

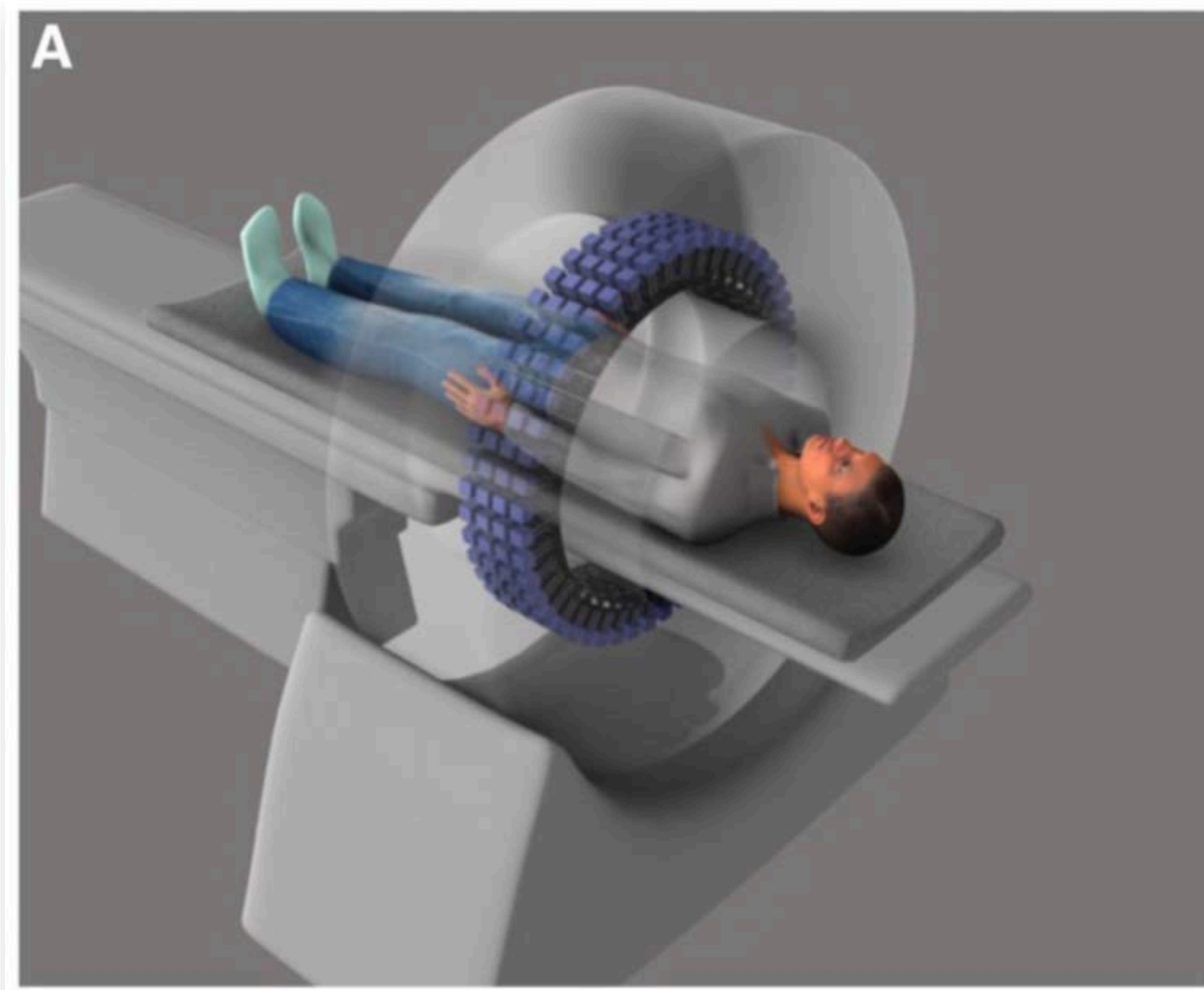
The Total-Body PET project

Belgian Nuclear Society / Christian Vanhove / 26/04/2018

Total Body PET Conference



Whole-Body PET versus Total-Body PET

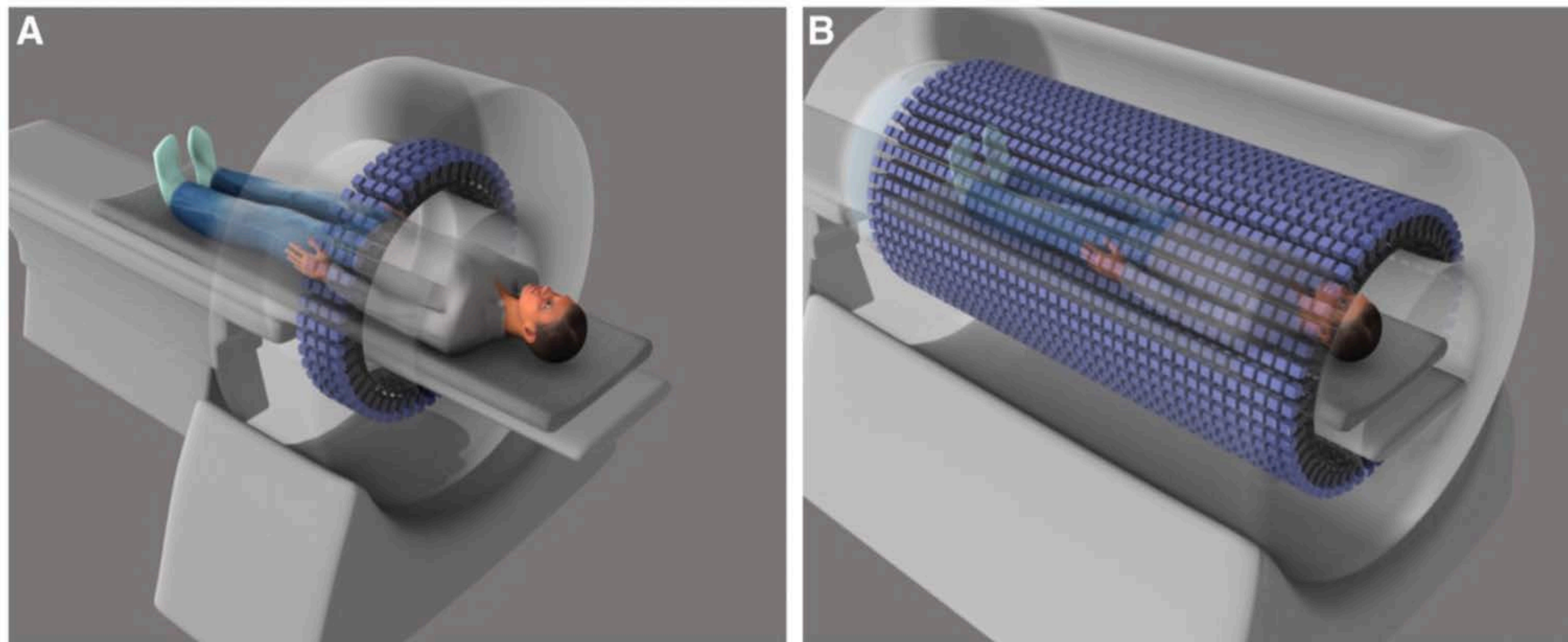


Point peak Sensitivity:
4-6%

Body imaging sensitivity (NECR):
7-21 cps/kBq

- Cherry SR et al. 2018. Total-Body PET: Maximizing Sensitivity to Create New Opportunities for Clinical Research and Patient Care. J Nucl Med 59:3–12.
- Cherry SR et al. 2017. Total-body imaging: Transforming the role of positron emission tomography. Sci Transl Med 9.

Whole-Body PET versus Total-Body PET



Point peak Sensitivity:
4-6%

X 3-5

Point peak Sensitivity:
12-24 %

Body imaging sensitivity (NECR):
7-21 cps/kBq

X 30-50

Body imaging sensitivity (NECR):
200-500 cps/kBq

- Cherry SR et al. 2018. Total-Body PET: Maximizing Sensitivity to Create New Opportunities for Clinical Research and Patient Care. J Nucl Med 59:3–12.
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Impact of Total-Body PET

$$\text{Image quality} \approx \text{SNR} \approx k\sqrt{S \times A \times T}$$



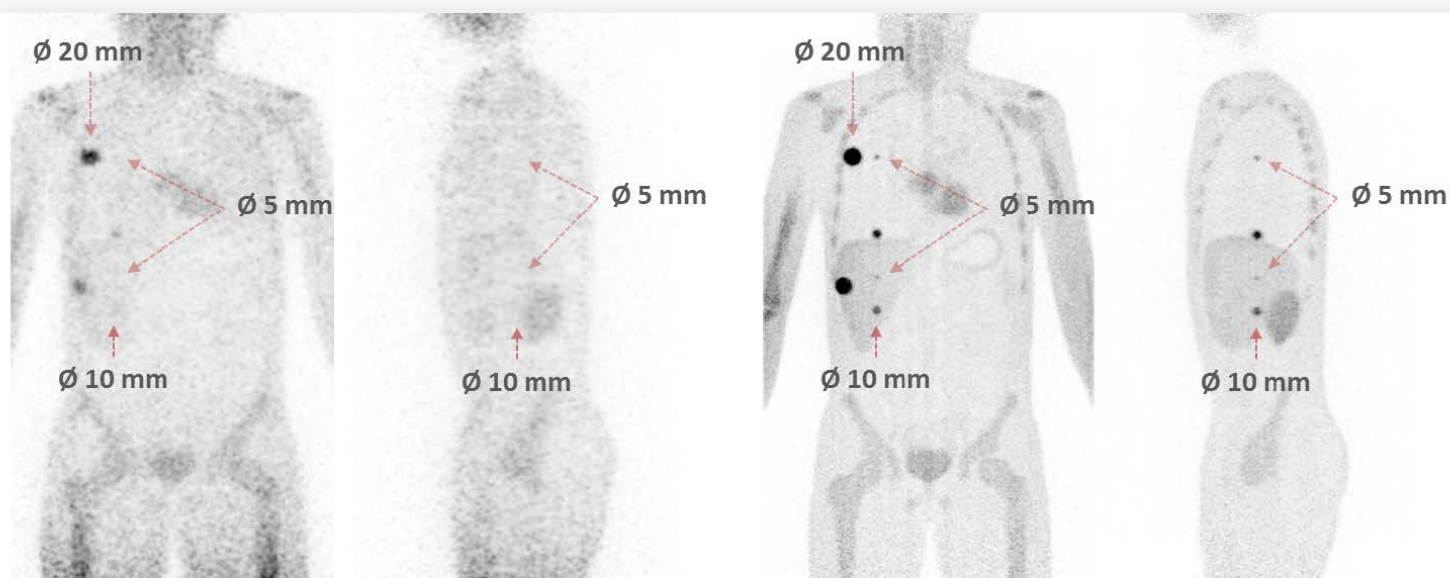
S = Sensitivity

A = Injected activity

T = Acquisition time

2m PET → 40x more sensitive → 6.3x more SNR

1. Sensitivity gain can be used to increase SNR (6.3x) using the same acquisition protocol (same A and T) to allow detection of 'lower-density' lesions, such as micro-metastases.



Equal low activity of 40 MBq & equal total acquisition time of 3 min

Courtesy of Stefaan Vandenberghe

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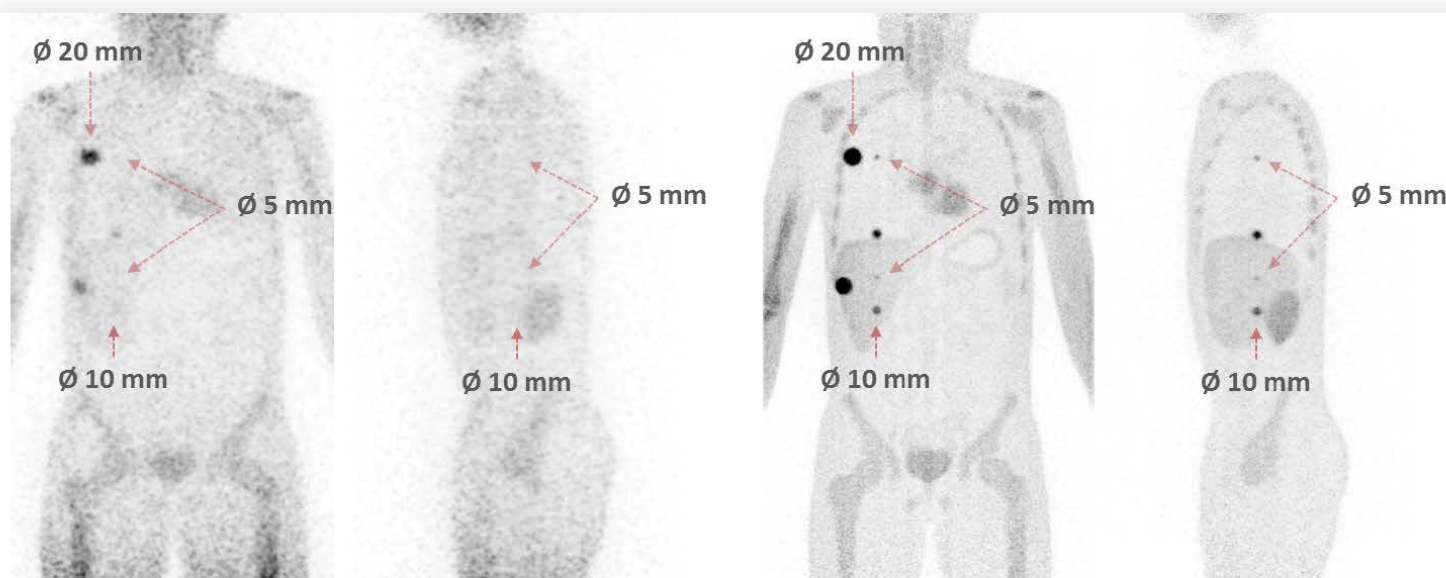
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2. Reduce acquisition times by a factor of 40 (**from 10-20min to 15-30s**), while keeping the current SNR. This might also further increase image quality due to less motion and possibility of breath-hold PET.



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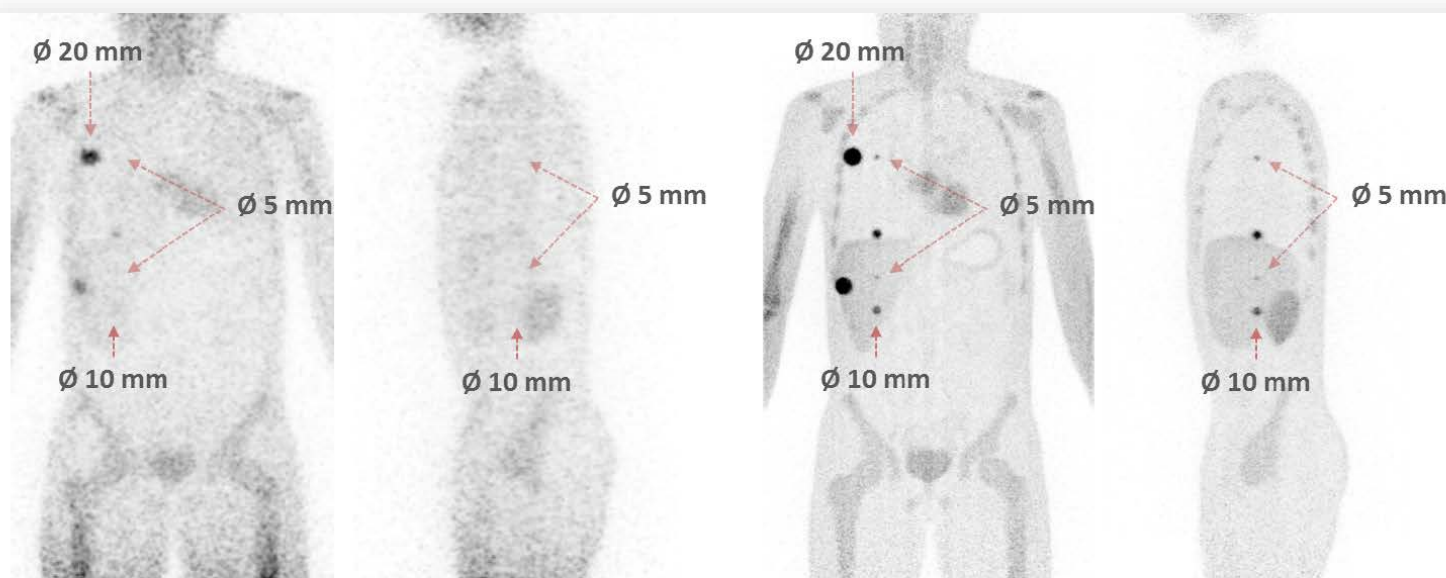
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3. Reduce dose by a factor of 40 (from 370MBq to 9.25MBq; **from 8mSv to 0.2mSv**), while keeping the current SNR. This would allow:
 1. Multiple injections for longitudinal follow-up of patients
 2. Expansion of PET to more sensitive population, such as children
 3. Screening tool



Equal low activity of 40 MBq & equal total acquisition time of 3 min

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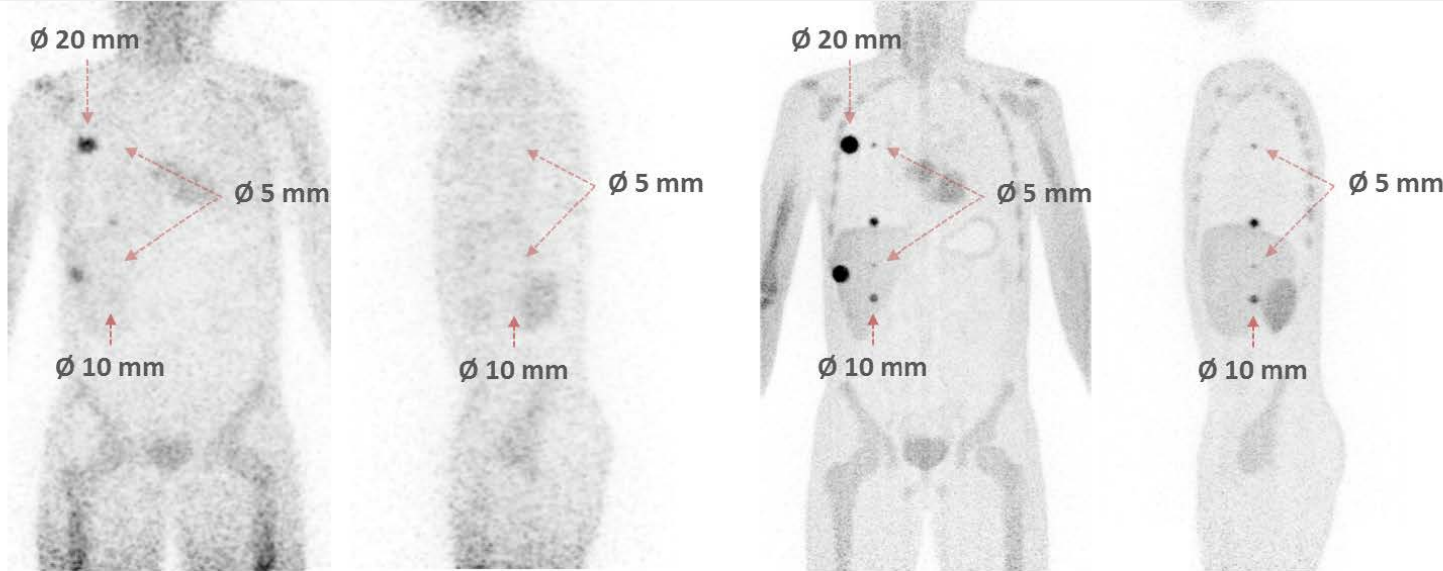
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4. Radiotracers can be followed for a longer time before the signal decays in pharmacokinetic / bio-distribution (PK/BD) studies (**5-6 additional half-lives** above the ± 3 half-lives on current systems).
 1. 18 hours for F-18
 2. 3 hours for C-11
 3. 30 days for Zr-89 (tracer clearance of larger molecules)



Equal low activity of 40 MBq & equal total acquisition time of 3 min

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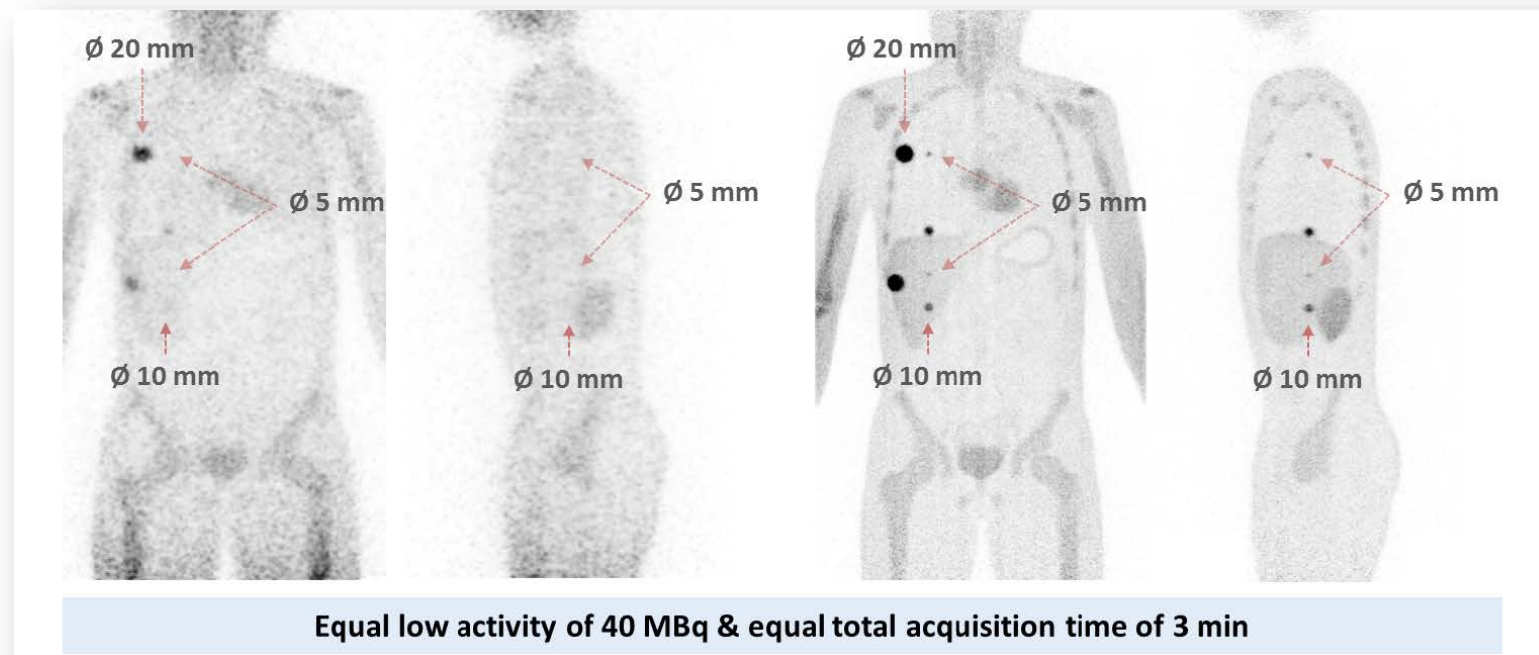
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5. Kinetic modeling
 1. Higher precision
 2. Shorter time frames
 3. Image derived input function
 4. Whole-body parametric imaging (inter-organ interactions)

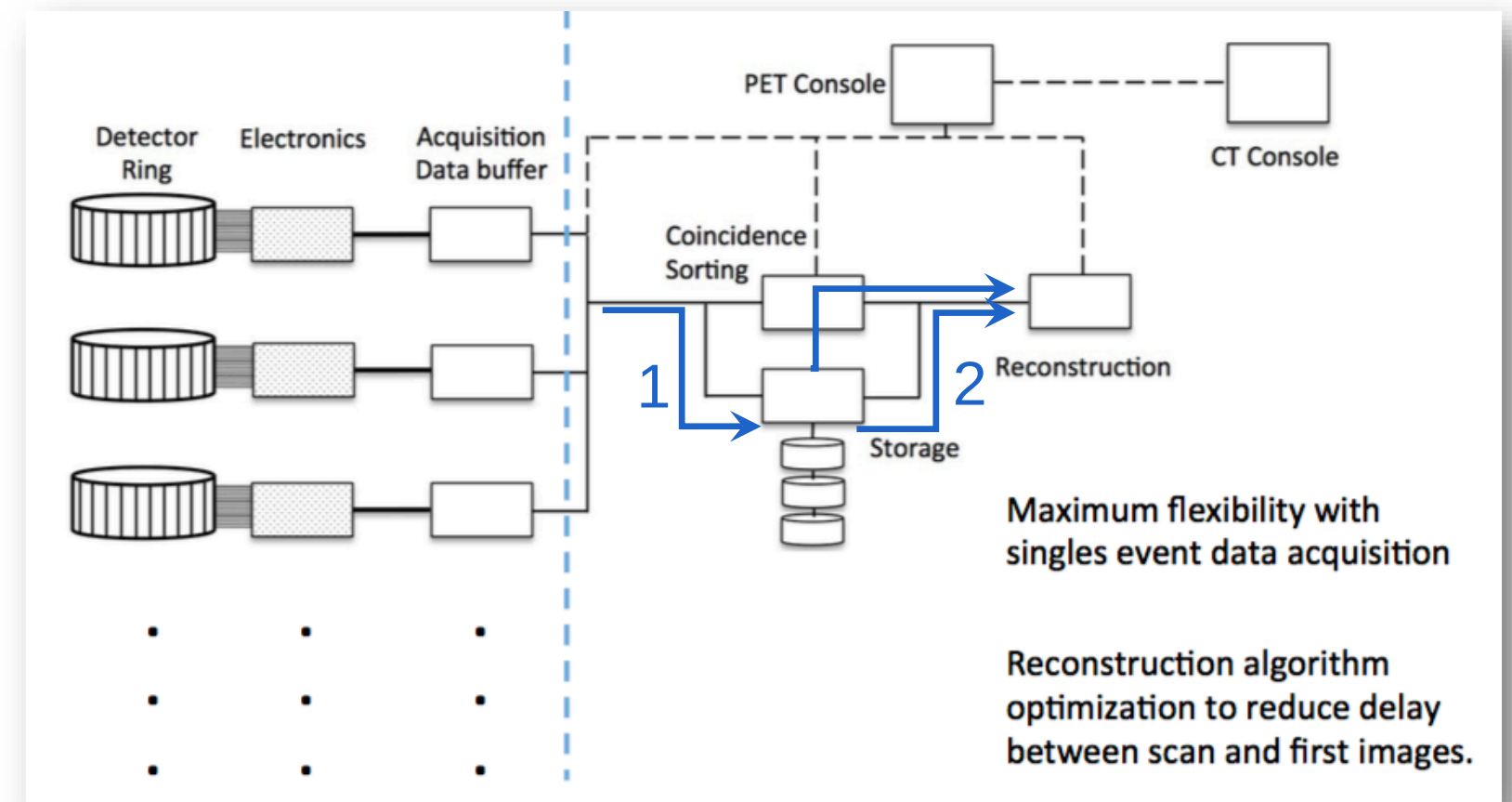


Courtesy of Stefaan Vandenberghe

Challenges of Total-Body PET

Engineering challenge

1. Rather engineering challenge than scientific challenge: expansion of existing systems
2. The rate at which single events are detected by each detector module is more or less the same as in current systems
3. Coincidence electronics → Extract coincidences in software using list-mode data
4. Large amount of data (3GB/s) to be collected
5. Image reconstruction likely to be the bottleneck. Ideally processing time should be in the order of the acquisition time.
6. Mechanical challenge
 1. Long cantilever of the patient bed
 2. Cooling
 3. Accessible for maintenance and replacements



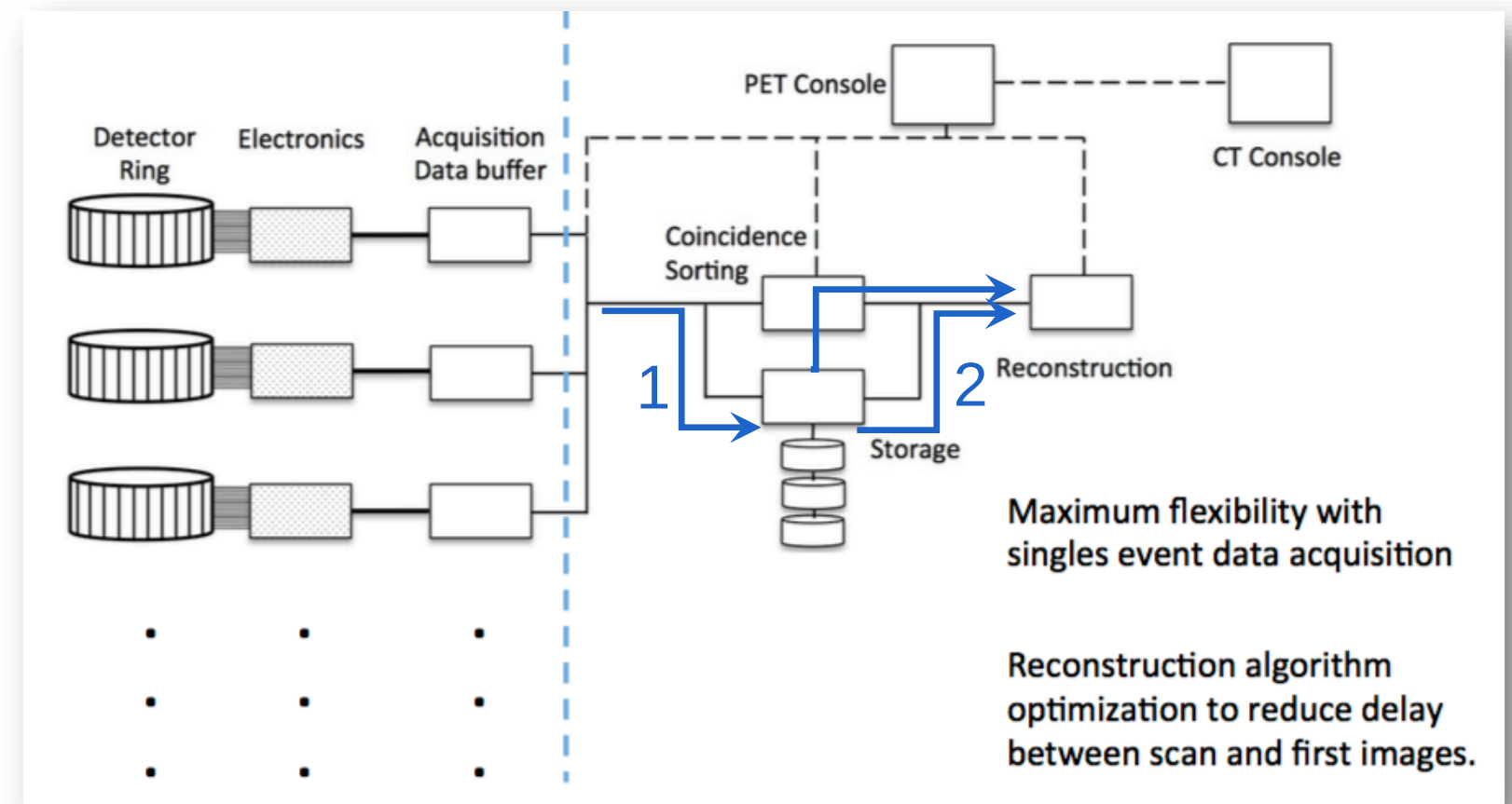
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Economic challenge

1. **We don't know the cost-to-benefit ratio. Time will tell.**
2. Cost current PET systems is $\pm \$2\text{M}$. Total-body PET system is not 10x more expensive. Estimated costs $\pm \$10\text{M}$.
3. More or less same price of 7T MRI. Currently, 50 installations world-wide.
4. One total-body PET can be the workhorse for multiple PET systems.
5. More patient doses per synthesis of radiopharmaceuticals.



