David C. Madoff, MD  I would like to welcome you to this podcast which will discuss an interesting article being published in the September 2017 issue of Radiology entitled “High-Intensity Focused Ultrasound for the Treatment of Symptomatic Benign Thyroid Nodules: A Prospective Study.” I am Dr. David Madoff the Deputy Editor of Radiology for interventional radiology and I am joined today by Dr. Brian Lang who is Clinical Associate Professor and Chief of the Division of Endocrine Surgery in the Department of Surgery at the University of Hong Kong Queen Mary Hospital in Hong Kong China. He is the lead author on this study and we just have a number of questions we would like him to address. Welcome Dr. Lang.

Brian Hung-Hin Lang, MS, FRACS Thank you very much. It’s a pleasure to be here.

D.C.M.   Thanks. So just to start off, can you review with our audience the clinical issue surrounding the management of benign thyroid nodules, when should intervention be considered, and what are the standard methods used to treat these nodules?

B.H.L.   Alright as we all know thyroid nodules, benign ones, are very common in our population and the majority of them don’t need any treatment. But we know that about 10% of nodules will get big over time. For those that are sized more than 4cm in diameter or those who are causing symptoms, obstructive symptoms or pressure symptoms. The situation when surgery is generally indicated. As a surgeon this is a very common problem for me and that’s the reason to look at. But because surgery has risks and we try to look at less invasive way of treating nodules. So we try to preserve those who have benign problems with less invasive option. I think high-intensity focused ultrasound is an attractive option for patients generally, because most of these patients are females. Obviously for other techniques such as radio frequency ablation or laser ablation or other ablation techniques they only need a needle to be inserted into through the skin and into the nodule. And that’s very minimally invasive but nevertheless you know you still need to puncture the skin. What HIFU or high-intensity focused ultrasound can do is can ablate an area without ever puncturing the skin and I think that is an attractive way of treating nodules. Also our patients who come in for treatment they actually don’t need to change, just wear the normal clothes, they come into our treatment room, have the treatment and then they go home within hours after treatment. And so I think that’s, for me, that is probably the least invasive way of treating the nodules. And also as you are aware there are of course multiple, many applications on radiofrequency ablation, laser ablation, but there has been very few studies on high-intensity focus ultrasound and that’s the reason why our centers really want to focus on this area. Just for your information, we have been treating high-intensity focus ultrasound liver lesions as well as well as uterine lesions. So this is not new for us. The liver lesions we have been treating for over 10 years. I don’t do it personally, but my colleagues they do the liver ablation and for me I do the thyroid ablation because this is part of the endocrine surgery. So my breast colleagues are using the same machines for the breast lesions. This is what we like to do over here and that’s why we’re doing it.

D.C.M.   Well thanks. Can you just explain the technology and the mechanisms of action of HIFU since many in our audience may not be all that familiar?

B.H.L.   To put it in very simple terms, basically it’s about focusing an ultrasound beam into a very small focal area underneath the skin. The depth of treatment is usually around 1 to 2 cm. If it’s too close to the skin then you worry about burning the skin. The wave length of, the (inaudible) wave is obviously a low frequency transmission. It’s an ultrasound guided treatment so it’s real time imaging focusing an area, and so for a nodule around 3cm the machine actually can actually divide the nodules into different subunits and automatically ablate the area. As long as we achieve a certain temperature change around...
Okay thanks. So for this particular study, what was your hypothesis and what previous work led to the hypothesis?

D.C.M. The hypothesis was that, well previous studies have shown that ablation will shrink the nodules, so it’s not surprising that applying for HIFU the nodule will shrink. What we’re trying to show is that not only the nodule shrinks, but patients feel better. That is feel better and quality of life will improve as a result of the shrinkage. I think in our study we have two groups of patients, although not randomized. One group had the HIFU ablation; the other group just has surveillance over a 12 month period. As we expected, we found that those who had ablation the symptom score improved relative to the controls and also the quality of life was improved. (inaudible) that we got from the ablation, physical shrinkage, there was also a symptom improvement as well as a quality of life improvement.

B.H.L. Right. Patients were, well first of all they need to have to benign in nature, so we will do a fine-needle aspiration before – at the first assessment to see if they are benign nodules. That is a Tesla 2 on cytology and also these patients are symptomatic which means that they complaining of either pressure or some sort of choking sensation we asked them; and also patients who didn’t want surgery. So these are the patients who were reluctant for surgery that we would offer ablation or observation and it’s up to them to choose. And over that period of time were at 22 patients who would desire to have treatment and 22 patients who desire not to have treatment. And we just followed them up through the 12 months and the results are showing in the papers.

D.C.M. So was there any specific laboratory values that you were looking for, any imaging findings that would make one be more likely to do HIFU as opposed to any other kind of therapy?

B.H.L. Okay. Imaging-wise apart from the cytology of course I think the nodules needs to be needs to have a low suspicion pattern which means they are (inaudible) and also they have to be well circumscribed, no suspicious features or malignancy for ablation. Does that answer your question?

D.C.M. Yes, that was very good. Thanks. Just to I guess you had already.

B.H.L. (inaudible) blood test all the patients have to be new fibroid that means the thyroid function has to be within the normal range.

