Integration of advanced 3D SPECT modelling for pinhole collimators into the open-source STIR framework

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STIR User's and Developer's Meeting
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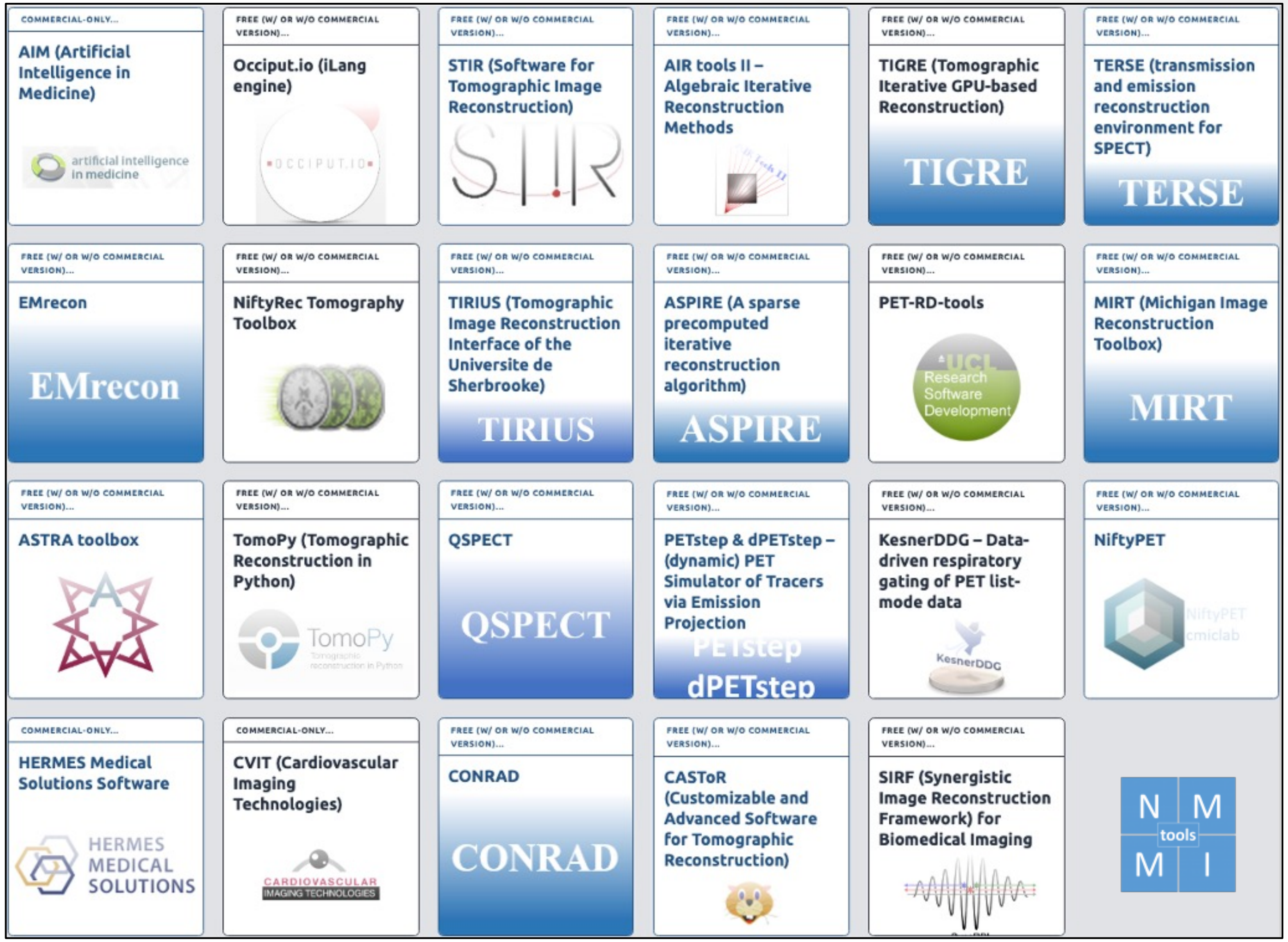
Disclosures

- The IWK Health Centre and Cubresa share an academic-industry research collaboration

Preclinical and clinical pinhole-SPECT is becoming increasingly important

Tomographic reconstruction software is widely available



Tomographic image reconstruction software (NMItools)

← Open source and commercial software for PET, SPECT, and CT image reconstruction

- Analytic and iterative 3D and 4D reconstruction algorithms
- Mathematical, physical and physiological modelling
- Data manipulation and presentation

What do they all have in common?

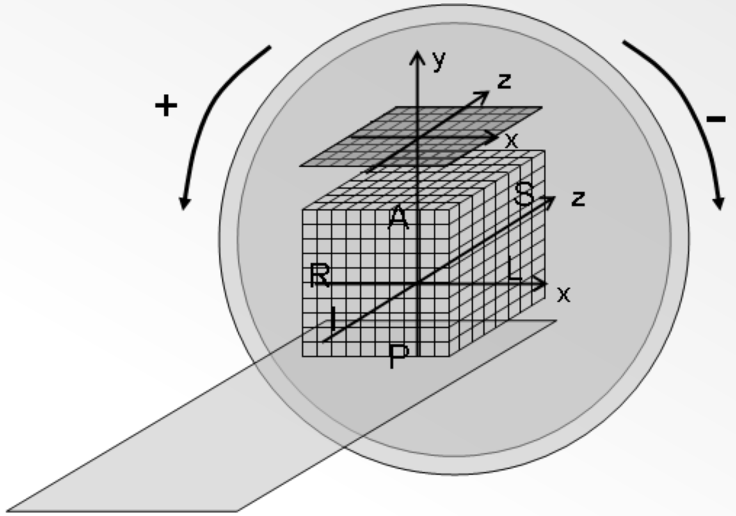
- **No open-source support for pinhole-SPECT**

