Predictors of Recurrent Stroke in Patients with Ischemic Stroke: Comparison Study between Transesophageal Echocardiography and Cardiac CT

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Albert de Roos, MD My name is Albert de Roos and I'm the Deputy Editor for Cardiac Imaging at Radiology and I am today joined by Dr. Hur, Associate Professor of Radiology at Yonsei University in Seoul in Korea. And we'd like to discuss his paper entitled “Predictors of Recurrent Stroke in Patients with Ischemic Stroke: Comparison Study between Transesophageal Echocardiography and Cardiac Computed Tomography.” Welcome Dr. Hur.

Jin Hur, MD, PhD Hi. I'm very glad to be here Dr. de Roos and thank you for your kind introduction.

A.d.R. Thank you. So we were very interested in your article and we'd like to discuss a few points which will highlight the background of your study. So as an introduction, could you give a short summary of the purpose and the motivation of your study?

J.H. Well I will start with the background of this study and motivation. As you know since Dr. Manning's study which was published in the New England Journal of Medicine in 1993, transesophageal echocardiography (TEE) has become the reference standard modality for the detection of potential cardiac embolic sources. However, TEE is a semi-invasive test and usually performed under sedation. Because of the excellent image quality, cardiac CT can also be used in the evaluation of potential cardiac embolic sources. During the past few years we have studied the diagnostic performance of cardiac CT in the detection of cardiac embolic sources and we found that cardiac CT is quite a sensitive modality in detecting cardiac sources of embolism in comparison with TEE. So going one step further, we wanted to investigate whether cardiac CT finding can be used in the cardiovascular risk stratification compared with TEE findings in ischemic stroke patient. Therefore we have conducted this prospective center study.

A.d.R. Okay and you focused specifically on patients with ischemic stroke. Can you explain the purpose of that and the motivation for just selecting those patients?

J.H. Yes, it is a good point. As you know, stroke is the third leading cause of death in the United States and the second leading cause of death in Korea. Furthermore, it is the leading cause of serious and long-time disability in the United States. Therefore stroke population is very important and according to a classification system, acute ischemic stroke can be divided into five categories and among them cardiac embolic stroke has been estimated to be the causing factor in twenty to forty percent of all stroke cases. Because cardiac embolus is a treatable source, identification of cardiac embolic sources in stroke patient is important for proper therapeutic management.
A.d.R. Okay so that’s the background, but in your study you didn’t make a one-to-one comparison between techniques, but you looked actually at the outcome and the recurrence of stroke. Can you explain that approach a little bit?

J.H. Yes. In the study we prospectively enrolled 374 stroke patients undergoing cardiac CT and TEE and followed them for about one year to investigate whether cardiac CT finding can predict stroke recurrence.

A.d.R. Yes so you looked at the outcome and not to the one-to-one hat-to-hat comparison between techniques. And you looked for the outcome for recurrent stroke and what was the main results you showed from this study?

J.H. The major finding of our study was that the complex aortic plaque determined by cardiac CT and TEE was associated with an increased risk of stroke recurrence. In addition, we found that the cardiac CT parameters of aortic plaque had equivalent risk of predictive prognosis compared to TEE parameters. So our result demonstrated that cardiac CT seems to be a promising non-invasive modality in the prediction of stroke recurrence.

A.d.R. So that is an interesting finding that especially aortic plaque was predictive of recurrence of stroke, but you defined plaque as complex plaque and simple plaque and you considered complex plaque as the more predictive feature. So what do you consider complex plaque? Can you explain that a little bit?

J.H. Yeah okay it’s a good point. Many studies reported that aortic atheroma is strongly associated with stroke. It’s known that a complex aortic atheroma is more likely to embolize than a simple atheroma. A complex aortic plaque is defined when the plaque thickness is greater than 4 mm, has ulceration or has mobile compounds and all these three factors are all known to be independent risk factors for increased risk of a stroke.

A.d.R. And when I read your article correctly, I think CT detected more aortic plaques than echo. Is the aortic arch somehow a blind spot for echo? Can you comment on that?

J.H. Yeah I think that compared to TEE, CT is much more useful for measuring plaque thickness, discovering ulceration and examining its components because cardiac CT can more easily detect aortic plaque because compared to echocardiography because echocardiography has a blind spot in the proximal aortic arch. So therefore, a cardiac CT can more easily detect many complex aortic plaques. But we have to keep in mind that cardiac CT is static imaging; therefore, it cannot evaluate the plaque mobility.

