

Thanks, Steve. We'll switch around and talk a little bit about ultrasound and maybe carry on a little bit with the theme of can we do better. A lot of people associate ultrasound with relatively poor resolution but I think if you look at some of the images that can be acquired in, let say in the first 5 centimeters from the skin line, ultrasound does a quite nice job. I'll talk about here is a little bit about the clinical applications emphasizing, I guess, the peripheral nature of ultrasound. I'll also talk a little bit about scanners specifications to get..kind of set your stage as to what the performance is going to be like for an ultrasound scanner and where the limits might be. I'll review a little bit about instrumentation and particularly the use off coded excitation, something that would give ultrasound a chance to get to even finer resolutions. And the use of the coded excitation, I'll make a case of some novel flow display techniques that we do, and finally finish up with what we can do with some of that higher resolution work.

I'll just skip that one fairly fast but ultrasound methodology, I mean I..I think the two big tools that I'll be talking about are B-mode imaging and Doppler. So here's a nice right common carotid artery. There's a rather sizeable plaque there. There's a centimeter..centimeter scale here so that's for 4 centimeters. The diameter's in the order of .7, rather 7 millimeters, in that ballpark. And there's this big hulking plaque here and as you look right there in the middle there's a big hole wear, and it's a ruptured vulnerable plaque. The cap has broken off right at that spot. The..if we now turn Doppler on, we get this rather nice image of the flow that's happening in the vessel, the flow is going in this direction. You can see that there's actually communication with the inside ear because we're getting a swirling blood here. The color change corresponds, you know, one blood is going away, one is moving towards the transducer. There's a high speed area right in the middle. And what's really kind of neat is the swirling pattern here where you can

actually see the individual swirls and eddies that this plaque is generating, you know, in this constriction plus the added swirl coming from here. So you can get a good idea of..of what's kind of happening here. All of this stuff is happening inside a blood vessel in the order of 6 to 7 millimeters. So obviously the needs that we have improve resolution, I guess you never have enough resolution as well as greater penetration. Those are the two big challenges on the B-mode side. On the Doppler, the speed of sound unfortunately is pretty slow. So since we have to acquire a lot of data to generate this info, we run into frame-rate problems, and we will need more and better detail flow information. I'll show you some techniques that we've come up with. To give you some of the numbers involved here, for most of the instrumentation out there right now, people use 5 megahertz for perhaps leg veins to look at deep venous thrombosis, and one of the manufactures has come up with a 17 megahertz device. We don't have too

much data on that yet but the typical numbers that you would get with, let's say a 5 megahertz you can easily go well past 7, you probably can go to 10 centimeters. With the 17, I'm not too sure you're going to go much more than 2 centimeters into tissue. This number actually we can probably beat. We're probably closer to 100 microns in terms of lateral resolution. Let me emphasize here in the terms of fairness and honesty, these are test tank numbers and what quite often happens to ultrasound as it propagates in human tissue, not only is there a Beer's law kind of an attenuation that reduces the effective operating frequency but there are also refractive effects that will distort your beam so you will lose resolution as you go into the body. But this is what..what kind of numbers we can get in a glass patient. Aperture size on a typical scanner, this

is..that's available today, it's about 25 millimeters. Now with some of the scanners that are very shortly coming out, that number can probably be doubled. And if

you loo..just look at a quick sketch approximation here for the ultrasound beam with its wave length times the focal length divided by the aperture, and of course that's equal to wave length times the f-number. So right..in today's systems we can go 1 inch into the tissue and retain f-number 1 operation, which means that all of these numbers here in this range are available to us, you know, including going down to 100 micron. If we now go even beyond that to a 50 millimeter aperture which could be possible, we can obviously get into some more impressive numbers, although f-number half might be a little tough. Let me talk about the challenge that we have, back off a second here. Obviously we'd like to increase the frequency, we'd like to operate in this end but we'd also like to be able to penetrate, you know, into these kinds of numbers so we..we have fundamental problem there. And one of the chall..solutions for that problem is something we call coded excitation. The conventional ultrasound scanner will transmit they

say a 2-cycle burst and wait for the echoes to come back from that. Now as we increase the amount of pressure that we ap..apply, acoustic power, there are FDA guidelines on B-mode imaging that act..called a mechanical index limits that prevent us from going to that stage. So if we really wanted to increase the average power we'd have to make the pulse longer. But if we make the pulse longer we immediately lose axial resolution, and you'll see later in a couple of images that axial ..resolution is really critical. So codes and coded excitation can solve this. What are codes? Code is any sequence of transmitted patterns which can be decoded to yield a short duration signal. Now what I just proposed a second ago is that we transmit a long pattern. Now this could be inside this small box could be a 2-cycle burst so this could be just the repetition of that 2-cycle burst until we get, let's say eight cycles. The processing that's used in these systems is matched filtering so we actually convolve this guy with the match filter data in an

