

Good morning and welcome to this morning's continuing education session on managing respiratory motion in radiation therapy and this is... there are some it's about 15 page sort of short document available on the APM website, meaning... under the meeting, which you can download, not the slides, but an actual sort of document, which has got a lot of references and explains what we're going to be talking about in more detail. So, I'll be talking about gating interaction and talking about the problems of respiratory motion during radiotherapy and also what their magnitude of these respiratory motion is and how the different people have measured respiratory motion. As most people don't have some respiration, explicit respiration motion management devices, for treatment delivery, then we'll talk about what we can do in the absence of respiration,

respiratory management devices and then I'll hand over to Gig who will talk about the, the, the different methods that are commercially available to explicitly account for respiratory motion in radiotherapy, as well as the quality assurance of these emerging technologies. And finally, I'll give a summary and some recommendations. I should also acknowledge the, the contribution of the members of Task Group 76, who have contributed a lot to this, to this work. Okay. So, intrafraction motion, in particular respiratory motion is becoming, you know, important. There's a lot of talks in this, in this meeting and it's all sort of part of the image guided therapy and you'll see a big emphasis of that downstairs, in the exhibit hall and there's a... for a good reference on this there was a, an, an issue of symposium radiation oncology, which was dedicated to

intrafraction motion and in particular respiratory motion. So, respiratory motion is important, but it's just one of the many, many geometric areas in radiotherapy and you know, we gotta take this into account here, especially when we go designing margins that we have typically set up here as for particularly for lung cancer, 3 to 5 mm, one standard deviation. The... obviously there's physiological changes to the tumor during treatment. If we're radiating with several regions of atelectasis that can change the tumor position, the tumor can shrink during treatment. If the tumor is obstructing a bronchiole and we radiated it, it can free up the bronchiole, which is going to change both the tumor position and the oxygenation status. We've got the heart beating with concurrent chemotherapy and potentially, hormones. We've got weight loss, intra and interobserver differences,

published variations for lung cancer GTV's vary by up to 400% or eight...and in some cases 8 cm superior to inferior distance. This is what different physicians think the GTV is and that's 8 cm and we're off of respiratory motion talking on the order of, you know, mm to cm. So, it's just... really want to emphasize that it's just one of the many areas in radiotherapy. So, intrafraction motion itself, goes by skeletal muscular motion and this is so that the patient actually moving, and this is tied into respiration management devices and that we want to keep the treatment time as short as possible, in order to minimize the chance of the patient moving from their simulation position or as much to these... or all of the devices that I used, actually increased the treatment time and have thus likely to potentially increase the set up error, if the patient's on the table for a longer time. We

also have gastrointestinal motion, which is not very predictable and, but still changes the

time during the course of treatment. Cardiac motion and... cardiac motion is something that potentially we could, account for, if it became a problem by gating because the heart spends about 70% of its time in rest, so that it could possibly be, be gated and respiratory motion, which is what we're talking about today. And this is just to keep everyone awake. So... respiratory motion affects all parts, all sides in the thorax and abdomen. The, the one that gets the sites of most interest, lung cancer, that accounts for about 28% of, of cancer deaths and we, we see a lot of lung patients. The liver is probably the most mobile organ in the body and also the pancreas; probably move a lot more than lung tumors, in general. However, we don't see that many, relatively, see that many pancreas

and liver patients. However, the motion and depending on the patient can go all the way down to prostate and cervix, particularly if the patient's prostate is well within. There was a publication about the 6 mm of prostate motion, if you treat in the prone position. So, some, some facts about lung cancer; 173 thousand cases estimated in the U.S. this year and 160 thousand deaths, note the first small differential between, between these two numbers and also, as I mentioned lung cancer accounts for about 28% of all of, of cancer deaths. One thing about that differentiates lung cancer from some other cancers is that, it's, it's very poor survival. We, we don't treat lung cancer very well, at all. This is 15% five year survival was averaged over all stages and what we seen in radiotherapy, typically, not the early stages, what you've got about a 60 or 70% chance of five year

survival, but the later stage, it's the stage 3A, stage 3B. So, for actual radiotherapy, we're doing even, even worse than this. And that's, that, that's why such methods or improvements in technology give us some potential turn and some hope to try and increase this number. And, you know, why, why may radiotherapy help? Well, Mary Martel published a paper saying evidence of tumor dose response at, of 50%, 30 month local progression-free survival at 85 gray and you know there are very few people here, treating at, at 85 gray. Most of us, probably around the 60 to 66 gray region. So we're like, well down on this curve and if, if that's... if you need 85 gray to get 50%, we're treating with 60 gray, 20 gray or less than that, then there's probably, you know, some, some reasons why, why this is so low. Numbers for limiting the ability to increase the

