the atrial fibrillation? Or would you like to wait until you have atrial fibrillation and then be exposed to procedural risk for a second time?

I choose the first, do it while I'm open. Makes sense, right? Less costly to the healthcare system. They can ablate but they don't have to worry about the atrial. The atrium is a source of failures with an ablation. It's the WATCHMAN device does not electrically isolate the appendage. We electrically isolate the appendage, an added benefit of the surgical technique for managing the appendage. So there's no downside to this to doing it at the time of cardiac surgery.

Now if I said, Suraj, you're in the pathway to have atrial fibrillation, I want to prophylactically take you to the operating room and clip your appendage right now and you don't need a heart surgery. I'd be nuts, right? So it's just a point in your life where we can do things for you predicting future events.

Operator^ Welcome Dr. Soltesz to the floor.

Edward Soltesz^ Rich, that was great, and thanks for inviting me down here. Welcome, everyone. So I wanted to talk a little bit about today that same topic we just were discussing, which is prophylactic ablation. So if any of you have had surgery or know anyone who's had heart surgery, I would hazard a guess that they would say number one, they remember that day very clearly.

And number two, it was a very significant day in their life that they certainly don't ever want to repeat. And I remember my own family member. My father is 100 years old right now. He had heart surgery when he was 64. I remember the day specifically. I can see it very clearly. And I can tell you, he remembers it, and he's still -- he's 100. He remembers it very clearly. He's been through obviously a lot over his 100-year lifespan.

But the point of fact here is that cardiac surgery is a very unique event. Your chest is open. You're on the heart-lung machine. You have one opportunity to do what you need to do and do it correctly and do it well. This is something that we train our residents to do, to think through what needs to be done. And we know that around the 90,000 patients or so in the United States, out of about 1.2 million open heart surgeries that occur in the United States annually, about 90,000 patients have preoperative atrial fibrillation.

We now have guidelines, Class Ia level guidelines that would suggest that we need to treat these patients with a concomitant ablation and management of their atrial appendage. We're not -- we don't -- we don't follow that guideline 100%. We're moving in that direction. There are a number of things, I think that are responsible for that. But the key is that we have guidelines for surgeons to suggest that we should treat those patients at that one time in their life where their chest is going to be opened.

Now what if we also had the opportunity to prevent, to prevent the most common complication of cardiac surgery and potentially also impact significantly the development of a major complication in patients' lives, that being atrial fibrillation at the time of their open heart surgery? If we could predict which patients may be need this, these high-risk type of patients, what if we could do that?

And there's probably about 200,000 patients annually in the United States without preoperative atrial fibrillation who have high-risk features, who would benefit from a prophylactic ablation. That is this concept of preventing not only postoperative atrial fibrillation but also impacting long-term development of atrial fibrillation. So what is postoperative atrial fibrillation? Well it's something that keeps me up at night. It keeps up -- keeps all cardiac surgeons up at night. In reality, it keeps our residents and fellows up at night as they treat these patients. But it occurs in about 30% of our patients.

And I specifically remember this, I specifically am impacted by this problem because a good friend of mine, who is a tennis partner of mine, a few years older than me. I operated on him 5 years ago. It was right during Covid where he called one day and said, I just went to the hospital. I have triple vessel coronary disease. That chest pain that I was getting when we were playing tennis that I thought was my esophagus because I eat too much at night was actually my heart. And so otherwise, this guy is very healthy. He maybe drinks too much alcohol in the weekends at parties. But otherwise, very healthy tennis player. (inaudible) even know USTA, he's a 4.0 tennis player.

So here he comes and I'm operating on him them. I did an all arterial four-vessel bypass, everything went beautifully, we're high-fiving everyone at the end of the case. Two days later, he gets postoperative Afib. That's where everything started. And unfortunately, to this day he has Afib. It's on and off. He's had an ablation. He still has Afib. He's on anticoagulation. He went mountain biking and fell and a lot of bleeding because he's on Eliquis, too.

So this is the type of patient we're talking about. We're not even talking about that 75-year-old patient high risk. If we can prevent postoperative atrial fibrillation and the subsequent development of atrial fibrillation in patients who are high risk, I think we can make a significant impact in the field.

So postoperative atrial fibrillation is much more common in valve surgery but still occur significantly in coronary bypass. Of course doesn't occur in heart transplant. That's really not an issue in heart transplant. Typically anywhere between two and five days postoperatively. When you look at the why behind postoperative atrial fibrillation, I think it's really -- it's a perfect storm.

When we operate on patients, we open the pericardium, there's inflammation naturally from that opening, there's some atrial injury, there's also some sympathetic and parasympathetic dysregulation that occurs, there's always some undrained blood products, which stimulate inflammation in the pericardial cavity, and there's some metabolic changes, potassium goes up and down postoperatively. That together with predisposing factors such as age, hypertension, obesity, alcohol, like my friend, and atrial myopathy that we may not have detected yet on any imaging study, that is the perfect storm.

And I put up a I put up a tornado here because in Cleveland, we get tornadoes, but that is -- it's destructive. It's not benign, postoperative atrial fibrillation is not benign. It is

increasing length of stay. It increases costs. It's something we talk about at our staff meetings all the time how are we going to reduce postoperative atrial fibrillation rates because we're doing 5,700 open heart surgeries at our main campus at Cleveland Clinic. And if we can reduce this, we're going to be able to operate more and we're going to have more opportunity for and more access for patients. It can lead to heart failure in the immediate postoperative period. But I think even worse you can get clinical atrial fibrillation like my friend.

So that is to say if you still have atrial fibrillation after one month after heart surgery, it's termed clinical atrial fibrillation, no longer postoperative atrial fibrillation. Then as we know atrial fibrillation begets atrial fibrillation through the whole complex mechanisms of development of atrial myopathy.

So this is a real problem. It is not something benign. If you look at the numbers, if you look at the actual outcomes, you can see that it leads to a significant increase in hospitalization, almost a doubling of mortality, doubling of stroke rates, there is also an increased risk of myocardial infarction in these patients.

I think importantly, it is a four or fivefold increase in clinical atrial fibrillation. So postoperative atrial fibrillation really is bad for the patient. It's bad for their family. It's bad for their surgeon, if their surgeon happens to be their friend. It is, unfortunately, a significant cost to the healthcare system.

So this is definitely not benign. But right now there's no FDA-approved therapy for adequately treating postoperative atrial fibrillation in these patients. And as I said, postoperative atrial fibrillation is really the tip of the iceberg because what exists below the surface is this continual hazard in these patients of developing clinical atrial fibrillation over the ensuing years. That, of course is an additional burden to the healthcare system and significant burden to the patients themselves.

So what are we doing right now to prevent postoperative atrial fibrillation? We've had this problem now for the past 40 years of heart surgery, have we come anywhere with the treatment strategy. Well we can use medications. We always use beta blockers postoperatively in almost all patients. We -- if patients develop atrial fibrillation, we started amiodarone. We've tried trials of prophylactic loading of amiodarone as an antiarrhythmic agent to combat postoperative atrial fibrillation. We've tried [colchicine], all of these have some benefit but nothing substantial. And unfortunately, a lot of the complications of these and the logistics of starting these limits their practicality in our practices.

What about surgically? Well we can overdrive atrial pace, that's something that was looked at many, many years ago, over 25 years ago. We can do a posterior left pair of cardiotomy, that's cutting a small hole in the back the pericardium that's been opened. So blood products drained into the left plural space, so it doesn't insight inflammation in the pericardial cavity and presumably then reduce atrial fibrillation rates or we can even do a prophylactic surgical ablation, right?

So let's look at our atrial overdrive pacing. This study here was a randomized controlled trial. As I said, 25 years ago, looking at seeing whether bi-atrial pacing postoperatively, improves postoperative atrial fibrillation rates. And certainly it did. If you look over here in the older age group, at significantly reduced postoperative atrial fibrillation rates. But there's problems with bi-atrial pacing. You need to keep people in the ICU almost always at least and our nursing protocols demand that. Sometimes the atrial wires don't work. Many times, the atrial wires start working and then stop working, and you're back to square one. And length of stay is prolonged actually with this therapy.

In my 17 years of practicing at the Cleveland Clinic, either myself or any of my partners, how many times have we used this as a prophylactic measure for preventing postoperative atrial fibrillation? Zero. And I would hazard a guess that there are very few places, if any, in the United States or in fact, even the world that do this routinely to prevent postoperative atrial fibrillation.

So it's very theoretical, but it is not practical. What about doing a left pericardiotomy? This study over here was a randomized controlled trial very recently, three or four years ago that randomized 120 patients undergoing CABO-JVR or aortic surgery. Two, cutting a hole in the posterior pericardium to let that blood products drain to try to prevent that inflammation driving postoperative atrial fibrillation. They showed a 44% reduction in the postoperative atrial fibrillation rates.

Now interestingly, when you do subgroup analysis, the patients who you would want to benefit the most are not benefiting. And this is the problem. Greater than 70 years old, no benefit, low ejection fraction patients, high chadsvasc and most common cardiac surgery operation CABG, not a significant benefit. So while this is theoretical again it is not necessarily practical and it doesn't target the patient population that we need to target for postoperative atrial fibrillation.

What about prophylactic ablation? So prophylactic ablation is not new. This is not a new concept. We've talked about this for many years. This is a feasibility study, a feasibility trial that was a randomized trial of 60 patients to get a bilateral pulmonary vein isolation and appendage placement in higher risk patients for postoperative atrial fibrillation and long-term clinical atrial fibrillation. And they showed a very significant decrease in the rate of postoperative atrial fibrillation.

So this really got the dialogue started that this really could be something that might be beneficial. And notice here, this is a pulmonary vein isolation and there's a significant difference between doing a pulmonary vein isolation surgically versus using this, which is a -- what's called a non-atriotomy surgical ablation, which is the EnCompass Clamp, okay?

The EnCompass Clamp, of course doing a full box lesion, but for a surgeon, for a cardiac surgeon, it is very simple to do an EnCompass Clamp. The placement of the EnCompass

Clamp is simple. It's like starting a car versus if I ask you to go and jump a car to start it, connect it up to another car, that's an advanced level. Not everyone can do that.

So this was a retrospective study at about 132 patients who are undergoing CABG, right, most common operation in the world for cardiac surgery, without preexisting atrial fibrillation and notice, if you just put a clip on, 40% of those patients got a postoperative atrial fibrillation, if you did an EnCompass clamp, they're calling it NSA non-atriotomy surgical ablation, and Appendage Clip 4.7% incidence of postoperative atrial fibrillation. And again this is in the higher risk patients.

