Correspondence

Response to "Comment on 'Large area CMOS active pixel sensor x-ray imager for digital breast tomosynthesis: Analysis, modeling, and characterization' " [Med. Phys. 43, 1578–1579 (2016)]

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To the Editor,

This letter is in response to "Comments on 'Large area CMOS active pixel sensor x-ray imager for digital breast tomosynthesis: Analysis, modeling, and characterization' " [Med. Phys. **42**, 6294–6308 (2015)] by Dr. Chan.[1] The main purpose of the paper of Zhao *et al.*[2] was to describe the properties of a 75 μm pitch CMOS active pixel sensor (APS) detector and to investigate its possible application to DBT. The goal of the paper was not to compare the performance and capabilities of CMOS APS and amorphous silicon thin-film transistor passive pixel sensor (a-Si:H TFT PPS) detectors.

Figure 11 shown in the paper of Zhao *et al.*,[2] that is at the origin of Dr. Chan's comments,[1] is only used in support of a simple contrast-to-noise ratio (CNR) calculation. The content of this short section does not affect the main focus of the paper of Zhao *et al.* which shows that a high resolution, low noise, and a high detective quantum efficiency (DQE) can be achieved using the CMOS APS detector. The comparison, described in the paper by Zhao *et al.*[2] (Figure 11), of the calculated CNR of microcalcifications for the Dexela 2923 MAM CMOS APS detector with the CNR values extracted experimentally for two digital breast tomosynthesis (DBT) prototype systems, (a) the Dexela 2923 MAM CMOS APS detector and (b) the a-Si:H TFT PPS GE GEN2 detector, is based on results presented by Park *et al.*,[3] and Lu *et al.*,[4] respectively. The CMOS APS (Refs. 2 and 3) and a-Si:H TFT PPS (Ref. 4) detectors used in these two DBT prototype systems are very different in terms of technology. PPS and APS are based on low (~0.5 $cm^2\ V^{-1}\ s^{-1}$) and high mobility (200–1000 $cm^2\ V^{-1}\ s^{-1}$ at room temperature) a-Si:H and crystalline silicon (c-Si) semiconductors, respectively. It is commonly accepted that CMOS APS, in comparison to a-Si TFT PPS, has (i) higher resolution, (ii) lower electronic noise (by around a factor of 10, i.e., higher detector sensitivity), (iii) better detector response at high spatial frequencies (>5 lp/mm), and (iv) allows full integration of the driving circuits.[5–7] The electronic noise of a-Si:H TFT PPS cannot be reduced to less than 1000 e^-, which can degrade both the DQE and thus signal-to-noise ratio (SNR) especially at lower doses.[8]

The responses to Dr. Chan's specific comments are:

1. We agree with Dr. Chan that the CNR data using 11 projection views (PVs) would have a mean glandular dose (MGD) of about 1.31 mGy rather than 2.5 mGy. Since in Ref. 4 the phantom images were reconstructed from 11 and 21 PVs by SART (corresponding to a MGD of 1.31 and 2.5 mGy, respectively), we assumed incorrectly that a fixed radiation dose of 2.5 mGy was used for all the acquisition conditions described in their paper. We believe that the impact of dose reduction from 2.5 to 1.31 mGy would be minimal on data discussed in our paper. Because of space limitation here, we will attempt to support our view with a more in-depth discussion elsewhere.

   Since the detector pixel pitch of the GE GEN2 detector is 100 μm, the probability of detecting microcalcifications smaller than 200 μm would be limited by its spatial resolution (described by blur, sharpness, high-contrast, or details visibility) and background noise level (with direct impact on visibility and detectability). Also the electronic noise for an a-Si:H TFT PPS detector is around ten times higher than that of CMOS APS detectors. Hence, we would expect a poorer image quality (in terms of CNR) especially for small objects (e.g., microcalcifications <200 μm) detection at low radiation dose conditions. For larger microcalcifications (>500 μm), the electronic noise has a lower effect at higher dose (2.5 mGy) and both detectors would expect to have a similar performance.
2. In agreement with Dr. Chan's comments, our simple calculation presented in Ref. 2 ignored a number of factors that could affect the CNR values. We clearly stated that "*It should be noted that 3D image reconstruction is not currently included in our model.*" and "*To simulate the 3D reconstructed image quality for DBT, additional information of detector performance at various angles, image reconstruction, and ray tracing techniques is needed.*" Therefore, the limitations of the proposed CNR calculation have been clearly acknowledged in our paper. The obtained calculated results need to be verified through future analysis under different conditions to prove its general applicability. It was also understood that the calculated 2D CNR values may be inadequate for quantitative comparison with the CNR values extracted from experiments. For a quantitative comparison of these two different detector technologies, the same experimental conditions should be applied, which might be rather difficult to realize from a practical point of view.

