Well good afternoon, first of all, I would like to thank the organization for inviting me and it's a great honor for me to give this presentation on the acquisition of 4-D tomographic data. First of all, some acknowledgments, we working in close collaboration with members of the Elekata Synergy Research group, Christie Hospital, Beaumont Hospital, Princess Margaret and Elekta oncology, and part of this research is also sponsored by the Dutch Cancer Society. Just as an introductory example, the context of 4-D CT, the mathematical model of computer tomography relies on static objects and the movie on the left clearly shows that that presumption is not met in the lung region and the upper abdominal region. So we get immense artifacts and the figure on the lower right, which I got from a publication of Yvette Seppenwoolde where they studied the

magnitude of these motions, indicates that especially in the lower lobe of the lung, amplitudes with a peak-to-peak amplitude up to, and more than two centimeters can occur. So this gives rise to motion artifacts in computer tomography data and in this slide, two examples are shown. In these figures coronal, sagittal images of a single slice spiral CT with a typical slice by slice deformation and for instance the diaphragm that's broken up into several pieces. And then the lower figure, an example of a Cone-BeamCT on a linear accelerator where these , motion artifacts manifest themselves differently, basically blurring of the moving structures over the trajectory and why is that? This is an example of how Cone-Beam CT system installed in Amsterdam and due to the fact that this Cone-Beam is installed in a LINAC, and LINACs are very heavy objects and due to

safety regulations their rotation times is about one minute, one rotation per minute and during acquisition around a phantom in this case, head a neck patient you aquire a set of projection data and in case of a lung, there are multiple respiratory breathing cycles during this acquisition mode and all these data has acquired simultaneously and use in the reconstruction of all the data. So therefore you don't have the slice by slice deformation but a blurring of the object and typically we use a four minute acquisition time for a lung patient. Well, there's been a large interest in the 4-D CT over the last few years and just a short overview Ford et al. and Vedam et al. submitted an, manuscript within a single month and got published a year later on the use of a single slice helical CT acquisition mode and 4-D reconstruction. Subsequently, Low et al. and Rietzel et al. for example,

published on the use axial or cini-mode CT acquisition mode but then using multiple slices. Finally Keall et al. recently published the use of multiple slices and a helical mode to get 4-D data. For the cone beam there's less extensive literature yet, Taguchi published interesting data using a smart windowing algorithm to get cone CT but that's not related to the slow cone beam scanning CT that I will refer to later in this talk but on the fast scanning cone beam and get optimal time resolution for that. Well we introduced the concept of respiratory correlated cone CT last year at the AAPM in San Diego and this morning and very interesting presentation by Doug Moseley on that similar concept. Due to the fact that 4-D spiral CT on the sort of the regular CT systems have been discussed extensively this morning already , inthis talk I will focus a bit more on the cone

beam acquisition mode. Roughly all except the Taguchipaper use a similar way to get 4-

D data and that’s what we call retrospective sorting. Suppose you have a CT data, a stack of data and mostly there can be axial CT slices or projection data and cone beam. You have a data sorter that tries to correlate this CT data to the breathing phase, the breathing signal and then creates subsets of these data sets and put different CT data in different subsets and by such correlating the corresponding breathing phase to the slices and put them into subsets and these subsets are consistent due to the fact that they correspond to breathing phase, there's hardly any motion present in these data sets and these data sets are there for consistent with the computer tomography mathematical model and should have reduced amount of artifacts and this whole stack together, so this is sort of the fourth dimension including the time of the breathing cycle. So we need a breathing signal in order to correlate the CT data with breathing signal, or the breathing motion and

the internal motion and there are sort of two different flavors available, quite different types. So on the one hand you have external measures to capture this breathing signal to get a surrogate for internal motion like the abdominal height, spirometry, thermistorsand a resipi-band. Alternatively, you have internal measures to obtain information about internal motion in the lung like measuring the tidal volume per CT slice, fluoroscopy with or without markers. This morning I've listened to a presentation about the use of ultrasound for gated radiotherapy and I think that that could principally be used to get an internal signal as well as the use of electromagnetic fiducials to obtain a respiratory signal. There is an issue in the use of external signals and this has been discussed yesterday in the motion tracking session extensively already and this is an example of

