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TRANSCRIPT - GR 08 12 22 ***"Assessment of Myocardial Function, Viability, and Ischemia: Stress MRI"*** – Amit Patel, MD from the University of Virginia

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Okay welcome everyone.

- 00:17:51Hello hello, and then, welcome to those out in the zoom universe as well today i'm excited to introduce Dr amit patel.
- 00:17:59Dr patel completed his internal medicine residency at the University of Chicago he then went on to do a fellowship in cardiology.
- 00:18:08At temple university and then advanced fellowship and cardiac imaging and research here at university of Virginia.
- 00:18:15Then moved back to his Alma mater the University of Chicago to establish really robust research and clinical career, where he served as the director of the university's departments.
- 00:18:26Of cardiac MRI cardiac CT and cardiac pet lucky, for us, the cold weather, it takes a toll on everyone and Dr patel chose to continue his illustrious career back here at uva.
- 00:18:38You is appointed to the position of full professorship and joined our faculty earlier this year as the director of non invasive cardiovascular imaging.
- 00:18:48His research focuses on the development and validation of novel ma models to quantify cardiac function and the evaluation of myocardial scheming and infiltrate of heart disease, such as cardiac sarcoidosis in amyloidosis so please give a warm welcome to Dr amit patel.
- 00:19:13Well, thank you very much it's it's certainly a real privilege to be here University of Virginia and to speak to this illustrious audience.
- 00:19:26Is i'm going to try a little experiment with you, using these little qr codes.
- 00:19:32So i've put them all through through the talk so if is this one doesn't take you anywhere good, but the rest of them takes you to the actual paper that I might be referring to in case you wanted to learn some more.
- 00:19:46So here are my disclosures.
- 00:19:50Alright, so I think most of you probably know that the American college of Cardiology and American heart association recently published new guidelines on the evaluation of chest pain.
- 00:20:03And they think what they do is first of all divide chest pain into two different syndromes one being acute chest pain, the other just stable chest pain.
- 00:20:12And they'd make a lot of emphasis on not doing testing when it's inappropriate so, for example, asymptomatic patients and low risk patients, you would really need to do any any testing on them, however.
- 00:20:28In the situation, a chronic.
- 00:20:31Chronic chronic chest pain, you may take patients who are intermediate risk and or at high risk for having coronary disease and and.
- 00:20:39And need to do further non invasive imaging and this really what they do, that is very new and new to the field is.
- 00:20:49tell you that you can choose either anatomical imaging which really translates into coronary CT or you can do functional imaging and they group all the non invasive functional test together and so that includes stress MRI stress pet stress nuclear stress that go and even.
- 00:21:08Other other forms of stress testing, on the other hand.

- 00:21:12If you have a acute chest pain, then, if the patient is only an intermediate risk, you may consider either anatomic or functional testing, however, if you have high risk features or evidence of acute coronary syndrome, this is when you'd want to go straight for invasive coronary angiogram.
- 00:21:30Now I want i'm going to try to go a little bit into the weeds I don't know how many of you guys realized that.
- 00:21:37My credit perfusion imaging and stress testing much of that was invented or really mastered here at university of Virginia during the time of Dr George feller.
- 00:21:48And so I want to get into some of the basic principles that apply to really all of the stress test.
- 00:21:54first thing is that there's a relationship between the degree of stenosis that you have.
- 00:22:00And the type of abnormality on the heart, you may develop So if you just have a mile stenosis perhaps you will just start with a little bit of what we refer to as a profusion defect.
- 00:22:12As the degree of stenosis gets worse, you may develop diastolic dysfunction systolic dysfunction ekg changes and then finally chest discomfort.
- 00:22:24And we often in a stress test are going to try to bring out these symptoms, by introducing exercise to help enhance our ability to detect these symptoms.
- 00:22:36So with stress MRI, which is what i'm going to mostly focus on here we are really talking about my Cardio perfusion imaging and that's the same thing we're talking about when we're doing nuclear stress testing and so.
- 00:22:48So I want to take a moment to help explain how what the basic path of physiological principles we're taking advantage of when we do this sort of testing.
- 00:22:58let's take a healthy person who has no coronary disease, all of us in this room are resting my Cardio blood flow is probably one mil per gram per minute Okay, however, if we exercise then.
- 00:23:15We will have increased demand, and we will require more myocardial blood flow, so we have we tap into what we refer to as our coronary flow reserve to increase our myocardial blood flow three or four or five fold higher than normal okay now.
- 00:23:34Now that's taken a disease state so as the severity of coronary stenosis increases.
- 00:23:41It turns out during resting and conditions, there is no decrease in your myocardial blood flow, even after you get to an 80 or 90% stenosis there really isn't any decrease in your myocardial blood flow.
- 00:23:56And the reason for that is we are tapping into that coronary flow reserve or another term my Cardio perfusion.
- 00:24:03reserve to kind of keep.
- 00:24:07Maintaining that resting blood flow, but what that means is that, when we try to exercise we no longer have that capability, or that my Cardio perfusion reserve or that coronary flow reserved to increase our blood flow because we're using it up just to sit here in the room.
- 00:24:24Now, what are the consequences of that well when it's.

Unknown Speaker

00:24:28mild.

UVA ERC Room 2407

00:24:30We develop engineer or ekg changes, however, if it's very severe.

- 00:24:38You.
- 00:24:39For example, and someone who has.
- 00:24:42A 99% stenosis and their coronary artery having acute chest pain what you're going to see is a decrease in profusion of course and then you're going to have an associated decrease in function, however, once you revamp the rise, the patient, the perfusion will improve.
- 00:25:01However, the function may still remain decreased.

