**Supplementary material**

1. **Material decomposition**

**Beer-Lambert equation**

|  |  |
| --- | --- |
|  | (S1) |

where and are intensities after and before traverse the sample, is the thickness of the sample, is the energy of the X-ray beam, and is the attenuation coefficient. For a breast tissue with micro-calcifications, the integral term can be written as:

|  |  |
| --- | --- |
|  | (S2) |

with , as the attenuation coefficients of two types of micro-calcifications, and as the attenuation coefficient of the breast tissue. The energy-independent integrals, , correspond to the projected thickness of each material. If is the total projected thickness of the sample, then the Beer-Lambert equation is

|  |  |
| --- | --- |
|  | (S3) |

|  |  |
| --- | --- |
|  | (S4) |

images at different energies, *,* are taken to retrieve and using matricial methods as:

|  |  |
| --- | --- |
|  | (S5) |

And inverting the matrix equation for as

|  |  |
| --- | --- |
|  | (S6) |

**Verification of equation S6**

Images were acquired for two types of micro-calcifications—alumina and hydroxyapatite (HA)—at five different radii, embedded in a standard breast tissue with a thickness of 5 cm. The corresponding imaging energies were 20 keV, 24 keV and 28 keV (Figure ), forming a matrix for . The objective is to retrieve the projected thickness of alumina and HA, using their attenuation coefficients at these energies to construct the matrix .

|  |  |  |
| --- | --- | --- |
|  |  |  |
| keV | keV | keV |

Figure . Images acquired at 20 keV, 24 keV and 28 keV of standard breast tissue with micro-calcifications of alumina and hydroxyapatite of five different radii.

|  |  |
| --- | --- |
| Alumina | HA |
| Theoretical | |
|  |  |
| Material Decomposition | |
|  |  |
|  |  |

Figure . Projected thickness maps of Alumina and HA, retrieved by using equation S6 (Second row). A comparison with the theoretical projected thickness maps (First row) is given with the profiles thickness profiles (Third row).

The results are presented in Figure , where the algorithm successfully retrieves the projected thickness of both materials. A comparison between the expected and retrieved projected thickness profiles—obtained by projecting the projected thickness images along the horizontal axis—is shown for both materials.

1. **Simulation-Materials**

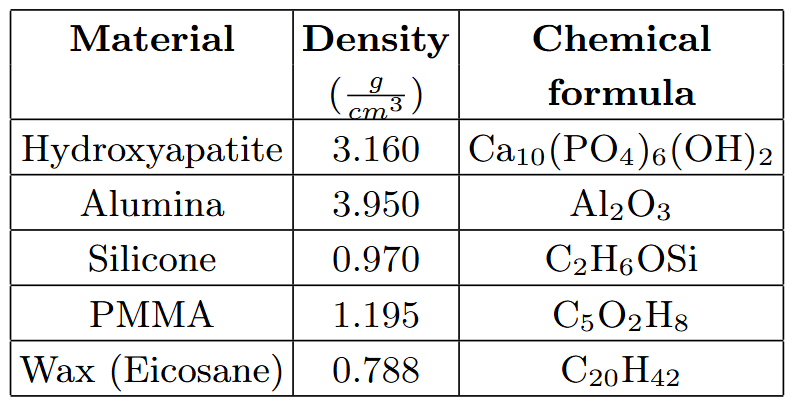


Table . Information of materials used in GATE, providing their density and their chemical formula [R1].

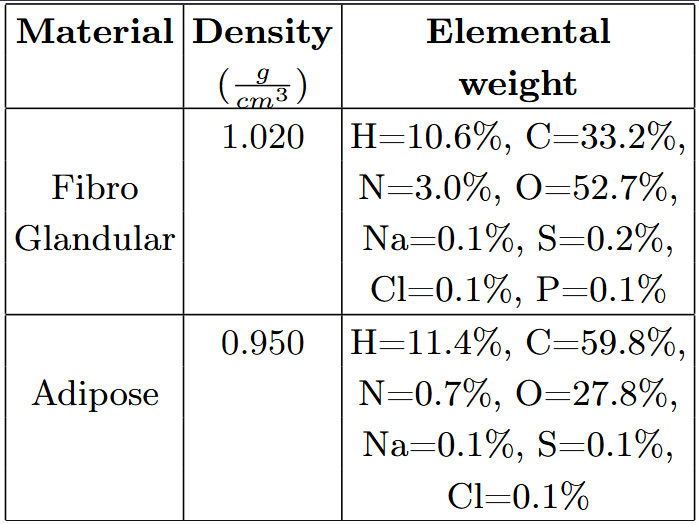


Table . Information of the material Fibroglandular and Adipose used in GATE, providing their density and their elemental weight according to [R2].

1. **Characterization of the Timepix3 detector**
2. **ToT vs. E. Using Timepix3 in Pixel mode.**

