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### Detecting Thyroid Cancer Using Ultrasound Elastography

Have radiologists uncovered a new epidemic with ultrasound? You are listening to ReachMD XM160, The Channel for Medical Professionals. Welcome to Advances In Medical Imaging. I am Dr. Jason Birnholz, your host and with me today is Dr. Theodore Dubinsky, who is Associate Professor of Radiology Obstetrics/Gynecology, and Reproductive Health Sciences and Director of Body Imaging at the University of Washington in Seattle. Today, we are discussing thyroid nodules and a new ultrasonic technique for identifying thyroid cancer.

#### DR. JASON BIRNHOLZ:

Hi Ted, thanks for joining us.

#### DR. THEODORE DUBINSKY:

You are welcome.

#### DR. JASON BIRNHOLZ:

Well, I wonder if we can just get into this topic kind of indirectly by having a little background on thyroid nodules and thyroid cancer.

#### DR. THEODORE DUBINSKY:

Well, I think as you know, as we have been doing more imaging, ultrasound imaging, and CT scanning of people, we have been finding more and more thyroid nodules and the prevalence has been reported to be about 3% to 8% in the general population, but that increases significantly as people age and it's actually greater than 50% in people over 65 years of age. We are finding more and more nodules in people all the time. In reality, because we are finding so many more benign nodules, the risk of cancer of any given nodule is actually decreasing, as we are doing more imaging. Somewhere between 5% and 15% of all nodules have been reported as being malignant, but more recently that number seems to be declining just because we are finding more benign nodules.

#### DR. JASON BIRNHOLZ:

Well, finding nodules, you are talking about using imaging method, is palpation still worthwhile?

**DR. THEODORE DUBINSKY:**

Well, palpation works if the nodule is greater than 4 cm in diameter, but the vast majority of nodules we are talking about are a centimeter to 2 cm in diameter and palpation is completely insensitive for these. So, imaging is really where these are being detected.

**DR. JASON BIRNHOLZ:**

I mean, should our colleagues be referring more patients for ultrasound or should radiologists just be doing more thyroid ultrasound when patients come into them?

**DR. THEODORE DUBINSKY:**

I think if there is concern about a thyroid problem, ultrasound is the study of choice. These cancers are generally fairly slow growing. Many of the nodules that we find are incidentally detected and ultrasound is probably the best study to evaluate them and determine what their risk is for being potential malignancies. However, because they are all slow growing, there really is time to follow these for a few years even to determine if they are enlarging before anything what has to be done.

**DR. JASON BIRNHOLZ:**

Okay, you say that most are slow growing, but not all.

**DR. THEODORE DUBINSKY:**

No and that's why any give nodule that we find it's probably prudent to follow it whether we think it's benign or malignant and as you know, Jason, none of the criteria for predicting malignancy are a 100% perfect.

**DR. JASON BIRNHOLZ:**

No, even though it seems to be that the situation of the thyroid cancer is very much like that of prostate cancer before PSA came along and that is you have a very frequently occurring problem that often tends to be ignored, what you have that ignored in the past because many of them are slow growing, but not all, the bad ones are very bad.

**DR. THEODORE DUBINSKY:**

I think that's a good analogy actually and right now there is no good serologic screening test for detecting thyroid cancer or determining which of the nodules are going to be highly aggressive types of cancers and which are going to be the slow growing less aggressive types.

**DR. JASON BIRNHOLZ:**

Okay, well let's turn this amount. If you want to define as many cases of thyroid cancer as early as possible in the population, what would you do?

**DR. THEODORE DUBINSKY:**

Oh, I think ultrasound is clearly the best screening test for looking for thyroid nodules. We can detect nodules as small as 2 or 3 mm and we can tell whether they are cystic or solid and then of course you can evaluate them for microcalcifications and irregular borders and hypoechogenicity and other factors that would either increase or decrease the risk of that nodule's malignant.

**DR. JASON BIRNHOLZ:**

Okay, so you are doing basically what radiologists do in every other part of the body as you are identifying something and then applying a series of criteria to try to classify what that problem is and to rate how bad it is in many ways. Does this require any special kind of ultrasound equipment?

**DR. THEODORE DUBINSKY:**

It does. You need high-resolution linear transducers and you need state-of-the-art ultrasound machines because of the difference in particularly to detect the microcalcifications. They are very small. The difference in echogenicity between them and the surrounding tissue is therefore not that great and clearly since this is the highest risk finding for predicting malignancy, the better the equipment, the better the ability of the radiologist doing the exam to make this distinction.

