An application-specific small field of view gamma camera for intraoperative dual-isotope parathyroid scintigraphy

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Loughborough University

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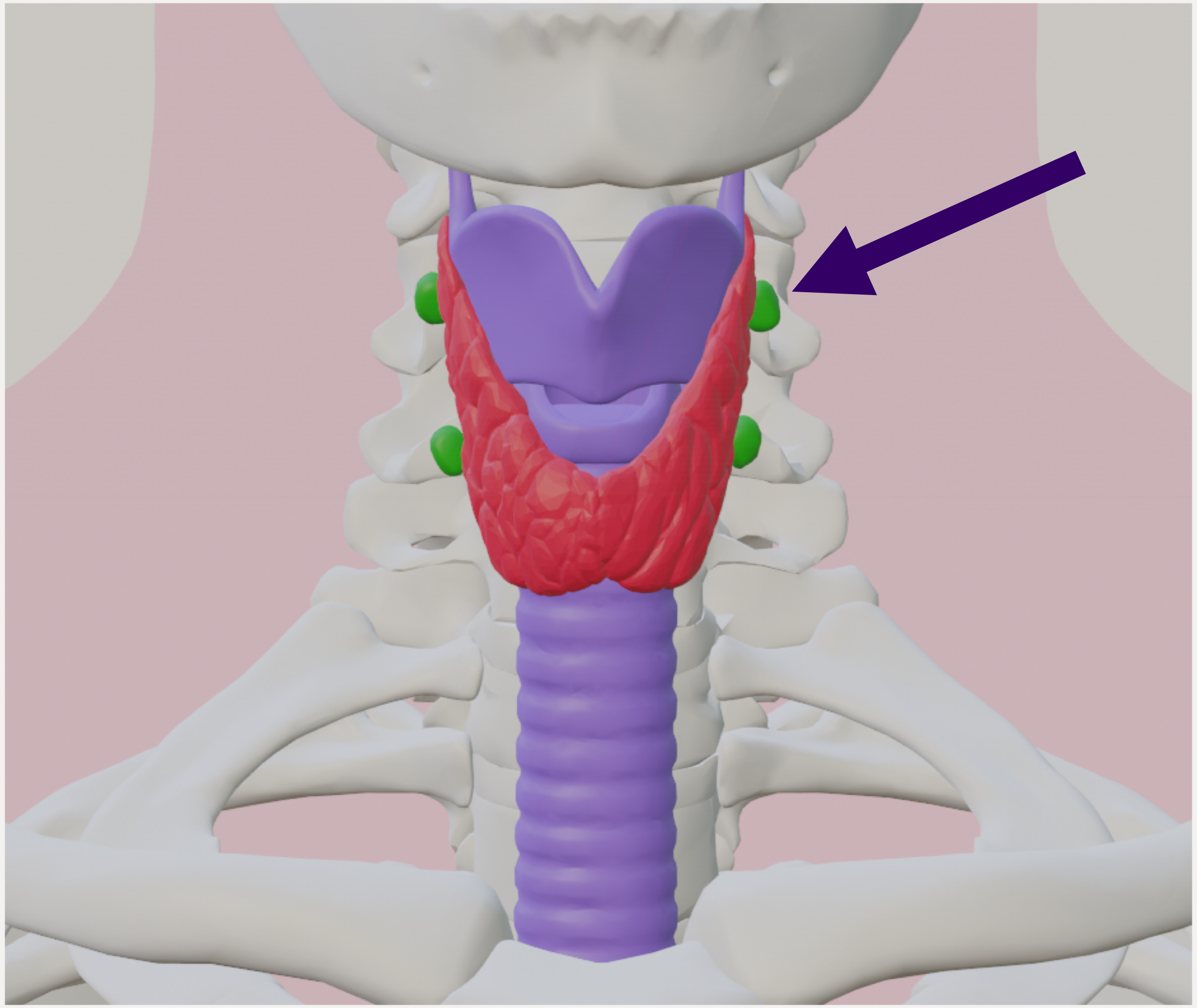
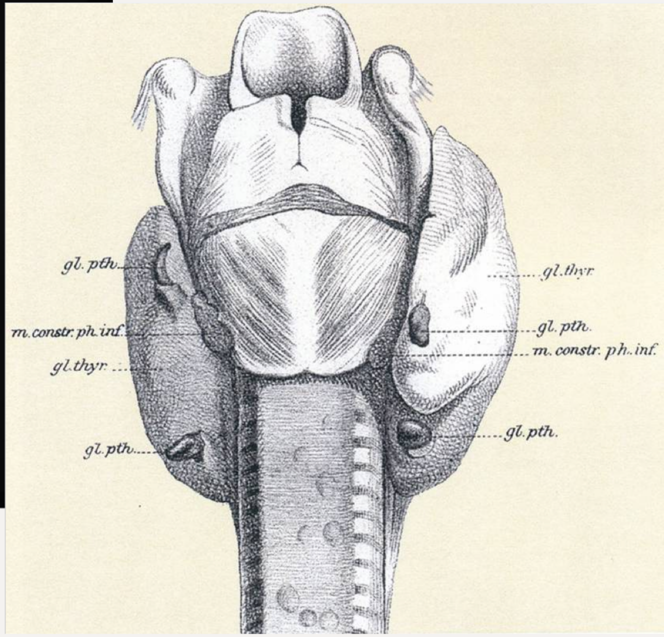
The Parathyroid Glands



- Four bean-shaped glands
- Behind thyroid
- 20 - 45 µg
- <7 mm long-axis diameter
- Highly variable gland number and location
- Control Ca metabolism by parathyroid hormone secretion (PTH)

(1) Walker, Marcella D., and Shonni J. Silverberg. "Primary hyperparathyroidism." *Nature Reviews Endocrinology* 14.2 (2018): 115-125.

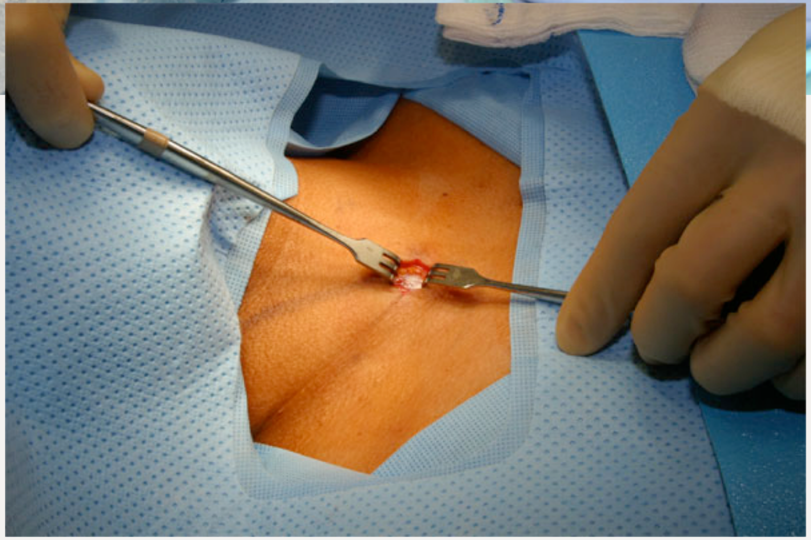
Parathyroid Dysfunction



- Diagnosed by blood test – PTH level
- Hypoparathyroidism
  - PTH supplementation
- Hyperparathyroidism
  - Skeletal, renal, cardiovascular and neuropsychological impact
  - 0.84% incidence for primary hyperparathyroidism in UK
  - 85%+ Single parathyroid adenoma
  - Parathyroidectomy only treatment

2) Zheng, Feibi, et al. "Skeletal effects of failed parathyroidectomy." *Surgery* 163.1 (2018): 17-21.
3) Soto-Pedre, Enrique, Paul J. Newey, and Graham P. Leese. "Stable incidence and increasing prevalence of primary hyperparathyroidism in a population-based study in Scotland." *The Journal of Clinical Endocrinology & Metabolism* (2023): dgad201.

