Of course I have to disclose that, that I have a financial interest in TomoTherapy, Inc. One of the components of image guidance and radiation therapy, in fact, most of these, the audience is extremely familiar with. The first two, multi-modality image acquisition and the fusing of those two, produce a composite image set, is what most of you are familiar with in modern 3-D treatment planning and two of the other areas setup verification and setup adjustment and adoptive radiation therapy are just coming into the fore and finally assessment and follow-up and integrating assessment and follow-up back into the original plan. A planning session is really still on the horizon. In fact, it's interesting that this is the second time that this slide has been shown and I think it's a really shows that the paradigm of surgical planning and surgical delivery is very similar

to the paradigm of radiation therapy treatment planning and the delivery of radiation therapy. Essentially what you have to do is form a patient specific model, do the planning and then during the delivery you have to update the model and update the plan and essentially this is the process that we're just starting to do, the adaptive radiation therapy is something that has been built into the paradigm of surgical planning because obviously the patient is changing throughout the course of surgery and we in radiation therapy have always felt that the patient's are like a block of concrete and in varying with time and I think that's the big difference, even though radiation therapy treatment planning is far older than surgical planning, they in a way have been developing the model that the patient isn't invariant with time. So the chain of radiation therapy process

is from the positioning originally of the patient before scanning and then the planning and the transfer of the plan to the machine in which it's delivered, the validation of the plan, the verification of the positioning of the patient and finally the delivery. It is a extremely long chain of processes and of course in the analogy of a chain, it's only as good as the weakest of these links and in fact, the weakest of the links has, I think, been the validation if, in fact, the patient is the same as they were planned. Well, let's get started at the beginning and look at imaged guided planning and, in fact, many people when they think of imaged guidance they think of the planning aspect only and of course it is extremely critical and it's the part that the physician is playing most of the role and I think, and in far…in terms of the physician, this to them is the central role of radiation

delivery and of course having multiple types of images greatly assists the physician in trying to determine what the GTV is and MRI is starting to show where probably the tumor really is located and in fact if you compare that web with a CT you can see that there's a huge difference in the both the information content in the prostate and even in the sense of structure surrounding it and for example one can determine where the apex of the prostate is with far more reliability using magnetic resonance, often. And that's just really started to come into radiation therapy treatment planning and it's limitation of course is the fact that it's geometric fidelity is far poorer than that of CT and when we think of the fusion of the two we probably should start to think of the defamation of one into the other to make sure that they're aligned properly and in fact the issue of

registration of images together is probably most critical with PET because a PET image itself doesn't have a lot of anatomical information, but when combined with a CT scan and a PET CT or a CT PET, then the one is able to really put the function onto the anatomy and so for example it's quite easy to see sometimes where the target volume really is when in fact it might not be visible at all in a conventional CT. And I think one of the most difficult things facing our, the planning issue today is the issue, especially with intensity modulated radiation therapy, is the need to do exquisite contouring of both the GTV, the Gross Target Volume, and the Clinical Target Volume and so, for example it takes extraordinary skill to know where the nodes are because you know the nodes are not really visible here, it takes the knowledge of the physician's and that knowledge of the physician with respect to the anatomy and landmarks that they can see for them to be

able to draw the nodes and in fact we're starting to experiment with a different paradigm where, while we are outlining what we can see, which is mainly the normal tissue structures, including the skin and then treating a much larger volume, but conforming, avoiding treating, for example, the cord or the skin or the parotid glands in head and neck, just another example and of course then the issue of imaging in a treatment planning is one about being able to design where the beam trajectors are coming and being able to then look at a dose volume histogram that's based upon volumetric data that has been contoured such that one is getting a quantitative assessment of a plan's quality with respect to some other way to do it and for example one of the great issues is the high gradience that exists between an object that one is trying to avoid and the target volume.

