Colorectal Polyps Missed with Optical Colonoscopy Despite Previous Detection and Localization with CT Colonography

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B. Dustin Pooler, MD • David H. Kim, MD • Jennifer M. Weiss, MD • Kristina A. Matkowskyj, MD, PhD
Perry J. Pickhardt, MD

Herbert Y. Kressel, MD  Hi. This is Herb Kressel and welcome to the Radiology podcast. Today I’m delighted to be joined by Dr. Perry Pickhardt, Professor of Radiology and Chief of Gastrointestinal Radiology at the University of Wisconsin. Welcome Dr. Pickhardt.

Perry J. Pickhardt, M.D.  Hi. It’s a pleasure to be here.

H.Y.K. Dr. Pickhardt and his colleagues at the University of Wisconsin wrote a very provocative article entitled “Colorectal Polyps Missed with Optical Colonoscopy Despite Previous Detection and Localization with CT Colonography.” It’s a very interesting title and you certainly have a very, very interesting experience with CT colonography. Can you tell us a little bit about the CT colonography program at the University of Wisconsin?

P.J.P. Sure. So we’ve been in existence now as a screening program, a standalone program, for over a decade now; really on the heels of the Department of Defense trial where we validated the modality for screening in general and shortly after that when I came to the University of Wisconsin, we were able to meet with the medical directors of all the major HMOs locally and were able to get coverage for screening. So that’s been the unique aspect of our program is that it’s covered by most insurers here locally for our hospital only really and that’s been the case now for going on 12 years here.

H.Y.K. So how do patients learn about the program? Are you advertising, or you having sort of seminars or reaching out to primary care doctors? What’s the basic route of patients being referred for CT colonography?

P.J.P. It’s a multi-pronged attack, but initially just the publicity related to the trial and the attention that received and the attention on the news that this is now a covered exam, but after that quickly faded away, it really took a lot of interaction, brand rounds, a lot of meet-and-greet sort of lunch meetings out at the clinic just to try to get all the primary care providers on board with this. It turns out they’re the gate keepers – are really our primary care providers; the internists, the family practitioners, with the gastroenterologists really being a secondary role for the incomplete studies and less so for the screening exams, but having said that, we really need the gastroenterologists on board as they’re really looked at as the keeper of the colon so to speak. I think our primary care providers really want to see their blessing which we’ve had for quite some time.

H.Y.K. So in Massachusetts typically our primary care doctors would refer people for CT colonoscopy so in your setting the primary care doctors would make a determination or have a discussion with patients as to which they prefer, either to go the optical or the CT route. Is that correct?

P.J.P. That’s right and actually we have data now that shows when patients are given that option, when they that the insurance coverage for both, that it actually is elevating all screening rates across the board both for CTC and even for colonoscopies, so we think it’s that discussion that’s increasing adherence rates. That’s hopefully going to be a future manuscript.

H.Y.K. In general what percentage of those coming to your center are for screening versus for further evaluation of definite signs and symptoms?

P.J.P. Well just in general for colorectal cancer screening it’s still about 90% are done by optical colonoscopy and we’re doing about 10% with DC or CT colonography and of those CTC patients the vast majority at our center are for screening and at least 90, 95 percent, I think around 95, which is obviously much different than pretty much any other center where the majority I believe are still by incomplete you know for incomplete colonoscopy.

H.Y.K. Right and how many exams are you currently doing per year?

P.J.P. We’ve averaged over 1000 per year. Admittedly though the volume has plateaued and even dropped off in the last four or five years I think partly because of the uphill battle of just winning this public perception with the guidelines not aligning, so it’s been a bit of a struggle lately but we’re still overall averaging about 1000 per year.

H.Y.K. Great. So Perry tell us a little bit more about the study now. What was actually the motivation for your study? What kind of drove it? It looks like a lot of work. People have been talking about lesions that are missed
on colonoscopy for quite a while. So what was going on as you decided to tackle this?

