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New Advances in Head & Neck Cancers at Penn Medicine

ReachMD Announcer:

Welcome to Medical Breakthroughs from Penn Medicine, advancing medicine through precision diagnostics and novel therapies. Your host is Dr. Lee Freedman.

Dr. Lee Freedman:

Treatment for cancer of the head and neck can often be devastating for patients and that loss of the ability to speak can be a result. What are the new advances in treating patients with head and neck cancer and what are some of the new trials in sparing a patient's voice box? To answer these questions and more is Dr. Alexander Lin, Assistant Professor of Radiation Oncology at the Veteran's Administration Medical Center and the Pennsylvania Hospital. Dr. Lin is a radiation oncologist with a focus on head and neck cancers. Dr. Lin, thank you so much for being with us.

Dr. Alexander Lin:

Thank you so much, it's an honor to be here.

Dr. Lee Freedman:

Why don't we start generally and maybe you could describe for us your role at Penn Medicine.

Dr. Alexander Lin:

Sure, I'm an Assistant Professor as you'd mentioned. I'm at the University of Pennsylvania. I'm the section chief of the head/neck cancer section in the department and I'm also the Director of Clinical Operations for the Roberts Proton Therapy Center here at the University of Pennsylvania.

Dr. Lee Freedman:

So a lot of different hats that wear and I know that some of what you do involves collaboration with otolaryngologists. Can you describe what you do in conjunction with them?

Dr. Alexander Lin:

Yes. I work very closely with our head, neck surgeons here and with our medical oncologists and radiologists. And essentially what we believe is that head and neck cancer is a disease and a problem that needs to be addressed, often in multiple ways. We have experts in surgery, experts in chemotherapy, experts in radiation. And what we hope to do here for all of our patients is to tailor individualized therapy so that we can maximize a chance for a patient's cure and do so in a way that minimizes their side effects and long-term toxicity, and maintain their quality of life after treatment is completed.

Dr. Lee Freedman:

So multidisciplinary approach to try to optimize outcomes and reduce morbidity from the treatments.

Dr. Alexander Lin:

Yes, that is correct.

Dr. Lee Freedman:

Now as an internist I know very little about this but I sometimes think about ENT cancers as being related to the human papillomavirus, is there any utility in thinking about these as HPV-positive versus negative?

Dr. Alexander Lin:

Yes, very much so because we are seeing that patients that have HPV-positive associated head/neck cancers tend to behave very differently in terms of how they respond to therapy. Those with the HPV-positive cancers tend to be younger. And when they're treated, even with very advanced disease, the cure rates can be as high as 90 percent. Whereas patients with HPV-negative disease, even with similar stages compared to those with HPV-positive disease, when they're treated unfortunately their results tend to be consistently not as good, their chance of recurrent cancer tend to be quite a bit higher.

Dr. Lee Freedman:

And is that felt to be related to any specific treatment that targets the virus or we just don't know why there is that difference?

Dr. Alexander Lin:

We don't really understand very well at this point. It seems to be that the HPV-negative head/neck cancers seem to be more induced by a heavy exposure to tobacco and smoking. And for some reason, that seems to make these cancers more biologically aggressive and less responsive to treatment. Moving forward, I think we are going to start to try to tailor it, figure out why HPV positive cancers are so responsive and try to tailor treatments to respond to that. Meaning maybe we can get away with less dose of radiation, maybe we can think about less aggressive chemotherapy, maybe we can tailor vaccines that are specific for HPV. On the other hand, for patients who have HPV-negative cancer, we need to find out why they're so resistant to treatment and to target the pathways that lead to resistance.

Dr. Lee Freedman:

Well why don't we continue by talking about one of these particular types, the way that you might approach an HPV-positive ENT cancer.

Dr. Alexander Lin:

Sure, these patients again, like I said, tend to be young, very healthy, and are cured on a higher rate. And they're likely going to live a long time after their diagnosis and treatment. So our goal is to maintain their quality of life and making sure that we're maximizing their cure rates. One of the problems up until now with head/neck cancer treatment whether it's with surgery, or with radiation or chemo, is that often it comes at a price. It comes at a price of side effects during treatment and even after treatment. And often when I sit with patients, they're grateful patients, they're years out from treatment, but when I sit at a meal with them and talk to them, I can tell the impacts that our treatments have had on their lives. They have dry mouth, they can't taste some of their foods, they can't eat certain foods, and so it really does kind of hit close to home when you see the effects of our treatment. For these patients who are going to live a long time, we want to maintain the quality of life.