So this led us to even further data in support of an EnCompass-type lesion for a prophylactic ablation to prevent postoperative atrial fibrillation and development of long-term clinical AF.

Now whenever you're doing a prophylactic operation, first and foremost, it has to be safe. It absolutely has to be safe. You cannot add something prophylactic to a patient's operation if it's not going to be safe. So looking at the data here, you can see there's no minutes of cross clamp are added to the surgery to do the EnCompass ablation. I think that's absolutely critical. Cross Clamo is when we -- cross clamp the aorta, arrest the heart, so the heart gets stopped. That's a very critical period.

We know that the longer you have dure of a cross clamp 45 minutes, 60 minutes, 75 minutes, the higher the risk of postoperative complications in general, okay? Cardiopulmonary bypass is a little bit different. We know at least from studies from the Cleveland Clinic that you can add 44 minutes of cardiopulmonary bypass time with no significant difference in outcomes and very good propensity match studies. So we're adding 12 minutes of cardiopulmonary bypass times here, which is really not significant. There's no increase in cost in this study here.

Of course the whole concept is no added risk. You can't add risk. It looks to be from the data that we're seeing here, at least in the initial studies, highly effective in reducing postoperative atrial fibrillation. So when we look at all these studies, particularly the randomized and this is a meta-analysis of seven randomized studies, taking non-Afib patients undergoing heart surgery and who are getting prophylactic ablations, the pooled estimate shows a relative reduction of 43% of postoperative atrial fibrillation.

Again I think this is some very, very strong evidence that this is effective. We know it's safe, and it's now effective. If you look at further development of clinical atrial fibrillation, that's that holy grail of preventing something of prophylaxing against something that might happen in the future. 75% relative risk reduction and development of clinical atrial fibrillation after a prophylactic ablation. So I think there really is evidence right now to suggest that we should be doing a multicenter randomized trial in this area.

Now if you look at trying to understand who should we target this trial for, if you look at the the risk factors for postoperative atrial fibrillation. We know age and CHA2DS-

VASC score are important predictors of postoperative atrial fibrillation. If you are over 65 years of age and CHA2DS-VASc of three or more, you have a 40% chance of developing postoperative atrial fibrillation after routine cardiac surgery, not including transplant, of course.

So that will be the target of course of any trial. So this is the BoxX-NoAF trial. This is what has led to the conceptualization of this trial. I think you will see is that the hypothesis, which is that the intervention, the combination intervention of ablation with the EnCompass Clamp, which is the BoxX part of it, with the Appendage Clip will reduce postoperative atrial fibrillation by 33% and long-term clinical Afib by 36%. This is going to be a prospective multi-center randomized controlled blinded study, it's going to be powered for superiority and 960 patients with around five sites in the U.S., Canada, EU and Australia.

The design is as follows. It's a one-to-one randomization. We put index surgery here because at the moment that is more than likely going to include the clip, but that is -- we can talk about that later, but control over treatment, and we're going to have primary effectiveness endpoint of postoperative atrial fibrillation out to 30 days. The safety endpoints will be major adverse events, that hopefully will drive the PMA for the postoperative atrial fibrillation indication. Then we need to wait some time of course with follow-up to get information on our secondary effectiveness end points of clinical AF out through three years. And that, of course hopefully, will drive the longer-term indication for this as well. So what I want to point out is a significant difference in using the EnCompass Clamp to do this lesion compared to using pulmonary vein isolation independently. There is a significant difference.

We looked at this within our resident cohort at the Cleveland Clinic over the last few years, and it takes our residents, two cases to become confident with an EnCompass. It takes them around 12 cases to become confident with a pulmonary vein isolation. So there is a significant difference, and if you haven't seen the EnCompass and sort of the way the device is placed, it is very straightforward to open two areas in the pericardial reflections that allow you to put in the EnCompass Clap, very, very safe, very, very effective.

And of course I'm not going to speak much about the appendage conclusion because I think most surgeons that's very straightforward as well. These are the devices, of course that will be part of the trial fairly straightforward, the EnCompass Clamp and the clip.

So what I would say to everyone, I think is that is that cardiac surgery really does offer a unique opportunity to intervene. It is really something that we have to understand completely what we can offer to patients. If we can offer them a prophylactic ablation that is safe and effective and it is easy for the surgeon to do, and that's important because the surgeon -- cardiac surgeon will do a procedure if it is safe, if it is effective, it makes a difference and if it is easy, okay? There are surgeries. There are things that we can do that are very, very complex and you will not get surgical buy-in. But if you have those three

components, you will have many, many patients getting prophylactic ablation. This trial, hopefully, will add to that data to support the safety and effectiveness.

So I'll be happy to take any questions.

Unidentified Speaker^ We've got time for about two to three questions. If you don't mind, please do wait for the mic so we can make sure that everything is picked up on the webcast.

Samantha Munoz^ Samantha Munoz from Piper Sandler. I guess one question from us is what proportion of these postoperative AA patients actually progress to clinical AF? And are there any sort of patient characteristics that you can kind of identify ahead of time for those patients?

Edward Soltesz^ Yes. So the progression of -- from postoperative Afib to clinical Afib typically are in those high-risk patients, CHA2D-VAS score two or three or greater, over seven years old, the cardio-metabolic patients who are hypertension, hyperlipidemia, some alcohol use, potentially obesity. Those are all the risk factors that go into the development from postoperative Afib, which is about 10% to clinical Afib. 30%, of course of all open heart surgeries get postoperative Afib and with coronary bypass being the most common operation and also the highest risk operation other than valve surgery, it's a substantial number of patients.

Richard Whitlock^ Just a comment on that. So because we studied this quite in-depth. So William McIntyre published about 2 years ago. So we put implantable loop recorders in these patients, and we followed them for two years. By 18 months, the patients who developed postoperative fibrillation, 36% are in clinical age fibrillation by 18 months. It keeps going up because these patients are -- a lot of these patients are developing POF have these substrate for clinical atrial fibrillation. So that's the number.

Suraj Kalia^ Dr. Soltesz. So for the BoxX-NoAF for the index surgery, how do you balance? Because this is a trial designed for superiority. How do you balance in the control versus treatment arm, patients who might have more valve surgery versus just isolated CABG because the risk of post-op AF is different, right? So how do you balance for that? And what should we read because cardiac surgery is just a bucket. So I'm curious how you've thought through in the trial design to make sure that it is balanced specifically on these attributes.

Edward Soltesz^ Yes. So your question really is when you look at valve surgery, right valve surgery is a much smaller volume than CABG volume. So CABG volume will be certainly the most common patient that gets -- CABG patient will be the most common that gets randomized. At the moment, do we have any -- have we thought about how to look at that?

Richard Whitlock^ Response to the question. So trials over 500 patients, the chances of having an imbalance between the groups greatly diminishes. So there's type 1 error, type

2 error in trials. That chance greatly diminishes when there are certain variables like that, which you're mentioning, where you're very concerned about imbalance, you do something called stratification of randomization. So indeed, by surgery type, there's going to be some stratification or randomization as well as by center. So that is a way of mitigating the risk of imbalance between the groups. But you're correct. It is devastating to a trial to get imbalance. This is a near 1,000 patient trial. It would be exceedingly rare for imbalance to occur between baseline characteristics.

Unidentified Speaker^ Any other questions?

Unidentified Participant^ Yes. So I guess just as you look at the different cardiac surgeries, you gave risk of post stop Afib. But have you found that any have a higher risk of clinical AF? Mean is there a surgery that might -- I think you gave the 10% number, but any of the surgeries that might see just a higher clinical just for any reason?

Unidentified Speaker^ Any valve surgery will, by far, any valve surgery, much exponentially higher rate. But that also is partly because of probably undiagnosed atrial myopathy as part of that valve lesion. I think as we begin to understand atromyopathy more and the imaging characteristics of that we'll be able to more greatly predict that. The highest risk (inaudible) is mitral valve as then atrial valve and then (inaudible).

Vinayak Doraiswamy^ I think we are skipping the break for time. So we're going to switch gears, and this talk will be -- this whole session will be on hybrid therapies and the impact of PFA. So I'm Vinayak Doraiswamy, the Chief Scientific Officer for AtriCure. It's just by way of context, coming from the CONVERGE AF trial, which is very successful, it shows that both epicardial and endocardial hybrid ablation is superior to endocardial ablation alone, right? And they used RF technology in that for endocardial -- with time now we have seen a number of PFA devices coming to the market. Those have had an impact on the hybrid therapies.

So today we are fortunate and we have the privilege of having two physicians in our room distinguished physicians who incorporated both hybrids and PFA in their practice, so they can speak firsthand experience on those two. So we'll hear from them shortly.

So just for logistics, I'll go ahead and introduce both of them, and then they'll go one after the other, and we'll reserve the Q&A for the back end, okay. Slightly different than the way we had before.

Our first speaker is Dr. Kevin Makati, Dr. Makati is an electrophysiologist. He is the Director of the EP Program at St. Joe's in Tampa. He is a key opinion leader. You might have seen him at the podium at big meetings like HRS, AF Symposium and so on. He's been on the cutting edge of research. He has a number of publications and studies under his belt. I'll name a few. He participated as an investigator in the first-line ablation for (inaudible) using cryoablation that paper. Then he was -- he is also currently an investigator in the persistent trial for PFA. He also authored the very first paper on the methods and best practices for CONVERGE, our trial, how to use it, and we also

authored the paper on the registry for TracAF registry, which we used for getting the CONVERGE approved. So he's been on a number of those papers. So he can -- he is also incorporated both PFA and hybrid induced practices. So he can bring that to us.

So Dr. Makati, welcome.

Our second speaker will be Dr. Nitesh Sood. Dr. Sood is also an Electrophysiologist. He is the Director of the Atrial Fibrillation Wellness Program at Southcoast in Massachusetts. Dr. Sood is also on the cutting edge of research has authored quite a few papers and has been a global PI and a national PI and site PI for a number of trials.

I'll just cite two. The first one is the cryoablation trial, for which his publication was in New England Journal of Medicine in 2020. He also was an investigator and a co-author for the Pivotal trial, which was the first IDE FDA trial for PFA. So he uses extensively PFA in his current practice and also CONVERGE in hybrid. So we'll hear from as well.

With that two brief introductions, I will now hand it over to Dr. Makati to kick us off.