dose is lung toxicity and also for lung cancer radiotherapy, esophageal toxicity is, is quite important, as well. So, there is some evidence of tumor dose response. There's strong evidence of lung dose response and so several greater than one hundred patients studies show that almost linear relationship between toxicity, which is prominently for lung pneumonitis with dose. And so if we can reduce those to the lung, then we will reduce lung toxicity. That's a, a very high correlation. So, what... what is the problem of respiratory motion during radiotherapy? This is a frost B video of the right lung. We see the diaphragm here. This is under normal respiration. There's no... the, the patient wasn't inhaling deeply. We have... we can see the heart beating here. Also, adding to a geometric error and the tumor here is about 4 cm in diameter, attached to the diaphragm

and it's moving about 2 cm, just with free breathing. And, another thing to note that there, we see the diaphragm moving here about 2 cm. This sort of, as we get further up, in the lung, then there tends to be less motion, though, even though, this is a, this is a

trend, some tumors in the upper lobe can still move up to, up to 3 cm, it's been published, which is quite surprising. And what happens when we image moving targets? Well, we get artifacts, of course, and this isn't just... we don't just get artifacts in CT, we get artifacts in all imaging modalities and particularly relevant for lung cancer or PET scans. And so essentially, smearing out the signal and if you smear the signal out with small tumors, then you might, might miss them... miss the tumors on the diag.. when you do the di, diagnosis. Also, if you, on the image moving tumors then the normal anatomy, as

you can see here, we've got the lung, the liver and this is a, a, a lung tumor, it's all sort of mixed up together and if we don't, if we're not predicting the normal anatomy, well, then by inference we're not predicting the tumor anatomy correctly, either. As we see here, and this was taken with a gated CT scan and here we see the, the normal anatomy is more clearly defined. So, we can have confidence that the tumor anatomy is also where it, where it actually appeared at the time of imaging and it's not in the wrong place simply due to respiratory motion. Another important point from... on the gated CT scan, is that, even though these respiration motion management devices can improve things, then yet, there are still... they're not going to work perfectly every time. So you can still get artifacts during imaging and potentially during treatment, as well. So they're not gonna

solve all the problems for you, but hopefully they're gonna minimize them to some significant level. And so, if we try and draw tumor contours on here, then we've got much more confidence, obviously, when we can delineate the boundary where as inside a region such as here, we're not really sure whether this is the diaphragm or the liver extending into the tumor or the tumor extending into the liver, but obviously would want to include that anyway, just to be sure that we were treating the tumor, during delivery. Get, getting on to margins, if obv, obviously respiratory motion is, is a geometric error. One of the many geometric errors that we need to account for during the radiotherapy process and if this, if this is a significant part of your CTV to PTV margin, if there's a lot of respiratory motion, then potentially, you can reduce the CTV to PTV margin, if,

provided that you understand the error sources and also provided that the respiratory motion is a dominant error source. And... another reason for, and I think, a big reason why people don't use respiratory motion for lung cancer radiotherapy, is because of this interplay fate between the anatomy and MLC leaf motion. So we may plan a uniform dose, however, when the tumor is moving around and the MLC is moving in an unsynchronized manner, then what will happen, the accumulation of dose on a day to day basis will have hot and cold spots and this has been shown experimentally and theoretically, though the, the magnitude, both the magnitude and the affect of this over multifraction treatment, I guess, are, are still being debated. So, this may not be a problem, but it's definitely perceived to be a problem. So how do we... what is the

magnitude of respiratory motion and how do we measure it? One... what are we doing? So, breathing we're facilitating oxygen and carbon dioxide exchange and it's in, involuntary activity, meaning, you know, we do it when we're asleep, we do it when we're unconscious and it's important that, it's not rhythmic. It's not like the cardiac cycle, which is very... looks the same from, from cycle to cycle. Breathing patterns

change, as we're sitting here, we're breathing, some shallow breaths, a deep breath, some shallow breaths and it's not very unlike the cardiac cycling. Predicting respiratory motion is also very difficult. Inhalation tends to be active, so the muscles are, are contracting and if we're just at, at rest, as we're sitting here then the exhalation is a passive process. So, although, I'm distressed then exhalation can also be, be active. And

