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MD782 – REPORT

Improving brain tumors perfusion imaging techniques: combined high spatial and temporal resolution SRCT with MAXIPIX-CdTe detector

Proposal Summary

We want to take advantage of new hard X-rays 2D detection technologies developed at the ESRF to achieve combined high spatial and temporal resolution quantitative brain perfusion imaging using Synchrotron Radiation Computed Tomograghy (SRCT). This project will use the Maxipix-CdTe detector[1] and the first bolus pass contrast agent follow-up technique. A systematic study on phantoms including contrast agent mixtures (Gadolinium and Iodine) will be performed. This step is mandatory to characterize the quantitative aspect of SRCT using the Maxipix-CdTe in perfusion conditions. The technique will then be validated with *in vivo* perfusion SRCT imaging on rat brain tumors.

Effectively used shifts: 9 + additional preparation time on MDT days

Experimental set-up:

DETECTORS:

DETECTOR SOLUTIONS

DETECTOR	DETECTOR TYPE / PIXEL SIZE	CHARACTERISTICS	
Multi-element GERMANIUM DETECTOR	Direct detection 1D Detector 2 arrays of 128 strips 350 um strip pitch	- High sensitivity - High temporal resolution (1s) - Low spatial resolution (0.35 x0.35 x 1 mm^3)	
FRELON CAMERA (CCD Camera)	Indirect detection 2D detector 2048 x 2048 pixels 50 um pixel size	- Medium sensitivity - Low temporal resolution (10s) - High spatial resolution (0.05 x 0.05 x 0.05 mm^3)	
MAXIPIX – CdTe (Hybrid pixel detector)	Direct detection 2D Detector 768 x 256 pixels 55 um pixel size	- High sensitivity - High temporal resolution (2s) - High spatial resolution (0.06 x 0.06 x 0.06 mm^3)	

More details about detectors:

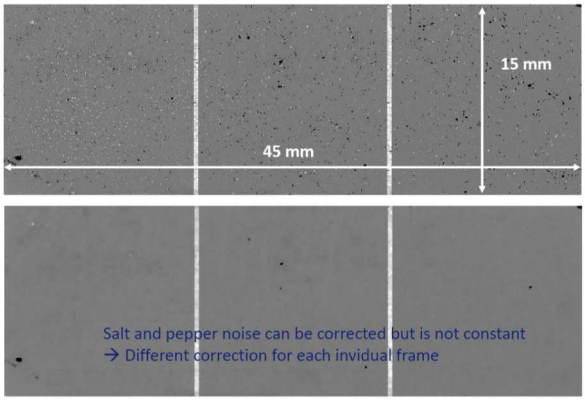
1. Germanium Detector:

Direct detection, 1D
3 mm thick germanium crystal with two lines of 432 pixels of 0,350 mm
Crystal size .....: 160 x 27 x 3 mm
Useful volume .....: 151,2 x 20 x 2 mm
Number of pixels ...: 2 x 432
Pixel height .....: 10 mm +/- 2 microns
Pixel step .....: 350 microns +/- 2 microns
Pixel width .....: 300 microns +/- 2 microns
Entrance windows ...: 2 x 0,5 mm of beryllium
Crystal to Beryllium : 15 mm

2. Maxipix-CdTe:

Direct detection, 2D
1 mm thick CdTe single crystal: 100% photon detection efficiency at X-ray energies up to 60 keV
768x256 pixels at 55 um pitch, effective dimensions 45 mm x 15 mm (3 x Timepix chip, 300 um gap in between chips)
Linear single-photon counting ability for fluxes up to 107 photons/mm2/s
Background noise suppression using the thresholding feature.
Tomographic spatial resolution: 0.06x0.06x0.06 mm^3
No entrance window
Parallel read-out of the full matrix, theoretical speed 300 frames per second (fps)

Flat-Field image (upper image => uncorrected ; lower image => corrected) :



The Frelon Camera was not used arguing that while the spatial resolution is similar the achievable speed of the Frelon (30 fps) is far below that of the Maxipix (> 150 fps expected) and results from the comparison of both detectors wouldn't be of an outstanding added value.