Pinhole-SPECT images can now be reconstructed with the open-source STIR framework

System matrix estimation software translates data between detector and image space

- Reconstruction for **single- and multi-pinhole SPECT** applications
  - **Data and configuration files**
    - Interfile format
    - Collimator, detector, and reconstruction/correction parameters
  - **Corrections**
    - Full/simple attenuation (ATT)
    - Point spread function (PSF)
    - Depth of interaction (DOI)
  - **Masking**
    - Default cylinder, attenuation map, explicit mask

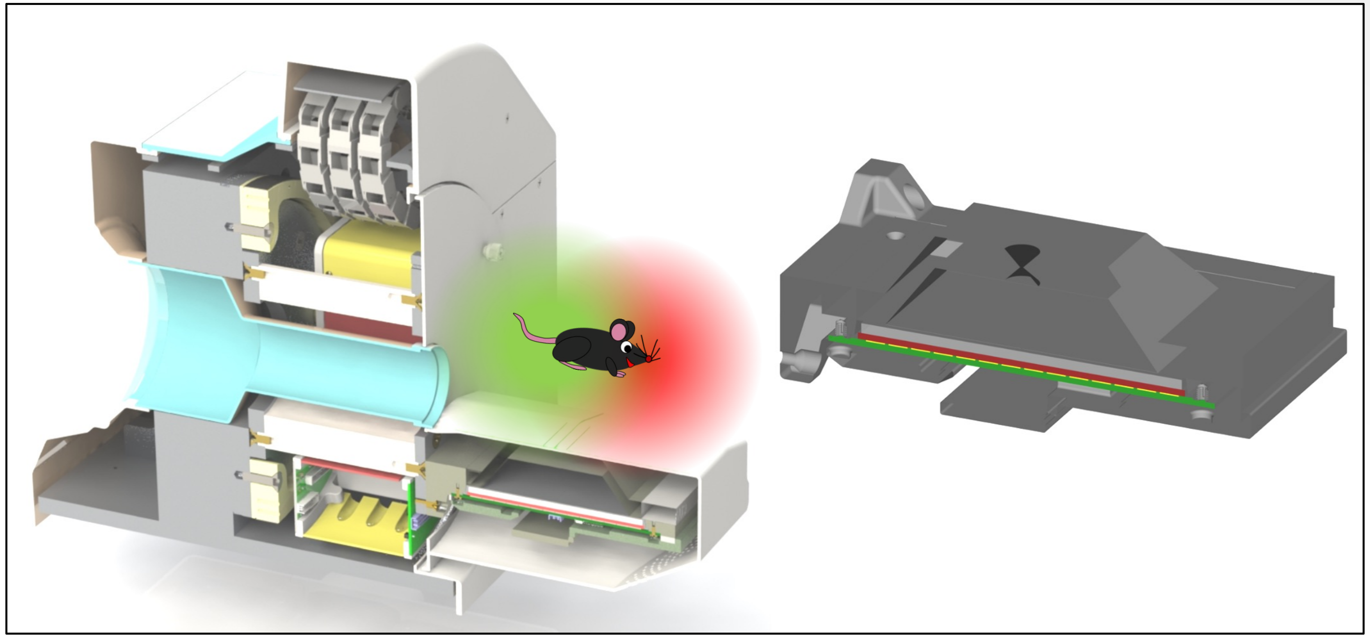
STIR is the first open-source platform providing configurable support for complex pinhole-SPECT geometries!



System matrix and coordinate system illustration

(Thielemans, 2012; Fuster, 2013)

STIR's forthcoming pinhole-SPECT capabilities are demonstrated with the Cubresa Spark preclinical system



Manufacturer's model and GATE model cutaway of the Cubresa Spark

- 10 mm-thick tungsten collimator
- 3 mm-thick CsI(Na) scintillator
- 14×14 SensL C-series SiPM array with 6 mm sensors

- **This study utilizes measured and simulated pinhole-SPECT data**

Cubresa Spark geometric and ^{99m}Tc performance specifications

Parameter	Value
Pinhole diameter	1.0 mm
Radius of rotation (ROR)	28.0 mm
Detector ROR	54.75 mm
Intrinsic resolution	0.85 mm
Energy resolution	14.7%
Planar sensitivity at ROR	33.8 cps/MBq

GATE simulation model validated against the **NEMA NU 1-2018 Standard for Performance Measurements of Gamma Cameras** with **differences on the order of ~3%**

(Strugari, 2022)

Image quality was analyzed with simulated phantoms of ^{99m}Tc

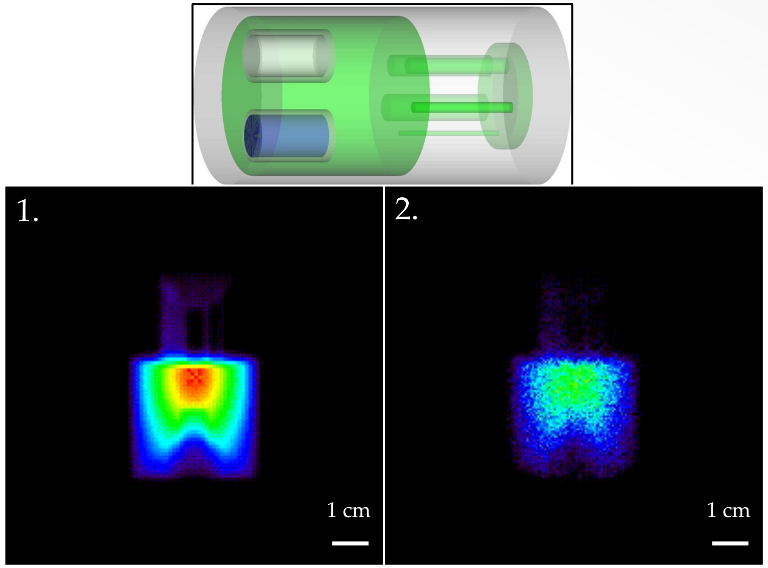
Micro-PET IQ phantom
($\varnothing_{ID}$ = {1, 2, 3, 4, 5} mm)