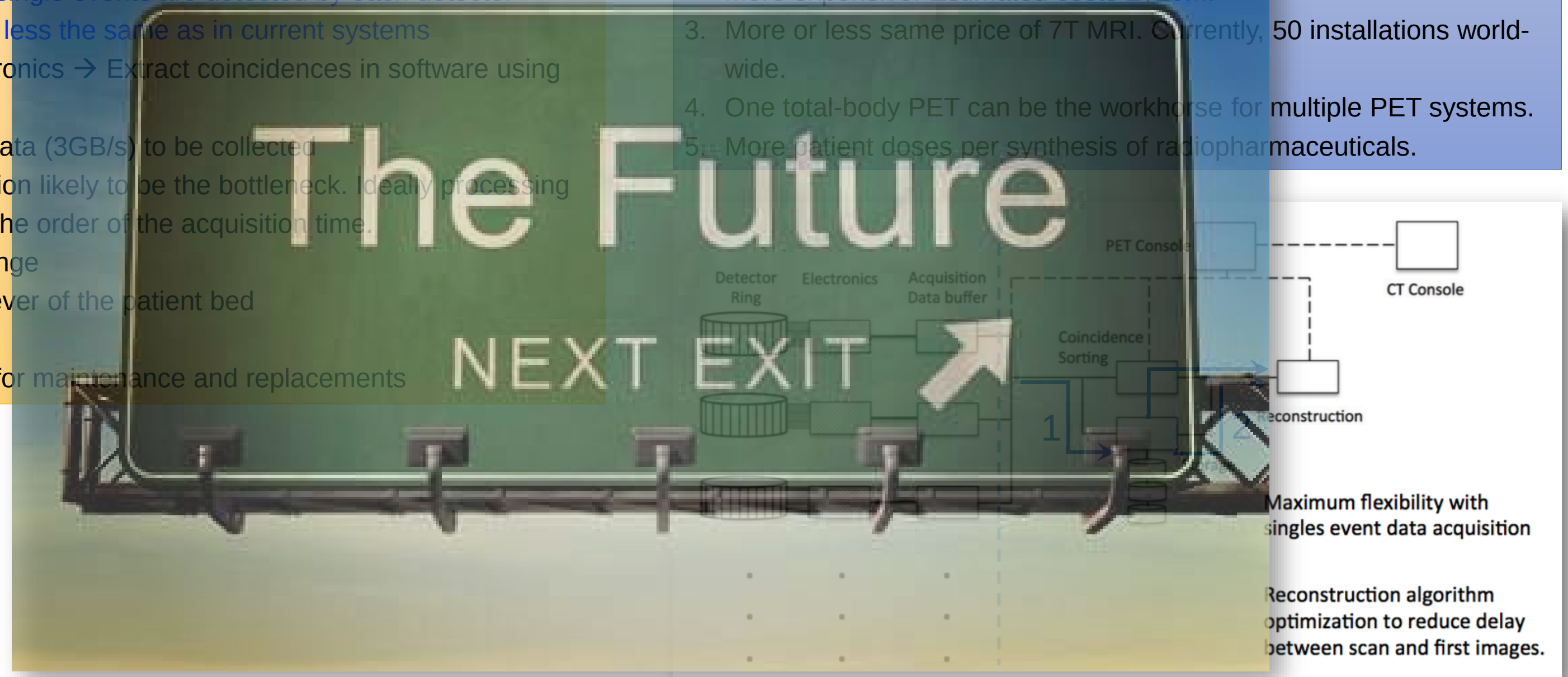
Challenges of Total-Body PET

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Current running initiatives



GE discovery MI

GE Discovery MI
3.95 x 5.3 x 25 mm LYSO
20 cm long
85 cm bore

13 liters LYSO
0.5 m² SiPMs

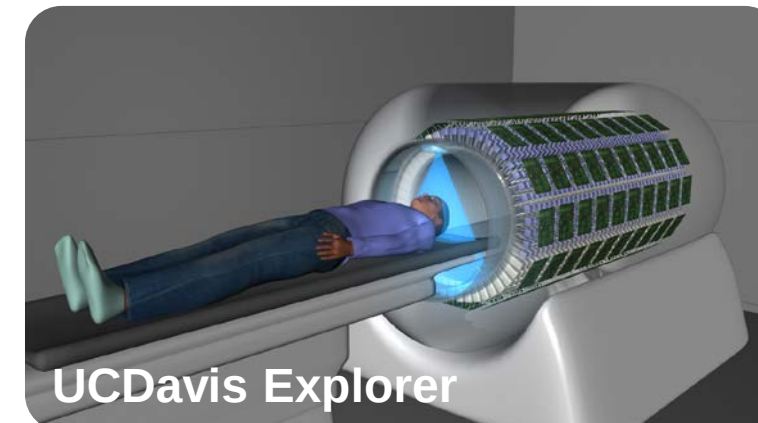


PENN PET Explorer

Philips Vereon based
3.9 x 3.9 x 19 mm LYSO
140 cm long
76.4 cm bore
30x more efficient

64 liters LYSO
3.4 m² SiPMs

2 Phases
From 70cm to 140cm



UCDavis Explorer

United Imaging SensL based
2.76 x 2.76 x 18 mm LYSO
198 cm long
78.6 cm bore
40x more efficient

88 liters LYSO
5 m² SiPMs

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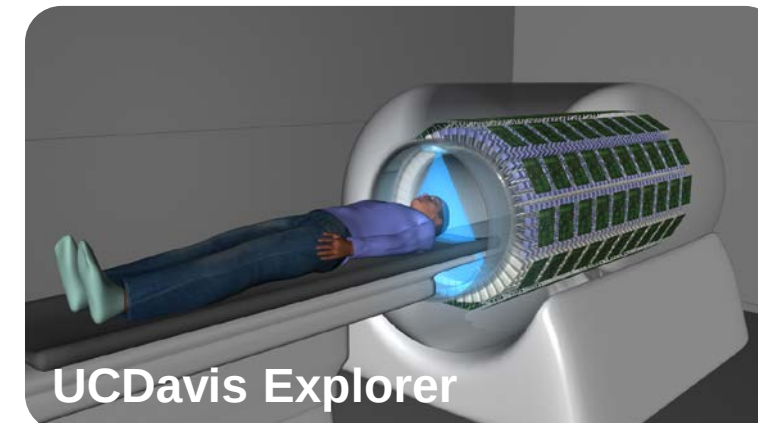


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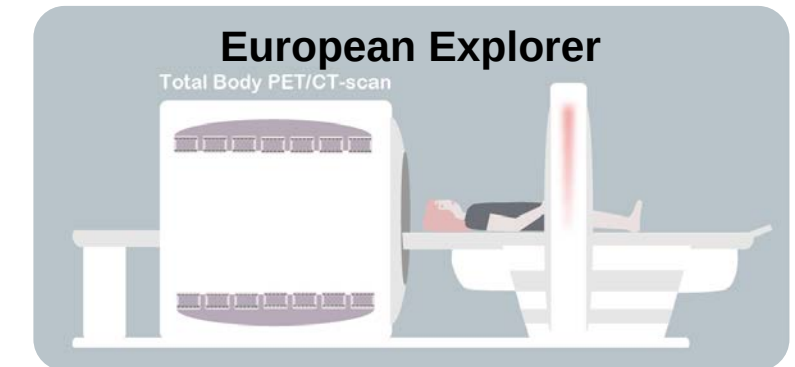
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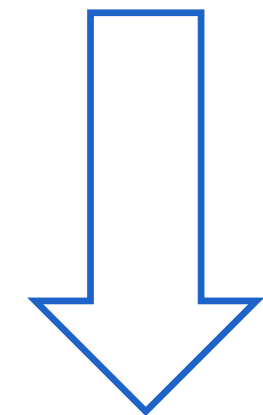
European Explorer

Total Body PET/CT-scan

SPHYNX Project

Monolithic
16 mm thick LYSO
100 cm long
65 cm bore
20x more efficient

33 liters LYSO
2 m² SiPMs



Most cost-efficient
Best spatial resolution

SPHYNX-project or PET 20.0

Studying **PHY**siology with **NeXt** generation molecular imaging

Large-scale research infrastructure UGent initiative

Lead: Stefaan Vandenberghe



GHENT UNIVERSITY
20.0
A HISTORY FOR THE FUTURE

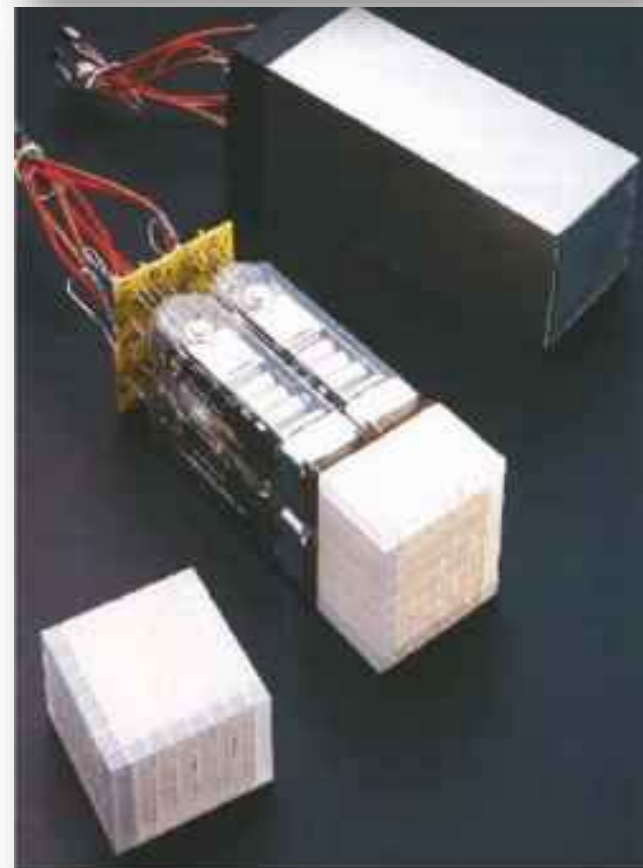
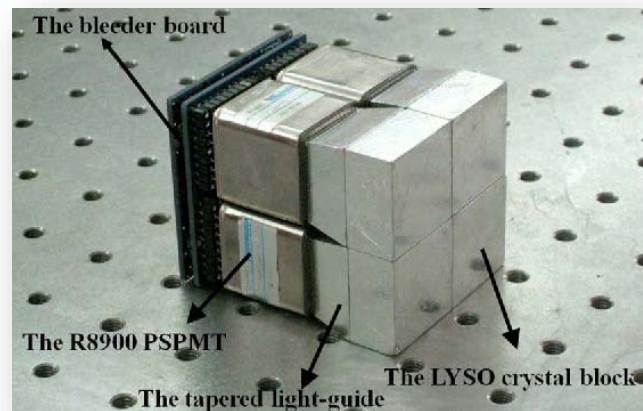
PET 20.0

- 200 years UGent
- 2 x 20.0 years of PET experience (first installation in 1977)
- 2.00x sharper
- 2.00mm spatial resolution
- 20.0x more sensitive
- 20.0x faster routine PET
- 20.0x dose reduction
- 20.0s time frames
- 2020 deadline

Total Body PET – From mice to men



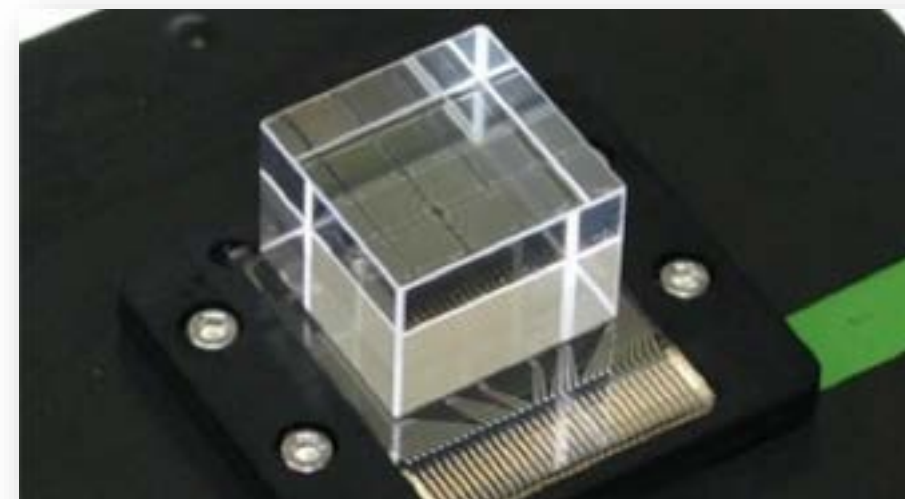
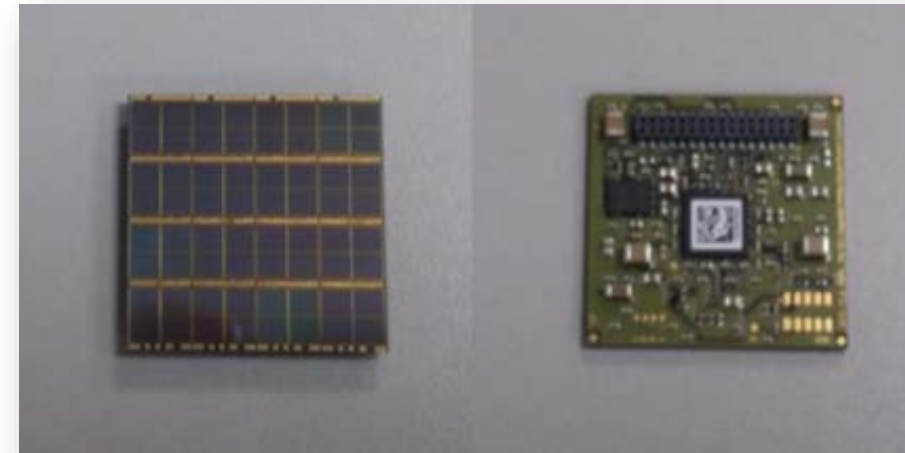
From mice to men – Monolithic SiPM detectors



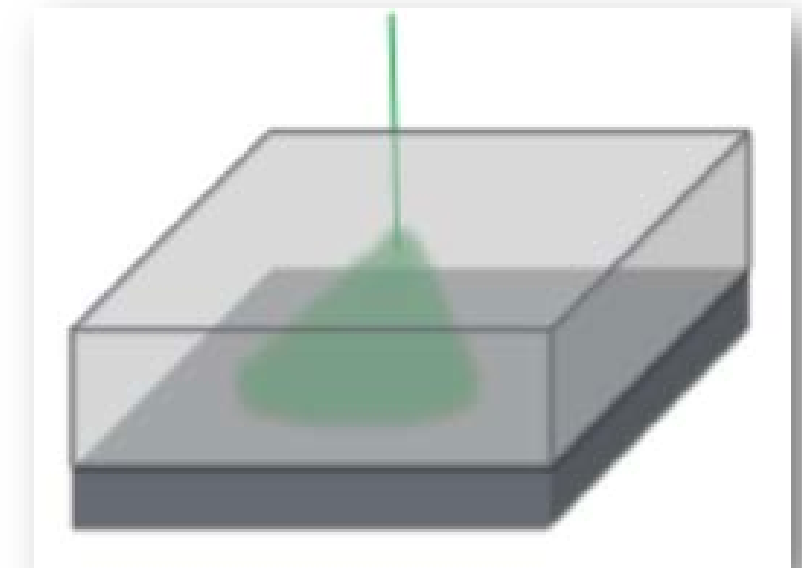
Conventional PET detector

- Pixelated crystal
- PMT pr PSPMT

Silicon Photomultiplier



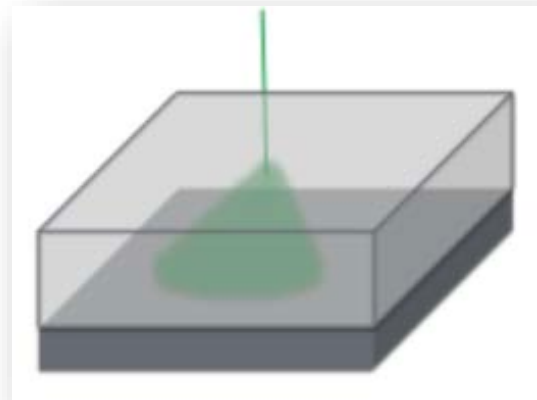
Monolithic LYSO crystal



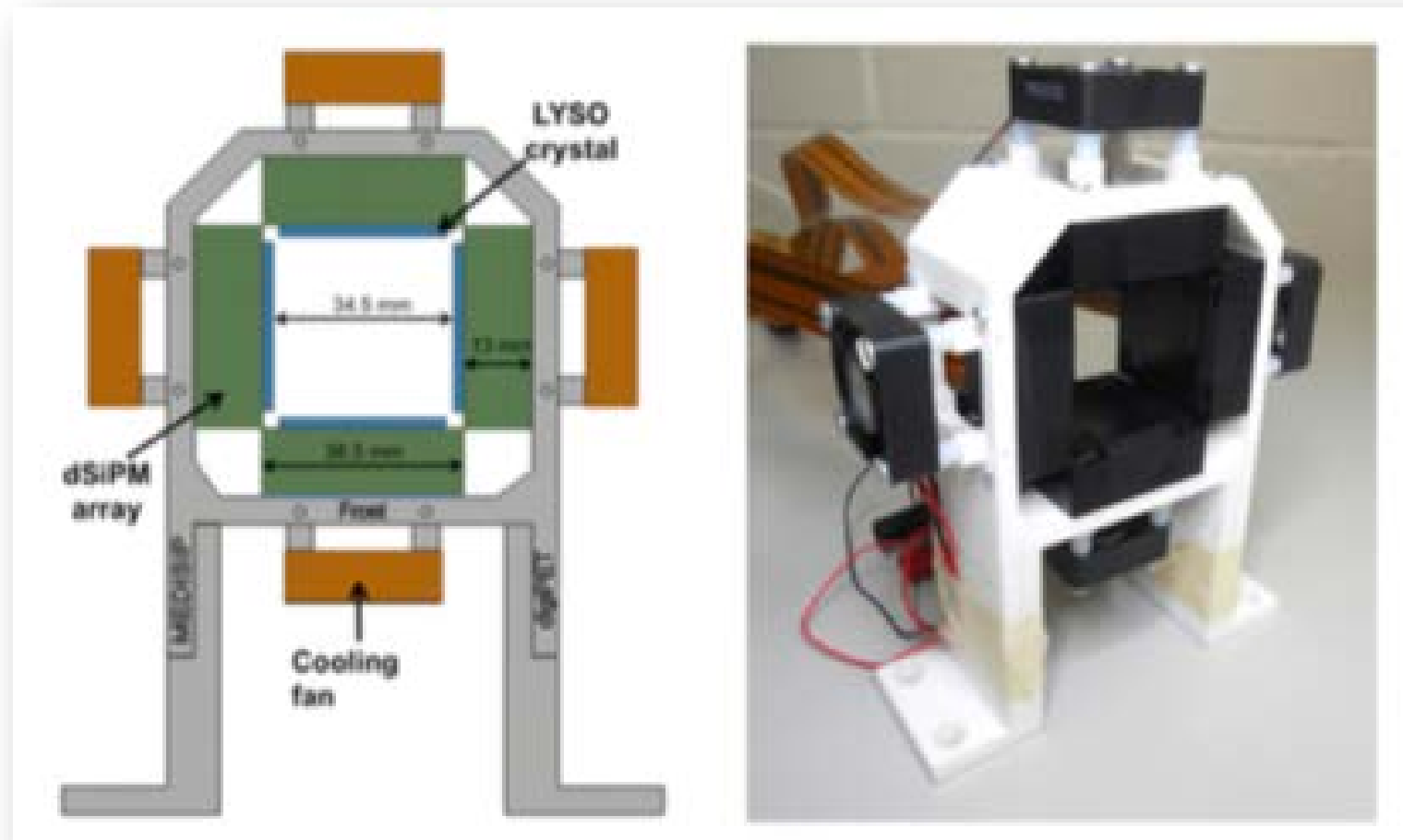
Courtesy of Molecubes

España et al, 2014. DigiPET: sub-millimeter spatial resolution small- animal PET imaging using thin monolithic scintillators. Phys Med Biol 59: 3405–3420

From mice to men – DigiPETv1.0



32 x 32 x **2 mm crystal**
32 x 32 mm SiPM (8x8 cells)
Digital SiPM



DigiPETv1.0

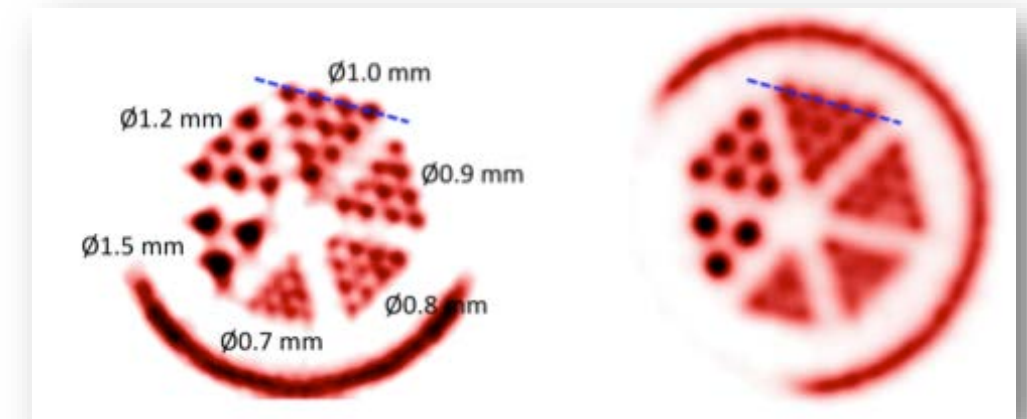
4 detectors

32 x 32 x 32 mm field-of-view

External dimensions of 115 x 150 x 38 mm

Sub-mm spatial resolution (0.7 mm)

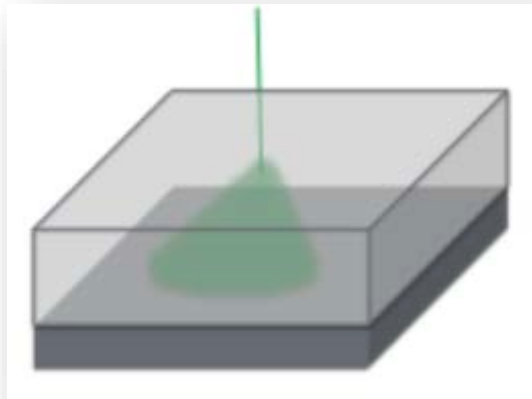
Sensitivity 6-10 less than commercial systems due to thin crystals