SAMPLE STAGE:

SSRT rotating chair
rotation speed from 6 °/s to 180 °/s

Rotation speed	Nb of projections / image	Acq time / projection
6 °/s	1024	50 ms
60 °/s	1024	3 ms
180 °/s	256	4 ms

PHANTOMS AND LIVING ANIMALS:

- Steady-state protocol:

Plastic tubes filled with different concentrations of Iodine (Iomeron 350 ®): 0, 0.1, 0.25, 0.5, 1.5, 2, 2.5, 5, 7.5, 10, 17.5, 25 mg/L.

- Dynamic protocol:

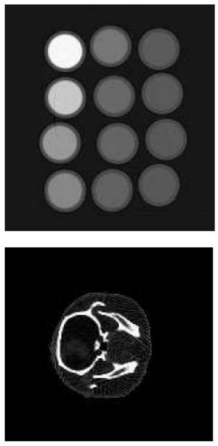
1. Flowing water circuit
2. Programmable injector which empties a syringe filled with Iodine (Iomeron 350 ®)
3. Plastic tubes in front of the beam filled with water in which 15 mL of iodine are slowly added. When injection stops the iodine is washed out of the tube under study by the flowing water, until its concentration falls to 0.

- In vivo imaging:

4 Fisher rats (Charles River) were injected with 10^4 F98 cells in the right caudate nucleus 9 days before imaging.

0.5 ml of Gadovist 75 ® or Iomeron 400 ® (5 animals each) will be injected in the jugular vein with a remote controlled injector at 1.5 $ml.s^{-1}$ and imaged each second with the Maxipix-CdTe and germanium detector over 3 min (first bolus pass protocols). Second, the same rats will be infused with the same amount of contrast agent but at 0.5 $ml.s^{-1}$ and imaged each 10 s over 20 min (steady-state protocols) with both Maxipix-CdTe and Frelon detectors.

IMAGE RECONSTRUCTION:



- Full tomographic slices : 1 image = 360 ° rotation

- Image reconstruction + correction for salt and pepper noise on the detector → μ values

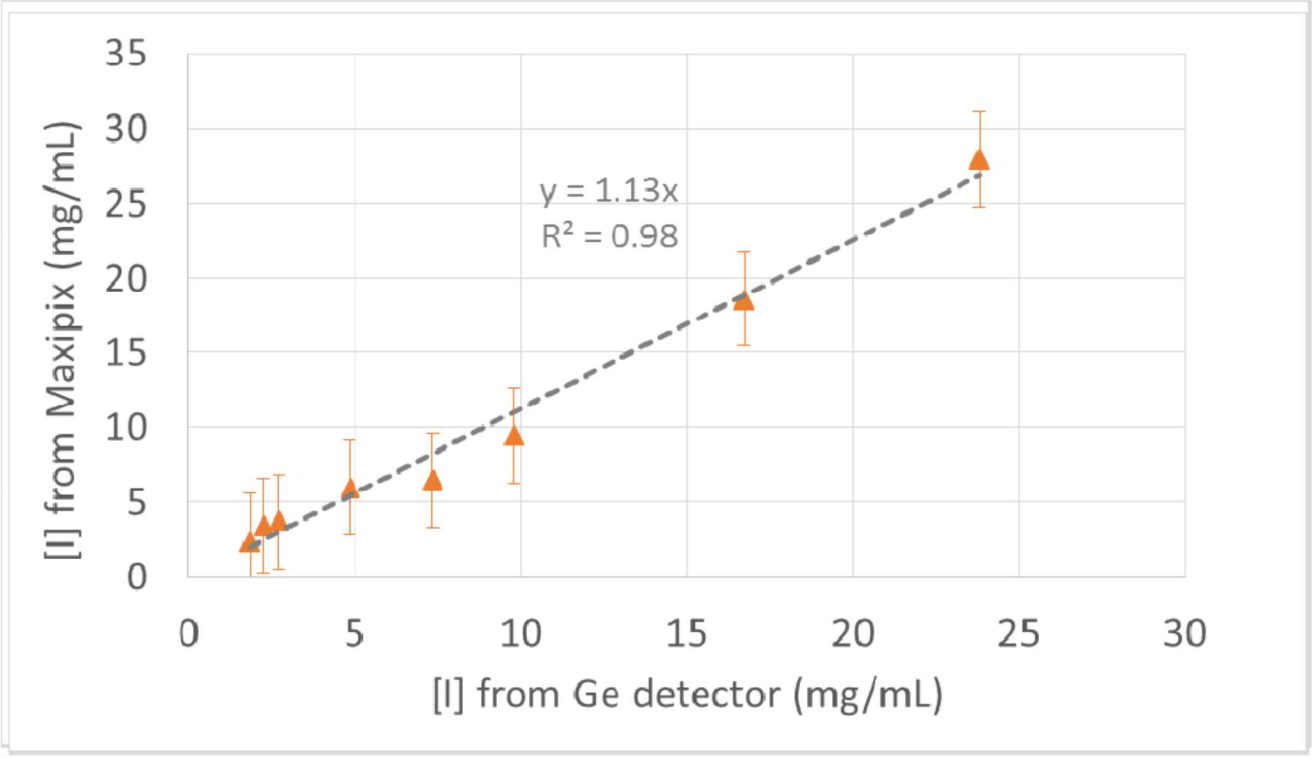
- Calculation of the iodine concentration :

