

Well I appreciate this opportunity to come and be part of this symposium. As Ken alluded in his presentation, I spent a lot of time in x-ray and actually my first few years were doing ultrasound imaging and so it's kind of fun to put all these topics together at this time and see how they all relate to the same, the same set of problems. So I'll try and talk about MR, I've been doing MR angiography research for the last 15 years and had a lot of people contributing to things that I'm going to talk about and the gauntlet is thrown and actually let me say right at the onset that it, it's great to, to have the gauntlet thrown. I think, I think that the best thing that can happen to the alternative modalities is if CTA and those that are really super high resolution can achieve sufficient resolution that, and, and they do become gold standards because that's so important to all of us, is to be able

to do inter comparisons and to try and understand what truth really is. I, so I, I'll just talk about MRA and talk about some of the fundamentals, I'll do a major focus on intracranial because that's where most of our research is, talk about some of the display techniques, quantitation that you can do and maybe the future, how we can go to higher resolution. So first, to review some of the techniques; MR, the reason I've enjoyed MR and have really turned my career over into that area, is because the incredible flexibility of what you can do, the relative safety of MR too is nice that you can do experiments on normal people if you're very careful and have your institutional review board approval, there's a lot of things you can do. These are the typical methods of getting contrast for MRA angiography, phase contrast, which I won't talk about, where you can actually measure

blood velocities. Most of our work we do is with time of flight which just implies that the blood is flowing into the region you're imaging and it brings a bright signal, but I will mention some things about black blood where you can look at lesions in the wall and, and then some of the importance of contrast agents and I would mention that as far as the gauntlet goes, the contrast in MR, the agents that they have typically right now are very, very safe and we have IRB approval to use those on normal individuals, they're, they're, the incidence of reactions are so extremely low. Time of flight method basically you have a region that you're imaging, you image it so rapidly that you suppress a signal of anything that isn't moving and then blood flows in and gives you a very bright signal and that's the essence of the physics of this modality and so one of the early things that we

recognized was that if you wanted image in extended length like the carotid artery, that you run into problems if you try to do the whole length because your signal saturates so we developed a technique of just doing these multiple little slabs and that way you get reasonably good information in a small region and you end up with these slab boundary artifacts which you can see there when you try to tile it all together. When you tune it up and you, this is a graphic from David Steinman and the group in western Ontario, but if you, if you tune up the technique and do the best you can, you can get a reasonably good luminography image. If you don't tune it very well, you end up with slab boundary artifacts and so Bryan Rutt, in London/Ontario came up with technique of Slinky, where this is my Z direction, this is the KY phase encoding direction so we talk about case base

in MR and I'm not going to go into details on that, but suffice it to say that you need a lot

of measurements in these directions, case base being before you transform the original of your, your image. So he acquires his measurements in the manner that I'm illustrating, where he's phase encoding at different positions, he acquires a slab position that's sparsely sampled and then he interleaves and acquires another slab position and so on until he's covered the entire region that he wants to image and then he has enough information in that region that he can reconstruct an image between the top line and the bottom line and there's very minimal artifact in that region, the slab boundary's essentially gone as it illustrates here and that actually works quite well. We also demonstrated that you could do the same thing with projection reconstruction techniques,

the nice thing about MR is again, is it's totally flexible how you do things and you can do CT-like acquisitions and so instead of doing a rectilinear 48 transform you can acquire on the radial lines and then do CT-like reconstruction and you can also then interleave in such a way that it looks like the Slinky-type acquisition and the nice thing here, if you, if you randomize the order in which you acquire these, you, you actually end up with a larger extent because as Ken was pointing out, you can do fewer projections and so these edge slices have fewer projections as you see down here, there's fewer projection lines but they're spaced widely enough that I can do a reconstruction and so a high contrast object actually does reconstruct quite well and so this sliding interleaf projection reconstruction or SLIPR works quite well, but it's never been adopted by manufacturers

so it's just kind of sitting out in the ether right now, comparison of these many different techniques. And so the only point I wanna make here is that with magnetic resonance, there's so much flexibility and what you can do. Now I want to spend time on, what are the issues, how can you do as well as you can? It turns out that the receivers in magnetic resonance are probably the biggest key to making things work as well as possible. Here I've got identically the same technique for imaging again the carotid arteries and the same pulse sequence, the same individual, everything's the same. The only thing I've changed is here I'm using a, an old, non-optimized anterior neck coil that was initially thought to work well in the neck, and I've replaced it with coils that were just, there's four elements here, one element here and the elements are very small and they're placed very close to