**DR. JASON BIRNHOLZ:**

However, this is generally available all across the country, isn't it? It's not just 1 or 2 places that will do this.

**DR. THEODORE DUBINSKY:**

Oh no, this could be done in most radiologist offices around the country.

**DR. JASON BIRNHOLZ:**

When a patient comes in and you have gone through all of your work and you say, well this is very likely to be a thyroid cancer, what happens next or what was the standard before your current work?

**DR. THEODORE DUBINSKY:**

Well, I think the standard has always been to do a fine-needle aspiration using ultrasound guidance. We can put a needle into the thyroid gland and sample some of the cells to determine whether they are malignant or not, but there are problems with doing fine-needle aspirations particularly that at least 20% of time the yield is inadequate for an interpretation and the other problem is that frequently these are follicular-type nodules and it's very difficult for the pathologist to distinguish follicular carcinoma from follicular adenoma and frequently in that situation we end up following them to determine if they are growing or not any way, so FNA is an imperfect means for determining whether something is malignant or not.

**DR. JASON BIRNHOLZ:**

If you have just tuned in, you are listening to *Advances in Medical Imaging on ReachMD, The Channel for Medical Professionals*. I am Dr. Jason Birnholz and I am speaking with Dr. Ted Dubinsky at the University of Washington in Seattle and we are discussing thyroid nodules, thyroid cancer, and ultrasound diagnostic, specifically a new variety of ultrasound elastography.

Well, Ted you were just saying about failure rates of biopsies and I presume that there is also a complication rate as well, although it's low.

**DR. THEODORE DUBINSKY:**

It is low. Hemorrhage is the most common complication that we encounter. Infection is certainly possible and I suppose it would be possible to perforate a large vessel, a carotid or jugular, if one weren't careful. The good news is that using ultrasound guidance, the complication rate really is quite low, but it's not zero as you mention and clearly there is some risk involved in doing these.

**DR. JASON BIRNHOLZ:**

Well, I wonder if we can move on to elastography. Can you give our listeners kind of an overview of what elastography attempts to achieve?

**DR. THEODORE DUBINSKY:**

Elastography is a technique for measuring the hardness of a nodule, a substance, or a nodule that is harder than another nodule can actually be imaged and what's been done historically, particularly in breast imaging, is that a transducer, an ultrasound transducer, is put over the lesion in question and then just the certain amount of pressure is applied to that nodule and that nodule will deform. As you push on it, it will get less tall and it will get wider and it's quite possible to measure the difference in size that occurs with these nodules and that's called strain and we can actually see these nodules deform. Now, the limitation of elastography has been that by doing external manual compression, there is no way really to quantify how much pressure someone is putting on the nodule. So, if you were to push on this nodule and I were to push on this nodule, we would be pushing with varying degrees of force, which is not very accurate and so what we have done for thyroids is rather than using external compression, which is quite inaccurate, we have actually used the carotid artery as the compression source and everybody has a carotid artery that's adjacent to their thyroid gland and believe it or not, we can actually measure the strain that's put on these nodules from the carotid artery. Most people have a fairly consistent blood pressure in their carotid arteries and the deformity that occurs in the nodules is in the range of micrometers. So, using very high-resolution ultrasound images, we can measure the nodule during diastole and then during systole and then by comparing these 2, we can determine how hard the nodule is and what we do is we get a measurement of the deformity of that nodule and then we just compare it to the soft tissues adjacent to the carotid artery, which are assumed to be normal and this normalizes the strain that these nodules undergo for every patient and therefore we can tell, okay which nodules are really harder than the adjacent soft tissues and which nodules are softer and deform more readily in the soft tissues and the data from our paper, we've had 2 papers on this, really

does seem to indicate that this technique works and that we can really tell the papillary carcinomas from the remaining nodules because they are significantly harder.

**DR. JASON BIRNHOLZ:**

So, the rationale for this work is doing sort of an exquisite and sensitive mapping of the firmness or softness of a field of view and so I guess the rationale is kind of like doing an ultimate physical exam is something hard or soft, is it rock hard or very soft or squishy.

**DR. THEODORE DUBINSKY:**

That's exactly right and I think for years this type of analysis has been done by physical exam with palpable nodules, is the palpable nodule hard, is it soft, is it mobile, and even during biopsies there has been papers written or people try to make this distinction by how hard it is to biopsy the lesion when you put a needle in it. I think all of us know if the lesion is hard, the risk that it will be malignant is much higher than if there is a soft lesion we are trying to biopsy.