research that we did comparing breathing signals obtained using thermistor, the diaphragm and the skin both used from fluoroscopy and then you see that that can be substantial amplitude as well as phase differences between the skin, the diaphragm, or the thermistor and the diaphragm. So if you use surrogates for breathing you have to be very careful to know what these signals represent or whether they have any amplitude or any phase differences and be careful to use them, because both phase and amplitude differences can cause artifacts. With respect to cone-beam CT , we have developed a method to acquire the breathing signal from the projection data and that’s a very attractive method because the projection data for the one hand is used to reconstruct the CT data, if you can extract the breathing signal from that and they are sort of intrinsically

calibrated and there are no potential phase differences In short this method is enhancing diaphragm-like features, projecting these on the cranial-caudal axis, subsequently combine these into an image and from this image determine of region of interest and extract the breathing signal. Now in a little bit more detail, this is an example of the enhancement of diaphragm-like features so you clearly see the diaphragm but you also see all kinds of other structures like the ribs. We compressed this data to a one dimensional signal, by projecting them on the cranial caudal-axis, you can do this for all projection data acquired for a cone beam sequence and then you get a 2-D image that we, tend to call the Amsterdam shroud From this shroud you clearly see a nicely temporal varying image or signal in the region where the diaphragm moves up and down. We can crop that image from the shroud and do a line by line comparison and the least square fit to fit subsequent lines and this is the result of the fit which nicely gives you the breathing signal There is a small trend visible due to the fact there was also some variation as a function of gantry angle but such a trend can easily be removed by signal processing tools. So we have now measured the amplitude changes over the course of breathing but we would like to obtain the breathing phase in which phase inhale exhale mid ventilation towards inhale, etc., to extract from the signal Some commercial packages give you this phase automatically although there can be some differences as we've heard this morning. We used a Hilbert transform from the amplitude signal to extract the phase and the nice property about the Hilbert transform from the respiratory signal is that together with the

respiratory signal itself, if you take the inverse tangents of that, you get a momentary phase of the amplitude so you can actually get a phase signal and subsequently you can divide them into bins and, that represent exhale, mid-ventilation, etc. So then we can finally go ahead to obtain 4-D data , our planning CT scanner is sort of an old fashioned CT scanner and we are in the process of finally getting a multi-slice CT scanner but with this relatively old machine we have to sort of crank it up and find a reasonable setting of data to obtain sufficient data and essential is that you get a over sampled data set. An example is shown over here, we use a slice thickness of .3 and a very low pitch yielding a slice distance, this is of 0.9 millimeters a gantry rotation time of 0.8 seconds and this is sort of the maximum we could get out of this system and basically it’s not enough if you

look at it in about 2.4 seconds the table travels in the order of the slice thickness and as the average breathing signal is more than this 2.4 seconds, you're going to miss some data. That’s what we see in the results, so we resort the slices into the phase bins and reconstruct the scans and do some interpolation in phase and space to obtain 32 phases and due to the fact that we have sort of not over-sampled our data set enough, there's some under-sampling in the reconstructed data so there's still artifacts and that’s the main cause. For the planning CT we use a thermistor to measure the temperature difference between inhaled and exhaled air and there might be some issues there as well in terms of phase changes. So a reasonable moving object with still some artifacts and we’re looking forward to obtaining our helical multi-slice CT scanner and go ahead with that, and we’re

very confident that we get nice and clean images with also the results that have been presented today to clean up the phase signal. So back to cone beam, as already stated, blurring of the data of all slices, so this whole retrospective sorting procedure doesn’t work for such a data set and there's a lot of motion going on. This is sort of the acquisition mode that we use for respiratory collated cone beam, quite a bit of projections in the order of 650 to 700 over an arc of 200 degrees and taking about four minutes to acquire and that’s pretty slow ,if you see a Gantry moving around four minutes over 200 degrees you hardly see it moving and occasionally the technologists thought the machine thought it wasn’t moving at all and it stopped the acquisition. So instead of selecting slices, respiratory correlated cone beam CT, is a selection of projections before

