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Feasibility studies of a novel ultra-low dose stationary tomographic molecular breast imaging system utilising 3D position of interaction CZT detectors

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The Newcastle Upon Tyne Hospitals NHS Foundation Trust

UCL

Innovate UK

Outline

- Molecular Breast Imaging (MBI) and its role in breast cancer screening
- Kromek's new Ultra-Low Dose MBI (ULDMBI) technology
- ULDMBI prototype
- Upgraded detector simulation model
- Current experimental results
- Summary and future work

Breast density factor in breast imaging

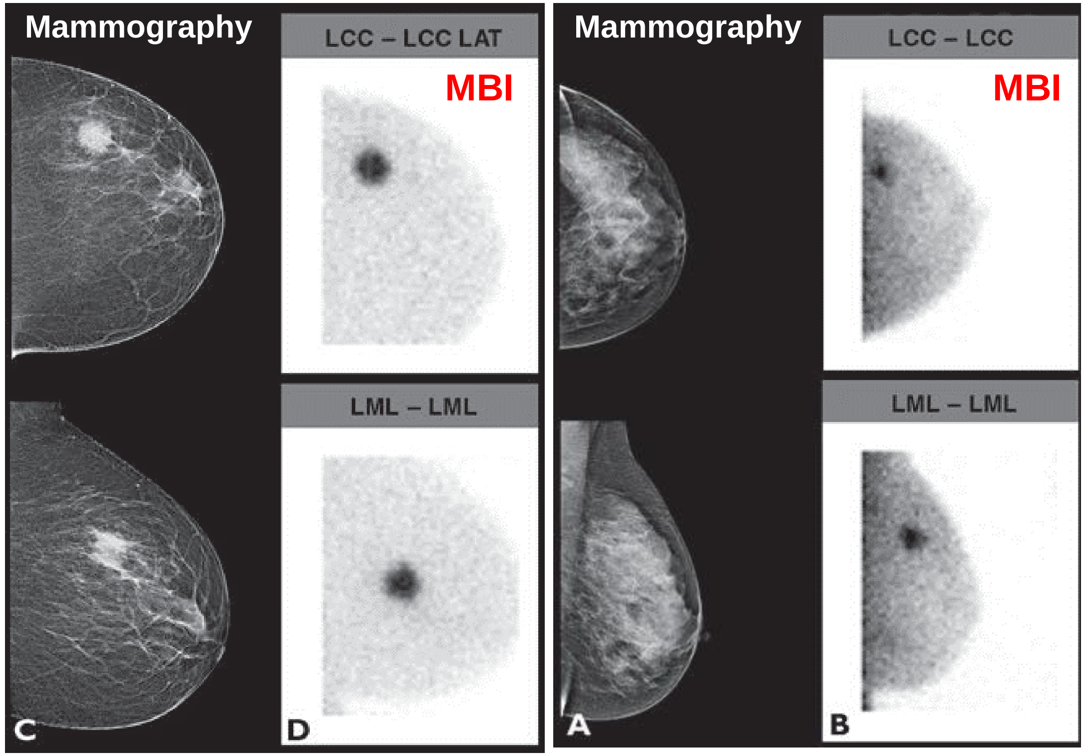
- Mammography is the most common modality used for breast imaging.
- Sensitivity for lesion detection is limited in patients with dense breast tissue.
- About 25% - 40% of women have dense breast tissue, depending on age, genetics, ethnic origins, hormone therapy, and other factors.
- Molecular Breast Imaging (MBI), a nuclear imaging modality, has been shown to be effective even for dense breasts.
- Mayo clinic's clinical trials for women with dense breast tissue:

  (mammography vs MBI + mammography)

  ✓ Cancer detection rate:
  3.2 vs 12.0 per 1000 screened

  ✓ Sensitivity: 24% vs 91%
  (true positives)

  ✓ Specificity: 89% vs 83%
  (true negatives)



Rechtman LR, Lenihan MJ, Lieberman JH, Teal CB, Torrente J, Rapelyea JA, Brem RF. *Breast-specific gamma imaging for the detection of breast cancer in dense versus nondense breasts*. AJR Am J Roentgenol. 2014 Feb; 202(2):293-8.

AJR Am J Roentgenol. 2015, February 204(2): 241–251.

MBI technology and ULD MBI project goals

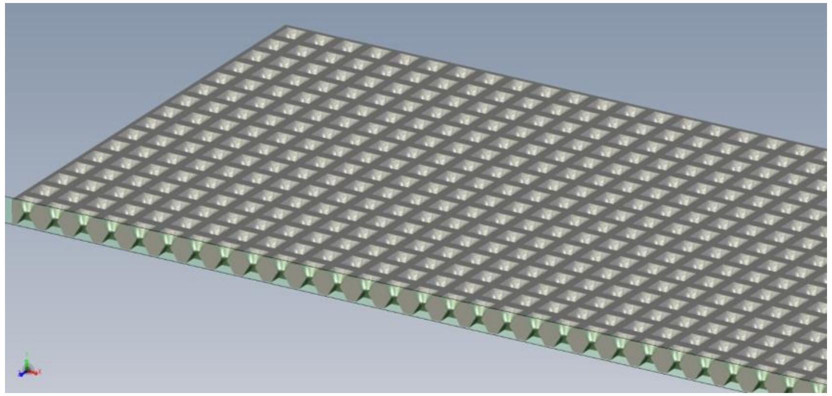
- Barriers to the widespread adoption of MBI:
  - Patient effective dose is considerably higher than in mammography (~0.5 mSv):
    - BSGI or scintimammography: injected dose of 740-1110 MBq, estimated effective dose of 6-9 mSv
    - CZT MBI: 300 MBq, estimated dose of 2.4 mSv
    - Lowest CZT MBI dose measurements published by Mayo clinic: 150 MBq, estimated dose of 1.2 mSv
  - Longer imaging time: 40 min (4 views x 10 min each) vs < 10 min total scan time in mammography.
  - Reluctance to change the existing pathways in the clinical practice using x-ray based techniques.