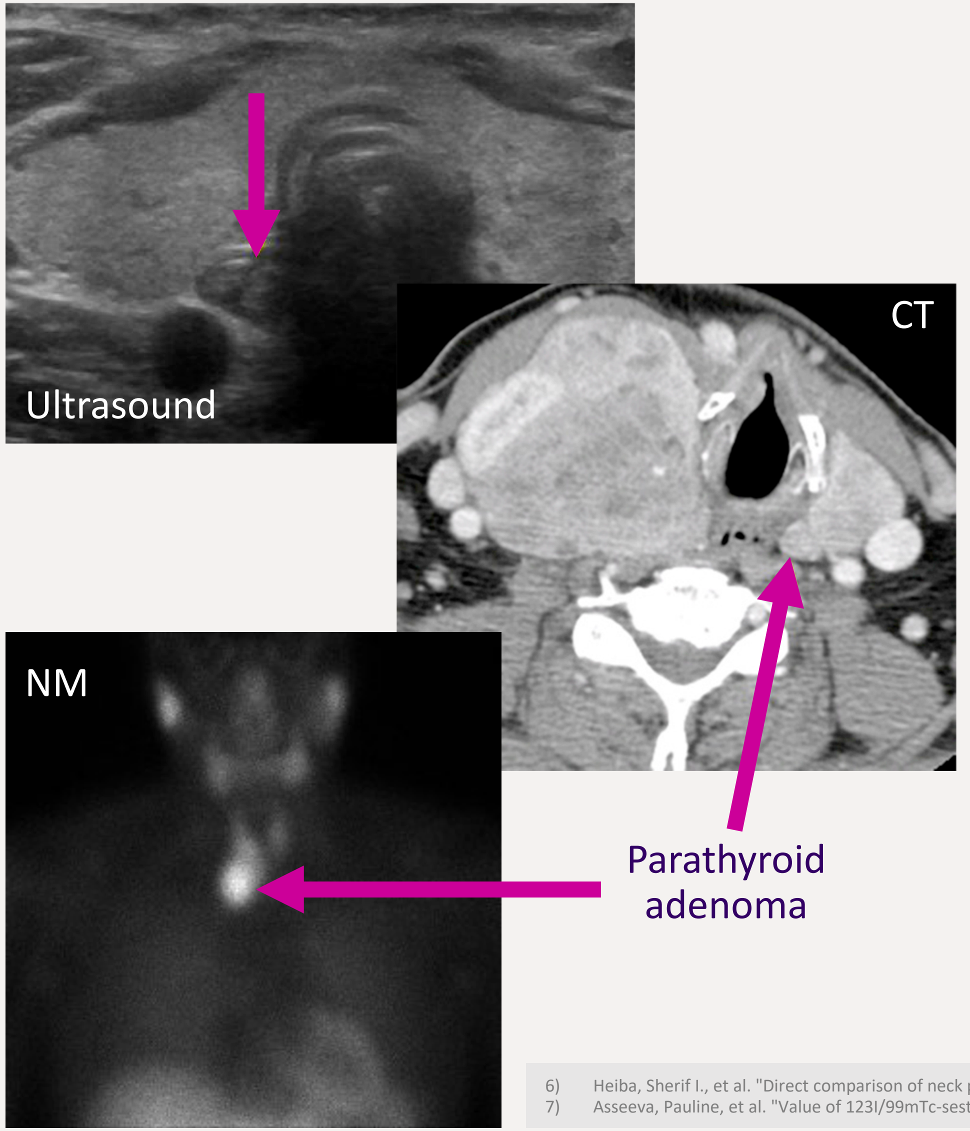
Parathyroidectomy

- Challenging – highly dependant on operator skill
- Minimally invasive parathyroidectomy
  - Requires known gland location
  - Lowest failure rate (4% vs 5-7%)
  - Best patient outcomes
  - Failure to find requires neck dissection
- Repeated surgeries must be avoided
  - Higher complication rate
  - Poor patient outcomes

4) Bagul, A., et al. "Primary hyperparathyroidism: an analysis of failure of parathyroidectomy." World journal of surgery 38 (2014): 534-541.
5) Lim, Ming Sheng, et al. "The utility of the radionuclide probe in parathyroidectomy for primary hyperparathyroidism." The Annals of The Royal College of Surgeons of England 99.5 (2017): 369-372.

Parathyroid Imaging



- Known gland location is key predictor of surgical success
- Nuclear medicine imaging is current gold standard
  - Dual-phase and dual-isotope protocols
  - Dual-isotope slightly superior
  - Sensitivities:

Ultrasound	Planar Dual-Isotope	SPECT Dual-Isotope
91.7%	88.9%	93.0%

  - Specificities:

Ultrasound	Planar Dual-Isotope	SPECT Dual-Isotope
38.9%	72.2%	66.7%

- Intraoperative interpretation complex

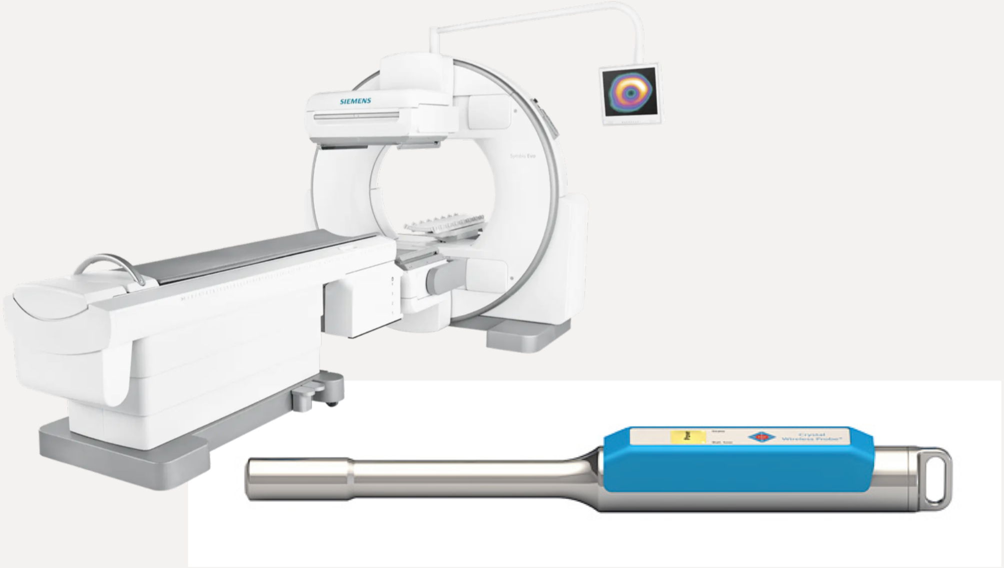
6) Heiba, Sherif I., et al. "Direct comparison of neck pinhole dual-tracer and dual-phase MIBI accuracies with and without SPECT/CT for parathyroid adenoma detection and localization." *Clinical nuclear medicine* 40.6 (2015): 476-482.
7) Asseeva, Pauline, et al. "Value of 123I/99mTc-sestamibi parathyroid scintigraphy with subtraction SPECT/CT in primary hyperparathyroidism for directing minimally invasive parathyroidectomy." *The American Journal of Surgery* 217.1 (2019): 108-113.

Intraoperative Parathyroid Localisation

- Intraoperative testing vital for adequate resection
- Current surgical practice recommends use of 1D gamma probes
  - Improve surgical success rate
  - Limited by lack of anatomical information
  - Confirmation, not localisation
- Single-isotope Intraoperative scintigraphy currently not currently recommended
  - No significant impact on surgical success
  - Poor agreement between interpreters

8) Schneider, David F., et al. "Predictors of recurrence in primary hyperparathyroidism: an analysis of 1,386 cases." Annals of surgery 259.3 (2014): 563.
9) Lim, Ming Sheng, et al. "The utility of the radionuclide probe in parathyroidectomy for primary hyperparathyroidism." The Annals of The Royal College of Surgeons of England 99.5 (2017): 369-372.
10) Creighton, Erin Weatherford, et al. "Utility of intraoperative digital scintigraphy in radioguided parathyroidectomy." Head & Neck 43.10 (2021): 2967-2972.

Intraoperative Imaging Issues



- High sensitivity (87%)
- High Specificity (95%)
- Improve success rates (+5.4%)

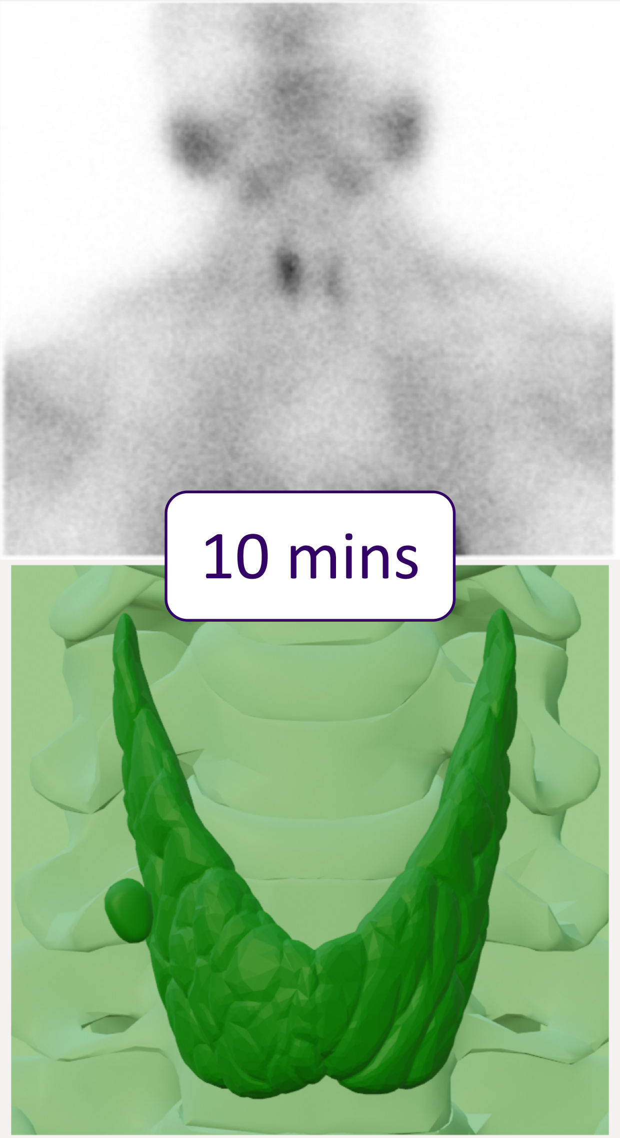
- Poor sensitivity (51%)
- Poor Specificity (50%)
- Does not improve success rates
- Provides anatomical information

All measure same physiological information!

10) Creighton, Erin Weatherford, et al. "Utility of intraoperative digital scintigraphy in radioguided parathyroidectomy." Head & Neck 43.10 (2021): 2967-2972.