A.d.R. Okay. Do you have an idea of how common aortic plaques occur in patients with stroke? Is that a large percentage or a small percentage? Do you have any idea?

J.H. I think that it’s quite a large percentage of aortic plaque detected in ischemic stroke patients because stroke is systemic atherosclerosis. There are many combined atherosclerosis in artery including carotid or aorta or coronary artery.

A.d.R. Okay so I’d like also to ask you a question about your CT protocol because I think you give up some specific tips and tricks to not only look aortic plaque but also for thrombus in the left atrial appendage and other abnormalities which may go along with recurrent stroke. Can you explain the main tips and tricks of your CT protocol?

J.H. Okay well, I will explain the cardiac CT protocol in more detail. As you know, presently there is no standardized imaging protocol for detection of cardiac embolic sources using cardiac CT. According to previous data, CT is a sensitive modality for detecting cardiac thrombus with a sensitivity ranging between 70 to 100 percent. But it is well known that its past predictability is quite low, ranging between 30 to 50 percent. This is because blood stasis can also cause filling defect, thereby mimicking a thrombus. Therefore we developed several new aortic cardiac CT protocol to differentiate more accurately between thrombus and blood stasis. One method was to add an additional delayed phase scan. Blood stasis phenomena appears when a dysfunction causes an incomplete mixing of contrast agent and blood. Therefore the delayed phase scanning will allow for a complete mixing of contrast agent and blood. However, the limitation of this two phase cardiac CT protocol is increased radiation dose due an additional delayed-phase scanning. So to minimize radiation, we proposed an alternative dual phase cardiac CT protocol which will be applied in this study. This protocol used double injection of contrast agent and the scan was performed only once in delayed phase, three minutes after giving the first contrast bolus. So using this technique, thrombus can be differentiated from blood stasis by different contract attenuation. I think that this protocol is much more useful and more accurate than with just one scan.

A.d.R. Okay but you also noted some limitations of the CT protocol, that patent foramen ovale (PFO) may be difficult to visualize by CT.

J.H. That’s right.

A.d.R. Better with ultrasound, but you also discussed that it may be not so important as a risk factor. Can you comment on that?

J.H. According to our data, many medium risk sources such as PFO are missed by cardiac CT. This is because PFO need provocative [unintelligible] for their precise diagnosis which is impossible to do with CT. However, in terms of therapeutic management many medium risk sources had limited therapeutic guidelines in current data. So in terms of therapeutic management, identification of high-risk sources such as thrombus is more important.
Okay I understand. As a final point, can you actually summarize some of the clinical implications of your study because people may think do we have to look more carefully for aortic plaque and what are the main issues that have clinical implications. Can you discuss that a little bit?

Okay. Our present data proved that cardiac CT has equivalent risk predictive prognosis compared to TEE. In addition, we found that complex aortic plaque determined by a cardiac CT was strong and independent predictors of recurrent stroke. Considering its impact on therapeutic decision and prognosis, it is critical to quickly determine the mechanism of ischemic stroke especially with embolic stroke. In that respect, we believe that a cardiac CT can be used as a test for detecting potential cardiac embolic sources in selected stroke patients instead of TEE because it is non-invasive modality with high reported disability. However, based on current guideline, cardiac CT is not allowed to be performed for the initial evaluation of cardiac embolic sources for risk assessment in stroke patients. Therefore, we should all be aware of the purpose of cardiac CT scan in stroke population. And lastly, we also have to keep in mind that cardiac CT imaging has fundamental disadvantages including radiation dose and use of contrast media.

Okay I think we have highlighted most of the interesting points of your study and we look forward to publication of your full article and I'd like to thank you for your contribution.

Okay. Cynthia tell me what was the rationale for the study you undertook? Why did you worry that low contrast objects might have decreased visualization using these iterative reconstruction techniques?

Part of our quality assurance program and part of accreditation with the American College of Radiology is to actually scan a phantom with these low contrast objects. And so we’ve been doing this on a continual basis and once we started turning on the iterative reconstruction, we noticed visually, you know we were very used to these phantoms, that we just couldn’t see these objects as well.

Okay. Cynthia tell me what was the rationale for the study you undertook? Why did you worry that low contrast objects might have decreased visualization using these iterative reconstruction techniques?

