

Good morning. In this part of the talk, I'll be, as Paul described, discussing methods to explicitly account for respiratory motion in radiotherapy. Those methods I'll be touching on are gated radiotherapy, either with an external monitor or internal fiducials. We'll follow that up with a (review of) breath hold methods, deep inspiration breath hold, active breathing control, held breath self-gating, abdominal compression and finally internal fiducial tracking. (To conclude,) I'll discuss patient related Q. A. methods. Respiratory gating refers to dose delivery within a portion of the respiratory cycle; this portion is referred to as the gate. The width and positioning of this gate are based on a respiratory signal from the patient, either by means of external monitors or internal fiducials. The ratio of the gate interval to the average respiratory period is called a duty

cycle and can range from 20 to 50%, or even a larger range, depending on the particular technique. This gate interval is a trade-off between the residual motion that occurs within the gate, and the increased treatment time that results from the narrower gate interval. There's been a number of publications of clinical studies of gated radiotherapy with different types of external monitors. The Japanese have been pioneers in this area, with a report (by Ohara) 15 years ago using an airbag and strain gauge. More recent studies have used laser displacement on the patient's surface. Minohara used an infrared LED and camera. Kubo in this country, in conjunction with Varian Medical Systems, developed a system using infrared video technology. More recently, this group (Hara) in Japan, used a laser displacement system to gate high dose per fraction treatments of lung cancer. As a

number of investigators have reported on the use of a commercial system, I want to talk about that (in more detail). The Varian Real-Time Position Management System consists of a passive infrared reflecting block that's placed on the patient and monitored by a video camera. In every session that one begins with this system, one begins with a so-called tracking session, in which the system learns the minimum and maximum marker position as it moves with respiration. From there, one goes into a so-called recording phase, in which one sees the respiration trace versus time. There are two modes (of gated operation). I'll talk about one of them, the so-called amplitude based gating mode, in which the user specifies a treatment point in the breathing cycle by setting these threshold values. When the signal goes within the thresholds a beam enable signal is given, which

will then either gate the accelerator or trigger the CT. These thresholds are usually set to a point where the tumor motion is expected to be a minimum, usually at end expiration as indicated here. Now I'll talk about our studies at Memorial Sloan-Kettering to give you a flavor of what the clinical process is like. For patient selection in non-small cell lung cancer, patients are indicated for respiratory gating if the physician believes the tumor is mobile, while in cases of liver carcinoma, if margin reduction is a priority for the attending. Patients must be able to follow audio prompting, that is, simple "breathe in, breathe out" instruction, in order to regularize the period and the rhythm of the respiration. We've treated almost 50 patients since '99, slightly less than half of them with IMRT. Simulation lasts about two hours. This starts with patient training using

audio/visual prompting. In addition to the audio prompting we use an LCD monitor

positioned over the patient's head, which shows the respiration trace superimposed on a (blue) field indicating the minimum and maximum limits of the respiration, set initially based on the patient's uninstructed breathing trace. The patient then aims to maintain a consistent amplitude in his breathing. So, these (audio/visual prompting) are complimentary functions. We usually use amplitude gating around end expiration with this range of duty cycles (30-50%). This is set for the particular patient. We use fluoroscopic movies to evaluate the residual motion, either by looking at the diaphragm, or the tumor if it's visible on the fluoro, to evaluate, again, the residual motion within the gate. This is followed by an RPM triggered planning CT, which because only one slice is

taken per respiratory cycle, lasts about eight to nine minutes. The treatment plan may use either conformal static fields or sliding window IMRT. In the latter case, this is indicated if the tumor is larger in size and the planner finds it difficult to meet the planning criterion. So, it (IMRT) is often used (in combination with gating). Treatment is delivered at the highest available dose rate, which on our machines is 600 MU/min. Usually these treatments are scheduled for 15 to 20 minutes including setup, so they're only slightly longer than our standard treatment slots. (In addition,) we use AP radiographs to monitor interfraction constancy. From our studies of patients, we've seen that one standard deviation interfractional variations of the diaphragm (position are) on the order of 5 mm. These are important to keep track of and I'll come back to this.