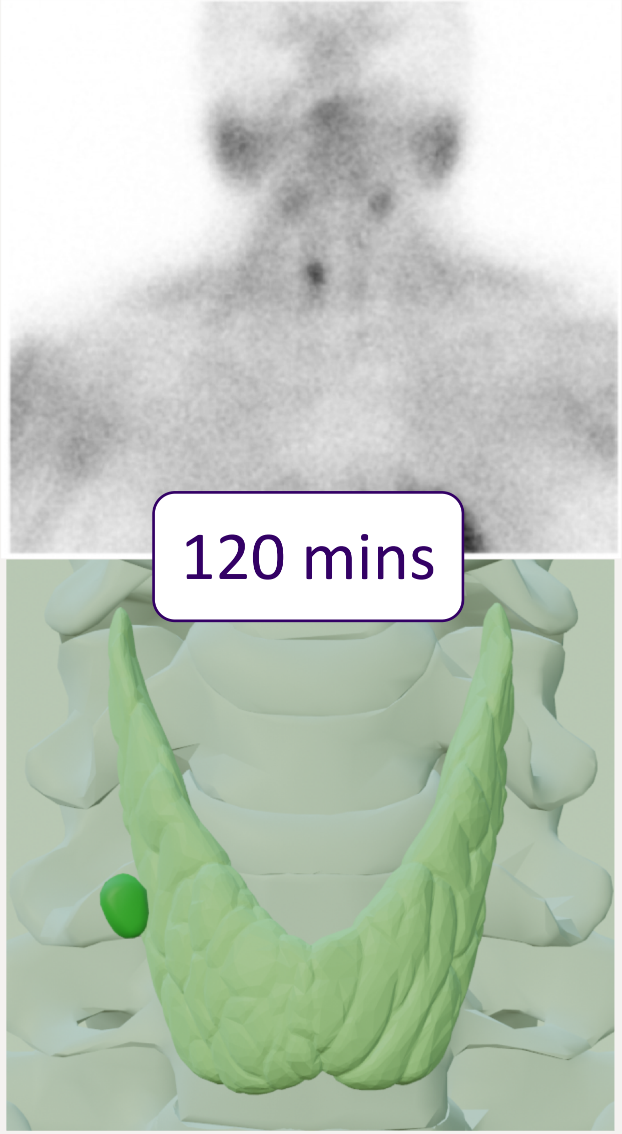
11) García-Talavera, Paloma, et al. "Efficacy of in-vivo counting in parathyroid radioguided surgery and usefulness of its association with scintigraphy and intraoperative PTHi." Nuclear Medicine Communications 32.9 (2011): 847-852.

Dual Phase ^{99m}Tc-Sestamibi Scintigraphy



Single-isotope technique

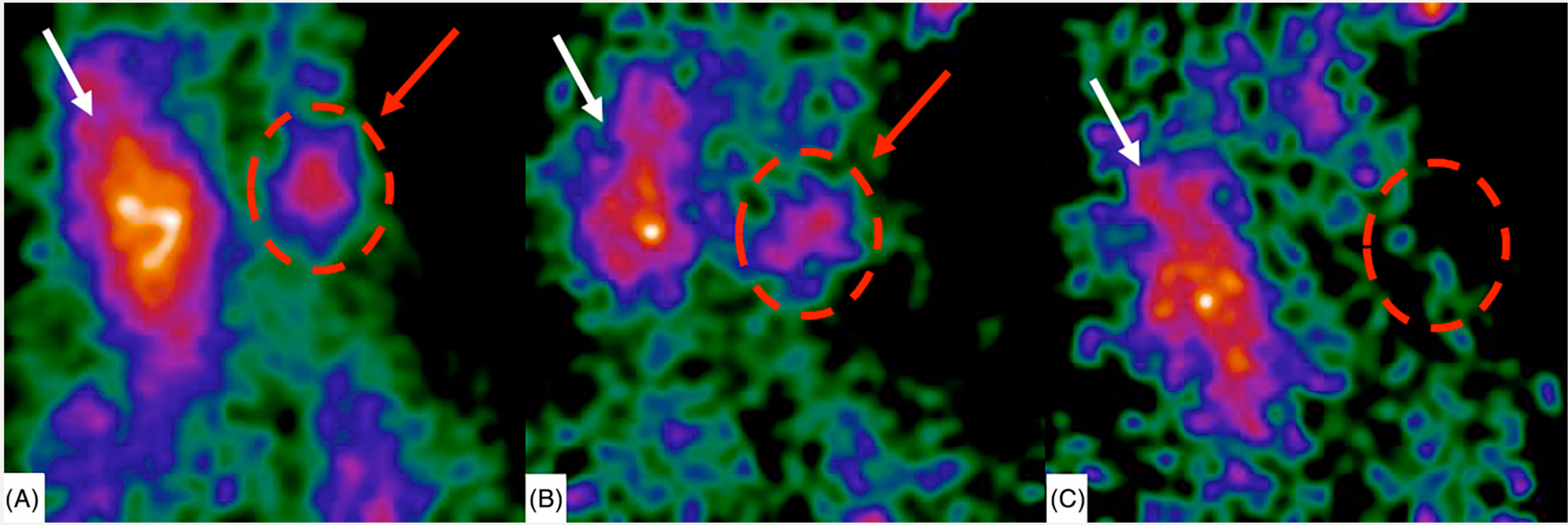
140 keV Photopeak images



12) Carral, F., et al. "Factors associated with negative 99mTc-MIBI scanning in patients with primary hyperparathyroidism." Revista Española de Medicina Nuclear e Imagen Molecular (English Edition) 40.4 (2021): 222-228.

Intraoperative ^{99m}Tc-Sestamibi Scintigraphy

- Single imaging time-point



Pre-incision

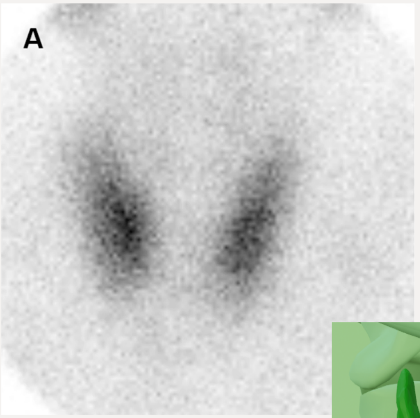
Open surgical field

Post-resection

140 keV Photopeak images

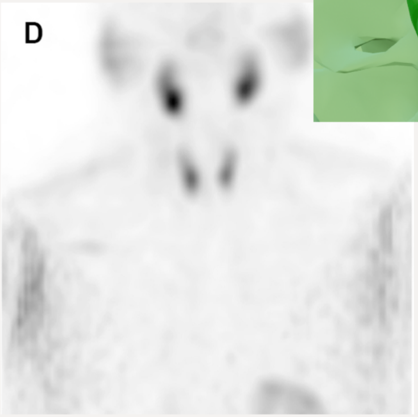
10) Creighton, Erin Weatherford, et al. "Utility of intraoperative digital scintigraphy in radioguided parathyroidectomy." Head & Neck 43.10 (2021): 2967-2972.

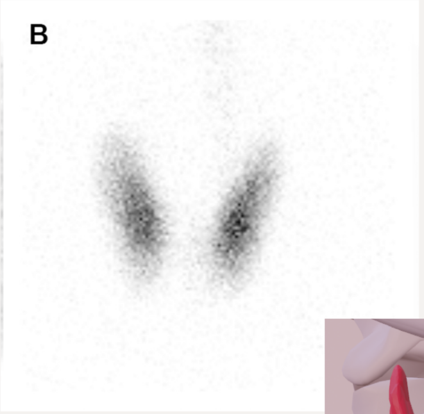
Dual-Isotope ^{99m}Tc-Sestamibi/^{123}I Scintigraphy



^{99m}Tc

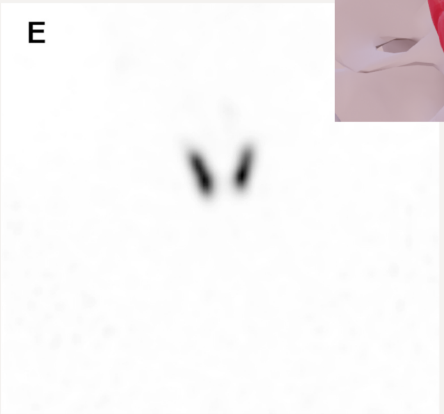
(140 keV)

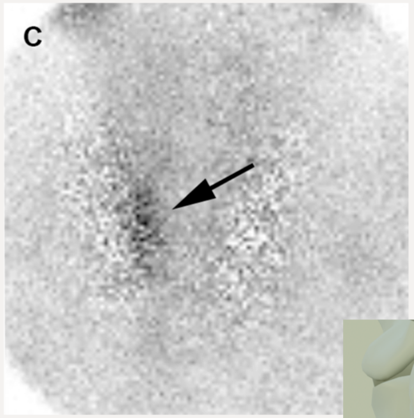




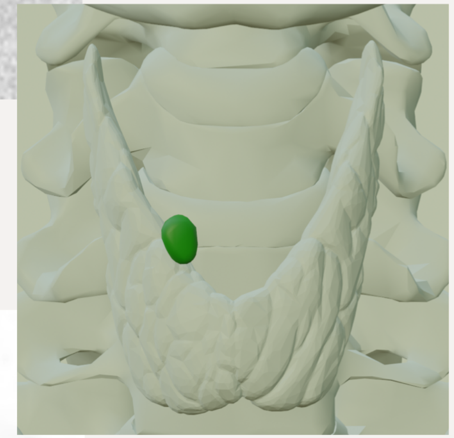
^{123}I

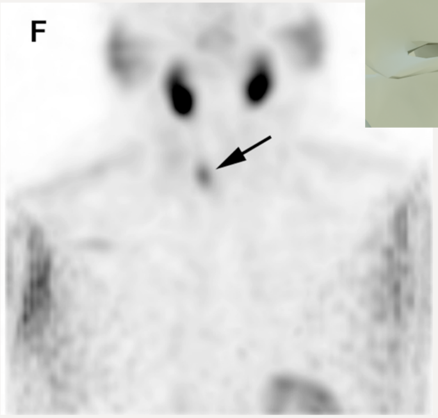
(159 keV)





^{99m}Tc - ^{123}I





7) Asseeva, Pauline, et al. "Value of 123I/99mTc-sestamibi parathyroid scintigraphy with subtraction SPECT/CT in primary hyperparathyroidism for directing minimally invasive parathyroidectomy." *The American Journal of Surgery* 217.1 (2019): 108-113.