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Unknown Speaker

00:25:06Okay.

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UVA ERC Room 2407

00:25:09And this may persist for some, while on the other hand, in the situation of my cart of hibernating myocardial you have chronically abnormal or chronically reduced my Cardio perfusion This leads to chronically reduced.

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Unknown Speaker

00:26:36Okay.

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00:26:38Great So if you heard what I said.

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00:30:37Okay, yes.

- 00:30:42Yes.
- 00:30:45All right, so during the previous pause I told you, the secrets of life and in the last part I hope everyone wrote down the winning lottery numbers it's about $1 billion, so you can quit your job if you got those numbers, so I to the residency program everyone just walked out the room.

- 00:31:05All right.
- 00:31:07i'm just gonna I don't know where you stopped hearing me but appreciate that if you do have a severe stenosis essentially you're going to get.
- 00:31:17A lot less tracer going into the myocardial distal test of your stenosis you're going to get a lot more tracer going distal to a normal coronary artery.
- 00:31:28We cannot because of this roll off phenomenon here, we cannot actually measure how much blood flow is there, we can just look at relative differences.
- 00:31:38And this is going to really turn out to be meaningful, as you'll see here in a few slides i'm just going to look at the chat here great sense of humor Thank you.
- 00:31:49All right.
- 00:31:51Okay, in Mr so that's where this is supposed to be talked about MRI, and so what is the tracer we use an MRI.
- 00:31:58gadolinium we use gilliam based contrast agents, and this is a pair of magnetic agent which shortens T one times of nearby water protons and so essentially anything that shortens to one time will create a brighter signal on MRI So what we do is we.
- 00:32:19inject a visa director record Dennis on or adenosine We then inject the gadolinium and it's going to go wherever blood flows.
- 00:32:29And then we're going to take pictures of the heart we're going to get multiple slices of the heart every single heartbeat for many, many.
- 00:32:37heartbeats and generate a video so here just to show it to you slowly.
- 00:32:44You can appreciate here's, this is a cross section of the Left ventricle right here, and you see there's no white signal here so there's no contrast here.
- 00:32:52As we've injected the contrast you see it starts to show up in the right ventricle and then it starts to show up in the lungs here.
- 00:33:00Finally, returns into the Left ventricle and then starts to enter into the myocardial.
- 00:33:06As we go down further you'll see this area, which is a normal area takes up a lot of contrast, and has an increase in signal and this area out here remains dark or black, and this is territory is a schema.
- 00:33:22And we can look at that as as curves here, so you can see here's the contrast coming into the lb cavity the signal goes way up.
- 00:33:29And then, here it is coming into a normal tissue and then here it is coming into an abnormal tissue alright.
- 00:33:35So what does it look like when we actually do it in clinical practice like this, so this would be a representative slice So you see the contrast is for going through the different chambers of the heart.
- 00:33:44And then here in the anterior wall you see there's lots of contrast, coming up and then here, where the big arrows are.
- 00:33:50You can see that there's a large severe perfusion defect there and just for comparison during resting conditions, this is what it looks like and you see the blood flow is equal, the signal intensity is equal everywhere.
- 00:34:04And so here's the coronary angiogram and you can see, really severe coronary stenosis in the proximal and mid RCA all right now.
- 00:34:14Why is this any better than what we're already doing nuclear stress testing being the most common way we do it well, first of all.
- 00:34:22MRI has much higher spatial resolution.
- 00:34:25And I showed you that if you have one coronary stenosis you're going to get a decrease in blood flow in that territory, but in the second territory if it's normal you won't and you just look at the difference.

- 00:34:36Well, what happens if all the coronaries are severely stenosis everything is going to look exactly the same and we have.
- 00:34:42We will just say that Oh, it looks all the same, so it must be normal so that's referred to as balanced ischemia.
- 00:34:48Well, with MRI because it has very high spatial resolution you guys may remember from from Medical School.
- 00:34:55ischemia already always starts along the sub into cardiac and works its way out towards the outer boundary of the heart okay that's called the wave front phenomenon of ischemia.
- 00:35:07And so, with MRI and spatial very high spatial resolution, you can see here this black ring.
- 00:35:14profusion defect along the sub into carpe diem and it's failing the EPA carpe diem here, and you see that on all three slices on the stress images.
- 00:35:22And if you look at the rest images, it looks equal everywhere.
- 00:35:26And then, if you look at the nuclear image, you can see that you can't see anything this disease in its most severe form is invisible for nuclear at in some way, there are tricks, but in on big picture perspective it's hard to appreciate.
- 00:35:39And here, you can see the patient actually had a critical left means to gnosis which matched the anatomy the stress testing results.
- 00:35:48yeah no problem is when we inject the nuclear tracers they go into the bloodstream eventually gets collected up in the gallbladder and then dumped into the.
- 00:35:59into the bowels and in the bowels will oftentimes right up right against the inferior up against the diaphragm.
- 00:36:05right next to the heart and because the resolution is relatively poor, we can actually very easily differentiate part muscle from uptake in in the GI system.
- 00:36:15And so we can not appreciate what's going on here in the inferior wall similarly.
- 00:36:21Radio tracers injected into you goes to the heart and then the signal is emitted out of the heart to camera and then the camera captures whatever.
- 00:36:31radioactivity is coming out of the body, however, if there's something in the way, like breast tissue or a big abdominal gut.
- 00:36:40Then you'll the camera doesn't know why there's no signal there it just knows that there's no signal there and calls it, a defect.
- 00:36:46Well MRI you don't have that problem and so here in this patient which you would interpret the nuclear images as essentially normal.
- 00:36:53You can see on the MRI actually there was a severe defect here in the inferior wall and and the patient here has a severe coronary stenosis So these are kind of the technical reasons why.
- 00:37:04Stress MRI may be advantageous one of the data show when we actually compare different stress testing modalities again against each other, and I like to study.
- 00:37:14called a see mark study was published in The Lancet about a decade ago, and here every single patient underwent.
- 00:37:22They had chest pain that was their indication for entering the study.
- 00:37:26Every single patient underwent a nuclear stress test and MRI stress testing and invasive coronary angiogram it didn't matter what the non invasive tests showed everyone had to get all the tests and what you can see.
- 00:37:38Is that the sensitivity of MRI for detecting a severe stenosis is 87%, whereas the sensitivity of spect is only 67%.
- 00:37:48And this happens without a sacrifice of specificity and, if you look at the area under the curve, you can see the accuracy, the AUC value for stress memorize point eight, nine and for nuclear is point seven four.
- 00:38:01And this year's data from a Meta analysis of multiple stress test modalities and.

