Tumor-Specific ^{99m}Tc-Sestamibi Quantification in Molecular Breast Imaging with Monte Carlo Simulation

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Motivation for Present Work

Motivation

Quantitative functional breast imaging could aid in lesion detection, treatment planning, and treatment response assessment, complementing the physiologic data of mammography/ultrasound

However, MBI currently lacks accurate quantification of ^{99m}Tc-sestamibi in lesions

Our long-term goal is to develop MBI image acquisition and processing techniques to help standardize interpretation and quantification

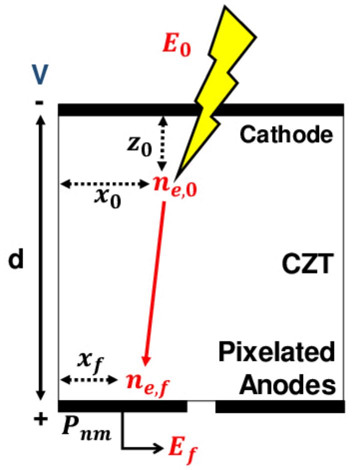
To help achieve our goal, we have developed a Monte Carlo simulation of the GE NM750b system with Cadmium-Zinc-Telluride (CZT) detectors

Outline of Poster Content

Part 1		Overview of physics and model parameters of pixelated CZT detector response used in Geant4 Monte Carlo
Part 2	A	Optimizing model parameters to match simulation output to measured performance characteristics
	B	Validating optimized parameters using a clinically realistic image quality phantom
Part 3		Evaluating quantification accuracy of simple scatter and attenuation techniques on simulated ^{99m}Tc sources

Part 1: CZT Detector Model

Simplified Model[1] Implemented in Geant4 and MATLAB



Photon deposits E_0 keV at (x_0, y_0, z_0) and generates N_{sub} clouds of $n_{e,0}$ electrons each

$$N_{sub} \times n_{e,0} \sim 1D\ Gaussian\left(\frac{E_0}{\epsilon}, f \times \frac{E_0}{\epsilon} + \sigma_{enc}^2\right)$$

Each N_{sub} cloud is assigned to pixel P_{nm} corresponding to coordinates (x_f, y_f)

$$(x_f, y_f) \sim 2D\ Gaussian\left(x_0, y_0, \frac{4D(d - z_0)^2}{\mu_e V}\right)$$

All electrons assigned to pixel P_{nm} $(n_{e,f})$ induce a E_f keV signal

$$E_f = (n_{e,f} \times \epsilon) \cdot \frac{\lambda_e}{\lambda_e - \tau_a} \cdot \frac{exp\left(\frac{z_0 - d}{\lambda_e}\right)}{1 - \exp\left(-\frac{d}{\tau_a}\right)} \cdot \left(1 - exp\left(\frac{z_0 - d}{\lambda_e}\right)\right)$$

Model Parameter Definitions

Physics	Symbol	Parameter Definition [Unit]
Charge Generation	N_{sub}	Number of electron sub-clouds [#]
	f	Fano factor [unitless]
	ϵ	Average ionization energy [keV]
	σ_{enc}^2	Equivalent noise charge [keV]
Charge Diffusion	D	Diffusion coefficient [mm^2/s]
	μ_e	Electron mobility [mm^2/V/s]
	V	Applied voltage [V]
Charge Induction	τ_a	Induction constant [mm]
	λ_e	Electron mean-free drift [mm]

Part 2: Optimizing and Validating Simulation Model Parameters

A. Optimizing Simulation Parameters

Final model parameters heuristically optimized through trial-and-error

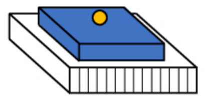
Starting parameter values for optimization from GE Healthcare or Pretorius et al.[1]

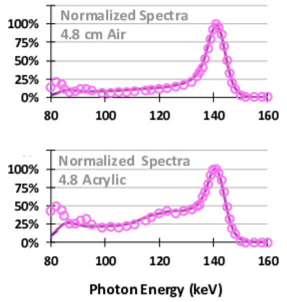
Good overall agreement in all standard performance characteristics between measured data (dark purple rhombus/line) and simulated data with final model parameters (light pink circles)

Energy Spectra and Resolution

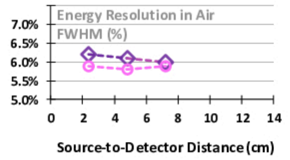
^{99m}Tc Point Sources in Air with/without Acrylic Slabs

