Thanks! It's a pleasure to be here. A few years ago, I've taken the habit to do my acknowledgements at the beginning for the simple reason that I often run overtime. Mike just told me that they came up with the D&C with the invention where they lower the podium when you run overtime. I'm not sure we have that one here yet. This one may just fold over to one side. So the work that I'm kind of we have seen how two presentation. One covering a lot of territory, one focusing on the single application and going really into that and I'm trying to do the cherry-picker approach. I'll just show you a few highlights of activities going on at the Brigham and Williams Hospital in Boston. The program that I am working in, and a member of is the image guided therapy program headed by Frank Gelais and I'm in charge of the image processing activities. This is

some of the most senior people involved the work that I'm presenting here and it's far from being complete. So, I'll talk a little bit about image analysis and display, a little bit about quality assurance. This is something that even now the field is becoming increasingly important. Probably something that we'll be able to from other physicist. Simulation and modeling, interprocedural imaging and if I get that far about robotics. So, when you try to do research in image guided therapy you confuse the commercial packages. The FDA approved packages are inherently trying to be stable and robust and closed. So, if you try to do new things, you have to have an open research platform and so we have worked over the years with different packages. The package that we have today is called 3-D slicer. It has grown by now to about three hundred thousand lines of

code, so we need the engineering staff just to maintain it and that is necessary to enable us to do image processing research in an interventional image guidance environment. We also were forced to double up our own standards like a for scene description, there was no standard that we were able to find at the time when we developed this package, so we ended up developing our own standard like ____ mail, but _____ mail, so we call it MURMAL. When you do image analysis when everything else fails and when you need to a prototype you need to do manual editing. So, basically outlining slice by slice, a few simple algorithms and that's one of the capabilities in this package. We've started working 3-D level sets and they are kind of unwieldy but in some specific applications you can make them work quite nicely and of course what you really want to have is the

automated segmentation. One of the problems that we have is that many of the structures we are interested in require some form of knowledge to be added to the analysis of the images. So, when we see an image, when we analyze it visually, we say, this is the brain and then inside the brain there is gray matter and white matter. There is a frontal lobe and the temporal lobe, frontal lobe and temporal lobe, but this is knowledge, it's not contrasting the image or it is local contrast. So, we need to take an external form of knowledge like an atlas, map this information into the data and help, use this to help us in the analysis of the data. In the brain we have a probabilistic out class that currently contains about 25 structures and that we can map into a brain MRI date within a few minutes and that algorithm under controlled of conditions of the calibration to particular

image study can be a particular acquisition. Sorry. It can be very robust and we've run into hundreds of data sets. Now, of course we're aiming at a moving target and new acquisition missiles are being developed or new modalities are being introduced which means that we have to develop novel approaches to deal with the data and giving here just one example in imaging one the exciting, relatively recent, development is the diffusion tensor imaging. Diffusion tensor imaging is based on the measurement of slow motion using a motion sensitive ______ physicians. You can basically look at the diffusion of water molecules in the data. Now, in the brain if you look at the white matter tracks the diffusion is limited in some directions but not in others. Using this fact, you can find white matter tracks using diffusion tensor imaging. The same approach works in other areas of the body, for instance, muscle fiber orientation can be also analyzed using

DTI. This means that our start data are not just scaler data sets where you have a single signal intensity but in every voxel you have a tensor of the description of the diffusion activity and so you need to develop processing methods. Now, when we take all the data, we would like to take the imaging data and link it to textual information. So, we do this analysis, you will remember I showed you the outclass before where we identify multiple structures in the data set. Now, we basically have a textual description of the patient's anatomy. So, for instance here, let's see if I can get it to obey, here is the superior frontal _____ in bright green. Now, if I have a patient who has a lesion in that area, I can link it to different other databases that are textual databases, once I have prepared the sling. This is again a new domain of research going on how to do this properly. So, I've just

given you a few highlights about segmentation and visualization. I would like now to talk a little bit about quality assurance. This is a very tricky topic and I'm presenting you here work that was done in the context of an NIH funded joint effort, which is called BIRN, Biomedical Information Research Network. A primary sponsor trade by NCRR, the National Center for Research Resources. There is a BIRN coordinating center that is developing a shared infrastructure and then there application burns in particular the brain morphology and the functional imaging BIRN and one of the things that you wanted to do is basically, oops, something happened… I really try to imitate Mike in everything. So, in the functional MRI BIRN we wanted to work on the multi-_____ ____, basically with the goal to do research in schizophrenia but using patient pools from multiple

participating sites. As it turns out those groups of different scanners from different vendors and so just developing protocols that would work across the vendors and across the sides with a project that involved tons of people and took over two years and as part of this we actually earlier this year had a group of five volunteers, human phantoms so to speak, traveling the country visiting those participating sites and undergoing the FMRI testing in each of those sites. What you see here is one subject, subject 106, two of the repeat studies done at the same site. What this is is a simple breast hold task where you would expect basically the entire gray matter to light up and the one thing that you can say confidently if you look at those images so the orange data is the FMRI data overlaid over a MRI gray scale data and it's pretty obvious that kind of overall we're in the same ballpark, but if you go voxel by voxel there's a lot of variability. Now, it gets worse, this is the same subject, same anatomical level on four different scanners, different field strengths, different vendors and one thing that I'm trying to point out here is that there is a lot of variability in the imaging data. So even with the FMRI task, just the underlying imaging data is very variable. However, we've found out it's expected a lot of this is a constant in each of the scanners so we can basically think of it as a systematic error and so when we do these comparisons, we can compensate for it. I also would like to point out for this particular slide I deliberately selected one where we see a lot of differences. The other ones where you have less differences. Nevertheless, when you do this then you