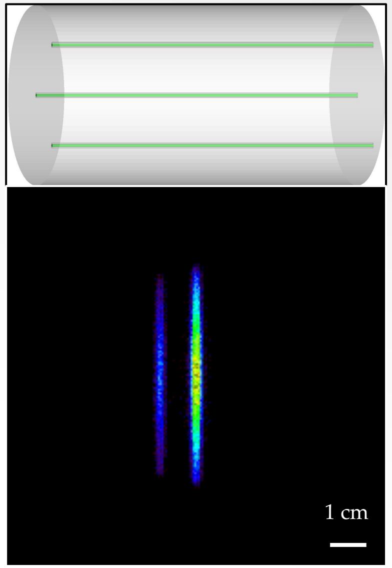
Mouse-sized NEMA triple line source scatter phantom
($\varnothing_{ID}$ = 0.4 mm)

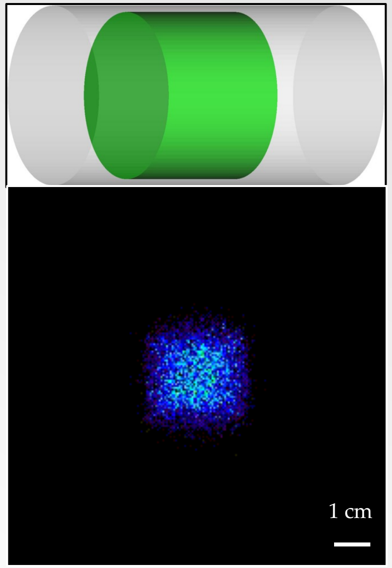
Volumetric cylinder
($\varnothing_{ID}$ = 26 mm)

Subject model:

Projections:







Analysis:

1.Memory and time
2.Hot rod SNR

Resolution

Uniformity
Coefficient of Variation (CV)

Summary of acquisition, reconstruction, and analysis.

Subject	Activity	Acquisition	Projections	Projection matrix	Reconstruction matrix	Reconstruction*	Analysis **
Micro-PET IQ	50 MBq	Forward proj 3600 s	64 (8 subs.) 91 (7 subs.)	104×104 px, 1.0 mm 208×208 px, 0.5 mm	120×92×92 vx, 0.5 mm 230×184×184 vx, 0.25 mm	OSEM OSEM, OS-OSL-MRP, OS-SPS-QP	Memory and time Hot rod SNR
Scatter Phantom	30 MBq	5460 s	91 (7 subs.)	208×208 px, 0.5 mm	230×184×184 vx, 0.25 mm	OSEM	Resolution
Volumetric Cylinder	20 MBq	910 s	91 (7 subs.)	208×208 px, 0.5 mm	230×184×184 vx, 0.25 mm	OSEM	Uniformity; CV

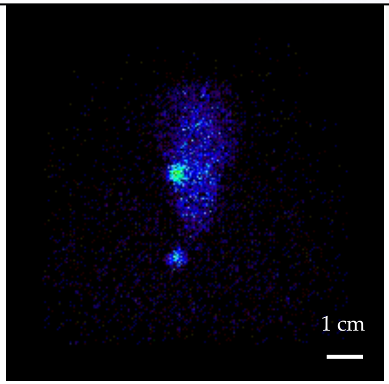
* OSEM: Ordered subsets expectation maximization; OS-OSL-MRP: Ordered subsets one step late with median root prior (penalization factor, PF = 1.0); OS-SPS-QP: Ordered subsets separable paraboloidal surrogate with quadratic prior (PF = 0.3). ** SNR: Signal-to-noise ratio; CV: Coefficient of variation.

In vivo image quality was assessed qualitatively with ^{123}I

B6SJLF1/J mouse injected with ^{123}I-labelled cholinesterase agent intended for Alzheimer's disease diagnosis

Subject model:

Projections:



Analysis: Qualitative investigation of a potential radiotracer 2 h post-injection

Summary of acquisition, reconstruction, and analysis.

Subject	Activity	Acquisition	Projections	Projection matrix	Reconstruction matrix	Reconstruction	Analysis
In Vivo Mouse	28 MBq	3600 s	91 (7 subs.)	208×208 px, 0.5 mm	230×184×184 vx, 0.25 mm	OSEM	Qualitative investigation

Time and memory requirements

Reconstructions were calculated with STIR v5.0.2 using the PinholeSPECTUB class on an HP Z820 workstation operating Ubuntu 18.04.5 LTS with two Intel Xeon E5-2630 CPUs and 64 GB of RAM

- Reconstructed with the OSEM algorithm (8 subsets, 40 subiterations) and various matrix corrections