Moving on to (gated treatment with) internal fiducials, in this case, fiducials are implanted either in or near the tumor using, for the case of lung, either a percutaneous or bronchoscopic technique. The group at Hokkaido has developed a system together with Mitsubishi consisting of four kilovoltage imaging systems. You can see the x-ray tubes situated on the floor, and image intensifiers in the ceiling. The system uses, at any one time, two out of the four imaging systems to monitor the motion of implanted markers; the (right) screen shows two such views. The motion detection software has indicated the current position of the fiducial with a square, and the planned position is shown as a star. When the displacement is less than the indicated one of about 2 1/2 mm in any direction, shown here, this produces a gate, and two such gates are required from the two systems in

order to enable the beam. Patient selection in the Hokkaido studies first (involves) patient evaluation for tumor mobility, in order to maximize the benefit because of the invasive procedure. In addition, non-small cell lung (tumor size) is usually 4 cm or less. The patient has to be able to tolerate the implant procedure and satisfy other pulmonary function criteria, based on the recommendation of the pulmonologist who does the implant procedure. They've also reported on treatment of liver, prostate, bladder and rectum. During simulation there are three CT scans, a free breathing scan, one breath hold scan at end expiration and a breath hold scan at end inspiration. More recently, they have been designing their non-small cell lung treatments to deliver 48 Gy in four to eight fractions. Plans are designed on both the inspiration and expiration scans, using six to

ten fields; the oncologist decides on the basis of the dose distributions at which phase to treat. Usually, it's at end expiration because the duty cycles there are higher. For treatment, 30 images per second are taken, and as I mentioned, two gates are required. In

the earlier study (published) in 2000, they reported duty cycles of 10 to 30% for lung and liver, with treatment times being about three to five times longer than for a standard treatment. They also reported that the imaging entrance dose to the patient is approximately 1% of the treatment dose. This becomes significant when one goes to high dose per fraction treatments. Moving on to breath hold methods, at Memorial we've been using a deep inspiration breath hold method for reproducibly immobilizing the tumor and for moving the healthy part of the lung out of the high dose region. The

patient breaths through a spirometer and the integrated air flow showing, therefore, the lung volume as a function of time, is displayed to the therapist. The therapist then coaches the patient through this maneuver, which consists of a deep inspiration, deep expiration, second deep inspiration and breath hold. In this way the patient (achieves) a reproducible 100% vital capacity. Patient selection is for non-small cell lung tumors, where the size of the tumor (is such that calculated) lung toxicity limits the prescribed dose. Patients must be able to perform this (maneuver) reproducibly; we have found that approximately 50% of patients are able to do so. To date we have treated about 40 patients. Simulation lasts about one hour longer than standard simulation. This starts with patient training, followed by fluoroscopic evaluation, in order to evaluate the

stability of the diaphragm (during the breath hold), or using the tumor if it's visible in the fluoro. We also examine the reproducibility of the diaphragm from one breath hold to the next. This is followed by actually three CT scans, that is, one free breathing CT and two breath-hold CT scans, where each scan is sectioned into three to four segments of ten second breath holds each. The plan may be either a 3D conformal plan or in some cases, IMRT delivered dynamically, if the patient is able to hold his breath 15 to 20 seconds and it's possible to deliver an IMRT in a single breath hold. We have done this in some cases, using treatment dose rates of 600; the treatments are about 5 to 10 minutes longer than the standard treatment. As in the gated technique, we use AP radiographs to verify internal constancy. An earlier study by Dennis Mah (published in 2000), found 4 mm

interfractional variations of the diaphragm, which included set up error. Thus the reproducibility was found to be quite good. Results from a plan comparison of DIBH against free breathing in the initial patients is shown here, comparing lung volumes, PTV volumes and normal tissue complication (probability) using the Lyman model. We found that average lung volume increased a factor of 1.9 (with DIBH). This is illustrated here on the left, as a sagittal cut through a free breathing (and DIBH) scan. The GTV's are indicated here (outlined in white). One can see the substantially increased lung volume, while at the same time, the GTV volumes do not vary that much. In this case, one sees some (GTV) elongation, but there is also a corresponding narrowing so the volume remains largely the same, as indicated here (plot of PTV volumes on the right). The