can analyze the data and what you see here is just an example. This is a task again, a calibration task where the subjects at the same time saw flashing images, the female tapping paradigm like this and heard a sound combination. So we want try to, we were expecting to see activation in the sensor motor cortex in the ______ sensor motor cortex, ______ and in the optical cortex where you see just a little bit back here in the occipital lobe area there. These are two subjects, this is 103 and this is 104. If we take five subjects and average them, what you see here is basically the average activation area taken from five normal subjects who all are right-handed and I mean there's still variability but it's not as bad as the initial images that I showed you and surprisingly enough the results that we get kind of, it sounds a little bit pedestrian, but yes, if you have

a three or four Tesla system and you an FMRI you get better results as with the 1.5 Tesla system. So, it's kind of going in the right direction in terms of the results that we are finding verses our expectations. Now, just to get to this based on the data that we have was about six person months worth of effort in terms of analysis, after two years of set up work. Ok, quickly, modeling, I'll just show one quick example. So one way to think of modeling and simulation is it's a way to replace data that you don't have. So, here's one example, electrocorticography, so the surgeon sometimes, neurosurgeon sometimes intraoperatively will use an electrode, put it to the brain surface like this and apply a small current and depending on how this is done, this can activate or fluctuate an area of the brain and you can use this for functional testing intraoperatively if you do the

neurosurgery under local anesthesia without full anesthesia so that the patient is awake. Now, what we want to do is to understand better how the current gets a spread when we do this, when we apply this electrode. So, we take pure _____ data sets, we develop the model of the brain and in the skin, then we use diffusion tensor imaging to give us an idea of the orientation and location of white matter fibers in the, in the region of the activation. The reason being, that you get different electric conductivity along the fibers that are perpendicular. We build a finite element model and reuse, and this was a Master's Thesis, we used the software package from the University of Utah to actually do the inverse solution and what you see here is basically the simulated model electrical field distribution based on the location of the electrodes. So, what you see here, the two

loose fields of the electrodes, this magenta structure is a isodensity surface model and what you see in brown here is FMRI activation in the same subject based on the speech parodyne. So, the data is pretty much in conjunction and what you see here in green is the actual tumor, which was of the course the reason why the surgeons were interested. So, you see the tumor is very close to the speech area. Now, Mike mentioned in his talk that surgery's really based on this hand/eye feedback loop. So, the surgeon looks at something and then cuts and then sees what is going on. Now, when we do image guidance we basically replace or augment, depending on the situation. The eye with whatever imaging modality we use, now we can use things other than a mechanical device to augment the hand and I'll show you brief, a little bit of work that _____ and his

people are doing on focused ultrasound. So, the idea is the following, you have an insight MRI scan and you have a transducer dish down here with good contact and we are using for a ultrasound is a method to deliver energy. In this particular case it's a face array. We see here the signal intensity changes in this large oval area, which is basically heating use changes in the MR contrast. Now, if you have a faced array available you can have a large focus or a small focus and with the small focus, you basically scan the target area one by one. By the time you are done scanning every time applying sufficiently high energy to heat the tissue, you have basically treated that area and that basic principle can be used even clinically and then our side, there has been a clinical effort going on to use this for a fibroid ablation in the uterus. Here you see the before

image and after image. So, the after image basically shows you this large ablated fibroid. Now, focused ultrasound can be also used to do many other tricks. What you see here is basically concept work that is moving forward to develop the capability to do transcranial-focused ultrasound. You have to overcome several problems, technical problems but it is feasible essentially to get to a point where you can do transcranial treatment. Now, once you can do this, this would allow in the future, we hope, to on one hand do tumor ablations and on the other hand also to use ultrasound to do, reversibly open the blood brain barrier. Another capability that you could do with ultrasound that we are thinking about in the future is to combine it with systemic delivery, so you deliver an agent systemically, then you use focus ultrasound to activate the agent in a very

specific area. Ok, I'm almost through, so I'll just talk very quickly about some of the plans that we have, so this is the environment that manual for imaged guided procedures going on in the last ten years, we've done, I believe close to two thousand procedures in this environment. So, it's not an MRI scanner but it really is an operating room equipped with an MRI scanner. We are now kind of in the design phase for developing a next generation environment, but basically we will have not only MRI, but also other imaging modalities available and in interest of time, just one quick example why it would be nice and potentially useful to have PET CT for instance available. Again, this is just an example, so of course what PET will allow is to distinguish behavior. Two masses here one, and here one visible on CT, but clearly in PET you see that only one of them is

metabolically active and having this type of information available intraprocedurally could help again in shaping the therapy targets. This can be potentially used also to help in bracket therapy. Now, how am I, it's ok. So, Aaron wants to talk about robotics and I agree with him that this is something that again a module that we will need in the future and we have been doing technological infrastructure development in that respect. We would like to use a graphical user interface to what we think of as point-and-click surgery. For the first concept development, we are working on needle procedures because that's essentially five degree of ____ problem. If you set aside the issue of needle bending and orientation of the needle and what we decided to do is basically let the ideologies push the needle so that we don't need to deal with it for the initial

prototype development. We have healed the needle hole, though this is in mock-up with a volunteer. He received a needle holder. You see here, the optical tracking system attached to the actual needle holder so that we have an independent evaluation of needle position and the actual contraption that we have is an MRI compatible robot that can be installed in our MR operating room and so the idea is basically you define the trajectory in the virtual world and then you push a button, the needle gets positioned and then you move the needle into location. What you see down here is actual phantom experiments where we basically had little beads with a two-millimeter opening and were positioning the beads with the help of the robot and I think that's a good place to stop. Thank you very much!