Kromek's goals in the project

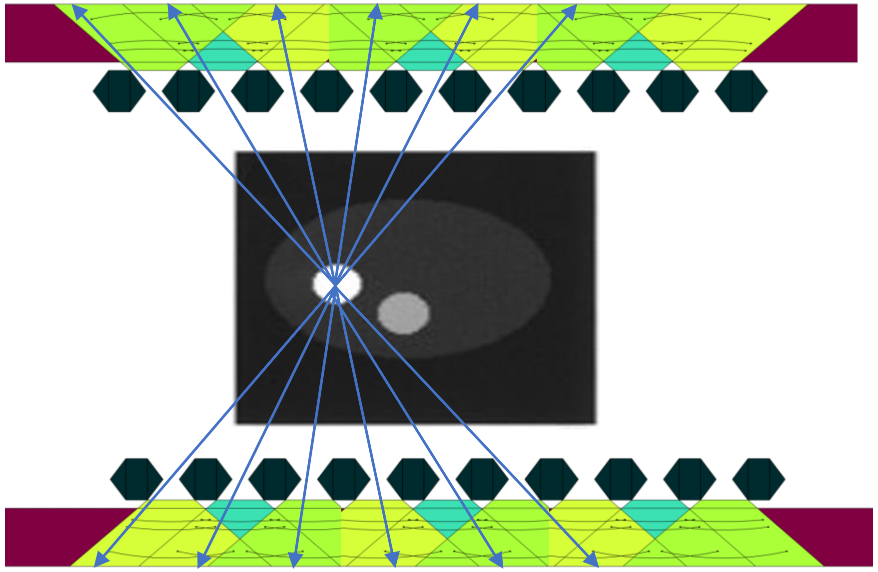
- Retain or improve clinical performance comparing to the current MBI performance.
- Reduce the dose/time combination by a factor of 10 (relative to 300 MBq dose) to be at the same level of patient dose and scan time as in contrast imaging in DBT or Breast CT (~1 mSv, ~10 min per 4 views).

New concept of imaging

- Tomographic imaging system comprised of a pair of stationary opposing detector arrays with densely-packed multi-pinholes (MPH) collimators.
  - ➢ Use collimator with hundreds of pinholes
  - ➢ Results in higher sensitivity
  - ➢ Improves angular sampling but results in significant multiplexing
  - ➢ Which varies with the detector depth-of-interaction (DOI)

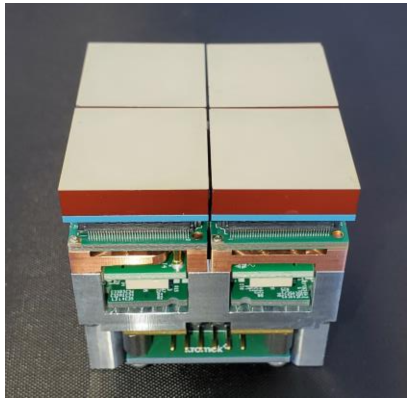


- Use high intrinsic position resolution CZT detectors to obtain 3D interaction position including DOI.
- DOI is used in de-multiplexing algorithms (patents pending) to reduce artefacts in the reconstructed image.
- 3D tomographic imaging results in lower background which improves Contrast-to-Noise Ratio (CNR).
- Detector FoV is comparable to the physical size of the imaged object.

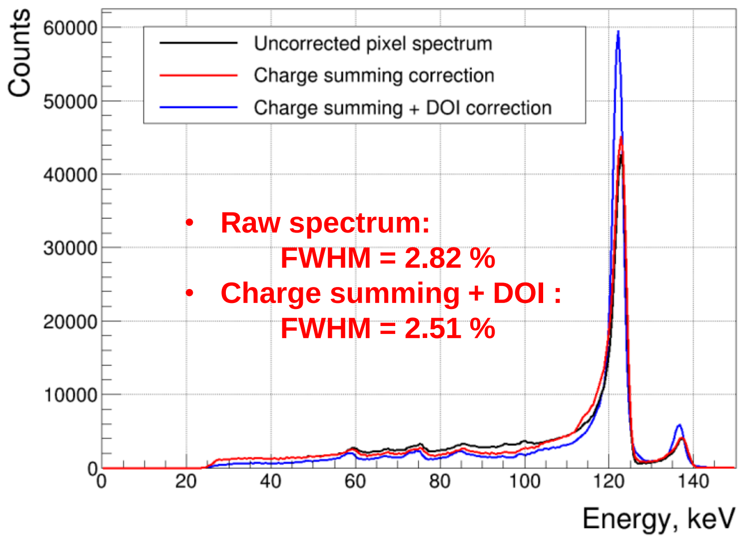


ULDMBI feasibility prototype

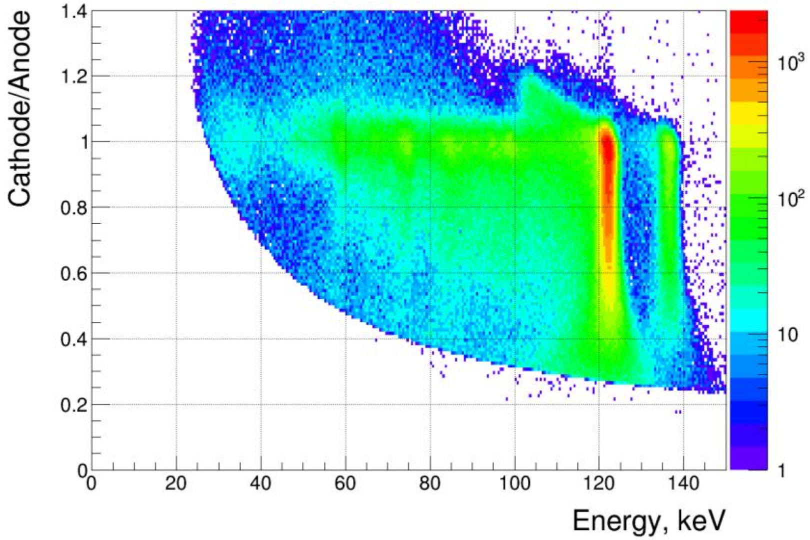
- The prototype is made from 5 mm thick CZT detectors with 11x11 array of 2 mm pixels
- Uses a new Kromek D-Matrix R2 module based on our KHR ASIC:
  - 128 anode and 2 cathode channels.
  - Amplifier gain – 20 mV/fC, 40 mV/fC , 80 mV/fC , 240 mV/fC.
  - Peaking time – 0.5 µs, 1 µs, 1.5 µs, 2 µs.
  - Readout mode – sparse (single pixel), enhanced sparse (pixel + neighbours).



