Thank you very much. Its' an honor for a doctor to get to speak to a group of physicists, believe it or not, so I, I hope that the information that I'm going to be imparting to you is, is useful. I'm not gonna do any equations at all, so I want to apologize for that up front. I don't do much math. I first wanna thank those people that really had a role in this, first I'd like to thank Eric and APM for actually having me here to speak and also the folks that helped with this work. Ken Forrester, of course, was the, this is the physicist that I worked with at Anderson now for many years who is now moved on to UT Southwestern to be head of physics there. Steven Frank, who is the first author on the paper that I'll be speaking about at the end and Paul Keel who provided some slides and Mike Gellen as well. So the premise that I'm gonna start with, is that the most radio resistant tumor cell

is the one that's not in the radiation field or not in the high dose region. Lung cancer radiotherapy is lousy today. We have as high as an 80 percent infield failure rate. Part of that is because we may not calculate the doses right, but if we want to get more dose into the tumor, which I would argue that we need to do, some data from the University of Michigan suggests that in fact we need to be in the 100 to 180 gray range. If we wanna try to increase those doses, we're gonna have to narrow our margins and we better know what dose we're actually delivering. The second premise that I'd like to start with today, is if you were picking the way that you calculate dose to lung cancers today, would you choose a less accurate way to do it? I would argue that you probably wouldn't since we have high speed computers that can do this all pretty quickly. So the rationale that I've

heard in banter about our department for why you would not want to do heterogeneity corrections are really these three; first, we're gonna be going to Monte Carlo in a few years, why should we bother making the transition today, let's wait. The second issue, is boy this is going to be really hard to change, maybe we should just wait another 20 or 30 years and the third thing is that we've never used them before, so how will the data or how will the dose calculations that we get today, how will we use the historical data to decide what doses that we wanna give. Well first I would argue that we know that we don't wanna use the doses that we've been using, we know we need to go higher. So that argument isn't, isn't quite so important but I'll go through all of these. So the, my responses and the, again with Ken Forrester, our responses to these, are, are first that

Monte Carlo is very similar to convolution super position and the errors are actually quite small or the differences are very small between convolution super position and Monte Carlo. However, if just, changing to the use of heterogeneity corrections is actually a much larger difference. Implementing heterogeneity corrections is also not very hard even in a busy clinic and they're more accurate and what you can then do since you actually take the heterogeneity into account is that your block margins can be made more sensible, your beam weighting can be actually based on the patient's anatomy and the energy will be chosen more correctly. So, how different are Monte Carlo for convolution super position and pencil beam and the answer is as you all probably know, not much. These are some slides I borrowed from Paul Kiel and basically they compare Monte

Carlo in the solid line to convolution super position and pencil beam and what you can see is that in fact in doses in the 60 to 70 gray range, there's a slight difference between convolution super position and Monte Carlo but not very much. Also in the area where we worry about lung damage, somewhere around 20 gray, there's also not much difference so in fact convolution super position is a pretty good approximation of Monte Carlo calculations. But isn't it hard? Nope, sure isn't. Five years ago, when I started, actually now six years ago when I started MD Anderson, we basically did two to two and a half D radiotherapy planning, we transferred the CT information onto simulator films, orthogonal simulator films and the CT's weren't even done with the patient in the treatment position. There was at least one centimeter from the tumor edge to the block edge, that's GTV to block edge, I would argue that that is hugely too small and that, the dose was calculated to mid plane in a homogeneous patient. This is five years ago at MD

