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The Role of Tissue Acquisition in Diagnosing Non-Small Cell Lung Cancer

Announcer:
You're listening to *Deep Breaths: Updates from CHEST* on ReachMD. The following episode is part of a four-part educational campaign brought to you by CHEST in collaboration with AstraZeneca.

Here's your host, Dr. Gerard Silvestri, Hillenbrand Professor of Thoracic Oncology of the Division of Pulmonary and Critical Care Medicine at the University of South Carolina.

Dr. Silvestri:
When performing diagnostic procedures on patients with non-small cell lung cancer, clinicians can uncover a wealth of information directly from their patient's collected tissue that can help inform treatment decisions. In today's program, we'll be discussing the importance of tissue acquisition, proper handling of specimens, rapid onsite evaluation during EBUS-TBNA procedures, and much more.

Welcome to *Deep Breaths: Updates from CHEST* on ReachMD. I'm Dr. Gerard Silvestri. And joining me today to talk about lung cancer is Dr. Michael Machuzak. He is a Staff Member in the Department of Pulmonary, Allergy, and Critical Care Medicine at Cleveland Clinic. Dr. Machuzak, welcome to the program.

Dr. Machuzak:
Thank you, Gerard.

Dr. Silvestri:
My pleasure. We're going to talk about a few things today. But the first thing I want to talk to you about, Michael, is can you tell us why tissue acquisition has become such an important part of the diagnostic algorithm for non-small cell lung cancer?

Dr. Machuzak:
Well, I think there are several reasons why just going from the basics when someone shows up with lung cancer, there's an 80 to 85 percent chance they're going to have non-small cell lung cancer. And that's significant because we now have got targetable mutations and checkpoint inhibitors that we can use that have been shown to tell us about prognosis, but more importantly, actually, extend quality of life and progression-free survival in these patients. And many of these medicines do so with less adverse effects to the patients.

Along those lines, there are new therapies that are continually evolving. There are medicines that weren't in existence eight or ten years ago that are now commonly being used and being used as first-line, second-line, and third-line treatments. And these are the types of medicines that are having an impact in our patient care.

Dr. Silvestri:
And so let me ask you this question. What if I gave somebody who might have had a target immune mutation chemotherapy rather than one of these EGFR inhibitors like Tarceva? Wouldn't they do about the same?

Dr. Machuzak:
Yeah, that's a great point. And I think that is one of the paradigms that we're trying to change. When patients first presented with lung cancer, there was a very broad view of what chemotherapy was. It was a platinum-based doublet. And now that we are able to target certain mutations, and these mutations can turn off the cancer and kill the cells, we now are seeing clear improvements in survival, and survival that we thought was really not possible, traditionally, with standard chemotherapy in lung cancer care.

Dr. Silvestri:
With that in mind, what's the biggest mistake made during the tissue acquisition process? If we know that this is important to get tissue in to get it sent off, what is the biggest mistake you see when patients are referred in for a second opinion to the Cleveland Clinic?

Dr. Machuzak:
I can tell you that getting additional tissue, in particular tissue with the idea that we're looking for these targetable mutations, is probably the largest error that we see. Now that goes back to a couple different reasons. Years ago, we weren't very good at TBNA. And we were happy just to establish a diagnosis of cancer or normal lymph node. That's not the case anymore. So what we really need to make sure is that we've got tissue that confirms a diagnosis and tissue that we can use to send off, whether this is going to the next generation sequencing or whether it's something that is done in house, but tissue that will tell us how are we going to guide therapy today and potentially therapy down the line. So number of passes is really important. And then making sure that we got a visible, large sample of tissue in our containers in our fixative or in our formalin.

Dr. Silvestri:
So how many passes do you generally get when you do a bronchoscopy, where you know you'll be sending for molecular analysis?

Dr. Machuzak:
So that's another great question, Gerard. I think the key is making sure that we've got plenty of tissue in there. And the way that we tend to approach it is, we know that there's kind of a plateau at three to four passes for diagnosis. But that's not it. We need to go in additional three or four passes past that to make sure that we're getting good tissue that can be evaluated. So we're talking about no less than five passes, and maybe eight or nine passes, depending on what we visually see in the container.

Dr. Silvestri:
So Michael, is there a preferred needle that you use for these procedures?

Dr. Machuzak:
Yeah, I hear that a lot. And what I can say is, whatever needle you are most comfortable with is going to be the needle you should stay with. Now that has to be tempered by taking a true critical look at yourself and looking at your own diagnostic yield. We know this is a procedure that should have a high yield and a low failure rate for getting molecular markers sent off. And if we're not achieving that, then maybe you need to look at changing the needle. But in general, the data has shown that the size of the needle or the type of the needle does not change how we do.

Dr. Silvestri:
Okay. And you said that there's should be a high likelihood of being able to do molecular. Is that over 80 percent? Over 90 percent? What would you say is high if someone's going to really start checking their own outcomes?

Dr. Machuzak:
I think if you go back and quickly review the data in the literature, we're looking at something that should be less than 5 percent for a failure rate. So we're talking about a 95 percent success rate when we're sending off for this type of tissue. And this type of tissue analysis.