^{57}Co pixel spectrum



DOI ~ cathode/anode



COMSOL model for detector simulation

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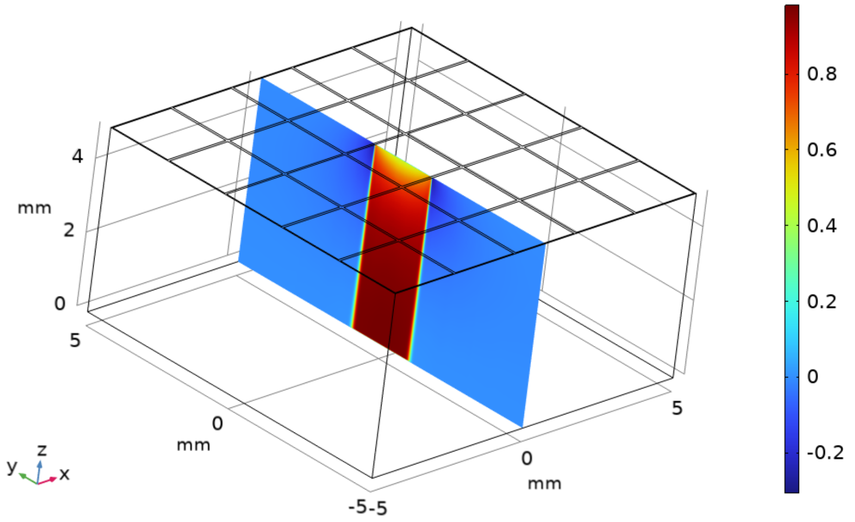
Charge Induction Efficiency (CIE) is calculated in COMSOL Multiphysics using the well-known method of adjoint continuity equations described by T.H. Prettyman (1999):

$$\frac{\partial n^{+}}{\partial t} = \underbrace{\vec{\nabla}(n^{+} \cdot \mu_n \cdot \vec{\nabla}\varphi)}_{\text{Drift}} + \underbrace{\vec{\nabla}(D_n \cdot \vec{\nabla} n^{+})}_{\text{Diffusion}} - \underbrace{\frac{n^{+}}{\tau_n}}_{\text{Trapping}} + \underbrace{\mu_n \cdot \vec{\nabla}\varphi \cdot \vec{\nabla}\psi_w}_{\text{Generation}}$$



- ✓ The recombination term – driven by trapping/detrapping since the recombination in CZT is dominated by the trap assisted Shockley-Read-Hall process.
- ✓ The generation term - interaction between the weighting potential and the drift field.
- ✓ Charge cloud expansion model - implemented in COMSOL using Einstein diffusion and Coulomb repulsion terms basing on the analytical model published by E. Gatti (1987):

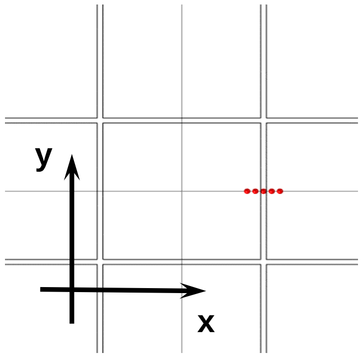
$$r_{Ein}(t) = 1.15 \cdot \sqrt{2Dt}\ , \quad D = \frac{\mu k_B T}{e}; \qquad r_{Coulomb}(t) = \sqrt[3]{3\frac{\mu e}{4\pi\varepsilon}Nt}$$

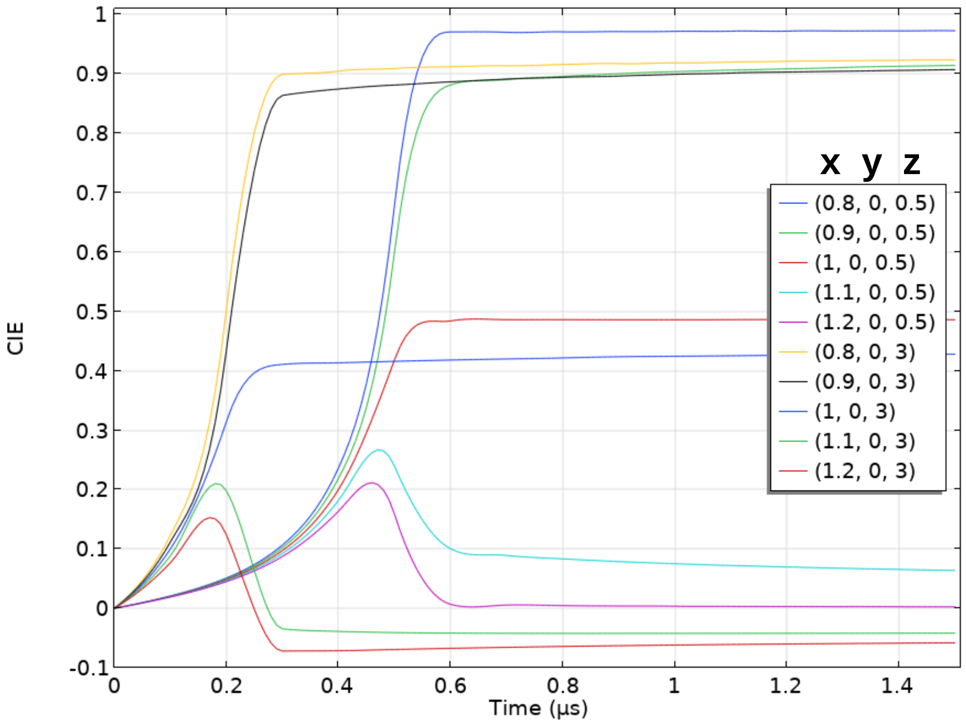
A. Cherlin et al., "Spectral performance, characterisation and simulation of 5 mm thick CZT detectors hybridised to a Timepix ASIC", iWoRiD 2017, Krakow, Poland.

M Bettelli et al. "A first principle method to simulate the spectral response of CdZnTe-based X- and gamma-ray detectors", NIM A, vol. 960, 163663, 2020.