P.J.P. Well you’re right in that this was probably one of our more challenging studies. It was really over a decade in the making. And we realized over time from the validation trials, we know that missed lesions if they are not found at the initial colonoscopy in a validation trial, even with segmental unblinding, there’s really no way to arbitrate or say that it was a colonoscopy miss, you simply don’t have the follow-up that’s needed. So even though we showed initially a validation that over ten percent of large polyps might be missed at colonoscopy even when they know or whether or not they know the CT finding, CTC finding, we had no real evidence in terms of what happens with those lesions that are discordant; that is we call a lesion at CTC and they don’t find it at colonoscopy even though they are unblinded. So that was sort of something that can’t be accomplished in a sort of artificial validation trial and really requires our actual clinical practice experience. So admittedly though this takes many years to develop. What we do and what we’ve always done is for every discordant lesion we have two radiologists, CTC readers, who didn’t read the initial exam review the study and come up with a game plan basically putting it in a category of likely CTC false positives in which case we don’t pursue it further; or if it’s a potential miss at colonoscopy or a false negative on their part, then we push a little further and we need to hopefully do a follow-up CTC depending on the size of the lesion, the location that would obviously impact when the follow-up gets done. In some cases the patient went straight to colonoscopy at a follow-up date, but we really prefer the CTC to reconfirm those findings with the fear that if they miss it again at colonoscopy without an additional CTC they might continue to think it’s a false positive. So long story short, it’s a very important study, but it’s important to really understand what this means beyond all the validation trials.

H.Y.K. Sure. Now there’s a lot of numbers in the paper but ultimately over 9000 exams were looked at and there were 180 unconfirmed polyps and 66 of these at the initial re-review were not felt to be lesions and I wonder what did you think these were?

P.J.P. So most of those cases, and I don’t have the exact numbers off hand, but a lot of those cases involve patients with other obvious lesions. So these were maybe a second, third, or fourth positive finding in which case they were soft-called if you will, they might be possibly adherent poorly pegged stool. We always use contrast tagging, so that’s actually a very uncommon cause of a false positive, but there are cases of thickened folds, poor distention maybe causing a pseudo lesion and other less common things, but even some of these of course we feel may have in fact been true lesions but we’re below our threshold to push for another exam because it’s asking a lot to have a patient redo an examination. So in some cases it was close to the 5 to 6 mm size threshold, we might have just called it a false positive even though there may be an outside chance of a true lesion. It’s a complex group of false positives.

H.Y.K. So the quality and the prep and the feces was not kind of the most common source. I think that’s kind of an important thing because most people would think that that was where you’re going to get hung up.

P.J.P. Yeah again that actually is an important subset so although we have our prep is very robust, if patients don’t follow the instructions there are certainly cases where we just simply can’t exclude a true lesion amongst a sea of residual stool. It is an important point even in our practice that’s not uncommon.

H.Y.K. Now the heart of the paper, at least from my perspective, was 31 out of 144 lesions were colonoscopy false negative on reexamination. That’s really the heart of what you’re reporting and can you tell us what type of lesions were these, where were they located?

P.J.P. Sure. To clarify a little further, those lesions that you’re talking about the 31 false negatives, was out of 78 discordant lesions where we felt there was the need and we did get follow-up. So we can only really talk about – so actually that’s 40% of cases where we thought it was potentially a false positive and went on to further testing so you know a little less than half proved to be true lesions; and interestingly the vast majority of those, I believe 80% of those that were resected, found and resected, were neoplastic meaning they were some sort of adenoma, serrated lesion, and even more importantly of the advanced histology, the advanced neoplasia, 90% of those were located in the right colon which we’re really starting to recognize that CTC has definite advantages for right colonic evaluation compared to physical endoscopy where there’s limitations just due to the distance and looking behind folds, et cetera. So I think that’s really a take home point is that most of these, the vast majority of these, are potentially precancers and that many of the – most of the very important ones are right-sided. So we have a complementary role I think in detection with CTC and colonoscopy.

H.Y.K. Yeah you may or may not know that I used to do a lot of barium work early in my career and when we looked at this with double contrast, the right colon was probably the most common by far. Again, tucked behind folds and they can’t flex the scope back enough, and the other place surprising was right at the rectum where again they have to flex back to look frequently and if they don’t do it right there’s some blind spots. Those locations are important. One thing that was kind of striking to me, I was surprised that most of them were sessile or polyoid lesions rather than these very flat lesions. You have some serrated lesions and I would have suspected that the flat lesions which you are detecting at CT colonography would be the ones missed. Any thoughts about – were you surprised at that or they’re just so uncommon?
P.J.P. Well yeah that’s an interesting question. We are certainly finding more and more flat lesions. In fact we will have some upcoming data on our serrated detection. Because these flat lesions (inaudible) with contrast we think the diluted harium that is increasing our detection rate for these, my concern is when we do have a discordant flat lesion that either on review we’re calling those likely false positives because they are often quite subtle and also that they’re being missed on repeated colonoscopy is another option. But in the back of my mind I’m also thinking too that most truly discordant lesions are probably in that flat range but we just don’t have a good handle on how to correlate those, how to confirm those, and they remain a definite challenge. But I think our detect rate for both is improving.