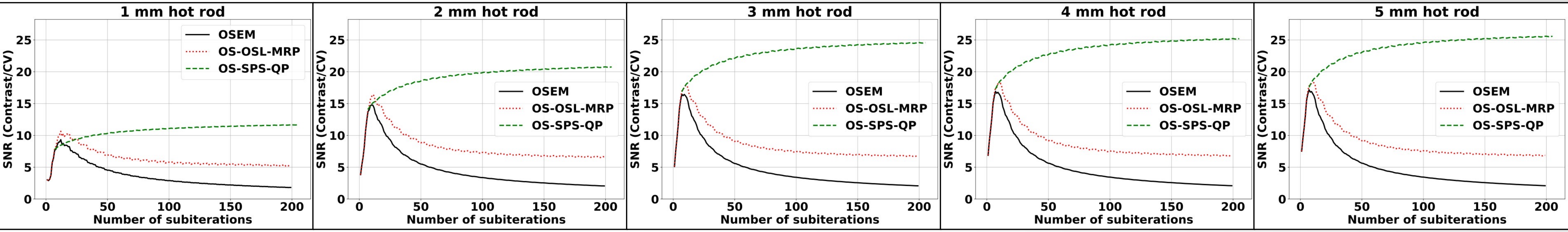
Maximum RAM and CPU time required in single-pinhole SPECT reconstruction.

	Matrix in memory		Matrix on-the-fly	
Correction type*	**Max RAM (MB)**	**CPU Time (s)**	**Max RAM (MB)**	**CPU Time (s)**
N-C	4519	57	172	162
ATT-C	4528	227	181	1141
DOI-C	7877	632	225	3484
PSF-C	12025	137	298	422
PSFATTDOI-C	17012	1417	378	7802
PSFATTDOIM-C	9875	780	264	4334

* N-C: No correction; ATT-C: Attenuation correction; DOI-C: Depth of interaction correction; PSF-C: Point spread function correction; PSFATTDOI-C: PSF, ATT, and DOI correction; PSFATTDOIM-C: PSF, ATT, and DOI correction using default mask (⌀ = 34 mm).

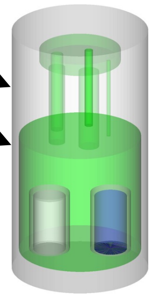
← PSF correction provides the greatest improvement in image quality in this study with a marginal increase in computing time

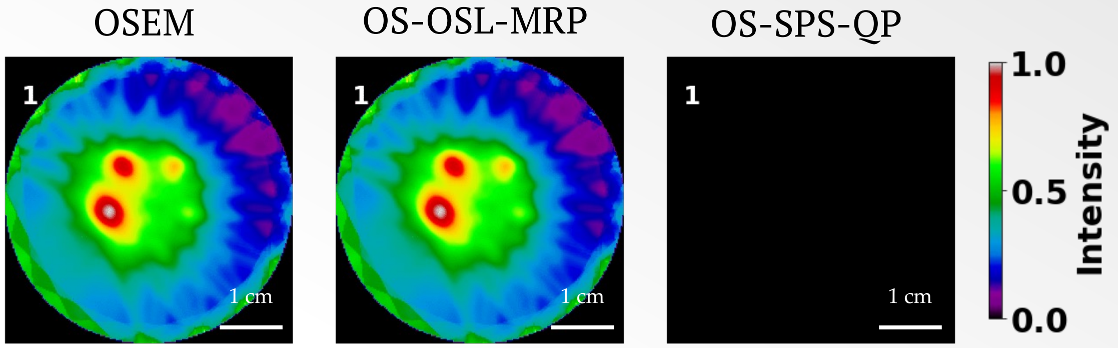
Signal-to-noise ratio of IQ phantom hot rods



SNR of IQ phantom hot rods (50 MBq, 3600 s) comparing OSEM, OS-OSL-MRP, and OS-SPS-QP algorithms (7 subsets, no corrections)

$$\mathrm{SNR} = \frac{\text{Contrast in rods}}{\text{CV in uniform vol}} = \frac{\left(\frac{|\mathrm{I_{rod}} - \mathrm{I_{ref}}|}{\mathrm{I_{rod}} + \mathrm{I_{ref}}}\right)}{\sigma/\mu}$$