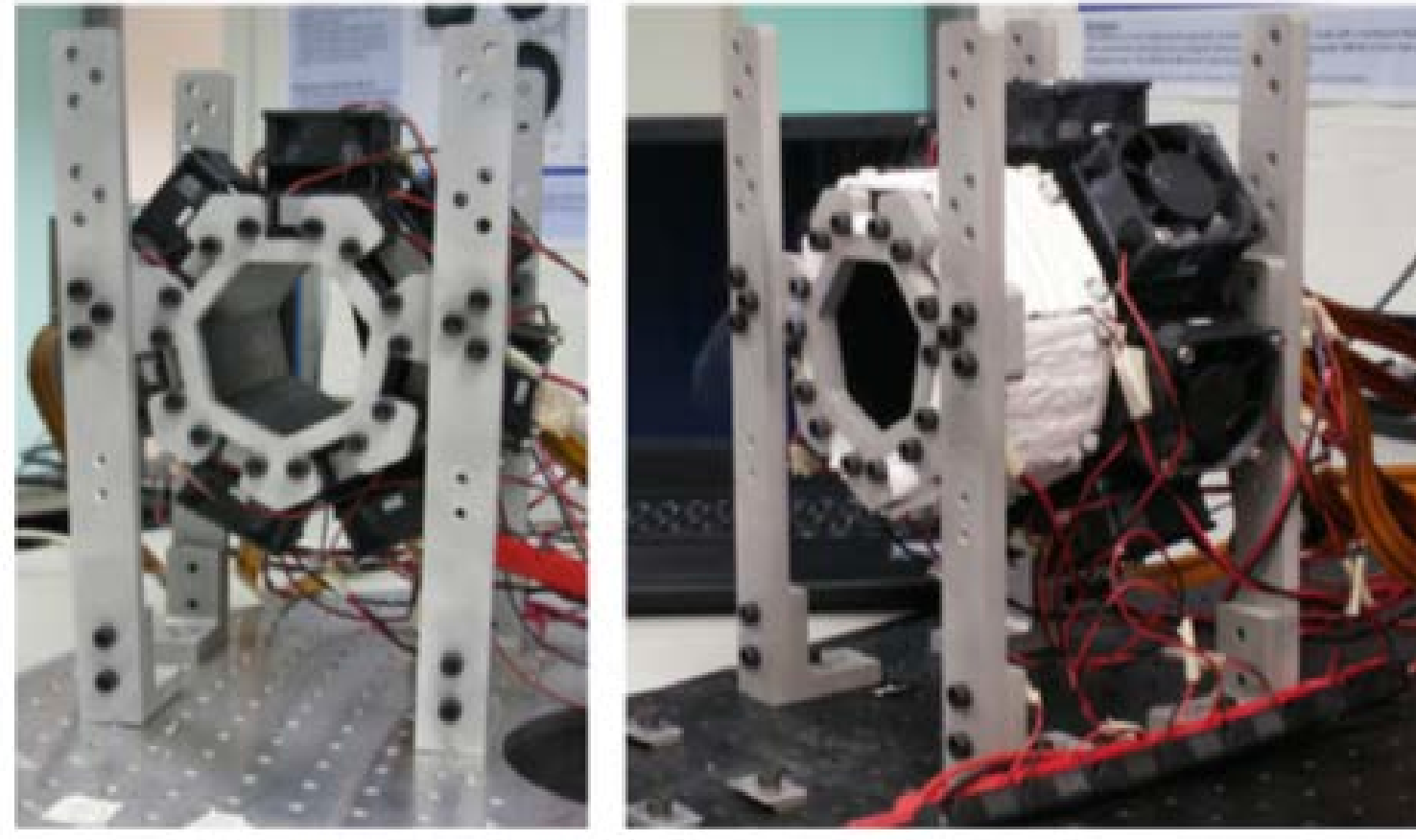
DigitPETv1.0

LabPET8

From mice to men – DigiPETv2.0



32 x 32 x **5 mm crystal**
32 x 32 mm SiPM (8x8 cells)
Digital SiPM



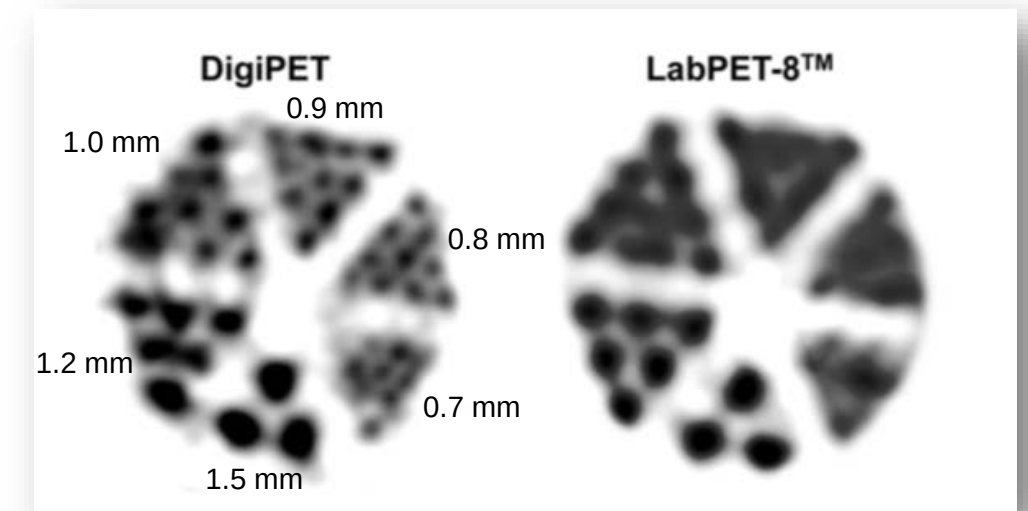
DigiPETv3.0

7 detectors

72 mm diameter – 32 mm axial field-of-view

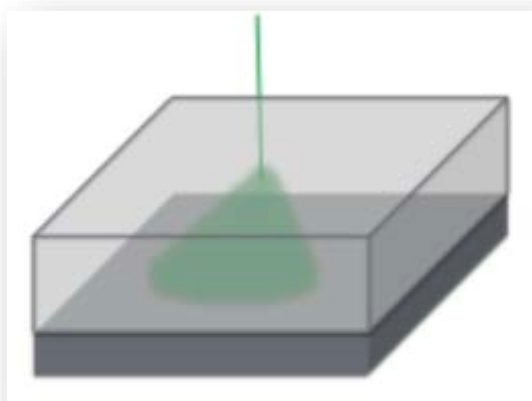
External dimensions of 220 diameter x 150 mm length

Sub-mm spatial resolution (0.750 mm)

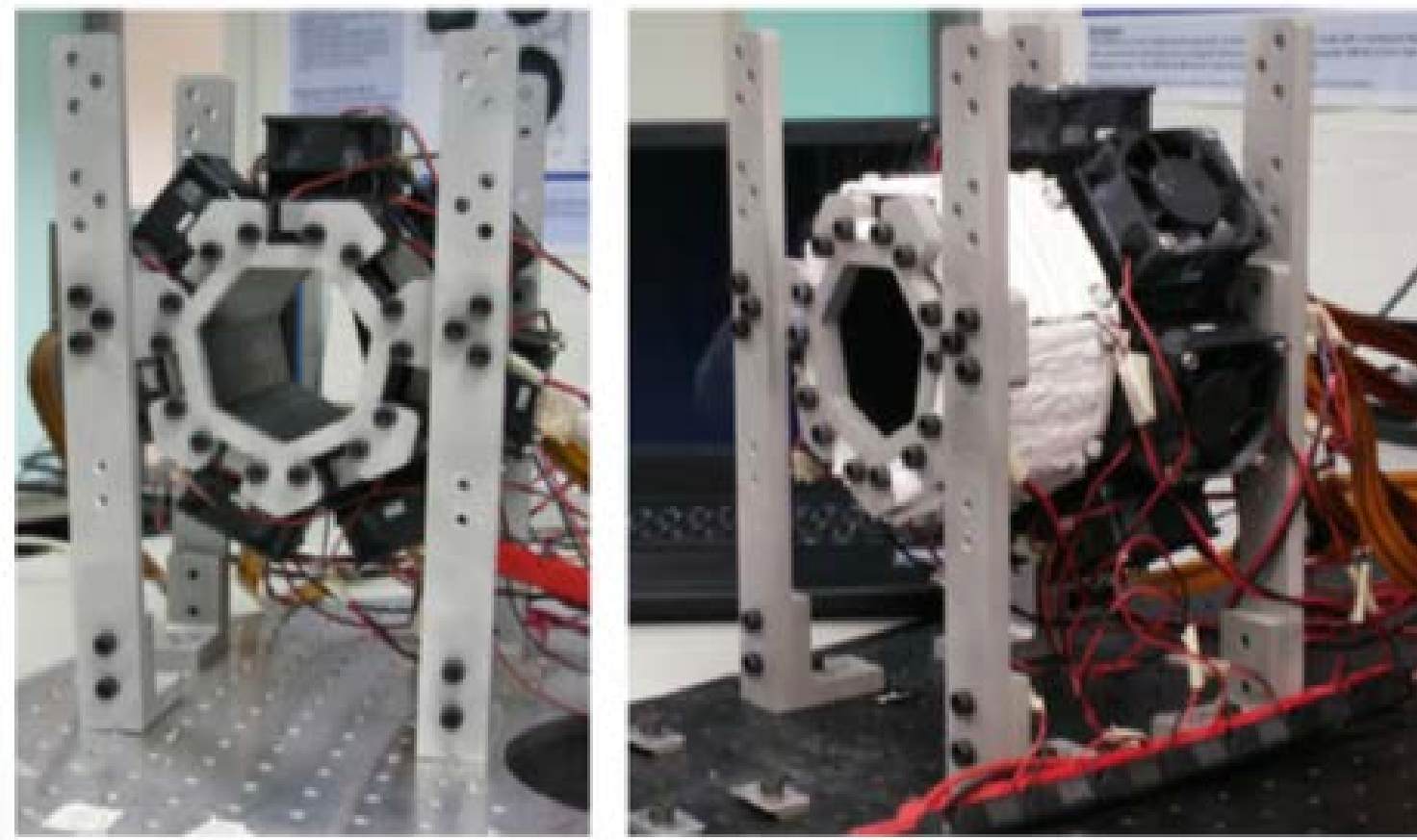
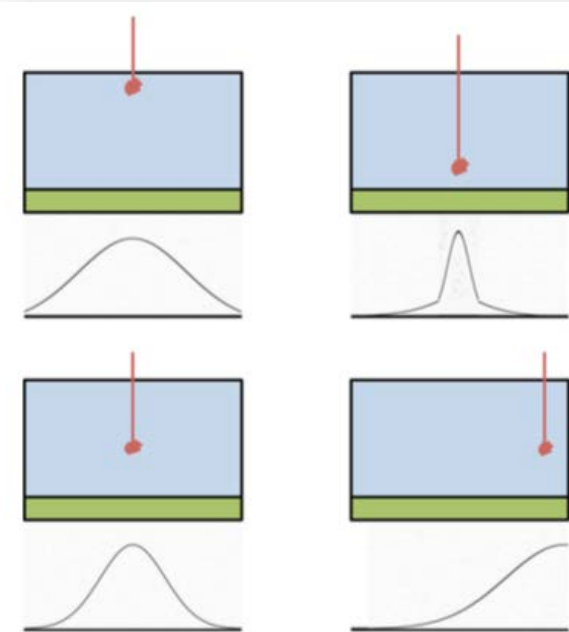


- Marcinkowski R et al. 2016. "Sub-millimetre DOI Detector Based on Monolithic LYSO and Digital SiPM for a Dedicated Small-animal PET System." Phys Medicine and Biology 61: 2196–2212.
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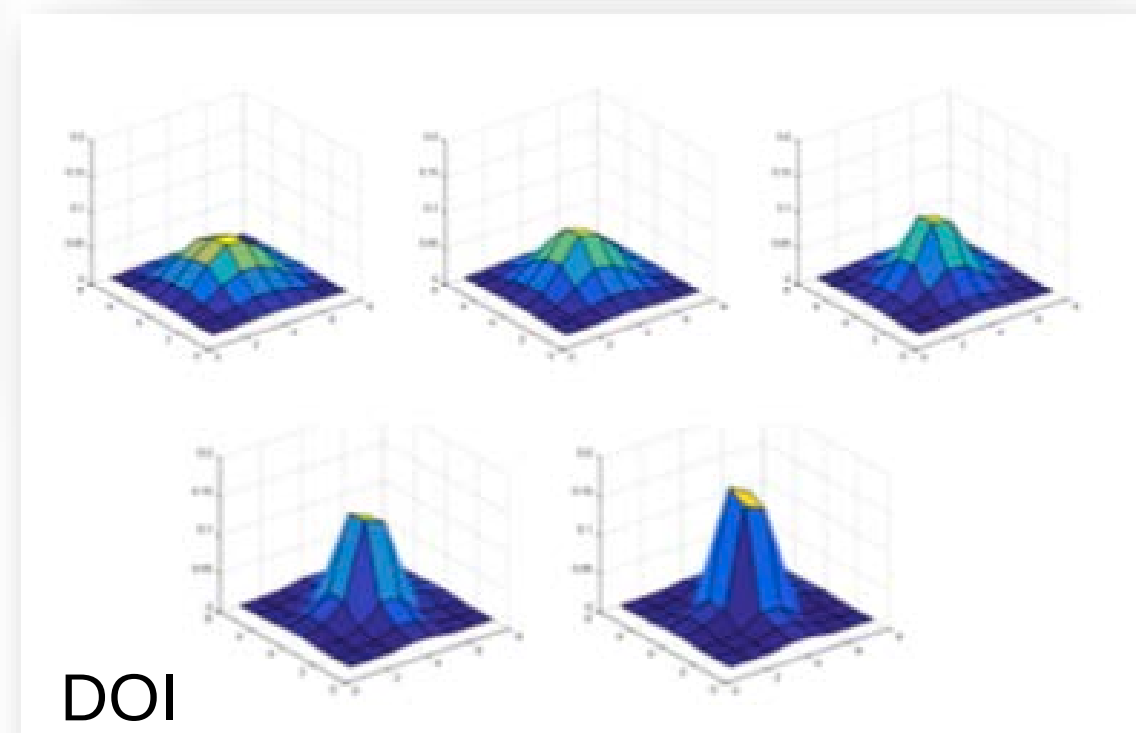
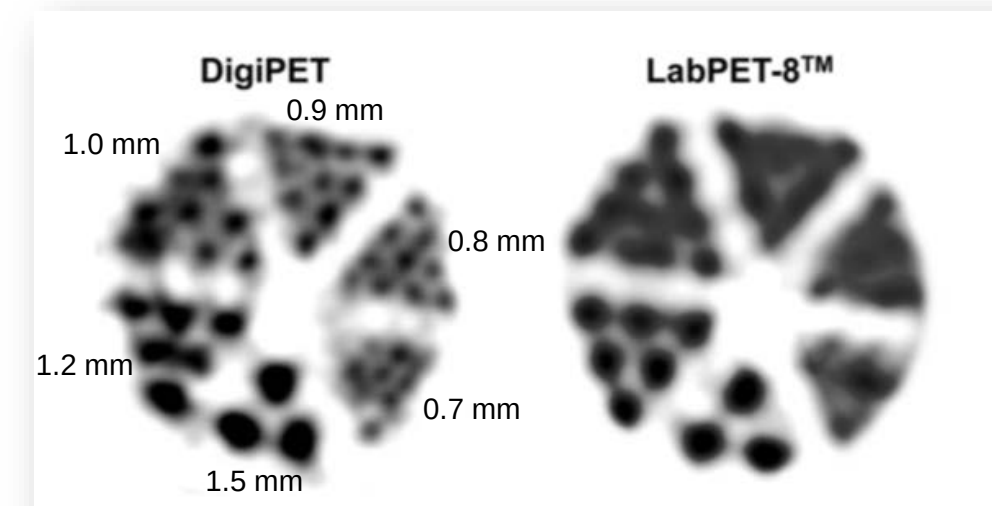
From mice to men – DigiPETv2.0



32 x 32 x **5 mm crystal**
 32 x 32 mm SiPM (8x8 cells)
 Digital SiPM
 DOI: x, y, z positioning



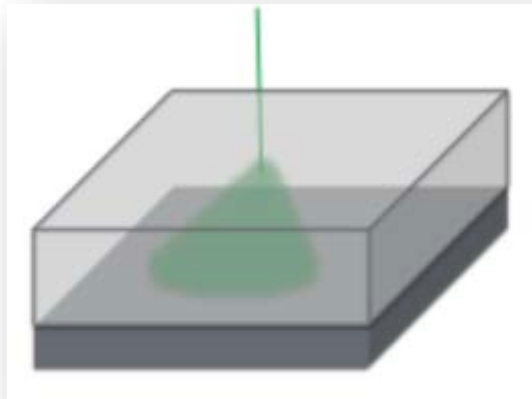
DigiPETv3.0
 7 detectors
 72 mm diameter – 32 mm axial field-of-view
 External dimensions of 220 diameter x 150 mm length
 Sub-mm spatial resolution (0.750 mm)
 Good sensitivity
 Problem: read-out rate digital SiPMs



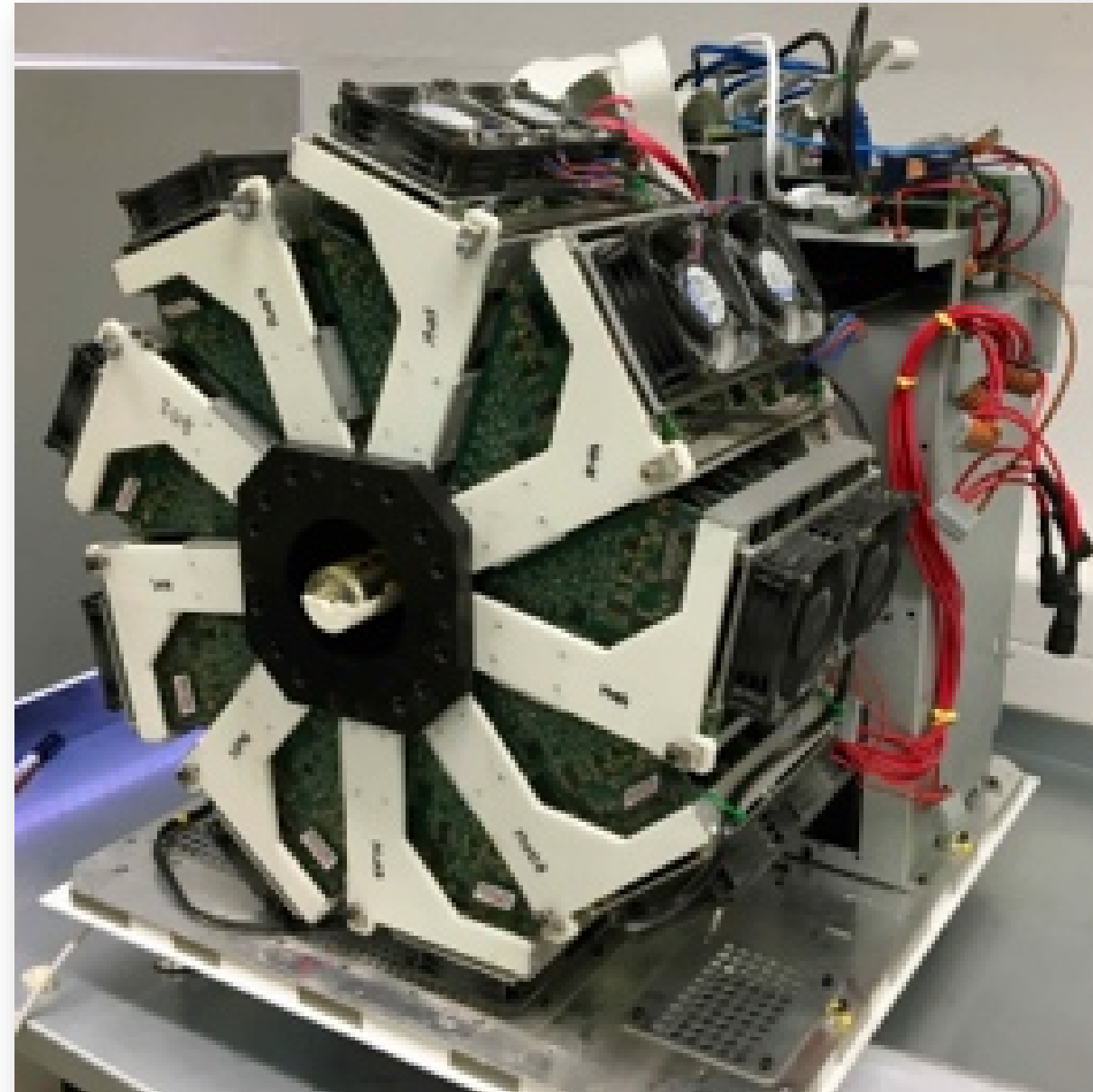
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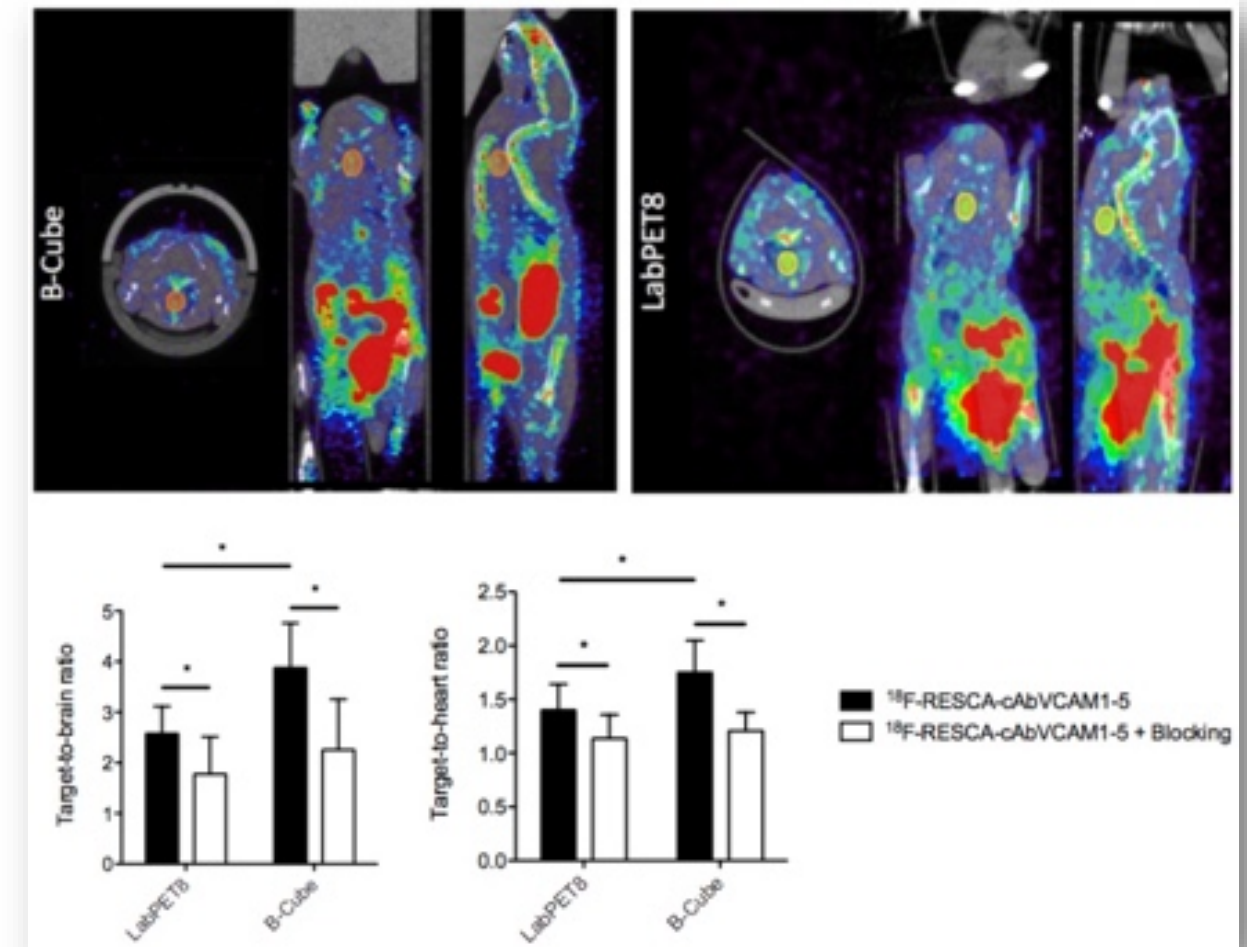
From mice to men – Beta-Cube prototype (DigiPETv3.0)



25.4 x 25.4 x **5 mm crystal**
25.4 x 25.4 mm SiPM (8x8 cells)
Analog SiPM
DOI: x, y, z positioning



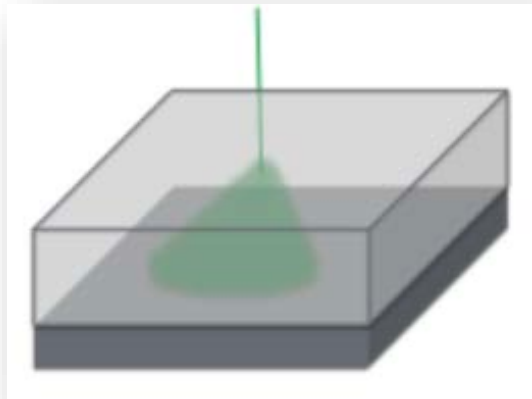
9 detectors per ring, 5 rings (45 detectors)
72 mm diameter – 130 mm axial field-of-view
Sub-millimeter spatial resolution (0.750 mm)
High sensitivity ($\pm 6\%$)



Plaque detection aortic arch
F18-labelled VCAM1 nanobody
Collaboration ICMI (VUB)

- Mollet Pieter et al. 2017. "The beta-CUBE, a high-end compact preclinical benchtop PET for total body imaging." Annual Meeting of the Society-of-Nuclear-Medicine-and-Molecular-Imaging (SNMMI), Denver, June 10-14 2017.
- Bridoux J et al. 2018. "Improved detection of molecular markers of atherosclerotic plaques using sub-millimeter PET imaging". European Molecular Imaging Meeting, San Sebastian, March 20-23 2018.

From mice to men – Molecubes Beta-Cube

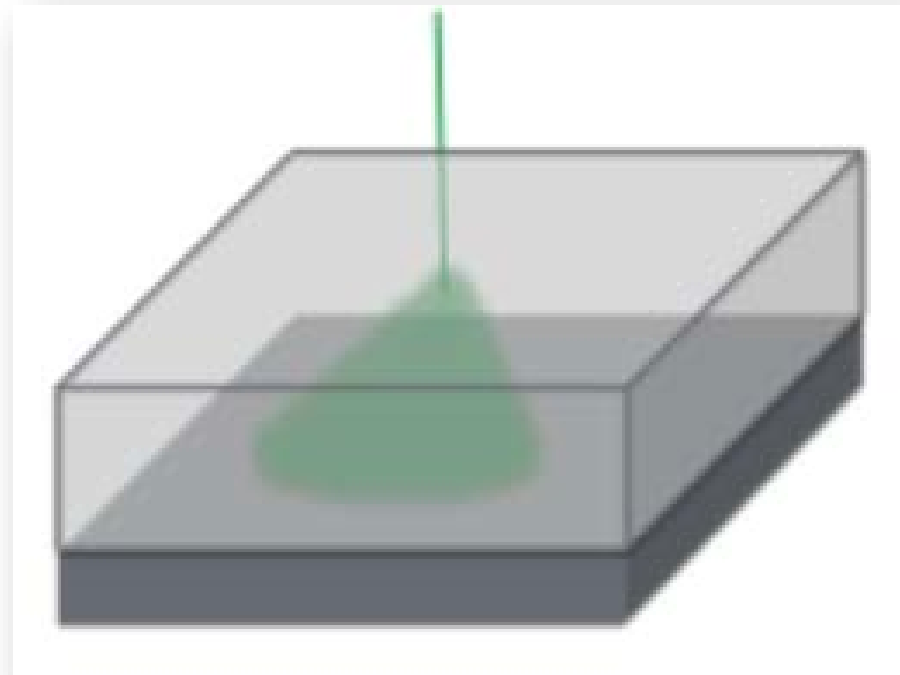
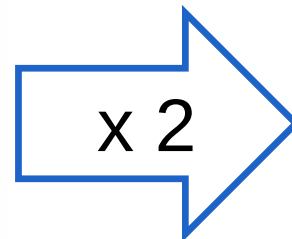
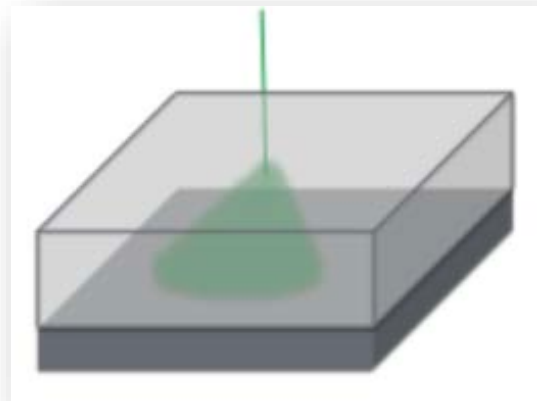


25.4 x 25.4 x **8 mm crystal**
25.4 x 25.4 mm SiPM (8x8 cells)
Analog SiPM
DOI: x, y, z positioning



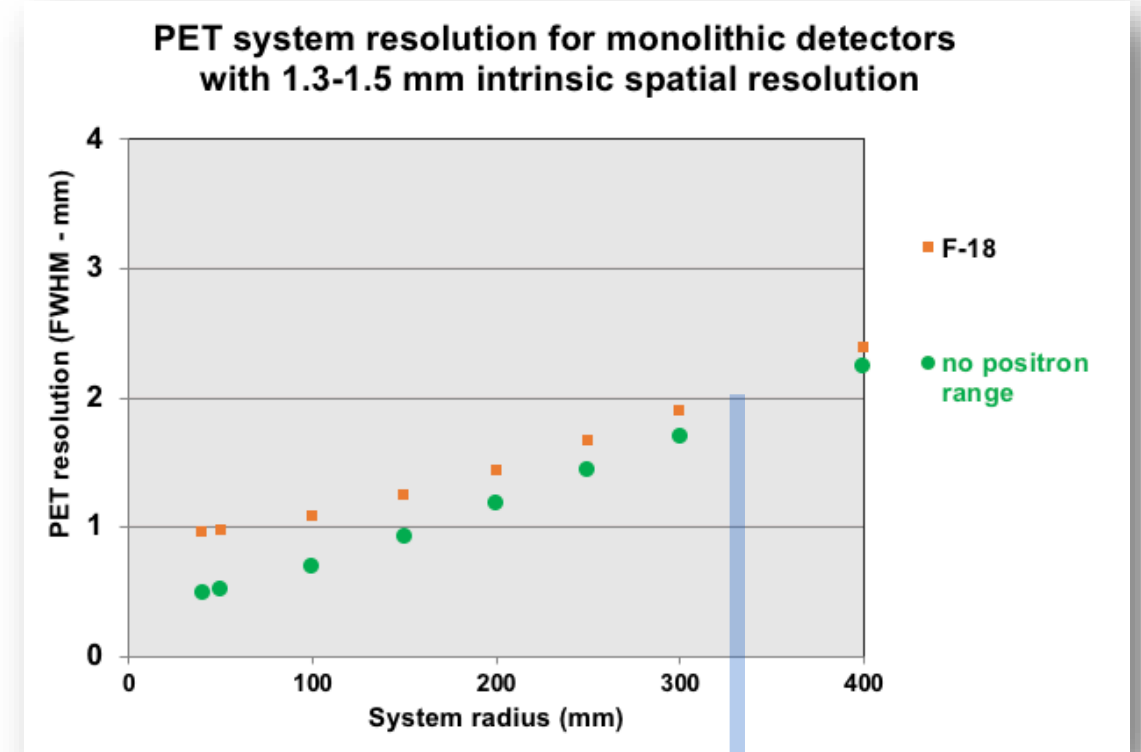
9 detectors per ring, 5 rings (45 detectors)
72 mm diameter – 130 mm axial field-of-view
Sub-millimeter spatial resolution (0.85 mm)
High sensitivity (12-13%)