H.Y.K. Yeah I think that my impression is that that is another non geographic blind spot and the Japanese of course use these vital dyes to bring out those subtle surface pattern changes to help the detection of these lesions and they’re still not done widely in the U.S. so it’s perhaps something to look at in future. Were you surprised at the findings of your study?

P.J.P. Well not really. Over time as we’ve accumulated our clinical knowledge of this and see that the false negatives coming out year after year, I was hopeful that the results would be in this sort of ballpark. Of course to actually sit down and execute the study was a whole another level of challenge and I’d like to acknowledge Dustin Pooler, one of our residents, who’s done a lot of CTC research with us and he really painstakingly tried to follow-up all these lesions. But no I guess I’m not surprised only because of our unique experience in dealing with these year after year, but I hope this sort of – I hope the gist of what we’re reporting comes through and that colonoscopy is clearly not an infallible gold standard. There are complementary nature to CTC and colonoscopy and we’re certainly not trying to denigrate colonoscopy which is the therapeutic gold standard of course, but I think we still have a lot to learn in how we can help each other and reduce the overall cancer risk by putting these studies together.

H.Y.K. Sure. What’s been the impact of your findings? Has it affected how patients with unconfirmed polyps at CTC are now managed where the gastroenterologist surprised at the findings?

P.J.P. Yes I’d have to say I think they were one more level of awakening. I think the first time we reported our results back in the trial days I think they were surprised that we – their missed are essentially doubled for large adenomas. Now we’re adding a whole another layer of misses that are only found at subsequent evaluations. So I think they’re finally believing us when we tell them what the discordant lesion, where we think there’s a legitimate chance that something was missed for geographic reasons as you’ve noted, or morphology reasons; and that it’s worthwhile to not only repeat examinations but do that by doing the CTC first with same day colonoscopy to follow if we reconfirm that lesion. If we have a very high confidence and good reason for a miss, we’ll go straight to colonoscopy. But I think our endoscopists are now on board with this sort of line of reasoning whereas initially they either would kind of just dismiss it outright or maybe do a repeat colonoscopy and not see it again and we’d still be in the dark, so it has really has helped in that area of confusion.

H.Y.K. Good. Thank you very much. Before we end, I want to get to sort of the money shot. Where are we now in terms of having broadly reimbursable CT colonography services available in the United States?

P.J.P. It’s a mixed picture really. We’ve made significant strides with some of the private insurers I think and that’s not well appreciated I think. The degree of coverage that’s already out there, it’s just not well advertised or there’s a lack of awareness, but the big issue of course whether it’s symbolic or not, is to have Medicare coverage even though that’s 65 and older generally and we’re going for 50 and over, I think we really need that level that blessing from both the U.S. Preventative Services Task Force and CMS. I think we’ll have it from CMS as long as the picture becomes more clear from the USPSTF and unfortunately that got furthered muddled in the sense that they may not be individually grading these tests rather putting them in primary and alternative listings which is causing a lot of confusion and we’ll know probably within a few months as to whether or not we were successful in alerting them to the potential confusion. So stay tuned.

H.Y.K. Well good luck and thank you very much for this very informative discussion. I want to thank you for joining us.

P.J.P. Thank you I appreciate it.
Maegan V. Prummel, MPH • Derek Muradali, MD • Rene Shumak, MD • Vicky Majpruz, MA • Patrick Brown, PhD • Hedy Jiang, PhD • Susan J. Done, MB BChir, PhD • Martin J. Yaffe, PhD • Anna M. Chiarelli, PhD

Deborah Levine, MD Hi this is Debbie Levine, I’m the Senior Deputy Editor for Radiology and I’m here today talking with some of my co-scientists about an interesting study on digital compared to screen-film mammography, measures of diagnostic accuracy among women screened in the Ontario breast screening program. It’s going to be published in the February issue of Radiology. I have with me here Maegan Prummel, who’s an MPH and Senior Research Associate from Cancer Care Center Ontario. So welcome Maegan. And I also have Anna Chiarelli who is a PhD and Senior Scientist Cancer Care Ontario and Professor at Dalla Lana School of Public Heath, University of Toronto. So welcome Anna. And then I also have Dr. Etta Pisano who is the Vice Chair for Research at the Beth Israel Deaconess Medical Center and who wrote an editorial on this article and we felt that this was sufficiently important topic to warrant an editorial and sincerely thank Dr. Pisano for writing it. So welcome Etta.

Etta D. Pisano, MD Thank you. I’m happy to be here.

D.L. So this really was an interesting study and I think it’s quite important. I’m wondering Maegan if you can just tell us a little bit about what you did and what you found.