the neck and by doing that I can get a substantial increase in the signal to noise ratio and the visibility of the structures within the object and that's, this is a clue, I think this is an extremely important observation that, that MR techniques are really going to mushroom now that we're having systems developed now that have as many as 32 receiver channels where we could have, now have 32 coil elements and really tile some very nice designed coils around the object we're trying to image. And just to give you an idea, these are measurements of signal to noise ratio as a function of position on a human volunteer from the arch to the circle of Willis and commercial coils are down in this region, what, just what's available. But if you build special purpose coils and tile the artery, for example, the four element carotid coil that our RF engineer constructed, gives almost a factor three

or four improvement in the signal to noise ratio. So huge improvements can be attained with these special coils. It was pointed out, as Dr. Rudin pointed out, the time that it takes to acquire an MR image can be quite long, at least at high resolution. These images

acquired very quickly, but they're low resolution and I just want to kind of give you an idea. But here's the problem you face in vascular imaging with MR, if you want to go to high resolution, the object you're looking at is bouncing around and especially in the neck and with the pulsations of blood flow so the timing on these images is probably 200 to 300, milliseconds and so it's not very, it's not a very good temporal resolution for imaging cardiac events. But it gives you an idea of what's going on with the respiration and other things and just kind of do them both here and those vessels are bouncing

around a lot. And so typically that's a problem that's going to blur the images if you have a long acquisition. Let me just talk briefly about acquisition techniques again, one of the advantages of MR too is to be able to suppress the signal from blood and just image the signal from tissues and where, if you want to see the morphology of the plaque detail and this is a timing diagram of how you might acquire suppressed blood signal and bright tissue signal in a couple of slices and examples without the suppression and with the suppression you can see a little bit better detail in the little bit of reduced blood signal here, images are noisy, but a lot of work to be done then and these vessels are relatively normal. And then one of our students decided that there was not enough dead time that he could acquire other types of images and interleaved multiple slices in there and can get

reasonably good contrast of a multiple types of contrast so proton density and T2 weighting and T1 weighting showing different morphologic features in these different types of contrast. The theory being that by combining multiple types of contrast, we can tease out the information of the characteristics of the plaque and that's what we're hoping to be able to do. These are just some comparison images, this triple contrast technique compared against standard techniques and again on a reasonably normal volunteer and then going to a subject with a herniated plaque, you can see the detail and the indentation there in the plaque and these are the proton density, the T2, and the T1 weighted images at two different locations so just to give you some comparisons. Now this next image is combining the time of flight image which shows bright blood at the same slices with the

black blood slices, showing that there's higher resolution available in the same amount of time. We actually do quite well with the bright blood techniques and, but the morphologic detail is very complementary between these and again there's several groups out there, including ours, that are trying to look at the different information detail that you can get out of this. And by combining this, I just wanna show this one little bitty, it's hard to see it I'm sure, those of you in the back will have a hard time seeing this but one of the interesting problems with magnetic resonance is that we don't see calcium very well. Of course calcium shows up as shadows in ultrasound and CT would show the calcium very well but it may not show the soft tissue morphology well, but by combining these multiple contrasts, you see this dark spot about right there, I guess I can look on my

little screen here, here it is. I look more closely, so there's little dark spot there and over here it's dark and the bright blood and it's dark in the other contrast and, and so you can pretty well safely infer that that's probably calcium because it's dark in everything. If it were blood, it would be bright in one of them and not, etc., so we believe that you can even tease out the lack of signal illustrating probably calcium in this case. So I want to

spend a little bit of time on intracranial MR, MRA, I'm gonna talk about, again, some pulse sequences, coils and field strength issues and processing and display that's essential. Some of the measurements that you can make, and just to give you an idea, I'm going to show some comparison images. This was typical of about 1993, when we were first starting and it wasn't too back, one and a half tesla. About 1998, we just pulled an

image off the assembly line and compared the two, and we're getting much higher resolution, we're also doing some things a little differently at that time and seeing a little bit better detail in some of the smaller vessels, and then I just pulled an image I'm gonna a little bit later that we acquired very recently and this is a three tesla and, and has some advantages, better coiled, some, some of the things are just better that are done here. So the images are a little better and you can see we're making improvements, but sometimes the improvements appear relatively minimal, it's just a continual progress that's going on. So coils, just to give you some comparison, this one's a conventional head coil, typically available in late 90's, we built some phase-to-ray coils, four element phase-to-ray that did quite well near the periphery and actually for, for imaging blood vessels and the cortex of