Kevin Makati^ Okay. Thank you for the invitation to speak about the integration of PFA in the current market of conversion and surgical AF ablation, which I'm very passionate about. So -- thank you, any for the introduction. Just to reiterate, just so you understand my perspective in the space. I'm not only an electrophysiologist with experience with catheter ablation trials and PFA specifically. But I also have a surgical colleague back in my home institution, we codesigned a surgical ablation procedure. So I'm articulate in the surgical AF ablation space and very passionate as far as the application of that technology as well. We'll talk a little bit about that at the end of the presentation.

So I'm going to say this while everybody is awake so that everyone hears it first. There is no better time. I've been practicing for 16 years. There's no better time for the management of atrial fibrillation than today. The advances in technology, the indications, the progress that we've made, it's unbelievable in the past couple of decades like I've never seen. And so how we're going to walk through this discussion is to understand a little bit about market dynamics, the tailwinds as well as some of the challenges that we faced in the space and then some solutions that were already in acting to help increase the penetration of some of these procedures and get patients the procedures that they need and then finally wrap up.

So let's talk a little bit about surgical AF ablation. We have some great presentations from Dr. Whitlock and Dr. Soltesz and you've seen this figure, but let's look at it closely. Here on the left-hand side, you see all the societies around the globe, and here are the level indications that they have approved in 2017 and then just recently. When things get approved as a Level one indication, that's what sets the standard for practitioners and it finds its way as Dr. Whitlock has mentioned, in-quality measures. So this creates a benchmark that everyone has to follow and people get sanctioned if they don't follow.

So it's really important that when you see a Level one indication that you're going to expect that the market is going to respond by starting to increase the frequency of some of these procedures. We have that with surgical AF ablation and appendage management. That's here. That is contemporary. So societal guidelines established practice behavior, and that's important to understand. The second phenomenon is that for surgical procedures, it requires expertise, dexterity, proficiency. You have to have an established network of educational programs, and that is happening here.

So you can see here's a couple of examples of different programs around the globe that AtriCure has participated, and they really set the standard for other companies as far as what a professional educational system needs to look like. It is because of this that we see the market expansion of different procedures. It's not going to happen by itself. You have to set an infrastructure.

So the second point to make is that to allow for scale for any type of procedure, you have to have the infrastructure for professional education and you have to be slick and mature in deploying that for any procedure to scale. That is a requirement. Well what also has happened in our market. Well the indications for doing something procedurally in a patient with atrial fibrillation in the last 5 years has exploded.

So this happened after Covid, it used to be that if you had a patient with atrial fibrillation, the older data would have suggested in the past that you can leave that patient in atrial fibrillation and it would be just fine, no longer. The data that has emerged in the last couple of years states that you should never leave a patient in atrial fibrillation that you have a higher chance of morbidity, mortality, hospitalizations. This is huge.

So no longer is it acceptable for a patient with atrial fibrillation to come into the hospital to leave with an atrial fibrillation. We have to do something procedurally. Then comes heart failure patients with atrial fibrillation. The data is rife with the level of evidence that suggests that doing an ablation, specifically ablation that doing an ablation in a heart failure patient with atrial fibrillation is going to improve outcomes. There's little doubt here. So now we've got a huge subset of patients with comorbid condition that really could stand to benefit with ablation.

Then the last thing is -- it used to be in our practice pattern that you had to fail medications first to then be eligible for an ablation procedure, gone. So we published this. Dr. Sood and I were co-authors in the New England Journal of Medicine Paper that showed that doing a catheter-based procedure as opposed to failing an antiarrhythmic agent is the right thing to do.

I'm also -- right now we just closed a trial to validate this in the persistent population. I'm hoping that, that's positive as well. And if it is, we've got our arms wrapped around the entire segment of AF patients who don't need to fail antiarrhythmic medications, which is huge. It expedites and improves the efficiency of patients moving through our system with getting them the procedures that they actually need.

So if you look at the accessible market for potential patients that could have ablation procedures, it's huge. Last five years, it's huge, like we've never seen it in the last couple of decades. Traveling along with that level of expansion is the expansion of technology.

What you're looking at, starting from right to left is where we were in the past with radio frequency catheters that we've been using since the late '90s. Then with laser cryotherapy and the most recent is pulse field ablation. Where PFA really shines -- and we're going to walk through this, where PFA shines is that it is efficient and it is safe but not more effective. It is safe and efficient. So ablation tools now have allowed us to lower the threshold of recommending procedure because we can do it with the confidence that it's going to be safe for our patients, and that's huge.

So what are the challenges? There are challenges that we're facing despite all of these benefits. Well let's talk about surgical AF ablation for a moment. This is the blueprint of a Cox-Maze procedure.

Now -- this is complex for me. It's complex for new surgeons starting off, and you have to follow this cookbook to a "T" to see the level of efficacy that study show. It's a complicated procedure and to show you proof of how complicated it is, this is a publication that came out a couple of years ago that shows the penetration of adding surgical AF ablation to patients who are going for cardiac surgery. And as you can see, this is not the graph that we want to see when we were trying to scale a procedure. It's flat. So despite all the education and the promotion and the indication and expansion of level of indication, it's just been flat. The reason for this is that it's a complicated procedure. So it's a hard thing to learn on the fly, but I'm going to show you some solutions as to how we can get around this.

So scaling Cox-Maze has been difficult because of the educational component. Well what about in the conversion market, we have some headwinds there as well. So PFA, the 800-pound grill in the room, the potential competition, this is a technology that was first identified in 2012. Then it took this many years to find the secret sauce to fine-tune PFA because, as Dr. Whitlock had mentioned, not all technologies are applied to every single company.

This is something that is very unique to this catheter, with the amount of algorithms that are applied to that catheter and they can't be modified. You can't tweak this catheter. You change your parameter and you suddenly change its risk-benefit ratio dramatically. So what you see is what you get, and then when you provide some evidence that it's safe, that's where we see the skyrocket of the number of procedures performed. But it is with this algorithm and with this catheter only and that you can't modify that.

So when you put yourselves in the shoes of being a physician standing in front of the patient with persistent atrial fibrillation, it's confusing. There's a lot of noise in the space now with potential decision-making and how do I apply a particular technology, should I choose PFA? It's safe, it's efficient. I can get patients home the same day that seems pretty easy. And it doesn't take many tries to get to some level of proficiency. So it's got a

pretty flat learning curve? Or do I do a convergent procedure that shows more efficacy, by the way there's no better efficacy than convergent, and that's proven time and time again. I can add appendage management. So I can address that at the same time.

And by the way it has the only FDA label, so when I'm asked about what I should do with a long-standing persistent patients, if you look at the level of evidence, it's the only thing that has been FDA approved for long-standing persistent, nothing else in the space.

So how did we get to where we are with PFA? Well this was the pivotal trial that compared PFA with cryo versus radio frequency. What this trial showed is that it's just as effective, no more effective. So you're getting the same level of efficacy as what we have been using for 20 years. But here's the difference. The safety is perfect. We get zero of the most dreaded complication of catheter ablation, which is called (inaudible), which is basically burning a hole through the esophagus into the -- from the left atrium to the esophagus and it's nearly fatal all the time. The reported incidence of this is basically zero.

So this is where you see the expansion of PFA. But if you look at the efficacy in the persistent market, we're only getting 60%, this is really the Achilles' heel. And we've not been able to approve this. And by the way you'll hear 60% quite often because that is what any catheter has ever shown in the field of electrophysiology when it comes to the persistent AF population.

We have not gotten past that, accept that they use a hybrid approach. You can't get it with catheter ablation. And by the way the durability when you take patients who have failed that procedure and you bring them back into the EP lab and you audit the work that you've done, you're only getting 70% durability, especially in the back wall, which is where CONVERGENT works the best.

So this is a problem. The reason that that's probably happening can be seen on this slide. So what you're looking at is a bench case where they apply PFA and what it does is it sears stake, but it doesn't get it well done. This is because this device has been tuned to be optimal for the safety efficacy window so that it doesn't cause complications, but the adverse effect of that is that you're only getting an ablation thickness about 4 millimeters, two to 4 millimeters. And by the way it doesn't ablate fat, and if you've got a structure on the other side, you're definitely not even approaching that. That's a big deal.

In our field, in our lexicon, that is the epicardium. So we now appreciate that there are structures on the outside of the heart that contribute to the maintenance of atrial fibrillation, and it's separated by fat. So if I'm driving energy from the inside out, and I got a lot of insulation. I'm not approaching those structures.

I'll tell you this is a big deal. This is a figure that was taken from the European consensus guidelines that were published last year, and they have a special call out to instruct operators that you better be careful because you've got structured on the outside of the heart that are important that you may not be able to get to. So we don't have a solution for

this in the endocardial space. So PFA has so so efficacy with persistent atrial fibrillation around 60%. It's likely we hypothesize because there are structures on the epicardium you just can't get to, especially in the posterior wall.

So why not the most logical thing is why not just turn up the volume on that console so that you overpower the lesion? Well this is some of the internal research that has been done with PFA that shows the exposure time once you start the ablation and the energy output from that catheter and how that device is designed is to live in a sweet spot. When you increase the energy you turn that catheter into a radio frequency catheter with thermal energy and all the complications that get engendered with that. If you turn it down, then you get reversible lesions.

So to answer the question, what's going to happen with PFA, well you would have to validate a more powerful device and go through the whole process of validating safety and efficacy, all over again. what you see with this catheter in this technology is what you get currently. And it's not going to improve unless you invest a lot of R&D to revamp the entire thing. And if you're wondering why don't electrophysiologists mention this? Or how come there isn't a buzz?

Well just recently, there has become a lot of discussion around this issue. This -- my colleague in New York wrote an editorial on a recent publication to ask the question what's going on here with reconnection rates. It's time that we temper our enthusiasm when it comes to this technology. There is a sweet spot for it. It's probably early AF, but as you get to more advanced forms of atrial fibrillation, we need to really call our enthusiasm and check as to what the level of evidence is showing us, and durability is a question. There's no argument with that.

So the real question that everybody wants to know is, does PFA provide an existential threat to hybrid technologies? Well you answer that question. And I'll answer that question by giving you a little history. I started CONVERGENT in 2011, three years later, there was a small company called Topera that was bought by Abbott in 2014 for a $250 million acquisition. What they purported is that the single procedure efficacy was 88%. I remember this very clearly because my colleagues, we taught a lot of conversion at that time. My colleagues would tell me that procedure is over. There is this new procedure called Topera that does roller-mapping that has 80% for persistent atrial fibrillation, it's going to revolutionize everything.