From mice to men



25.4 x 25.4 x 8 mm crystal
25.4 x 25.4 mm SiPM (8x8 cells)
Analog SiPM
DOI: x, y, z positioning
0.7 mm intrinsic spatial resolution

50 x 50 x 16 mm crystal
50 x 50 mm SiPM (8x8 cells)
Analog SiPM
DOI: x, y, z positioning
1.3-1.5 mm intrinsic spatial resolution

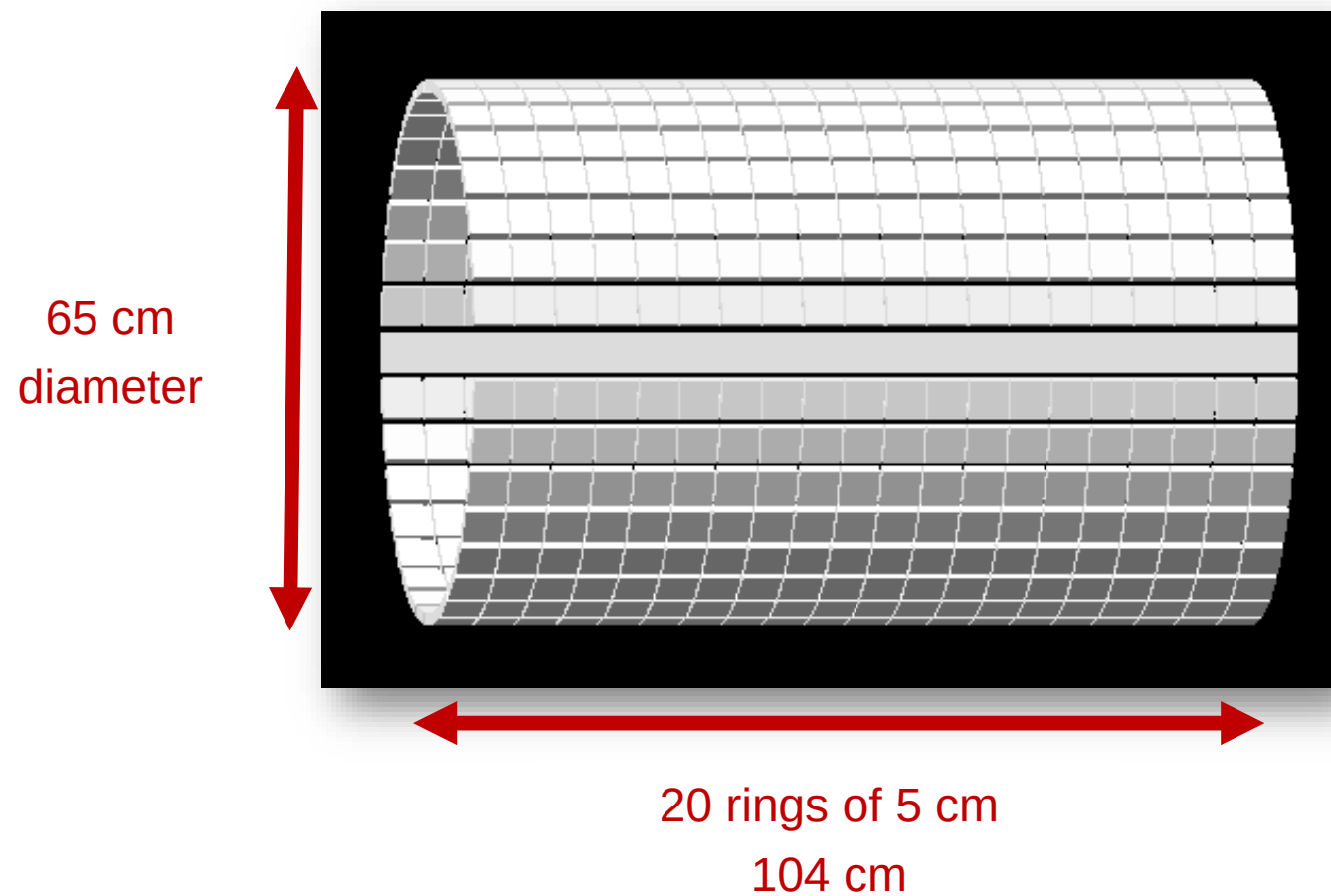


System level spatial resolution: 2 mm
Expected spatial resolution for 65 cm bore



From mice to men (SPHYNX - PET20.0)

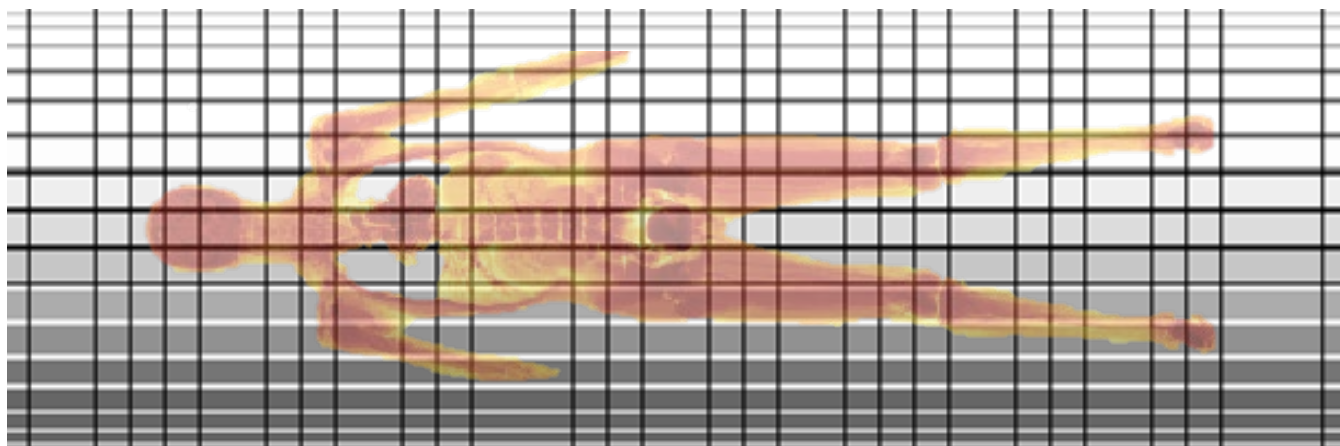
Compact bore
PET 20.0 design



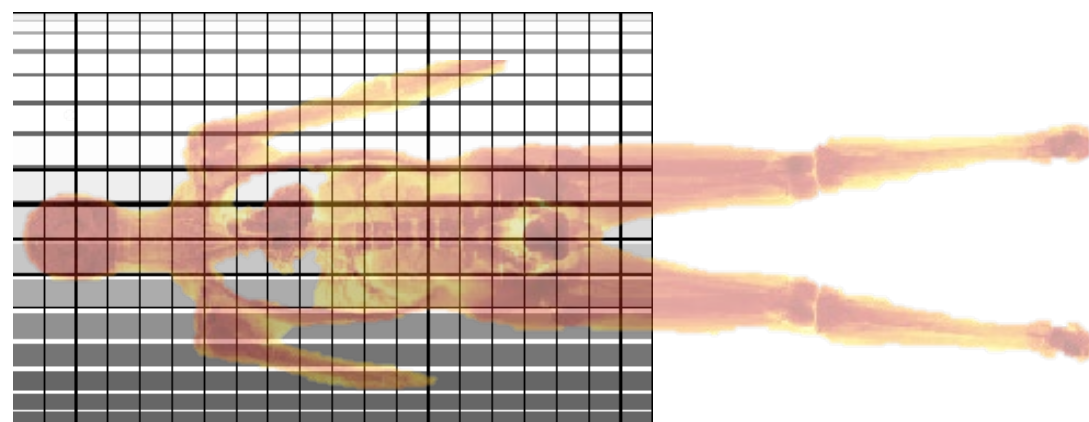
Motivation for design with compact bore (65 cm), 1m axial field-of-view and thin monolithic LYSO PET detectors

- High detector cost is the main limiting factor for introduction of total-body PET (lowest cost compared to other initiatives)
 - 36 modules per ring
 - 20 rings
 - 720 modules
- Thin detectors
 - Better spatial resolution and time-of-flight
 - Lower cost
- Monolithic detector technology has DOI
 - Full bore can be imaged with uniform resolution
 - Best spatial resolution compared to other initiatives
- 65 cm bore (just above PET-MR)
 - 25 % less detectors (lower cost)
 - Larger solid angle (114 degrees; higher sensitivity)
 - Suitable for nearly all Euro/Asian patients

Pros and cons for 1m-2m system



- + A 2 m system sees total body of any patient (excl some basket players)
- + Total body dynamic imaging
- + Very high gains for long objects (40x more efficient)
- Very Expensive
- Claustrophobic (but short investigation times)
- Gains compared to a 1 m system range from only 3 % to a factor 2x

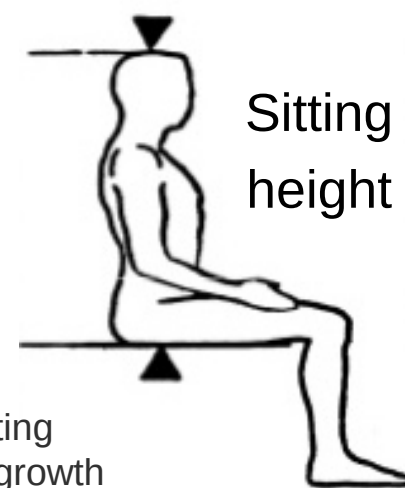


- + A 1 m system sees interesting part of all patients
- + Head to leg dynamic imaging
- + Gains compared to a 20 cm system range from factor 2.5x to factor 20x
- No Total body dynamic imaging
- Still high cost

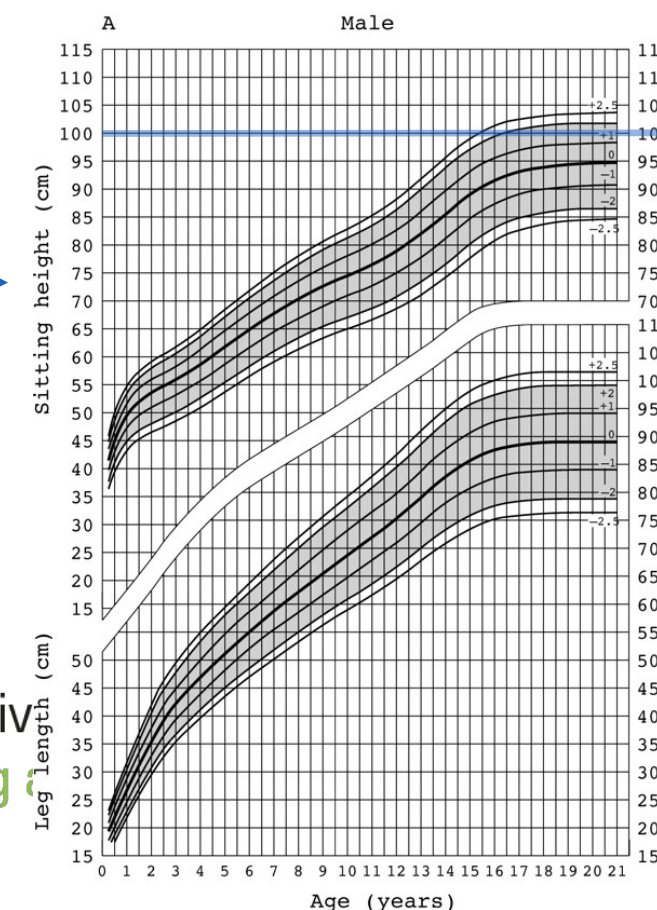
Netherlands is the tallest country in the world, where the average height of men is an incredible six feet (1.83 m)

<http://adc.bmj.com/content/90/8/807>

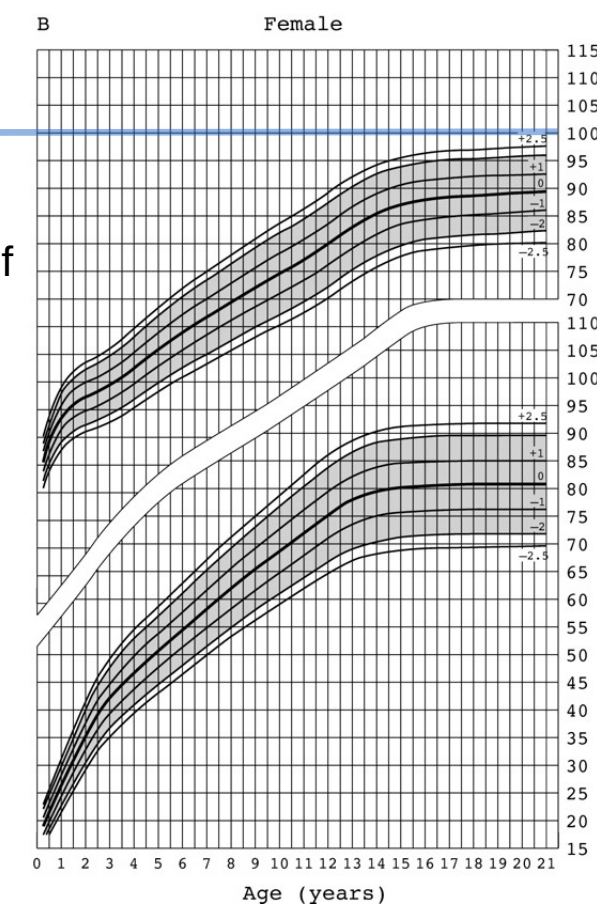
Nationwide age references for sitting height, leg length, and sitting height/height ratio, and their diagnostic value for disproportionate growth disorders



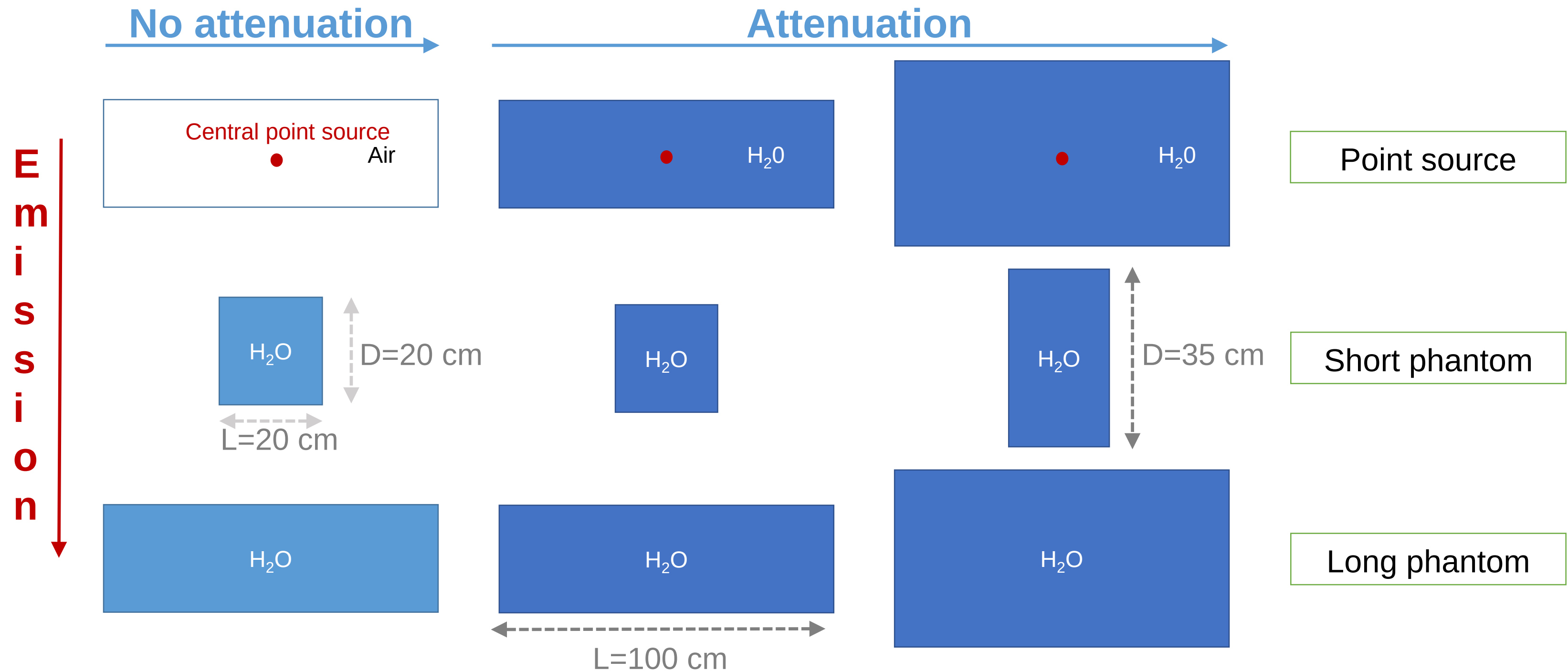
Sitting height



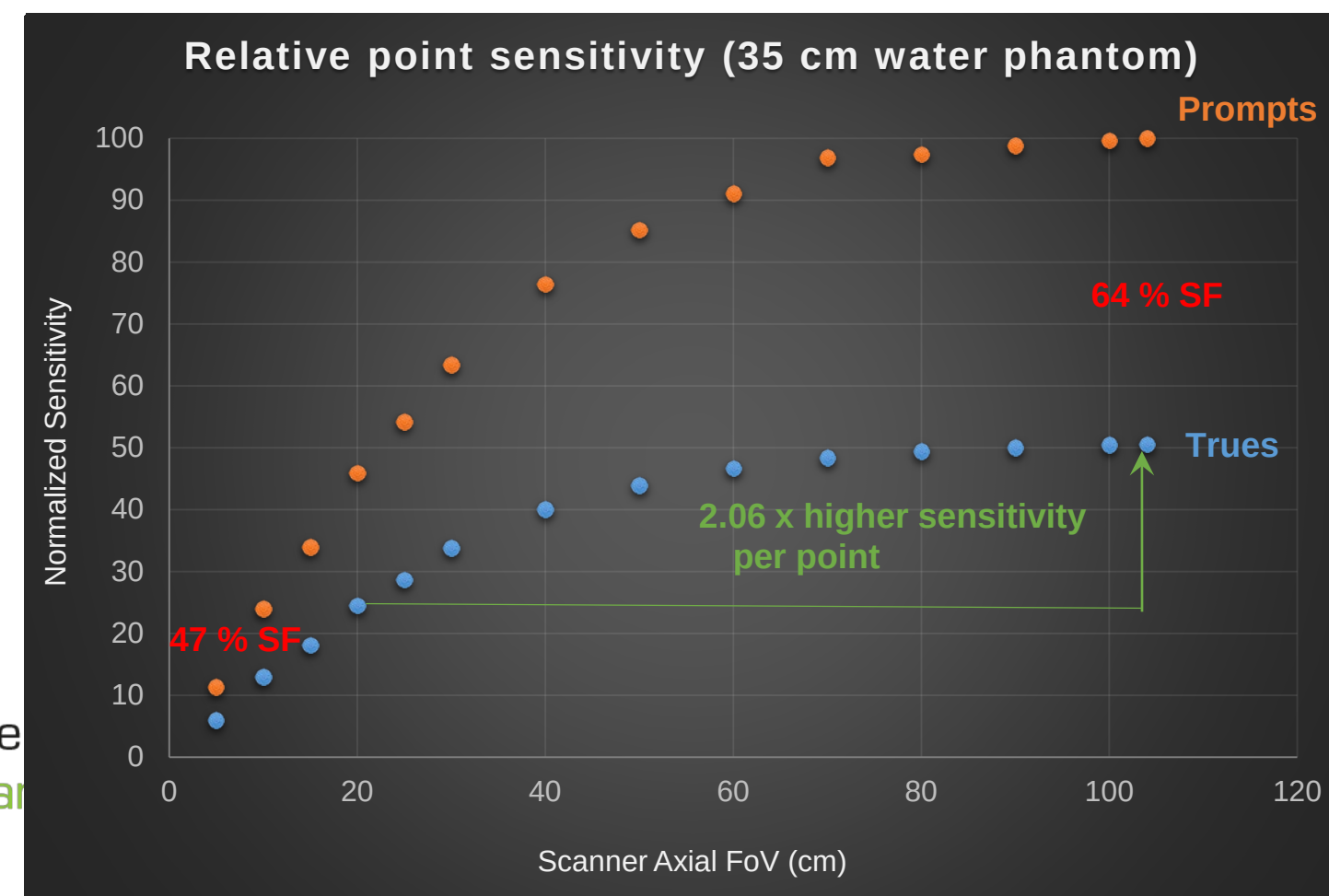
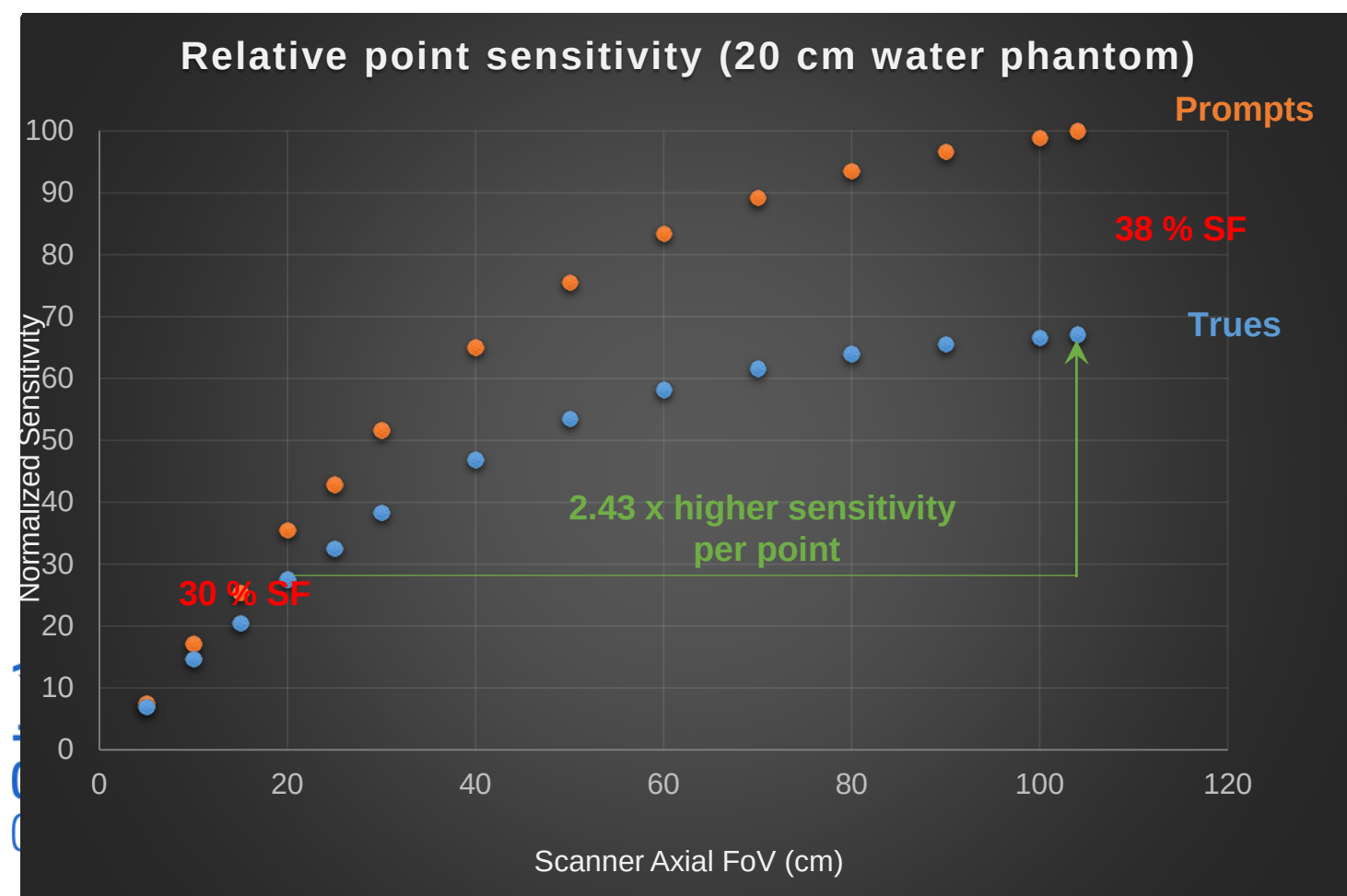
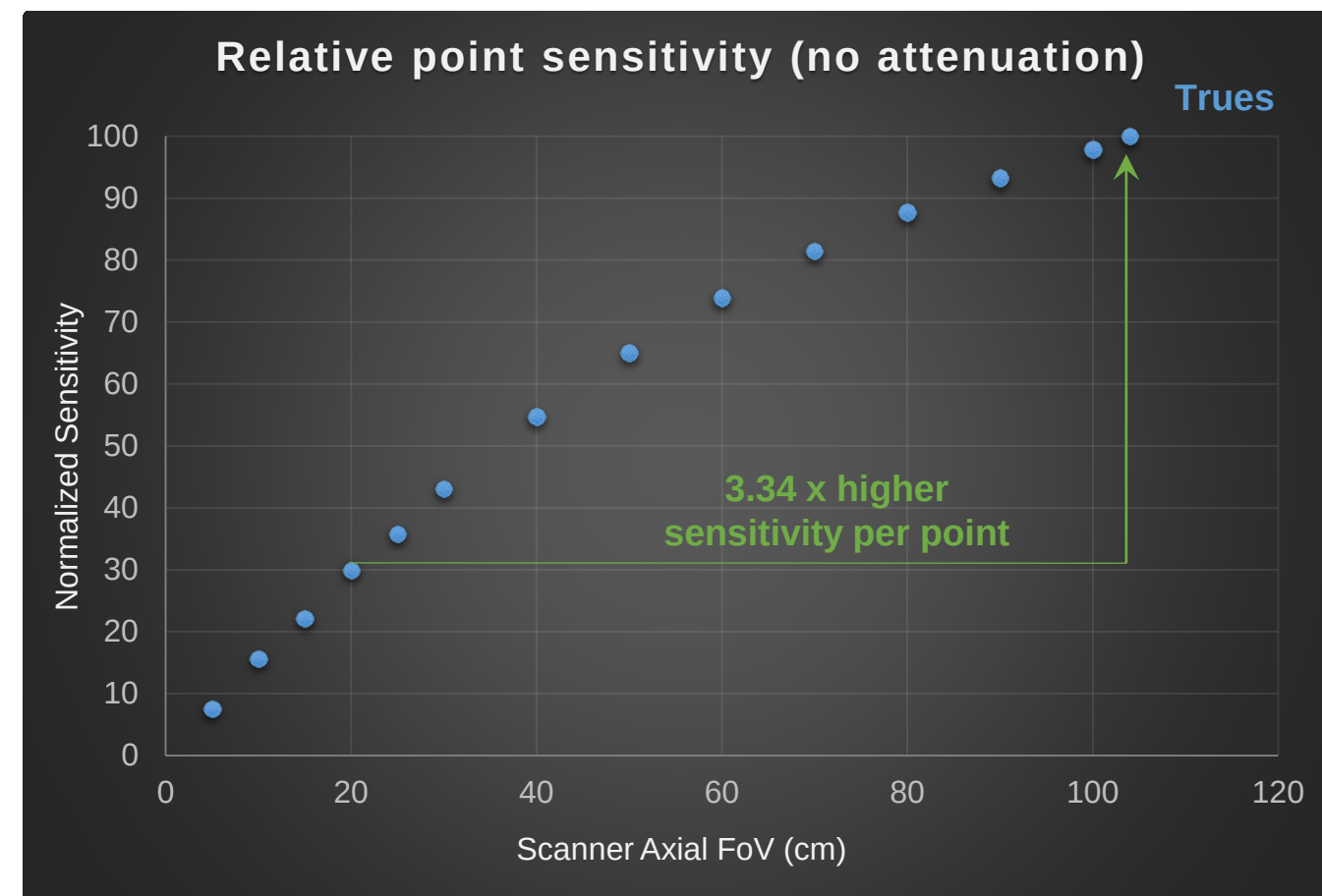
More than 90 % of Dutch man and 99% of women below 1m sitting height