Upgraded model for detector simulation

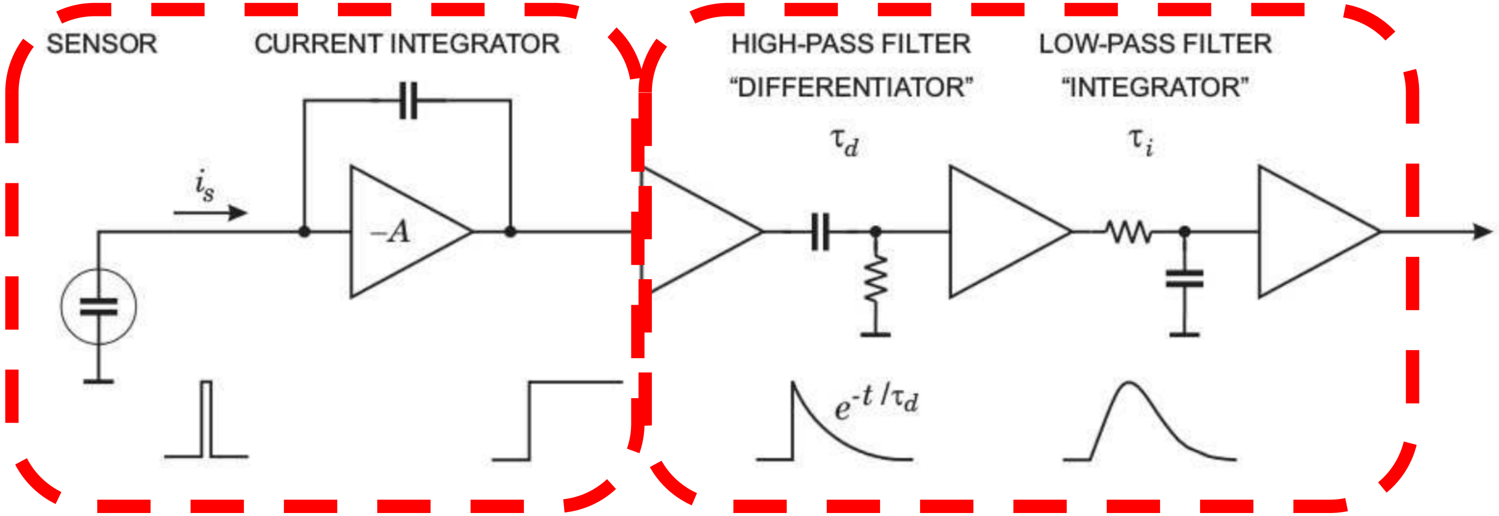
1. Charge pulses produced in COMSOL emulate the output of CSA without reset.





Upgraded model for detector simulation

1. Charge pulses produced in COMSOL emulate the output of CSA without reset.
2. The shaping amplifier is emulated by “differentiator” and multi-staged “integrator”.
3. Gaussian noise is added to the pulse shape at the shaper output. The noise sigma is chosen to match the energy resolution in the measured data.
4. The peak detector output is obtained by measuring the height of the final pulse.



(Image source: Spieler H., *Analog and Digital Electronics for Detectors*)

$$v'_{out} + (RC)^{-1} v_{out} - v'_{in} = 0 \quad (differentiator)$$

$$v'_{out} + (RC)^{-1} v_{out} - (RC)^{-1} v'_{in} = 0 \quad (integrator)$$

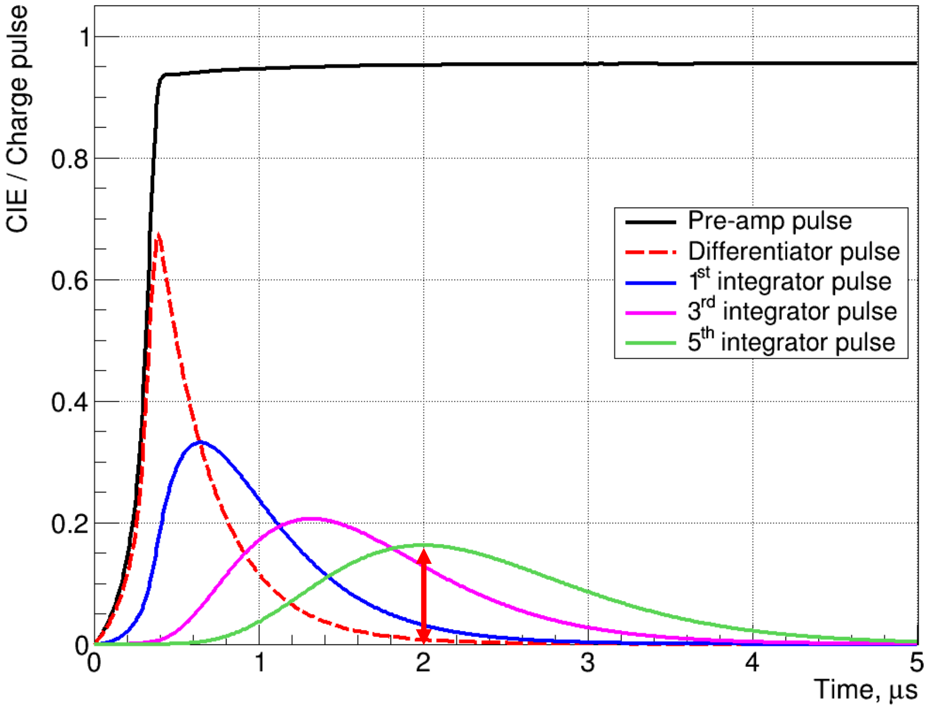
$$where\ (RC)^{-1}\ is\ the\ shaping\ time$$

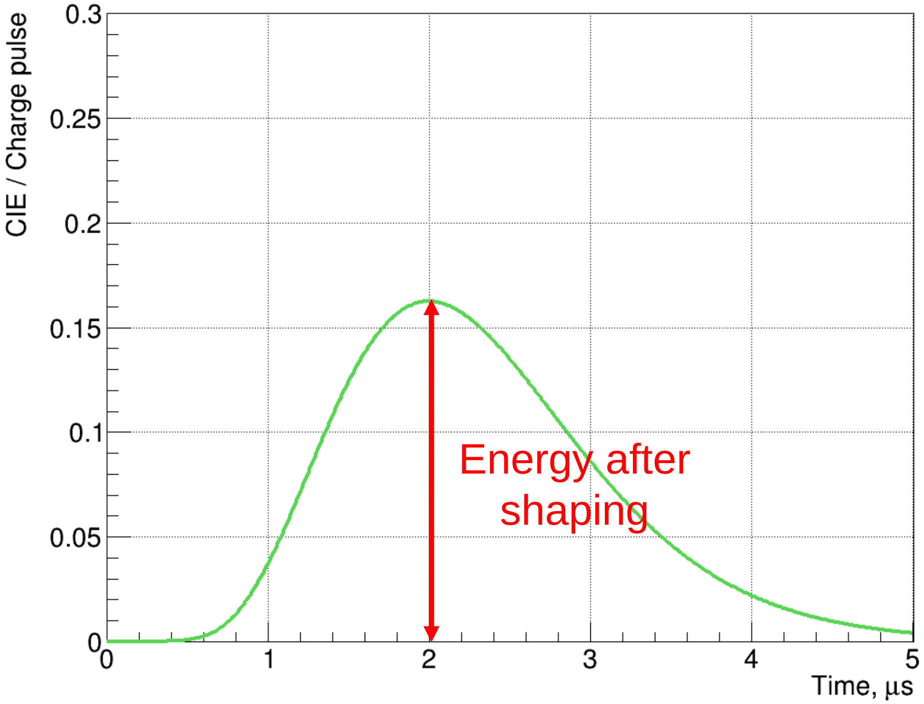
A Makeev et al. “Modeling CZT/CdTe x-ray photon-counting detectors”, Proc. SPIE Vol. 9412, 94124V; 2015.

