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Radiation Approaches for Localized Non-Small Cell Lung Cancer (NSCLC)
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GRACE, the Global Resource for Advancing Cancer Education, is pleased to provide the following presentation on Radiation Approaches for Localized Non-Small Cell Lung Cancer, by Dr. Quynh Le, Radiation Oncologist and Professor at Stanford University. Dr. Le spoke at the GRACE Non-Small Cell Lung Cancer Patient Forum in Seattle in September of 2009, a program supported by OSI Pharmaceuticals and Swedish Cancer Institute.

Thank you. Early stage lung cancer, if the patient can go through surgery that's the treatment of choice. Unfortunately, we have a small population of patients who cannot go through surgery then the question is, is there anything that we can do for these patients? And in traditional radiation treatment in the olden day where we really couldn't really visualize a tumor very well, we treat the patient through six or seven weeks of radiation. The results are not that good. We're talking about 30% cure rate in this population if it's a frail population, we're talking about. But now we have new technologies immerging and so the question is can we use this new technology to change our pattern of practice and to improve the cure and results of these patients.

So there are some advances. You've heard about the PET/CT and the PET/CT allows to diagnose a cancer early and hopefully at earlier stage. I'll show you some pictures of the tumors moves with the lung as you've heard before and when you breathe the tumor the tumor moves, when will respire -- it does a lot of things. And with us focusing the radiation for your spot, it doesn't' help, we didn't take care of the tumor motion in the past. Now, we learned that we can do that with the newer radiation and we can actually aim the radiation much better. And we actually have new software now that allow us to improve the radiation delivery and new hardware that we can image the patient while they're on the table to look at tumor motion and where the tumor is. And so that allow us now to give the radiation more accurately.

This is the first linear accelerator ever be in the world. It was Stanford University in 1956. As you can see in that picture, since then we've gone a long way and these are new linear accelerators and we use them to deliver the radiation, generate the radiation. And these are new linear accelerators that are out there. All of them ability to image patients with CT scan or chest x-ray so that we can see the tumor. In the olden day, we treat the radiation through and through, so front and back. So you see that the radiation being traversed a large area of the lung. Now we have ability to just focus the radiation around the area of the tumor, so less radiation to less area of the lung so less toxicity to the patient.

As you can see here, here's an image rendering of the lung of the patient. Actually the blue are the bronchus, the alveolar of the tumor and the tumor is actually in green here; it's hard to see. But you can see the tumor moves with respiration, so we had to take that into account when we do the radiation treatment. And with the PET scan, you can see that the PET, this is the location of the tumor at inspiration; this is the location of tumor in expiration. So you can see that when you take a PET scan, you lay on the table for 45 minutes or 20 minutes when we apply the PET scan, you can see this blurring approach. If we treat this whole region, that's a lot of lung for us to treat.

So there are ways now that we can do this. We can brace the patient. And this is what we call 4-D CT PET scanner. We put a block on the patient's chest wall and if you put your hand on your chest and you take a deep breath in and out, you can see that your chest wall will move with respiration. And so we use this as a surrogate marker to look at the respiration pattern.

So based on that, we actually can acquire CT images, and this is reconstruction of CT images that we acquire during respiratory cycle, so we can actually see where the tumor is during the respiration pattern. But now we can do the same thing with a PET CT. So now we can accurately target the tumor much better and sparing more normal lung tissue.

Other ways people are doing that is they can actually put a frame, kind of a chest plate on here to minimize your respirations so your respiration will be a little bit shallower during the radiation treatment, but then you treat less lung. Or you can put a fiducial into the tumor and track the tumor. Also during the radiation we can rotate, change the leaves so the radiation deliver in the top of the accelerator and the leaves can be changed during the radiation treatment while we're moving the beams around the patient so we can conform our radiation dose better to the patient.

So, let's go back to what we call this new terminology which is stereotactic body radiation. We learned that from brain tumors. A patient will have brain metastasis we know that we can give big dose of radiation to these lesions -- many years ago and because your brain doesn't move within your head. These tumors are fixated and in addition put a frame on in order to best target that. We know that we have a good control rate with these pre-metastases. So the question now, if now we can account for motion for the lung tumor can we do the same thing for the lung tumor. And that's where the SBRT field comes from.