the brain, these coils are very, very good but we found that a, just taking a coil like this, reducing the volume so it just barely fit around the head, and it was very snug to put your head into, you could actually do a little bit better and uniformly over the entire brain. Now we actually use a, an available eight element phase-to-ray of three teslin that does even better than this. But coils turn out to be extremely important. Another thing in time of flight imaging, if you're trying to image a reasonably large volume, you end up saturating the detail around, the detail in the peripheral of the image and so you want to do what we call a ramped RF where our minimized tip angle that you're applying here, so, and maximize the tip angle of the exit of the slab so that you can, you can do a little bit better in this capacity. Excuse me. Another problem that you run into with time of

flight imaging is the timing of your encoding and this is a timing diagram, slice selection occurs when the gradient has this shape, you apply the RF to do the slice selection and that gives you the position in Z, you phase encode in Y and Z to, to give you a, well I'm sorry, this really gives you your positioning in Z, this gives you your, your slice, your slab that you're looking at in Z and then the X position is encoded during the readout gradient so there's a time difference between these and if you have oblique flow, as you see here, the vessel can appear shifted because of the time when the frequency of coding occurs is, excuse me, is later than the time when the phase encoding occurs, and so the vessel itself appears to be shifted. And that can be actually remedied by using bipolar phase encoding gradients, so that you actually shift the time, it appears to shift the time to

be back at the center of the readout gradient and the vessel is more true and this just is some examples of that, just using this cross-section we meet you at the circle, near the circle of Willis, this middle cerebral artery. With no correction, it looks like this, with full correction looks like this, and, and like this and the other is just an elliptical way of acquiring the case base measurements so you can actually get distorted vessels if you're not careful and you can correct that in this manner. Contrast has a very interesting effect in magnetic resonance, without the contrast, you see primarily arterial detail, there's very

little venous flow that's fast enough to give you a bright signal and so this is actually a more useful image if you inject contrast, you can see smaller vessel detail and I'll talk about that in just a couple minutes, but the venous detail becomes substantially increased

and can be very distracting to the arterial detail that you're trying to see. The technique we're using here actually gives us a little bit better contrast between them because of venous detail and this is not quite as bright, there's still some time of flight enhancement in this image, but contrast will have a big effect in what we want to do. And then comparing one and a half to three T, I've already shown you a little bit of that comparison, these are basically taken using the same techniques, unfortunately the slab position wasn't quite the same, but you can see a little bit better peripheral vessel detail and lower noise in the three T as compared to the one and a half T. The higher the field strength, the stronger the signal that you get and it, and it turns out, it also lengthens the relaxation time of the background tissue so that it's, it actually suppresses the background

tissue and gives you a stronger blood signal, so increase in the field strength is a big effect for improving MR angiography. Going to higher resolution is an interesting thing because if you have any phase dispersion, we're looking at magnetization which is precessing, if it's all precessing in the same direction, we get a strong signal. If it's not all in the same direction, we end up with a minor problem and we lose signal and so making the voxels smaller can actually improve the detail that we see because with the same phase dispersion, we have a smaller region for that phase dispersion to interact over and we actually get a stronger signal over that smaller volume. Here's an example, I, it's not a totally fair example, it's on the periphery of the brain, it's very hard to image with a very high resolution or at the time it was that this was acquired and so just doing the best

comparison we can, you can see a little bit better vessel detail with a 10/24 by 10/24 acquisition. The 5/12 by 5/12 has stronger signal, but the pixels are a little blurrier and some detail that you just can't pick out at all so in principle, going to higher resolution can improve things, but I'll talk about that in just a second. Let me just say a word about magnetization transfer, the blood does, blood has some protein in it, but not as much as the soft tissue and, and there's a phenomenon where the water molecules where you're getting your signal will absorb onto protein or the large biomolecules and in this capacity, it doesn't give any signal, but it has a very broad resonance and so by applying, by applying an RF pulse, strong RF pulse, off resonance, we can actually saturate the signal of the bound water and that exchanges then in the tissues with free water and suppresses

the signal of tissues even more and that turns out to be very important at lower fields, at higher fields it's not quite as important, but it's still important, but these are older images, the quality's not as good, but it illustrates the concept of without magnetization transfer and with magnetization transfer you, you suppress a lot of the tissue signal when you've added magnetization transfer and these are just two different coils. One of the interesting things is, magnetization transfer greatly increases the RF power that you're putting into the subject and you can decrease that by just applying it for the very central regions of case base and that actually works quite well as, as these slides show. And I'm, I'm going