Maegan V. Prummel, MPH Sure. So this was an observational cohort design study. We examined women who were screen in the Ontario breast screening program from 2008 to 2009 and who are age 50 to 74 and we followed these women forward for two years which is the standard interval in the Ontario breast screening program to ascertain whether they have been diagnosed with a breast cancer. We further identified three different cohorts based on the type of mammography that the women were screen with. So there were three types that we looked at; digital mammography with computed radiography, digital mammography with direct radiography, and screening film mammography. So the major differences between these types are that for screening film mammography which is sort of a standard type before digital mammography was introduced. It’s an image that is produced on film and the radiologist would view it all on hard copy on a film view box. Digital mammography is viewed on a computer screen. For computed radiography type the image is recorded on a cassette and is removed and viewed on an external reading devise. Whereas for the direct radiography type the detector is part of the imaging unit, so when the image is recorded, it’s viewed in real time. So our major interest for the study was to look at interval cancer rate and sensitivity and specificity of each of the different screening modalities, and we compared direct radiography and computed radiography to the standard at the time which is screen film mammography. What we found is that for computed radiography the sensitivity was significant lower than for screen film mammography and we also found that interval cancer rate was substantially higher though that result was not statistically significant. And for DR conversely we found, or direct radiography sorry, we found that the interval cancer rate and sensitivity were similar to screen film mammography while the specificity was somewhat lower.

D.L. So Anna it’s clear that you were not surprised so much by your results since the computed radiography has physical limitation that you nicely document in your study; and your group also had a piece on screening mammography and assessing CR specificity previously. It was personally for me the 38% difference in sensitivity between modalities that I found so astounding, and I was wondering if you were surprised at this level of difference found in your results?

Anna M. Chiarelli, PhD Yes we were surprised. So the earlier study actually looked at cancer detection rate. So the first study that was published, and I think it was the only study that had found this at the time, was it found a 20% lower cancer detection rate for computed radiography compared to screen film mammography. So we had expected that the sensitivity would be lower, but you’re right it was greater than we had expected and no other study to our knowledge has published differences in sensitivity for computed radiography versus screen film mammography. They’ve only looked at specificity.

D.L. Right. So one criticism of your study might be well this coming a bit late, this is old technology and computed radiography is on the way out. I’m just wondering is it ever too late for this type of finding or should we apply similar concerns for other technology in use today?

A.M.C. Well I believe that computed radiography may
still be used so I think it’s important to look at these results. And in fact when our earlier results came out, which was about two years ago and we found a lower cancer detection rate, at that point in Ontario we did actually transition all of the machines that were computed radiography to direct radiography given that evidence at the time. So we didn’t wait until we looked further into the sensitivity. We felt that that data was enough at that point to make the transition. But since then, as I said, at that point there was really no clinical evidence that computed radiography was different than direct radiography, although like you had said I think there had been physics had shown some differences but there was no clinical evidence to that effect, so I believe that it’s important to – and in fact it’s also interesting because sometimes you need a sufficient sample size to look at this and I think our study was one of the first to have the sample size and as well we looked at cohorts screened in the same time period, so concurrent cohorts. So sometimes designs of studies are different and some earlier results may not show the differences, so I think it’s important that even though, because as I said until the study was done it didn’t seem that there was any difference in computed radiography. I felt that we still had to continue to seek further even though we knew there was lower cancer detection rate, whether or not accuracy was also different.

D.L. Okay well thank you. Etta you wrote a very nice editorial to accompany this article and I’m wondering if you could tell us a bit about your thoughts.

E.D.P. Well I agree with what was just said that it’s not too late to study this topic. There’s still a lot of CR systems, computer radiography systems, in clinical use in the United States and probably worldwide. Sometimes we get a very North American-centric view of the world, but in fact with the cost of digital mammography and tomosynthesis being as high as they are, many places in the U.S. are still using CR. I don’t know about Canada, but in the U.S. there are still places using CR, and I think around the world maybe even a higher percentage of places are using CR. I believe this is definitely a timely article and I believe that the breast cancer surveillance consortium data could be analyzed to evaluate this exact issue in the U.S.

D.L. And again that would be worth the time and expense because you think it would end up changing the way that we evaluate studies or we could actually mandate that CR if that were to be replicated would no longer be used?

E.D.P. Well I actually have a question about whether you know this was a large study and very well done study, but every clinical practice is slightly different and it wasn’t a randomized trial it was an observational retrospective cohort study, a very well done study. But each practice and each radiologist should look at their own data and figure out if their cancer detection rates are lagging. It’s possible that their, especially with the differences in screening in the United States; I mean we don’t screen every two years, we screen every year, that there are practices that are performing up to standards for computer radiography and so that’s why I believe you know every center, every radiologist really does need to evaluate his or her own data before we generalize too broadly about this. It’s possible that there are centers performing at appropriate standards with CR.