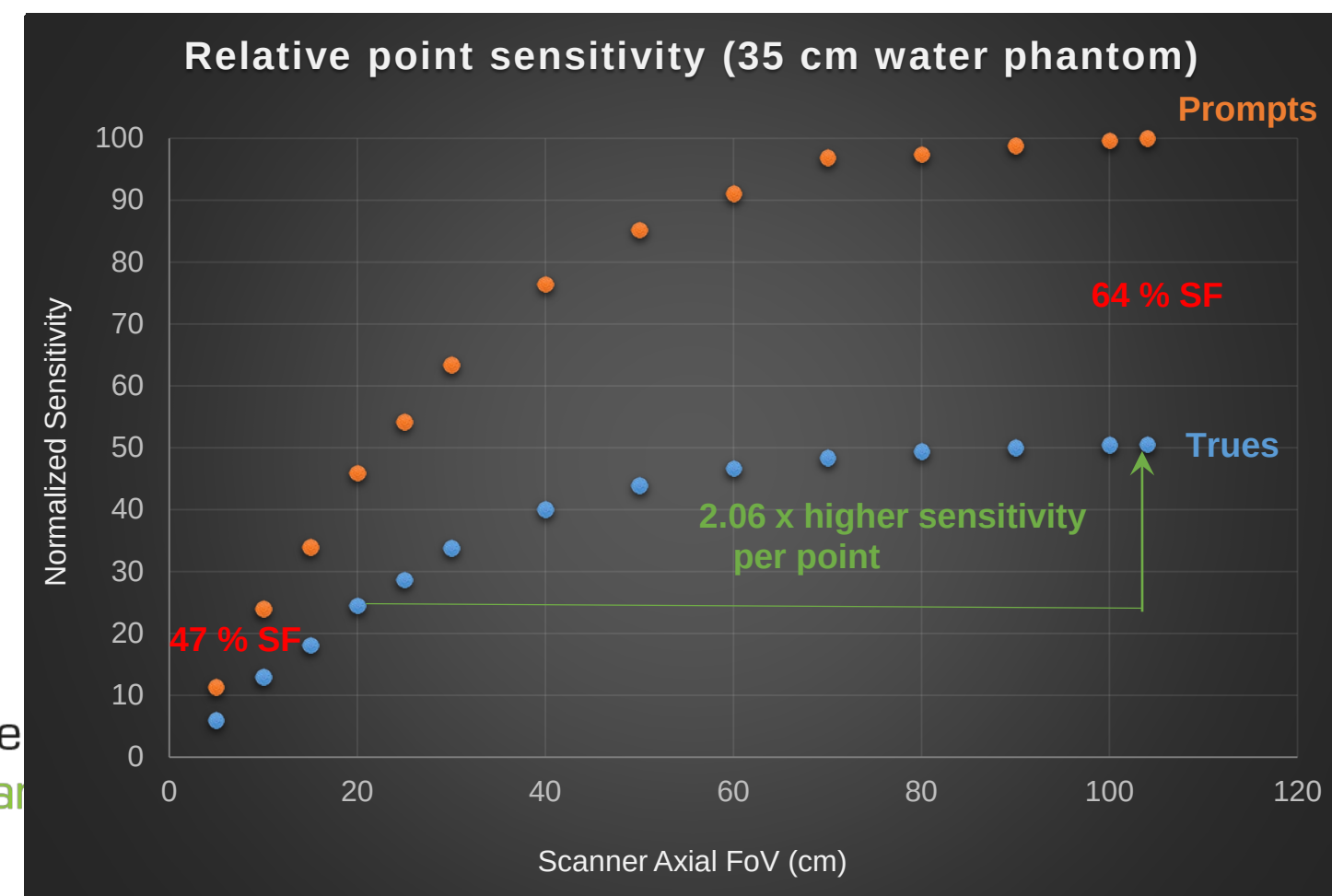
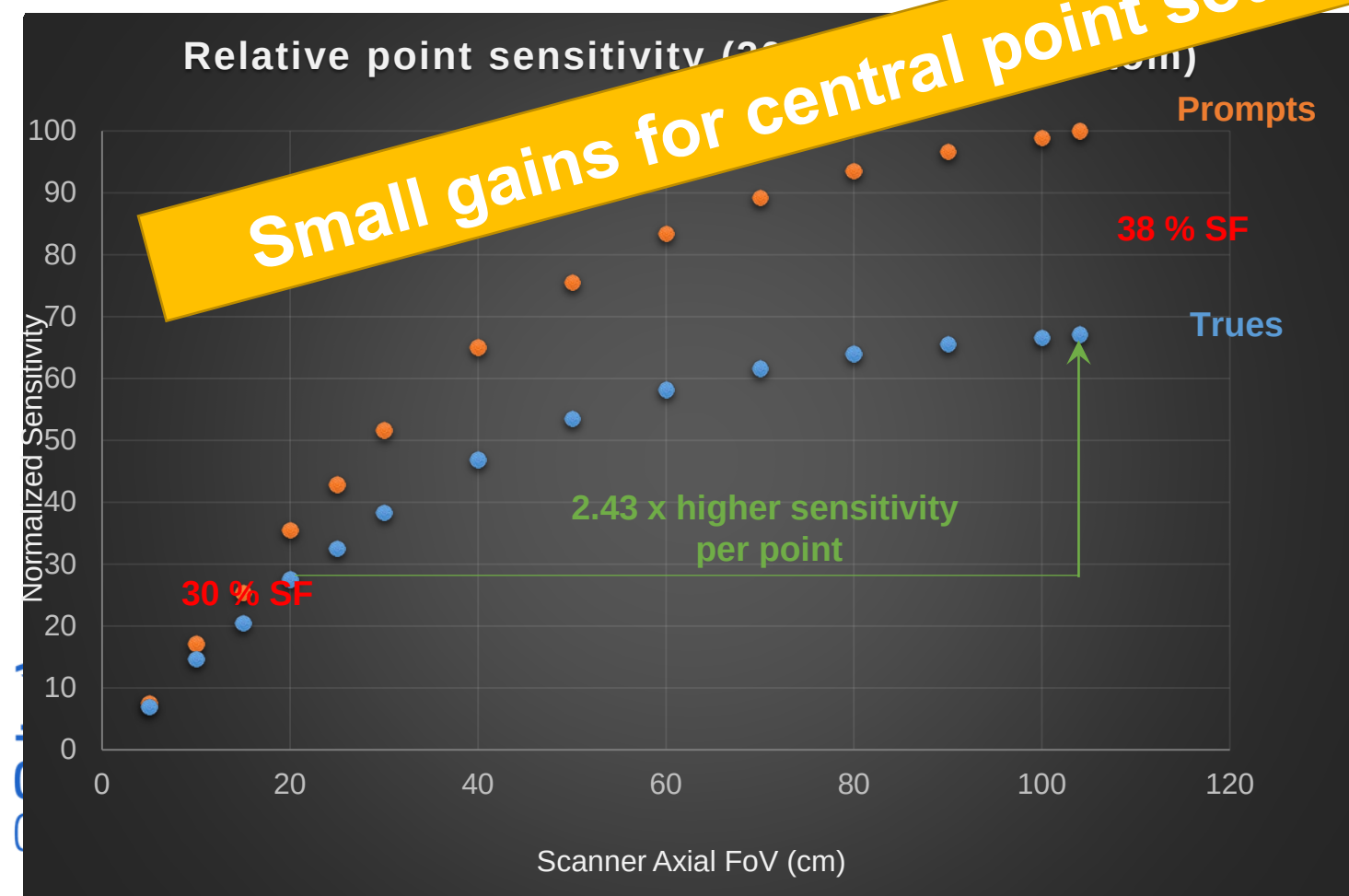
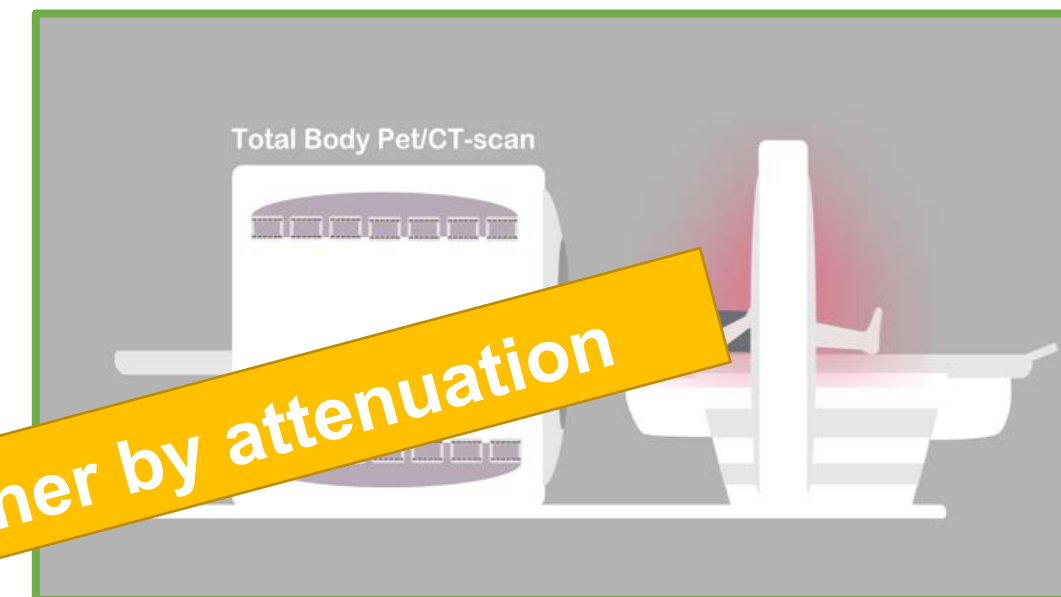
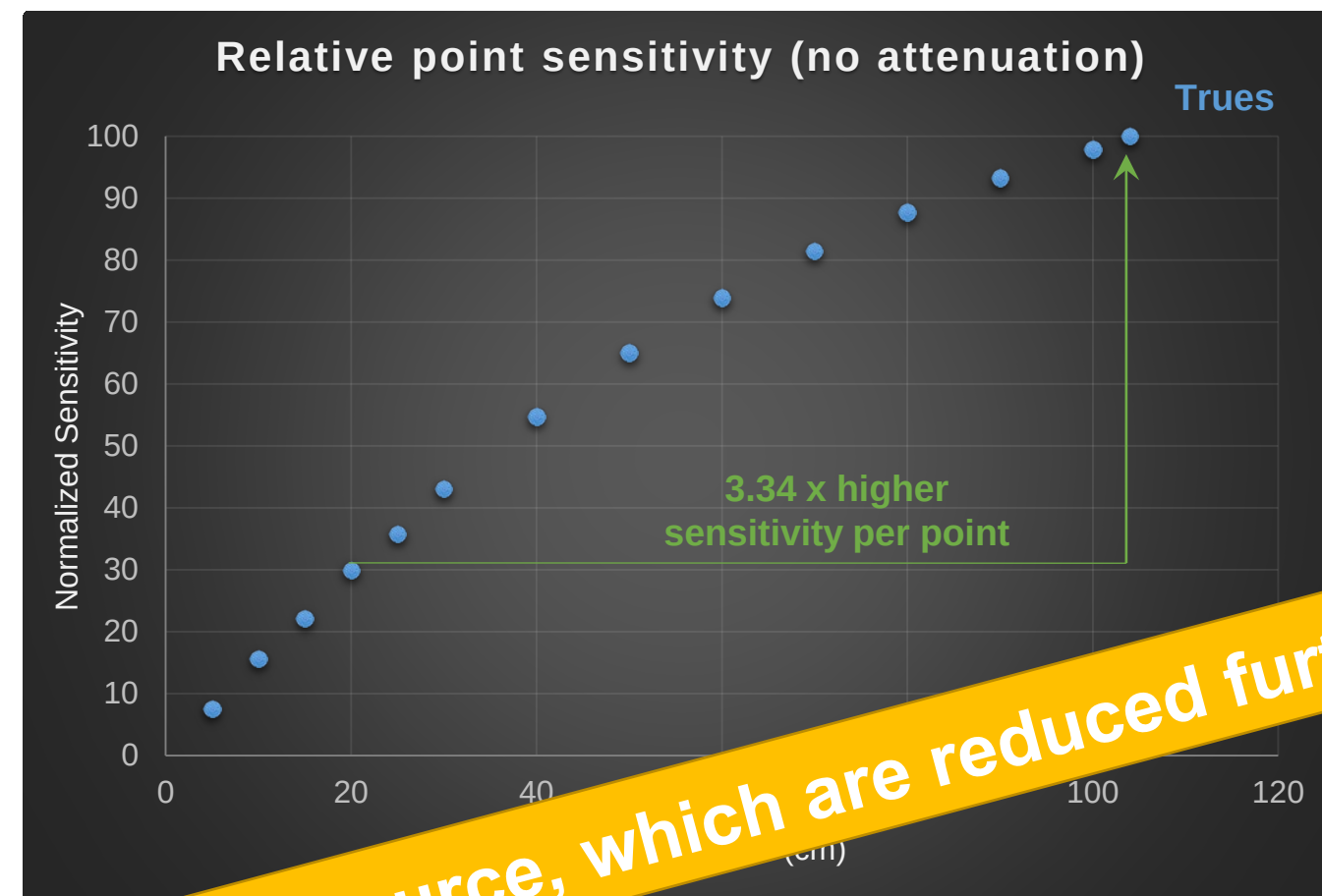
Simulation study: 20cm versus 1m



Point source

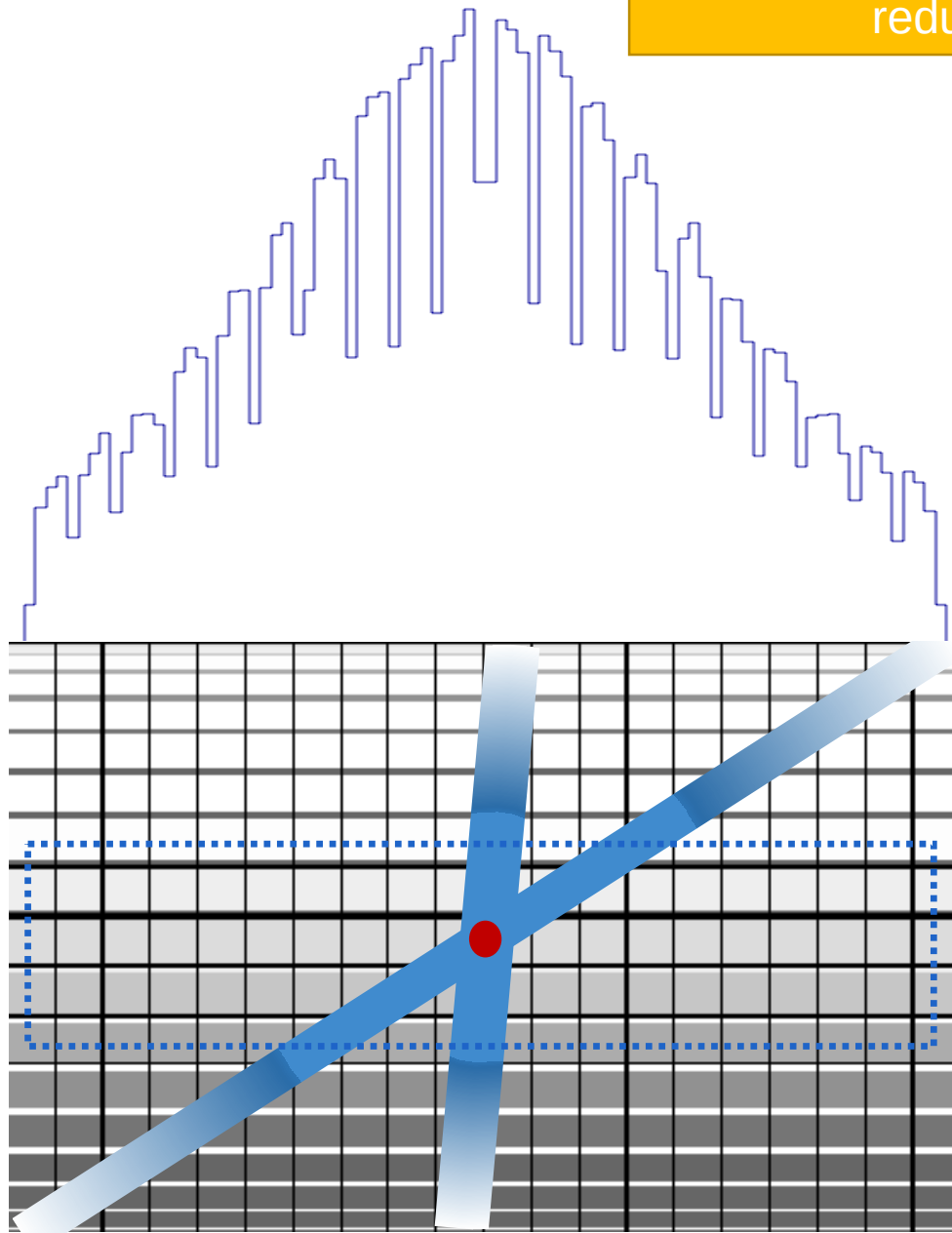


Point source

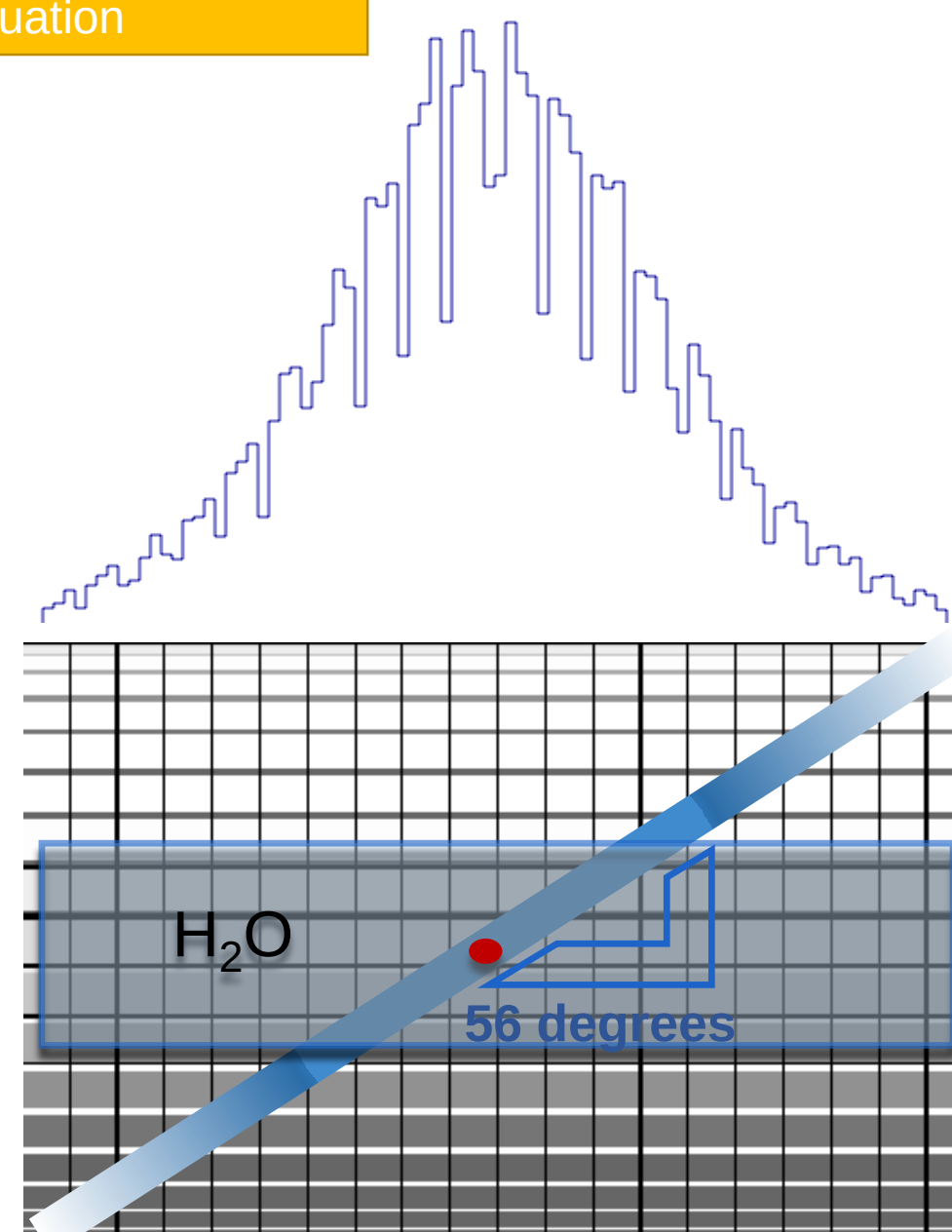


Point source

Small gains for central point source which are reduced further by attenuation



Solid angle reduces significantly with obliqueness due to larger distance to detector (32.5 cm → 60 cm)

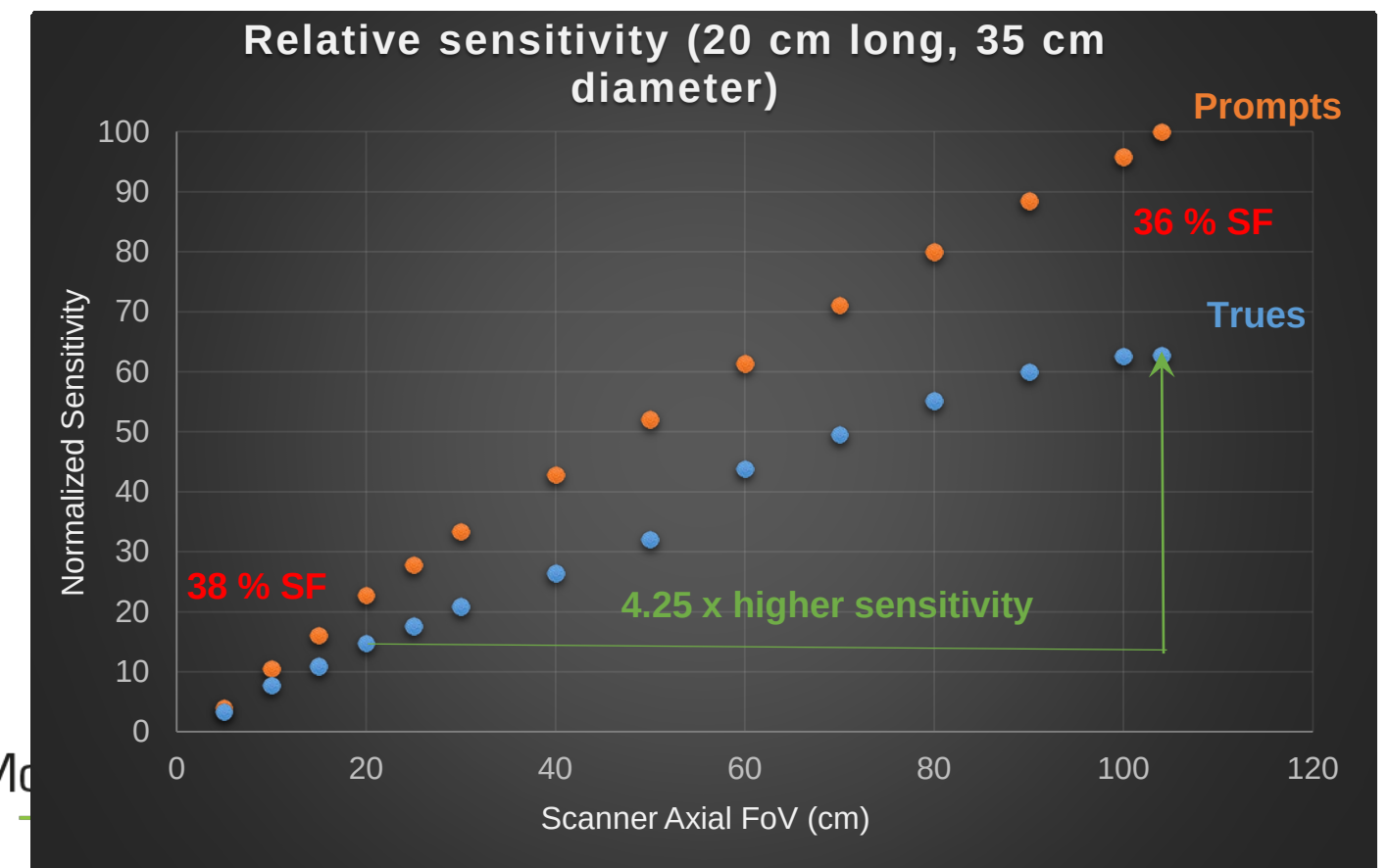
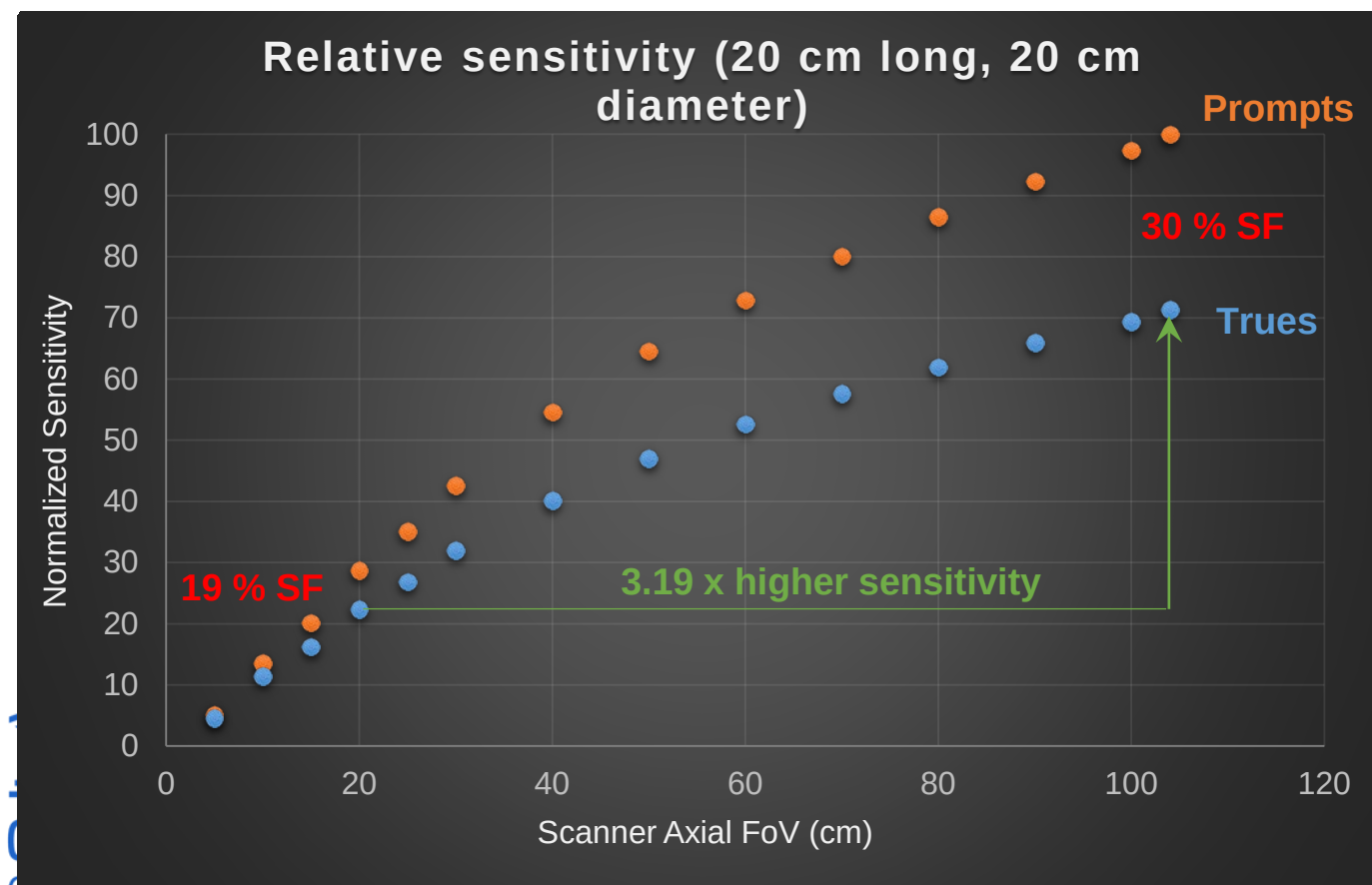
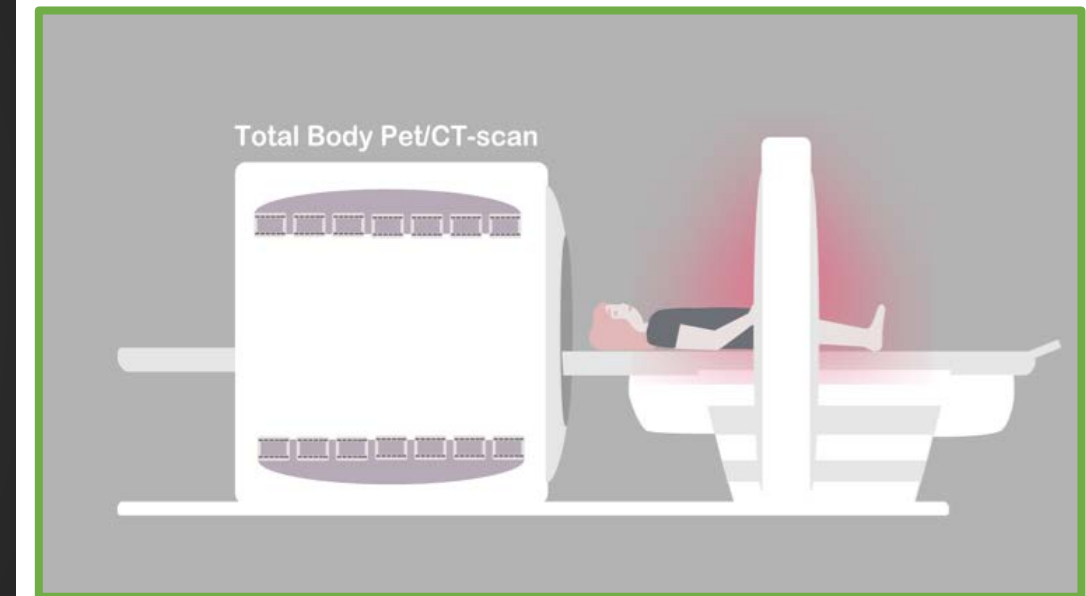
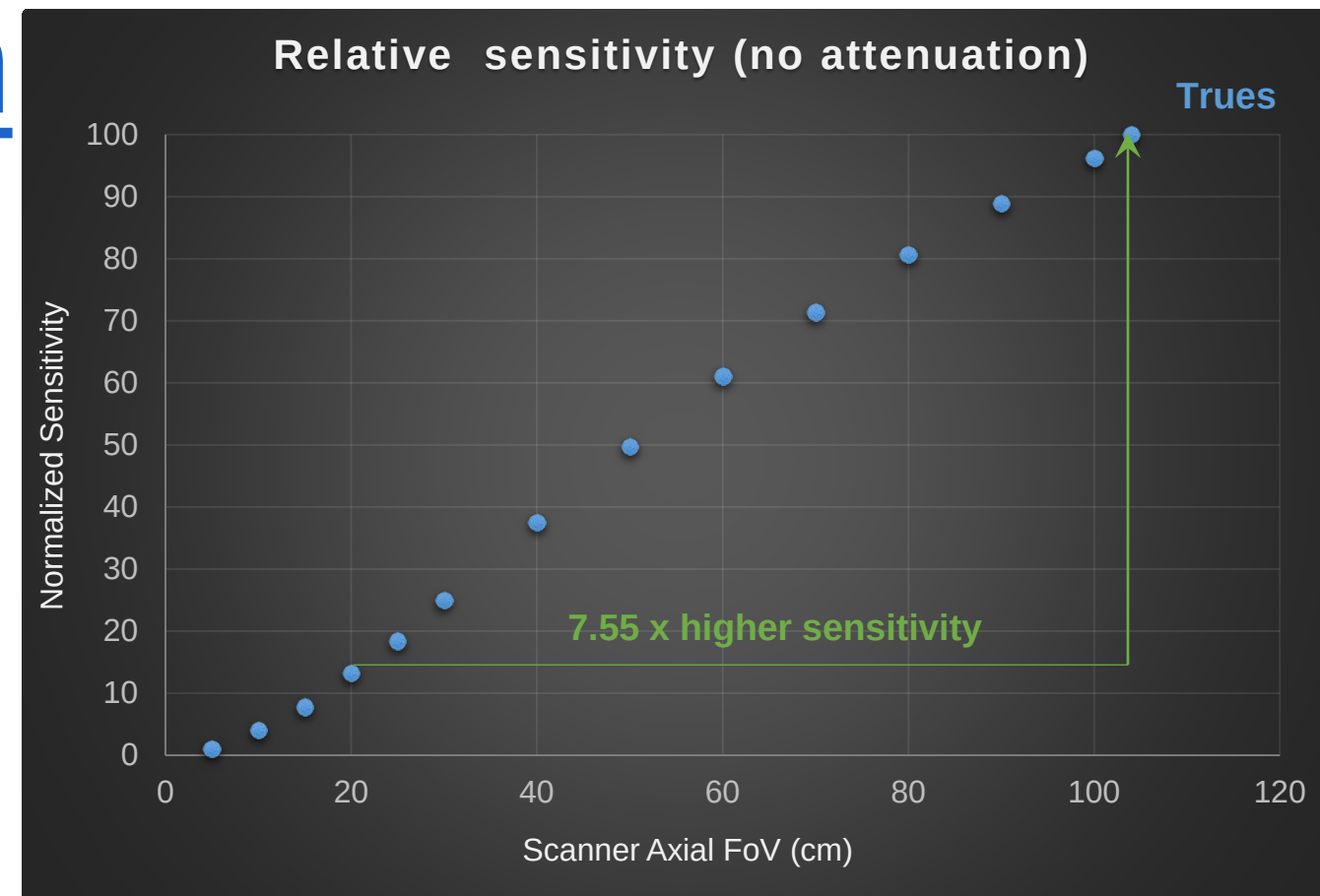


