Good morning. My name is Eric Klein from Washinton University in St. Louis. I'll be co-speaking today with Dr. Craig Stevens from MD Anderson Cancer Center. Nikos Papinikolou is another contributor; he is chair of task group 65 on inhomogeneity corrections. He's actually in Greece right now, but still provided, quite a bit of information for this talk and I will discuss about TG-65 in terms of the report which is being published this year and most importantly, recommendations for transitioning to using heterogeneity corrections in your clinic. Now, everything with heterogeneity corrections has to go back to algorithms and why, because the effectiveness of therapy does depend on tumor control probability and normal tissue complications and obviously these are sensitive to absorbed dose and I mean accurate absorbed dose. Clinical trials are, and we just had a lecture on, on clinical trials and the physicist's role, but the outcome of clinical trials does depend on the accuracy of recording data and I will talk a little bit about the historical analysis that's been done on previous clinical trials and some thoughts how you at your own institution should conduct your own clinical trial about how to transition a, corrections and whether prescription changes are needed. Now physicists have been involved with changes in, in prescriptions, actually how, how dosage should be prescribed by analyzing changes in physical quantities. I think we're all aware of the TG-43 recommendations version one, two and three about how for, for prostate seed implants because of the air kerma strength changes for particular seeds based on NIST Standards Those who were involved in Gamma Knife were aware of what happened with the four millimeter output change and how that affected prescriptions using that particular helmet size, historically trigeminal neuralgia, when that was an eight percent change in actually the prescription, not so much the output, but the prescription in order to maintain the dose that was previously given. I think physicists have also been involved with changes from LDR to HDR and in terms of getting a little bit into the biological aspect about prescriptive changes and IMRT, especially in terms of hot spots and the EUD concept; physicists are becoming very involved with prescriptive changes and information. Now looking at clinical trials that within homogeneity corrections, Colin Orton 1998 published a paper based on RTOG-8808, 88 by the way, stands for 1988, which is when this trial began and basically it asked the physicist to calculate what the dose was using a heterogeneity corrections at their institution in order to find out what was really given using the same modern units of given dose how the patient was treated and now again, keep in mind the year. This year '88 was when the trial started and these patients then were treated from '88 through probably about 1992. And obviously they found that the, what was found in correction factors, you know, accounting for the, the lung and this, in this case for this particular thing this was non-small cell and obviously found that based on the algorithms there calculated were predicted to be, , as much as 17 percent high, there was still a lot of cobalt in those days, and a mean of five percent. So certainly this showed that the, that, , corrections weren't absolutely necessary. In other words, basing a patient on water calculations and then applying the correction post facto finding out these corrections. However, again, this is

1989 through 1992 so we’re thinking about ratio TAR and at best be the equivalent TAR at that time for algorithms. One important paper that came out a couple of years later, by Cathy Mah and Jake-Vandyke, looked at 100 thoracic patients, looked at what happens by not correcting and what they found out that the probability of lung damage was underestimated by greater than five percent. This is a fairly significant number and again, though this is again using these primitive algorithms, which I’ll discuss. And here, here's a caveat with that error and, and in fact if some people are still using these algorithms, and I know there are some planning systems that are still, haven’t gone a convolution super position, and are still even using some version of modified Batho that

if you look at dose delivery versus prescribed dose and this is basically a correction factor, inverse correction factor, , this for ten MV, you find the homogeneous versus Batho, depending on the depth and low density media, there actually is, is not a correction for increased transmission but there's actually no correction until you get to very, very deep depths and if you're using ratio TMR or ratio TAR, you can see you're going in quite a different than Batho. So again, the point of this is that the algorithm can make a huge difference. Now the other too is that how, how things, how you're actually taking your lung information and applying it to come up with corrections and then what this shows, it’s very important, is that the, if you use bulk density, you can be making, make some very significant errors depending on, for example, if the patient has

emphysema or if you're looking at, , real lung average, a total lung average lung age-related depth, densities can vary quite a bit too and when you get to very low densities, as you go lower, then it makes a much more significant impact. So TG-65, on inhomogeneity corrections for megavoltage beams chaired by Nikos, tried to analyze the, the effects, of corrections for all media, not just lung and with a, with eventual recommendations. So just a little bit about the physics problem, we want to account for, , every-, everything possible, not just the primary photons of course, but what happens for secondary scatter electrons, scatter photons and electron transport. And one thing we can do quickly is we can just quantify these parameters. For example, just something simple, was percentage of total dose – how much of that is scatter? Scatter being the more

complicated aspect to correct for. And you can see that percentage of scatter obviously increases as energy decreases and also as depth increases, the percentage of scatter increases. These things have to be considered obviously and in any type of algorithm and the range of scatter electrons certainly increases with energy both in the forward direction and lateral direction, especially pay attention here to what happens with 18MV for those that are using 18MV. So to account for, for these, these simplistic parameters and the more complicated parameter such as transport and what happens with interfaces and penumbra, algorithms have to be derived. Measured based algorithms that rely obviously on, on measured data are in water that need to account for internal anatomy and that these are, or some examples of these are Clarkson algorithm and equivalent TAR whereas