So this was sort of an observation made during routine quality assurance for the scanners, is that correct?

Correct.

And I understand that you made the observation on a phantom originally, but why use a phantom for something like this? What are the advantages and disadvantages as opposed to the study that J.G. did using a bunch of observers and clinic data?
C.H.M. One of the things about the phantom is it’s a set object that’s not going to change on us. If you do patient studies depending on the patient, the contrast, injection, the same lesions or same types of lesions could end up with different brightnesses; so we had a fixed, low contrast and then we could take that phantom from scanner to scanner. We could scan it over, and over, and over, because low contrast is a little bit, well very much subject to the influences of noise and so occasionally you’ll get a picture that looks great, but the next ten images in a row, it doesn’t look so good. And so there’s this statistical nature that we wanted to be able to scan many times and get the truth.

H.Y.K. Well it’s interesting when we started to receive the research papers on these iterative reconstruction techniques, as you note in your paper, they were all evaluated on the basis of image quality comparing with it turned on and turned off just looking at the quality of the images without any observer performance data or anything like that. And I remember in our discussions that we were very, very nervous about this, about making the claim that these were equivalent just on the basis of overall image quality assessment. So in your study exactly what did you do? Can you tell us?

C.H.M. We used the American College of Radiology phantom which is very well known and established in the U.S. and we scanned it on two different manufacturer systems. We scanned it at three dose levels and then we reconstructed with and without the use their iterative reconstruction and we used both a moderate setting and a strong setting because the looks of the images are different with the strengths of the iterative reconstruction. So that came to a grand total of 1800 images because we scanned each condition 100 times and so then we had three medical physicists who as part of their jobs review these phantoms and grade these phantom scores, go through in a darkened room, with calibrated monitor, we set the light level to the right ambient light level and had them go through and read them in a random fashion as to whether or not it would definitely pass, pass, maybe pass, I don’t remember the exact words that we used, but we had a graded scale so that they had to tell us would this pass easy our accreditation? Can I see those four nodules or those four rods accurately?

H.Y.K. Now the figure of measure you used you termed low contrast spacial resolution. How did you actually define that?

C.H.M. Low contrast spacial resolution is actually defined in terms of how much contrast there is between the background and the test object. So in this case it’s really low contrast. It was 6 Hounsfield units so not a very bright object.

H.Y.K. Good. And what did you find? What were the key results?

C.H.M. Well the key result is that if the object is visible in the filtered back projection conventional image, then using iterative reconstruction to reduce the noise and made a more pleasant image, but if you couldn’t see it in filtered back projection at the lower doses which is what happened, you couldn’t really see it in the iterative either. The iterative reduces noise but it also reduces the contrast and you don’t get benefit for these really low contrast objects.

H.Y.K. So very cautionary. Now there was a slight difference in the results between the two manufacturers. What sorts of factors might relate to manufacturer differences in terms of the ability to visualize low contrast lesions?

C.H.M. Since iterative reconstruction was introduced, it has gone through lots of generations for every manufacturer and so what we tested was not the most current that’s out on the market today. They are on a lot a lot of scanners out there and so they are relatively current, but the algorithms handle subtle contrast slightly different and the example I like to give is noise are these subtle fluctuations of the CT number. Well if that fluctuation is about the same magnitude, 6 Hounsfield units, the algorithm doesn’t know is that noise that that pixel change by 6 Hounsfield unit and I smooth it out, or was that really a 6 Hounsfield unit signal and I should leave it there. They must have slightly different ways in which they make that decision.

H.Y.K. I see. Now J.G. you studied a related but somewhat different question, you had a large number of readers and a group of political images on patients, what was actually the back story for this study? What was the rationale? Wasn’t Dr. McCollough’s work convincing enough for you on the phantoms?

J.G.F. Well there’s a lot of things that we scan in abdominal imaging and we actually have like fifty-something abdominal protocols and then there’s multiple sites and we all kind of have our own protocols and we were looking around for some benchmark data where we can achieve a certain level of performance and in discussing this with my colleagues in multiple practices throughout the Mayo system, we needed something to hang our hat on. And I needed some reference point; even convince my own colleagues in Rochester to lower the dose, because they felt very differently about it. They felt that the doses that we are using are very justified and result in overwhelming benefit for patients with suspected cancer or known cancers and so they didn’t want to sacrifice that observer performance so we needed some data to say we could lower the dose without sacrificing that performance.