to just move into some issues of post processing here, these images, if you look very closely, I don't know if you can this, there's difference here and here, the vessels here are

jagged, vessels here are much more smooth, it's identically the same data, but a, the only difference is, is that we've applied zero field interpolation and just to show you what's going on here, the point spread function in magnetic resonance looks like this, it has a kind of a rounded curve in the center, has these oscillations which cause what we call Gibb's artifact or ringing. This is because we're sampling the 48 transform of the object and we have a limited amount of frequency range that we can out to, so I'm gonna shrink this done, I'm going to overlay on top of that, and we're just gonna look at the central region case so just expanding that out, looking at that central region, this is what it looks like and I call this the voxel sensitivity function if you will, or it's the point spread function in MR. But if you, if you look in a volume image, if you go from the center of

the voxel, to the side of the voxel, you're going to lose intensity. So if you have a very small pointed object, and this is partial volume effect, so if it's within, within your voxel and MR and you take that vessel and you move it to the side of the voxel, you're going to lose intensity. If you move it to the, what I call this edge of the voxel, you're going to lose even more because that's the point spread function squared and if you go to the corners, the point spread function cubed and so you can lose a lot of signal, that's a incredible hit in signal just because of the position of where that vessel is. Well it turns out that your reconstruction grid is totally arbitrary in MR, you could put it anywhere you want because you've sampled the 48 transform of the object and you can apply a linear phase to it and you can put it anywhere you want so here's an example of a vessel just

cursoring through a grid and what the grid intensities look like. If I do this interpolation, all I'm doing is reconstructing more grid points and I'm, wherever one grid, whenever one voxel sensitivity function exceeds the value of another, I just eliminate it, I'm just displaying the maximum values here by factor two and, and so you can see with a factor of two, I end up with a, this is the corner one that was so bad, it's much reduced and by factor four it's almost completely eliminated. It doesn't improve the spatial resolution but what it does do is it gives you very smooth vessels. It doesn't improve resolution, but on the other hand, you can see things that you couldn't see before so it turns out to be very important in MR angiography. I'm not going to, there's not a lot of time to talk about display so I'm, let me bounce over that. But basically, well actually, okay, let me

just show this then. If you do a densitometric projection through your data, you end up losing a lot of detail. But if you, if you do a maximum intensity projection, which is what people do, you end up, you know, losing a lot of the background signal, this looks better, but it's highly artifactual. The problem is you're only picking up the maximum value and that's what this is showing, you're only picking up one value along here and that maximum value may or may not be the vessel that you want to look at if, it may be shading the vessel. But it does increase information content in a single image, so this maximum intensity projection's a very useful thing to do as long as you remember that it's artifactual. Well, here's an example of a, maximum intensity projection of a, it's a very interesting arteriovenous malformation. If I just do a shaded surface rendering, if I

segment the vessels up, do a shaded surface rendering of them, I can actually get a lot more detail and turns out I can leave where the segmentation didn't work or it may have missed a vessel or two and just leave the original mip in there, so I would argue that I'm not losing any information, but I actually see more information by using alternative rendering techniques and we've been playing with this for quite a while. I'm not going to do that, but here's some example MR angiograms with this segmentation and rendering, you can see aneurysms in these, there's an aneurysm there, can't remember where it is over here and then there's one here at the tip of the basilar. So you can see reasonably good vascular detail of these, the blood vessels, talk about resolution in just a second. Just a word on quantitation, using some histogram processing, this isn't, this is kind of

based on segmentation, but it's really more based on the statistics of the background of the vessel signal, we can actually do multiple scans on the same individuals, segment out the same aneurysm after it's been registered and make quantitative measurements of the aneurysm's size and I'll know through the gauntlet back on that because this is really something that's convenient to do with magnetic resonance and, and there's no x-ray risk to the subject and there's no contrast injected either. It's just taking a normal individual and you know he's got an aneurysm, you wanna know if it's changed in size and you put him down and this one we scanned over the course of a couple of years, and there doesn't necessarily appear to be any movement in the size of this aneurysm. This is research, and we tell the people that it is just research and we're, you know, we're hoping to learn