- 00:38:07Five different ones plotted here, and you can see that really these curves are dividing up into two groups, you have these two curves which clearly have lower performance and these other three curves up here.
- 00:38:18What are these two curves well that's those are stress ECHO and stress nuclear most commonly used stress testing techniques that stress MRI stress pet and even stress CT, which is an up and coming technology all outperforming significantly are more standard imaging test.
- 00:38:36Now we don't want to just know, is there a schema there or not we'd like to know how much ischemia is there because we believe the amount of ischemia correlates to how patients going to do and predicts their prognosis to some degree.
- 00:38:50And so here, these are data from the spins study, which is a about 10 or 15 centers across the United States all performing stress MRI.
- 00:39:01And you can see those patients who have no ischemia they have the best prognosis as you go from mild to moderate to severe burden of ischemia you can see that their outcomes are worsening in a stepwise fashion.
- 00:39:16And this holds true this prognostic ability holds true, no matter which subgroup of patients, you look at.
- 00:39:23Patients without a prior history of coronary disease patients with the history of coronary disease patients with normal ejection fraction abnormal ejection fraction prior Am I know prior Am I diabetes women obesity.
- 00:39:36All of these subgroups of patients have been tested at and consistently MRI is able to risk stratified these patients.
- 00:39:45Now, what we really want to know is, which patients need to be revascularization and the current standard.
- 00:39:55state of the art way of doing that is to do a coronary angiogram.
- 00:39:59If you see a coronary stenosis put a little wire through that coronary stenosis and measure whether the pressure drops off distal to the stenosis.
- 00:40:09And that would tell you that distance gnosis is hemodynamic Lee significant and that's called invasive FF R Okay, the problem with that approach is is invasive study and and it takes time and whatnot.
- 00:40:22And so here's a randomized control trial call the Mr informed state was published in New England journal.
- 00:40:29Three years ago now, here they randomized patients to get invasive FF are guided revascularization or stress MRI guided revascularization.
- 00:40:40And what you can see, is in the FF are guided arm everyone got an invasive corner angiogram obviously that's, the only way, you can do FF far.
- 00:40:49And then half the patients actually did not have Fr positive findings and half did, and of those patients who had abnormal Fr most of them were revascularization as you would anticipate.
- 00:41:01Well, what happened in the stress MRI arm well half the patients and normal stress MRI so they did not get an invasive coronary angiogram the other half got.
- 00:41:15Cast because they're stressed everyone was abnormal and 80% of those hat were confirmed to have severe stenosis and get re vascular rise.
- 00:41:23Overall, fewer patients were very vascular eyes in the MRI arm, then in the invasive Fr arm and that begs the question well did we miss critical disease and are we having poor are we going to have poor outcomes, because we missed that disease.
- 00:41:38And you can see, when you when these patients outcomes were followed for one year after after being enrolled in the study and being revamped guys you see their outcomes for exactly the same between the two groups, so we were not.
- 00:41:52hurting patients by not revascularization and by using a non invasive strategy.