56 degrees
36 cm path through 20 cm phantom

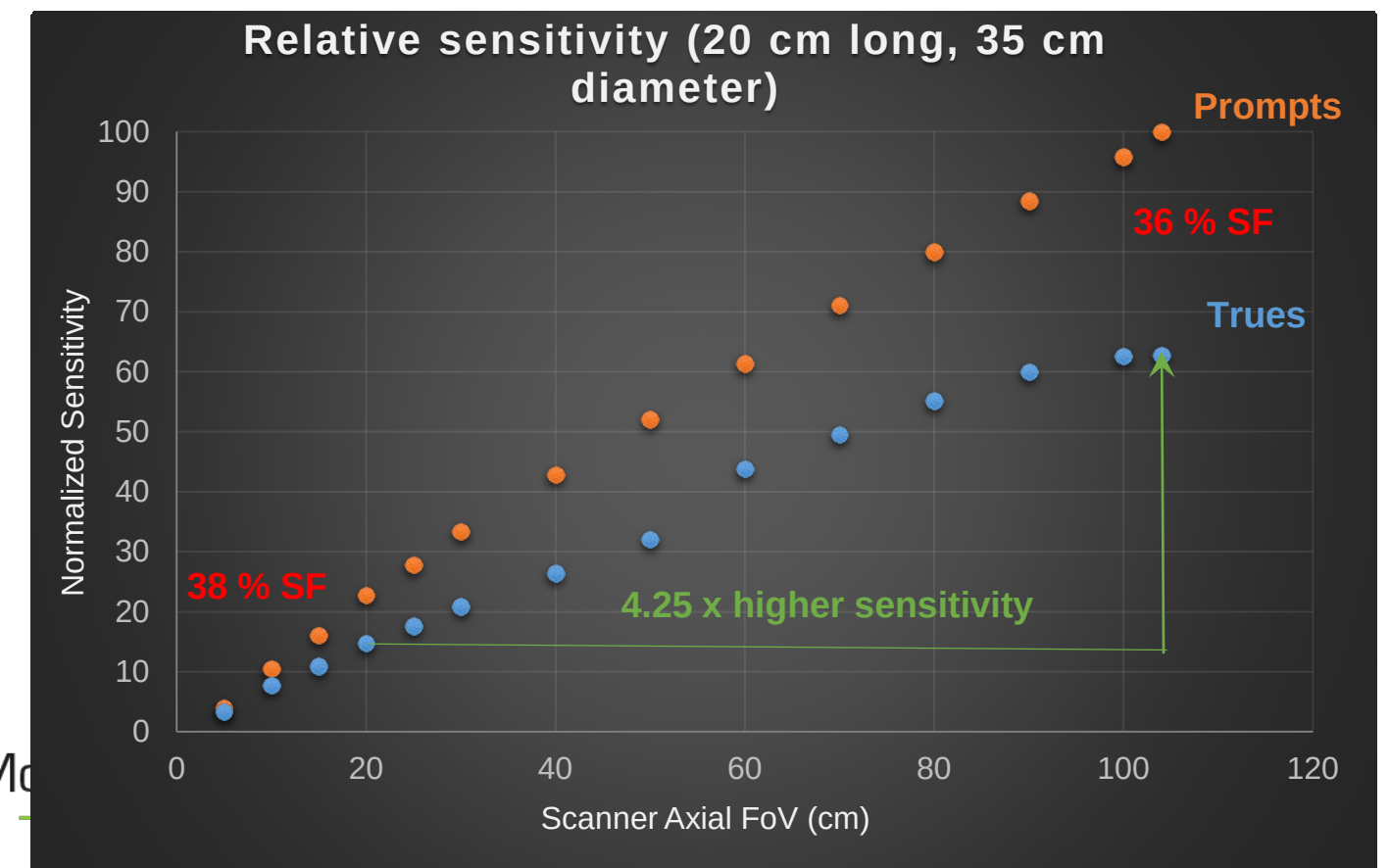
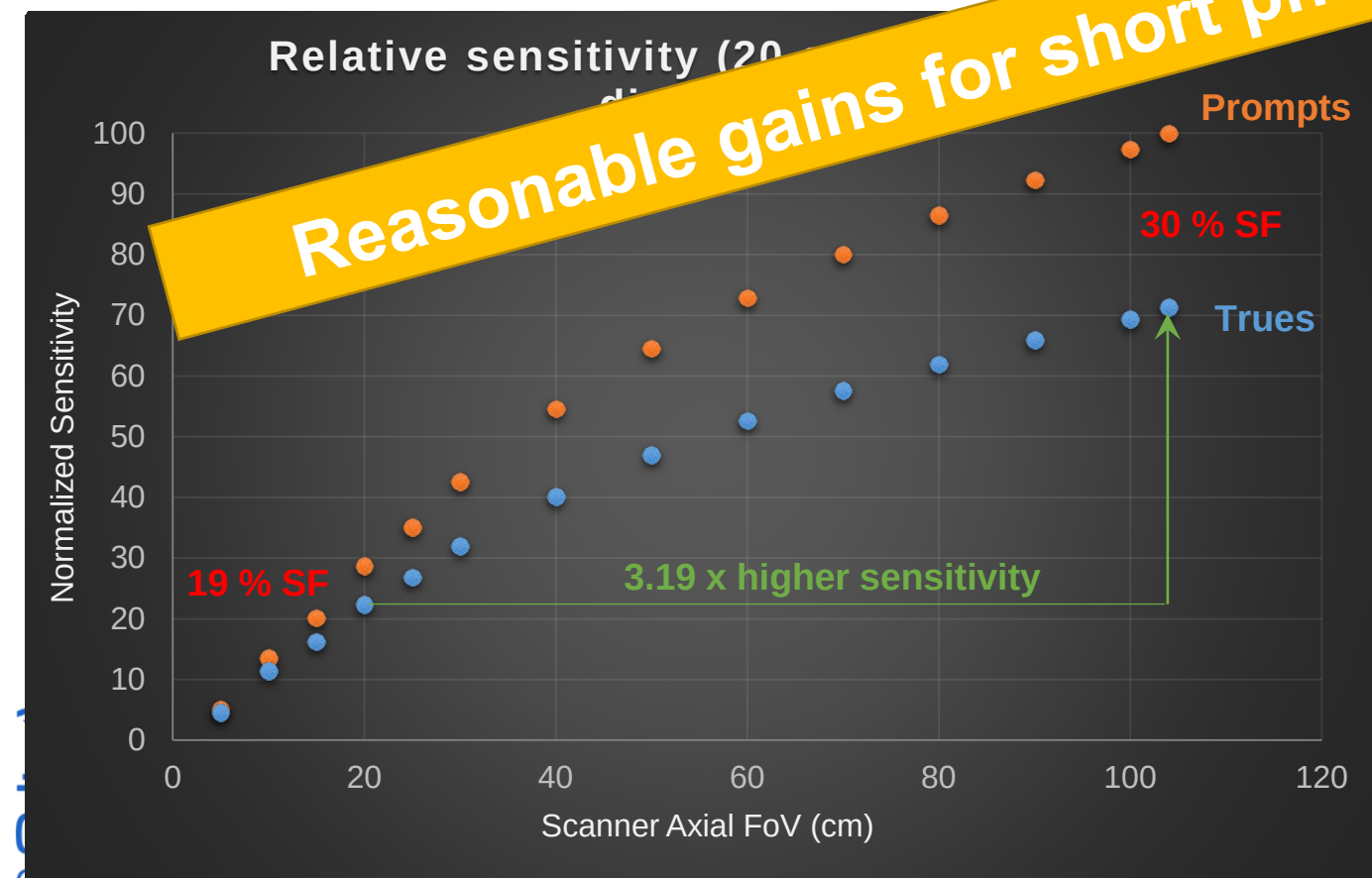
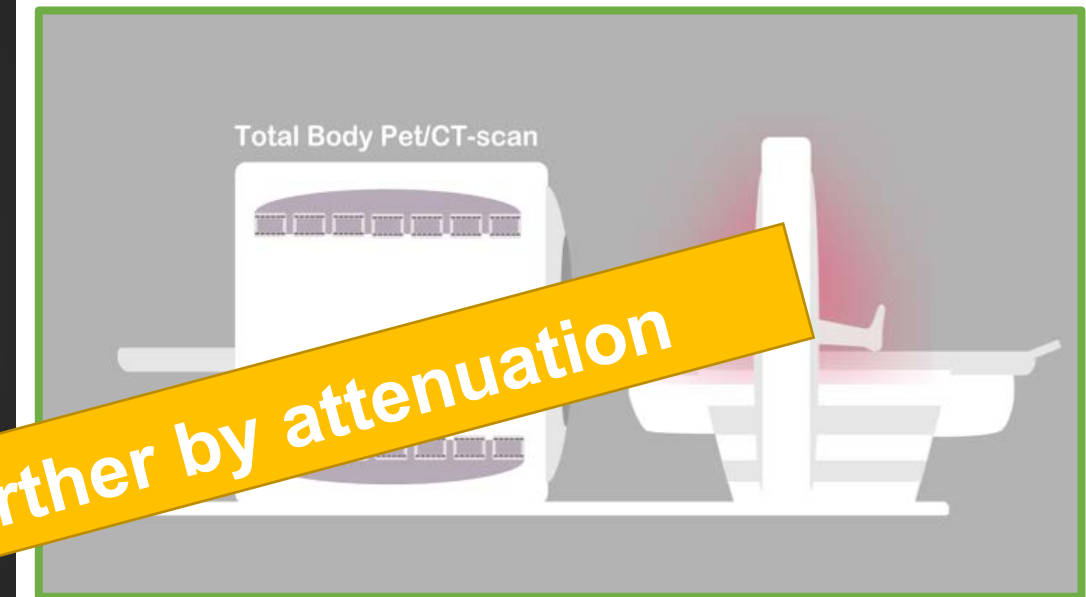
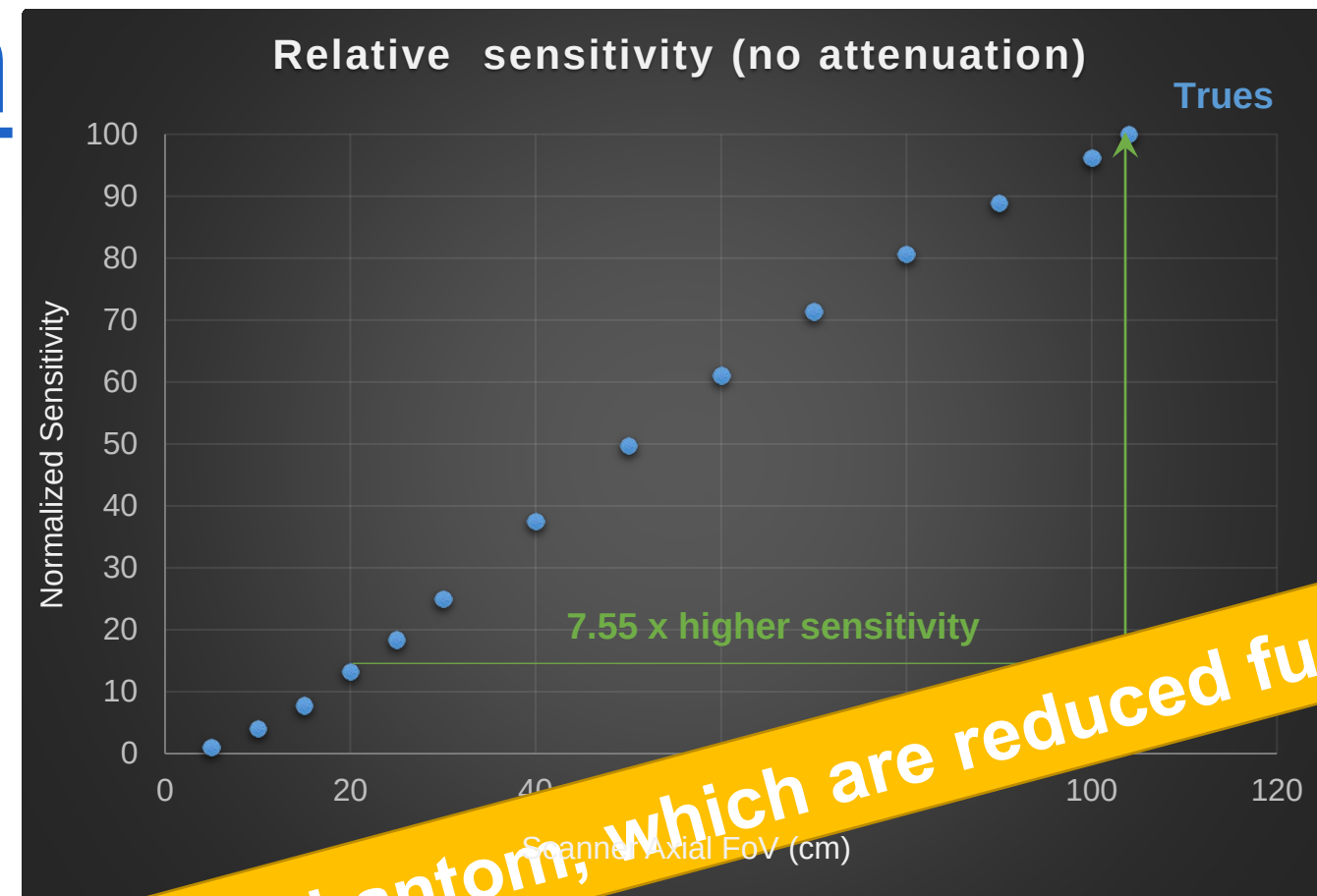
511 keV photon pairs not attenuated:

- 20 cm path: 14 %
- 36 cm path: 3.1%

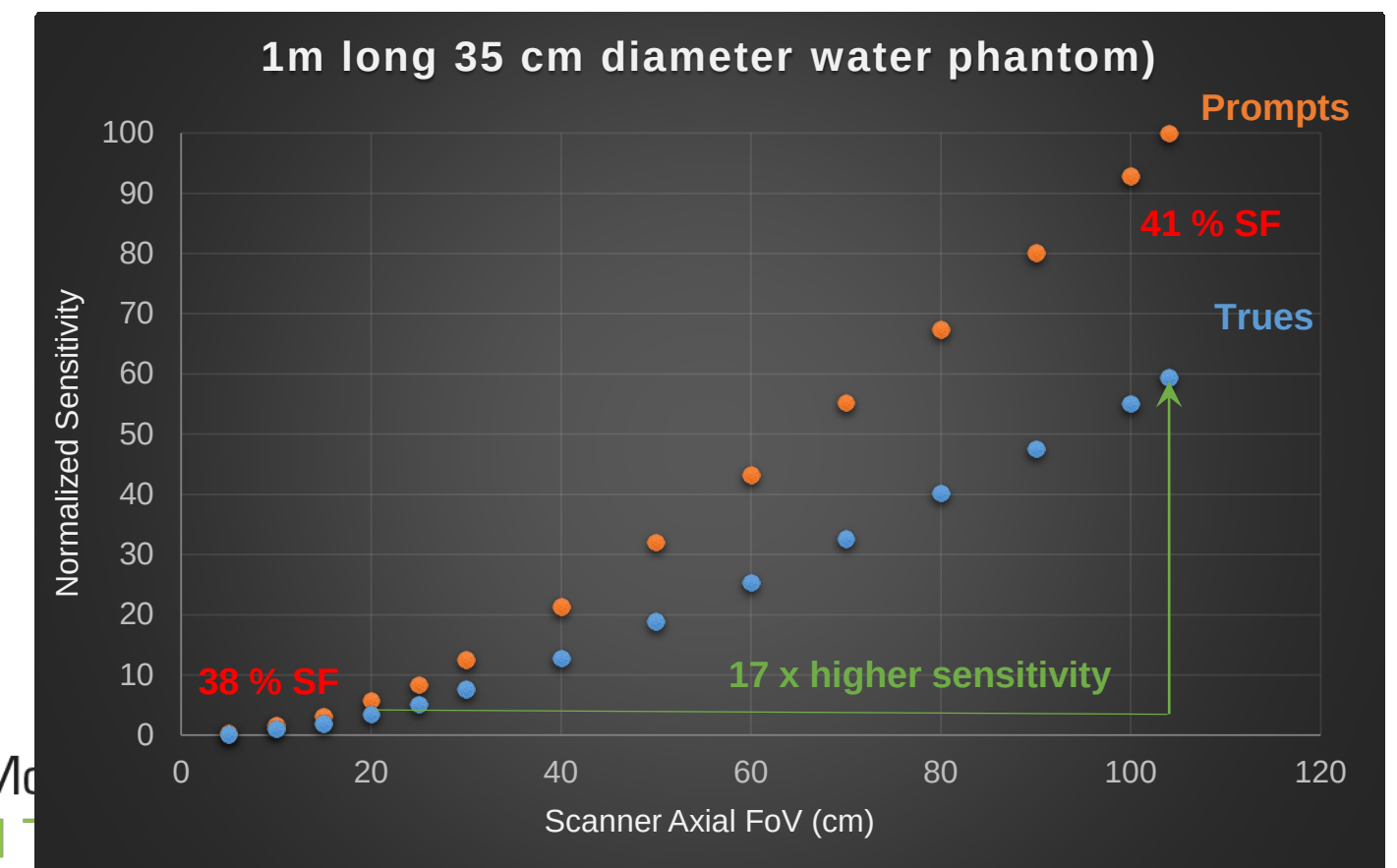
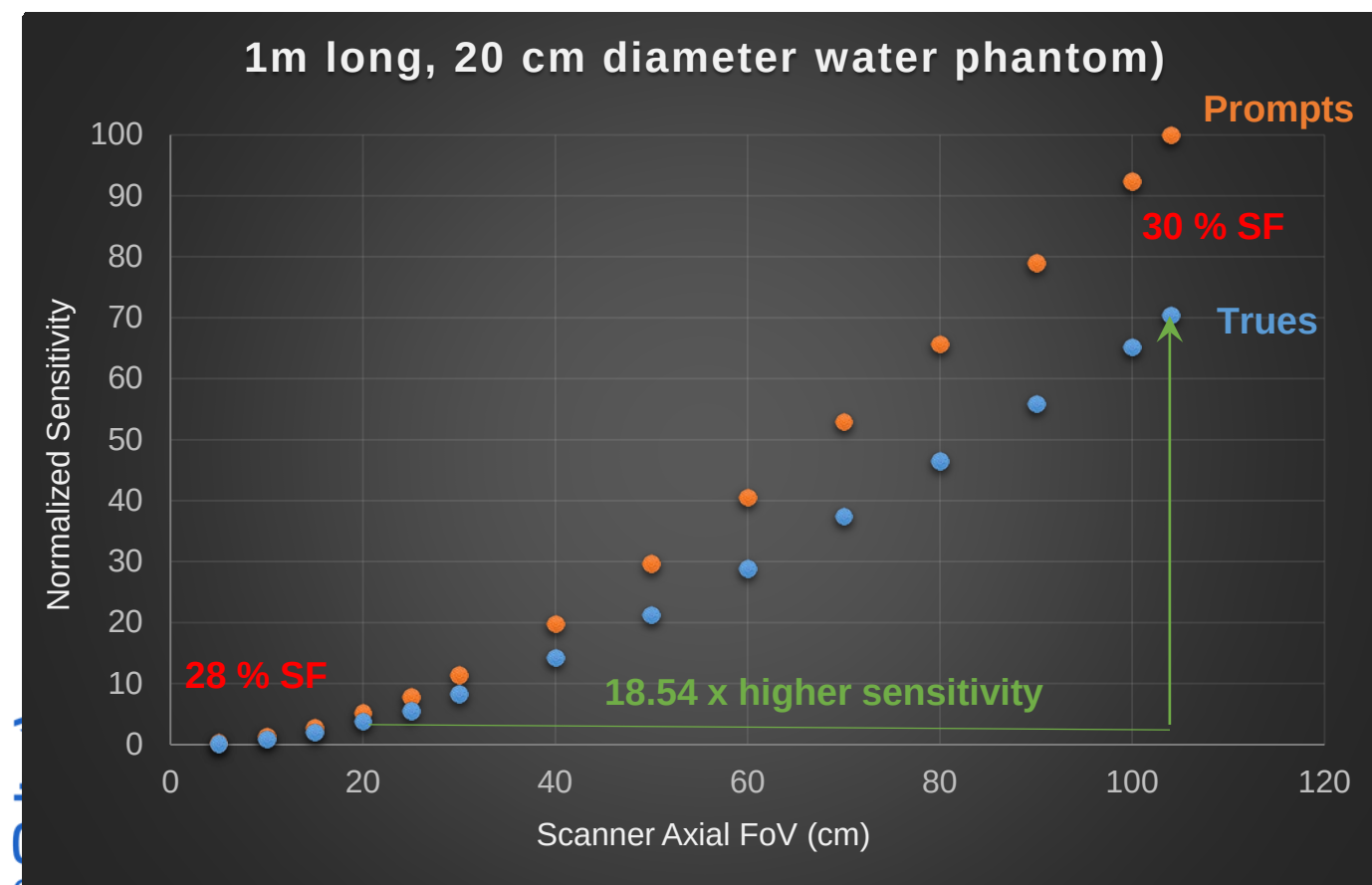
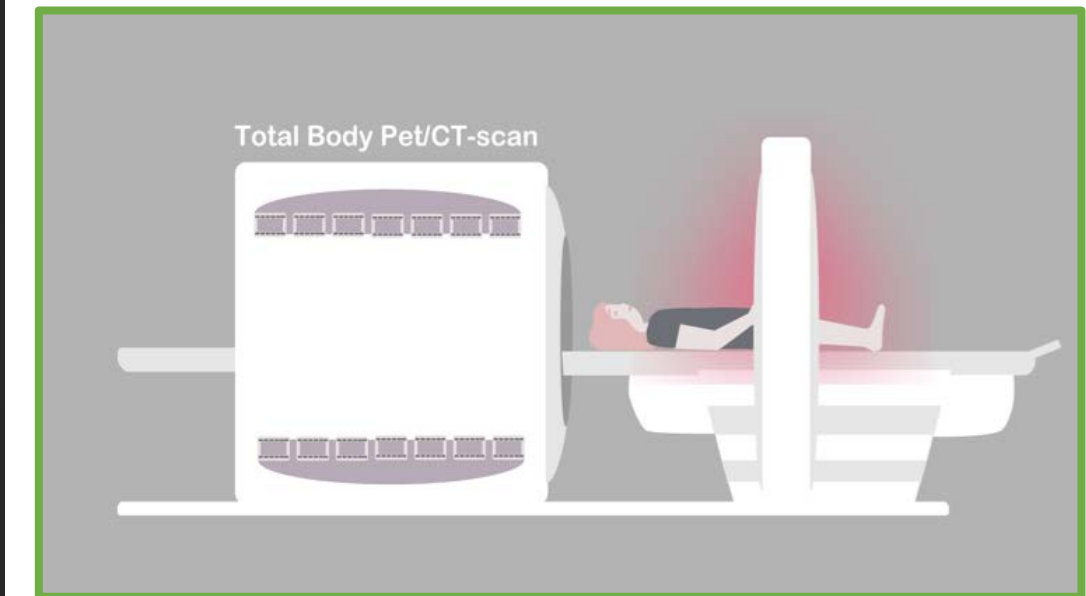
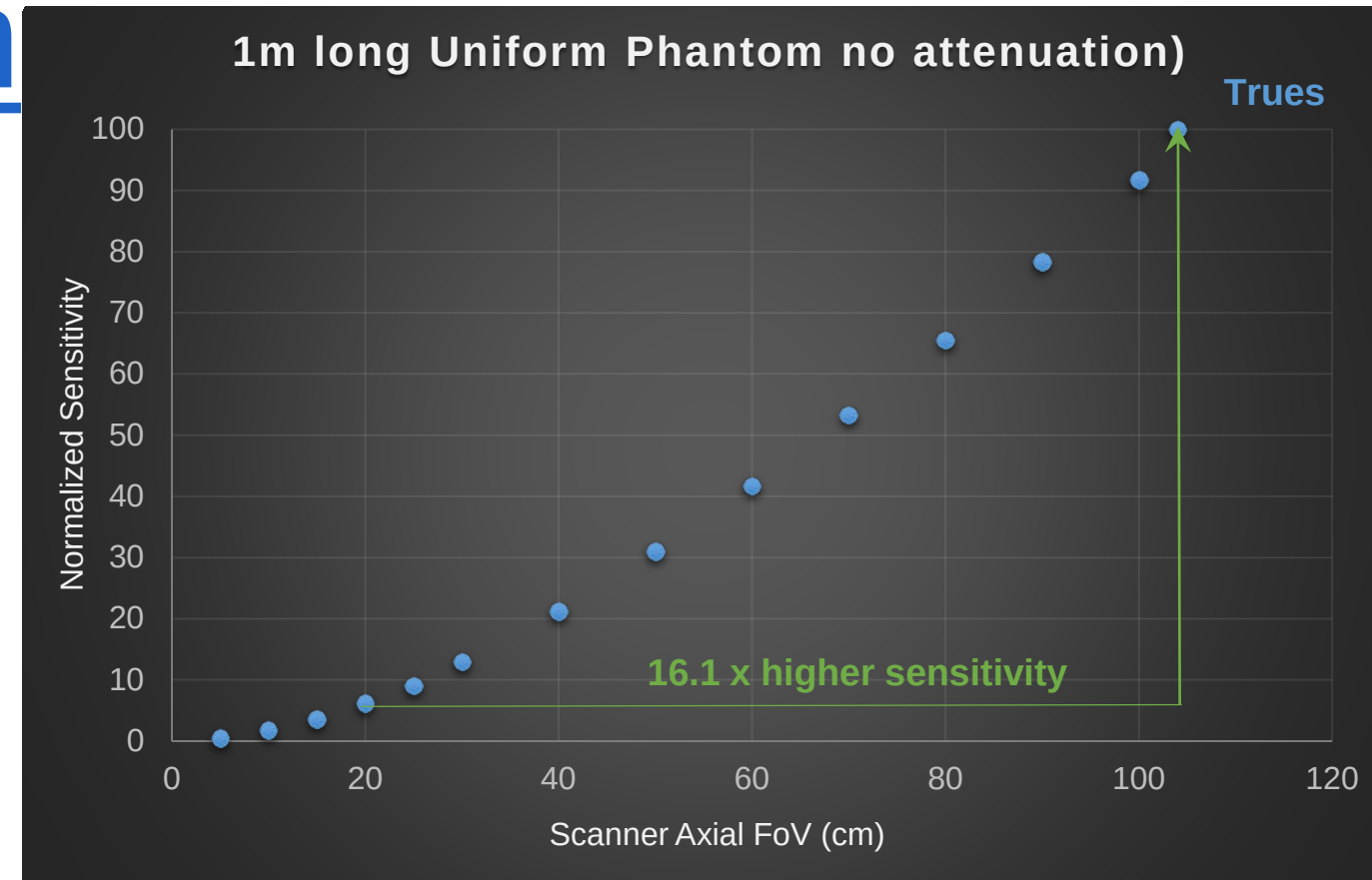
Short phantom