**DR. JASON BIRNHOLZ:**

Well, I think your wrinkle of using the carotid artery as you are vibrating or stressing a target is really unique and clever and sort of built in, everybody has one if they are sent for an exam. Now, what about differentiating other kinds of cancers. Like, for example, do you ever get a clue that something like the anaplastic cancer, which is the one you really want to find early, are even harder or is it too early to say?

**DR. THEODORE DUBINSKY:**

I think it's too early to say. We've had so few of those in our data that I don't think we can draw any conclusions from it. Looking at our own data, there is quite a bit of overlap with some of these nodules and for example a Hurthle cell carcinoma, we really can't differentiate from the other cancers, the follicular cancer really seems to fall into a normal range. So, so far of our data, the papillary carcinomas are the only one that are significantly different and I don't know that we have had any anaplastic cancers come through yet.

**DR. JASON BIRNHOLZ:**

Now, are these techniques commercially available or is it something in the research stage, it's going to take years before it's available.

**DR. THEODORE DUBINSKY:**

Well, there was, as you know, some reluctance on the part of the manufacturers to go into elastography because they didn't see the clinical application, but since our manuscripts have been published, at least one manufacturer is actually going to put elastography on their machines and you know in our manuscripts, we basically state that currently Hitachi has it on their system and they are the machine that we have been doing our analysis on, so we use other machines to acquire the data and then we actually offload the data to an Hitachi to make our measurements currently, but it is our hope that this is going to become available very quickly. I think this has real utility.

**DR. JASON BIRNHOLZ:**

Well, I guess, as always, the referring clinician needs to talk with his local radiologist and find out what's available and what's best for the individual patient.

**DR. THEODORE DUBINSKY:**

Right, I think right now, it's not widely available and more than just predicting, which nodules are malignant or not malignant, it really does appear that we can tell what part of the nodule is malignant and that the entire nodule turns out not to really have carcinoma within it and I think that's extremely exciting and important because that can guide where to do your biopsy and improve the yield of FNAs and I think it's a significant discovery to realize that when we see a nodule, it isn't as though the entire nodule is filled with malignant cells, that may only be a small part of it and therefore even watching it or using other criteria to determine if it's malignant or not are probably not going to work as well.

**DR. JASON BIRNHOLZ:**

We tend to think of a cancer as being a discrete nodule and filling it as opposed to being a small area that goes bad and then spreads. I think that points out the limitations of the skinny needle biopsy for example.

**DR. THEODORE DUBINSKY:**

Exactly. I think that's probably why there are so many failures from FNA really.

**DR. JASON BIRNHOLZ:**

Well, that's great. Just in closing, I would like to have a small summary. Thyroid cancers are very, very prevalent and involve millions and millions of people in our population. What do you think Ted, how should we deal with this new epidemic.

**DR. THEODORE DUBINSKY:**

I think the problem is going to be ultimately distinguishing those cancers, which are going to be troublesome and highly aggressive and metastatic from those that are really slow growing and more benign and then of course the bigger challenge is to distinguish the cancers from the background of benign nodules at all. I think there are not enough resources available to biopsy every single nodule that is discovered and therefore it is incumbent on the radiologists to try to make some educated prediction as to whether a lesion is going to be malignant or not and I think the elastography is a significant help and a significant start in that direction. I think in the future predicting what malignancies are really going to be aggressive will become important and whether ultrasound and elastography will play a role in that is yet to be seen. It's possible that some other molecular or functional-type imaging may be necessary to do so, but it's clearly the ones that like the anaplastic carcinomas that are highly aggressive and malignant that we want to find early and prevent from spreading if we can. The rest of them that are more benign in appearance, I think there is time to follow them, determine whether they are malignant or not and then remove them as necessary, but the 5-year survival for the slower growing cancers is very, very high. It's over 90%, so there is not the urgency to treat these less aggressive lesions like there would be for more aggressive one.

DR. JASON BIRNHOLZ:

Seems to me that's very, very important.

My thanks to Dr. Ted Dubinsky, who has been our guest and we have been discussing thyroid cancer, thyroid ultrasound, and ultrasonic elastography. I am Dr. Jason Birnholz and you have been listening to Advances in Medical Imaging on ReachMD XM160, The Channel for Medical Professionals.