- 00:41:58The next kind of major criticism we all hear about mris it's very expensive and we can afford to do it, and this is, I think a really nice study looking at.
- 00:42:08proving that concept to be incorrect indeed stress MRI use of stress MRI results in cost savings not cost increase, and this is just looking at the degree of cost savings across the world, and so, if you're in Europe.
- 00:42:21or in Mexico and you get a stress MRI your you if you use stress MRI instead of invasive coronary angiography you're going to have a 50 60% savings in the US, we would anticipate saving 40%.
- 00:42:34And then, Brazil, would be only about 20 30% savings, but still no matter what the healthcare system, there was a savings associated with the non invasive approach now.
- 00:42:47One of the major advantages of MRI is that it can be very quantitative okay I showed you that we generate these curves and they represent the amount of ischemia that is present present.
- 00:43:02And if we would apply mathematical modeling to these curves we can actually quantify myocardial blood flow and milligrams a milliliters per per gram per minute of units and So what does that look like so here.
- 00:43:19First of all, let's look at this example on the bottom left this is resting blood flow it's Nice and equally Gray everywhere, and then you look at the stress image.
- 00:43:29The Gray parts look exactly the same than theirs is darker area, right here, which is a scheme yeah.
- 00:43:34But if you look at the great part looks the same you can't tell that actually this has increased in blood flow relative to rest.
- 00:43:41But let's look at the quantitative blood flow map you see it's green everywhere and green let's say equals one meal per gram per minute a blood flow.
- 00:43:50And then at stress look at this normal area becomes orange which corresponds to about three meals per gram per minute, so we can see that the blood flow actually increase from one to three here.
- 00:44:00And here in this schema segment it remained green so continued to be abnormal OK now let's look at the situation of triple vessel disease so here, you see, is equally Gray.
- 00:44:10You can appreciate here, there is a profusion defect everywhere Okay, but look at the blood flow it's green at rest and it remains green at stress the blood flow doesn't increase at all and that's because this patient has severe.
- 00:44:24stenosis involving all three coronary territories, and this is just looking at the stress my Cardio blood flow measurement here and healthy volunteers, you can see, goes up to about three and a half during stress and then a patient with coronary disease, it remains at one.
- 00:44:42Well, this is important because now, you know we were University of Virginia and we.
- 00:44:48helped develop this this technique here at uva.
- 00:44:51But how do we get it everywhere, because there's not that much expertise and it turns out, these quantitative maps help a less experienced.
- 00:44:58person perform, as well as a more experienced individual So these are different levels of training Level one level two and Level three and and you know, Jonathan pan here's level Point five.
- 00:45:11down here, but when you which which you can see is that the quantification performs as well as a level three expert.
- 00:45:22And outperforms a level two and Level one train person, so you can see how this technology is going to really.
- 00:45:31Make make make make dressing room more available other places, now, when I was an imaging fellow here at the privilege of of.
- 00:45:41Of course, learning from Chris Kramer and working with Dr Fred Epstein here who'd actually developed a some of the early ways of quantifying my Cardio blood flow.

- 00:45:53And, and what we wanted to understand what was the other clinical added values of quantifying the the blood flow.
- 00:46:00And so, if you look at these images in this patient underwent stress MRI you can see there's a perfusion defect down here in the Info lateral wall and here.
- 00:46:08This would correspond to a single vessel coronary disease, a SER complex tear to circle FLEX to gnosis.
- 00:46:14And and that's great we might medically managed single vessel disease, however, when we quantify the blood flow actually all of these red areas.
- 00:46:21Were abnormal and and you would have anticipated that the patient actually had severe three vessel coronary disease and sure enough when we did there coronary angiogram they had severe three vessel coronary disease.
- 00:46:34And, and what we found was that when you looked at, when you divide it.
- 00:46:38Patients at between those three vessel disease and those who had single vessel disease and just look at the images.
- 00:46:43which you would find is that the qualitative estimate estimation of how much scheme and you saw was the same in patients with single vessel and three vessel disease.
- 00:46:52However, when you quantify the blood flow, you will see that patients who had three vessel disease had extensive Ischia.
- 00:46:59Whereas those a single vessel only have a little bit of a schema as you would have expected, and so the quantification lets you better distinguished between patients with single and triple vessel disease.
- 00:47:11And, and this was shown again just a couple of years ago, using far more sophisticated techniques and we were using 15 years ago.
- 00:47:20So the concept holds true and it turns out, it also is true with other imaging modalities like stress pet so it's really a universal.
- 00:47:28thing that's happening now, this um, so I think we're as we start to enter the world of quantitative profusion imaging we want to ask again, what does this last predict outcomes and here you can see.
- 00:47:44Depending on the stress myocardial blood flow you're able to achieve Sure enough, those who individuals who achieve higher blood flow.
- 00:47:52have better outcomes than those patients who don't achieve as high of a blood flow.
- 00:47:56And what you thought what we find is that for every meal per gram of minute decrease in your stress my Cardio blood flow.
- 00:48:04there's a two fold decrease in the death rate, so I think that the the the amount of ischemia you, you can get it is indeed a very important prognostic Lee.
- 00:48:15Now, most of the talk up to this point has been focused on.
- 00:48:20detecting obstructed coronary artery disease or epic Cardio coronary disease and here's just an image of what the EPA Cardio coronary arteries look like.
- 00:48:28However, the vast majority of the coronary circulation is in the micro vasculature and here's an image of all the micro vessels that we're not even talking about Okay, well, it turns out, when we quantify myocardial blood flow, we can.
- 00:48:42start to understand what's happening in the micro vasculature.
- 00:48:46And, and I think it's increasingly being recognized that we need to know what's going on in the micro vasculature and there's many disease types like patients with diabetes insulin resistance chronic kidney disease.
- 00:48:59Actually, women, many women in general who can have coronary micro vascular disease and and it's and as we.