Upgraded model for detector simulation

- We start from a charge pulse simulated in COMSOL.
- The first stage of shaping is high-pass filter, or “differentiator”.
- It’s followed by 5th order low-pass filter, or “integrator”.

- Energy is obtained by measuring the height of the resulting pulse.





Comparison with real data

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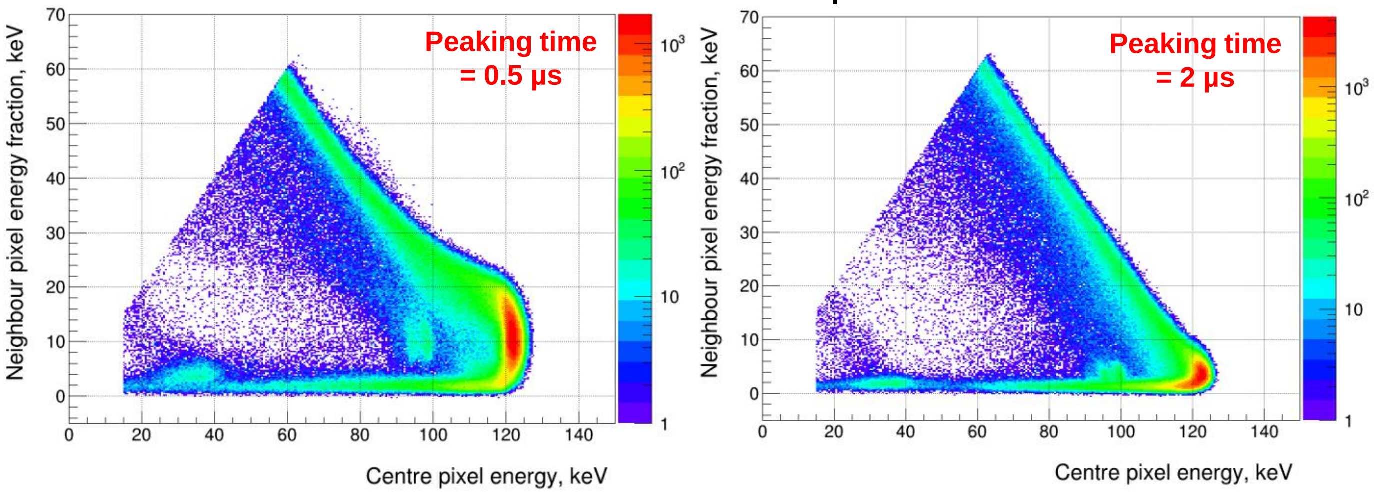
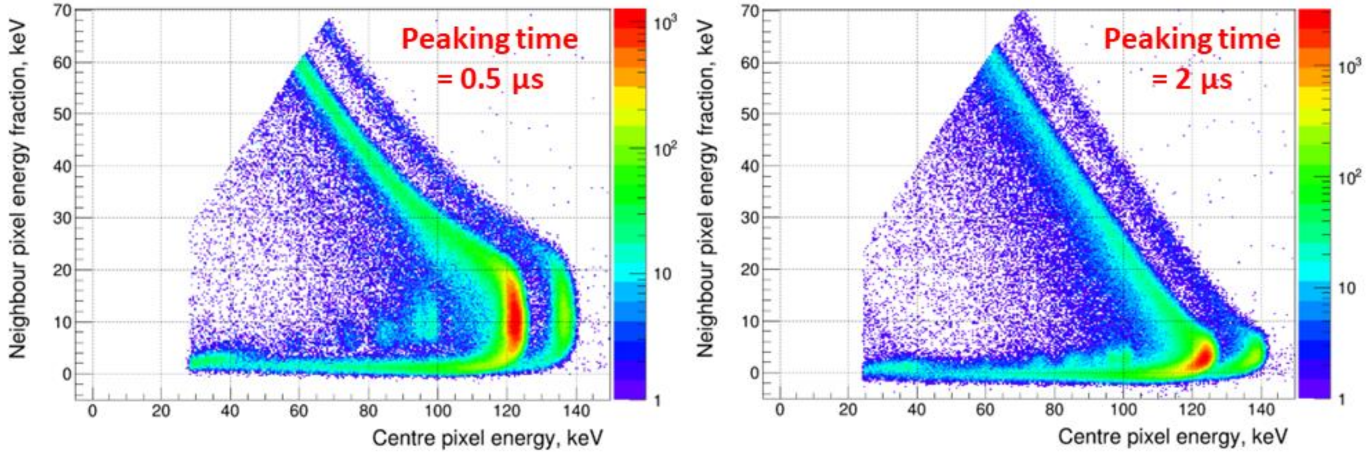
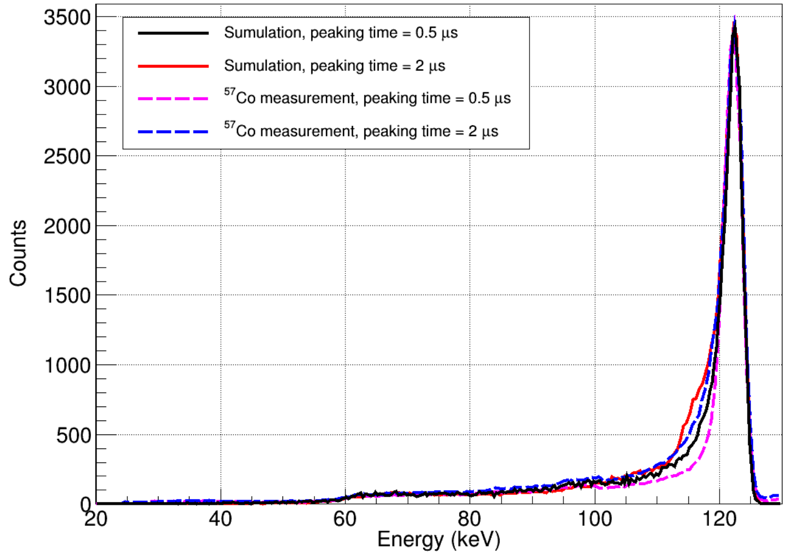
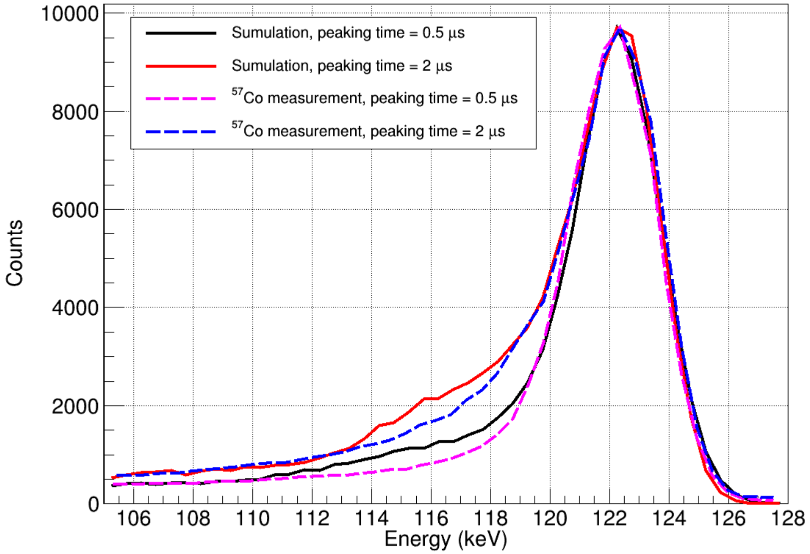
Simulated 122 keV spectrum