Well 5 years later, it was dead. Now the only remnant of Topera is probably as a goodwill impairment or a depreciated asset on a balance sheet. That's all you'll hear of that technology. So we learned from our mistakes. Now let's talk about some pathways as to how to get through some of these challenges? From the surgical space, well you iterate. So as was mentioned by Dr. Soltesz and Dr. Cox has mentioned this, you can have the best procedure. But if it's too complicated and you can't teach it, no one's going to ever do it. So with all the tools that we have available today that AtriCure has designed, we can create a Cox-Maze like procedure that's easier to do and we believe it's going to be just as effective.

That's what we've done at our hospital, we call it the TAMPA2, you can call it whatever you want. This is an abstract that we published, and it utilizes the EnCompass Clamp, a cryoPROBE and a Clip. So we could basically reconstruct all the work that you do with the Cox-Maze, but we can do it much simpler with elegant tools and the efficacy still needs to be borne out, but we believe it's going to be effective. And this is how you get around the plateau and the penetration rate of that procedure is that you iterate. That's what we can do.

And to give you some proof, we taught a course this past weekend in Tampa and literally, Twitter is -- we get all our information from social media now literally, the next day people are tweeting about this new procedure. In fact, the surgeons in the room, were actually learning about it and then doing it two days later. This is the adoption rate that we all want to be able to scale procedures.

So when you can do something that quickly, and leverage the elegance of new surgical elation tools, this is how you get scaling. Well what about the CONVERGENT procedure? Well I'm going to answer that question by showing you the MANIFEST data. So the MANIFEST data, PFA started in Europe and then to the states. So they have a lot of outcome data already built. And MANIFEST was a 17,000 observational real-world trial that just followed patients. They looked at all the patients that had PFA and they follow them over time.

And this is a breakdown of the demographics in that trial. And because it was a real world, it wasn't randomized, it's got pretty decent application to our setting here in Ohio or Tampa. Most patients are paroxysmal. This is our low-hanging fruit. Then you've got a middle section of persistent atrial fibrillation patients, moderate severity and then a small fraction are long-standing. So here's what happened after following these patients for 12 months. This is before they were ablated and this is what happened after. So here's all the success rates of the patients that were successfully treated and this is the fraction of failures. My real-world practice of inversion is long-standing, persistent is persistent, but where it shines is also covering these failures. Because if you treat every patient like a nail and use the same hammer and expect a different outcome, you're just asking for failure. This is what's happening with PFA.

I tell people it is the best customer segmentation tool ever because it has a very predictable failure rate. And what do you do with all these failures? You could apply the same technology, but you can expect a better outcome because we already know very well what the effectiveness rate is. That's what's been a boon to the conversion procedure, and it's coming, just like the (inaudible) is that there is a bolus of patients that are undergoing PFA and they will have failures. Then the question is what do you do with these patients?

So in closing, with novel appliances and techniques, I think we're being -- we're in a better position to be able to scale a very complicated procedure Cox-Maze for the first time since the invention of Cox-Maze, which is exciting. PFA is market disruption.

There's no question about it. But combining the expansion and indication, pouring more patients into the mix and having a very well detailed failure rate is a boom for procedures that play well in moderate to severe atrial fibrillation, which is what CONVERGENT is.

Then finally, there's no question that adding appendage legation to both the hybrid market and to surgical procedures. Everybody agrees that this is a good thing, and we see this in our community practice as well. And with that, I would like to close.

Dr. Nitesh Sood ^ Perfect. Thank you, so much. Thank you, AtriCure for having me here. Thank you, to being here. I'll start with an apology because you will learn a lot more about EP than you signed up for today in my talk. My talk is a lot more clinical than financials. So bear with me as I walk you through my mental process of where we stand with PFA and the CONVERGENT procedure in our practice.

So we are a big health system south of Boston. Once you are in Boston, you cannot turn a corner without finding a hospital, right? Once you leave Boston, you can only find us, which is where the beauty lies. So we work in Southeastern Massachusetts, a nonacademic large healthcare system. My disclosures, and that's my goal today.

Talk about PFA, talk about hemolysis, which nobody has talked about yet with (inaudible) ablation and then touch on where hybrid stands in the era of PFA. Some background, we all know this. There's cryo, there's radio frequency. There's pulse field ablation. Ablation is now first-line therapy. Very proud of this paper and being an author on this.

Of course being Indian my mom pointed out, I was third author and hopefully, I can strive to be first author next time. This is a true story. And -- but EJM is, I think the zenith of achievement for anybody in medicine. So we are very proud of this paper being -- so it's been a 5-year journey with IDE studies starting with this clinical study, which put ablation as frontline therapy.

Then, of course social media, right, because if it's not on Twitter, it's not true, and this is a treat I borrowed from Dr. Sanders, who was a co-author on our -- on the pivotal study. This is just after we started doing these cases. He put up this case of a PVI and posterior wall ablation. And his comment was, this has become too easy.

Somebody asked how long does it stay that way, and that is the big question. We don't know. I'll share some clinical cases, real life clinical cases showing that. Our current experience at Southcoast where we are, we were lucky enough to do the first IDE case of the world as in any clinical study, which was a big feat.

We are also -- I'm a PI on the PERSISTENT as first-line therapy, which is just completed as of last month with Farapulse, part of the IDE study for Abbott for VOLT. Obviously an author on the pivotal study, which was the first IDE study. This is just last week or two weeks ago, I was at the National PFA Summit as a faculty member. So there's a lot of PFA coming out.

We're also part of the Affera launch. So there's a 25 center launch, as I'm sure some of you guys know we are part of that initial launch. So I always tell people this, there's PFA coming out of our pores. We have four, five different systems, pretty much everything that is to offer with PFA. So I have used and have experience with pretty much all the different systems for Pulse Field.

I'm not going to waste too much time and I know that all of you already know the data. But here's the reason why I put these slides, they might be redundant, but -- the initial promise with PFA was great, 70%, 80%, as Kevin pointed out, just like with (inaudible). There is an interesting fact with PFA data that nobody is talking about. There's a huge drop off.

If you look at outcomes at six months versus 12 months, which is what we have is a sudden drop off. This is not something we've seen with previous technologies, with radio frequency and with cryo, this is so-called 3-month blanking period, where whatever you get after three months is what you get at one year.

With pulse field ablation, you get excellent outcomes at six months. For some reason, the drop-off is pretty dramatic at 12 months. Is it the blanking period that's longer? Well it's not true because most recent guidelines because of Pulse Field changed that blanking period from three months to eight weeks. And actually what is supposed to be four weeks, but it was a compromise between two different fractions.

So the blanking period has actually gone down to two months. So we know this is not an inflammatory based drop-off in outcomes. So what's going on? Anyways, the first IDE study showed about 55% to 65% outcome with the Medtronic catheter, of course followed up next month with the Boston Scientific catheter, which showed a slightly higher efficacy, but again no difference between Radio Frequency and Cryo and Pulse Field.

Of course being part of the steering committee for Medtronic, we immediately redid our data. Our argument was that we looked more so we found more. So we reanalyzed our data with the Boston Scientific Monitoring, and we also got 75% efficacy. So it's -- I guess if you look more, you find more concept, but I would say the efficacy is about 65%, 70%, depending on how you look. Posterior wall ablation, again not to get true academic. There's been arguments about, does it work? Is it important? We know it comes from the same embryonic origin as the pulmonary veins.

This is a more recent well-done study, which showed that if there's a diseased posterior wall, there is benefit of ablating the poster valve. Again I won't spend too much time here. What about Pulse field? You've heard about the esophagus, that being an issue, with radio frequency and cryo damaging the esophagus, with pulse field is safe. So what have you found? This is the MANIFEST registry that Kevin showed. And at one year, there was no difference between doing just the veins versus veins and posterior wall for persistent AF patients and about 60% outcomes.

But again this is a retrospective data. This is industry-sponsored. So what about something else? This, I think is a very important paper that hasn't really gotten the press it deserved. This is a prospective registry data out of multiple centers in Europe. They were ahead of us in Pulse Field. They looked at patients who were sort of real-life patients.

I'll just pause on this slide for a second. They looked at patients who were persistent, long-standing persistent, failed paroxysmal.

Interestingly, only about 30% patients were first-timers patients. 70% In this study were re-dos of some sort. What they found was if they did PVI versus PBI posterior wall, there was no difference in outcome. The outcome was 53%, freedom at one year, which we would expect is a little visible. Well then why was it? About 80% patients or 80 patients had recurrence. Out of the 80 patients, 26 patients underwent a redo procedure. Well we can say Pulse Field is not durable and the poster all must have been reconnected, right? Or the veins are reconnected. It didn't work. It was new operators. They didn't know how to do the procedure well.

Well out of the 26 patients who underwent redo procedures, Red is (inaudible) here. So hopefully, you guys will be all 3D mapping experts when I'm done with you here. I can't find the pointer, but thank you. But just to get a sense of what these 3D maps look like, red in this is CAR. So if you look at posterior wall and veins in the patients, again not all patients who had recurrence underwent redo operations, but people who did there was 85% durability of lesions, even though the follow-up of the study was about eight to 10 months.

So if these patients who so-called had durable endocardial posttrial wall and venous ablation. Why are they having Afib? And that's the question that we need to answer. So this has another interesting twist I was actually doing grand rounds the month that this paper came out at Temple, which is a big institution. The Chief of EP at Temple had just written this editorial on this paper that I was unaware of and of course I was going on and on about how Pulse Field is great and we can do posterior wall. And he said, well have you heard about this paper that there's no benefit and the results are visible. I said, I haven't -- he said, Well I wrote the editorial, you should read it.

So and this is from our field, you know Ed is part of the guideline committees, but why are we not able to get the outcomes? Is efficiency the only thing we desire? And that is a big question that we need to answer as a society as a field for these persistent and long-standing persistent patients? And again so the conclusion is, it appears to be safe. There is a risk for hemolysis, but the outcomes are about 50%. It's like tossing a coin. It's really not good enough. If there is durable endocardial posterior wall ablation, with Pulse Field, then why are we not getting the outcomes that we think we should be?

I won't spend too much time on hybrid data, but every time somebody has done a study, independent or industry sponsor, the (inaudible),the CEASE-AF, which is a randomized

study published in Lancet, showing benefit of hybrid versus endocardial therapies. Of course you've all seen the CONVERGENT study, the CONVERGE data.

Again I won't spend too much time but just build that narrative at each time anybody has done a study comparing epicardial and endocardial ablation to just endocardial ablation. No matter what technique they've used, they have shown benefit beyond that 50% to 55%. So there must be something going on is not absolutely clear. Again long-standing persistent, the outcomes are even better. Again you've all seen this data, so I won't spend too much time.