- 00:49:08start to identify which patients have it, there are a lot of therapies you can't stand a micro micro vessel, of course, but there are a lot of other therapies like St lt two inhibitors.
- 00:49:19out that tone that can potentially treat this micro vascular disease, so there is a need to detect it.
- 00:49:27And indeed, no matter what degree of epic Cardio coronary artery disease, you have the presence of micro vascular disease in the severity of that micro vascular disease.
- 00:49:39Is adds it provides additive risk to the to the patient now with my blood flow assessment, I showed you.
- 00:49:49That we can a healthy individual may have a blood flow around three three and a half a patient with severe coronary disease will be considerably lower well, it turns out, patients with micro vascular disease fall smack in the middle of those two groups, so we.
- 00:50:04are in a position to really find cut off values, where we can say Okay, no you don't have micro vascular disease, and you have micro vascular disease or you don't have micro vascular disease, you have EPA cardiac coronary disease.
- 00:50:17And so I think a lot more research is needed in this area, but this is very promising.
- 00:50:22And I think this is a data from Fred Epstein here who like I said, has pioneered a lot of this work, looking at detecting.
- 00:50:31myocardial blood flow in mice believe in, and I assume stress MRI and mice and and and.
- 00:50:37feeding them a high fat diet and what you can see, first of all is that when you feed these mice a high fat diet their.
- 00:50:44Stress blood flow decreases considerably, however, if you treat them with in this case at plant known you regain some of that.
- 00:50:54myocardial blood flow, so you you he's starting to show that there are treatments that it can improve your micro vascular function or your your my Cardio blood flow.
- 00:51:04Now this says Well, this is now we can start to really understand other diseases like let's there's a pandemic going on right so coven, we know that covert.
- 00:51:16The virus infects the endothelial so we would be led to believe that it causes micro vascular disease.
- 00:51:25And maybe all of us have had covert and so now we're left to wonder well do we all have micro vascular disease well.
- 00:51:34We we studied this we took patients who had mild coven who are not hospitalized just you know stayed at home.
- 00:51:40didn't show up to work and what you can see is that doing resting conditions both Kovac patients and people who never had coven had the same resting mark aria blood flow.
- 00:51:51They also had after you know few months of recovery, the same stress my Cardio blood flow and the same myocardial perfusion reserves, so this is maybe reassuring to some of us to know that.
- 00:52:03Perhaps when we have mild coven we aren't developing.
- 00:52:07Micro vascular dysfunction now we don't know about what happens when you have more severe covidien you're hospitalized and that sort of thing but but we're starting to be able to understand really specific pathophysiology issues now.
- 00:52:22Stress MRI is not just perfusion the exam takes when we do it efficiently 30 minutes.
- 00:52:30In addition to all this perfusion stuff I showed you we also look at function and viability and scarring Okay, and so i'm going to switch gears a little bit and talk about that So how do we measure function with cardiac MRI well we get videos like.
- 00:52:48shown here okay dynamic beating heart images of the beating heart.
- 00:52:53And then we essentially get these images starting all the way in cross sections from the apex of the Left ventricle all the way through the base of the heart, we look at every centimeter of the heart.

- 00:53:04And then we get a series of cross sections, as shown here and we simply draw the a circle around the end of cardio boundary any of us can see where exactly to draw that circle.
- 00:53:15We know the area inside the circle, we know the thickness of the slice so we know the volume there we add all these different volumes together, and now we know the total volume.
- 00:53:25If you do that, and I asked Italy and you do that in Sicily, you can very easily calculate the ejection fraction and I would propose that anyone can figure out where to draw this circle okay.
- 00:53:36And so it turns out, we can all do this extremely reproducibility so the measurement is accurate and precise.
- 00:53:43And what does that mean well if you wanted to let's say design a study, where you intended to detect a 3% change in ejection fraction.
- 00:53:52If you use cardiac MRI as your marker to measure ejection fraction you only need 15 patients in your study.
- 00:53:59Well, how does that compare to mugu or ECHO, while you would need 40 patients, if you use makkah and you need over 100 patients, if you use the ECHO so that just tells you something about the precision of the measurements right.
- 00:54:12almost always where do we get our ejection fraction from ECHO and every time i'm rounding i'm asked well how does this, Mr what's more accurate the MRI measurement or the ECHO measurement because they sometimes different from each other.
- 00:54:24And so here's a study of several hundred patients, looking at the correlation between the ejection fraction.
- 00:54:31These units are wrong, the ejection fraction measured by MRI and ECHO and you see that the our value is only 0.66 so just a modest correlation in the ejection fraction between the two modalities.
- 00:54:43And indeed, if you look on the bland all in plot, you can see that you can have a plus minus.
- 00:54:4915 or 20% difference in your ejection fraction measurement if you start to go patient by patient.
- 00:54:56Now, I think we can do better we do better than this here and our data is better than this, but this is what's out there in the published literature.
- 00:55:03doesn't matter, so what we don't measure the ejection fraction very accurately who cares well look what happens here if you divide patients up is by by those who had an E, F greater than 35 patient.
- 00:55:17Up 35% as determined by ECHO, of course, the patients do better than those who have less than 35% ejection fraction, but when you.
- 00:55:27Make the measurements that, in the same patients using MRI you see the two curves separate a lot more, and so this is telling us we're better classifying your patients risk with that more precise measurement.
- 00:55:41Now, one of the challenges is that making these measurements can be extremely time consuming and and, frankly, as we get busier it becomes harder and harder to make these measurements in a timely fashion and so.
- 00:55:54With the with the artificial intelligence really being pervasive in medicine, now there are many software's that just do this automatically they've been trained.
- 00:56:07To make the measurements without user interference and what you can see, is when it comes to measuring left ventricular ejection fraction actually the software's do quite well they clearly better with.
- 00:56:20MRI gold standard measurement than the ECHO does you can see our values of point nine three and pointing three here so quite quite good, what about the ability to predict outcomes so here's our speakers showing.
- 00:56:31That the ability of the software automated measurement from the software is every bit as good as the clinical expert when it comes to predicting patient outcomes.