uncoded setting where we just by brute force increase the average power by lengthening the pulse, we get something that looks like this which is definitely going to have fairly crummy axial resolution. There are codes though that are called Barker codes and these come directly from the radar literature and we..we steal shamelessly. And for example, this is one particular Barker code. If we now look at it's match filter and we do the convolution process, we can see that the main beam here in the temporal domain, in the range resolution domain has gotten a lot shorter. There are some side lobes here, there are some side lobes there. But we've already gotten a little bit better and I'll talk in a second about Golay codes which improve the situation even further, and chirps. Just to go over quickly a typical ultrasound scanner. We, in this case, with a coded excitation will apply a code to the transmit beamformer through a transmit/receive switch that'll be applied to a transducer, the codes come back, time gain compensation

to compensate for the **Beer's law** kind of attenuation delay some, and then we go through the decode processing, this match filtering and up comes the image. So Golay codes are great but they're a big problem as they do require two transmits, but this is what happens, this is a Golay code pair, 1 1 and 1 and -So these would be just the 2-cycle burst here, a 2-cycle burst here, both of the same polarity so it would be four pulses in sequence. This one would be a positive 2-cycle

burst, and then negatively going 2-cycle burst. For now do the transmit once on this one, store the data after match filtering, we transmit this group, do the match filtering, we wind up with this dataset. If we now add these we get zero side lobes, we get perfect cancellation of the temporal side lobes. That's something that works very nicely in ultrasound. Chirps are the next type of code and chirp is just a swept frequency. We can now do a similar match filter processing on that and we can see that the temporal side lobes are in a -50 kind of a domain

so that..that's going to work nicely for us. Although that's perhaps still a little bit marginal and there's some peaks out here in the -45 range. If we actually put this into a test phantom, here's..we were applying 7 megahertz here, in this particular case we're getting penetration..in this particular phantom we're getting penetration of 15 centimeters. If we now go into the Golay code mode, we actually easily get out to 18, we see all of these structures way out here, and if you look at any of these wires here in the near field there's no increase in their size even if..even these wires here are brighter so you would expect them to have more physical extents so we may actually have gained in their as well. So we are definitely getting superior penetration, you know, without any loss in axial resolution. I'll say, mention in passing in spatial compounding 'cause that's another technique that going to play here and what we do in spatial compounding is we ac..acquire the image with number of beam steering directions and then combine

those incoherently and that actually reduces some of the speckle noise. So here's a carotid bifurcation and just with conventional acquisition and with spatial compounding. And you know you can see so much more of the fine structure here. This is sternocleidomastoid muscle, the..some of skin and fat layers here. You can see the lining here on the..all the surfaces of the common carotid and the internal and the external very nicely. Once again, the distance scale here, this is 2 to 3 centimeters so we're talking about something like 6 millimeters and these are in the order of .6 millimeters, the thickness of the layers. So spatial compounding is a good thing. I had to put in, I didn't realize that the previous two speakers were going to make a big deal out of stents. I..if I had known that I would have pulled out all stops but this will have to do. You know, we didn't really break any sweat here doing this stent. This is 2 to 3 centimeters from here so this is about 6 millimeters and, you know, we can see all the minor structures there very

nicely. One of the things we've been looking at very closely lately is vulnerable plaque, vulnerable lesions and I'll be talking a little bit about intima-media thickness and adventitia here. The basic theory right now is that to have the foam cell formation lipid core and then once that gets inflamed there's an inflammatory process, the cap gets very, very thin, and you finally get the rupture coming through. Well, here are some cases where we've been able to demonstrate that very nicely using some of the new flow display techniques. B-flow is a technique we developed in my lab and it's based heavily on the coded excitation process that I just described. When we did one of our early clinicals we happened to run into this patient down here and it's one of those cases where it's really great to be lucky. So if you look at this particular image you can see the..where the plaque is you can see clearly that the cap has broken off from here.