Any time one is high, one has a high gradient then a small positional variations in the patient are going to either mean that the target volume is going to be under dosed or that the sense of structure is going to be overdosed and so one really does need the second big series of steps which is, how does one then verify that the patient is in fact being setup correctly and, or in fact the organs on the day of treatment are the same as the organs on the day of delivery and so there's lots of things that have been tried and rigid immobilization works when in fact the organs can be immobilized in fact the brain inside the cranium is a pretty good model of that cement block and that it doesn't move very much, probably less than a millimeter and so being able to rigidly attach frames to patient's skulls and guaranteeing that the setup of the patient at the time of delivery is the

same as the imaging is possible. 2-D plus time portal verification where one has the ability then to electronically image with an x-ray set at the time of treatment determines a two dimensional image of the patient but one can do this fluoroscopically and determine that the patient hasn't, is both being setup correctly but is also not moving. Ultrasound guidance then is a, has the ability to locate where the prostate is on a daily basis and might also be able to determine where, for example, the liver is, or the chest wall, but it has generally limited applicability in radiation therapy planning, probably the future is going toward CT guidance with a CT scanner in the treatment room. The CT on rales for example. Cone beam CT or helical TomoTherapy. So for example portal verification does give one information, but has limited contrast because one is determining image sets

that don't necessarily have a lot of contrast of soft tissue. Ultrasound has the ability to see the prostate with a high degree of reliability and is shown here one can clearly make out the fact that the contour sets here derived from CT are aligning up properly on the ultrasound images in orthogonal views and then if and then what essentially what one does then is move this, move the contour around until it has the best alignment and this gives you then the three offsets that one has to make in the setup of the patient in order to treat them correctly. And there are many systems being developed now for determining if the patient's been setup correctly using 2-D imaging systems. I say 2-D plus time because most of them can operate when the treatment is going on and most of them have the ability to locate the patient within a millimeter and so some of these are based upon even trying to do planning ahead of time and determining on the basis of digital

reconstructive radiographs how to setup the patient from the time of planning to the current manifestation of the patient and even robotics has entered radiation therapy just as it has entered surgical delivery and again there it's key that imaging systems are around to determine that the patient is aligning up correctly as a function of time. In fact, this particular system may take considerably longer to treat a patient with large target volumes and so it's critical that the patient is not moving during the treatment or if they are that the robot is correcting the delivery so that it takes into account the patient movement and it's a system that was developed in Japan and actually has a multiple of fluorographs. In fact, there's four of them in this room that are determining where the patient is. There's four of them because sometimes the gantry is in the way of two of

them and mounting accessories on the sides of LINAC is becoming popular both for fluorographic imaging and for cone beam imaging including CT. And of course the helical TomoTherapy's the integration of a LINAC onto a CT instead of the integration of a CT onto a LINAC and the image quality is improving with CT on LINAC. This is a coronal view of a thigh and in two minutes then one can acquire then multiple CT images. You notice at the end that there are some parts of the image that can't be reconstructed because it is a cone beam rather than a conventional CT that has a smaller fan angle. This is a transverse image, sorry, a coronal image of the pelvis and this is a transverse image of the head at a dose of about three centigrade. This is a CT image of a lung, both of a soft tissue window and a lung window using the treatment beam itself.

The LINAC is the source of x-rays at the same dose, at three centigrade and it's possible to see where the lung is at least with regard to the, sorry, the tumor is with regard to the lung side of the tumor. One of the interesting things about megavoltage images is that they don't have metal artifact problems. This is a GE light speed CT scanner and clearly there's metal artifacts here and when you're imaging then with megavoltage CT, then the teeth are properly displayed here even though they're full of mercury amalgam. This is an interesting case. This is a bilateral hip replacement and you can see then that you clearly make out on the transverse images here on the TomoTherapy CT the hip replacements without artifact and it's even possible then to volume render that. What does one do then with a CT while one registers the image that one just acquired with the planning CT?

That can be done automatically by either translations alone, translations plus roll of the patient including YAW or including PITCH. Now, typically, tables don't have the ability to PITCH, for example, so that's why it's important for one to select the automated procedure such that if you don't want to affect a PITCH then you find at least the best trend translations plus other rotations to align the patient as best as possible and of course there has to be other ways. A manual registration, such that you can align the patient and it's useful to be able to show the dose distribution that one's expecting to deliver to the patient, superimpose on the image of the day and this is the image of the patient as just setup properly and here the skin is misaligned in order to align the prostate. So, just