reconstruction, so a sort of retrospective gating in projection space. This is such an example that was also shown this morning, similar example. By selecting only dose projections that correspond to a certain breathing phase, you sort of freeze up all the motion, there's hardly any residue of motion within the bins selected and taking about 85 projections for this particular breathing phase. And if you did of all projections, you get a movie loop somewhat like this or in the bottom 3-D data sets at 670 projections and then the upper one a 4-D data set based on eight times 85 projections and now you nicely see that all that blurring has largely disappeared and you gain trajectory information about the motion of the tumor and all the structures. And having the ability of such a system on the LINAC, you're able to acquire such data just prior to treatment, you're able to see things you didn’t see before. Suppose we have the planning CT scan of that patient and

acquired a data set just prior to treatment which is shown here and now in a dual color overlook, purple is the planning CT, green is the cone CT. Well, first of all we do a bony alignment, get some contours there and this is basically how we treat the patient currently at that machine. If you get rid of the planning CT and see the contours based on the cone beam CT and play a movie loop, we clearly see there is a systematic imaging error occur due to the fact that we don’t have a 4-D planning CT data set yet available in the clinic, so systematic errors due to the the interference pattern between breathing and the scanning process and the planning CT scanner and currently we are in the process of implementing correction procedure where you will be able after bony anatomy match do an additional shift in the cranial caudal direction to compensate for such a systematic

imaging error and since that you have a symmetric motion weighted over time around the contour of the GTV and PTV and hopefully we’ll get this running in the clinic in about two months. So this system works quite robust and good for about 80 to 90 percent of the patients and 80 to 90 percent of those patients fraction. This is a typical example of the breathing signal that we obtain for such a patient, but for the particular patient that I'm showing today, t a breathing pattern of the same patient about one and half weeks later acquired and you see dramatic differences. On the one hand, large amplitude differences and also quite big changes in the pattern and the length of the breathing cycle. And if you use phase sorting in such a mechanism, you presume that each cycle represents sort of the same motion so you would presume that this point corresponds to this point and

corresponds to this point, which is obviously not true and you will introduce massive errors and artifacts in that. So alternative, what you could give it a try is amplitude sorting. So instead of putting all the inhale phases together, you just bin it in amplitude and get a bit more consistent data. However, as a consequence, you neglect histeresis and the data is sort of harder to interpret. This is a histogram of the phase and amplitude of this particular breathing cycle and then you see especially for the larger displacements, you have a very limited data so in order to acquire sufficient data, you have to use larger bins for the larger displacements and accept some additional blurring for these in order to get some reconstruction going at all. And this is just a very slow example in the left of phase sorting of the data set and on the right a displacement sorting of the data set and then on the phase sorting you see for the inhale phase, you hardly see anything at all ,the data's really inconsistent and hard to interpret. On the right movie loop, this displacement sorting, you still get reduced image quality due to the fact that you have sort of larger bins and, but compared to the phase sorting you can increase some image quality. Again be careful because you throw away the really big peaks so you clean up your image but you don't know what inhale and exhale is, it's purely positioned and you can't say this is inhale and this is exhale, it's just trying to get a nice image and if you want to use this data set for gating, be very careful. So finally some conclusions, well obviously your 4-D CT data set provides a 3-D data set at multiple respiratory phases, it improves the

identification of anatomical shape by reducing the motion artifacts in the CT data and very important, it provides mean position and the trajectory of the moving structures that are very important to increase your accuracy of radiotherapy and with the use of 4-D cone CT on a linear accelerator, you have the ability for 4-D verification and guidance and just prior to treatment. Future work, future directions improve the image quality of the cone CT using faster panel, getting more images and less view aliasing artifacts, but also trying to use interpolation methods, to get a better image quality but most importantly, we have to really focus on these breathing variations, probably some sort of coaching and training is inevitable but then you have to do that for each treatment fraction obviously. But there will be variations anyway, even after training it will be

some variation. I we have think about ways to incorporate that uncertainty in the variations that occur with respect to your 4-D data set. And finally, 4-D data set is still a snapshot so it is quite significant inter fraction variability possible. We are thinking about the concept of 5-D CT. so 4-D CT over multiple fraction are the 5th dimension, sort of the slow variation and the 4th dimension is presenting the breathing cycles, the quick dimension. And obviously we want to implement all these nice features in the clinic as soon as possible. Thank you.