benefit is largest for larger PTV volumes where NTCP limits the prescribed dose. In this case (Patients 5 and 6), for a prescribed dose of around 80 Gy the NTCP was larger than our criterion of 25%, but by going to a DIBH technique, we were able to reduce NTCP to acceptable levels, and this has allowed us to go to doses of 80 Gy and higher. Moving on to active breathing control, this is a method, which allows reproducible breath holds at

inspiration levels other than at maximum inspiration. This system was developed at William Beaumont Hospital by John Wong and colleagues. It is marketed by Elekta and called the Active Breathing Coordinator. It consists of a spirometer coupled to a computer controlled balloon valve. With this system the operator sets the volume, the inspiration level and the phase for the breath hold to occur, whether it is during expiration

or inspiration. The patient is coached to this preset volume, indicated here in green, and then at that point the valve is inflated. The breath hold is 15 to 30 seconds and it's set (at a level) so that the patient can tolerate repeat breath holds of that duration. William Beaumont has done a number of studies on reproducibility. This is one study done with breast patients that were coached to a moderately deep inspiration of 75% vital capacity. They examined repeat CT scans at the same session, and for some patients, (performed) a repeat scan some weeks later. They used alpha cradle and ABC immobilization, and examined the distance to agreement between 3D surfaces of the lung (from different scans). The (right figure) shows one example, color coded (to indicate distance to agreement). One can see the maximum differences, as to be expected, down in the

diaphragm region, on the order of 3 mm. They found, for same session CT scans and 14 patients, mean and standard deviation distance to agreement numbers of this sort, in the inferior 10% of the lung where the differences are largest, whereas the interfractional variations were 2 ± 2 mm, again in the inferiormost 10%. So, for moderately deep inspiration, this technique appears quite reproducible. William Beaumont has been using this technique for treatment of left breast. This shows a tangential field arrangement; for a free breathing plan based on a free breathing CT scan, one can see the heart (in purple) partly inside the field, whereas at moderately deep inspiration, the heart is completely outside the field. This technique is now routinely used at William Beaumont. Moving on to other studies of ABC, Cheung (et al.) have done a CT study of non-small cell lung

patients. In their study, they coached patients to what they call a comfortable inspiration level, whose inspiration level varied from patient to patient, nevertheless, once established, it was subsequently used for all subsequent studies of the same patient. They examined GTV centroid variation and found displacements of around 2 mm left/right and AP, but larger superior/inferior variations of about 3 1/2 mm. Because of this larger variation, they elected not to reduce their PTV margins. However, they also found that lung volume increased on average 42% compared to free breathing scans. Another study, by Wilson (et al.), examined moderately deep inspiration at 75% vital capacity and found no significant variation in lung volumes, although they examined lung volume, as opposed to GTV position in the other study. They also observed that the lung volume

receiving 20 Gy was reduced in all cases. The University of Michigan, Ann Arbor has been using active breathing control in combination with a kilovoltage imaging system to treat intrahepatic tumors. Their system consists of KV tubes situated on the wall and ceiling, and flat panel imagers, which detect the position of implanted micro coils, shown here. They use an ABC device for immobilization and (perform) daily imaging to (calculate) a couch correction, (applied) in the room. In the initial eight patients, they reported treatment times of 25 to 30 minutes and found setup errors were reduced from 4

to 7 mm, where this latter number is in the superior/inferior direction, down to 2 to... this (4 mm) should be 3.5 mm, after image based correction. A study by Dawson (et al.) examined the reproducibility of ABC immobilization for treatments done at end

expiration. They reported an intrafractional standard deviation of 2 1/2 mm. However, the day-to-day variation was 4 1/2 mm, which led them to conclude that daily imaging is necessary to reduce these numbers to a more acceptable level. Moving on to another technique called held breath self-gated radiotherapy, this technique involves the patient voluntarily holding his or her breath and indicating so by means of a switch, which controls a customer minor interlock on a Varian Linac. The sequence of events during treatment is indicated here. When the patient achieves a breath hold, he presses the switch, which indicates to the therapist that he can activate the beam. One of three things can occur: either the treatment completes and the beam automatically terminates; or, if the patient cannot maintain a breath hold for the (duration of the) field, he can simply