Intraoperative Dual-Isotope Scintigraphy

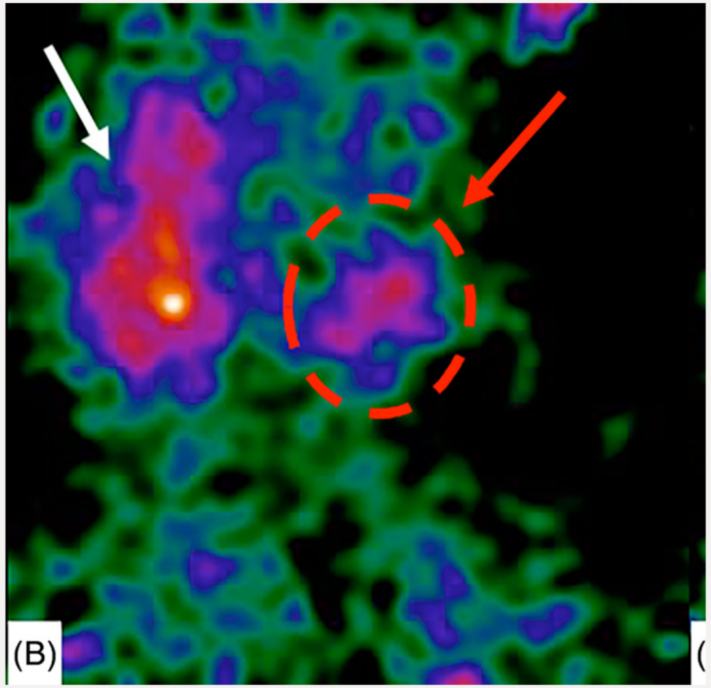
Benefits

- Overcomes single-time point limitation
- Removes background
- More physiological information
- Potential sensitivity and specificity improvement

Problems

- Still dependant on image quality

!!!



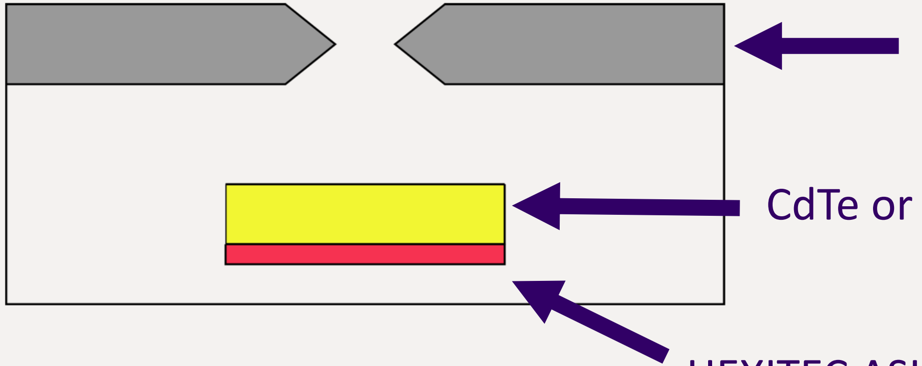
140keV Single time-point image

Application-specific dual-isotope camera

- CdTe/CdZnTe – HEXITEC system meets application requirements
  - Per-pixel spectroscopic
  - <1.2 keV (159 keV) energy resolution
  - 0 – 200 keV range
  - 80 x 80, 250 µm pixels
  - Room temperature operation
  - Small footprint (22 x 6 x 6 cm)

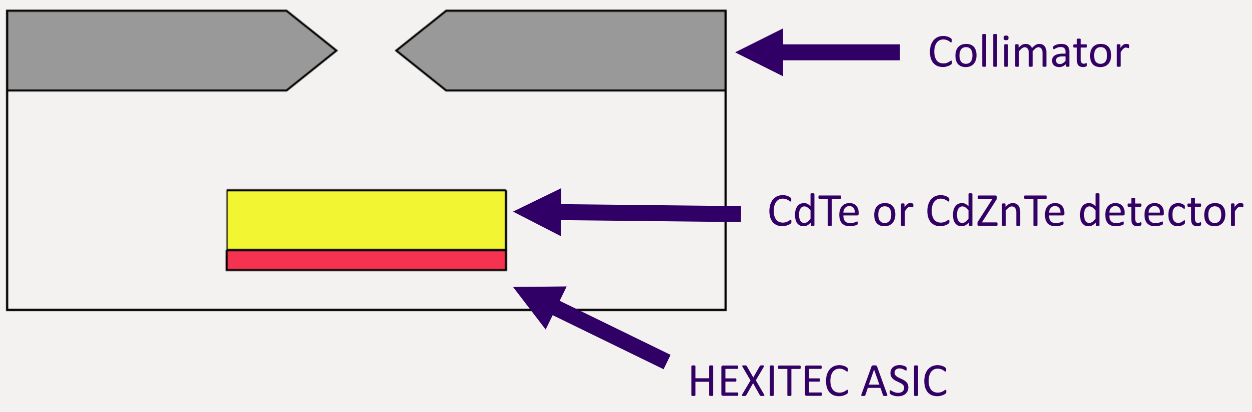
HEXITEC: A High-Energy X-ray Spectroscopic Imaging Detector for Synchrotron Applications

M. C. Veale,[1] P. Seller,[1] M. Wilson,[1] and E. Liotti[2]
[1]*UKRI Science & Technology Facilities Council, Rutherford Appleton Laboratory, Didcot, Oxon, UK;* [2]*Department of Materials, University of Oxford, Oxford, UK*



14) Scuffham, J. W., et al. "A CdTe detector for hyperspectral SPECT imaging." *Journal of Instrumentation* 7.08 (2012): P08027.

Unclear Medicine



- Small activities (kBq)
- Limited imaging times (10 mins)
- Tiny imaging objects (1 mm)

Choice between:

- ⌀1 mm Pinhole collimator
  - Geometric resolution: 6.7 mm
  - Geometric efficiency: $3.4 \cdot 10^{-5}$
- ⌀3 mm Pinhole collimator
  - Geometric resolution: 18.7 mm
  - Geometric efficiency: $2.5 \cdot 10^{-4}$

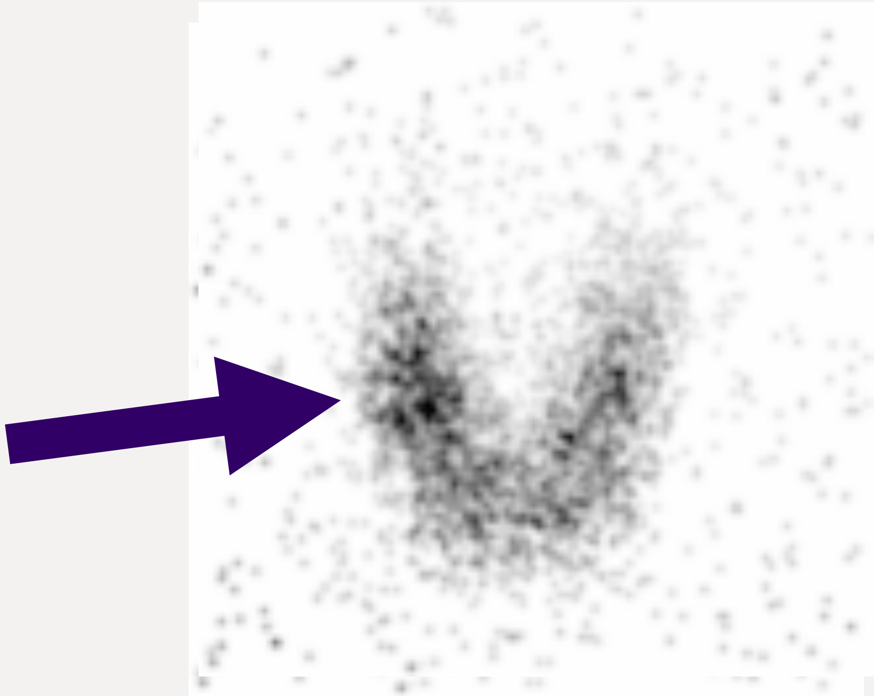
15) Accorsi, Roberto, and Scott D. Metzler. "Analytic determination of the resolution-equivalent effective diameter of a pinhole collimator." *IEEE transactions on medical imaging* 23.6 (2004): 750-763.
16) Metzler, Scott D., et al. "Analytic determination of pinhole collimator sensitivity with penetration." *IEEE transactions on medical imaging* 20.8 (2001): 730-741.

Unclear Medicine - 140 keV experimental images

FOV:

~85 mm^2

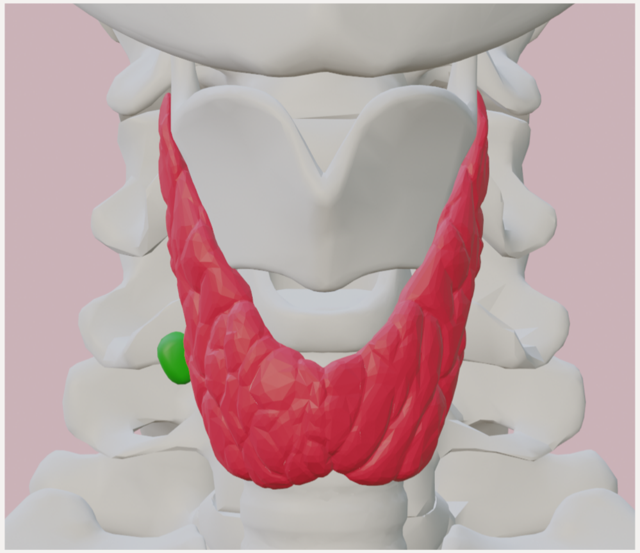
- Image counts: 507
- ⌀1 mm Pinhole collimator
  - Geometric resolution: 6.7 mm
  - Geometric efficiency: $3.4 \cdot 10^{-5}$