- 00:56:42well.
- 00:56:44We know that systolic function, what about diastolic function, we know that that is also very important, if you wanted to do it by MRI you'd have to just draw these little circles and every frame of.
- 00:56:55The cardiac cycle and would take almost an hour to make the measurement but with the software, it can do it automatically and generate these time.
- 00:57:03volume curves and from these curves we can measure things like the time to peak filling the diastolic volume recovery and variety of other measurements related to diastolic function and and these.
- 00:57:16measurements made by MRI correlate very nicely with the ones that we would normally get on ECHO.
- 00:57:22But with artificial intelligence, maybe we can do better so here, this is a great study published in the European heart journal, just a few months ago, where they took.
- 00:57:34Almost 1000 patients they trained and algorithm all of these patients had a calf and an MRI within a week or so of each other.
- 00:57:42They measured the wedge pressure and then they trained an artificial intelligence algorithm to use the MRI images to predict what the wedge pressure would have been.
- 00:57:52And then they tested it in the algorithm the patients, and so they derive this formula, so you all you need to really calculate your left atrial volume and your left ventricular mass and you can from that generate the wedge pressure.
- 00:58:08Now, so how does that happen so we shortness of breath so here when they tested it for patients with shortness of breath and suspected heart failure, you can see that.
- 00:58:19Several patients had in determinant using kind of this, the current standard.
- 00:58:25ECHO approach, about half the patients had kind of an indeterminate assessment of diastolic function, however, when you applied them to MRI we could reclassify a lot of these.
- 00:58:36indeterminate patients as having or not having diastolic function and Sure enough, the the the the you can see here the accuracy.
- 00:58:48Of this formula was about point eight one on rsc analysis so that's not bad it's not perfect, but it's not bad.
- 00:58:55And it did, allow us to risk stratify patients and and predict Sir survival so that's a good step in the right direction, are we all the way there yet, maybe not, but this is a big step forward now.
- 00:59:07I don't know if any of you ever had an MRI it does take a long time and it's many breath holes that are taken, in fact, to get this one.
- 00:59:16Data set oftentimes takes five to 10 minutes to get just those functional images and and here.
- 00:59:24Craig Meyer who's number one the biomedical engineers here at university of Virginia he's developed a technique.
- 00:59:30to actually do this without having to hold your breath in 45 seconds, we get all of these images of the entire heart so we're drastically changing what's going to become possible and just probably in the next five years.
- 00:59:45Now many of you, you know know have heard of a new kind of functional parameter referred to as strain in cardiology oncology this is now.
- 00:59:55kind of a preferred measurement that we like to do to track chemotherapy toxicity a variety of other conditions where where we like to measure strain.
- 01:00:04So what is strain well here's just a cartoon of the myocardial what i've done is i've drawn a little diamond here.
- 01:00:11As the ventricle contracts, you can see, this diamond gets stretched out so in this if it gets stretched out in this direction that's.
- 01:00:19referred to as Radio strain and but then you can see in the opposite direction and actually gets thinned out and that's referred to as circumstantial strain.

- 01:00:29So if you can do this in the third dimension in the longitudinal direction and calculate longitudinal string So these are kind of really.
- 01:00:40allows us to understand what's happening with the contractility of the myocardial itself let's say so.
- 01:00:47here's just kind of we can do that, we can actually make this measurement from these same sending.
- 01:00:52Images a functional images that we acquired routinely on MRI using a technique called feature tracking and here you can see.
- 01:00:59A healthy heart there's no scar tissue here, and you get a global longitudinal string value of minus 19% which is normal, on the other hand, here's a very diseased heart in the patient who has terrible cardiac sarcoidosis and they you get a strain value of minus 12%.
- 01:01:18Now it turns out that the strain measurement has its own prognostic ability, above and beyond ejection fraction so here, you can look at a study of a little over 200 patients.
- 01:01:32In this top group here our patients all of them have an E, F less than 35% and you can see, if your strain is relatively preserve your prognosis is good if it's bad if your prognosis is worse and that holds true even if your ejection fraction is higher, so the value is independent.
- 01:01:51Now again i'm so privileged to work with the biomedical engineers here they've actually developed fried epstein's lab again is developed a way to track the strain and every single pixel.
- 01:02:03Of the heart and so here, you can see the strain being measured very precisely in every voxel of the heart, and this is.
- 01:02:11All work coming from here at university of Virginia now I talked a lot about the way the gadolinium enters the myocardial.
- 01:02:20But it turns out the way it leaves the myocardial is also important, so in healthy tissue after you inject gadolinium it's going to refuse into the myocardial and then after 10 minutes it's going to start to wash out.
- 01:02:32However, if there's myocardial damage there the gadolinium is going to get stuck behind and then, if you image.
- 01:02:40The heart 10 minutes 15 minutes after you inject gadolinium you're going to be able to identify all the areas of the heart muscle that actually have injury within the muscle people refer to this as a virtual histology.
- 01:02:54And so here's just an example, this is a work seminal work done at northwestern where.
- 01:03:01They take a canine model here of myocardial infarction, and so this is a ttc stained heart here.
- 01:03:07And then next to it is the actual ex vivo MRI image and zoomed in you can see, this is the actual scar, this is the MRI image of the scar and I would tell you that I would say that those look awfully the same to each other, so this is a very.
- 01:03:23Precise accurate way to detect myocardial scarring and it turns out, when you look at the muscle, the more scar tissue is there.
- 01:03:33Well scar tissue is injured or dead myocardial essentially and so.
- 01:03:38If you if you have a lot of scar tissue there, and you try to revascularization that territory it's not going to get better because it's all scar tissue.
- 01:03:45On the other hand, if you have very little scar tissue there, and you read vascular eyes, a coronary artery supplying that area it's going to.
- 01:03:53It doesn't have scar tissue there, so it will improve that's the hibernating or stun myocardial I talked about the beginning of the presentation.
- 01:04:02So a couple of example this patient had severe chest pain didn't come to the hospital for a week many weeks later, and you can see.

