Deborah Levine, MD  Hi, I’m Debbie Levine, I’m the Senior Deputy Editor for *Radiology* and I’m here doing one of our podcasts for the May issue of *Radiology* and I’m talking with Dr. Christiane Kuhl who is the Chairman at the University Aachen Department of Radiology and we’re talking about her paper entitled “Supplemental Breast MRI Screening of Women at Average Risk for Breast Cancer.” So hello Dr. Kuhl.

Christiane K. Kuhl, MD  Hi, hello.

D.L.  Can you tell us a little bit about what you did and what you found?

C.K.K.  Yes, we had a group of women who were selected to have no specific risk factors that are usually associated with breast cancer like family history or a personal history of biopsy that was indicative of lesion that indicates a significantly increased risk of developing breast cancer or other sorts of factors that would somehow increase the personal risk of a given woman. So we had, if you want, selected a specifically low risk cohort of women, 2200 women were included, who then underwent MRI in addition to mammography. Women were selected to have a normal screening mammogram, double reading screening digital full field mammogram and in case they had residual breast densities also, a screening ultrasound. And then women underwent an additional MRI and we tracked the number of additional cancers that we found in these women and also followed women for a couple of years to see whether they would develop more breast cancers down the road. The findings were that we found additional breast cancers through MRI screening as you would also anticipate, and this translated into an additional cancer detection rate of 22 per 1,000 in the first screening round. Then in subsequent screening rounds, the so-called incidence screening situation the cancer detection rate dropped dramatically and we found an additional I think 13 cancers at incidence screening, and again most of these cancers were then MRI detected and not visible on mammography and ultrasound which were by then done in direct comparison. One of these cancers were also found by mammography. None of the cancers were only mammography or ultrasound diagnosed. So that is in a nutshell what we did.

D.L.  That’s great even though you said that the cancer detection rate decreased, it was still 6.9 per 1,000 of what was being seen with mammography so still an impressive amount. Can you talk a little bit about the cancers that were found by MRI that were not found by mammography and whether these could be biologically important cancers?

C.K.K.  Yes actually we found a relatively unusually high proportion of cancers exhibited a high nuclear grade indicative of rapidly growing tumors so that in somehow accordance with pathophysiological expectations, we had cancers found that compared with the cancers that we usually identify through mammographic screening were skewed to exhibit a more than usual higher growth rates than usual. They were by all histological means the majority of them had to be categorized certainly as biologically significant and somehow that makes sense because I forgot to mention that in this cohort of women that were followed by a total of 7,007 women-years we did not find interval cancers. It is somehow plausible to conclude that possibly through the MRI we found the cancers which would have been found with mammography only possibly later, plus the cancers that would not have been identified through mammographic screening and would have later become probable to cause the interval cancers that we are usually used to seeing with mammographic screening.

D.L.  I’d like to start and change a little bit the topic and discuss potentially false positive diagnosis because that’s a major criticism of any breast screening program, but in particular for MRI screening. For BI-RADS 3 you had 175 MRI studies or 4.9% that were categorized in that manner most of which were settled with a follow-up MR. Do you think that’s acceptable in a screening program that rate of BI-RADS 3 studies?

C.K.K.  Well I think it’s comparable again to mammographic screening for start. I think it’s still fairly the same with mammographic screening plus the fact that with mammographic screening for every positive screening result, you have to recall the patient and do a diagnostic examination which is not the case with MRI. The entire process of recall doesn’t happen with MRI screening because MRI diagnosis are more or less final.

D.L.  So when you then look at your BI-RADS 4 and 5 potentially false positive cases but this is also all the cancers that you found so you had a positive rate for BI-RADS 4 and 5 you 171 studies that were in those categories and a false positive rate of 2.9% and a positive predictive val-
ue for recommendation of biopsy of 35.7%. How do you think that is compared to other screening programs?