D.L. So if we see something that gives an added benefit to mammography and if we assume that CR is actually doing the opposite, it’s giving a negative benefit or making it a little bit more difficult, when do you get to the point where you think we should advocate for replacing new units because there always seems to be something new on the horizon and if we keep on waiting for something new, we’ll never replace our old machines and yet once we buy something it’s already on its way out for the technology. So Etta I’m just wondering because I know you have a large amount of interest in tomosynthesis when do we make that decision that we shouldn’t be using older machines?

E.D.P. Well you know right now we’re in the midst of a big controversy about screening in general. As you know the main issue is whether we’re over-diagnosing low acuity or things that are not going to kill women. So it becomes very complicated and that is why, exactly why, I’m saying that individual centers need to look at their data and assess their own performance because you know you have to look at your own population. That’s another issue with the Canadian data. Their demographics are substantially different than the demographics in the United States and may explain you know the sensitivity was lower than one sees with the breast cancer surveillance consortium data. So there are a couple reasons for that; one is probably the screening interval had an impact. Canada screens every two years, we screen every year. The demographics, the population may be a point as well. We know that our African American population is more rapidly growing breast cancers and there is small percentage of African Americans, a smaller percentage in Canada. So it may be that, and I don’t want to sound too skeptical about these results, I actually really believe these results and I believe they’re due to exactly what was said in the article that it’s about the physics of the detector. But screening is such a complicated process that to generalize to a different population and to a different screening paradigm is a little bit dangerous and so that’s why I’m actually hesitant to be too aggressively suggesting that all of the centers in the United States should go to a different system. I actually believe that it’s because we’re doing screening, not just diagnosis not just kind of the stuff that the rest of radiology does, we have to be cautious about adopting new technologies. We may end up doing more harm than good. I sound like a screening skeptic. I am not a screening skeptic but I have become more comfortable worrying about the paradigm of screening and what we do when we find things, how much harm we’re doing.

D.L. I think that’s a very good point. So Maegan I’d like to draw you back into the conversation. We always are
concerned about retrospective studies and study design and the biases inherent in them and we’ve mentioned a few of the issues that come up with that, but I wonder if you would like to mention any limitations that you see in your own study design that we should be careful of if for example we design something similar to do in the United States.

M.V.P. Sure so with respect to our study design, despite the fact that we were looking at this retrospectively, we did do a concurrent cohort study so all of the women that were screened in our study were screened during the same time period from 2008 to 2009 and some of the limitations to previous studies that we’ve observed are that the cohorts are designed in different time periods, so the study might be looking at historical screen film mammography cohort compared to a more recent digital mammography cohort. So we would highly recommend that any observational cohort study be designed using the same time period for the women screened in the study. I don’t believe that we had, despite the fact that it wasn’t a randomized study, we did look at the patient differences between the cohorts and there weren’t any major differences that were alarming to us. So that’s also something to be cautious about and to look at the slight difference in the cohorts before interpreting the results.

D.L. And Anna do you want to add anything to that?

A.M.C. Well I guess too also you just have to be careful about multiple comparisons and I think we did comment on that. Because we did a lot of the stratified analysis and sometimes things are significant just because of that, so to kind of be careful of that. And also I guess sample size, I think our study was quite large and that’s very important and especially if you wanted like for sensitivity you want to look at not only screen detected cancers, but interval cancers and those normally are rare and there’s a smaller number, so therefore you would need a large cohort, a very large cohort to look at interval cancers and also you know I’m not sure what the proportion of machines are that are computed radiography in the U.S. but in Ontario it was 25% of the machines so again you want to make sure you have enough numbers for these comparison groups otherwise you may not see differences. Those are a couple of things.

D.L. And then Etta you had mentioned obviously screening interval and patient population itself as being different between our two countries, what other factors do you think we should consider?

E.D.P. I think that we are pretty comfortable that Canadians and U.S. radiologists read very similarly. When you compare the data of the sensitivity, specificity, cancer detection rates allowing for difference for screening at interval, you really do see a very similar pattern of call backs and things like that. So I believe this really does apply to American radiologists in a very direct way. And so I don’t have concerns about that and I agree with the comments about the size of the study and the populations. The only real differences I see that worry me a little in terms of whether it’s generalizable the United States in the screening interval and the demographics of the population. And as I said, I think that the Breast Cancer Surveillance Consortium, you know even though they have limited funding at this point, they probably could do a similar study pretty easily and publish it and we’d have an answer.