This is definitely a case of a vulnerable plaque. You can see this blood swirling inside the plaque itself inside the core of the plaque. This dimension here is in the order of 6 millimeters so

you're getting an idea that we're looking at something in the 2 millimeter range. If you look at this dimension at 6, you can also see that this is probably about 8 to 9, and it shows the amount of pounding that the swirling here is doing on the edges on the walls of this carotid. So here's a case where one of these new techniques now is starting to pay off very nicely in a diagnostic case. Here's also a carotid artery and you can see the dark areas here corresponding to the plaque. You can see the remaining channel in the vessel and this thing is continuously pounding here. There's actually a lot of lateral motion in a media clip on this. Let me talk a little bit about how these B-flow images are formed. We have a digital encoder, we transmit a code pattern here. It hits various targets, gets back, we digitally decode it and just stick that as

a line on a B mode display. We transmit a group of these and we actually do a subtraction of adjacent echoes which will then suppress the static, the walls, the other parts of the structure. We've actually gotten a little fancier though so that we do some pretty clever filtering on that and then display those results. So the whole goal here is to emphasize the weak blood scatterers and show the amount of motion they have. So here's a typical set of numbers that we're working with. If you look at the tissue targets, they might be...if you look at this distance to the peak where the blood echoes, they might be some 40 dB down. Here's one of our decode filters which emphasizes higher frequencies, de-emphasizes the low. Here's the original image. If we apply this filter in here you can see that we're actually seeing the walls rather nicely but we're seeing a lot of flow here in the carotid and I believe this is jugular here. But we can play games and we've gotten to be pretty good at this actually so

we can alter the filter characteristics and, you know, you can see this guy drop by about 10 dB and then all of a sudden the red blood cell echoes are coming up quite a bit so I'll go back and you can just look at this part and see how we can emphasize, de-emphasize different parts of that. That's B-flow, that's how we have taken some of this technology in the area of tissue equalization and beam coded excitation and kind of pull that off. Let me talk a little bit about some of the trends that we're applying some of these things. One of them is in the area of surrogate indicators and the carotid intima-media thickness. For those of you who might not be familiar with this, this is an increasingly important risk factor for atherosclerosis and cardiovascular risk. The risk of acute myocardial infarction increases by 11% for each 100 micron increase in the intima-media thickness. So here's a case where there is actually a fairly thick intima-media thickness. By the way, I do this now once a day just to track mine and

see where I am. I'm about .8 so I'm getting a little nervous. The...on a young healthy post-doc, this is about .4 to .6 kind of numbers. Once this thickness here gets to be in the order of above 1 millimeter, that's usually associated with twofold greater risk of acute MI over a three year period. The interesting thing to hear from a signal, and image processing point of view, is that can we automate this so that we don't have to deal with people drawing lines and stuff, and one of the...there are several groups working on that, unfortunately there may not be sufficient standardization in this area. But the top image here is a B-mode image of the intima-media. We probably don't see the intima, it's all just the interface actually that we're observing here. And we almost certainly don't see the adventitia. If we now do a gradient image of that we actually see some barriers on that and the most common technique that people have been using are snakes or active contours to identify these two walls. And this particular effort was done

at University of Freiburg, but a number of groups have done this and it's probably an area where the FDA

should work on some standardization. Another key parameter that is directly related to these high resolution imaging techniques is flow mediated dilation. And the endothelium plays a critical role in this and this measurement is usually done on the brachial artery. And endothelial function is an imperative by all cardiovascular risk factors so it's a good thing to measure. The brachial artery is typically on the order of 4 to 5 millimeters in diameter. The procedure that's done here is you actually put a blood pressure cuff here. You inflate that cuff for about five minutes stopping all the blood flow in here. You then suddenly release the pressure here, there's a hyperemic response and increase in the diameter of the brachial and you observe the degree of that. Then you compare the response of the brachial to a nitroglycerine or a chemical intervention, chemical vasodilator and then compare those to get a quantitative measure. So here's the result that people are getting. On a baseline measurement here the cuff has been inflated, it's in percent. And think of this as being about 4 millimeters. We now release the cuff and there's a 4%

increase in the diameter of the brachial. It's a fairly small number but we can track that nowadays. There's a period it never really goes back to the original baseline but actually remains at a somewhat higher level, obviously because the cuff has been removed. And then later on we do the nitroglycerine and we can see the response of this. Usually these two are on a healthy individual are fairly close to each other. So a person in this study probably is having some problems. So let me summarize, what I've tried to do here is kind of give an idea on what's happening in the area of vascular ultrasound, what are some of the trends in instrumentation and how we're attacking the high resolution issue. And we're definitely getting in there knocking at 100 micron kind of numbers, both axial and lateral resolution. We're dealing with penetration, hitting high frequencies, and what we're also coming through is a whole bunch of interesting applications where I think we can take advantage of that added resolution. Thank you very much.