

Q&A Session: Post-Operative Radiation Therapy for Cancers of the Head and Neck: indications, Results, and Future Directions, with Dr. Alex Lin

Dr. Weiss: Dr. Lin, thank you for that excellent comprehensive introduction to adjuvant radiation therapy. In listening to your discussion in who needs adjuvant radiation therapy I saw the advanced nodal status and the highlighting of extracapsular extension and lymphovascular invasion. Is the size of the primary tumor or the extent of invasion of the primary tumor also a factor for you?

Dr. Lin: Yes, it is. In general, larger tumors are one's that are indicated for radiation. So I would say we stage tumors by their size and by their location and by what other areas they invade. So any tumor that's a T3 or T4 tumor that's been resected, I would counsel them to seriously consider post-operative radiation.

Dr. West: I wanted to ask, as well, what is used now to help manage the mucositis that patients are experiencing? Are there drugs or any other techniques that you're routinely offering to try to help patients navigate through that challenging time, or is this just something that you have to give hydration and a PEG tube and enough of a safety net so that they can struggle to get through it till the end?

Dr. Lin: That's a great question, and it's a major issue for a lot of our patients, but now that we're able to conform the radiation a little bit better, I think that maybe we're able to control the severity of mucositis. But that being said, the majority of patients are still at high risk for developing symptomatic mucositis that may require medication such as narcotic medication for pain control. There are several things that are on the horizon that I believe may be of benefit. One of them, we're conducting a trial here at Penn with Neurontin, and what we have found is that patients who are taking Neurontin, we believe that the mucositis pain has a very large neuro component to it, and patients who are on Neurontin will still have mucositis on examination, but they're subjective feeling of mucositis and the pain associated with it has been, at least on our preliminary evaluation, much less severe than what we would expect.

And we're also testing agents now that we believe may protect the mucosa. One of my colleagues here at Penn, Dr. Harry Kwan, is using olive oil for patients who are undergoing head and neck chemo radiation or even radiation alone; swish and swallow olive oil, extra virgin olive oil -- and we believe that the high levels of anti oxidants on the olive oil may actually protect that mucosa; sort of as an anti-inflammatory agent. So that's another agent that's out there that we're testing in a clinical trial now and the preliminary data have been promising.

So agents such as that, olive oil and medications such as Neurontin, may be able to combat some of the severe toxicities associated with severe mucositis.

Dr. West: As the newer radiation techniques become more honed, has that actually led in your experience to patients having less toxicity or are we primarily now using this to increase the dose a little more to the target region and still pushing and pushing to a newly defined maximum tolerated dose?

Dr. Lin: So far we've really used it more to try to decrease toxicity. Especially with risks such as xerostomia; what we've found is the ability to spare the salivary glands is really much better with IMRT compared to conventional radiation. There have been trials looking at dose escalation, right now that hasn't been something that's commonly used with photons. It's certainly something that we can consider with protons for the appropriate patients.

I believe that patients that are at very high risk of progression or recurrence or those that don't seem to be responding well to treatment, during the middle of treatment -- those are patients who would be candidates for dose intensification.

The ability of using IMRT also, I think, has led us to be able to treat areas that we previously couldn't treat. So one example would be nasopharynx cancer. Nasal pharynx cancer has a tendency to involve the parapharyngeal spaces which are wrapped right around the area of the spinal cord. And using conventional radiation techniques, it was really difficult to deliver adequate doses to the parapharyngeal spaces without overdosing the cord. So that was a real treatment limitation and now that we have the ability to sculpt out dose and deliver high dose to these areas close to the spinal cord, but yet protect the spinal cord what you're seeing is that results of the IMRT for nasal pharynx are excellent. Local control rates of 90% or above.

Dr. West: How do you discuss with a patient whether to place a PEG tube prophylactically at the beginning of their treatment versus trying to get them through it without that? How common is it for you to recommend a PEG tube, and is it based on the location of the tumor and the extent of radiation that you foresee, or how much of it is a patient's health going into this; just desire for or against it...things like that?

Dr. Lin: It's a combination of all those things. I will consider the extent of volume to be treated, the dose that I will need to treat to, whether they will be receiving chemotherapy or not, because that dose tend to increase the toxicity of radiation. And then also the shape of the patient: how healthy are they? Do they have good nutritional status currently? Someone who has poor nutritional status to begin with, I'm a little bit more concerned about their ability to get through treatment. And then the patients preference on how aggressive they think they can be. What I've found is that patients who are self motivated, who are healthy, who have good nutritional intake, can usually get through treatment with good supportive care and really maintain their nutrition.