$$[I]\ (mg.ml^{-1}) \sim 1000 \times \frac{\mu_I - \mu_{H_2O}}{\left(\frac{\mu}{\rho}\right)_{I\ ,\ 33.5\ keV}}$$

- Ge detector is the quantitative reference

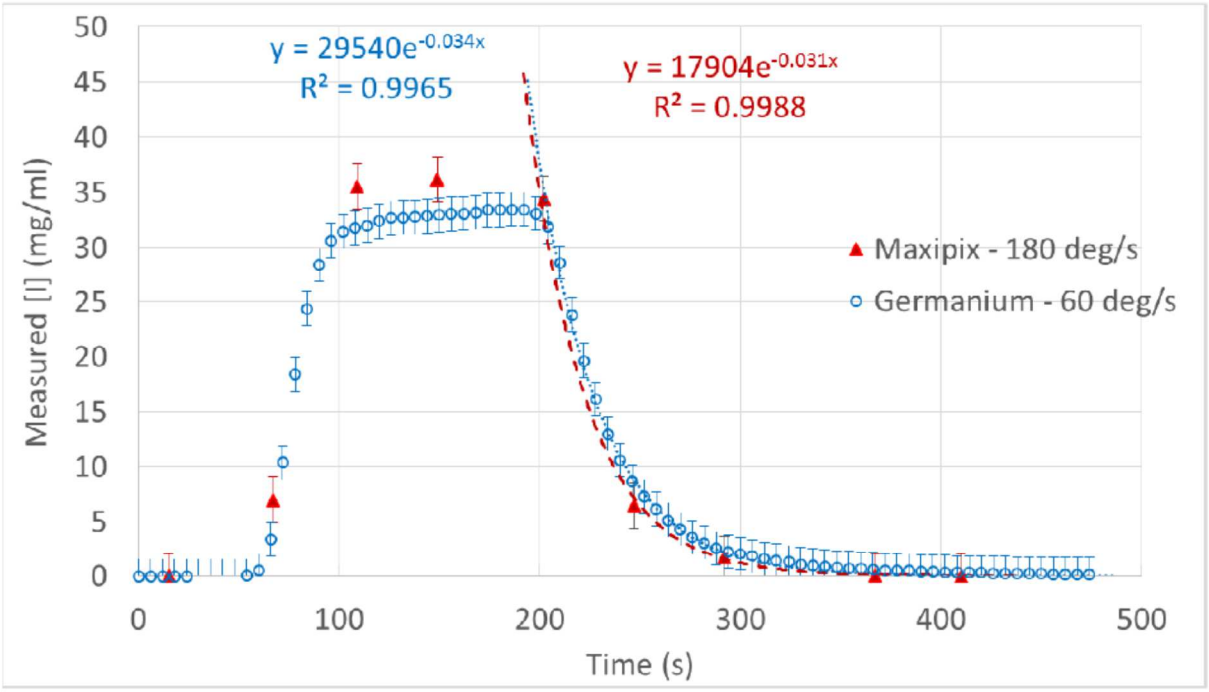
RESULTS:

STEADY-STATE Phantom



Fair correlation
Difficult to resolve concentrations below 1.5 mg / ml with the Maxipix

DYNAMIC Phantom



Excellent agreement between data from both detectors
Impossible to follow up with Maxipix at closer time intervals → RO deadtime too high

IN-VIVO IMAGING

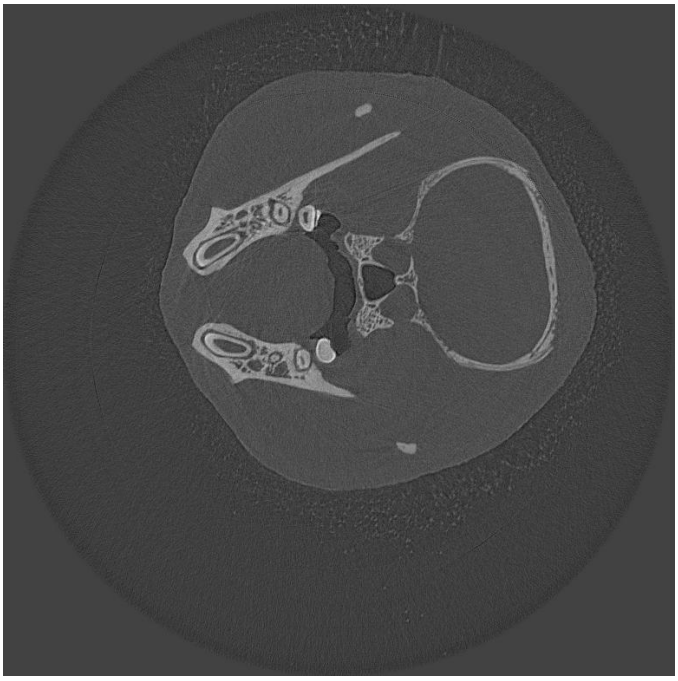


Figure: *Tomography slice obtained in vivo on a rat head during MD782 with Maxipix-CdTe detector (1024 projections over 360 degrees at a speed of 6 degrees per second, total dose 180 µGy).*

Reconstruction by C. Nemoz

N.B. One image is enough to obtain tomography slices over the full beam height with a 60 µm vertical resolution.

Besides a good image quality and the very low dose achieved, the tumor is not visible (iodine concentration into the tumor was measured with the Ge detector at 1.4 mg/ml, which is below the limit of detection for the Maxipix-CdTe).

CONCLUSION

We have shown during MD782 that the Maxipix-CdTe detector is suitable for such studies, on both steady-state protocol and for dynamic contrast-enhanced brain perfusion imaging, with phantoms and *in vivo* (see following image). Tomography images have been taken over 2s, 3s, 6s, and 60s. The high efficiency of the detector as well as its background noise suppression enabled very low dose imaging.

LIMITATIONS:

Low concentrations of iodine couldn't be resolved, this should be overcome.

The readout capabilities of the Maxipix-Cdte are expected to be improved, allowing a complete tomography temporal resolution of 512 (1024) projections over 360 degrees in 3 (6) seconds. Images need to be repeated without interruption during a total time of 8 minutes to follow up the contrast agent concentration. This was not possible during MD782. Data storage capabilities will then be optimized to overcome this limitation. Synchronization between the tomographic stage and the detector also need to be improved, as well as image reconstruction techniques.

Perspectives:

New proposal submitted March 1st, 2014.