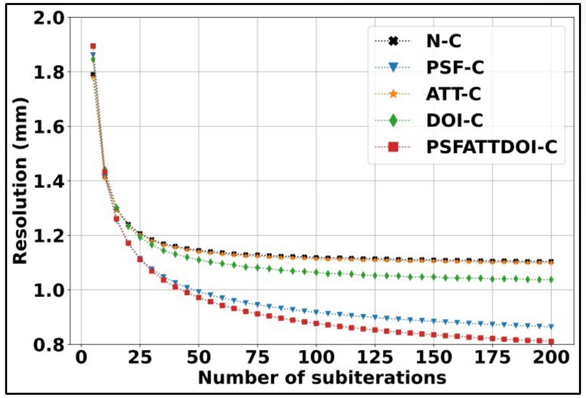




Normalized axial sum of hot rods with advancing subiterations

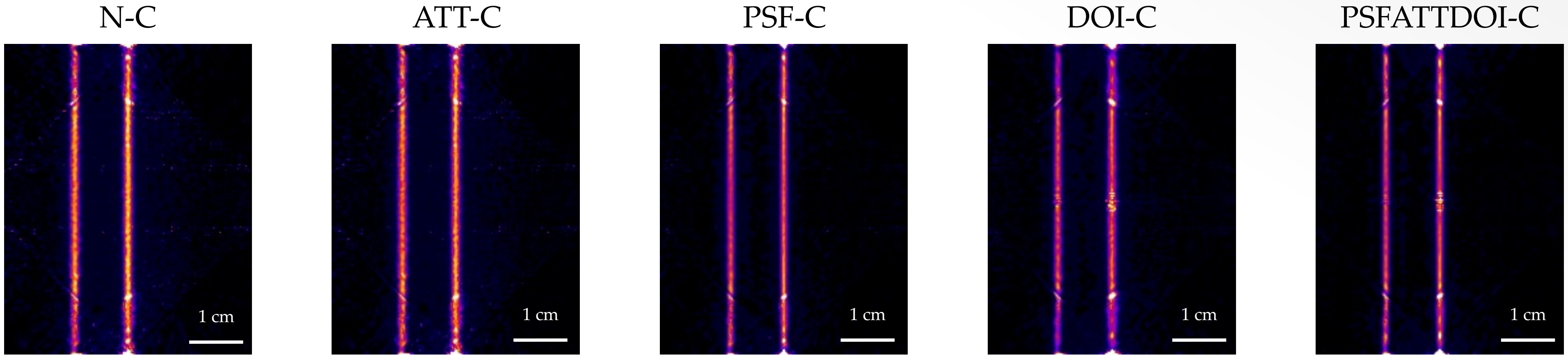
- OSEM shows increasing noise with increasing subiterations
- OS-OSL-MRP converges toward stable solution; **effectiveness in noise reduction, and preservation of spatial detail**
- OS-SPS-QP converges toward stable solution; **effectiveness in noise reduction**, no improvement in spatial detail
  - Initialized with OSEM image after 7 subiterations

Resolution in the mouse-sized NEMA line source phantom



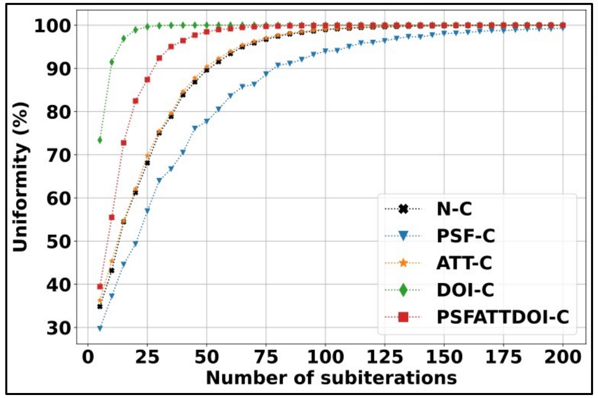
Resolution in the NEMA line source phantom reconstructed using OSEM (7 subsets)
Resolution calculated from the average FWHM in x and y directions in three 3.5 mm-thick slices: one at the center and two at ± 14.5 mm.

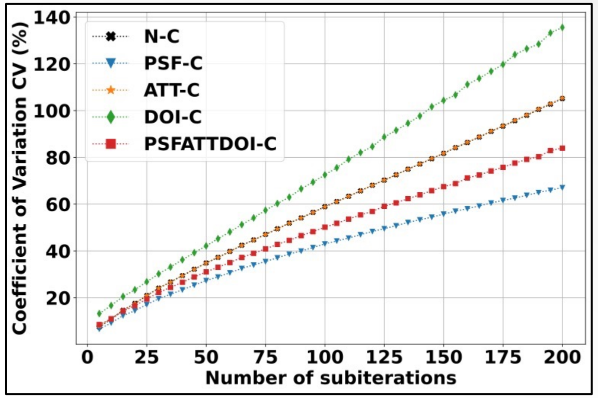
- **ATT correction** provides minimal improvement in resolution
  - Minimal attenuation effects in preclinical SPECT
- **PSF correction** provides greatest improvement in resolution
- **DOI correction** overestimates resolution improvement due to **bug affecting small angles from the pinhole axis**



MIPs of simulated line source phantom (30 MBq, 5460 s) reconstructed using OSEM (7 subsets, 105 subiterations)

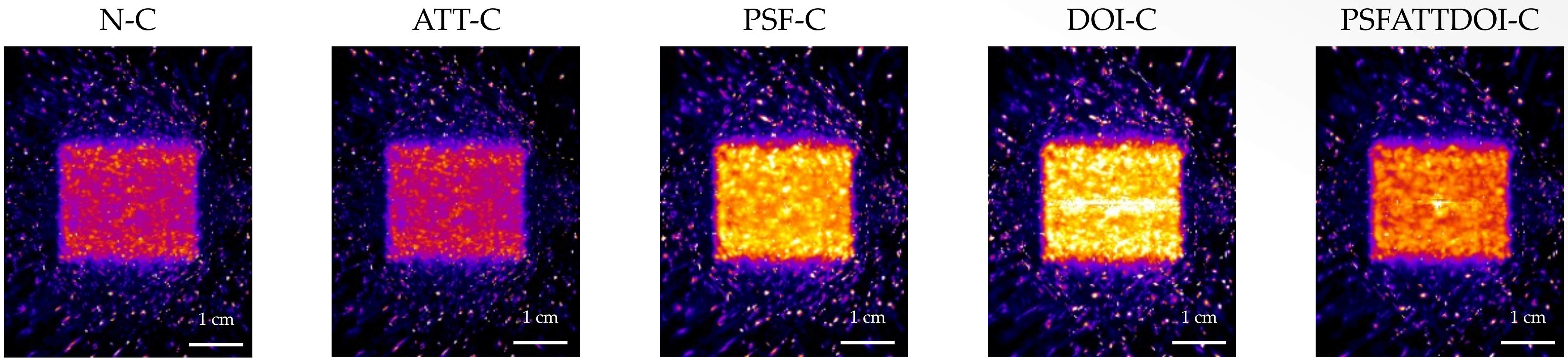
Uniformity and variability in the volumetric cylinder