the diaphragm is the most important muscle involved with breathing. However, the intercostal muscles also participate. So, what happens when you breathe? The diaphragm will push the abdomen down and forward during inhalation and that, that affects motion, the superior, inferior direction and also the intercostal, intercostal muscles are gonna push the ribs up and forward and so we also get anterior/posterior and medial lateral motion, though the superior/inferior motion is the... see, seem to be the largest from the measurements. And how can we measure the respiration signal? There's many, many different ways. An optical system, this is what the, the Varian RPM system, a Spiro meter what the elector system uses, I think the strain gauges, I believe what the Seaman's solution will be. People have looked at nasal thermistor, which changes the

temperature that the temperature changes as we breath in and out and so by measuring the temperature change, you can get a respiration signal and also pressure senses, also ma, ma, many ways to measure the internal respiration signal, as well. And obviously, what's most important is the tumor motion itself. There have been a lot of people who have measured breathing in a lot of different ways. CT and which is something evolving particularly with, with 4D CT and hopefully, soon, there'll be a lot more data about tumor motion based on 4D CT. Also MRs, can be a good technique used and there's also been developed such that the lung imaging is, is much better. Fluoroscopy has been used extensively. Ultrasound, nuclear imaging and also some portal imaging studies have been used. So, what are the numbers? I've got a bunch of different people here and

what's, what's interesting is that there's many different people come up with many different answers for, out the, the actually magnitude of, of motion, from some saying sort of not to 13, a similar, similar study again using, fluoroscopy 2 to 30. So, just different patients and almost, you know, two to three times the magnitude of, of measurements. So, it's I think... there's also more work to be done in how well do we, can we measure breathing. That was, that dye was full up lung the ovals had pancreas, liver, kidney, diaphragm, all of these organs also moved during treatment and you know, we do occasionally list, much less often then lung, lung cancer, but we do radiate kidneys, livers and pancreas and busy departments. Okay, so what do you do? Most people don't have methods that account for respiratory motion during delivery. So what

can you do during the imaging stage of therapy? And one, one method that, that is proposed is to do a slow CT scan. So, typically we'll do one second slices with our... most people have probably got single slice CT scanners and that, the one second slice gives the artifacts that were shown earlier. Whereas if we slow the scanner down to four seconds, and I think four seconds is generally the, the longest rotation time for most older scanners, then you tend to average the breathing. You'll average the breathing ration out so you'll get blurred images, but what you see should be a representative, should

represent the tumor motion integrated over the entire breathing cycle. And there are issues with this; because you tend to lose contrast everywhere, however, for peripheral untuneness then this is a reasonable approach. What is done at some institutions is the

inhale and exhale breath hold CT. So at exhale take a CT scan, draw the tumor volume and inhale take a CT scan, draw the tumor volume and then the target volume, at least to account for respiratory motion on the day of imaging, which of course, may change during the six weeks of, of treatment is then going to be the encompassing volume of the inhale and exhale CT. So again, this is something that can be done on conventional scanners that the breath hold, though the newer scanners can do a thorax in five seconds and which makes it much easier to do breath hold CT scans. Another way to, to do this in the clinic is if using 40 or respiration correlated CT imaging with basically via several methods, but you take a whole bunch of CT scans of the patient and you record the respiratory cycle and with post processing, then you can acquire a complete 3D data set at

inhale, mid-inhale and all the different phases of the respiratory cycle. And what you get, what you can get with 4D CT is a... you can quantify the motion of the internal anatomy. As we can see here, there is significant motion of the diaphragm going up and down. We can see changes in the mediastinum, but again we've also got artifacts. So, these methods are evolving and can be improved, though we could use such a scan, and on the different phases to determine what, what the motion of the tumor was, during the phases of free breathing and use that for our target volume. Some things important during the treatment planning, when designing your margins, if there are motion artifacts in the CT scan, then these are, are random in nature, but that they cause systematic errors during delivery. So if you scan a patient at free breathing ten times you'll get ten different CT

scan re, representations of the patient and different the artifacts will manifest themselves, differently. However, they're all, all of these are gonna cause systematic errors, if the position that, that you thought it was from the images, is not actually the true position of the, of the tumor. Also, we're gonna have respiration motion and heart beat during the delivery and respiration patterns change from day to day. The variations gonna be caused by the changing volumes of organs and it sort of really challenges the concept of the dice volume, dice volume histogram if the ya, your organ size changes by 20 to 30%, during respiration. What is the volume that your actually... of interest for your dice volume histograms? Also the tumor is gonna grow and shrink during treatment and there will be treatment related anatomic changes, such as reductions in the bronchial obstructions and

changes in regions of atelectasis. So, you know, many... there are still many errors that we need to account for. And of course, patient set up error is typically 3 to 5 mm, one standard deviation. And... I will pass over to Gig now, who will talk about the different respiration management devices, which are available and quality assurance and then I'll come back with some... the recommendations from the task group.