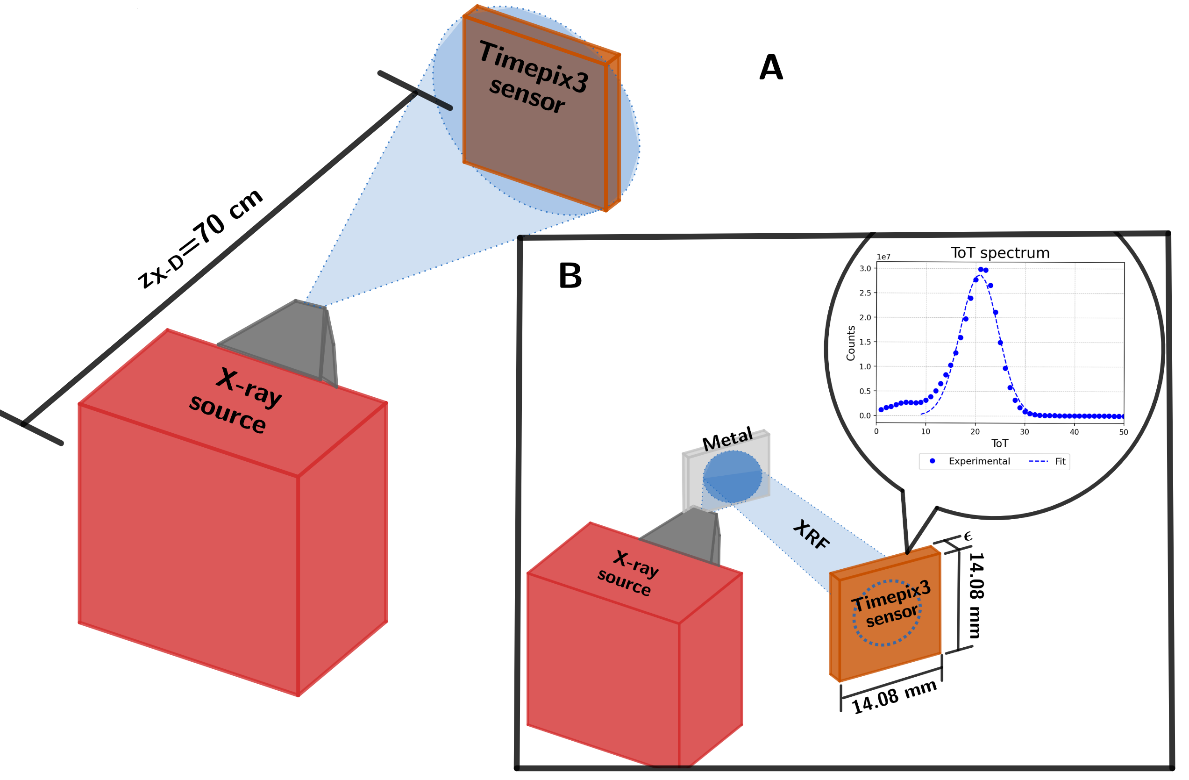


Figure . Panel A: General diagram of dose measurement, illustrating the X-ray source and detector. Panel B: General diagram used for characterization of the Timepix3 detector, to convert ToT to energy values. The detector is arranged so that a metal can read the fluorescence photons generated by it. The ToT distribution obtained for comparison.

The Timepix3 is a photon-counting detector that combines a 130 nm CMOS readout chip with a 1 mm thick CdTe crystal serving as the X-ray sensor [R3]. The sensor consists of a 256256 matrix of square pixels with a pixel pitch of 55 um, resulting in a total detection area of about 14.08 mm 14.08 mm. The detector operates in two measurement modes: the counting mode and the ToT (Time-over-Threshold)-ToA (Time of Arrival) mode. In the ToT-ToA mode, the ToA value is obtained by counting the total periods before the signal crosses the threshold, and the ToT value is determined by counting the periods while the signal remains above the threshold [R3]. Initially, charge sharing in the detector, where the generated charge by a photon in a pixel is spread among its adjacent pixels, is the reason for incorrectly reconstructing the ToT values at each pixel. This problem is solved by using a clustering algorithm [R4], which relates pixel clusters close in space and time to reconstruct the correct ToT value in each pixel.

The ToT value is proportional to the energy of the incident photon [R3,R5]. The relationship between ToT and energy is calibrated as follows [R5]: first, a ToT spectrum for a reference metal is acquired in ToT-ToA mode, with the detector arranged as illustrated in Panel B – Figure . The ToT value corresponding to the peak count is identified and associated with the X-ray fluorescence energy of that metal. Using four metals, such as Zr (15.775 keV), Rh (20.216 keV), Sn (25.271 keV), and Gd (42.996 keV), determining their respective ToT peak values (Left of Figure ), a calibration curve relating ToT peaks to photon energy is established (Right of Figure ).

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Figure . Left. ToT spectrum of four materials. Right. Calibration curve of ToT with energy.

1. **Spectrum of the X-ray source using the Timepix3.**

One of the advantages of measuring the energy of the incident photons is the possibility to estimate entrance radiation doses at any distance between the X-ray source and the detector. The incident spectrum on the detector is measured when the Timepix3 is placed at 70 cm from the X-ray source (Panel A – Figure ). Following the process described in [R6], could be obtained in the following way:

|  |  |
| --- | --- |
|  | (S7) |

* : Energy spectrum measured by the detector
* : Spectrum of the X-ray source
* : Detector response function

is determined by using the energy resolution of the detector. This resolution is determined by the fluorescence spectra of four materials: Zr ( keV), Sn ( keV), Gd ( keV), ( keV), as follows:

* Perform a Gaussian fit around the peaks of the spectrum (Left of Figure )
* Obtain and from each fit to obtain the energy resolution from each material.
* Graph of vs E (Right of Figure )

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Figure . Left. Energy spectrum of four materials, with Gaussian fits. Right. Dependence of Energy resolution of the detector with energy

Each element of is constructed from Gaussian functions, following the energy dependence of , as illustrated in Figure 6.

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Figure . Left. for E=8 keV (Black), E=17 keV (Blue) and E=27 keV (Red).

Measuring for each spectrum, with the setup pf Panel A – Figure , the Bayesian deconvolution method [R7] is used to determine from equation S7, as illustrated in Figure for Rh and Al at 28 kVp.

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Figure . Top. measured for Rh and Al at 28 kVp. Bottom, retrieved for Rh and Al at 28 kVp.

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