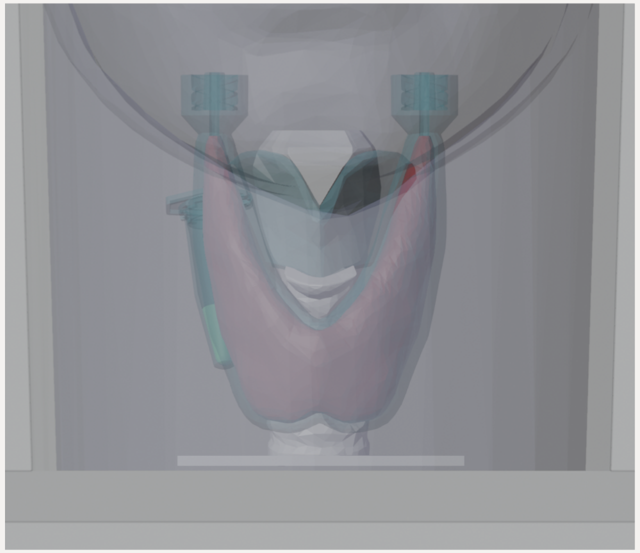


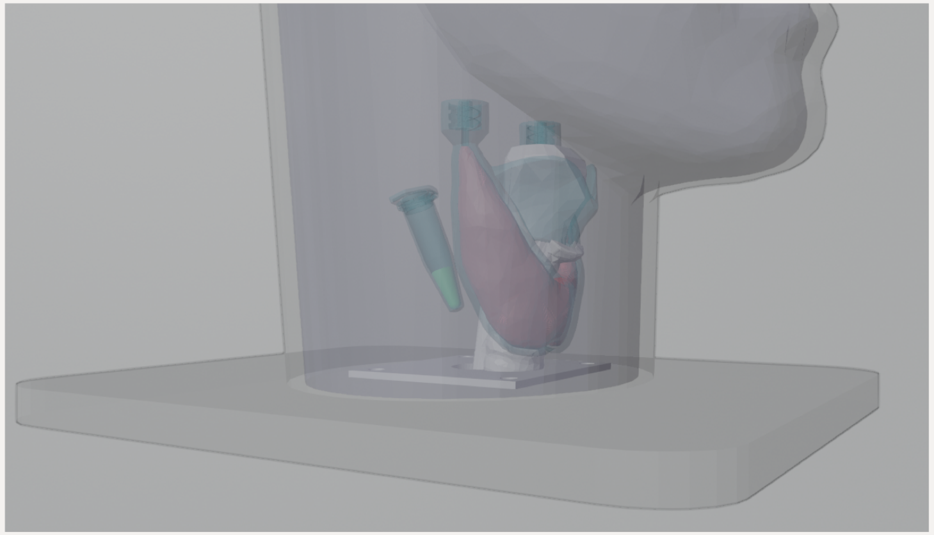
- Image counts: 3973
- ⌀3 mm Pinhole collimator
  - Geometric resolution: 18.7 mm
  - Geometric efficiency: $2.5 \cdot 10^{-4}$

15) Accorsi, Roberto, and Scott D. Metzler. "Analytic determination of the resolution-equivalent effective diameter of a pinhole collimator." *IEEE transactions on medical imaging* 23.6 (2004): 750-763.
16) Metzler, Scott D., et al. "Analytic determination of pinhole collimator sensitivity with penetration." *IEEE transactions on medical imaging* 20.8 (2001): 730-741.

Clinical-like Phantoms







17) Mitsuhashi, Nobutaka, et al. "BodyParts3D: 3D structure database for anatomical concepts." Nucleic acids research 37.suppl_1 (2009): D782-D785.

Predicting qualitative performance

Simulate expected imaging scenario:

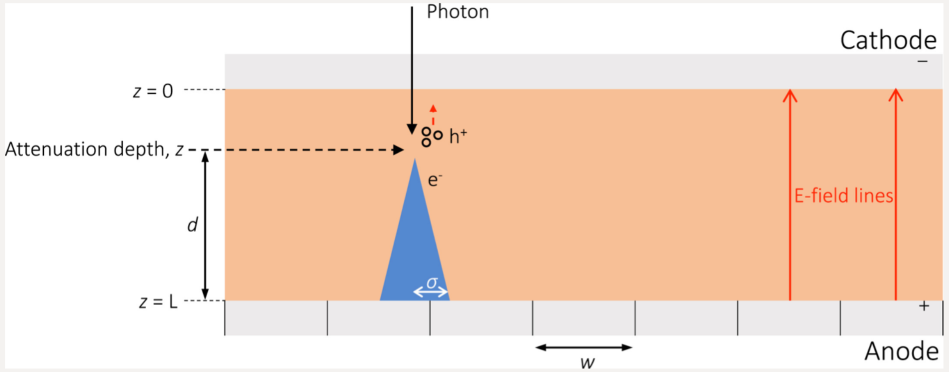
- GATE photon transport
  - Geant4-based
  - Anatomical-like geometry
  - Clinical-like activities
- HEXITEC Monte Carlo model
  - Charge carrier diffusion across pixelated anodes
  - Spectroscopic output including charge sharing

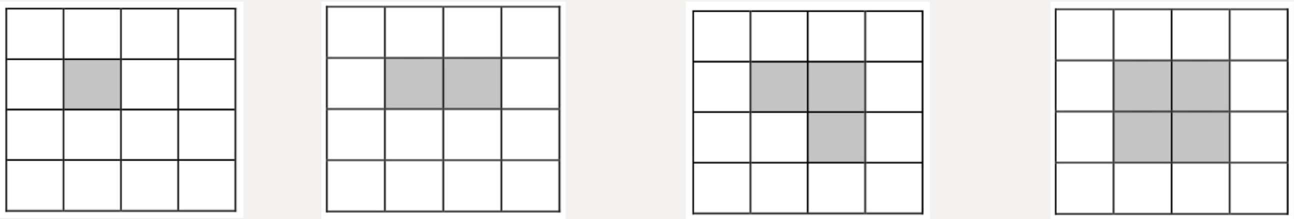
Produce clinical-like images for prospective system geometries

A spectroscopic Monte-Carlo model to simulate the response of pixelated CdTe based detectors

K.A.L. Koch-Mehrin [a,*], J.E. Lees [a], S.L. Bugby [a,b]

[a] Space Research Centre, Department of Physics & Astronomy, University of Leicester, LE1 7RH, UK
[b] Centre for Sensing and Imaging Science, Department of Physics, Loughborough University, LE11 3TU, UK





19) Sarrut, David, et al. "Advanced Monte Carlo simulations of emission tomography imaging systems with GATE." Physics in Medicine & Biology 66.10 (2021): 10TR03.

Predicting qualitative performance

Simulate exp

- GATE ph
  - Gear
  - Anat
  - Clini
- HEXITEC
  - Char pixel
  - Spec char

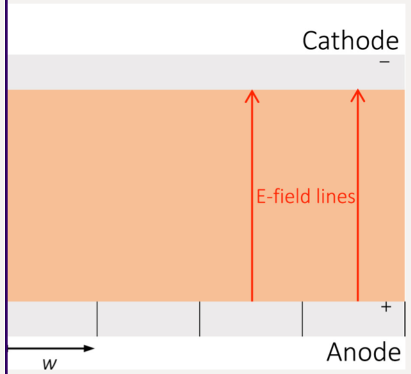
Produce c prospective

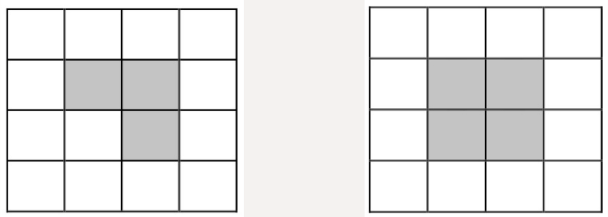
Review

Intraoperative Gamma Cameras: A Review of Development in the Last Decade and Future Outlook

Andrew L. Farnworth * and Sarah L. Bugby *

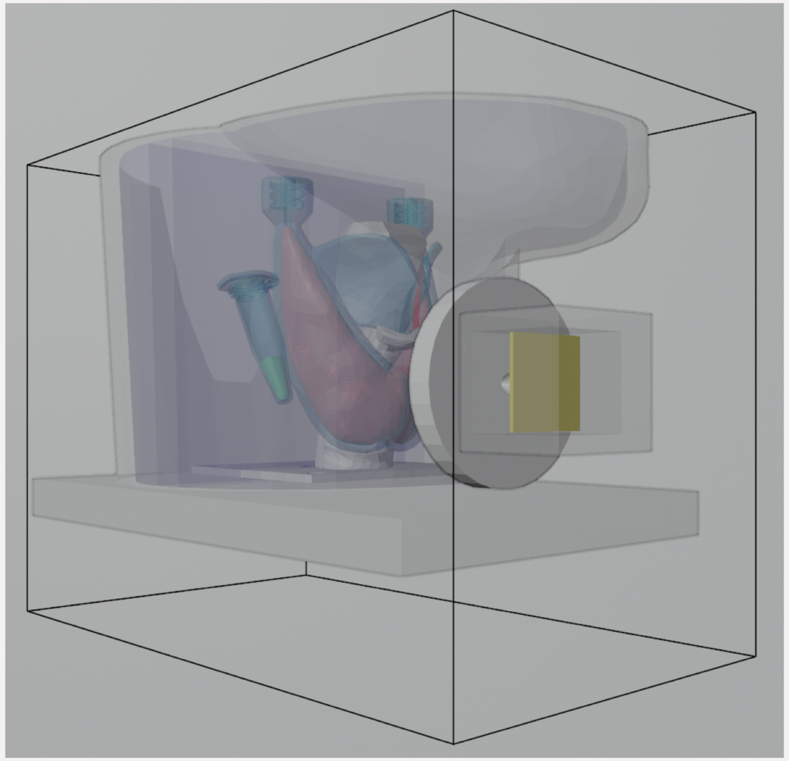
New design approach for area!





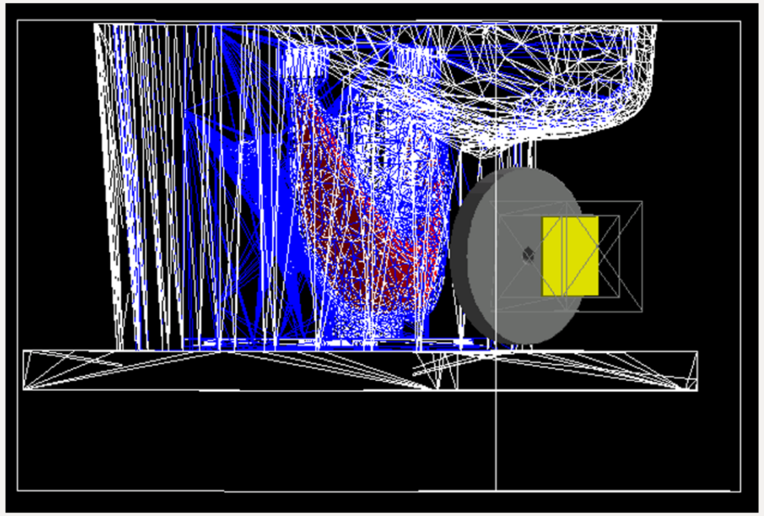
19) Sarrut, David, et al. "Advanced Monte Carlo simulations of emission tomography imaging systems with GATE." Physics in Medicine & Biology 66.10 (2021): 10TR03.