using skin marks then this patient would have been aligned incorrectly. I had just another example of a case where the yellow here is a verification CT done just before treatment and this is a planning CT and you can see that the bones are as there is continuity around the edge and one has to have the ability then to move this checkerboard pattern anywhere to be able to inspect the two image sets. Just another lung example here, in fact, this was the area that, sorry, this was the area that the patient was being treated. Oops, going in the wrong direction. Well, the process of doing predelivery imaging and then adjusting the setup is only really part of the adaptive radiotherapy chain. The other important processes are dose reconstruction, which is the determination of the dose that one has just delivered and a formal dose registration. Dose reconstruction, uses the signal itself from

the detector behind the patient during the patient's treatment. So, in other words, the image of the treatment being exiting the patient is used to reconstruct the dose based upon having the CT scan of the patient, the representation of the patient and so the dose distribution actually acquired that day is compared with the planning one, if there is no deformation of the patient. So, in other words, if the two images of the patient are identical then one can provide the geometric movements to align the patient and then add up the doses or compare the doses or add them up from day to day and then compare them, but if there's deformation, if the two imaged sets are different then one has to deformably register the dose distributions together in order to properly add them up, 'cause what you really want is you want the dose on each, if you like functional sub-unit

on the region of interests to be added up together so that you have a proper biological dose and so for example what one needs then is one needs the ability to have an accurate image of the beam exiting the patient and this is a interesting example where there's two brain mets being treated simultaneously on the TomoTherapy Machine, the axis of rotation is actually not at either of the target volumes, it's actually here and the scanner then, the detector seeing a sign pattern here for the more centrally located one in a larger amplitude sign for the one further away, so this is actually the raw data that is used then to reconstruct the dose to the patient. Well, then again if the patient is deformed then one has to be able to deform not only the imaged sets together in order to get the volume data but also to be able to add up the doses and compare them back to the planning CT and so

this then is the contour on the reference day and this is a computed contour on a subsequent day based upon being able to deform one contour, well the whole volume onto the whole of the first volume onto the whole of the second volume but also dragging the contours that one has drawn onto a position of the contours on the second day, in fact the contours are then used by the physician to verify in part that the deform of registration actually worked and so one of the things is you get then a displacement vector that shows how voxels are moving from one image set to the other or vice versa, so either an arrow from the planning CT to the delivery CT or vice versa. So, what do you do with all this information? Well, in principle then you could have a actual dose distribution for each of the fractions and so this is fraction one and this is the plan for fraction one and the dotted

lines will just go back and forth. This is the actual dose that fraction one got and you can see that it was delivered well. If we go to this fraction you see that there's a small deviation between the two but still it's not bad. What do you, how do you actually then process it if you didn't like what the dose distribution was? Well, the first thing you'd have to do is add up the fractions that you've delivered and compare them with what the dose that you wanted after you've delivered those fractions and so this then is the dose distribution comparison between the plan and the actual dose that you deliver. In fact, what happens you get slight blurring here of the dose distribution but you don't get accentuation of any particular badly delivered day. Well, what do you do about it if you then want to change it? Well, a tool here that I think is very useful even for general

analysis which is these vertical lines here indicating where or allow you to indicate on a DVH, where doses are between each of these lines, and so for example it's a way then of determining between two dose levels where those voxels are and so if you look the yellow line here and the red line that's painted here back on the image of this yellow region is, has dose values between this point and this point in dose and that one can then segment that and say that this is a new region of interest that I want to apply a little bit of dose to, a little bit of extra dose to because it didn't quite receive enough and so, one can then put that back into the treatment planning system just as a regular region of interest and apply a small amount of extra dose and then you have to say, well, when do you want this delivered to? Do you want it delivered on the fraction? Do you want it delivered

throughout the rest of the fractions? Do you it delivered in the next week, this extra dose, or this extra amount of dose, the change in the dose? And so, this is really an unknown issue, is when should we feed back? How often should we feed back? How much should we actually add? How many days should we add together to then, before we evaluate if we adapt the plan and then how many days do we apply this change? And so these are questions that we really have to have the capability to do adapted planning to really answer. So, in conclusion then imaged guided planning is enabling the target volume to be better defined and reducing the uncertainty of the clinical target volume should be a major role of the…of our current oncologic imaging and I think it's one that's been under-addressed. Imaged guided pre-treatment imaging is enabling margins for setup and

inter fraction variation to be reduced and adaptive radiotherapy is quality assurance for the whole course of radiotherapy and we've just begun to be able to explore this new avenue. Thank you very much!