So my conclusion looking at this is small big, randomized, observational, we've done a registry study. Each time we touch the epicardial space, along with the endocardium, there seems to be some benefit. And no matter what energy you're using? Is it cryo, is it radio frequency? Is it pulse field? And I think that will be the next foray into literature. We have some patients who are coming back after we've done Pulse Field -- and as we start doing them, we have two patients scheduled for the convergent, I'm super excited to see what the apricot looks like.

What does the Epicardium look like after you've already had post-real isolation with PA Hemolysis, something that is not talked about, but it's that of a dirty secret of pulse field. Now why is the hemolysis? Because these catheters are big. When you deploy the energy into the left atrium, only part of the catheter is touching the tissue. The other half or other three quarters or other third is the blading blood -- and this is what it looks like. You don't have to be a physician to see which one of these was PFA, which one of these was radio frequency. This is at the time right after the procedure, you can see red urine.

So these are urine samples taken after pulse field ablation and it's bright red. Now why is this important? This is important because -- this leads to cytotoxic effects. There's been reports of patients going on dialysis. After pulse field ablation reports are small, anemia, may not be clinically significant. But as we get into the realm of doing more and more with Pulse field during the posterior wall.

And by the way it takes about 50 lesions to get to this stage, it takes about 40 lesions to just get PVI. So 30 to 40 lesions for PVI, 50 for posterior wall and then you start adding SVC this, that whatever you're getting into 100, 150 lesions. And all it takes to get to this is about 50 lesions. So we have to be careful as we keep going up on what we are doing with Pulse field. These are not benign issues. A lot of our patients already have renal disease. So we have to be careful what we do.

So I'll finish with a few cases. This is where my apologies because this is a lot more clinical. I've never done something like this. So I only know one language, so please bear with me.

What is the current state of hybrid ablation? Hybrid ablation has come a long way. It used to be that the surgeon would go in, they would ablate and they would come out. They will look at the tissue, ablate and move on. But now it's a lot more sophisticated. This is just

an example of what it looks like -- and this is the 3D maps I showed you, we are now able to do this in the epicardial space. This is revolutionary, and this is a surgeon doing it themselves. You are looking at a lot of bad stuff here, looks like this. Once you're done, it looks great, which is what you want. But this is sort of improving the fitness of the procedure.

This is the endocardial portion. You can see that the surgeon has done the back wall. When I go in, there's a nice, clear demarcated gray zone in the posterior wall. And after I'm done, everything looks perfect. This is has increased the sophistication. Why is this it's important because what's happened in the TAVR world, surgeons and structures came together, and that has led to a successful, successful program. The problem in EP has been each time we have spoken to a surgeon is when something catastrophic has happened.

So we hate seeing the surgeon. It's once every six or eight months, thankfully, it's even less. But when an EP is interacting the surgeon, it's been something is not going well. It has not been a true marriage, but by surgeons adopting sort of our language and the fitness of mapping which has not been true for surgical ablation thus far, it has really bridged that gap between EPs and surgeons leading us to the same heart care team that TAVR has demonstrated. This is just an example of epicardial mapping.

I'll go on from there, and I'll finish with two cases of pulse field ablation and where the limitations might lie. What is the importance of contact -- now I do a lot of work, and we are part of a study ongoing study on contact, and this has sort of been my sort of big part of PFA training, proctoring, teaching -- but here's the problem. It's this thing here.

Now for all of you who have dealt with the ablation space, you heard about contact force being a big advantage with rate of frequency ablation. This is what happens. Let me sort of blow this up for you a little bit. The way we do an ablation. We look at tissue on a pre map. We say okay. There's electrical signals. We apply energy and we ablate it. We go back and look at it and say okay. This tissue is dead, we are done. It's a successful procedure. The problem with Pulse Field is this. If you are 4 millimeters or so, which is not a lot of distance from the cardiac tissue, and you apply energy, Pulse Field, this is (inaudible), you will get a nice broad lesion, but it's very, very shallow. You have to be at least to preferably in full contact with the tissue to get the same lesion, but get the depth that is needed.

If you look at animal studies, -- if you deploy a lesion almost in the middle of the atrium, the signals go away because you're applying an electric field, right, you're not destroying tissue. It takes an hour for that to come back. And electrophysiologist, the one thing you will -- if you ever met one, you will know patience is not a virtue.

If you also think about it, the big advantage of Pulse Field given the additional cost that it entails is efficiency. I have gone from doing two ablations a day last year to now doing four or five routinely. So I am not going to sit around, wait for an hour.

By the way that's if I deploy Pulse Field in the bloodstream in the left atrium. If I deploy it even 4 millimeters away or 5 millimeters away it can take a while for this to come back. The problem is I have no way of knowing right now because there's no contact force. There's no contact on these catheters.

The other issue is even if there was contact, these are large footprint catheters. If I'm pushing with something, some of the polls could be in contact, the others are not in contact. There's no real way of knowing that. So that's why I think there's a lot of tapering off of these lesions after six months.

So this is an example of the case I did. We are lucky and unlucky I say because if you look at Pulse field, it came to commercial use last March. That was the first time commercially available for people to use it. And most people have only used it for about four to six months. It has grown exponentially, but it's really been even less than a year that this market has grown, right? We have had cases because of the clinical studies, which have 3, 4, 5-year follow-up.

I'll show you a couple of cases. This is a patient I did, and this is a clinical study patient. And each time this is a circle is a lesion is deployed in the left atrium. You can say one thing, not knowing anything about EP and how we do these cases, subtlety was not a forte here, right? I mean there was no -- nothing spared. This, by the way the esophagus, the one thing that we worry about, and I had absolutely no problem being right on the esophagus and ablating as much as I could. I checked this right after. And as you can see, grades dead, you can see no signals here. I said you become experts in EP, but I'm done with you. But this is a case I did, and I checked my work and I had perfect results.

What else could I have done here? There's really not much else I could have done. I did this guy 1.5 years later because he was part of the clinical study, and this is what it looked like. So now everything is back. But it's not -- it's back and healthy, but you can see there's a lot of jagged lines here. When you see a lot of different lines and time difference between signals, that means it's injured tissue, which has returned.

So what you are seeing here not being electrophysiologists is that there's a lot of return of injured tissue about 1.5 years later. So that is -- we don't know that because nobody is done and followed these patients for 1.5 years yet because commercially, it's only been six months. The second case I did, this is part of our study that we are doing just as a proof of concept, and I'll finish with this, I promise. This is a case where I did.

Now the current mapping systems that you all know the ESI, Abbott Mapping System, the Cardamapping system, they can only tell you the out-of-box setting is about 7 millimeters. So they can tell you if you are within seven inches from the cardiac tissue. Now it typically didn't matter until now because our radio frequency catheters have grams in (inaudible). So it tells us how much we are pushing. So it doesn't really make a difference if it's seven or not. With cryoballoon, you're pushing with the balloon and you're injecting die, again it doesn't really matter how far the mapping system says you

are. But with Pulse field, we don't have that. We're not going to have that for a long time because they have big footprint catheters and there's a lot of playing of electrodes.

So what I did was we sort of generated our system to get down to 2 millimeters. Now we can only do that with the Medtronic system. The Ferapol system is a magnetic system, and all the mapping systems are what I call resistance or impedence-based systems. So they don't talk to each other. The best you can do with the Farapulse system is 6 millimeters. So what I did was I did the left-sided veins, the top -- the left upper here is 2-millimeter contact. So if you generate the system for 2-millimeter contact, you can see that I'm missing some areas here. But if I make that 4 millimeters, you see perfectly inset. Mind you, it's 7 millimeters out of box.

So this is four, and I remapped or checked my work. This is just what the lesions look like and how they sit. We checked our work right after we were done, looks perfect, right? There's a nice demarcation of tissue. Then I had to do the impossible: wait for 30 minutes. That took everything out of them. We went back and checked and sure enough, there were two spots. The ones that were not perfect contact, they were back and they had -- and you can see again injure tissue return. But again it's not happening in real life. This is not going on. This stunning effect of pulse field ablation is underappreciated. It is quick, but there is a significant amount of limitation with pulse ablation. This is just the settings. Again you can see an example here where you can see where the contact is. These are just shadows, which are internal to the shelf. But if you look at the post map, there's a lot more sort of a lot bigger lesion set than what you would expect with good contact.

So to conclude, there is a significant drop off from six to 12 months in the current data. However -- and there is stunning, short and long. But the big question I have is the study I showed you earlier even with durable pulse field ablation of forestry of wall endocardially, why are these patients getting atofibrillation?

Why does each time we do a surgical approach of combining the epicardium to endocardium. Why does that benefit? And this is something we've known all along is that the reason is that the Epicardium, or the outside of the heart is insulated from the inside by fatty tissue and it's almost like a different structure.

That is the reason why I would sort of argue are we really choosing efficiency over efficacy when we are doing pulse ablation for these sort of persistent and long-standing persistent patients. So in our institution, and I think that's going to happen a lot is when we see somebody who is long-standing persistent Afib, we are still offering them the convergence as an upfront therapy. So beyond 1.5 to 2 years. The interesting thing is -- and typically, what would happen is if somebody was persistent, I would do one ablation, I would do just the veins. If they had recurrence, I would bring them back then to the veins, (inaudible), yada, yada, yada, whatever sort of tackle the fantasy that day.

Then when they had their third ablation, and I was done with them, and there's nothing more I could do, I would then offer them the surgical procedure, that is the more typical

sort of workflow. But now what's happening, and I think what will happen as we get past that 6- to 12-month follow-up is now we are doing that all upfront with Pulse field, because we can. So we do PVI and postal and SEC because you can do it here, we can do it there and everywhere. These patients are having recurrence. We have seen the data from Europe is 53%. So when we have these patients who come back and we've already done what we need to do endocardially, what are we going to do? And I think that's where the hybrid approach is going to make a resurgence and be an option for these difficult-to-treat patients. That is it. Thank you.

Unidentified Speaker^ Okay. Great. So we'll take two to three questions for Dr. Sood.

Suraj Kalia^ Dr. Sood, a lot of good data presented, and I commend you for some of the things you said about PFA it's a rarity. So the question I have is the comments you made, and I'll just kind of randomly go reconnection with of PVIs after time drop off significantly after 23 months and analysis. Forgive me, maybe I missed it. Was it relegated only to persistent or also peroxisomal? So that's one thing. And the second thing is I'd love to be in your shoes and understand how you advise Medtronic or Boston for going into persistent AF and help us reconcile your comments here.