Short phantom



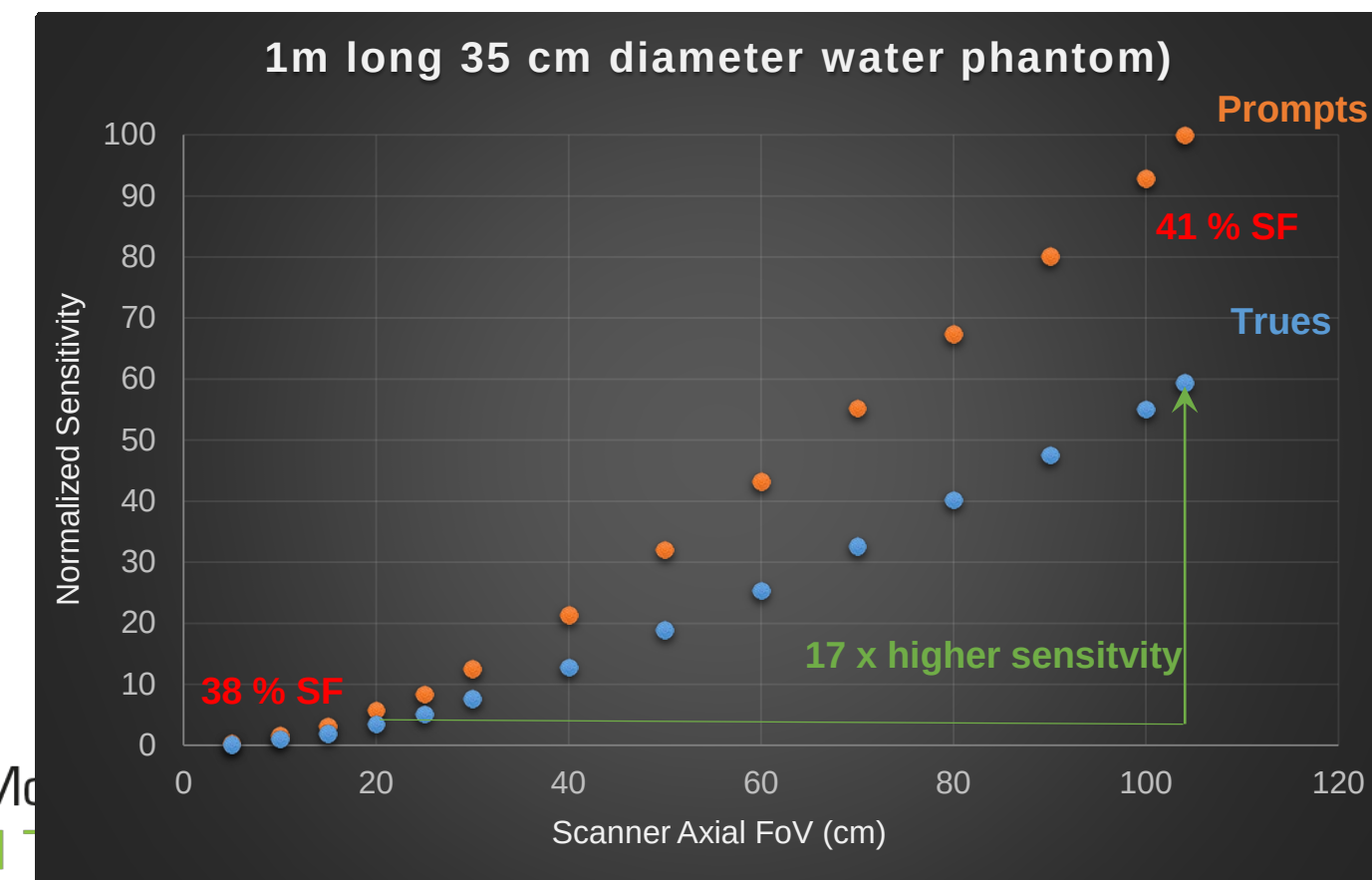
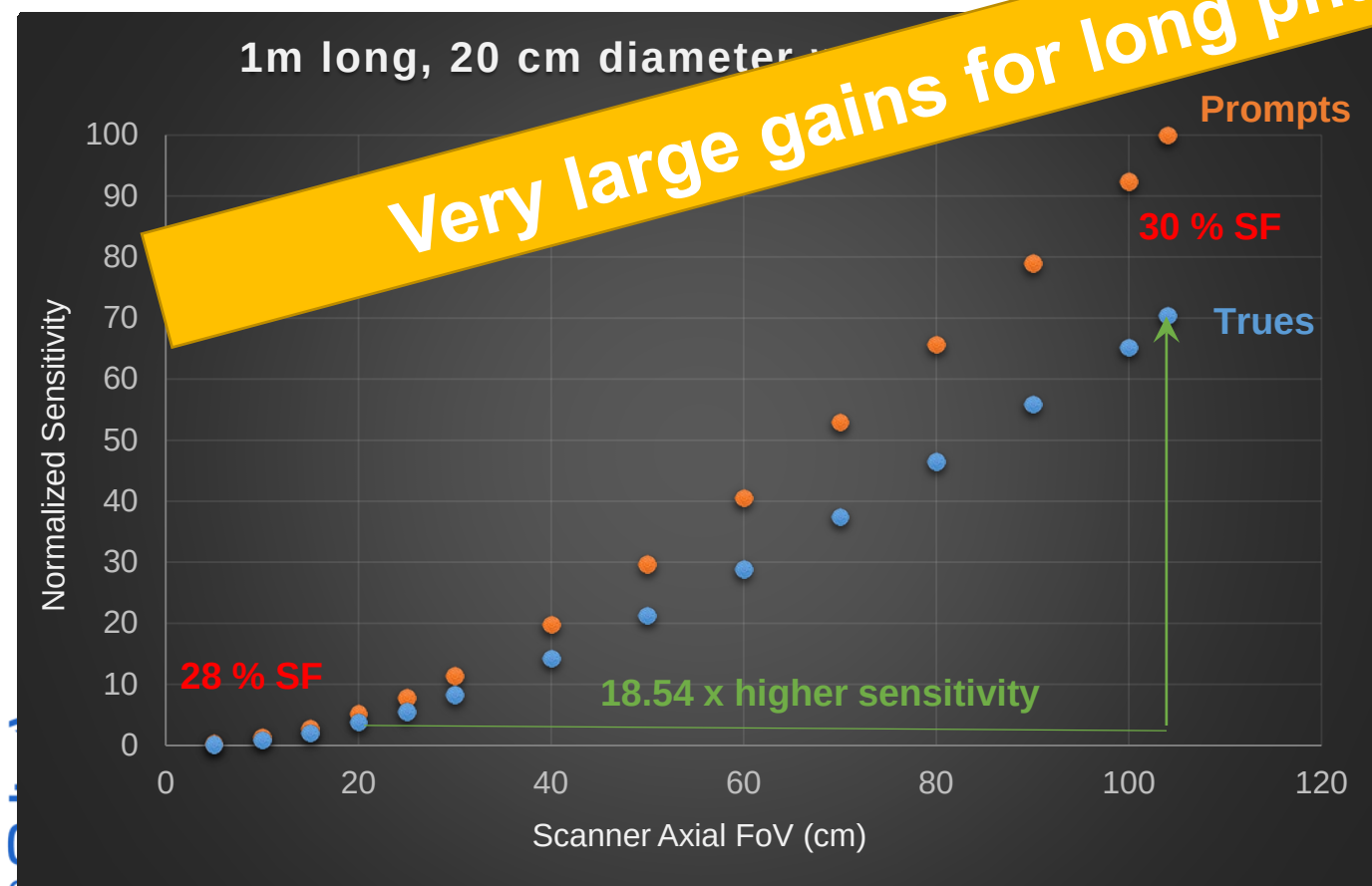
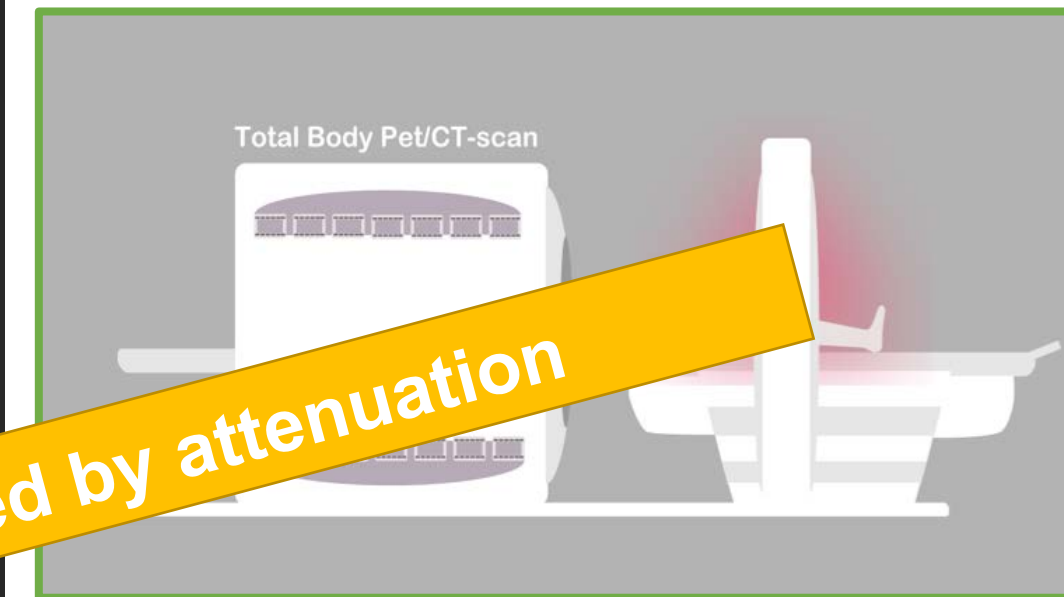
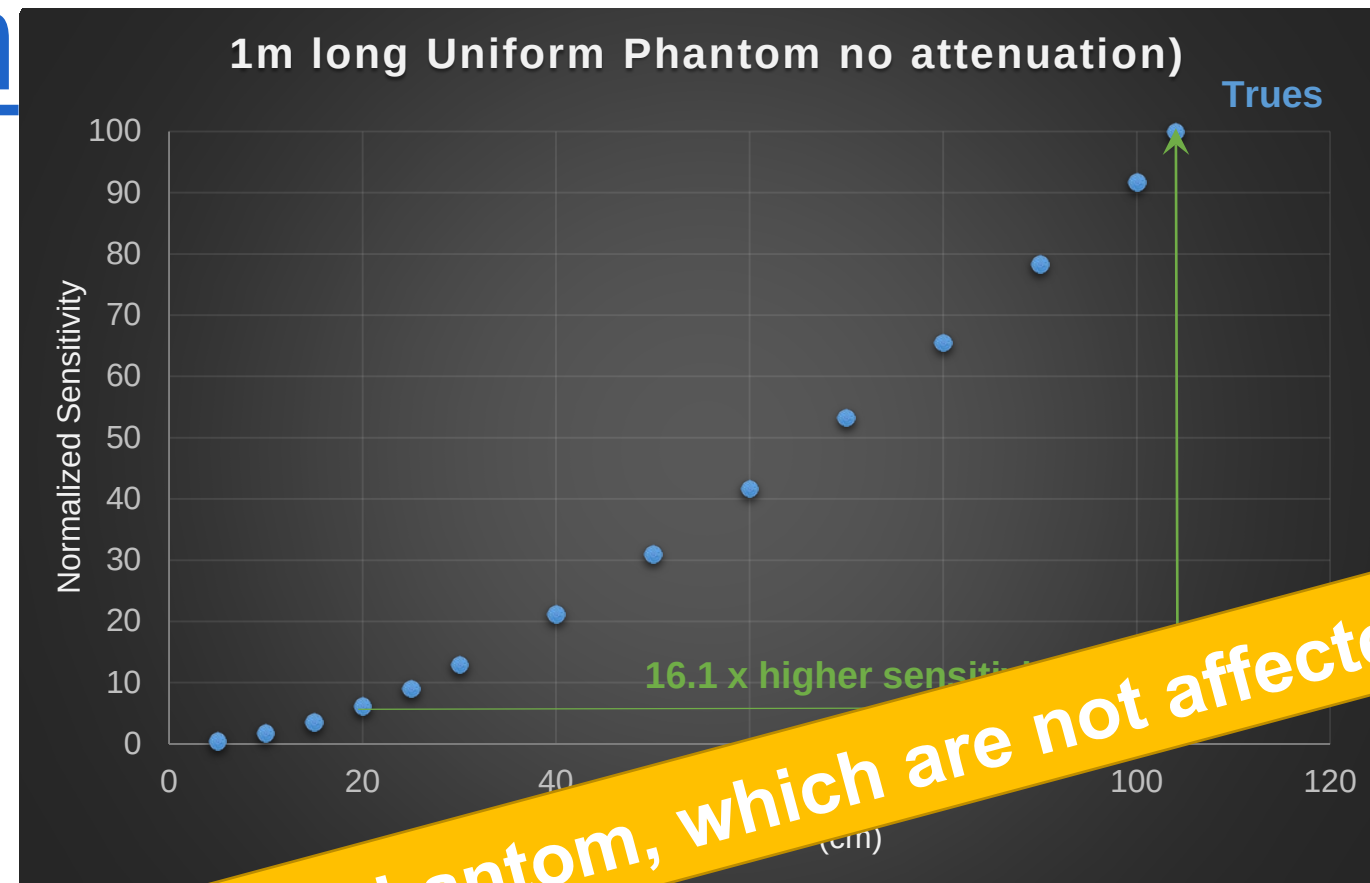
Long phantom



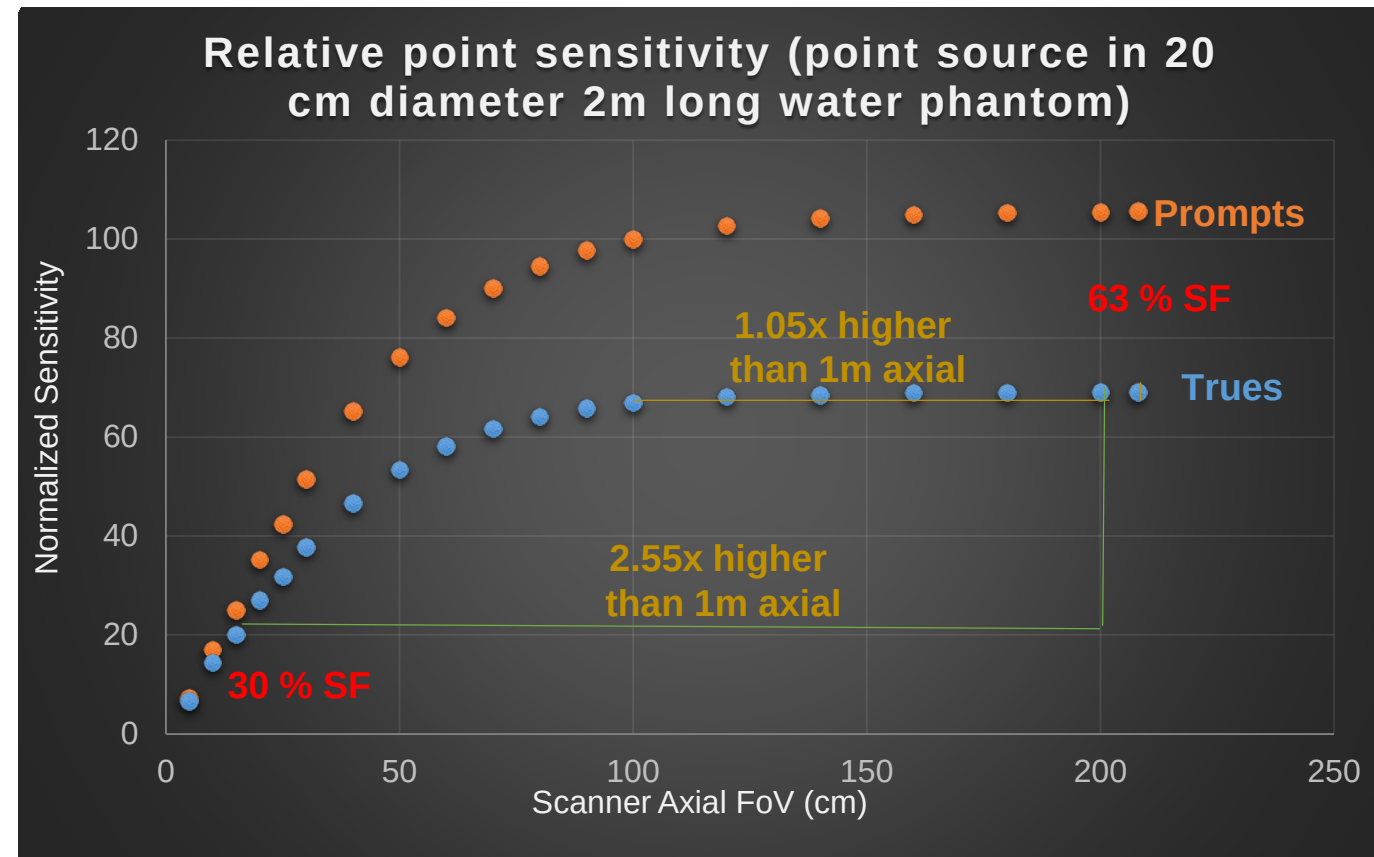
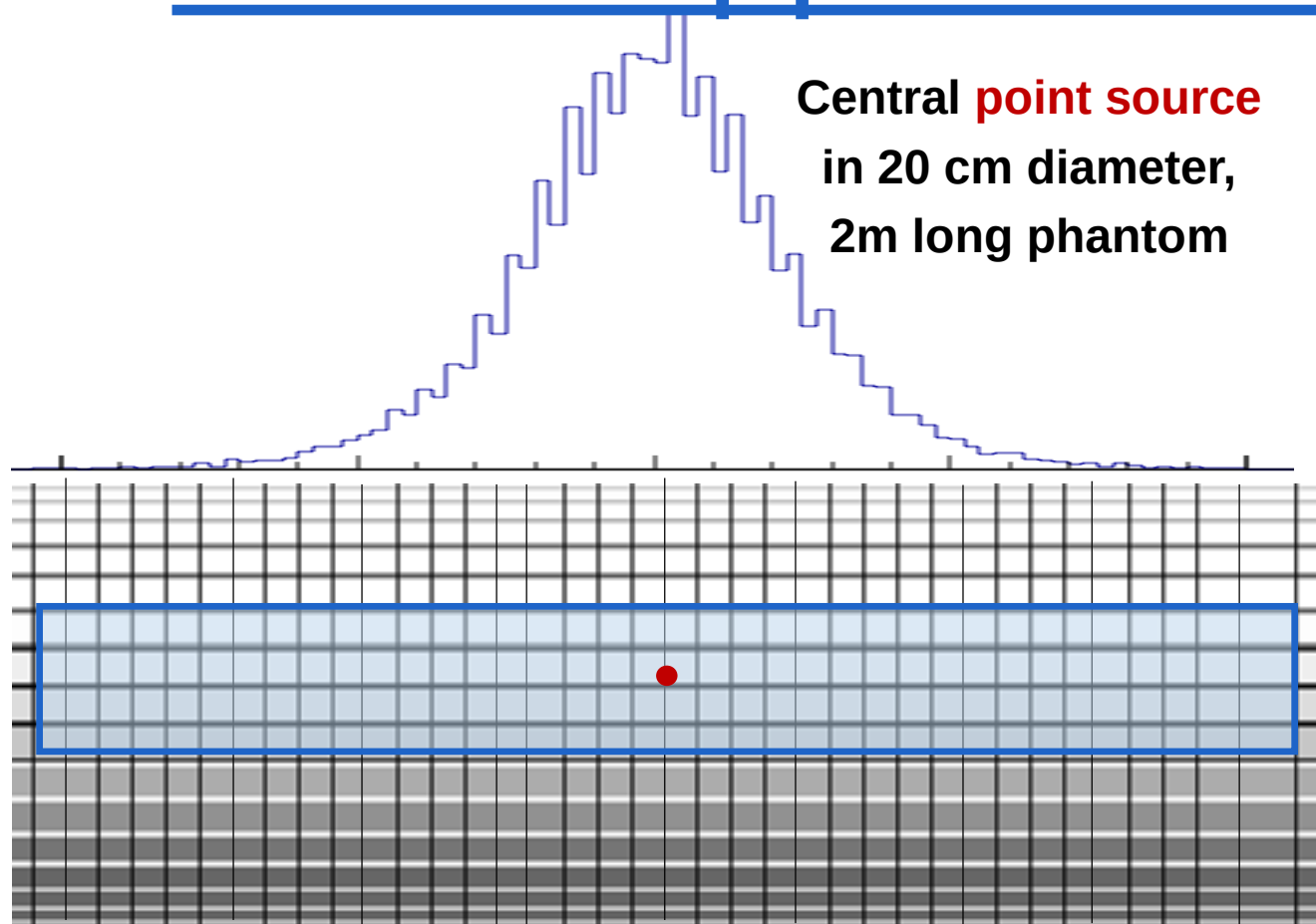
MIT

Innovative Medical
Imaging and Therapy

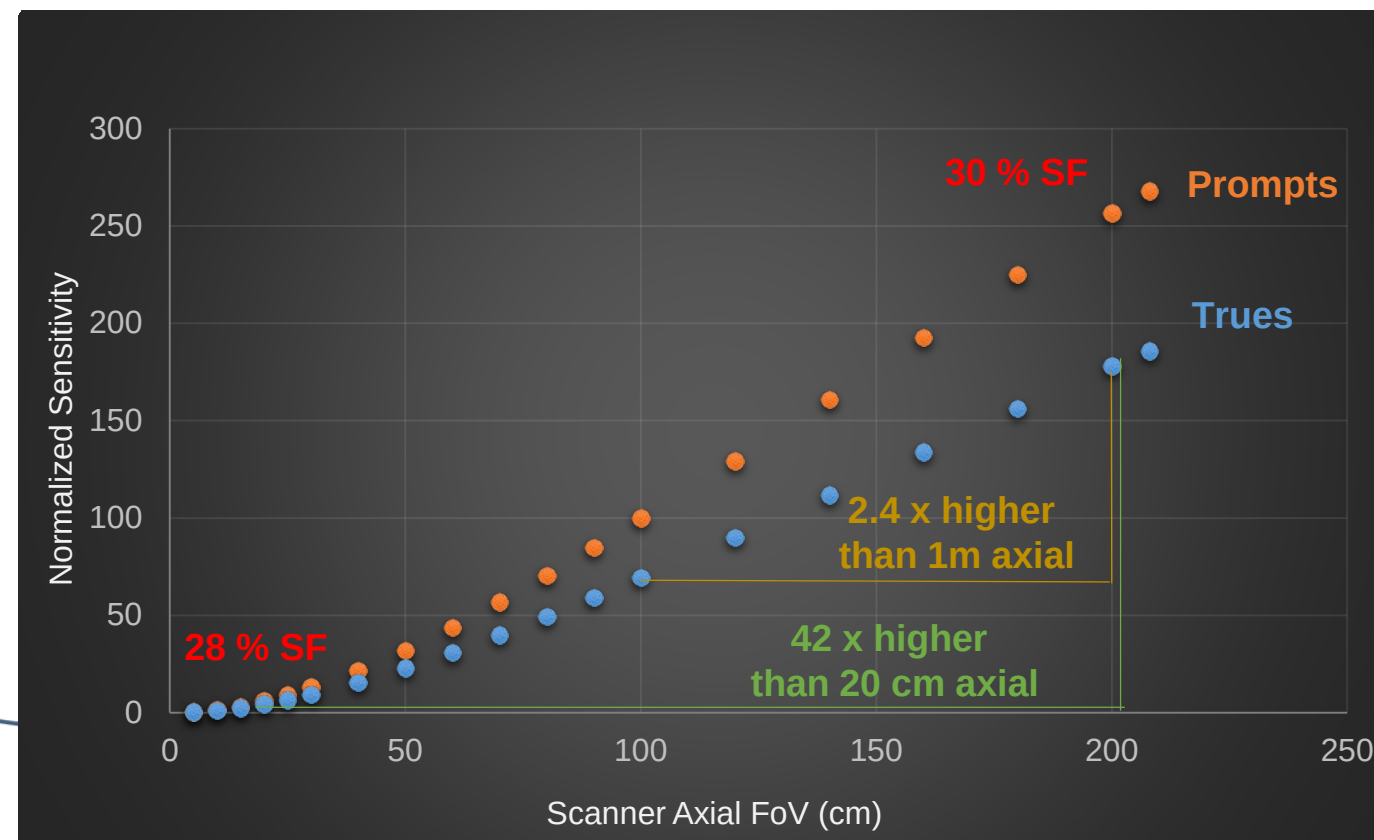
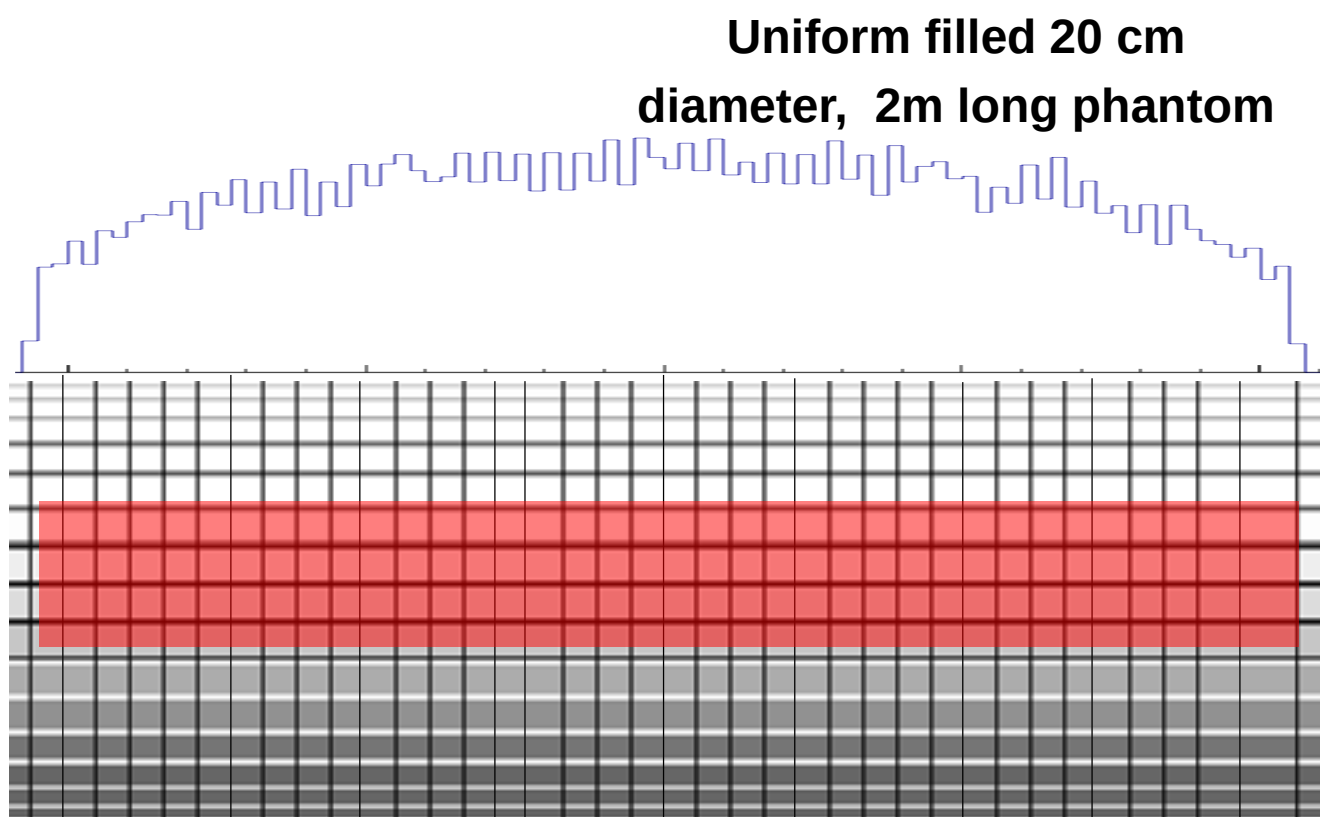
Long phantom



What happens in a 2 m long PET ?