So again, as I mentioned the standard treatment for early stage lung cancer is still surgery. But many patients cannot tolerate surgery, and the results of dose escalation study using the conventional radiation therapy has been disappointing. We only have about 30% survival rate for these patients. So this has been emerging promising option that we have for these patients.

What is SBRT? So, its highly focused radiation concentrated on small tumors and I emphasize only small tumors at this stage. I would give low dose to the surrounding tissue. It's a single or few treatments as big dose for treatments would also make it a little bit more convenient for patients. It's very precise delivery and we use all sort of image guiding that I've shown you before in the mobilization technique in order to accurately target the tumor. And as I mentioned, this is because we learned from brain tumor and we try to see whether we can apply it to lung tumor.

And so we have a lot of phase I, dose escalation studies going on throughout the world as well as in this country. We can use treatment in one fraction, we can treat it in three treatments, or we can do it in four treatments most of SBRT treatment is either between one to five treatments in the patient spread out between one to two weeks.

And here's the results of these are what we're learning how to treat these patients, what dose to give. We do these studies and we learn, try to figure out what the results are from these study. So based on this you can see the control rate in the patient. Again, these are early compared to surgical series, but it's promising -- two to three years anywhere between 80% to 90% control rate for these patients at this point.

So this is example patient who got treated SBRT. So you see the tumor melted away, but we do see changes in the lung and we need to follow this patients very carefully because we don't know what the late outcome side effect would be to the changes that we see in the lung.

This is data from the Japanese consortium study and they show, when they pulled the data together from many hundred patients that had been treated in Japan - they showed that actually what we call, this BED or biologically effective dose, the higher dose the better for the control rate for these patients. They also have a group of patients that they didn't want surgery for an operable patient the result outcomes are quite excellent as well.

So what are ongoing study or completed study right now? So for patients who are inoperable, so in situations where it's very dangerous to have treatment for the patient in terms of surgery the patient cannot tolerate surgery, then there are some of these studies that are going on or just completed. This is a Japanese study looking at 100 patients randomized between surgery and radiation the result will be available in 2010. There is a SPACE study which is a Scandinavian consortium study again look at conventional radiation versus SBRT, and hopefully that will be completed as well. There's an RTOG cooperative group study -- an early report that's just been completed -- showing a very minimal toxicity and an excellent control rate, about 96% at this point.

Going to the operable patients, I show you before the Japanese pooled their data and they showing that for people who can tolerate surgery have physiologic ability to tolerate surgery but refuse surgery period, they do have a subset of these patients and at least their results at this point is quite promising. This is the data from the SBRT compared to surgical series -- about 80% survival.

Surgery is still the standard of care for these patients but they are randomized study to take a look at whether SBRT can yield similar result as surgery. And so this is a study that is ongoing through RTOG is a Phase II study looking at outcomes for these patients. There are two randomized study, one of them is activated; the other one is about to be activated. One in the Dutch group and the other one has been activated by M.D. Anderson and these studies we're working together with the surgeons and patient will be randomized to either surgery or SBRT.

The main issue that I want to raise is that SBRT is not the standard of care in this population right now, because we don't really have late data, long-term outcome data for these patients and we don't have late toxicity data. And that's why it's very important to do the SBRT on a clinical trial, because we need to learn about what's going on with the late radiation side effects and also outcome.

We do have, in our study we do track the respiratory function of patient receiving SBRT and we are not affecting patient respiration. But we do learn that there are certain locations that it's not very feasible for SBRT. Those are the location very close to the central airway, because we cause more toxicity when we have those locations, so the lesions we're comfortable treating are in the periphery.

We do however make sure that we need to take care of the toxicity because we give these big doses like this, and we just use beams that go through and through we can have toxicities, skin toxicity look like this. So we have to be very careful, learning about new side effects of SBRT.

In conclusion, SBRT is a promising treatment modality for early stage non-small cell lung cancer patient who are inoperable. Early data suggest that it may also achieve high local control and survival rate in inoperable patients, but we need a randomized study to prove that.