Nitesh Sood^ Yes. That's a good question. So the data on drop-off is true for both paroxysmal and persistence because if you look at the MANIFEST data, what it shows is about 85% for paroxysmal and 70%, 75% of persistence, and that drops from 80 to 60 and from 75 to 50. So it's showing it for both. Now you could say it's early experience and they are learning and all of those things. But it's happening across the board for both paraxylene and persistent. As far as hemolysis is concerned, it's the same thing. Hemolysis depends on the number of lesions, not what patient you're using it for. The sort of crux is 54 lesions. That's typically the cutoff. If you have anything more than 50, 54 lesions, you will get significant hemolysis as it's described.

For all of these technologies, they recommend at least eight lesions per vein minimum. That's the recommendation from the manufacturers. So you do eight lesions minimum for vein. So you're already at about 40%. That's the basic minimum. And anything most of us are doing something beyond. If you want to do the posterior wall on an average, it takes about 30, 40 lesions more. So the only time you're not getting hemolysis is when you're not checking for hemolysis. Sort of everybody is now looking at that. As far as the future are advising people for Pulse field.

The big question is going to be is contact and how do you ensure good contact when you're doing these cases. But the bigger question, I think what I would like to also emphasize is even if you do have durable lesions, the patients who had new procedures in that serious independent series, nonindustry sponsored. People who had durable lesions, they are still having AFIP. So if they have durable lesions and we go in and there's not much for us to do as EPs endocardially. What is the option for those patients. Yes.

William Plovanic^ Bill Plovanic, Canaccord. So this is fantastic information for us. I guess my question is, when -- are there any specific studies or long-term follow-up where

this is going to go and hit the podium and that this will become a bigger topic. Then you're implementing, obviously some protocols of, hey, these are the patients that will treat with PFA frontline and then hybrid and what have you. How long do you think does that take to trickle down to kind of the rest of the community?

So -- and I ask is we're all waiting with bated breath for hybrid to take off. We see the opportunity, and we've kind of been waiting for this, okay. This is creating a bigger pool of patients. When does this become a standard of care? And what you're showing us, I think it was the Tampa 2, when does that become standard care and guideline.

Nitesh Sood^ So I think the answer is that you have to go through at least a year of follow-up on the initial pulsefield cases to start seeing the failures come through. If you look at even our practice last time this year or over the summer, we were -- our hybrid volume had gone down significantly. And now suddenly, it's ticked up and now we have booked out to the summer for the hybrid procedure because we are now seeing, because we were early on in the PFA world.

So now we are seeing those people come back and we have -- because we have done everything we normally would do in a second procedure already in our first procedure, I know I've run out of options. I know that, that patient will benefit from the hybrid procedure a lot better, especially because you can also manage the appendage electrically, which adds about 20% given if you look at which paper you look at. But efficiency and efficiency-wise certainly will be first line. There is no question. But I almost feel that it will bring that hybrid procedure up even sooner in the conversation because rather than doing 1,2,3 ablation you are doing that one two three ablation in that first ablation because you have pulse field in your hands.

John McAulay^ John McAulay from Stifel. Just sort of a simple question. You talked about how your conversion procedures dropped off. They're recovering. Can you just talk a bit about where your actual conversion volumes stand today and just your expectations over time as these PFA patients come back into the pool?

Nitesh Sood^ Yes. I think just Afib volume itself has gone up significantly. If you look at what we were doing five years ago to what we are doing now the kind of patients we are treating, the number of patients we are treating, it has all gone up. As far as you know PFA volume per se, one of the biggest limitations of the hybrid procedure is coordination and trying to get scheduling and lab time and all those things. But truly because it has become such a straightforward procedure with the subxiphoid approach, I envision that at least 10% to 15% of my patients with time will end up being hybrid ablations, either from a failed PFA first-line de novo, which in the past was not the case because we're just treating more and more patients.

Michael Carrel^ Well speaking of PFA, I guess before I kind of get -- you've heard from the physicians already today and I just want to -- if we could kind of give them over a round of applause and thank you for your presentation. Hopefully, what you got was a feel for the depth of studying and looking at the different markets and the things that

we're working on and the type of talent that we work with and get actually feedback from on a regular basis. Obviously we'll be open for other questions kind of at the end.

I'm going to give a real brief overview of kind of our PFA platform because I think it's -- I know we get asked the question all the time for those of you that haven't gone there, but we are obviously building our own PFA platform. We are not going to become an endocardial company on this front. This is really for the epicardial portion of it. We believe we need to be at the forefront our platform, though, is going to have a combination of RF and PFA.

It's important to note, surgically, we are already incredibly safe. We don't have safety issues. There's not an issue with that. All of our technology, you can check MAUDE databases and everything else, incredibly safe procedure to use the technology that they've got today. So there's not going to be the same safety benefit that you get from an endocardial standpoint and kind of saving the esophagus from that because we don't have those issues. From a procedural time standpoint, it does have a small effect on the cardiac surgery in the open chest procedure, but it has a very large effect procedure from a kind of EPi-sense standpoint or convergent. That's really where we see the benefit from a timing going in the market. So we're going to go to market with two different devices. If you go in and you can actually check this out in the engineering lab, the Encompass device is going to have that. We actually are working on that, and I'll give you some timelines here in a moment.

Then on the hybrid side, we're going to be improving the speed quite dramatically on that front. So it's important to understand the speed because you've heard this from many of the physicians and I just want to repeat it quickly. We have already seen by putting in the Encompass in people's hands, you're taking a procedure that can take up to 52 minutes to do all that work that Dr. Soltesz talked about earlier, the dissection to get access to the vein, we're bringing it down like 10 minutes.

We've solved the time thing with our Encompass clamp. That's super important. We can probably save two to three minutes with the PFA and obviously that will be incorporated within the Encompass clamp. However if you put it into our other clamps, you're not going to get all that other savings. So if you try to do the old procedure that was out there, you're not going to get the benefit, which is a bigger benefit, which is from the Encompass clamp itself and kind of the procedural portion from that standpoint.

Super important to understand that, but we will have that embedded. That is different than on the EPi-sense side, where we're seeing a significant reduction in the time related to this in terms of reducing the time for the ablation because every time you use the EPi-sense today it's about a 90-second burn every time you place it, then you can have anywhere between 25 and 40 burns. If we can take that 90-second burn and cut it in half, with PFA or some combination of PFA and RFA, you're going to be able to reduce that time quite considerably on that front. So the time savings is going to be really on the EPi-sense side and convergence side of the procedure, relative to that. So hopefully, that makes some sense.

On the timeframe for it, this is not something that's coming to market tomorrow. We're not giving -- we want to give you a kind of a peak into the future about what we're doing on that front, whether you hear from competition trying to enter into this. This is a required PMA product to get onto the market.

So our timeline is as such. We've made a tremendous amount of progress. We do have a generator, as you saw in the labs there. You can see on the Encompass clamp, we will be first in human this year. We will be starting an IDE trial in the beginning of 2026, enrollment into 2027, follow-up and then sometime later in the decade, you'll actually see that into the clamp. It takes time to do these trials and to do the long-term follow-up that is necessary to get that FDA approval. Then on the EPi-sense it's going to be a fast follow. You're probably going to be behind about three to six months relative to that in terms of getting it into the market from that standpoint.

So hopefully, you leave with we have confidence in what we're doing. We have done hundreds of animals already with this technology. We have a great technology already in place. We've got the design set. We are moving forward towards getting this into the market, and we are very confident in the process that we're kind of going through. But there's no near-term revenue spike or anything else that's there, but know that we understand it, we understand the technology incredibly well. So we thought that, that was an important piece because I know it gets asked on different calls, we won't go into too many much more detail on it.

I'm going to turn it over to my colleagues, Justin Noznesky, our Chief Marketing and Strategy Officer, and Sam Privitera, our Chief Technology Officer, and we're going to kind of shake your brains here for a moment and kind of get you thinking a little bit about cryo and kind of what's kind of in-store for us there.

Justin Noznesky^ Thanks, Mike. Well this is bunch of tough act to follow. We're going to lead you through a slightly different conversation and talk about our journey in pain management.

So Sam, do you want to take it away?

Sam Privitera^ So Mike started the day talking about how our market opportunities have expanded by us going into different procedural steps. I think it's important to know we're not a technology company, a single technology company. We've always been about solving the next clinical opportunity. We can do that because we're so close to our clinical partners.

So when we started, this room is the James Cox conference room. We work really closely with Dr. Cox to understand what he was trying to accomplish with the cut and sew and we developed an RF technology to mimic that or we actually better than that. who are less dramatic. But then it was, okay how do you test so we developed an interoperative mapping system? Then how do you create linear lines in areas where thermal ablation

with RF wasn't appropriate and we created our cryo technology. Then well we should deal with the left appendage.

So we constantly changed our technology focus to deal with the next clinical problem. When you look at pain management, it's been the same way there. We saw that as we move to minimally invasive procedures, we needed to start dealing with pain. Then it was, well if this -- we're doing this for arrhythmia treatment, what about thoracic procedures, and we developed tools specific to that and now we're moving towards extremities. So as we talk through this, all of these are logical steps in our evolution as a company.

Justin Noznesky^ So pain after cardiothoracic surgery is a huge problem. Mike already showed a derivative of this slide earlier, a significant percentage of patients who undergo cardiothoracic surgery report persistent chronic pain after surgery. The opioid epidemic, we don't need to talk about that too much. It's a huge issue. There's been a number of studies in this population of patients, cardiothoracic surgical patients, in particular, showing that these patients at a higher-than-acceptable rate develop an unhealthy addiction to prescription narcotics after surgery.

So when you look at the market, in particular, the market in thoracic surgery, which is done again primarily through the ribs is being driven by the prevalence of lung cancer. So lung cancer screening, as most of you probably know has increased the identification rate of this disease, which is great for patients. It's led to an increase in the number of thoracic surgeries, with that comes postoperative pain. So again a significant percentage of these patients experienced postoperative pain and a significant percentage of these patients report an unhealthy addiction to prescription narcotics after surgery. That is our opportunity is limiting postoperative pain and better treatment for patients.

Sam Privitera^ And there's really three parts to this. First, a non-pharmacological solution. The second is making sure that we're very specific on the peripheral pathways that we're affecting. The third is to have a predictable response. So predictable in terms of the analgesia we provide but also in the regeneration of the nerves.

So the goal here is Wallerian degeneration. It's a grade two injury, where we're affecting the axons but we're not affecting the sheet and -- or the multiple sheets that are associated with those axoms. So we need to be very specific in what we do, and we need to make sure that what we do yield a regeneration that will give the sensation back to the patients.