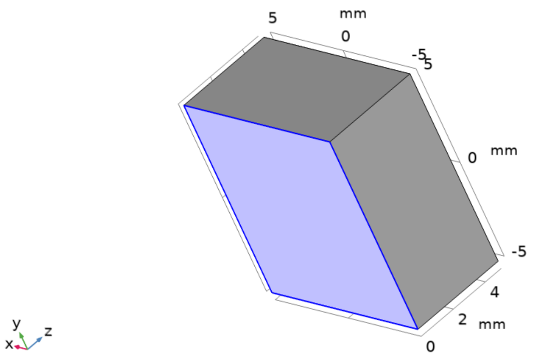
Measured ^{57}Co spectrum

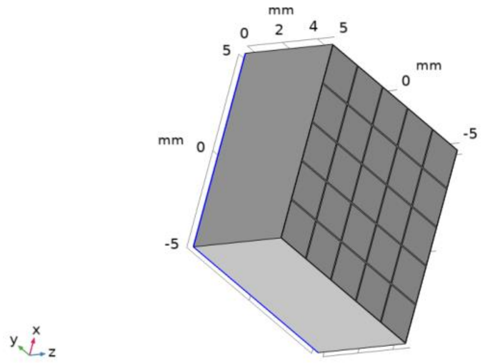


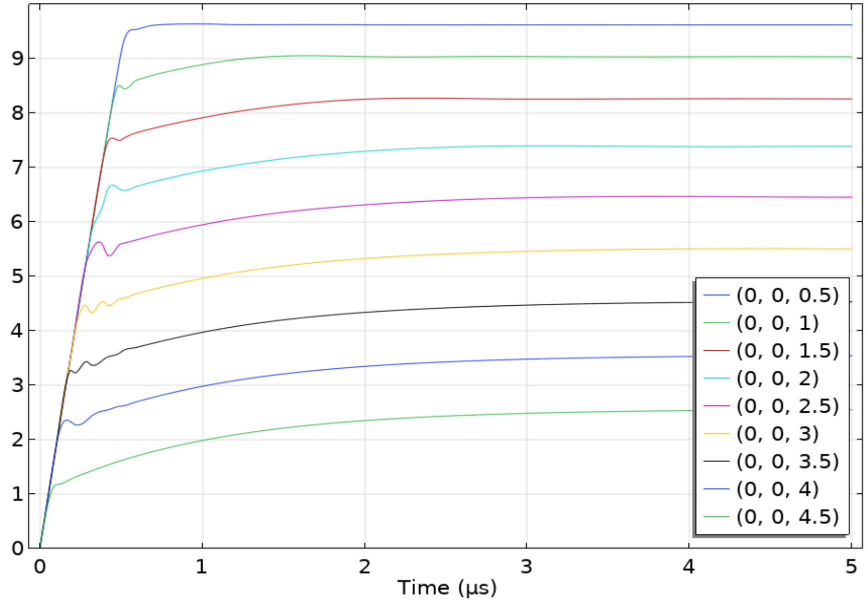




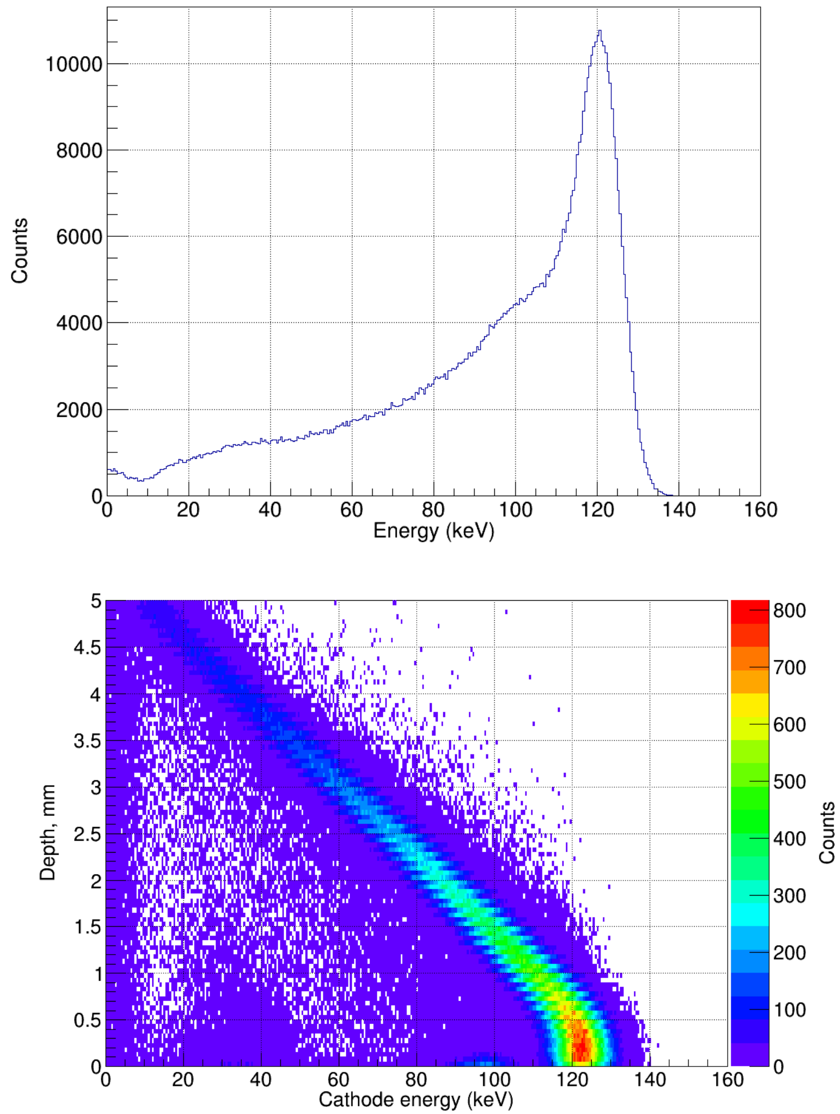
Cathode signal simulation





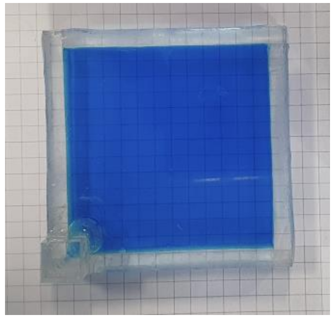


Simulated 122 keV cathode spectrum



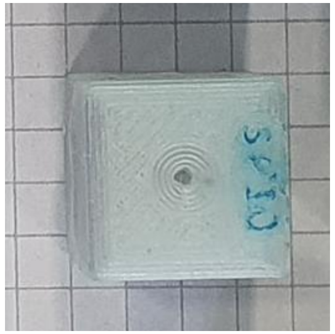
Dose/time reduction - phantom measurements

^{99m}Tc-filled phantoms represent spherical lesion over tissue background



"Tissue background"

30 x 30 x 20 mm box

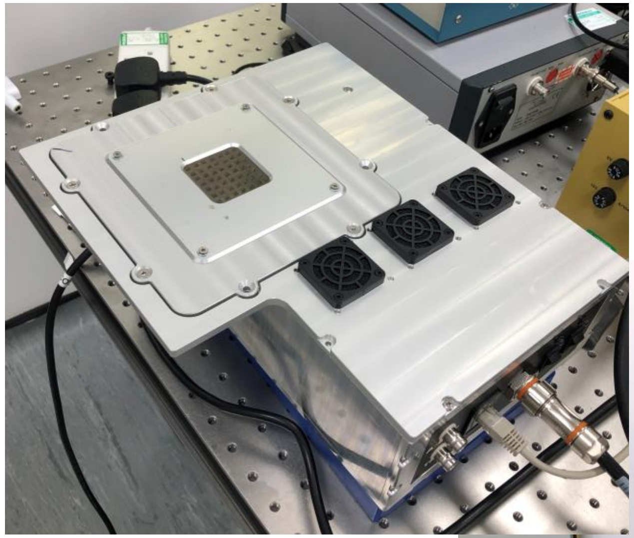


"Lesion"

6 mm spherical

cavity