D.L. Terrific. And then Anna Etta previously kind of alluded to this, when we look at sensitivities of different modalities it’s possible that just having increased sensitivity is not enough, that we might be finding something like low grade DCIS and the enhanced sensitivity is contributing to the so-called over diagnosis. Are there particular morphologies or histologies whose detection is either enhanced or it may be deterred by different imaging methods?

A.M.C. So in this study the majority of the cancers were invasive cancers and with about 80%, I think 20% were DCIS. Within the DCIS we weren’t able to look at the grade, we didn’t have the information on the grade of the DCIS, but the sensitivity although it wasn’t significantly different it was similar to what it was for the invasive. When we did the stratified analysis, so in that case, but that was the only information that we had for this study is whether or not it was invasive for DCIS.

D.L. Great.

E.D.P. It would be interesting to know if the cancers were ER, PR positive HER2 over expressed, those kinds of things and are you planning to do anything like that?

M.V.P. Yes so actually we do have a study that’s been published in Breast Cancer Research and Treatment on the prognostic features of cancers detected among women in this study. And so we actually found that for computed radiography the cancers that were detected were detected at a later stage and we did look at ER, PR receptor positivity but we didn’t find any significant differences there, but I encourage you to look at the paper to follow-up on more of those differences.

E.D.P. It would be nice to know about the ER, PR negative cancers because those are the – so if it’s ER, PR positive, HER2 negative and those are detected later, those may not matter to the woman’s prognosis, but if the ER, PR negative HER2 positive cancers are being detected later, that’s a very significant, worrisome result. So that would be an interesting thing to look at and if it’s in the paper I’ll find it, but you don’t remember I guess right now?

M.V.P. Off the top of my head I don’t, but I do know that we had lower, much lower sample size especially for CR cancers because of the smaller cohort, so I’m not sure if we would have been able to look at the stage of
ER, PR positive HER2 negative cancer specifically, but definitely something to follow-up on.

D.L. Yeah I think that’s a good point. So we’ve been kind of looking backwards in time talking about computed radiography and I’d now like to look forward because I know Etta you are very interested in imaging tomosynthesis and research on that. And so if we know something works better and think we’re all going to agree that tomosynthesis definitely works better, at what level of evidence do we need to guide clinical decision making and perhaps even to direct policy changes for breast cancer screening?

E.D.P. So you know when you say tomo works better we know it has a higher sensitivity, finds more cancers, and it has a reduced call back rate. I think the issue among the skeptics is again are we finding things, are we getting to the point where we find things that don’t affect patient outcome. So that’s the threshold, we have to prove that we’re affecting patient survival or patient morbidity. We have to – we can’t just use radiology end points to affect national policy. We have to actually show patient centered outcomes that are improved. And so that’s why you haven’t seen, that and the cost of tomo, is why you haven’t seen a gigantic rush to tomo. I think that there’s enough debate right now about what we’re finding. That’s why I asked the question about the zero types of the cancer if you will because we know that the ER negative, PR negative, HER2 positive cancers or just HER2 positive not matter whether ER, PR are positive or negative or not, those cancers are the bad actors. They’re the ones that kill women. Now there are some DCISs there are some, you know I don’t want to make it sound like it never happens; those are the ones that in general really hurt women. And so we’re not being pressed by the epidemiologic and scientific community to do something besides show improved sensitivity and reduced call backs. Those are radiology outcomes. We need to think of public health outcomes as our most important outcome measures.

D.L. And yet if you want to do that kind of study, and I know that you are attempting to do that kind of study, it’s immensely expensive because you need to screen so many women to find the cancers to have enough cancers to be able to do the kinds of analysis you want to do on the subtype of cancer and then show outcome differences.

E.D.P. Yeah it’s going to be a big study but I would say it’s probably one of the most important public health issues facing us today. We can’t keep telling women we don’t know whether they should be screened or not and how frequently they should be getting screened. I mean they are hearing very conflicting advice right now and it’s worth, in my view, spending 100 million dollars over a ten year period to answer that question and to have better data on that. The NCI’s annual budget is five billion dollars, annual budget, so if we spend 100 million over a ten year period, that’s a very small percentage of what they spend and it will answer the study that we’re proposing. In fact it’s already open in Toronto, this study, because we have some money from the Breast Cancer Foundation of Canada, or the Canadian Breast Cancer Foundation I mean. That organization has started the study in Canada and we can answer the question and it’s going to have a major public health impact. So I would say tomosynthesis from a radiologist’s perspective is better, but from a public health perspective, the jury is still out.