The way that we go about doing that is, number one, using an optimized gas. So nitrous oxide that we use is at the right temperature. If it's too cold, like an argon gas, we can damage the sheet. On the other hand, if we're using gas is that don't get us to the right temperature, we can stun the axons have an effect the last couple of days as opposed to a couple of weeks. The second thing we do is we make sure that we're transferring that energy that heat from the tissue into our probe most efficiently.

So we have specific end effectors that are shaped for our application and conductive materials that allow us to form the ice as quickly as possible. We're transferring gas at a high rate. So we're creating that cooling effect very quickly. We have an active defrost allows the therapeutic effect to continue after the probe is removed and lets the user get to the next application. Then all of that is done with real-time temperature measurement that is actually accurate. Other technologies, crowd technologies, use surrogate measures for assessing what that temperature is. We're measuring right at the point of the tissue interface.

Justin Noznesky^ All right. So how did we get here? In 2015, we pursued our first indication for peripheral nerve block for treating postoperative pain. So that was done with our legacy AtriCure cryoablation devices, the same ones that are used for cardiac tissue ablation in concomitant cardiac surgery. Fast forward to 2019, between 2015 into 2019, we built the Cryosphere platform, the Cryosphere probe.

So that's a purposely built device specifically for doing intercostal nerve block, as Sam mentioned. It's designed for specifically ablating intercostal nerves during thoracic surgery. In 2023, we expanded the use of this platform in its open sternotomy procedures using a very similar application, and then in 2024, which Sam is going to talk about the products that we launched recently in the last six months here in a second. We launched the Cryosphere Plus and the CryosphereMax platform, which significantly improves the performance of the device, and Sam's going to go into that here in a second.

Sam Privitera^ So with our platform here with the Cryosphere platform, this is the first time we've created a device entirely towards cryoanalgesia. So the original Cryosphere wise, we took the cardiac probe, we modified the distal to facilitate in our costal freezing. Here, we've changed the device completely. We've optimized the insulation along the shaft to protect all the surrounding tissue that might be associated with thoracic procedures like lung procedures. The valuable zone, we made it easier for the user to bend to orientations that might be more specific thoracic than cardiac procedures, but for that shape to stay so they can apply pressure in the intercostal space, and then we've adjusted the tip.

And through all of that, we've found quicker time to temperature. We've been able to cut the therapeutic time itself from down to 90 seconds, and then we're defrosting quicker. That leads to roughly an 8-minute savings per side of the patient. Then we took that same device and we modified a tip from 8 millimeters to 10 millimeters did some other changes with it and this is now getting us down to a 60-second freeze. So it takes us 30 seconds to get from rib to rib, our ice formation and to make sure that wherever that nerve is between ribs, we're getting that nerve frozen at 30 seconds, then we hold for 30 seconds of therapeutic time for a total of 60 seconds. And so this is half the time of the original Cryosphere product, half the nitrous oxide used in a much more efficient procedure.

Justin Noznesky^ So in addition to product development in this area, there's been a significant increase in the science proving safety and efficacy and also a healthcare economic benefit and benefits to healthcare system.

So we've proven safety and efficacy in a wide variety of procedures in cardiothoracic surgery. A few of them are listed here on the left-hand side of the page, Pectus and nus, pectus excavatum chest repair for a patients, lung transplants, mid-cap robotics a wide variety of other procedures. The study we really wanted to highlight here is on the right-hand side of the page, this is a paper that was recently published by the Medical College of Georgia at the University of Minnesota.

So they took 532 patients. These are lung cancer patients getting a single lobectomy, matched 1:1 cryo nerve block versus no Cryo Nerve Block. What it showed is the significantly reduced length of stay significantly lower opioid use. The really exciting part of this was the long-term savings for the healthcare system. So over a 6-month period postoperatively, almost $15,000 in savings, cryo nerve block versus no cryo nerve block. So not only is it safe, not only is it effective, but it's saving the healthcare system money.

From a market development perspective to support all of our product development, all of the science out there and to really push this message out into the marketplace. We have a dedicated sales and clinical support team out in the field about 70 people dedicated just to this market. From a marketing and education perspective, one of the hallmarks of AtriCure throughout our history, it's been our physician education platform and programs.

We leverage all of that into this marketplace as well. We have a wide variety of ongoing field resource investments including the REDUCE clinical registry. So this is a company-sponsored registry our physician partners can put patient data into the registry and they can track outcomes for future publication support.

So with that, all of that experience in cardiothoracic surgery is now being leveraged into a new market, and we're going to talk about this here in particular, in extremity amputations. Then Sam is also going to talk about some next-generation product development that we have going on in this area and for a broader cryoablation platform. So if you look at extremity amputation, there's about 180,000 extremity amputations done every year in the United States. This is really being driven by the prevalence of diabetes and peripheral vascular disease. So think about a patient that has diabetes or lower limb disease, they're coming into the hospital, and this is an acute problem.

So typically, these patients need a limb amputated very quickly after they're diagnosed with peripheral vascular disease that's so severe that they're coming into the hospital. So you can see the breakdown in procedure types here on the right side of the page, but suffice to say this is a huge market. These patients are experiencing phantom limb pain. So phantom limb pain after an amputation is a huge problem. It's highly prevalent depending on what studies you read up to 80% of patients can experience phantom limb

pain after they undergo a limb amputation. So this is a huge issue for the system and a huge issue for patients.

Sam Privitera^ I started by talking about how we've moved from technology to technology application. We have a really good formula for how to do it. We get really close with clinicians that are experts. We study the anatomy, the physiology, we understand procedural application. And here with extremities, it's different, exposed nerve versus a nerve that's within muscle patients that may show up for a planned amputation versus a trauma, we had to go back and really understand the anatomy and physiology, understand how to engage in nerves, understand that these nerves can range from 1 millimeter to 20 millimeters and then come up with a technique and a design that will let us deal with that whole range of nerve sizes and then to be able to make the effect on the tissue that we see already in the intercostal space.

So we've come up with a configuration, we've worked really closely with clinical partners to do preclinical testing. We've completed all of that. All of our development is done. All of our manufacturing development is done. We've submitted to the FDA, and we're excited for having this first purpose-built extremities analgesia device.

Then beyond this particular application, we understand that there are more applications to come. We have big opportunities in this space. So we're developing a cryo generator system that will let us readily adapt to these individual applications to adjust our cooling parameters, the flow rates, time temperature and so on, specific to those tools and then to have the usability that we can go into an institution, train the team, that can become proficient at the procedure in a rapid way and then become independent of us quickly.

Justin Noznesky^ So to sum it up, this is a market in need. It's a market that is unaddressed by other technologies, and we're well positioned with differentiated products, clinical science investments sales, marketing and commercial investments to provide for a significant runway for continued growth. The kinds of opportunities that are out there expanding into extremities and potentially other applications down the road, that's our opportunity, and we're really well positioned to do it.

So with that, I think Angie is going to come up, and then we can take questions after that.

Angela Wirick^ Appreciate everybody's attention for the past almost three hours.

We'll have the management team available product demos available to go back into the room, if you like to, facility tours as well. Part of the reason we brought you here today was we wanted to showcase the bright future that we have as a company. You see large untapped markets already existing in AtriCure. You also saw a number of roads to expand our market through differentiated innovation in our clinical trials. That's been the basis of this program today. But what's even exciting above and beyond that is we're in a really special phase as a company as we start to see growth really complemented by growing profitability.

So AtriCure is and will always be a growth company, but you're also starting to see an improvement to the bottom line that we're really excited to share with you today. So we go back to the beginning of this decade, we started in 2021 coming out and saying, look, we are in a position where we're going to accelerate growth. We've delivered on that 19% CAGR over the past four years. We've also, in that same timeframe, expanded our product portfolio, a number of devices that you've heard today or on previous earnings calls, don't just benefit one quarter or one year. These are multiple years of growth driven by our innovation.

In that same course of time we expanded our investments in R&D. And as last year, we had 20% revenue reinvested in R&D activities. While that's a big expansion of our R&D initiatives at a larger scale in revenue, you also saw us achieve a really important milestone in our company's history, which was driving positive adjusted EBITDA in 2023 and 2024. It's a great setup. So we delivered on our commitment to accelerate growth. We also achieved and are driving improving profitability.

So we're off next with investors, with our analysts, people interested in the company, what is the strategy for capital allocation. I think this chart does a nice job summarizing primarily organic activities really focused on market expansion and driving adoption within each of the areas which we are providing benefits to patients.

So not stopping with the original clamp device in cardiac surgery and saying that’s a limitation to our long-term growth, something like an Encompass clamp where you heard the physicians talk about the speeds up and makes a procedure incredibly easy, it's a no-brainer for me to do, not stopping with innovation with our AtriClip devices continuing to make that device smaller, more usable, more effective.

So that has been our trajectory here. Innovate, study in clinical trials and surround each therapy with really robust training and education to drive adoption. That strategy has led to continuous and durable growth but also something that is the building blocks as you think forward.

So why many of you are here today we're here to share our vision, the framework that complements Vision 2030, creating standard of care what that translates to from a financial perspective. And this is an equally important part of our vision for 2030, really showing the value and the potential of our therapies.

So this past fiscal year, we had just under $500 million in revenue, around a 75% gross margin and achieved around a 7% adjusted EBITDA margin. As we work towards the end of the decade in the next three years, our goal, our target is $750 million plus in revenue in 2028, doubling our adjusted EBITDA margin to 14% and steady to improving gross margins as well as cash flow. Part of our guide for 2025 said AtriCure would drive positive overall cash flow in 2025.

What you're seeing here is an expansion off of that and building towards the end of decade target, so Vision 2030, creating expanding markets, building standards of care,

helping a lot of patients but doing so on a broader scale and a very profitable way. $1 billion in revenue is our target in 2030, nearly tripling our adjusted EBITDA margin to 20-plus percent at the end of this decade and most of that cash regeneration going back into the business. and the framework to carry us to $1 billion in revenue.

I think the good news is most of the foundational elements of growth already exist in the technology that we have today. You can see that on the far left-hand side there. But that doesn't mean that's where we're stopping. This innovation has multiple years of growth still ahead, which you can see continuous innovation as we work towards the end of this decade. You heard about a couple of them today just most recently, the Cryo-XT. You heard about the cryo platform, which will enable us to expand different opportunities, continuous generation of new AtriClip technologies, you also heard earlier a next-generation Encompass clamp. V1 was an excellent product. How can we make that product even better.

It's also nice to see at the end towards the end of this decade, some green shoots from the research activities that you heard about today. The BoxX-No AF trial two stages: first, studying acute post op-afib, having a PMA from that study by the end of this decade, but then also seeing letter by the end of this decade. And even more exciting is this is durable double-digit revenue growth. But as you exit this decade, you can see a number of the long-term investments that we're making are growth drivers for the company beyond 2030.