- 01:04:13This is her to Chamber three chamber for Chamber views of the heart and the first thing you can see it's not squeezing very well at all, this is a severely abnormal function and the myocardial is extremely thinned out here okay.
- 01:04:28What does the scar imaging look like so here it's called late gadolinium enhancement another term is delayed enhancement delayed hyper enhancement hyper enhanced they all mean the same thing.
- 01:04:37And what you can see, is this big white.
- 01:04:40rim of a cold lake i'm asking all the way in this kind of thinned out territory that's a large massive transmissible my car infarctions completely scarred out there's nothing.
- 01:04:52No revascularization you can do to help that thing contract more it's all scar tissue.
- 01:04:57So let's look at another example is another patient I saw again this heart is also severely dysfunctional maybe 20 25% maybe lower okay.
- 01:05:08But when we did there late gallium enhancement look at the myocardial it's black everywhere, so there is absolutely almost no scar here in this ventricle recent this patient for a cabbage bypass surgery and look.
- 01:05:23A huge improvement in their cardiac function almost totally normalized from 20% to probably 60% there, so the viability helps a lot now.
- 01:05:35This is just kind of a paper published in JAMA which really illustrates in a more systematic way they took a group of patients, all of whom had very thin myocardial.
- 01:05:48which normally you would assume to be dead and what they found was that if less than half the wall thickness was scarred and they revascularization there.
- 01:05:58The wall actually plumped up and started to function better, on the other hand, if the wall had more than half the wall with scarred it never improved.
- 01:06:08And then you could kind of just look at how much overall scarring there was on the heart and the less scarring there was them, the more the ejection fraction improved following revascularization.
- 01:06:21Now the beautiful thing about the technique is that I talked to you about earlier how it has a very high spatial resolution, that means we can actually detect a small it's amounts of scar tissue so here.
- 01:06:33Again this data collected northwestern showing literally small myocardial infarctions here here, and here, and on the MRI you can see it very nicely detects all of these small areas of scarring.
- 01:06:49None of that those small scars are detectable by buying a nuclear imaging.
- 01:06:55So it doesn't matter well yeah it turns out, it does, these are oftentimes referred to as unrecognized or my current functions, because you don't see them on ekg you don't see a wall motion abnormality.
- 01:07:06But you can detect them on MRI and it turns out, if it from the spins registry, we were able to show.
- 01:07:12That, of course, if a patient had no MIA at all their prognosis was better than if they had evidence of a prior myocardial infarction This is called a recognized EMI.
- 01:07:24However, those patients, we did not know that they had an MRI but they incidentally had one discovered on on MRI.
- 01:07:30You can see their prognosis was equally as bad as those patients who had a recognized my current production so just because you didn't know that you had an EMI doesn't matter it's still just as bad for you.
- 01:07:44And it's important because look what happens to how we treat these patients, when you have a patient who has a known EMI you're going to give them aspirin.
- 01:07:52you're going to give them a Staten you're going to give them beta blockers etc, but.
- 01:07:58These patients who had unrecognized myocardial infarctions well we didn't know they had an infection, so they weren't getting any of the appropriate medical therapy.

- 01:08:06And, and of course this means that there's a real opportunity for us to provide real guideline directed medical therapy to these patients in whom we recognize the scars.
- 01:08:17Now, one of the challenging things is that we would like to quantify how much scar tissue there is exactly because in a whole host of cardiac conditions hypertrophic cardiomyopathy cardiac amyloidosis cardiac sarcoidosis.
- 01:08:33Non schema cardiomyopathy in all of these conditions, the amount of scar tissue you have directly correlates to your prognosis.
- 01:08:41However, to actually measure and quantify the amount of scar tissue you have is extremely time consuming, and if you start to try to manually measure diastolic function systolic function, the myocardial scarring.
- 01:08:54One case is going to take you easily over an hour to interpret and that's just not a clinically viable solution and so again to brag about my my colleagues here at uva.
- 01:09:06Miami I was saying in our lab again using artificial intelligence to automatically identify this scar tissue and to quantify and here just preliminary data.
- 01:09:16giving us a lot of hope that she's gonna really be able to allow us to do that automatically so i'd like to summarize by saying that typical stress MRI provide you information related to ischemia function and viability.
- 01:09:32It allows us to accurately.
- 01:09:35For the accurate detection of chemo dynamically significant epicurious coronary disease, and we hope micro vascular disease.
- 01:09:44It can help us guide our revascularization strategy, it allows us to accurately and precisely assessed both global and regional cardiac function.
- 01:09:54It can allow us to accurately detect my Cardio scar and us assess for my Cardio viability and the technology comes with a very large body of prognostic data now, and with that i'd like to say thank you very much and be happy to answer any any questions.

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Unknown Speaker

01:10:22In.

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UVA ERC Room 2407

01:10:27The chat here they're definitely some questions related to microphone problems, hopefully, they were resolved.