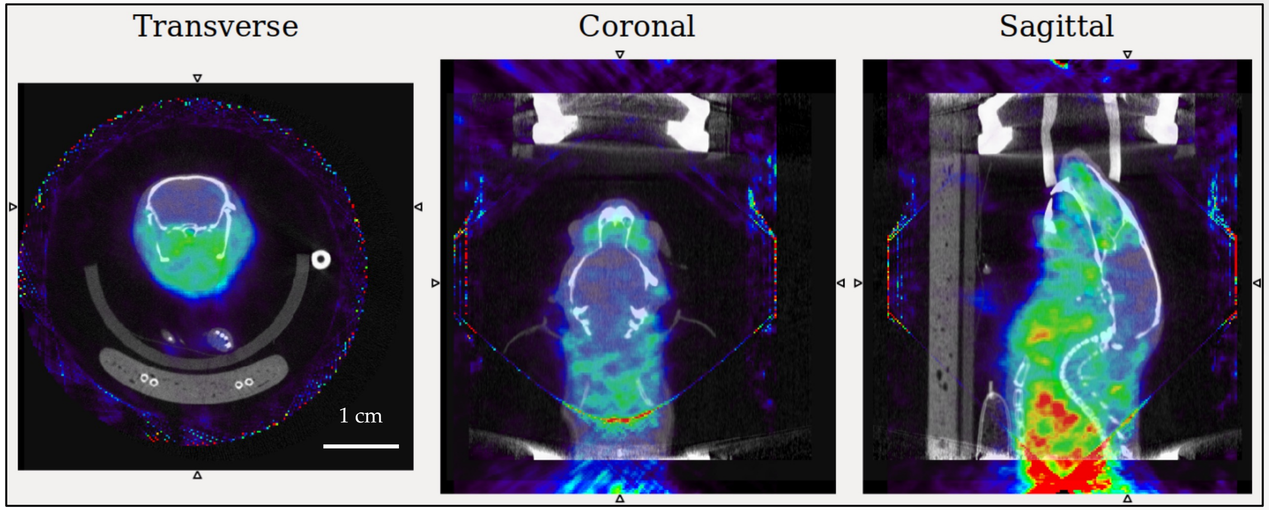
Uniformity (left) and variability (right) in the volumetric cylinder reconstructed using OSEM (7 subsets)
Analysis performed within the filled volume.

- **ATT correction** provides no apparent improvement in uniformity or variability
  - Minimal attenuation effects in preclinical SPECT
- **PSF correction** provides greatest improvement in uniformity and variability
- **DOI correction** degrades uniformity and increases variability due to **bug affecting small angles from the pinhole axis**



MIPs of simulated volumetric cylinder (20 MBq, 910 s) reconstructed using OSEM (7 subsets, 35 subiterations)

In vivo test study demonstrates indicative image quality



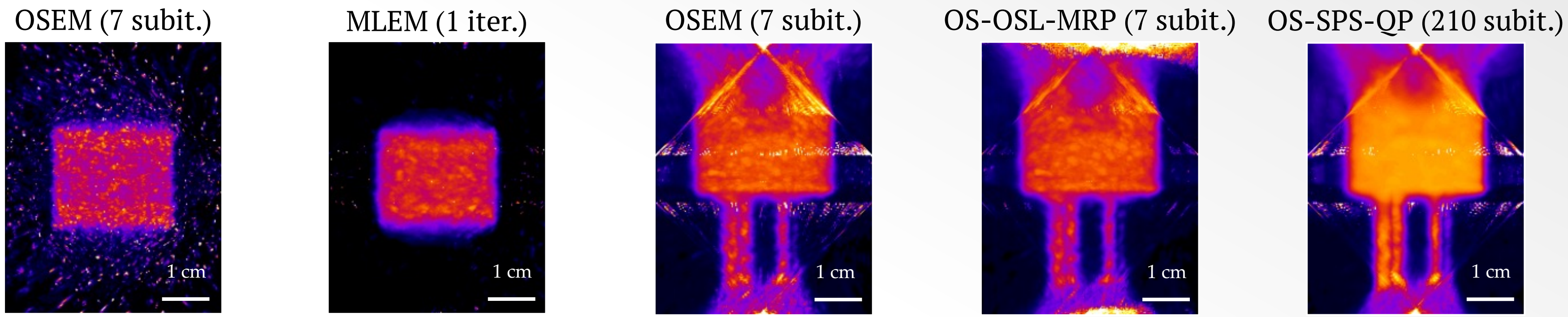
Slices of experimental *in vivo* data (28 MBq, 3600 s)

reconstructed using OSEM (7 subsets, 7 subiterations, no corrections)

- *In vivo* SPECT/CT fusion shows ^{123}I tracer under investigation for Alzheimer's disease diagnosis
- **Radiotracer is not persistent in brain 2 – 3 h post-injection**
- Uptake can be observed in eyes, thyroid/salivary glands, and heart

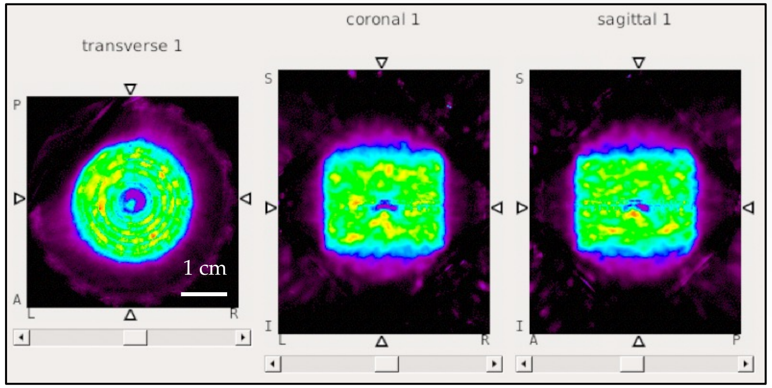
Discussion

- Data acquired with the single-pinhole collimator have relatively **low count statistics**
  - Directly affects figures of merit: contrast, coefficient of variation, resolution, etc.
  - STIR produces quality results in all demonstrated cases with various algorithms and corrections