C.K.K. I think it’s a very high positive predictive value. Actually in the upper range of what you would expect to see with tomosynthesis which has been known to improve the PPV3 of mammographic screening. With tomosynthesis the positive predictive value that has been published for tomosynthesis is around 30ish percent so it’s just above 30% so with 36% positive predictive value we are as good as tomosynthesis for screening which has been shown to be better than mammography. In any case, we’re not worse than mammography. I think the claim that MRI is associated with a high false positive rate is certainly not true even on average risk women.

D.L. Your findings with the initial screen having a much higher detection rate than your subsequent screening rounds, could you imagine a scenario where breast MR is integrated into a breast screening program but it’s only done once or perhaps done at a long interval between exams to make it more cost effective.

C.K.K. Right, I think that would well be conceivable. I think that is actually the most important aspect of this study because that it shows that we can indeed possibly increase the screening intervals. We had a couple of women who underwent screening only every three years or every two years and an interval cancer, none of them an interval cancer arose. It took from a negative baseline MRI until the first only MRI diagnosed cancer it took three years on average. I think this data could at least be used to encourage further trials that would address this question, but if you ask me, that is certainly something that is conceivable.

D.L. For your study reporting now, you did a ten minute MR protocol and obviously time is an important factor when you’re using an expensive machine like an MR. How fast do you think we can go with these exams? That’s part one of my question and the second part is are we always going to need intravenous contrast?

C.K.K. Well that’s a difficult question to start with. The second one you will need intravenous contrast, there are a lot of studies right now going on that address this question, specifically using diffusion weighted imaging. For the time being I think we still have to use or rely on contrast agents. On the other hand, there are also studies ongoing that try to get rid of at least of the gadolinium based contrast agent. For the time being I think we have to stick with contrast, but I think it is actually less problematic than it is sometimes discussed in the scientific and medical community for the time being at least.

D.L. And how fast can we go with our protocols? How much time do you need for everything?

C.K.K. We, as you know, we published on abbreviated breast MRI for screening where we used a study protocol that just included one pre and one post contrast acquisition that just takes about three minute amount of time which is certainly the quickest we can go for the time being. But I’m quite confident that this is also doable in the future as a regular screening tool outside clinical trials. And there’s right now, as you know, the Akron Trial is recruiting on abbreviated breast MRI. The Akron Trial accepts I think an imaging protocol of ten minutes or so which is longer than the one that we published on.

D.L. For this current study you were comparing your MR results to regular mammography, full field digital mammography, but tomosynthesis is around now and I’m wondering how you think your results would differ when you add MR as supplemental screening for tomosynthesis?

C.K.K. Well it’s difficult to speculate on data that you don’t have or didn’t generate, so what I’m going to say it’s just a speculation. If you just take the published numbers, tomo increased the cancer detection rate compared with digital by 1.4 per thousand so that is a very moderate increase. With MRI we had an additional cancer detection rate of 22 per thousand in the first screening round compared to 1 per thousand. I think there is a big radiant still between what MRI can do and what tomosynthesis will be able to do. So I think tomosynthesis is not – probably the data would not have been much different if we had been using tomo instead of digital mammography.

D.L. Great, thank you. So we’ve touched on a couple of other topics that your group is working on now and I know you probably have way too many different projects to discuss, but what is really exciting to you that your group is working on now in this area of either breast cancer research or screening.

C.K.K. Well one of course is to use non-contrast enhanced screening to use diffusion weighted imaging that’s for one. Radiomics, I think everybody works in radiomics to see whether we can use imaging biomarkers to predict the behavior of breast cancer. I think that is something that I really find interesting because I’m convinced that we can add diagnostic and prognostic information by using these types of more refined mathematical modeling on our imaging data sets, because you know people are right now focusing very much on genomics and I think that what we can add as we observe a living cancer, if you want, and can better see what the cancer is actually able to do in its local, specific environment. So I think that is something that will be very interesting and these are I’d say the most important aspects we work on right now.

D.L. Well great. Well thank you so much for taking the time to...

C.K.K. Thank you.

D.L. …talk with me today and for all of the wonderful research that you do.

C.K.K. Thank you. Thank you.