Good agreement of spectra between 100-160 keV in-air and in-scatter conditions



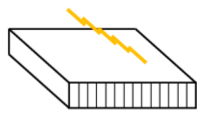


Good agreement of photopeak FWHM in air for sources 2-8 cm from detector

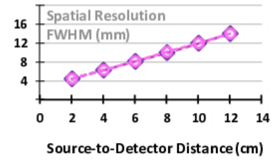


Spatial Resolution

^{99m}Tc Line Sources in Air

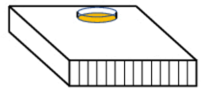


Good agreement of line profile FWHM[2] for sources 2-12 cm from detector

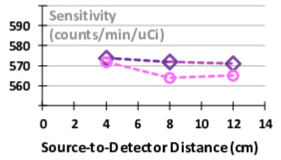


Sensitivity

^{99m}Tc Thin Film Sources in Air

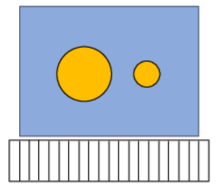


Good agreement for sources 4-12 cm from detector (*570 cpm/μCi ≈ 0.026% efficiency)*



B. Validating Parameters

Final model parameters validated by assessing image quality of a 5cm-thick phantom with 2 spherical sources (center 3cm from detector)

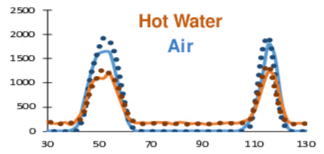


Source:	Large	Small
Ø (mm)	18	10
μCi/cc	340	1280

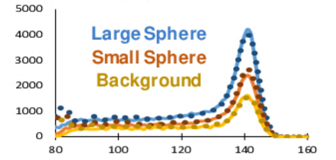
Background Conditions		
Air	Cold Water	Hot Water (11 μCi/cc)

Good agreement in (*Left*) line profiles & (right) energy spectra between measured data (*solid lines*) and simulated data (*dotted lines*)

Photopeak window count profiles through spheres



Energy spectra within 30mm Ø ROIs for different sources in hot water



<5% error calculated in all simulated 30mm Ø ROI counts in photopeak window

Condition	Bgd.	18mm Sphere	10mm Sphere
Air	--	3%	-1%
Cold Water	--	-4%	-5%
Hot Water	5%	1%	3%

Key Takeaways

Validated simulation of GE NM750b allows us to perform idealized experiments to construct physics-based quantitative MBI

Geant4 toolkit is used to track and record particle interactions (e.g. photoelectric, Compton scatter, etc.) throughout the simulated world

Simplified model of charge generation, diffusion, and induction can be easily adapted for other pixelated semiconductor detector

Initial simulated experiments with simple ^{99m}Tc sources highlighted the dependence of source quantification accuracy on ROI size

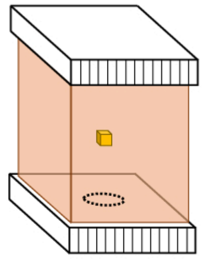
Part 3: Testing Accuracy of ^{99m}Tc Quantification

Simulation Experiments

Background: 10cm thick Air or 50/50 Breast Tissue (non-radioactive)

Sources: (2.5mm)^3 ^{99m}Tc Cube at 20 distances from center of detector (150M histories/simulation)

Measurement: Counts-per-1M-decays (*cpMd*) recorded with 12 ROIs of radius 0-75mm on photopeak image



Quantitation Techniques Evaluated for each Photopeak ROI *cpMd*

1. *NC cpMd*

Photopeak window counts with no corrections

2. *AC cpMd*

NC cpMd with geometric mean attenuation correction[3]

3. *SAC cpMd*

NC cpMd with dual-energy-window scatter correction and geo. mean attenuation correction[3]

Mean ± σ of relative errors in *cpMd* (*ΔcpMd*) for sources in air and in breast tissue.
[*Error relative to NC cpMd with r=75mm ROI for source in air (assumed gold standard)*]

ROI Radius	*Sources in Air*			*Sources in Tissue*		
	NC ΔcpMd	*AC ΔcpMd*	*SAC ΔcpMd*	*NC ΔcpMd*	*AC ΔcpMd*	*SAC ΔcpMd*
Single Pixel	-82% ± 18%	-87% ± 2%	-89% ± 2%	**-87% ± 18%**	**-87% ± 2%**	**-89% ± 2%**
7.5 mm	-7% ± 9%	-7% ± 4%	-19% ± 4%	-46% ± 26%	**2% ± 5%**	-14% ± 5%
15 mm	**-0.3% ± 1%**	**-0.3% ± 0.4%**	-13% ± 0.4%	-41% ± 24%	16% ± 3%	**-5% ± 2%**

Key Lesson: Quantitation Accuracy Depends on ROI Size

Due to the relative inclusion of primary and scatter signal in tissue ROIs:

- Larger ROIs (e.g. 15mm) required **both** SAC (mean error of -5%)
- Smaller ROIs (e.g. 7.5mm) required **only** AC (mean error of 2%)
- Single-pixel ROIs never accurately quantified activity (mean error of -88%)

Extensive studies on quantitation underway with newly validated MBI simulation

Acknowledgements

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References

[1]. Pretorius et al. IEEE Trans Nuc Sci, 2015.
[2]. Siman and Kappadath. Med Phys, 2012.
[3]. Bache and Kappadath. Med Phys, 2017.

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