H.Y.K. So how did you go about addressing this question? What did you actually do?

J.G.F. What we did is we collected cases of patients with lesions that we could prove. So for a period of time we collected the CT projection data and then we would wait to see if patients got follow-up or surgery. And then some of
the patients were just undergoing routine abdominal CT, some were undergoing dedicated liver and pancreas CT, and then once we had the collection of positive and negative cases that we thought we needed, we had a validated way of inserting to noise in the CT projection data to generate very realistic low dose images. For each patient we would have a routine dose, we would have a lower dose via this noise insertion method, and then we would have a lower dose with a denoising method and that denoising method for all the patients was an image based method which is vendor independent, you could just do that from the images themselves, and we called that adaptive non-local means. Then we have a vendor method called iterative reconstruction that we could do on the cases that were performed on the higher end scanners.

H.Y.K. What was the rationale for using the, I call it the homegrown noise reduction method? Why use that as opposed to I'm sure you have scanners from different manufacturers, why not use some of the existing techniques?

J.G.F. Well if we could buy all new scanners every year we would, but the truth is that we're limited in the number of CT scanners that we can purchase. So there's an element of realism here. What do we do with all of these old scanners? They may not have – we want to extend the benefits of lower dose imaging. Do we have to buy something really expensive for these older scanners or not and do we have to go to the triaging patients to different scanners, is very problematic when you're scanning 75,000 patients a year.

H.Y.K. I can imagine. So what did you find? How much dose reduction can you achieve without iterative reconstruction or noise reduction techniques and actually preserve diagnostic performance because I think that was one of your key questions?

J.G.F. We had a limited pot of money, of course, to do the research study so we had to take a stab at a single dose level. So we didn't try to go super low, we tried to go with what we thought was probably achievable and reasonable. So for the abdominal CT we reduced cells for about 25 percent dose and for the liver and pancreas CT, which started out at a higher dose to begin with, we reduced those about 40 percent. So those were the dose reductions that we tested.

H.Y.K. What did you find?

J.G.F. We found that for the abdominal CT scans that you don't really need the noise reduction to result in an equivalent level of observer performance. The images with the noise reduction either image based or commercially based with a CT vendor might look better but you're doing just as good at detecting the hepatic malignancies.

H.Y.K. So you could reduce the dose by about 25 percent and still use filtered back projection and get equivalent results?

J.G.F. Yes. When we looked at the liver and pancreas scans what we found out was that the performance was equivalent with the noise reduction methods but not with just filtered back projection alone.

H.Y.K. Okay so you could denoise them and get the same result as an iterative reconstruction, but you couldn't do that with filtered back projection?

J.G.F. We could get the same observer performance with the denoising methods at with a lower dose.

H.Y.K. What do you think accounts for the difference in results by protocol; slice thickness or?

J.G.F. Well we really didn't want to answer that question until you made us. It's really two things; number one, part of it is statistics and that is the way we say something is equivalent or not is by estimating the difference between the two levels of performance. So if you have a narrow, if you're very precise, it's going to be more easy to be equivalent than if you're wider, if you have less precision. So it turns out we had less precision with this diagnostic question. The other one though kind of goes back to our original protocols and just observational radiology. We had higher doses and thinner slices for our liver and pancreas exams because our practice felt that those lesions were more difficult to identify. It turns out that those lesions, there was any difference in size, but they did tend to have less of a CT number difference compared to the background liver.

H.Y.K. That's interesting.

J.G.F. So they were more low-contrasty.

H.Y.K. That relates to Dr. McCollough's paper. Looking at this, what are the take home lessons? Someone listening to the podcast and reading these articles, what do you think the major points that should be drawn are? Dr. Fletcher, J.G.?

J.G.F. I would say that there's multiple ways to deduce your radiation dose without hurting your patients. You can just lower the dose by a moderate level and just keep you filtered back projection. People get used to looking at these noisy images. Mark Baker from Cleveland Clinic, he's done a bunch of these studies, and he's told me that that the radiologists that complain the most at the beginning like it most at the end. That's because I think there are certain radiologists that are very picky about how their images look. They will get used to the noisier images over time. The second is that besides just lowering the dose, there's multiple ways to denoise an image. We're really in the infancy of comparing the differences between different denoising approaches you know like Cynthia has studied.