D.L. It’s been wonderful to talk with the three of you today. I am just so impressed with the research that all of you do. It’s wonderful when I get papers like these to read because I find them interesting and clinically important right away and that’s just wonderful and so I want to thank you for your time and for being with me.
on adhesive capsulitis of the shoulder also known as frozen shoulder. It is characterized by loss of glenohumeral motion and in clinical practice we treat it with oral medication, physical therapy or ultrasound guided intraocular injection of steroid. This method may reduce pain and improve shoulder range of motion especially internal reflection. However, its rotation usually remembers treating because it limits the patient’s ability to do some activities of daily living such as hair washing or dressing. From text hook we know that the coracohumeral ligament is the main restraint of shoulder external rotation. And previous studies using ultrasound or MR imaging have shown that the thickening of coracohumeral ligament is associate with frozen shoulder and it has been proposed that tightened coracohumeral ligament may restrict external rotation in patients with frozen shoulder. But the comparison of the elasticity of the coracohumeral ligament in frozen shoulder patients has never been conducted. Therefore we are interested in this and so that’s why we conduct this study.

A.G. Why do you think this is important? Why the acknowledge of the elasticity is important at this point? What is the implication and treatment for example?

C.H.W. Previous treatment focused on the whole joint capsule. For example, hydro dissection or intraocular steroid injection, but in our experience the external rotation is rarely treated by these conditional therapy. Do we want to know how what is the role of the coracohumeral ligament in these patients. Maybe we can do some intervention to the coracohumeral ligament to make the patients have better external rotation. And that’s why we...

A.G. Thank you Dr. Wu. I’m going to turn to Dr. Rosskopf and ask her the same question. So why did you do this study?

Andrea B. Rosskopf We wanted to evaluate the shear-wave ultrasound elastography in the rotator cuff because up to now there are no data available using our ultrasound machine with this technique and we thought that this technique could add important information to assess muscle quality. Because up to now radiologists only talk about the fatty mass of infiltration of the rotator cuff and about muscle volume atrophy, but we think that the muscle stiffness can also add important information for assessment of the rotator cuff muscles. Because we know that our surgeons when they operate on patients with rotator cuff tears with full retraction, they have difficulties when they want to reattach tendon muscle unit that is really stiff. So in these patients it can be very helpful for evaluation of the muscle tissue preoperatively.

A.G. So you think the stiffness would be clinically or ultrascopically related to what you see on or correlated on with what you see in or correlated with what you see in shear-wave histography?

A.B.R. This can be. Of course we have no proof yet, but this can be an interesting topic for the future.

A.G. Dr. Wu I come back to you and I want to just say that adhesive capsulitis as you introduced is a clinical diagnosis. So my question would be what is the add value of shear-wave elastography measurements to the clinical diagnosis itself, or simply do the ultrasound, conventional ultrasound?

C.H.W. For diagnoses, that’s just my opinion. Let me explain our studies results briefly. Imaging the coracohumeral ligament as this rubber band. It is normal and it is thin. We can easily stretch it, but in the frozen shoulder patients the coracohumeral ligament is thicker and also very tight and we cannot stretch it easily. So we hypothesized that, maybe we can target this ligament in those patients who cannot do external rotation easily. For example, doing steroid injection just into the coracohumeral ligament.

A.G. That’s actually a good point and if I turn now to Dr. Rosskopf, I found actually your data a little bit intriguing and actually as a conclusion you concluded that the findings of the study showed here the shear-wave tends to decrease with the increase of infiltration and that’s Goutallier stage one, two, three, but when it comes to Goutallier four which is a huge I mean a big fatty infiltration of the supraspinatus then your actual shear-wave results will increase. Can you just tell us a little bit about what happened here?

A.B.R. Yeah normally you would expect that with increasing fatty infiltration your shear-wave velocities would drop. So you would have the most decreased values in Goutallier four. But that is not what we found. We don’t really know why we found these measurements, but one explanation could be that the fatty infiltration Goutallier four we found in patients with full thickness tears with a full retraction of the supraspinatus muscle. It is known from animal studies if you detach a muscle then first your stiffness in the muscle decreases in the days after the detachment, but then after a few weeks, it’s known that the stiffness reincreases in this muscle. So perhaps our measured patients they were detached for a longer time and that could be an explanation why we measured higher values in these patients.

A.G. Okay, if I go back actually to the practical measurements here, Dr. Wu can you tell us a little bit about the time needed for the shear-wave elastography to be performed?

C.H.W. You mean the learning curve right?

A.G. I would say yes the learning curve is a very good and interesting question and also what time you add for the ultrasound, conventional ultrasound to measure that shear-wave elastography of the coracohumeral ligament? Is it two minutes?