For patients who are having a hard time swallowing or have baseline dysphagia already from their surgery or from their cancer, I think it's going to be really hard to get them through without a PEG tube.

Some of the drawbacks of putting in a PEG tube up front are a risk of complication or infection risk from the PEG tube, and also the potential reliance on the PEG tube when they physically can still eat and drink and swallow.

So it's really an evaluation of a combination of factors.

Dr. West: You had said that having them to continue exercise and not lose the ability to swallow over that, having the PEG tube I imagine would be some compromise of that.

Dr. Lin: Yes and it's my preference actually to try to get through treatment without a PEG tube and for the patients who can't do it we can then consider inserting a PEG tube during treatment if they really can't maintain adequate oral intake.

Dr. Weiss: At the initial evaluation, patients sometimes make a very difficult decision between surgery and radiation, and we're planning in the future to discuss definitive -- meaning curative intent radiation and chemo/radiation on GRACE -- but for the patient who chooses surgery who is then told later "you need to go back and now you need radiation also", they're often a little bit frustrated, and they often want to know what the surgery was for, and they also wanted to know how that radiation is different. Can you describe how you treat the adjuvant patient differently from the patient for whom radiation is going to be their primary curative modality?

Dr. Lin: Yes. So the difference between definitive chemo/radiation and post-operative radiation is that, in general, patients won't need as high of a dose of radiation. The typical treatment course will be anywhere from 5 ½ to 6 ½ weeks, whereas with patients who are getting definitive chemo/radiation, they're treatment course will be upwards of 7 weeks.

So they will receive a higher dose if they haven't received surgery. And also I can use the information from the neck dissection to kind of tailor what areas of the neck I would need to treat and to what dose. So for patients who don't undergo surgery, most likely they would have a larger area of the neck radiated, whereas that may not be true in the post-operative setting.

I do think it's important, however, for patients who are trying to make the decision between surgery versus non-surgical options with chemo and radiation to see a surgeon as well as a radiation oncologist or medical oncologist to discuss each approach and the pros and cons, so that they have a full understanding of what they're getting into before they undergo major treatment.

Dr. Weiss: I have another post-op question for you. At Penn, tumors of the oropharynx, meaning of the tonsils and the base of the tongue, a lot of these patients get trans-oral robotic surgery as a new surgical technique. I was just recently at the tumor board of another institution where there related technique, trans-oral laser surgery is very commonly used and I heard a very interesting debate between two radiation oncologists about whether every trans-oral laser patient needs adjuvant radiation therapy or not. Do you have an opinion on that?

Dr. Lin: That's an interesting question and it's really an evolving field. I think the potential advantages of trans-oral surgery are that for the carefully select patient -- I believe that the robot is actually FDA-approved for T1 and T2 primary tumors -- they may be able to receive a non-invasive surgery, and it may buy them the ability to receive a lower dose of radiation or they may not need chemotherapy, whereas before they might. And it also may cut down in the incidents of long term swallowing problems.

We talk about organ preservation with radiation, but there are publications out there of higher rates of PEG tube dependence than what we see here at Penn. And so the thought is by doing trans-oral surgery you may be helping them to de-intensify their chemo and/or radiation and thereby potentially reduce the risk of long term toxicity. The question of whether to irradiate those patients -- what I've been trying to do is use the same standards for post-operative radiation as someone who undergoes an open resection. So we look at high risk pathologic factors. If they have any factors

such as number of nodes, a large node, nodes on the contralateral side of the neck, extra-capsular extension or at the primary tumor site if they have close margins or lympho-vascular invasion, or perineural invasion; all of those things are still indications for radiation. I don't think we can safely omit radiation in this specific population.

Dr. Weiss: Well great. Thank you very much.

Dr. West: I really would like to thank you, Alex, for a terrific overview, not only of radiation in the context of head and neck cancer, but a really good historical context, and also a great summary of what a lot of people with a wide range of cancers might ask about how they should think about radiation and whether it applies for them.

So thank you so much.

Dr. Lin: Thank you very much. It was a pleasure to be able to participate.

Dr. Weiss: Good night.