H.Y.K. I think one of the other features is that not all of these denoising methods are exactly the same and you need to sort of keep that in mind. Cynthia what do you
think those reading the articles and watching and listening to the podcast should take away from these papers?

C.H.M. I think the main message we want to get across is that you have to use a little bit of caution when you start turning down dose. If you can still see it in the filtered back projection, which the radiologists are good at reading through the noise and they can, the iterative won’t see your prettier and maybe easier, but if you can see in the filtered back projection you’re probably not going to see it in the iterative. There’s such pressure in our community to lower dose that people buy the new scanners, they applications people come in and say cut your dose in half, turn this on and you'll be great, and most of the images you will. Things with high contrast, kidney stones, even moderate contrast appendicitis, you'll probably be fine. But for things like liver lesions or maybe brain stoke imaging, things where it’s subtle you may not be fine. That’s our biggest take home message. So proceed with caution.

H.Y.K. Yeah, J.G.?

J.G.F. You know sometimes for the radiologist that don't know all the physics, it’s easier to, a phrase that I like that really helps me is that iterative reconstruction has contrast dependent spatial resolution. And so if it’s high contrast, I'm not going to sacrifice a spatial resolution so there I can really reduce the dose and use the iterative reconstruction as key in helping me. When I have the low contrast, then I'm sacrificing spatial resolution and I have to be careful. So contrast dependent spatial resolution is a catch phrase that helps me.

H.Y.K. What you said about sort of people getting used to the changes in noise and adjusting, I'm one of those people that really doesn’t like a noisy image and when I look at them, I just have problems looking at them. It occurs to me that where you have these situations where you have a fleet of scanners and one radiologist can be reading from different sites using different techniques, do you think this might affect their performance, because when I read I sort of set a bar. I know where I am. I kind of understand how much noise I'm accepting and what’s a lesion and what's variability on the image, but if it's shifting all the time, I wonder how it would affect my own performance. Do you have any information on this J.G. or any thoughts?

J.G.F. I have some thoughts and it really varies on the task, but one thing that I've observed is that as you drop dose people start, at the low levels of dose reduction, there are some people that are uncomfortable, but they’re not really doing any differently. They’re just more uncomfortable. At a certain point, people start to drop off in performance, but there’s a wide range where people might be less comfortable but they’re still doing great.

H.Y.K. Okay. Cynthia in your study you actually had readers looking at different types of iterative reconstruction and different dose, I assume they were mixed up. Did you have any sense that it was affecting people’s performance rather than giving them, everyone would look at the same dose levels and the same reconstruction methods?

C.H.M. I don’t think so. I don’t think it changed their performance. We really had to randomize it to do the study appropriately. The images have a bit of a different look to them, but not enough to explain the findings that we had.

H.Y.K. Well very good. I want to thank you both for a stimulating discussion and for two very fine papers. Nice talking with you both about this. Thank you.

C.H.M. Thank you very much.

J.G.F. Bye-bye.
and then matching them. Can you talk a little bit about what specifically you ended up with as far as your patient population and your results?

**C.D.L.** Yes, we went to a very large database that is linked to a tumor registry that gave us the ability to look at lots of women that had undergone screening MRI at the Seattle Cancer Care Alliance, and we were able to follow them to see which ones developed cancer after that screening MRI and which ones didn’t. We selected those women. There were 23 that developed breast cancer and we matched those. So we used a case control design. We matched those to women that were similar except they never developed breast cancer. So by that case control design, we could then assess whether or not there seemed to be differences in the patients that ending up developing breast cancer versus those that didn’t.

**D.L.** And so you ended up with 23 women in each group, which even though you started out with a huge number obviously, those that end up getting cancer are going to be a much smaller percentage of that and interestingly, you found out that women with mild, moderate, or marked background parenchymal enhancement were nine times more likely to have breast cancer. I’m wondering looking at these for the enhancement pattern that was a qualitative assessment that you had people do at the time of imaging. Is this something that can be computerized for more standardized assessment or is this qualitative assessment good enough do you think?

**C.D.L.** We are very excited about the approaches being used to try to be more quantitative. Whether we’re talking about breast density on a mammogram or a breast parenchymal enhancement on an MRI, we tend to have studies where we have very subjective qualitative assessments. We look at the mammogram and we put it into one of four categories of breast density or we look at our MRI and following ACR BI-RADS lexicon terms we use one of four categories of the breast parenchymal enhancement. Is there none to minimal, is it mild, is it moderate or marked, but that’s somewhat subjective. There’s some fabulous techniques and tools that are being developed to try to be more objective in this. Our prediction is that that would make us even better at assigning risks to patients based on this feature.