whether or not we can see a difference, but, but in the individuals, five individuals that we had done at this point in time, they've been no change and this is an ongoing project know to see what we can see. If we just did thresholding to try and make that measurement just as a function of the threshold, it's very sensitive to the threshold that you pick and so to be able to get these kind of measurements precision over multiple visits over a couple years is, I think, is really cool. We're find, trying to find center lines doing some automated processing and from that we should be able to do some more vessel quantitation. And now let me just talk future, how far can we push resolution? This I can skip through pretty quickly, but with MR there's a huge hit in signal to noise ratio. If you try to trade off resolution, try to go to higher resolution, take a huge penalty

in noise and I just give you the, suppose we try to improve the resolution in X and Y, we leave Z constant. We do this, I'm not going to go through where this equation comes from, it's very, it turns out to be very straight forward in MR the signal's proportional to the voxel's volume, so I've cut the volume by a factor of four, the noise is proportional or related to the square root of the total number of samples that I've made and if I keep the number of samples constant so that my imaging time is constant, so for the same imaging time, I cut my resolution, I improve my resolution by factor of two in two directions, I lose signal to noise by ratio, by factor of four. If I decided I wanted to back to the original resolution, I could combine those two, those four voxels and average them together and I'd get a square root of four improvement so going, taking, going back to the

original resolution, I've taken hit by fact of two, so if you go to high resolution in MR,

you've lost signal to noise ratio and you cannot get it back, that's a big hit. So, what is the resolution that you want to use? Clearly you want to go to high resolution, but let's talk about what this means. This is a contrast detectability diagram, if you will, from which you can obtain one anyway. The intensity is decreasing from right to left and top to bottom and the size of the wholes is increasing, you know, going in that direction. So big objects you can see to much lower contrast. Small objects, you just can't see as well as is, typical perception problem. So I'm gonna define a score from which I can do a detection of the object size and this, the more,  $N$  is the number of points covering the object, I'm going to assume that my background is really large so I just have to worry

about how many points are covering the object, I end up with a Z score that looks like this, and it's just signal difference divided by the pixel noise and multiply by the square root of number of pixels in my region. For x-ray imaging, it turns out, let me just give you the answer here, turns out, that it's independent of your resolution and so I get plots that look like this for my contrast detectability curves, the bigger objects I can see with lower contrast for given x-ray dose, but for my detection system, if I make my detector smaller and smaller and smaller, it doesn't change my ability to see big objects and this is really true for CT as well as standard x-ray, Ken Hansen made some nice proofs of that in the early, late 70's, early 80's. But I can really improve my ability to see small objects and these lines are almost vertical in x-ray, it's pretty incredible. So that's detectible

there, not detectible here, I can see the big objects with same contrast, small objects I can do better on if I make my detectors smaller and if I wanna go to, if I wanna push this line down, I just have to increase my x-ray dose. With MR, just quickly going down, go through the same reasoning, I get these detectability curves and this region's detectible, this is not detectible, if I make my detector, my voxels smaller, these lines go up so I can't see these large area, low contrast objects as well, but I have a better chance of seeing these here. This line is not vertical, in fact, it may actually have come out at an angle, depends on how well the system's designed. You actually may do better with lower resolution all the way along for detecting an object. You wouldn't be able to resolve it, but you might detect it. So, just this, this is just my ending, and I apologize I've taken so

long. These are the same individual, same imaging region with different resolutions on our three T system, just to show you what happens as you change resolution going finally up to higher resolution. In principle, I should reach a point where the image quality is getting worse and I think I would argue that it is getting worse on this one, it's a little, maybe a little hard for you to see in the back, let me change the brightness here so it's a little easier to see and I've added the times that it's taken to acquire these. So this was, you know, one and a half minutes roughly, 3.9, eight, 23 minutes to go to .4 millimeter resolution and 24 minutes to go to .3 millimeters, and this is isotropic resolution and I would argue that I'm starting to lose detail here at this point so that's a problem. The only way we can improve things is to increase the acquisition time and 23 minutes is

getting pretty long as it is. Well we can also improve the coils that, and by reducing the coils, this is a mouse from group in Japan, we can probably do better. Let me just conclude and I apologize here, looks like we're limited to about .4 millimeter isotropic

right now. We can make coils better, get to higher field strength, maybe use contrast agents, improve the acquisition techniques, maybe get some post-processing techniques and just have to end with the picture from last night. This, I'm very embarrassed I have a cold nose, this was from that, if those of you were out at the activity, this thermal imaging system, standing next to my friend who doesn't have a red nose and I just, I have no idea what happened here, but imaging is fun. Thanks. (Applause)