Anderson. Today, we do GTV's contoured on treatment planning CT's, always with FDG PET scans done in the treatment position and in fact every patient treated for cure today gets a 4-D CT and gets the tumor tracked through the entire respiratory cycle as well. The CTV's are based on the literature, we know microscopic extension from the, the work by Giroux should be about eight millimeters. Our PTV's are measured in every single patient and we've also measured our setup uncertainty and we know that two standard deviations is about seven millimeters and then we add a block edge to that. So on top of the motion that we've measured, we add eight millimeters GTV to CTV, excuse me, seven millimeters for the setup uncertainty and then about seven millimeters to the block edge. That's much more than a centimeter I would argue and we now prescribe our

dose so that 95 percent of the PTV gets the goal dose and I, and this is a very important point in that if you don't prescribe the dose correctly, you don't actually end up with the same Isis center doses from a, from the approaches that, are from comparing homogeneous to heterogeneous. We were able to do this on a service with eight attending physicians on the lung service, two physicists, six dosimetrists that rotate, 12 treatment machines and actually it's about 1,000 therapists, they travel in packs like wolves. So, this is, this was possible in a very, very, very busy clinic and this was all done while Implementing IMRT 4-D CT, 4-D PET scans, MR based treatment planning for prostate cancers, so while all of this is going on we were able to implement heterogeneity corrections so I would argue that it is really not that hard. So, the final, the

final issue is we've never done it before so how can we compare historical results, which again were lousy, to what we're doing today? What we found when we actually looked at this is that the changes to the Isis center dose were much smaller but in fact the doses to the PTV, which is again how we prescribe, is much better when you actually try to get the dose to the PTV, then if you just prescribe to the Isis center. So again, the assumptions that I'm making for the planning characteristics are that we're gonna do GTV, which is defined by the doctor, CTV of eight millimeters for all patients, which is based on this data from Giroux, which I would encourage you to send to all of your physicians to read. The CTV was then expanded by ten millimeters for PTV 'cuz in this particular case we didn't actually measure the motion, and we added another ten millimeters for block edge. So that's pretty similar to the, the numbers that I showed you before. And we kept the beam geometries and prescriptions, which were 60 to 66 gray, for those used for actual treatment of the patients in question and all the beams were 6MV x-rays. I should say that in our clinic, because we use heterogeneity corrections, we don't limit ourselves to only using 6MV x-rays. We often treatment patients with mixed beams, especially if the tumors are immediately adjacent to the mediastinum and the beam is traversing the mediastinum. So in fact, I'd say that probably 20 or 30 percent of our plans are actually mixed beam, but we feel comfortable with that because we're using heterogeneity corrections. So we calc-, we did three different plans, the first was to basically use our old treatment planning approach, that is we're gonna calculate the dose

to the Isis center in a homogeneous patient, assuming that the patient's full of water. I don't recommend filling the patients with water, that isn't good for them. The second plan was to basically take the monitor units from this plan and then apply the heterogeneity corrections. And the third plan, is to adjust the beam weights so that 95 percent of the PTV is treated to the target dose. And here's one example, where again we were prescribing to the Isis center, we're prescribing 66 gray which is in white and what you see in fact is that a good bit of both the GTV and the CT, the CTV and PTV are in fact not getting 66 gray. When we took the monitor units from this plan, and plugged them into a calculation algorithm where heterogeneity corrections were used, what we see is what we would expect, that is the doses are actually a little bit higher than what we

thought they were, however, there are still some cold spots. And if we now actually try to treatment the patient, to treatment the target to a, to full dose, what we see is in fact the doses are different still and in fact we're able to get the target volume coverage that we'd actually hoped for. When we look at the DVH of the PTV, what we see is for the, the case number three, where we actually tried to get the dose to the PTV so that 95 percent of the target dose, 95 percent of the PTV received the target dose, in fact we're able to do that, when you actually look at what we would have delivered with the homogeneous patient, you see that it's about 70 percent. However, the effect of using heterogeneity corrections, has almost no effect in the range at which you see lung toxicity which is somewhere between 10 and 20 gray. All of these effects are in the high dose region,

okay? So, you would not expect this to change your normal tissue complication probabilities range. Did it change the monitor units? Not very much. Basically we had about 300 modern units when we did the homogeneous plan and about 300 monitor units when we actually took the heterogeneity correction into account. So it didn't actually change the amount of energy that went into the patient, all it changed was the beam waves. So why did it, did this change? Well, it turns out that the tumor's more anterior so probably your beam weight should be a little bit more anterior and there's a lot of lung posteriorly so get more transmission from your posterior beam. So the bottom line is that the weighting should have been more anterior/posterior. In the second example, this was a little bit larger tumor, our goal dose was 66 gray to the isis center and here you can see