Detector system with collimator on top



Measurement facility

Dose/time reduction - phantom measurements

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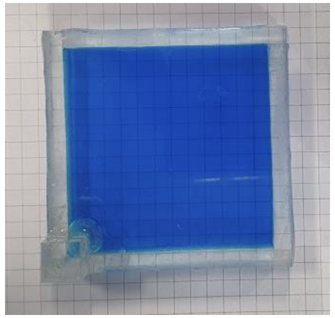
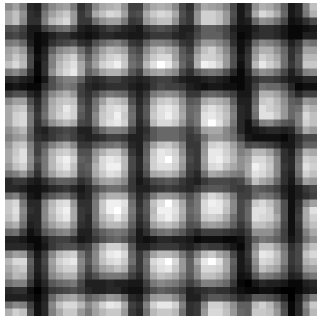
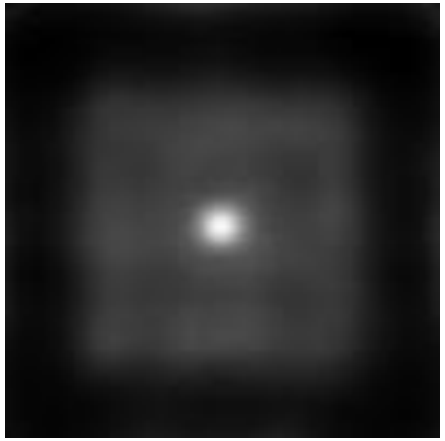
^{99m}Tc-filled phantoms represent spherical lesion over tissue background

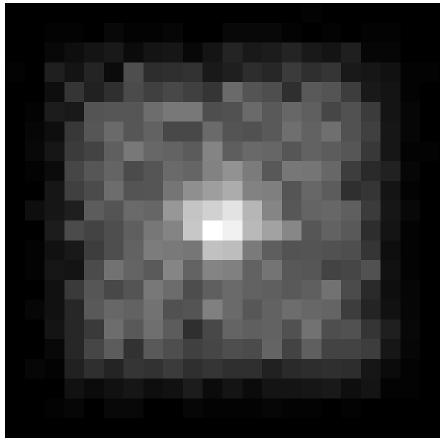


“Tissue background”

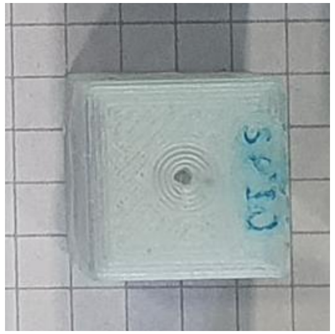
30 x 30 x 20 mm box





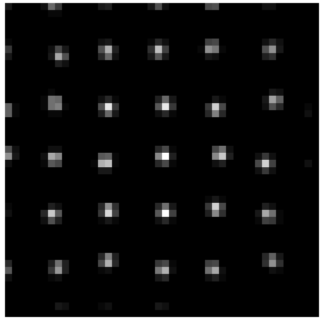


Corresponding 2D parallel collimation data (simulation)