model based algorithms still have to be accurately verified by measurements and some initial parameters have to be derived by measurement and again, these, these do go back to more basic laws of, of transmission and transport and these are, show up in convolution, particularly super position and Monte Carlo. Now in also understanding some things to, to look at especially in, in learning as, as these algorithms have developed is how many dimensions are we concerned with and, the main thing is that a dose cloud displayed on a 3-D running dose planes does not necessarily suggest a 3-D algorithm. So then you'll be careful of. The other thing too, that I want to emphasize, is the calculation grid you use can make a big impact on what you're seeing in terms of accuracy. Now just going back historically and thinking about those clinical trials, those early clinical trials

based on the error ratio of TAR and some of you still using old systems may actually still be using this, that ratio TAR basically just a transmission correction based on effective but it knows nothing about size, shape or location of the heterogeneity. So, you know, it doesn't do a unreasonable job on central axis and a very unforgiving and very forgiving situation, but in complex geometries, it obviously does very poorly. Batho at least took a step further and took into consideration the proximity of the heterogeneity from the calculation point and, and did it in a very, in, in empirical fashion to, to relate the, the differences in densities and so forth in the proximity and to account for algorithms so it was definitely a big improvement over ratio TAR. However, it's not sensitive to the width of the heterogeneity, it's still really central axis based and it's, it will lead us to

under correct for a low density and over correct for high density. Now, one thing that happened, and this is sort of getting now post data from Orton, was to come up with, use a simple scaling theorem about the size of a heterogeneity, O'Connor's scaling theory where basically you could take a density and, and compress it or compact it for variations of density of one and there give you, therefore the effective, so here's a high density, gives you, what is it effectively in water equivalency you can see basically by scaling it, that by scaling it by the densities you come up with the, effective scatter area, and, and scatter contributions. This was applied in equivalent TAR which I know some systems are still using so basically what happens is by accounting for radii-, by coming up with equivalent radii for the scatter contributions, that this today, isI one step above certainly

what ratio TAR and TMR were doing. However, now this is from Rock Mackie, the very early it showed was, some measurements and good measurements that certainly things were doing a better job if, if a beam was traversing through a heterogeneity, what happens after the heterogeneity well beyond, yes improvements were being made but once you get close to the interface, all these algorithms were, were still failing because they were under predicting, over predicting the dose by, under predicting the effect of what happens at the interface. Here's just, an example of work that I had done by what happens let's say if you plan a patient for 70 gray, 20 gray of that being an A-PPA boost with 18MV for a small coin lesion and all this is, is a plug and rando phantom plug replacing the lung media and what we find if you, but what we found is that by

calculating for 70 gray, based on homogeneous, that even, even with the lung transmission, you weren't quite getting 70 gray. Why is that? Small narrow fields through lung for 18MV are terrible and basically you're not being compensated for this lack of scatter by a small, small lesion, very small lesion in this case. 6MV is not as bad but the, again, we measured lower than what simplistic algorithms, and this is again, and this is based on an ETAR type of calculation that again is still with, that the measurements were showing differences for what the calculations would have predicted. So finally we get into an error now that, that we're able to hopefully come up with an algorithm that will do much better job of not only in, for taking care of the primary beam but, but seeing such as the penumbra and interface region. Again now, the, what to keep

in mind is that the clinical trials that have shown you need to do corrections, here's the direction the corrections were based on, weak algorithms. Fine for their time, but again, but again they really weren't corresponding with reality. So, you know, just, just to, just to show a quick example for the coin lesion, convolution where we apply terma and then apply a kernel that, that depends obviously on energy and, and spread is predicted from, from measurements and so forth and we come up with a, with the actual dose which then accounts for the multiple, multiple dispersions of the depositions to come up with hopefully inaccurate/accurate distribution and so how does this work? The convolution dose computation, you, we break these all up into small compartments for a particular beam and then each of those compartments contribute basically a deposition that

depends, , that actually gives you a composite distribution. Then we apply the super position part of it to account for the heterogeneity and again, you still look at the same, same deposition here but then applying the correction and what we see then is we start to see the spread accounting for the heterogeneity and therefore you see the widening of, the distribution and lung and also effects at the interface. So, theoretically, this looks to be counting for what's needed and how well does it work, , that, again, from, from what measurements have shown that it actually works fairly well. Here's what happens though, just to show where, where you go from, from going from water based which would be homogeneous, primary and scatter. So a single AP field going through lung and this was the result. If you apply just the correction based on the primary only, the

primary only, you can what happens with the increased transmission and so forth and how that impacts exit dose to the cord and so forth. But this is only accounting for primary and what the convolutions or position is able to do then is to also take you to accounting for primary and, and scatter and you can see what happens with the widening of the penumbra and even some, some changes in doses near the periphery, the boundaries of the lung and the media. So again, what I wanted to do here, was just give an introduction of, of historically what's happened and then therefore how in your clinic would you take your algorithm and start applying corrections and then also recommendations for what you do for margins and for prescription. So what I'd like to do now is to bring on Dr. Stevens to discuss their history at MD Anderson and how they went about their transition and what they learned for these corrections.