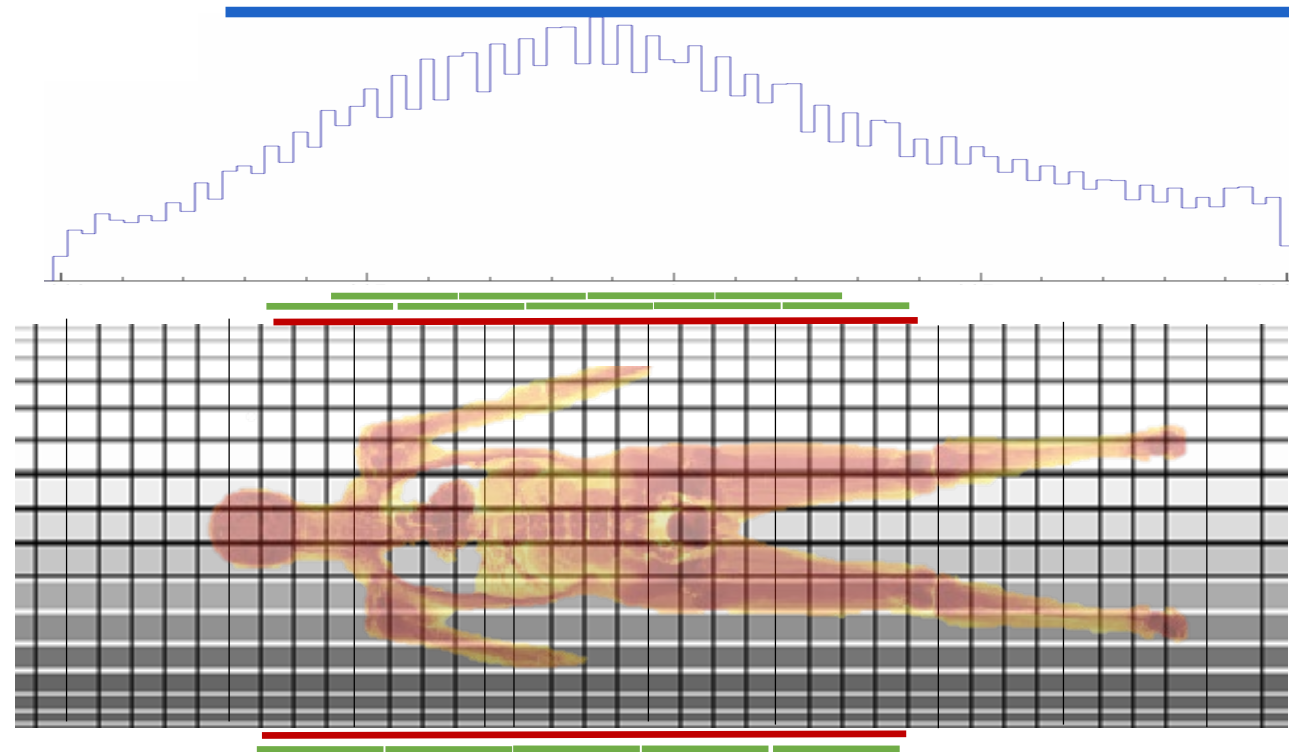


- 2m PET is only 2.5 times more sensitive than 20 cm
- **Only 5 % extra true** coincidences in 2 m versus 1m scanner
- More scatters than trues are added by extra 1 m



- 2m scanner is **2.4x more sensitive** than 1m scanner
- 2m scanner is **42x more sensitive** than 20 cm scanner
- 1m scanner is **18x more sensitive** than 20 cm scanner

Patient simulation

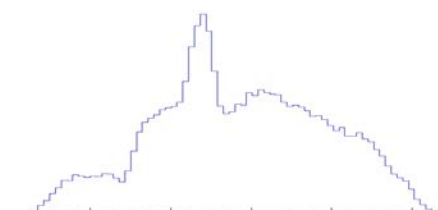


1m scanner vs 2m scanner
9 bed positions (50% overlap) of 20 cm

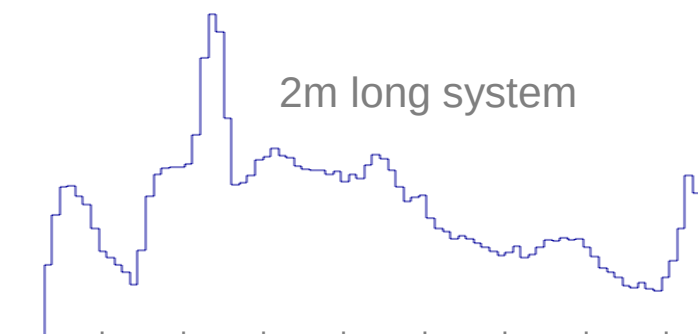
9 bed positions (50% overlap)
of 20 cm long scanner



1m long system

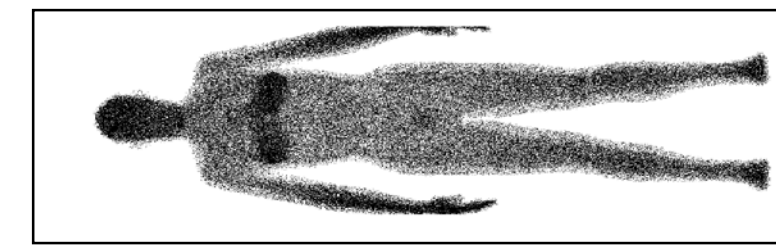


2m long system



Detected
coincidences

Summed axial
emission profile



emission map

with body
attenuation
(factor 12-14)

Simulation of 1 s
acquisition
total body activity
10MBq
=
270 microCi

without
attenuation

4837
Total Coincidences
0.048 %

20.1 x more

97302
Total Coincidences
0.97%

1.97 x more

192110
Total Coincidences
1.92%

69037
Total Coincidences
0.69 %

17.2 x more

1 119 342
Total Coincidences
11.92 %

1.85 x more

2 217 649
Total Coincidences
22.17 %



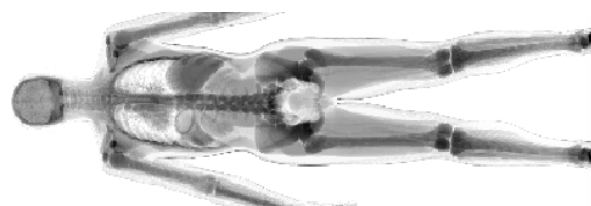
1cm thick slice

Emission map



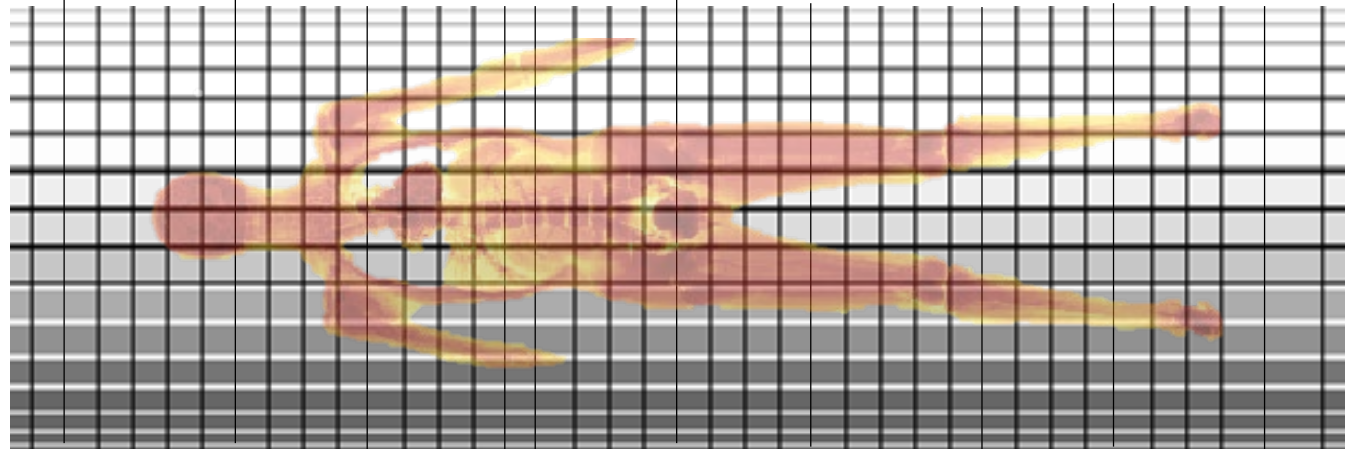
1m64, 74 kg female

Attenuation

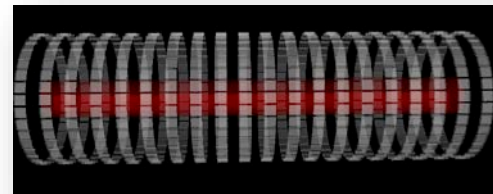
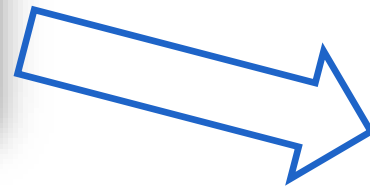
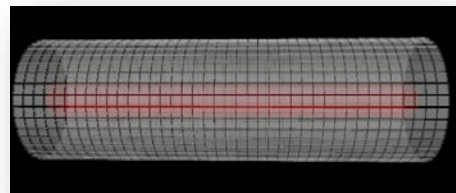


Alternative scenarios with a 1m system

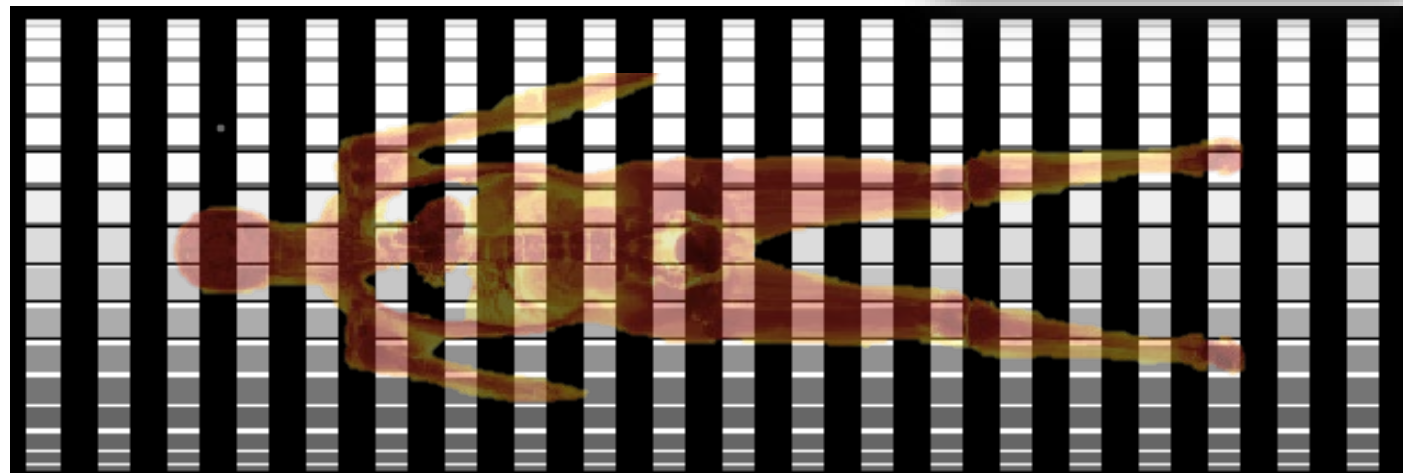
1m scanner can be reconfigured for 2m long objects (with some sensitivity loss)



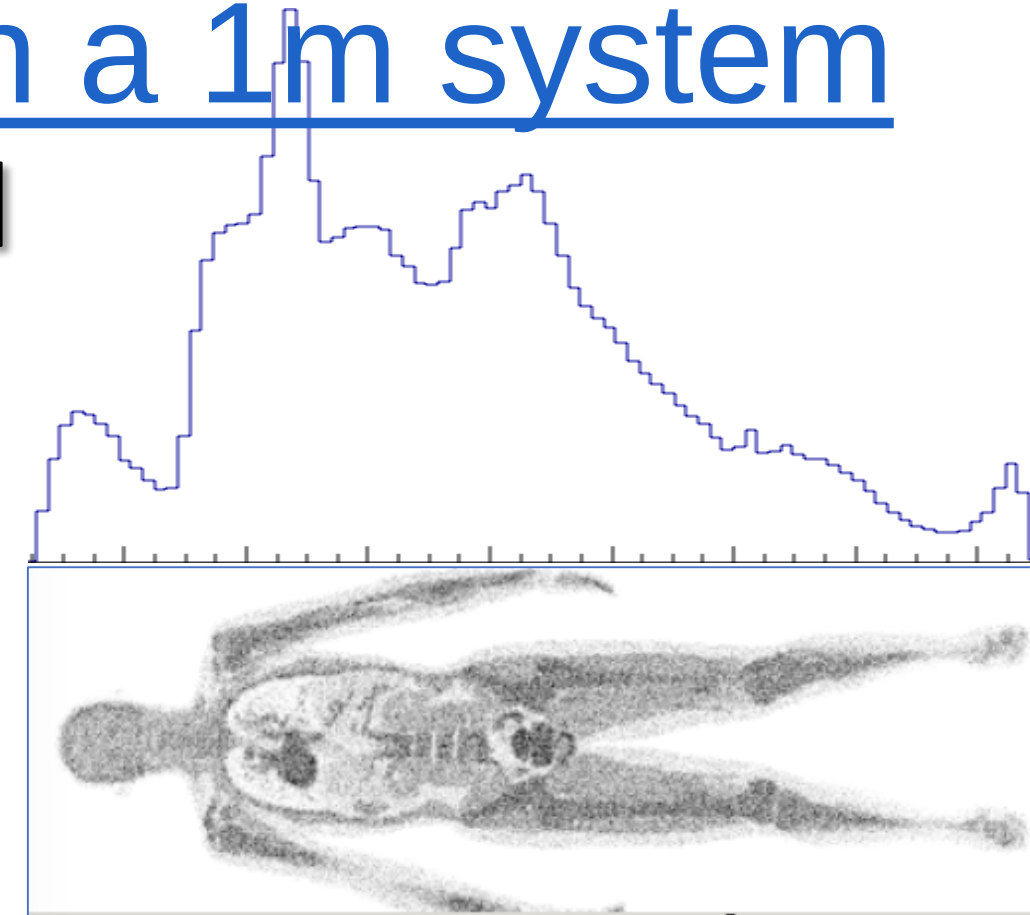
No gaps
2m long



without
attenuation

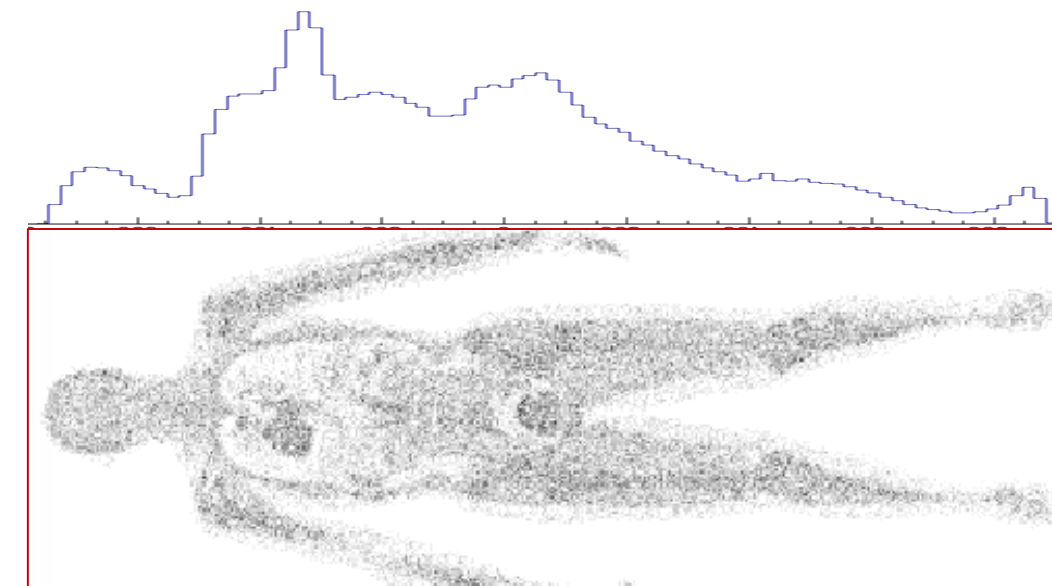


50 % gaps
2m long



2 217 649
Total Coincidences
22.17 %

1cm thick coronal
emission map
of detected coincidences

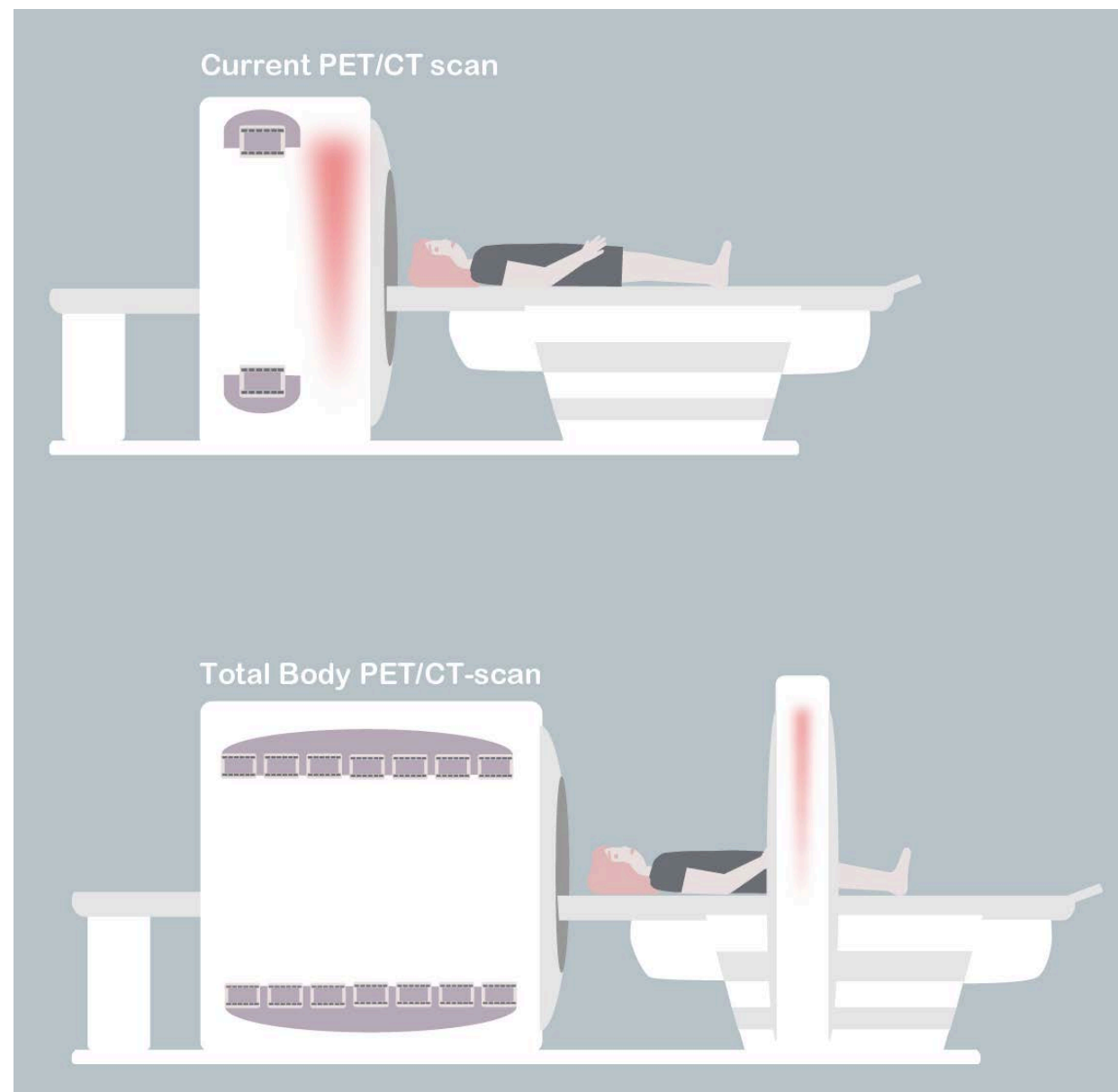


681088
Total Coincidences
6.81 %

1cm thick coronal
emission map
of detected coincidences

Conclusions

Proposed compact design

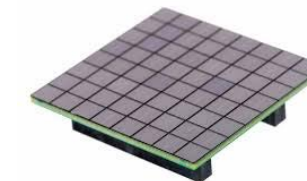


High resolution detector

16 mm
Monolithic
LYSO



SiPM



Expected 1.3 mm
intrinsic resolution

Time-of-Flight

Depth-of-Interaction

Cost effective scanner design

1 m long axial FOV

More scintillator than PET
with 20 cm axial FOV

Thinner crystal

Less scintillator than
2 m Explorer

Smaller (65 cm) bore

Predicted Performance

PET 20.0

20.0x Sensitivity

2.00x Sharper

20.0x faster routine PET

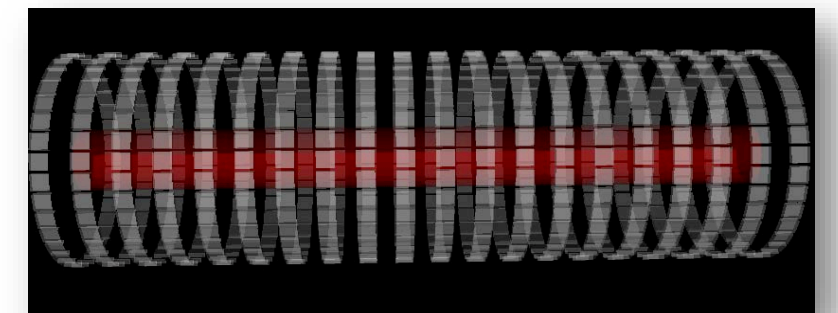
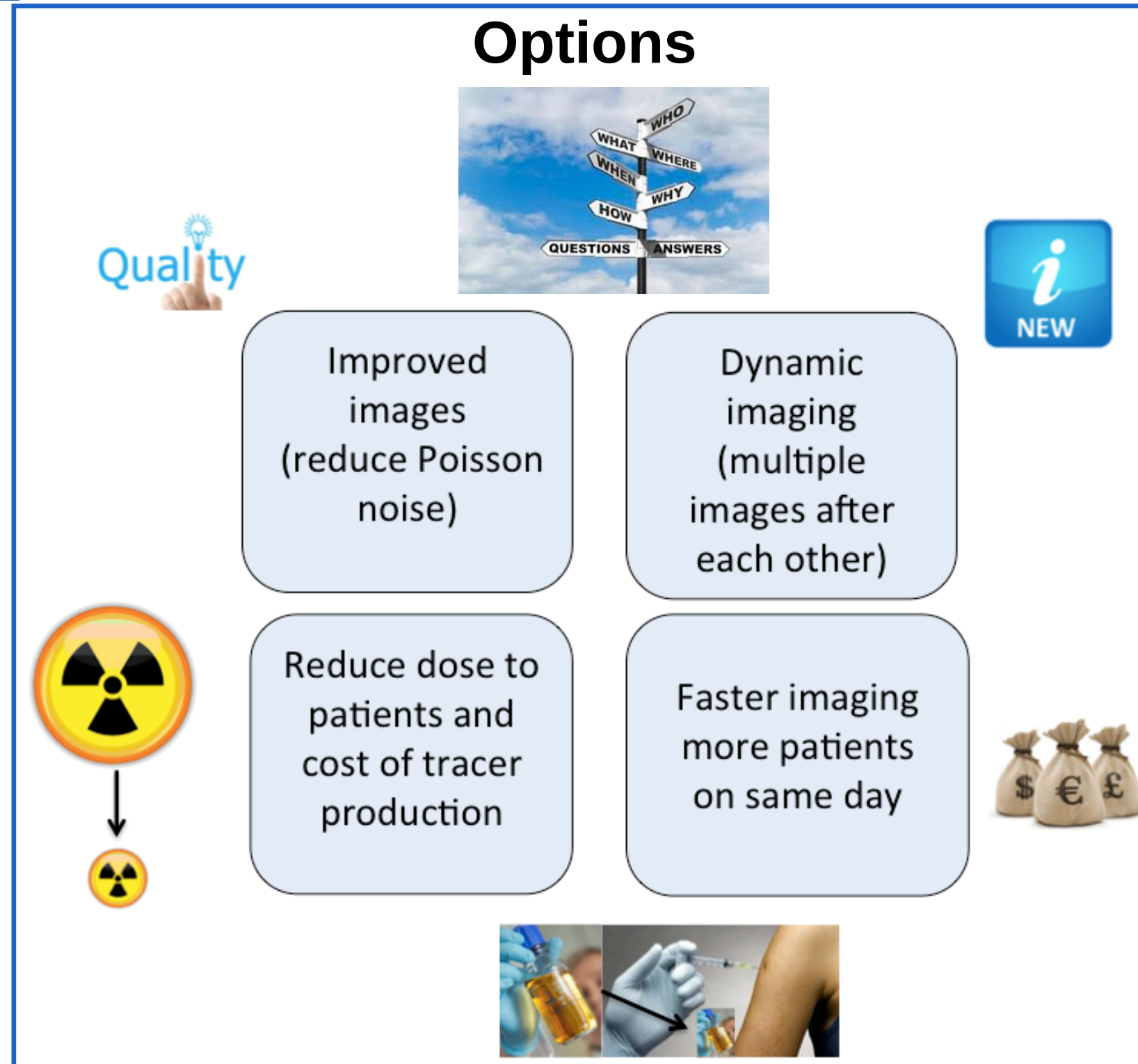
20.0x dose reduction

20.0s time frames

Up to 2.00m long objects

Conclusions

Options



Reconfigurable to 2m

Peoples involved



And many others...