D.C.M. Okay, so in terms of you had basically you had a brief overview of your results, but could you be a little more specific in what was actually found in terms of your results?

B.H.L. Okay, specifically I think in terms of nodule shrinkage the median, if I remember correctly, the shrinkage was around 70% in volume as compared to the baseline and also we found the symptoms in terms of pressure symptoms improved, and also the physical component of the health-related quality of life was improved from baseline as compared to the controls.

D.C.M. So in terms of quality of life measures, what specifically was evaluated?

B.H.L. We did the standard quality of life questionnaires. They filled in before treatment and 6 months and 12 months after treatment. We compared the values of the baseline with and we found the component improvement were mostly the physical component rather than the emotional component. The questionnaire was, if I remember correctly, was the SF HRQOL short form.

D.C.M. So I guess I was when reading your manuscript or reading your article I looked at a lot of the symptoms such as pressure, how do patients respond to – what exactly kind of pressure are they feeling?

B.H.L. Specifically there were either – they had – before treatment they had symptoms. When they lie flat they feel the pressure on the neck when they lie flat or sometimes when they try to swallow fluids, occasionally they have fluid regurgitating up so kind of choking, but it’s intermittent, it’s occasional.

D.C.M. So in patients that had more than one nodule because that often happens, how did you determine which nodule to actually treat?

B.H.L. That’s a very good question.

D.C.M. Assuming only one nodule was treated.

B.H.L. I think if I remember correctly about half of our patients had dominant nodule in a much larger goiter. So we would normally treat the dominant nodule in terms of – the dominant nodule probably would have caused the most symptoms. (Inaudible)

D.C.M. Okay, given that HIFU requires extreme precision, was this study performed under general anesthesia or moderate sedation and to that end how long do these HIFU sessions typically last?

B.H.L. We didn’t use general anesthesia, we used moderate IV sedation. The patients had a bit of pain. So they...
weren’t absolutely pain free. We asked about pain during treatment and most of them had pain, but the pain was tolerable, so in our series none of them were not able to complete treatment because of pain. It wasn’t general anesthesia. The kind of medicine we give was IV (inaudible) and (inaudible) which is a benzodiazepine. We found that an analgesia was more important so we give a high dose of analgesia. Sedation we didn’t want to give too much because that would affect the respiration. One other problem is if we give too much sedation is patients tend to have more heavier breathing and that could cause movement of the thyroid and that makes the treatment difficult and so the sedation is, the analgesia and the sedation is tricky to get the right balance. Typically the treatment takes around 45 to an hour depending on the size of the nodule. For most of the nodules around 3 to 4 cm it would take about 45 minutes.

D.C.M. Okay, great. So with regards to procedural safety, what complications occurred during this study and what are the potential complications that can result?

B.H.L. In our series about half of our patients had some sort of redness some swelling in the ablation sites and that’s not uncommon because as the analgesic goes through the skin into nodule the skin and the subcutaneous tissue and muscle actually absorb some of the analgesic and we think that’s the reason why you have neck swelling at least for the first few days. And that’s why usually we apply ice packing for the first few days, for the first few hours and after they go home they can also apply ice packing. We think that helps with the swelling, but none of them had any skin burn. We didn’t have anybody with skin burn. Potentially they could have vocal cord palsy. (Inaudible) nerve (inaudible) lies along tracheoesophageal groove if the nodule is very close or part of it is very close to the tracheoesophageal groove it’s possible you can get damage of the (inaudible) nerve and causing hoarseness of voice or vocal cord palsy.

D.C.M. So how difficult is it to identify the parathyroid gland given that you’re kind of in the same region?

B.H.L. Yes it’s almost impossible because a normal parathyroid gland you won’t see on ultrasound. An abnormal one yes of course you’d see but for a normal one you don’t see. Fortunately we have four parathyroid glands and so it’s pretty difficult to damage all four parathyroid glands because (inaudible.)

D.C.M. Okay great. So your study compared HIFU to active surveillance but not to any other ablative technology. How would you think that HIFU would have compared to other percutaneous methods that have already been tried?

B.H.L. I think that in terms of (inaudible) actually the radio frequency ablation or laser ablation or other ablation technique would be more efficient in terms of I guess the energy would bypass the skin and the (inaudible)
next steps now being done by your group to advance the understanding of this minimally invasive therapy for thyroid nodules?

**B.H.L.** I think one of the big areas to study, if you look at results, about 20% of nodules actually don’t shrink enough in the 6 to 12 months and we don’t know exactly why that’s the reason. We try to obviously since the study we have done about 120 treatments actually and we try to collect data to see whether there’s a particular kind of nodule or whether it’s the position or the power we use. I think the other things might predict who respond well to this treatment and who would not respond well to this treatment. That’s important information for patients to know so that for some patients we can select them this technology and for others that may be less responsive, maybe they should offer other thermal ablation or even surgery.

**D.C.M.** Well great. So Dr. Lang I would like to thank you for joining me today on this podcast to discuss your groups clinical work comparing HIFU to active surveillance for the management of symptomatic benign thyroid nodules. I definitely thought the discussion was very insightful and should give our viewers a good platform to understand the use of this exciting technology to treat symptomatic benign thyroid nodules as well potentially other solid lesions. We are looking forward to seeing your group’s future work. Thank you again.

**B.H.L.** Thanks very much.