MIPs of MLEM, OS-OSL-MRP, and OS-SPS-QP reconstructions showing effectiveness over OSEM for low statistics data

- DOI corrections exhibit a bug causing incorrect behaviour at small angles from the pinhole axis
  - Current approach uses Bresenham's line algorithm to subdivide scintillator
  - Future approach uses new algorithm



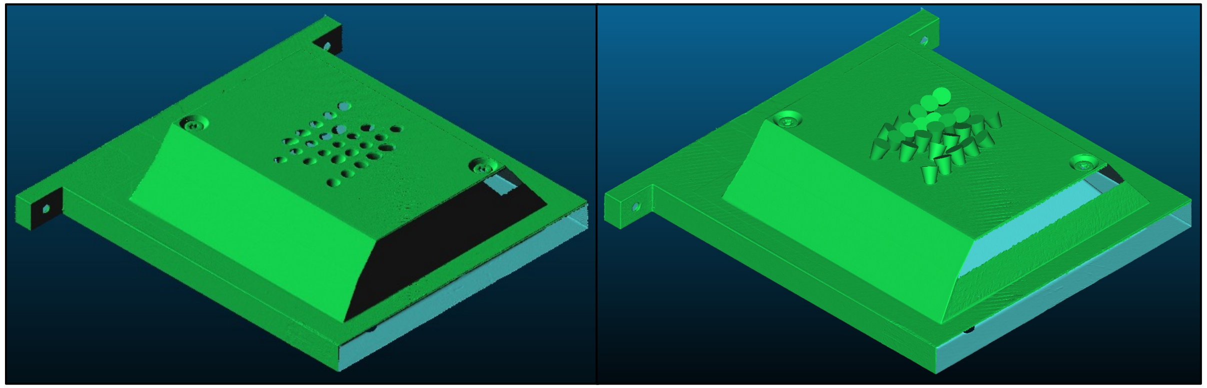
Conclusions

- This work demonstrates STIR's forthcoming capabilities using the pinhole-SPECT modelling tool
- Results show **measurable and indicative image quality** suitable for in vivo applications
  - PSF and/or ATT corrections improve image quality and accuracy
  - DOI corrections degrade image quality due to a software bug
  - STIR can be configured for complex pinhole-SPECT scanner geometries and used with many algorithms
- Pinhole-SPECT is becoming increasingly important in preclinical and clinical investigations of molecular imaging agents
  - **This marks the first open-source platform for reconstructing pinhole-SPECT images** which is important in the advancement of molecular imaging techniques and technology

Future work

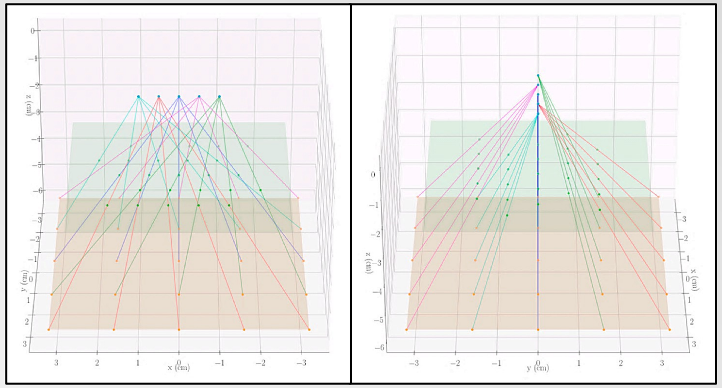
- Continue working on a solution for the DOI correction bug

- Test software **with simulations** of the multi-pinhole collimator

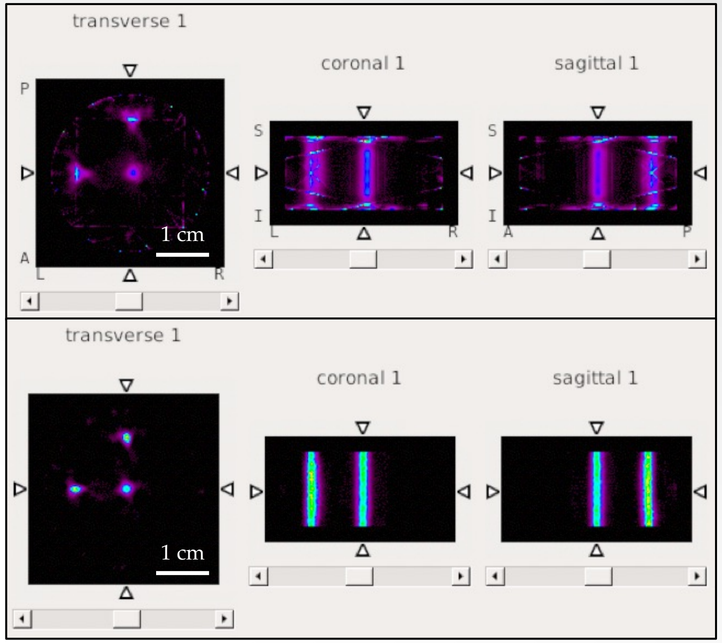


MPH collimator optical surface scan with registered double-cone pinholes

- Release the pinhole-SPECT software with STIR (and SIRF)



Extracted pinhole focal spots and orientations



Line source phantom reconstructed using MLEM (9 iterations) for **STIR result (top)** and manufacturer's result (bottom). Discrepancy likely due to extracted geometry.