C.H.W. Actually the measurements of the elasticity of the coracohumeral ligament is very difficult. To be honest I spend about 30 minutes for one patient because first coracohumeral ligament is difficult to identify. We need to do internal rotation and external rotation to confirm the
upper boulder and the lower boulder of the coracohumeral ligament. And also because we use the supersonic shear imaging and the elastography on the machine it changed in real time. So we have to wait until the imagery become very stable and then we take a picture, so it takes a lot of time and it actually needs practice.

A.G. So what is actually the time for practice as you said? What is the time needed to be a good shear-wave ultrastenographer?

C.H.W. I cannot say I'm a good ultrastenographer, but to obtain optimal image, actually I practice almost 30 to 40 patients. After that, I am competent that my imagery quality is good. It's a long time.

A.G. Thank you. Dr. Rosskopf how about you? That measurement of the elastography and shear-wave and the elastography of the supraspinatus muscle?

A.B.R. I think the time you need for the elastography depends on the tissue that you want to assess because if you want to assess a whole muscle so it's really easy to put a probe on the supraspinatus muscle and you can do the elastography in about two to three minutes. That's not a problem. But if you think if you have such a small ligament as the coracohumeral ligament, it can be really difficult to find and to do it.

A.G. Okay may question to you both because I thought that it would be much more easy to be honest but let's say now we have one of you is in Zurich and the other is in Taipei, and I'm actually sitting here in Boston, if I want to just do this, do you think that it would be a difference between machines that we use in different countries or different machines, different brands, there would be different results here or you think the results be the same? I will ask Dr. Wu to answer and then you Dr. Rosskopf.

C.H.W. It's a good question. Actually in our hospital we have only sonic shear imaging and Acuson S2000 that's an older one. So actually for the Acuson S2000 the region of interest on the elastography on the VTI and VTQ is too big for a ligament. So in my own experience we can normally use the supersonic shear imaging. I don't have experience on the Asuson S3000 so maybe we should ask professors.

A.G. What do you think Dr. Rosskopf?

A.B.R. I think from past data it's known that the absolute values of your shear velocity are different from one manufacturer to the other so you can only compare measurements if they have the same ultrasound machine and there are some other factors that can influence your measurements for example the orientation of your transducer, so for muscle tissue it's important that you align it parallel to the long axis of the muscle fibers because then you get other values then if you were to turn them perpendicular to the muscle fibers. It is known that measurements are dependent of your positions so for example if you have a normal position of the shoulder or the arm, you get other values than if you do a 90 degree abduction and for the more shear-wave velocity is dependent on the depths of the tissue, so if you have muscle lying very deep you get lower shear-wave velocities than in more superficial tissue. It is also known that it is dependent on the age of the patient. For example for a supraspinatus muscle it's known that with increasing age your muscle stiffness decreases. That's one point why we tried to match our patients with volunteers of the same age and same gender because these factors can all influence your measurements.

A.G. So the reality of these two papers relates to ultrasound shear-wave elastography measurements in the shoulder. One of them on coracohumeral ligament, the other one in supraspinatus elasticity, so from this point of view Dr. Wu how do you think the results of these two papers relate to each other in your opinion?

C.H.W. In primary frozen shoulder the supraspinatus tendon should be normal. It is disease of joint capsule. Because I don't have too much experience on the muscle, actually I cannot answer this question.

A.G. What about you Dr. Rosskopf, do you think there is actually any relationship in using actually those results together, the two papers here?

A.B.R. I think both try to add some information that cannot be found if you only do B mode ultrasound. So they try to assess stiffness of the tissue and you cannot do it with another imaging modality with ultrasound up to now so that's the strengths of the papers.

A.G. Let me know just you give a general impression here. So we have these results. They are there with actually communicating with you in this absolutely nice conversation; I can see that it's not easy. Very honestly I do think myself I don't do this elastography as a matter of fact, the ultrasound in my department. Let's say it looks like it's a little bit difficult to apply it, but I do think myself, it's a great venue for research and again for clinical practice so I want to just ask you Dr. Rosskopf what do you think the next step in clinical practice and in research to bring to the shear-wave elastography as an additional measurement to conventional ultrasound?

A.B.R. Of course we have to do research with some more patients and have bigger study population, but I think the problem if you want to compare the different study papers is that they are not consistent because some researchers they only publish the TM modulars in kilopascal and the others only publish the shear-wave velocity in meters per second and that it's really, really difficult to compare the results so I think we have to find some kind of consistency which do you report in our studies.

A.G. Well thank you very much. I do think it was a very interesting, actually a kind of conversation and I want to again thank you because of the time difference for joining us this morning and I hope that you find this discussion very interesting. Thank you.