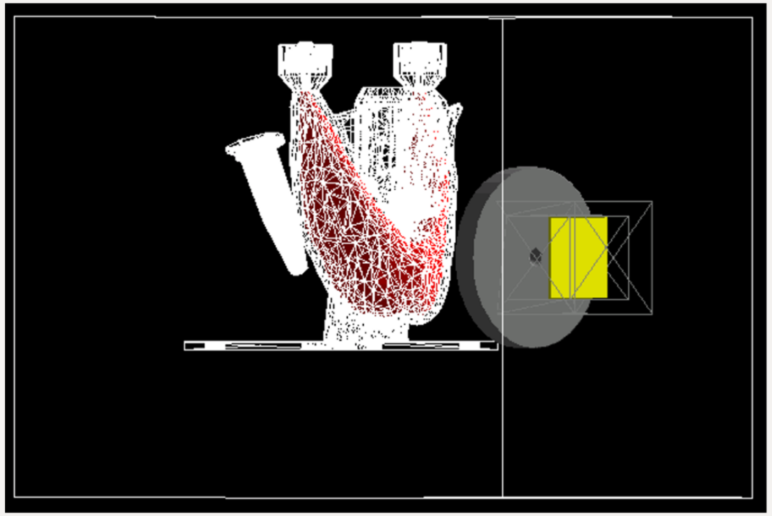
Clinical-like Phantoms



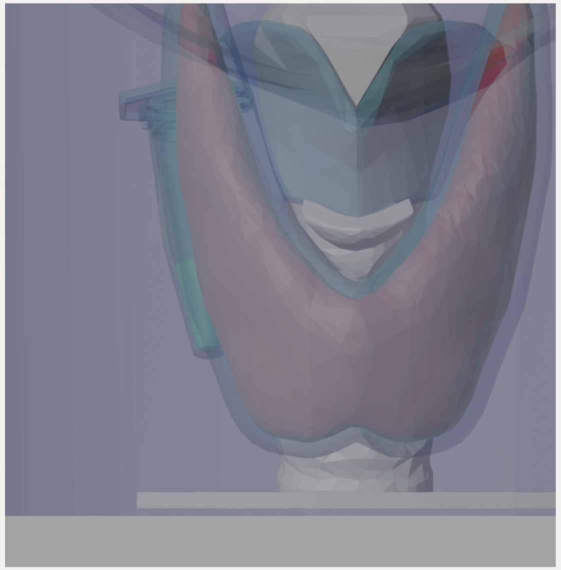
Simulation scenario:

- ⌀1 mm Pinhole collimator
- 1 x 20 x 20 CdTe crystal





Expected image

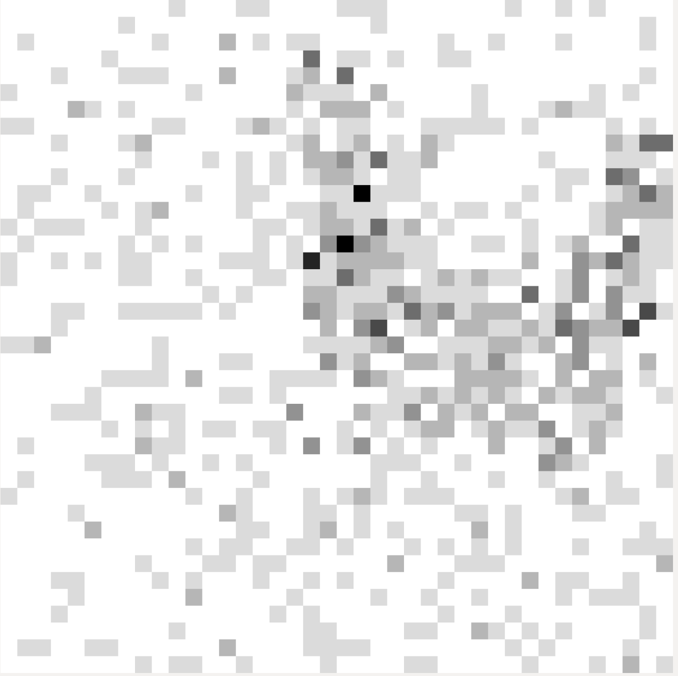


FOV:

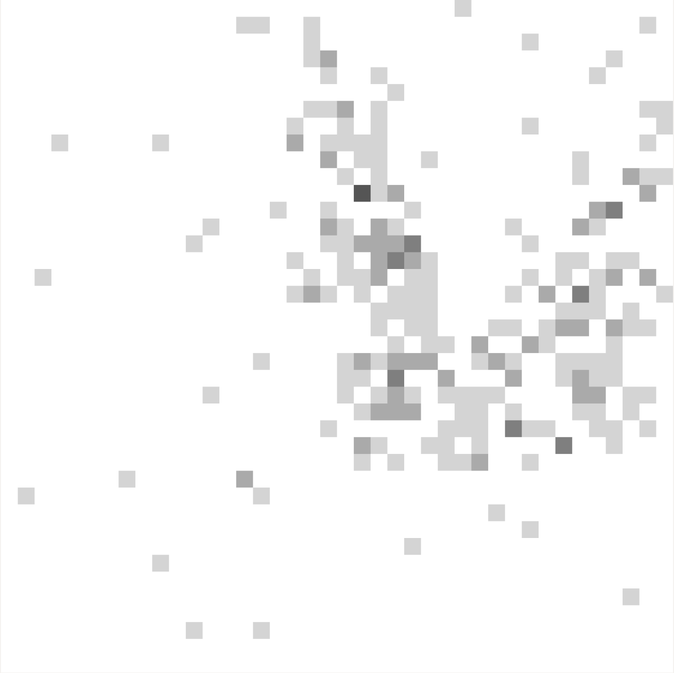
~50 mm^2

Simulation Output

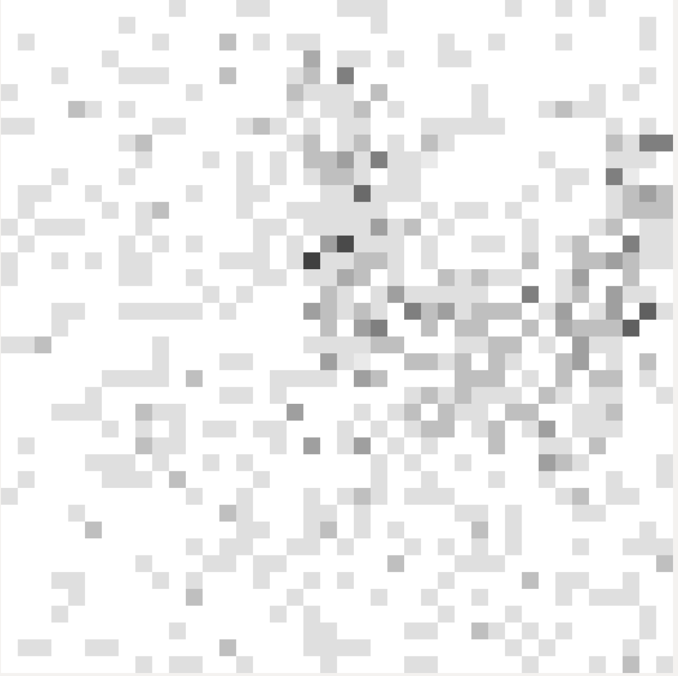
^{99m}Tc (140 keV)



^{123}I (159 keV)



^{99m}Tc - ^{123}I



- 500 mg parathyroid adenoma - 22.8 kBq ^{99m}Tc uptake
- 10 minute duration
- Single-pixel events only

FOV:

~50 mm^2

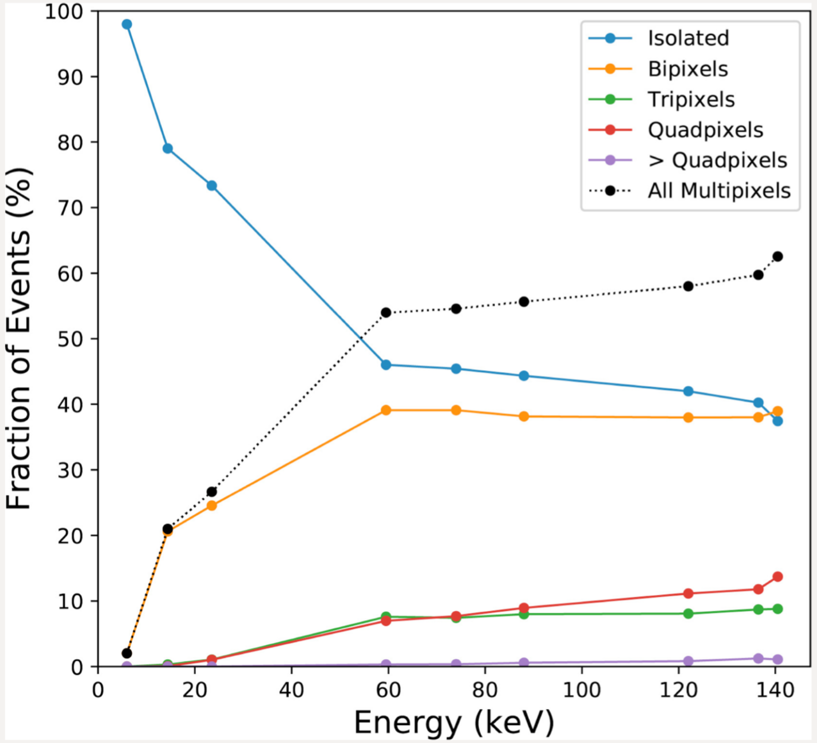
Simulation Output

^{99m}Tc (140 keV)