Dr. Silvestri:
Michael, once the tissue has been collected, how can we ensure proper handling?

Dr. Machuzak:
I think that there are several ways that tissue can be processed here. That there isn't one absolute right way. So my recommendation would be to sit down with your cytologist or your pathologist and have a conversation about how do they want it to go. And that may change. If we're talking about a situation where we may suspect lymphoma versus a non-small cell, we may process that tissue a little differently. So having an idea of what the cytologist or pathologist prefers is the first step. And once you do that, then ensuring that everyone that's involved in that procedure, from needle in the node to specimen in the container, are well versed in how it's handled.

Dr. Silvestri:
It's important for the cytologist and pathologist to really be involved with that, because they're the ones who now have taken that specimen, and to maximize yield, they need to get that specimen or format that they like it. And so communication between not just the pulmonologist and the pathologist, but also maybe even the oncologist to make sure that you're testing for the right things.

Dr. Machuzak:
And I think that's a great point, Gerard, especially because if there are discussions about a patient potentially going on to a clinical trial, that sample may need to be handled differently as well. So not just having a cytologist, pathologist, but also the oncologist involved, I

think is a fantastic recommendation.

Dr. Silvestri:
For those of you just tuning in, we're listening to *Deep Breaths: Updates from CHEST* on ReachMD. I'm Dr. Gerard Silvestri, and I'm speaking with Dr. Michael Machuzak about tissue acquisition for patients with non-small cell lung cancer.

Michael, we just spoke about some of the tools and procedures used to collect tissue. Keeping that in mind, can you give us a brief overview of rapid onsite evaluation for EBUS? And tell us what ROSE means to you, what ROSE means in your lab? And more importantly, what happens if you don't have ROSE?

Dr. Machuzak:
Another great question, Gerard. So ROSE, in general, stands for rapid onsite evaluation. And that can be done many ways. Probably one of the most common ways is there's a cyto tech that will process the specimen and take a look at it under the microscope. In some cases, you're fortunate enough to have a resident or a fellow. And if you're luckier, you have the actual staff involved. So what will happen is I'll take a sample of a lymph node, we will plate it, make a smear, one smear goes into a fixative, the other one gets air dried, and then goes through a DiffQuik treatment. And then our cytologists will take a look at it. And they can tell me, yes, you've got adequate tissue, that adequate tissue also shows lymphocytes, but no sign of cancer. And after a few passes there, I'll move on to the next lymph node. And then if we get the confirmation of malignancy, I can stop right then in there. So what's nice about that is my procedure can end at that biopsy station, meaning I don't have to go on and try and biopsy the nodule, the mass, or the parenchyma; I can focus on where I am.

But something that I think is just as important, if not more important in the situation is they can also tell me a little bit about the tumor itself. And if they're seeing something that looks like a non-small cell, then we know we really have to focus on getting adequate tissue. So we're going to process it a little differently. We're going to do additional passes, get lots of tissue in the fixative, lots of tissue in the formalin. And also if it is a malignant lymph node, but a malignant lymph node that doesn't have a high tumor burden, then I may need to look at another site. Because we want to make sure we don't just have cancer in there, but we've got cancer cells that can be evaluated for markers down the line. So having that conversation back and forth, I found to be incredibly useful.
And additionally, if you're just starting out with this procedure, I think having that rapid feedback, you know, this worked, what I did here didn't work, that can improve you as a bronchoscopist, and ultimately make this a more viable procedure for you and your patient down the line.

Dr. Silvestri:
And what if you didn't have that? I know that Cleveland Clinic course has that technology. What then do you tell your colleagues who may be in a smaller community hospital where they just don't have the staff? Are there other ways to get either some sense that you have rapid onsite evaluation, or what do you tell them to do with their specimens and the fact that there can be no one there?

Dr. Machuzak:
Yeah, I think there are a lot of levels to how this can play out. We can have staff in the room or just outside of the room, we can have a resident or a fellow or a cyto tech or your nurse RT or tech can also gain some knowledge and get taught how to process these. Additionally, there are also some new devices that are coming down the line that will do some processing for you. So having someone on site to take a look at it and depending on who that is will depend on what kind of information they can give you, adequate versus inadequate versus malignancy versus high tumor burden. But there's also additional technologies that are out there. And now, web-based cytology cameras are available. And you can take the slide, put it into the machine, and the cytologist can be across the street or across the country, and they can move the camera to evaluate that slide and give you a rapid evaluation of that sample right then and there. Technology has really advanced in the last five or ten years to make this a viable option if you're in a location that is remote or one that doesn't have a cytologist or a cytologist that's comfortable with rapid onsite evaluation.

Dr. Silvestri:
Well, skilled clinicians and the right tools will only aid in the quest to help our patients with lung cancer. And with those thoughts in mind, I want to thank my guest, Dr. Michael Machuzak, for joining me today to talk about tissue acquisition and rapid onsite evaluation during an EBUS-TBNA and a procedure for patients with non-small cell lung cancer. Dr. Machuzak, it was great having you on the program.

Dr. Machuzak:
Thanks, Gerard. I really feel honored to be included in this.

Announcer:
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