what it was that we were planning. What we were actually delivering, again, was a little bit higher dose than what we had calculated with the homogeneous patient. However, when we actually, again, tried to cover the entire PTV to the target dose, you see that in fact, we do a better job when we actually try to do that. What you can see here is that in fact when you look at the PTV's, that again we were achieving our goal, however, with the, when we were using a homogeneous case, we were only treating about 80 percent of the PTV goal dose and again there's no effect in the 20 gray range and this was uniformly the case for every patient that we treated and we looked, we, when we actually planned 30 cases like this, we didn't see any significant difference in the low dose region. When you actually look at the dose to the GTV, you also see that there's not much difference. There's only about two gray difference between what was actually delivered with the original homogeneous plan and with our approach of treating 95 percent of the PTV to

the target dose so it's a very small difference. Had we used 18MV beams, however, and just done our initial plan, this is what the plan would've looked like in a homogeneous patient and you see great dose distributions. However, what we actually would've delivered, would've been quite lousy and in fact, large amounts of the PTV would not of even gettin', gotten 60 gray. So, without heterogeneity corrections, do not use high energy beams. It's very bad. So now I'd like to tell you about a study that was reported by Steven Frank, a colleague of mine at MD Anderson, where we looked at 30 tumors in 29 patients, early stage cases, these tumors were not small, okay, these were large, some of these were very large tumors, some of them were very small. Some of them were surrounded by lung, some of them were adjacent to the mediastinum. And we asked

what effect heterogeneity corrections would have on the treatment plans. So again, we used exactly the same approach I described to you before. GTV to CTV of eight millimeters, CTV to PTV of ten millimeters, PTV to block edge of ten millimeters. This should not be a standard. You should measure tumor motion in every single one of your patients and you should also measure setup uncertainty with our techniques, with your mobilization techniques, with your therapists and your dosimetrists in your department because I would hope that you would all do better than the seven millimeters that we measured. But anyway, this is what we chose to use for the study. Again, the beam geometries and prescriptions were those that we used for the initial treatment. We did exactly what I just described to you in those previous two cases, calculate dose to Isis

center in a homogeneous patient, monitor units then plugged into a heterogeneous calculations and then for the, the third plan, was to adjust the beam weight so that we treated the way we wanted to, that is so that 95 percent of the PTV gets the goal dose. What we noticed was that there was essentially no difference in the Isis center doses, and here's a distribution you see in a few cases, there was a, a, a rather larger difference in the Isis center doses but in the vast majority of cases, it was about a three percent difference, not a big deal. The CTV minimum and CTV maximum doses, were similarly very similar between what we actually delivered with our initial homogeneous plan, and when we tried to cover the target volume to dose. Again, there was a few outliers, but in general, the difference was quite small, no statistically significant difference. And here's

CTV maximum dose, again, we see the same thing. So what about PTV? Let's look at PTV minimum and PTV maximum doses, again, very similar and not statistically different, PTV maximum doses. However, what really changed, was the PTV coverage and what we've found was that the PTV coverage could sometimes be terrible, if we just assumed a homogeneous patient. However, if we actually tried to treatment the entire patient, or 95 percent of the PTV to the goal dose, in fact that was achievable in every single case. So in summary, Monte Carlo calculations are very similar to convolution super position with heterogeneity corrections, heterogeneous planes are extremely close to Monte Carlo on average P, though the PTV coverage is much better if you actually try to cover the PTV, on case by case basis it can be quite different but in general, it will not

change your average doses. It's not particularly difficult, but your block margins, your beam weightings and your energies will be chosen so that an individual patient will get the best treatment they possibly can, this is absolutely essential before you move on to IMRT based treatment plans, and certainly before we start doing dose escalation trials so that we can actually deliver the doses that we plan to deliver. Thanks.