**D.L.** When you find it in mild, moderate, or marked and you clump those groups together, was that something you were planning on doing ahead of time or were your small subject numbers such that you had to combine groups to end up results like what you found?

**C.D.L.** We had planned to do that in advance. First we found that if we just compared the four groups, not doing the breaking into two large groups but across the four groups, there was a significant difference across the four. But what was the most pronounced was separating the groups into none or minimal parenchymal enhancement versus the other three groups. And that’s where we found this really pretty striking nine-fold increase in risk in those women who were in any of the parenchymal categories outside of none or minimal.

**D.L.** And then an additional analysis that you did was looking at whether parenchymal enhancement was central or peripheral and I’m wondering if you can talk a little bit about that. Why you thought that might make a difference and why you think your findings were what they were.

**C.D.L.** We love the ability in academic medicine to be able to observe things in the clinic and then ask and address that question in our clinical databases and many of us, across the country and around the world that were doing screening MRI, would talk to each other about these different patterns we were seeing. Early on those discussions helped us a lot in just recognizing patterns that were part of just normal breast tissue enhancement. It didn’t mean it was cancer, it didn’t need to be followed, it didn’t need to be biopsied, it was just a normal pattern. And some of them were pretty striking. Two in particular that we had all been discussing was a pattern that is peripheral enhancement of the breast tissue and one that has more central enhancement. We wondered if it’s those patients with really dramatic central enhancement of the bulk of the breast tissue rather than this rind or rim of enhancement around the outside that might be at high risk. We didn’t find that in our study. So we have small numbers, we still think the different patterns might be interesting, but we didn’t find significant differences in our study. You know it reminds me a little bit of the very early days of mammographic breast density and the Wolfe pattern, so not just how much breast tissue, but what is the pattern of it? And we were really having the same thinking around patterns of enhancement as well as amount and again this is where I think some of the really exciting computer programs that can assess both amount and patterns, could really be exciting for future research.

**D.L.** Since you brought up breast density, how does this interact? Do you think that this is a subset of dense breasts or are we looking at something completely different?

**C.D.L.** You know they seem really distinct. One thing that we’ll notice in the clinic is that we will have a patient come in with extremely dense breast tissue and no parenchymal enhancement at all and another woman might come in that has scattered fibroglandular density on the mammography, but every bit of that fibroglandular density is dramatically enhancing on the MRI. So they don’t seem to be the same thing. They really seem to be measuring different things and that intrigues us. We also were really interested, and this is something that many of our patients and our referring providers haven’t been aware of, that both our research and other studies prior to ours have shown that once you have a patient at high risk, if you have a patient who has a genetic mu-
ization or a very strong family history, mammographic breast density doesn’t confer additional risk. So there’s no further discrimination of risk based on breast density. But parenchymal enhancement does and we think that’s important for patients especially to understand because many of them become very anxious when they say here I have a strong family history and I have dense breast tissue, I sort of have a double whammy. We actually don’t think the clinical research supports that. We think that once you’re at high risk, it’s really the parenchymal enhancement not the mammographic breast density that we should pay attention to.

D.L. And so do you think this is ready for prime time, are your findings and those of others such that when women have a breast MR they should expect to hear about the parenchymal enhancement and use that for the future risk assessment?

C.D.L. I don’t think it’s ready for prime time as far as patients making decisions about whether or not they – with even a higher level of risk they should make treatment decisions. So for example, what kinds of decisions are women at high risk trying to make? Some of them wonder, if they are at very high risk, should they have prophylactic mastectomy and they talk with their doctors about the pros and cons of that. Do I think that if a woman was at high risk and had marked parenchymal enhancement that should push her toward mastectomy? I don’t. I think the research is much too premature to have that clinical application at this time. Other women are trying to decide whether or not they should have some kind of chemo prevention. Should they go on a tamoxifen or another type of agent that will reduce either their risk of a breast cancer or their risk of recurrence? Should they use parenchymal enhancement to influence that decision? I don’t think it’s ready for that either. What I do think it’s ready for is very active research in larger patient populations. We’re very excited to push that forward rapidly.