- 01:10:35So, Dr Lindner who actually just joined us in cardiology as well and tremendously brilliant echocardiography for doing amazing research as well, you should meet him nicest person he says.
- 01:10:48it's important to realize that the advantage of see Mr over to over ECHO for ldf ld volumes.
- 01:10:55etc becomes negligible when contrast ECHO is used, which it wasn't in the pond Thank you Dr Lindner yes, it is true, we can improve our ability or ECHO image quality by using ECHO contrast, and so I think it's really key that.
- 01:11:14You know we're working with our snog refers to really use that more often, because what we don't want is you send the patient for ECHO, we should be giving you guys the best possible answer.

- 01:11:25That we can without saying oh bring him back for another ECHO or now send them for an MRI whatever test you decide to send the patient to we want to be in a position to answer the question as best as we can.
- 01:11:45Thanks Adam tell really interesting talk.
- 01:11:47I know a lot of work being done from the city side on like plaque characterization hires features for ruptures or anything that we can do from an MRI side.
- 01:11:55To take a look at the plaques themselves, or is it more the my party and then we're looking at yeah that's great, so I think.
- 01:12:02We can look very accurately at plaque, especially when you start looking at the carotid the femoral arteries the order Dr Kramer is.
- 01:12:12Really, and others here have done a huge amount of work really characterizing the chronic component of a of a plaque and the hemorrhagic component of a plaque and.
- 01:12:24The soft limit component all of that can be done in the coronaries you know they're only like three millimeters.
- 01:12:31Around and spatial resolution of MRI is good but it's not as good as CT, as it turns out, and so it's a little bit more challenging.
- 01:12:39Several sites have used gadolinium because I get a lineage will be taken up into inflamed territory tissues as well and use lake enhancement to kind of look at.
- 01:12:50part are vulnerable plaques in the coronary tree, I think you bring up on the CT side they're really interesting area.
- 01:12:59Because I think there's a shift that's happening right a scheme IA and civilian stenosis is really about symptoms and improving.
- 01:13:09Our symptomatology and the disease itself is actually happening at the plaque level.
- 01:13:15And so we're now in a position with coronary CT to understand how much atherosclerotic plaque is there, how much disease is there and is the plaque calcified meaning.
- 01:13:24it's healed and not likely to progress, or is it still a kind of a limited late in plaque that is going to progress if you don't treat it aggressively with.
- 01:13:35status and PCs canine inhibitors are what whatnot so, so I think plaque stay tuned there's a lot happening with our ability to detect coronary plaque now.
- 01:13:50Alright looks like a.
- 01:13:53Question from.
- 01:13:55Dr Wang, thank you for.
- 01:13:58continents.
- 01:14:01may have been discussed earlier before I signed on any issues getting these MRI studies and patients with icd pacemakers and other.
- 01:14:11metal devices instance that's a great question traditionally we have felt that I CDs cerebral aneurysm clips pacemakers a lot of these things were contract indications for MRI turns out that that is probably that is not true.
- 01:14:31You can image almost any modern day icd with MRI, especially at 1.5 tesla maybe not three tesla.
- 01:14:40pacemakers We just need to have proper safety protocols in place and make sure we've turned off the defibrillator, for example, before we put them to the MRI scanner because the.
- 01:14:51radio frequency pulse of the MRI scanner is really fast and then a defensible thing gets vt and shockey and that's not ideal.
- 01:14:59And so we need to turn off the defibrillator reprogram it so that the pacing functions are kinda all stabilizing the environmental field.
- 01:15:08The magnetic field, but I think we can do it safely the the technical issue is availability and access it does require coordination.

- 01:15:17From the EP lab you need nursing support a CLS certified individual to be hanging around, and so, so it takes time and coordination, but definitely can be done safely and and in fact we do it all the time now.
- 01:15:38Alright well.
- 01:15:40yeah one more question.
- 01:15:43So I just have a question kind of focus towards your career a little bit.
- 01:15:49You know MRI certain at this point in my training i've seen a lot of interest put into cardiac MRI and it seems very intuitive to me that Oh, of course, taking more detailed pictures of the heart is always going to.
- 01:16:04yield better results for our understanding with trauma patients you've been doing this now for close to 10 years, maybe a little over 10 years.
- 01:16:12Was it is obvious to you getting into this as a young researcher that this was going to yield clear results or was there kind of doubt in the beginning of your your research career yeah I think.
- 01:16:26The first time I saw an MRI image of the heart was when I was applying for a during my medicine residency in 2000.
- 01:16:38And the minute I saw that slide I showed you about the myocardial infarction I had no doubt that this technology is something special and.
- 01:16:49By the time that image was published and that type of data could be collected my mind my mentor Dr Kramer had been doing them or I already for 15 years or 10 510 years before that so so really.
- 01:17:06I think MRI that what limits it real right now is at first was politics between departments, oddly enough, it go figure, and then the expense of the MRI scanner itself, these are you know, two $3 million dollar scanners sometimes.
- 01:17:24though they are everywhere and then having trained physicians to interpret these studies, I think we have a huge shortage in expertise and then actually the technologist you need technologists that can acquire these images and.
- 01:17:40You know and and and there really aren't formal training programs for people to go to and really learn how to acquire these these images.
- 01:17:50But I think at this point.
- 01:17:52I would be willing to bet first of all in Europe MRI is used far more than it is here in the US, I don't know why.
- 01:18:03And secondly, I would say, currently probably every major academic Center in the US has access to cardiac MRI and increasingly every large cardiology practice probably has access to cardiac MRI, so I think the technology is here and it's growing rapidly, but still has long, hard to go.
- 01:18:30Right well Thank you everyone and really appreciate.
- 01:18:35You joining me here today and inviting me to speak and all the good questions.