release the switch, which will activate the interlock and interrupt the beam, at which point, one resumes the sequence to complete the field. The third situation is if the therapist, for some reason, needs to interrupt the treatment, he can beam off to interrupt the beam and let the patient breathe. Patient selection is for treatment of non-small cell lung cancer, and requires that the patient be able to do a reproducible deep inspiration breath hold of at least 10 seconds duration. Simulation includes verification, under fluoro, of the reproducibility of the tumor or diaphragm position. The CT is broken into 10 second segments, where the patient is given a switch to indicate when he is holding his breath and ready (for the therapist) to initiate a segment. These studies have reported treating patients primarily using IMRT step and shoot, using either one to two breath

holds per treatment field, with dose rates of 600 MU/min. At the time of these studies, eight patients had been treated. Abdominal compression was originally developed for a stereotactic irradiation of non-small cell lung cancer. Here one sees the Elekta stereotactic body frame that has been used by investigators for this technique. Negoro, among others, have reported use of abdominal compression in their cases for treatment of solitary lung tumors with hypo-fractionation from 40 to 48 Gy with four fractions. They would use a small compression plate applied to the abdomen if the tumor excursion on the fluoro was observed to be more than 5 mm. What they found in their study is that the intrafractional tumor excursion was reduced from 1 to 2 cm, without compression down to 0.2 to 1 cm with compression. In their treatments they performed a daily portal film

verification, shown here from their publication, using orthogonal port films and compared against the simulator films. Because these are isolated tumors in lung, they apparently show up well enough in the portal films to make this comparison. They used a correction threshold of 3 mm and found that corrections were necessary in only 25% of the cases. I'll skip this slide. In the Cyber Knife case, this system uses a robotically controlled linac to treat tumors on the basis of detected fiducials by means of x-ray sources in the ceiling and flat panel (imagers), shown here. In the study published last year, the Stanford Group used 20 second breath holds during which treatment was

administered, whereas the Cleveland Clinic Group used respiratory gating by means of external LED's on the patient. These treatments involved 15 Gy delivered in one fraction

from a hundred beam directions. This shows the variation in the fiducial positions over a single treatment showing that, in any direction, the variations were less than about 3.8 mm. Now, moving on to patient specific Q.A. A key aspect of external monitor based techniques is maintaining internal constancy. This can be affected by the correlation between the internal anatomy and the external monitors and also by changes in the patient. In turn, this can affect the self consistency of the CT over multiple cycles, whether it be breath hold or gated, and also the constancy between simulation and treatment. Procedures common to breath hold or gated methods with external monitors is the importance of patient screening and training and frequent imaging to check this internal constancy. For patient screening, it is useful to do so already at the office visit.

That is, the physician may evaluate if the patient is able to understand and willing to cooperate. One can then follow up with an office visit screening, which would introduce the patient to the treatment equipment and the procedure and also already test the patient's ability to consistently perform it. At simulation it's important to start by training in the treatment position and do an evaluation, with breath hold, to establish the inspiration level and its duration, or with gating, to establish where to place the external monitor in the case of position-sensitive monitors, and also audio-visual customization. This is followed by a simulation, either with fluoro or cine CT to evaluate, for breath hold, internal reproducibility, or for gated radiotherapy, to evaluate the correlation between internal (anatomy) and external (monitor). Here's an example showing a one

second time lag between the tumor motion shown in black and the external marker motion shown in green (Fig. D). By gating on the respiratory signal alone (Fig. E), one would then gate not necessarily on the point of minimum tumor motion (Fig. F), so it's important to keep in mind that those things do occur, albeit not so frequently. Interfractional constancy: here is an example, for treatment with RPM gating, showing the diaphragm at simulation about two cm below the isocenter, whereas at treatment it is only half a cm below isocenter, that is, more superior than it was at simulation. This was a cooperative patient with a consistent external trace, but with a consistently superior diaphragm position, so it's important to monitor these kinds of interfractional variations. In the interest of time, I'll skip the summary and turn it back to Paul.