3. We agree with Dr. Chan's comment that we did not consider the phantom composition used in Refs. 3 and 4, when describing the 75 μm pixel pitch Dexela CMOS APS detector advantage in comparison to the 100 μm pixel pitch GE GEN2 a-Si:H TFT PPS detector based on experimental data presented in the respective publications. Taking into account this comment, a question could be raised if the difference in phantom composition (e.g., difference in speck attenuation coefficients) would affect our conclusion in Ref. 2. We believe it would not, because the background noise (background materials) is different for the two phantoms. Therefore, we suggest that one could not simply multiply the data collected by Lu *et al.*[4] by a factor of 1.7, without consideration of the phantom's background noise. To remove the impact of phantom composition on the experimental data, it would be necessary to use the same phantom for both detectors. The x-ray spectra and exposures would also have to be the same.

   Dr. Chan also indicated that an additional correction factor of about 1.24 [$(2\ \text{mGy}/1.31\ \text{mGy})^{1/2} = 1.24$] should be considered to account for the dose difference between Park *et al.*[3] and Lu *et al.*[4] The square root relation of noise as a function of dose is only valid when the total pixel noise is quantum limited (i.e., x-ray quantum noise >> detector electronic noise). The estimated quantum noise level is in the range of 250–1000 e^- (for typical DBT detector surface air kerma within 1–10 μGy).[2] Hence, the a-Si:H TFT PPS detector (with electronic noise of 1000–2000 e^- under DBT conditions),[8] in comparison to the CMOS APS detector (with 100–150 e^-), does not satisfy this assumption.
4. The pixel pitch of Dexela 2923 MAM CMOS APS and a-Si TFT PPS GE GEN2 detectors is 75 and 100 μm, respectively. If the Nyquist-Shannon sampling theorem is used to define the imager resolution for high contrast objects, then from the pixel dimension we can infer that the smallest individual object that can be resolved is 150 and 200 μm for Dexela CMOS APS and GE GEN2 a-Si:H TFT PPS detectors, respectively, due to the aliasing effect. Hence, in principle, it is expected that a-Si:H TFT PPS detector would not be capable to resolve (without aliasing) individual microcalcifications smaller than 200 μm when the CMOS APS detector would be able to resolve objects as small as 150 μm under ideal conditions. We acknowledge that, in general, the x-ray source focal spot size, magnification, and imaging system performance can affect the imager resolution. For the ACR mammography accreditation phantom used by Lu *et al.*, test objects are located about 3.4 + 0.35 cm = 3.75 cm from the bottom of the ACR mammography accreditation phantom. For the investigated Dexela CMOS APS and GE GEN2 systems,[3,4] the calculated magnification factors M are around $66.5/63.2 = 1.05$ and $66/(64 - 3.75) = 1.095$, respectively. Taking into account the magnification factors, the Nyquist frequency for GE GEN2 system can be improved from 5 to 5.48 mm^{-1}, which should not have a major impact on image resolution. In Ref. 3, the focal spot size for the Dexela imaging system is $a_f = 0.3$ mm, which is acceptable for DBT. The expected blurring introduced in the image using the Dexela CMOS APS detector is $B = a_f\,(M-1) = 0.3\ \text{mm} \times 0.05 = 15\ \mu\text{m}$.[9] This should not affect the image spatial resolution significantly. Another factor that affects spatial resolution is focal spot motion blurring. Since both systems use the step-and-shoot motion, the focal spot motion blurring should be negligible. Focal spot motion (shake) during the "stop" portion of the step and shoot acquisition may differ for the two imaging systems. This is out of the scope of our presented paper.[2] Finally, super-resolution in DBT is feasible independent of the detector used, provided that the detector has measurable modulation above the aliasing frequency and the reconstruction algorithm supports finer sampling than the detector in each reconstructed slice.[10] We recognize that there are other additional physical factors such as background noise level, scatter radiation, and object attenuation coefficient that can affect the probability of detection of microcalcifications; the sampling, aliasing, and image reconstruction methods will also affect that probability.[3,4] The probability of microcalcification detection will also depend on experimental/clinical conditions such as x-ray beam quality (target/filter combination at a given tube voltage), dose, breast thickness, and glandularity among others, for a given detector. In addition, an advanced reconstruction method could also enhance the observed CNR of microcalcifications by suppressing the noise.[11] Nevertheless, accepting that the modulation transfer function (MTF) is commonly used to define the intrinsic resolution of an x-ray imager from a scientific point of view, and if the scintillator and interface optical properties are assured to be the same for both detectors, simply reducing the pixel pitch from 100 to 75 μm will improve the MTF by about 25% at spatial frequencies around 5 lp/mm. But we agree with Dr. Chan that more detailed investigation is needed to clarify the microcalcification detection probability limits when a new high resolution x-ray imaging technology is considered for a DBT application.