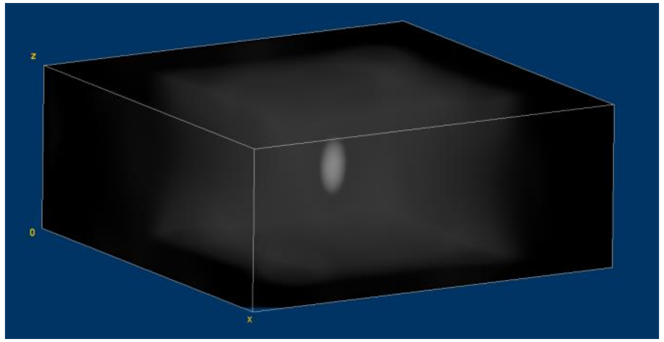


“Lesion”

6 mm spherical cavity



Multi-Pinhole projections with 10 depth layers



3D reconstructed images

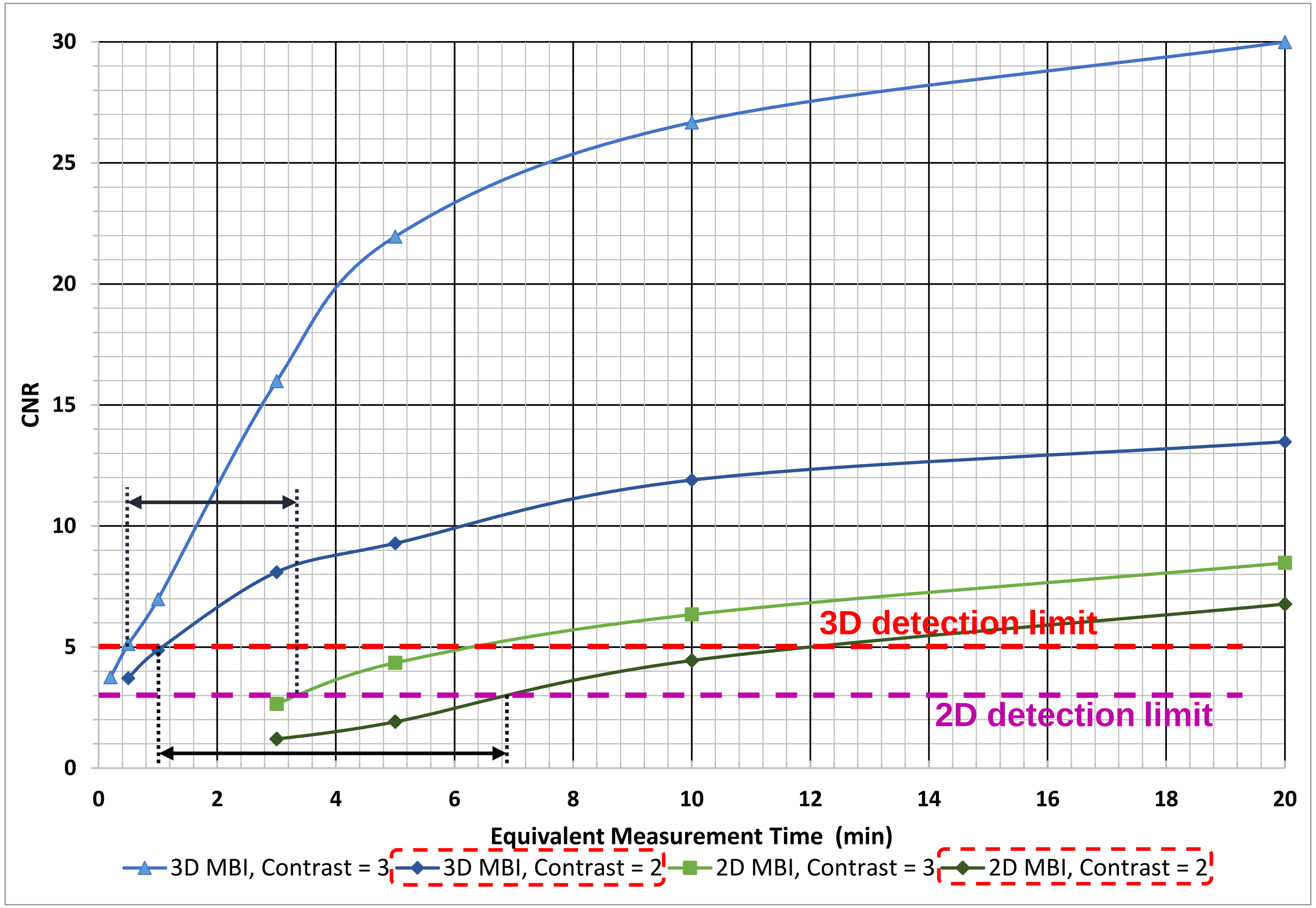
Numeric evaluation (CNR calculation)

Dose/time reduction - phantom measurements

- “Background” and “lesion” were combined with a weight factor ratio which defines contrast.
- 2D detection limit CNR = 3, defined by the “Rose criterion”.
- 3D detection limit CNR = 5, defined by modification of “Rose criterion”.

Contrast	2D MBI	3D LD MBI	Reduction factor
2	6.88	1.05	6.55
3	3.56	0.46	7.74

Average dose/time reduction factor ≈ 7



Summary and future work

- New simulation model reproduces the charge sharing and shaping effect with a good precision.
- Cathode signal simulation is also implemented.
- First experimental measurements with ^{99m}Tc show that the dose/time reduction factor of 7 has been achieved.
- The result is very close to the dose/time reduction factor of 8 predicted in simulation work.
- The results demonstrate a clear potential to position ULD MBI as a technology for dense breast imaging competing with x-ray contrast imaging achieving a similar combination of patient dose (~1-1.2 mSv) and measurement time (~10 min for a 4-view scan procedure) without using the iodine-based contrast agent.

Further work

- Implementation of negative energy simulation in non-collecting pixels and continuous reset after CSA.
- Further and more comprehensive comparison with measured data.
- Develop ML methods for subpixelisation and energy corrections using simulated data.
- A new project to design and manufacture a small FoV and full-size MBI prototypes is underway.

Acknowledgments

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