D.L. And I also think you know women who are in a high risk category a lot of times they get a breast MR and it looks okay or not okay or whatever, but then they think okay I’ve had my MR I’m done. But right now is the recommendation a yearly MR once you are put into one of these high risk categories?

C.D.L. We do and the American Cancer Society supports supplemental MRI screening on an annual basis in patients who are at high risk is defined by greater than 20 percent risk by a variety of models and methods, but predominately models that are based on a strong family history. So we do support supplemental MRI screening in patients that are truly at high risk. There is a lot of important research going on right now to clarify some of the groups of women where we don’t have enough data to give them clear recommendations. And the American Cancer Society has been really terrific in giving us a list of these populations of women that they hope to have more information on. What about a woman with no family history but a personal history? What about the woman who has extremely dense breast tissue and has a biopsy showing lobular carcinoma in situ? There are other groups that we need more clinical evidence to be able to guide their best decision making with their doctors.

D.L. Excellent and so one of the limitations that you mentioned in your study is that all of the women by definition had already had an MR of the breasts so were most likely at some increased risk, so you have a high risk population that you’re looking at. Do you think the associations that you found can be extended to low risk populations?

C.D.L. You know we don’t know it’s such an interesting question. In fact it would be interesting if we found high risk patents, its parenchymal enhancement not breast density, low risk average patients its density not parenchymal enhancement. We may be finding out more about what is it about these high risk patients versus average risk patients, but we don’t know. We do have areas where women at lower risk are undergoing screening MRI. We don’t support that. We really follow and support the American Cancer Society recommendations which are also supported by the Society of Breast Imaging and the American College of Radiology. But there are women at average risk undergoing screening MRI. We’re very excited about the breast cancer surveillance consortium database and the opportunities there to really address these compelling questions in a much larger group of women and a group of women that are at a really diverse level of risk.

D.L. What about menstrual cycle and menopause, how does that affect the background parenchymal enhancement issue?

C.D.L. That’s also an area of active research. Certainly we see trends. It’s similar to breast density. We see trends that as women go through menopause and move from pre-menopausal to post-menopausal, the parenchymal enhancement tends to decline as breast density tends to decline, but it’s not a black and white scenario. There’s variation. We also see that there’s some variation over the menstrual cycle, but not as much as was expected. Similar changes over the menstrual cycle with mammographic breast density has been reported, but it’s not as dramatic as we might think. What I’m really excited about is one thing that we notice when we have patients who have been undergoing routine MRI, perhaps they’ve had a personal history of breast cancer or they’re diagnosed with breast cancer, and they undergo treatment. If they go on a hormonal agent that blocks estrogen receptors such as tamoxifen or other type of chemo prevention hormonal agent, we can see really dramatic impacts on the parenchymal enhancement in almost all the patients, but interestingly not all of them. So I’m really interested in that. What does that mean if we have a patient whose breast tissue seems resistant to standard chemo prevention strategies and what does
it mean when we have a patient whose breast tissue is very sensitive? I don't know if it’s warranted or not, but I know I certainly like it when I see patients who start their tamoxifen and they move from being a patient with marked parenchymal enhancement to none or minimal. It feels like there’s really been an impact on that patient and her tissue.

D.L. Interesting. So usually at the end of a podcast I ask what you and your group are doing, but as we were talking about before we started recording here, you’re in the process of moving from Seattle to Boston and so you’re leaving behind known oncology database and cancer registry that you’ve worked with for quite a while. What are you own plans for ongoing research in Boston?

C.D.L. You know I don’t know if there is a more exciting time than right now in the area of breast cancer research and in overall imaging research and science. We have so many opportunities. I am beyond excited about this opportunity in Boston and also so very excited about the work that will continue to be done in Seattle with one of the most fabulous teams anyone could ever work with. We also all feel that we’re just expanding our community out. We’ve had such great examples of the community of scientists. Whether it’s through the American College of Radiology imaging network, the ISMRM, different groups where they really have international and national collaborations and I think that Seattle-Boston collaboration is going to stay really strong. With the team that I’m joining in Boston and the MGH group, I couldn’t be luckier or more excited about the future and we’ve got a lot of important questions to address for our patients and we’re ready to get started.

D.L. That sounds great and I’m looking forward to seeing you in town and thank you so much for your time today.

C.D.L. Alright, thank you.