References

DeBay, D. R., Reid, G. A., Pottie, I. R., Martin, E., Bowen, C. V., & Darvesh, S. (2017). Targeting butyrylcholinesterase for preclinical single photon emission computed tomography (SPECT) imaging of Alzheimer's disease. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, *3*(2), 166–176. https://doi.org/10.1016/j.trci.2017.01.005

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Thank you!

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Sample parameter file: OSEM.par

```
OSMAPOSLParameters :=

    objective function type:= PoissonLogLikelihoodWithLinearModelForMeanAndProjData
    PoissonLogLikelihoodWithLinearModelForMeanAndProjData Parameters:=

        input file := projections.hs

        projector pair type := Matrix
            Projector Pair Using Matrix Parameters :=
            Matrix type := Pinhole SPECT UB
            Projection Matrix By Bin Pinhole SPECT UB Parameters:=

                ; Minimum weight to take into account. Makes reference just to the geometric (PSF) part of the weight.
                ;  Weight could be lower after applying the attenuation factor (typically 0.005 - 0.02)
                minimum weight := 0.0

                ;Maximum number of sigmas to consider in PSF calculation (typically 1.5 - 2.5)
                maximum number of sigmas := 2.0

                ; Spatial high resolution in which to sample distributions (typically 0.001 - 0.0001)
                spatial resolution PSF := 0.01

                ; Subsampling factor to compute convolutions for mid resolution. This reduces temporally the PSF resolution to
                ; perform more accurate calculus and then down sample the final PSF to the bin size (typically 1 - 8)
                subsampling factor PSF := 1

                ;  Detector and collimator parameter files
                detector file := detector.txt
                collimator file := collimator.txt

                ;Correction for intrinsic PSF { Yes // No }
                psf correction := no

                ; Correction for depth of impact { Yes // No }
                doi correction := no

                ; Attenuation correction { Simple // Full // No }
                attenuation type := no
                ; Values in attenuation map in cm-1
                attenuation map :=

                ; Voxels not belonging to the cylinder defined by this radius are masked by default.
                object radius (cm) := 2.3
                ; Mask properties { Attenuation Map // Explicit Mask // No }. Default mask - cylinder object radius.
                mask type := no
                ; In case of explicit mask.
                mask file :=

                keep all views in cache := 0

            End Projection Matrix By Bin Pinhole SPECT UB Parameters:=

        End Projector Pair Using Matrix Parameters :=

    end PoissonLogLikelihoodWithLinearModelForMeanAndProjData Parameters:=

    initial estimate:= init.hv
    output filename prefix := out/OSEM

    number of subsets:= 8
    number of subiterations:= 40
    Save estimates at subiteration intervals:= 40

END :=
```

Configured for memory and time reconstruction (slide 9)

Sample Interfile data: projections.hs

```
!INTERFILE  :=
!imaging modality := nucmed
name of data file := projections.s
originating system := Cubresa SPARK
!version of keys := 3.3
!GENERAL DATA :=
!GENERAL IMAGE DATA :=
!type of data := Tomographic
imagedata byte order := LITTLEENDIAN
!SPECT STUDY (General) :=
!number format := float
!number of bytes per pixel := 4
!number of projections := 64
!extent of rotation := 360
process status := acquired
!SPECT STUDY (acquired data):=
!direction of rotation := CW
start angle := 180
orbit := Circular
Radius := 54.8
!matrix size [1] := 104
!scaling factor (mm/pixel) [1] := 1
!matrix size [2] := 104
!scaling factor (mm/pixel) [2] := 1
!END OF INTERFILE :=
```

Detector radius defined according to GATE setup

Configured for memory and time reconstruction (slide 9)

Sample collimator file: collimator.txt

```
Information of collimator

Model (cyl/pol): pol

Collimator radius(cm): 2.805

Wall thickness (cm): 1.

#holes#

Number of holes: 64

nh / ind detel (1->Ndet) / x(cm) / y(cm) / z(cm) / shape (rect-round) / sizex(cm) / sizez(cm) / angx (deg)     /angz(deg) / accx(deg) / accz(deg)

h1:     1       0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h2:     2       0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h3:     3       0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h4:     4       0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h5:     5       0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h6:     6       0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h7:     7       0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h8:     8       0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h9:     9       0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h10:    10      0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h11:    11      0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h12:    12      0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h13:    13      0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h14:    14      0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h15:    15      0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h16:    16      0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h17:    17      0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h18:    18      0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h19:    19      0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
h20:    20      0.      0.      0.      round   0.1     0.1 0.  0.  45.    45.
```

… repeat to h64

Collimator radius defined according to GATE setup

Configured for memory and time reconstruction (slide 9)

Sample detector file: detector.txt

```
Any comment here or anywhere in lines not containing parameters. Avoid
using two points character (colon) since it is reserved to indicate the
following value must be read as a parameter

number of rings: 1

#intrinsic PSF#

Sigma(cm): 0.0361

Crystal thickness (cm): 0.3

Crystal attenuation coefficient (cm -1): 3.61

\#....repeat for each ring ........\#

Nangles: 64

ang0(deg): 180.

incr(deg): 5.625

z0(cm): 0.

\#........until here..........\#
```

Configured for memory and time reconstruction (slide 9)