So what I hope you take away from today. We are excited for our future here at AtriCure, we brought you here because we're really proud of the company that we've built. We have an expanded portfolio, which gives us multiple opportunities to win in these really big markets. We are determined to drive growth and expansion as we operate and execute towards Vision 2030. Every day more than 1,300 AtriCure teammates get up every day very passionate about driving towards this mission. This is something that we talk about internally and has really rallied the company towards reaching and accessing these patients.

Financially, we've been known as a growth company. will continue to be a growth company, but also one that is driving enhanced profitability as we treat our patients, and it shows the value of our therapies at scale. Our focus is unchanged for our business, innovation clinical science, education awareness will remain at the forefront of our strategy for the rest of this decade. The why behind our mission is there's too many patients out there who could really benefit from our therapies and our technology and so many physician partners who are looking to AtriCure to help them give best care to their patients.

So I hope you share in our excitement. Thank you, everyone, for coming here today. I know it is a trip to make it to Cincinnati, Ohio. We do have some time for questions.

So I'll invite Sam, Justin and others up if you've got any questions.

Marie Thibault^ Marie Thibault from BTIG. A couple of quick questions, Angie. I wanted to quickly see if you were able to reiterate 2025 guidance. While we have you here and while we're talking about financials. Then secondly, is it right to think about an acceleration here toward the back half of the decade, it looks like you're talking about a little bit more of an acceleration. Maybe talk us through the cadence, I guess over the next five years as we think about 2030.

Angela Wirick^ No change in 2025 guidance.

I'll start there to answer question number one. You do see between the two milestones of 2028 and 2030 is a bit more of acceleration in growth. And part of that is the benefit of having data from BoxX-No AF thinking about more in earnest surgeons treating prophylactically those patients as well as LeAAPs.

So we'll have been through the trial, expect to have data before the end of the decade and believe that the data, like Dr. Whitlock said, will be incredibly compelling. You're also seeing a stack of innovation, thinking about our cryo franchise, for example, the growth that it drove year one, year two was excellent. But think about CryoXT for extremities and other things that will come contributing to growth as you exit the decade.

Lilia-Celine Lozada^ Lily Lozada, JPMorgan. Any chance you'd be able to share some more color how you're thinking about growth by segment qualitatively or quantitatively you would be willing to share and qualitatively some of the dynamics we should be thinking near to midterm?

Angela Wirick^ Yes. I'll leave the quantitative aspects to what we've already said relative to our 2025 guidance. We do expect as we're operating to the end of this decade and the $1 billion goal that each franchise is contributing to growth at the end of this decade. I think we know we're under pressure right now with hybrid. Our hybrid business is under incredible pressure with the distraction from PFA.

Our belief continues to be I think reaffirmed as of two positions you heard here today that there is a place for hybrid therapies. There are tons of patients in this particular market. There could be success for both PFA and AtriCure's hybrid program. So our expectation is, over time you will see hybrid continue to grow. In the near term, the growth drivers is similar to what we've talked about relative to 2025 guidance.

Suraj Kalia^ Mike, Angie, thank you for inviting us here and giving us a good overview. Mike, if I could ask you this 5-year LRP, how much of it is predicated on whether it's hybrid returning back to the original growth versus some of the new trials kicking in at least the incremental bolus. And as you lay out this plan, how do you factor in competition? There's been a lot of chatter of Penditure, right? And now there is chatter on Edwards tools I'm sure you know. Just walk us through how you came up with this plan given everything going on?

Michael Carrel^ Yes. I think I'll start, and I'll let Angie kind of add some context to it. We're very confident in the plan that you've seen in front of you today to get to $1 billion in 2030. I think it's everything that you just described. Now we've been conservative in the sense of the way that we look at all of those different markets in competition coming into the market, et cetera, I'll hit on each one.

So if you think about the clip franchise, what we saw when Penditure came into the market was what we talked about, which was that we going to acceleration in growth overall into that marketplace because having competition raises awareness. On top of that, we've continued to innovate with the Flex Mini device, which is a far superior device than anything else on the market. So we know we've got the best technology. You bring in competition, they are going to raise the bar overall in terms of awareness within this market whether it's Edwards or Medtronic or somebody else, we're expecting them to come to market.

As I said in my initial comments, when you're a leader in the field and you're developing that evidence and you're building that out, people are going to follow I've talked about it before. just look at the WATCHMAN market or the TAVR market. Both of those markets when a second level of competition came in, you saw accelerated growth rates in that market for a long period of time. We anticipate the same thing happening within the left atrial appendage management market.

Now we also have a benefit in that market, which is long term, as Dr. Whitlock talked about, there's not a class effect. When we get a stroke label, we will be the only ones in the market that have that stroke label to get and look at how you actually get that in the markets all over the globe because it is a global trial, and that will accelerate, we believe, the overall AtriClip kind of at the end of the decade and into the next decade, when you see data that is only applicable to the AtriClip device. So we're doing things to kind of help that competition. I think it's good to have it come in and raise awareness that help us beat the competition long term overall within that.

As it relates to hybrid, we've taken a very conservative approach as we kind of look at it. Do we think it's going to bounce back? Yes. We absolutely do think it's going to bounce back. We're not giving a specific date as we all know because you heard from that. It's going to kind of take some time for that huge tsunami of patients that kind of come through the funnel, but they are going to be coming through the funnel and actually have a benefit to us. whether that's in '26, '27, but you're going to start to see that and that does affect us kind of longer term with this. I think we have taken a very prudent and good approach, and we've got a tremendous amount of confidence to hitting that at the end of the decade.

Angela Wirick^ Yes. I think what's often underappreciated about our company is the ability to drive growth, and it may not come from the exact segment. We've had this discussion many times with investors from the exact segment, but you have multiple growth drivers within the business, that have delivered the numbers that we've committed have delivered to what we said we were going to do and that you can't get track record of

growth like you saw on the one slide that Mike opened with more than a decade, double-digit revenue growth, acceleration at a larger scale, and the continuation, our plan is a continuation of really strong double-digit revenue growth if you don't have multiple drivers within the business to get you there.

William Plovanic^ How should we think about the margin expansion by bucket? So whether it's gross, SG&A, R&D, where are the lever points, especially as you expand internationally and what have you on the gross margin?

Angela Wirick^ Yes. It's a great question. I'd say in the near term, with international outpacing our growth in the United States, it is a headwind when you think about gross margin. We do have some tailwinds with new product development that ultimately are accretive to the gross margin. So near term, I'd say very modest improvements to margin. We do expect over time that you're going to see more fulsome improvements, particularly when you start to manufacture some of these new products at size and scale. The way you get to the kind of the improvement to the bottom line is really driving enhanced leverage within SG&A.

So we've got a really robust sales and training teams. We've got what we need now. Yes. We'll continue to grow those based on overall kind of volume growth, but we've done the kind of the heavy lifting to get to this particular place R&D, while still a very strong investment anticipated in this LRP model, you will start to see R&D as a percentage of revenue moderate slightly down to the mid-teens kind of range. Look at a strong top line growth with strong to improving gross margins, real leverage within SG&A being driven and then let strong is mentioned R&D, but moderating slightly as you start to think through working through the rest of the decade.

Unidentified^ So I guess on that, all the new products coming in the plans out to 2030 how do you feel about capacity? Do you feel you build out manufacturing? Or I guess I haven't looked around the facilities yet, but do you have room or do you anticipate any large products, projects that might cause like a large cash outlay? Anything around there would be great.

Angela Wirick^ Yes. I'd say nice thing about this facility and some of the expansions that we've done since we've moved into this building almost 10 years ago now Sam, is we've got great capacity today. That being said, the team is looking further out and saying we've got big growth plans. So we are planning to expand our manufacturing capacity just south of here. We own some property there. And you may have seen that the state of Ohio and the city of Mason are supporting that growth with some grants.

So jobs based activity-based grants here. So we're financing that project. So that's not a big cash outlay for the company and ultimately, pretty moderate impact to margins that we expect to offset, puts us in a great position when you think about exiting 2030 to be able to handle capacity at even bigger size and scale than the $1 billion we're talking about.

If there were any questions for Justin and Sam, we did ask them to hold on that. If you had any questions about CryocXT this would be a time too. We just wanted to make sure we got through the materials. Yes.

John McAulay^ John McAulay from Stifel. Just one on encompass, actually, Mike, I can wait certainly better appreciating the impact that's had, procedure times, utilizing during CABG procedures as well at a greater rate than in the past. And maybe just if you could elaborate on where you are in terms of encompass adoption today? And where you see yourself throughout this LRP evolving? Or are we in the third inning, fourth innings in that terms might be helpful.

Michael Carrel^ I think you're in the early innings of it. What you've seen over the last really three years since we've had encompassing adopted is you're seeing kind of patients with Afib going from about 25% up to about 35% of those patients that are actually getting treated on that front. You've seen a nice uptick and really the fastest uptick that we've ever seen, quite frankly, in adoption, and Encompass has played a big role in that. But it's just starting to get adopted in a big way. As Dr. Soltesz said, he's now starting to train his residents on that at the early stage. That's really we're going to have a tremendous impact over the next decade or so.

So I'd say we're really more closely to the kind of second or third inning, to use your baseball analogy, even in just the Afib patients. I also think there's going to be a very large benefit from the trial box because what's going to happen is you heard Dr. Soltesz, it is the bane of the existence of a cardiac surgeon. They feel the pain for postop afib. They see the benefit longer term, but they feel the pain staying up nights, working weekends, coming in to see the patient, having to manage them more long term. You heard Dr. Soltez talk about that.

So they're going to now have a product to reduce that. And if we see anywhere near the results that you've seen in some of those trials, where you've gone from 40% down to 5%, you're talking about a huge time savings and quite frankly, something coming off of their backs and concern with the post-opera afib rate. I think that is going to be another reason. We've made it easy.

Now in addition to reimbursement, they're going to have actually a reason. I'm going to treat -- I think that's going to actually help our Afib adoption as well. And so I think you're going to start to see that kind of happen over the course of the next three to five years as we begin to roll out that trial. There is so much excitement with that trial because of it. So I think we're really at the early stages.

Angela Wirick^ Any other questions. Okay. I'll say it again. Thank you, everybody, for coming here to our campus. I hope you share in our excitement for the future. For anyone that can hang around, we're more than willing to take you back to the product demos. We've got the engineers back there at the table ready to go through that. And happy to go through a facility tour as well. Thanks, everyone.

Michael Carrel^ Thank you.