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[1]H.-P. Chan, "Comment on 'Large area CMOS active pixel sensor x-ray imager for digital breast tomosynthesis: Analysis, modeling, and characterization' [Med. Phys. **42**, 6294–6308 (2015)]," Med. Phys. **43**(3), 1578–1579 (2016).
[2]C. Zhao, J. Kanicki, A. C. Konstantinidis, and T. Patel, "Large area CMOS active pixel sensor x-ray imager for digital breast tomosynthesis: Analysis, modeling, and characterization," Med. Phys. **42**(11), 6294–6308 (2015).
[3]H. S. Park, Y. S. Kim, H. J. Kim, Y. W. Choi, and J. G. Choi, "Optimization of configuration parameters in a newly developed digital breast tomosynthesis system," J. Radiat. Res. **55**(3), 589–599 (2014).
[4]Y. Lu *et al.*, "Image quality of microcalcifications in digital breast tomosynthesis: Effects of projection-view distributions," Med. Phys. **38**(10), 5703–5712 (2011).

[5]I. M. Peters, C. Smit, J. J. Miller, and A. Lomako, "High dynamic range CMOS-based mammography detector for FFDM and DBT," Proc. SPIE **9783**, 978316 (2016).
[6]C. Zhao, A. C. Konstantinidis, Y. Zheng, T. Anaxagoras, R. D. Speller, and J. Kanicki, "50 μm pixel pitch wafer-scale CMOS active pixel sensor x-ray detector for digital breast tomosynthesis," Phys. Med. Biol. **60**(23), 8977–9001 (2015).
[7]Y.-S. Kim *et al.*, "Characterizing X-ray detectors for prototype digital breast tomosynthesis systems," J. Instrum. **11**(3), P03022 (2016).
[8]L. E. Antonuk *et al.*, "Strategies to improve the signal and noise performance of active matrix, flat-panel imagers for diagnostic x-ray applications," Med. Phys. **27**(2), 289–306 (2000).
[9]F. Ouandji, E. Potter, C. Engineering, and C. Oklahoma, "Impact of focal spot size on the spatial resolution of a digital x-ray imaging system for small animal studies," Proc. SPIE **4615**, 109–116 (2002).
[10]R. J. Acciavatti and A. D. A. Maidment, "Oblique reconstructions in tomosynthesis. II. Super-resolution," Med. Phys. **40**(11), 111912 (19pp.) (2013).
[11]J. Zheng, J. A. Fessler, and H.-P. Chan, "Digital breast tomosynthesis reconstruction using spatially weighted non-convex regularization," Proc. SPIE **9783**, 978369 (2016).

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