Energy-loss correction in charge sharing events for improved performance of pixellated compound semiconductors

S.L. Bugby [a,*], K.A. Koch-Mehrin [a], M.C. Veale [b], M.D. Wilson [b], J.E. Lees [a]

[a] Space Research Centre, Department of Physics & Astronomy, University of Leicester, LE1 7RH, UK
[b] STFC Rutherford Appleton Laboratory, Harwell Campus, Didcot, OX11 0QX, UK



^{99m}Tc - ^{123}I

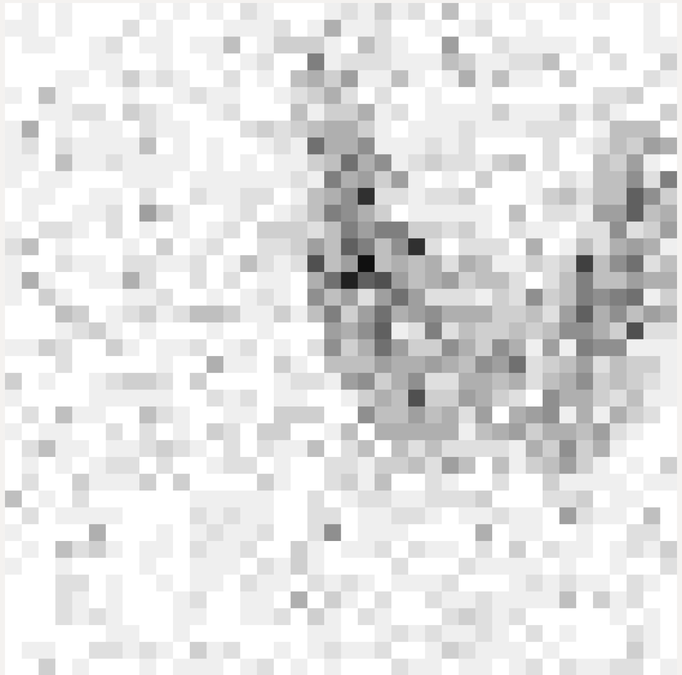
- 500 mg para
- 10 minute d
- Single-pixel events only

FOV:

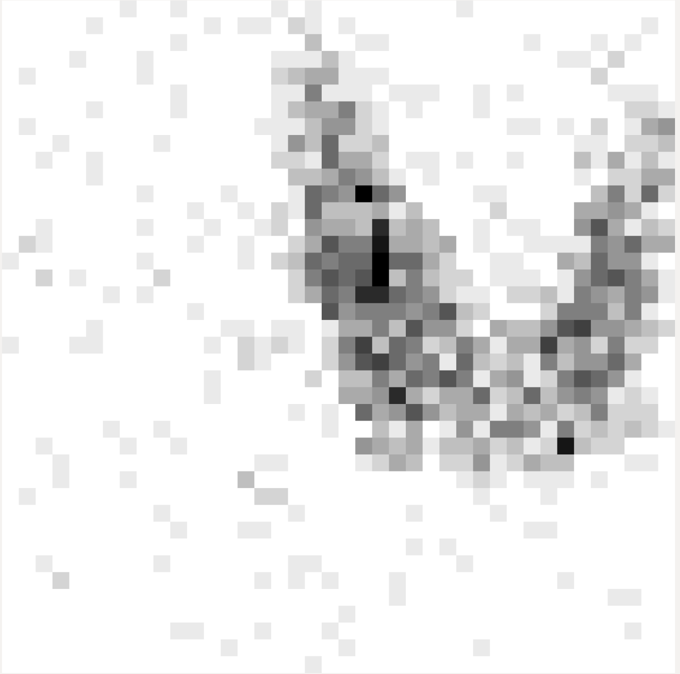
~50 mm^2

Simulation Output

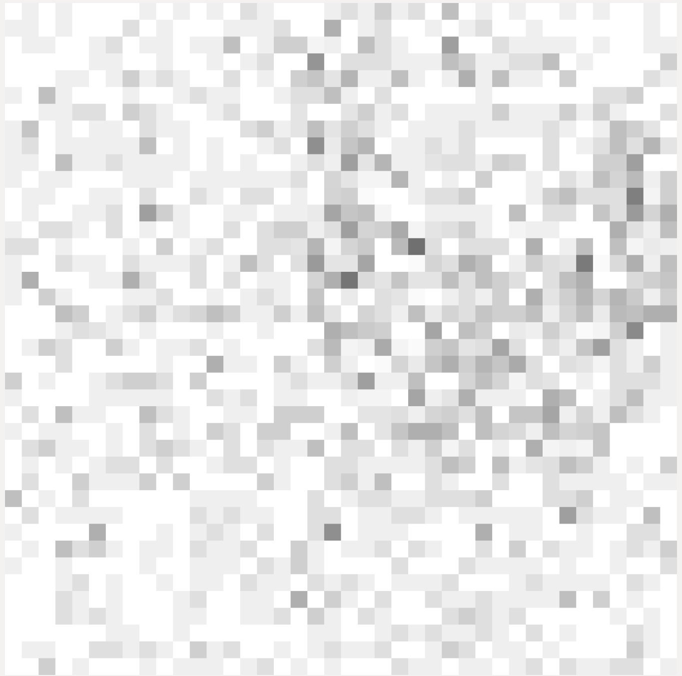
^{99m}Tc (140 keV)



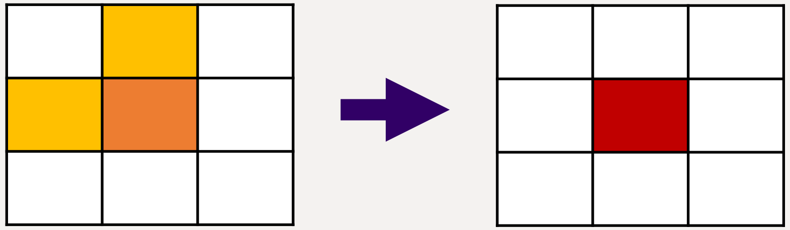
^{123}I (159 keV)



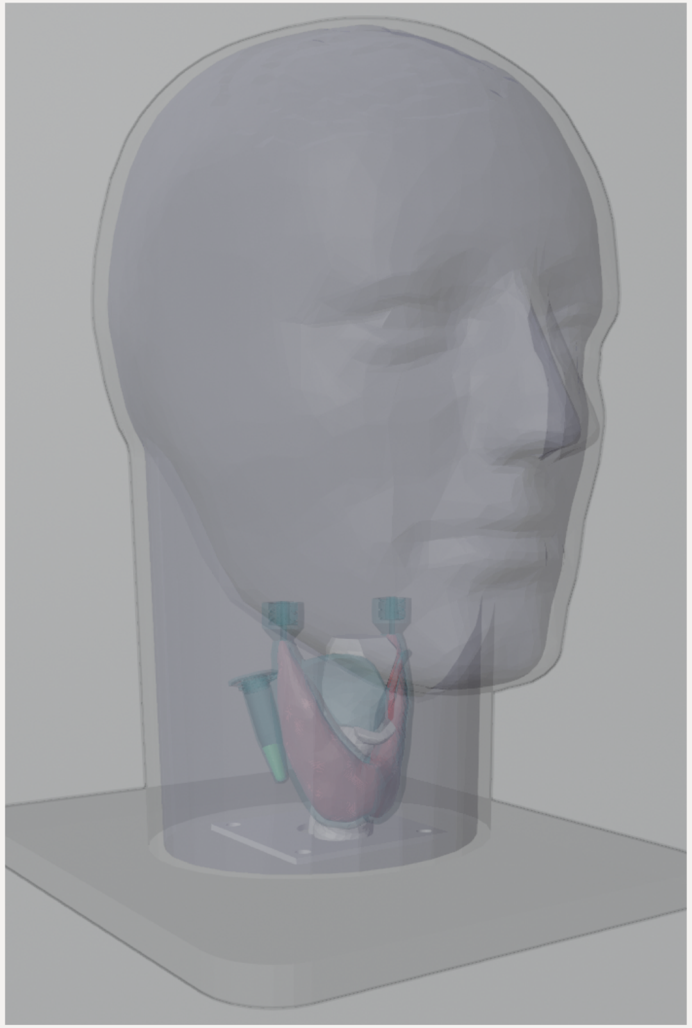
^{99m}Tc - ^{123}I



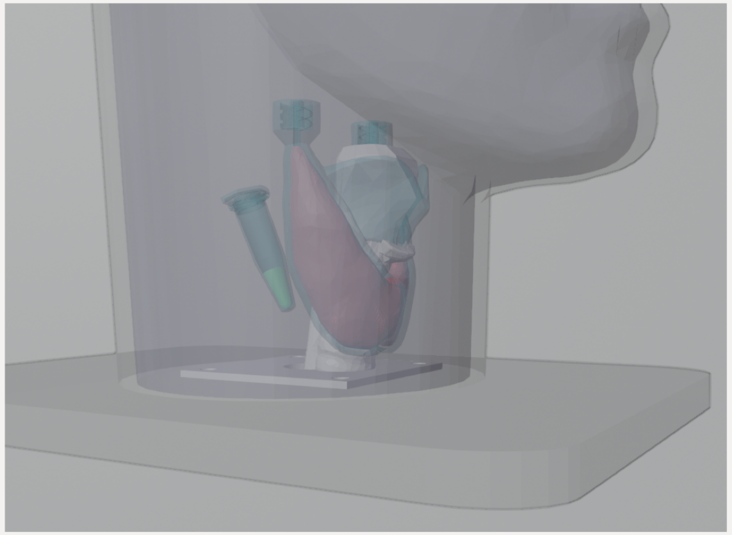
- 'Hottest-pixel' charge-sharing correction
- Sensitivity still insufficient!
  - Higher open fraction needed