We are now trying to think of ways that we can minimize the toxicity of surgery and radiation and chemo. At Penn we've pioneered for our otolaryngology department an approach called transoral robot, called TORS. Transoral robotic surgery was before, in order to resect an oral pharyngeal cancer, they would have to do a very expensive surgery, a very invasive surgery, or they'd have to essentially crack the jaw open in order to do get access to the base of tongue or the tonsil to resect that. Now they can bypass that and they can access that using a robotic arm. The advantage of this is that the recovery times are much quicker after surgery. Many more patients who previously would not have been a candidate for surgery can now get surgery. And in so doing, we can remove the very small cancers that arise on the base of tongue and tonsil that often spread to the neck where the bulk of disease is in the neck we're able to resect the tongue or tonsil cancer very easily now. The advantage of doing so, getting the bulky cancer out, getting the neck nodes out, means that once we're done with the surgery even if they need to get radiation, the dose of radiation we have to give is much less compared to before when a patient could not receive surgery and we had to treat radiation with definitive intent, meaning that we had to give radiation for intact gross disease.

Dr. Lee Freedman:

So this is a more extensive surgery, but done with less damage to the healthy and surrounding tissues that then allows a reduced dose of radiation.

Dr. Alexander Lin:

Right, I would even say that the surgery now, compared to before, is less expensive and allows more people to get surgery and in so doing, allows us to give less dose radiation.

Dr. Lee Freedman:

That's wonderful, and are there any unique side effects to this particular approach?

Dr. Alexander Lin:

Yeah, we've seen in some cases where after surgery and radiation, two or three months afterwards, sometimes patients can develop an ulcer in the area where they received their surgery and radiation in the back of the mouth, in the tonsil and the tongue. These areas heal up after a couple of months of treatment, but we also realize the impact that this can have in terms of pain and requirements for needing

to take medications for the discomfort. So we actually believe that for well-selected patients where the primary tumor is very small, cleanly resected, has no adverse risk factors that we can actually think about omitting radiation to where the tumor started but continue to give radiation to where the bulk of the disease has spread to in the neck. Now this is a study that we have open here at Penn and only at Penn. And again, it's an investigational study and one that we believe has great scientific merit in terms of still preserving a very high rate of cure while decreasing the risk of long term side effects, short term side effects from our treatment.

Dr. Lee Freedman:

So, really not needing to give radiation to the primary site in the selected patients.

Dr. Alexander Lin:

That is correct.

Dr. Lee Freedman:

Now you mentioned you do proton therapy, is there a role for proton therapy in these type of patients?

Dr. Alexander Lin:

We believe so. So we have a proton therapy center here at Penn. Proton therapy is radiation still, the only difference about protons is its ability to stop and to minimize exposure to tissues that are adjacent to the areas that we want to treat, meaning less potential collateral damage. We believe that this has great potential. And we are currently treating patients with proton therapy under study. And we are planning to be able to inform the community and the world about our data comparing protons to what is currently the standard of care, which is intensity modulated photon radiation with an eye on whether protons does as good of a job or better in terms of controlling head/neck cancers. As importantly, by doing so are we able to also reduce the significant side effects that one sees during treatment and afterwards?

Dr. Lee Freedman:

Well two very important studies in these type of patients at Penn. If you're just tuning in, you are listening to Medical Breakthroughs from Penn Medicine on ReachMD, the channel for medical professionals. I'm your host Dr. Lee Freedman and joining me today is Dr. Alexander Lin, Radiation Oncologist, talking about new treatments for head and neck cancers at Penn Medicine. Dr. Lin, maybe we should shift gears now and talk about those more recalcitrant patients, those with the HPV-negative cancers.

Dr. Alexander Lin:

Yes, we also think that's this is a very important area of study because these patients do not have as good of an outcome or result or a cure rate as those with HPV-positive. And if you look at the treatment paradigms for these patients, it's very similar now compared to ten or twenty years ago. Advances have been, I would say, somewhat oncoming in terms of the radiation techniques and such, but we haven't seen a major breakthrough in dramatic improvements in cure rates. And we start to ask the reason, well why is that? What is it about these cancers that make them so resistant? One theory is that these cancers may have a high level of hypoxia, an absence of oxygen in these tumor cells that make them less responsive to treatment. And the presence of hypoxia may then activate mechanisms that promote disease aggressiveness that may help them to spread to regional areas or even systemically to the point where a patient may become incurable.