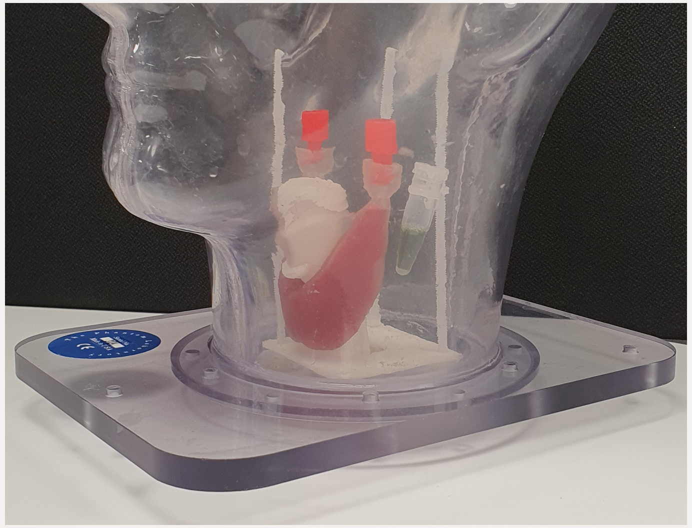


Future Work

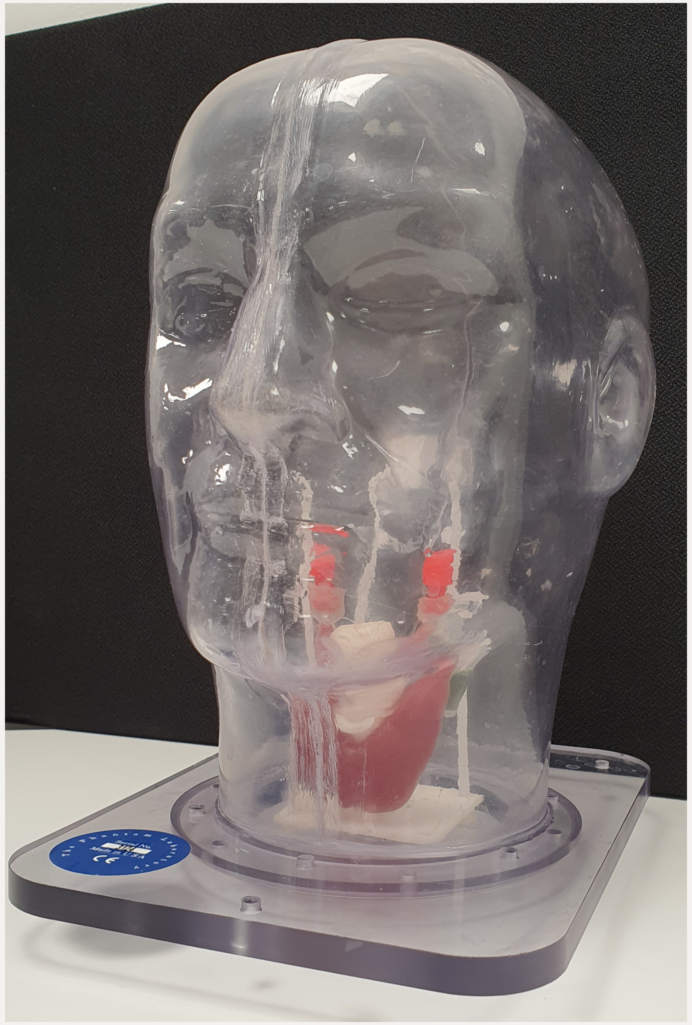


'Dennise'

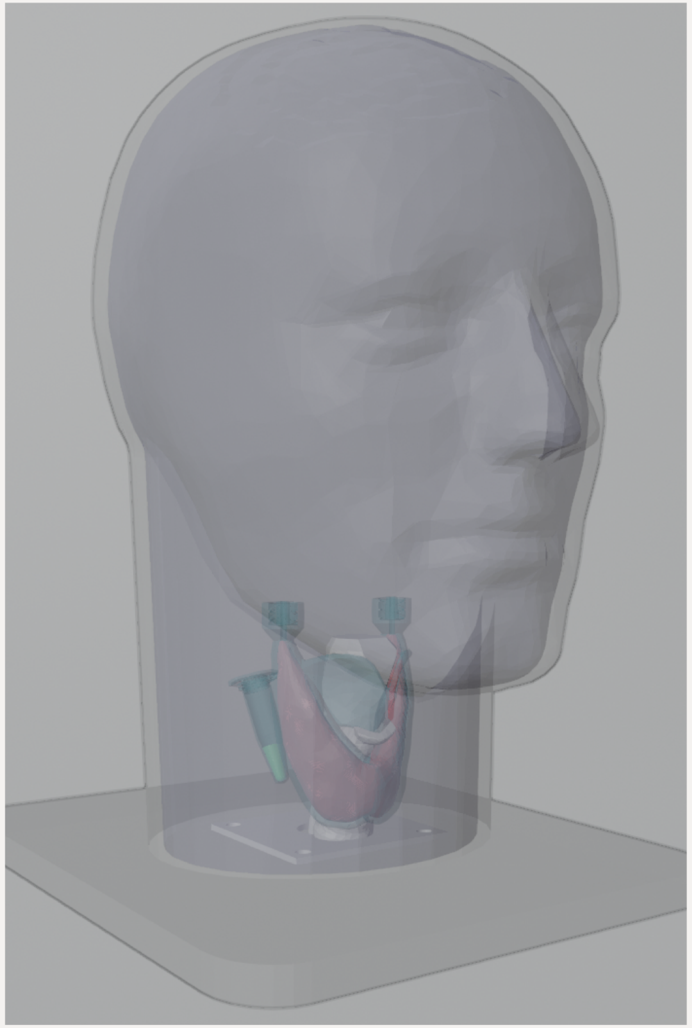




'Dennis'



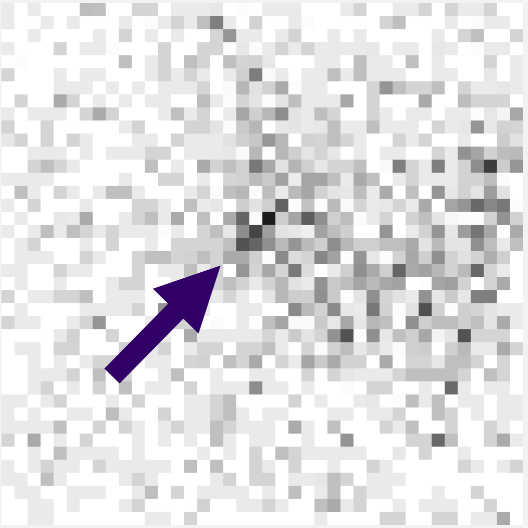
Future Work



Novel design pipeline with many uses!

- Optimise camera system design
- Optimise data analysis methods
    - Access to ground truth
- Optimise imaging protocols
- Investigate limitations of systems

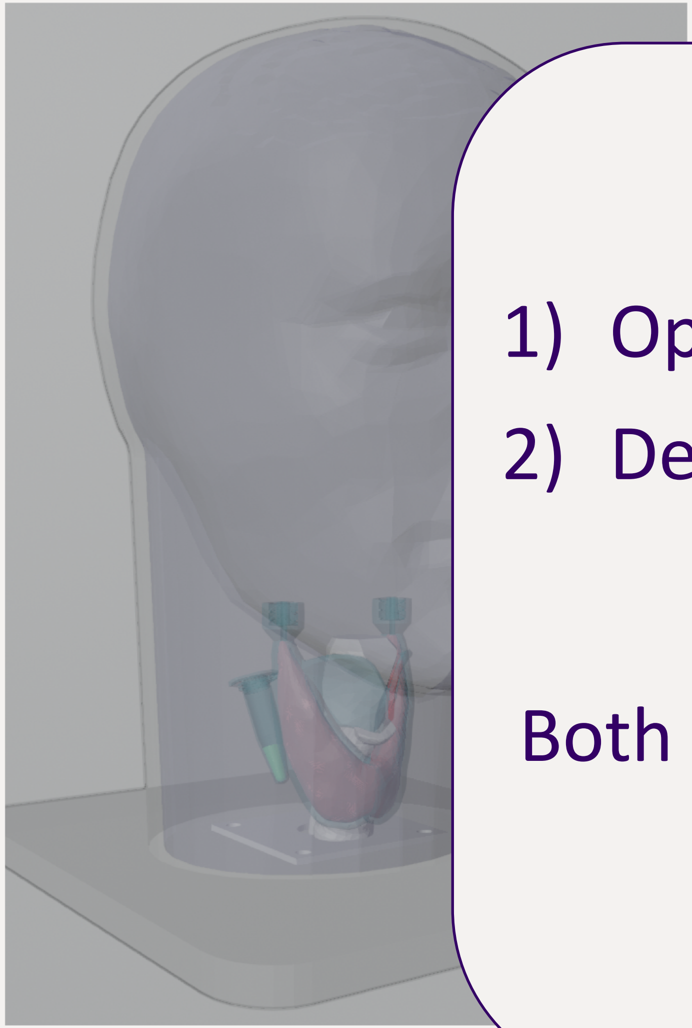
^{99m}Tc - ^{123}I



200 kBq Parathyroid

≈ 4 g

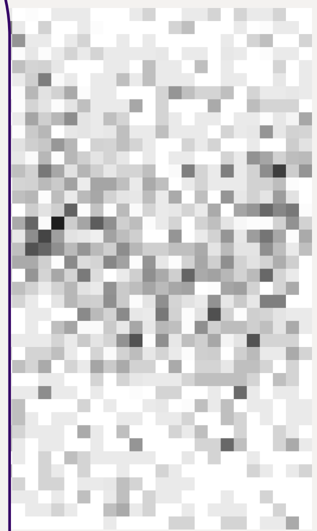
Future Work



1) Optimise image quality at system design stage
2) Define acceptable use-cases for system

Both have potential to improve patient outcomes

Tc - ^{123}I



Parathyroid

4 g