And so we've done a lot of work here at Penn researching the mechanisms and why these tumors may be resistant. We think that it's because of hypoxia. We've been able to measure head/neck cancer tumors showing that those are more hypoxic, patients who have more hypoxic tumors tend to have a worse disease outcome. We have a way to image hypoxia using a novel tracer through a PET scanning, called EF5 that was developed here at Penn. And we have a drug that we believe can actually improve tumor oxygenation and decrease tumor oxygenation consumption of these tumor cells. So by so doing, improving the sensitivity of these very resistant cancers to radiation. The drug is called Nelfinavir.

Dr. Lee Freedman:

Interesting, and to me that's a little counterintuitive in that. I know we treat sometimes other cancers or metastasizes by trying to cut off the blood supply and make them ischemic and this, if I'm understanding correctly, seems to be that these type of tumors actually are more resistant because of hypoxia and possibly ischemia.

Dr. Alexander Lin:

Correct, and the way that radiation actually works is by interacting with oxygen in our tissues to create these oxidated radicals which then go and damage the DNA of tumor cells. And so if we can improve the oxygenation we would then therefore improve the sensitivity of these cells to radiation therapy.

Dr. Lee Freedman:

Well that really sounds fascinating. Are there some trials going on with these agents and with this type of imaging that you talked about

that can identify hypoxia?

Dr. Alexander Lin:

There is, and we have a trial here, we've opened a single on phase two trial that's open now for the next five years. And this is funded by the NIH through an R01 grant and we're very excited in this trial. It's for patients who have HPV-negative larynx cancer. These are patients who, oftentimes, are offered the option of chemoradiation as their treatment, which their outcomes are not great or suboptimal compared to our HPV-positive counterparts or the other option is removal of the larynx in which the results are still equally suboptimal. And so, patients are having to choose between two not great treatment options knowing that their long-term outcome results are not as good as they can or should be. We here at Penn are now combining our strengths in imaging where we can image patients with this cancer and detect how much hypoxic is their cancer, give them a drug, Nelfinavir, that has been show to improve oxygenation in these tumors, repeat the imaging to see how much the hypoxia improves. And then we give them chemo and radiation and Nelfinavir for seven weeks, which is the standard way to preserve ones larynx and to treat the cancer without having to remove larynx. And we believe that by doing so, we will be able to improve the outcomes for these patients in terms of preserving their larynx and also curing their cancer.

Lee Freedman:

So you think that the outcomes in terms of curing the cancer will be as good or even better than with standard treatment that does involve removing the voice box?

Dr. Alexander Lin:

We believe so. We believe that these results would be better than the results seen with surgery followed by radiation for larynx cancer as well as standard chemo radiation for larynx cancer.

Dr. Lee Freedman:

That's very interesting and can you tell us more about this novel agent, Nelfinavir, and how it improves the hypoxia? Is it a vasculogenic type of treatment?

Dr. Alexander Lin:

We actually are not quite sure what the exact mechanism is. We have data in vitro and in vivo showing that it does improve oxygenation. We see that it improves intrinsic as well as extrinsic radiosensitivity. And part of it may be through the vasculature and part of it may be just through oxygen consumption or by improving oxygenation it may downregulate some molecular mechanisms that typically lead to more increased aggressiveness and ability to metastasize. And part of this grant is actually funding a lot of the mechanistic work that we're going to be doing on these patients tumors to see how this drug is working exactly.

Dr. Lee Freedman:

Is it a well-tolerated agent? Are there side effects?

Dr. Alexander Lin:

A very well-tolerated agent, in fact, we had kind of already conducted a phase one study. The patients receiving chemoradiation with Nelfinavir for locally advanced lung cancer and those results have been published in very highly respected journaling showing that it's safe, tolerable, safe to give, and well-tolerated by patients.

Dr. Lee Freedman:

Right, I very much want to thank Dr. Alexander Lin for speaking with us today about the new developments, particularly at Penn Medicine, but also in general in terms of the field of head and neck cancers. It sounds like we are developing many more tools that have the outlook much more positive for patients with this sometimes devastating disease. And again, Dr. Lin, thank you for your insightful comments.

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