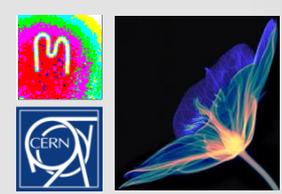




# **SINGLE PARTICLE DETECTION FOR SPECTROSCOPIC CT AND TRACKING IN HADRON THERAPY USING MEDIPIX CHIPS**

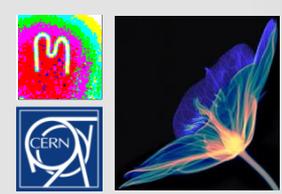
**M. Campbell, J. Alozy, R. Ballabriga, E. Frojdh, E.H.M. Heijne,  
X. Llopart, T. Poikela, E. Santin, L. Tlustos, P. Valerio and W. Wong**

**CERN, EP Department  
1211 Geneva 23  
Switzerland**

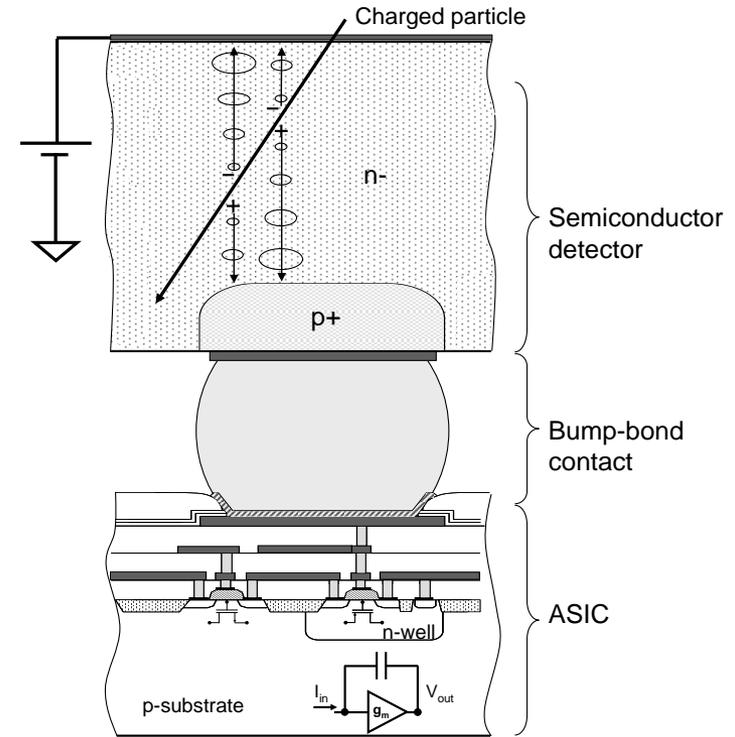
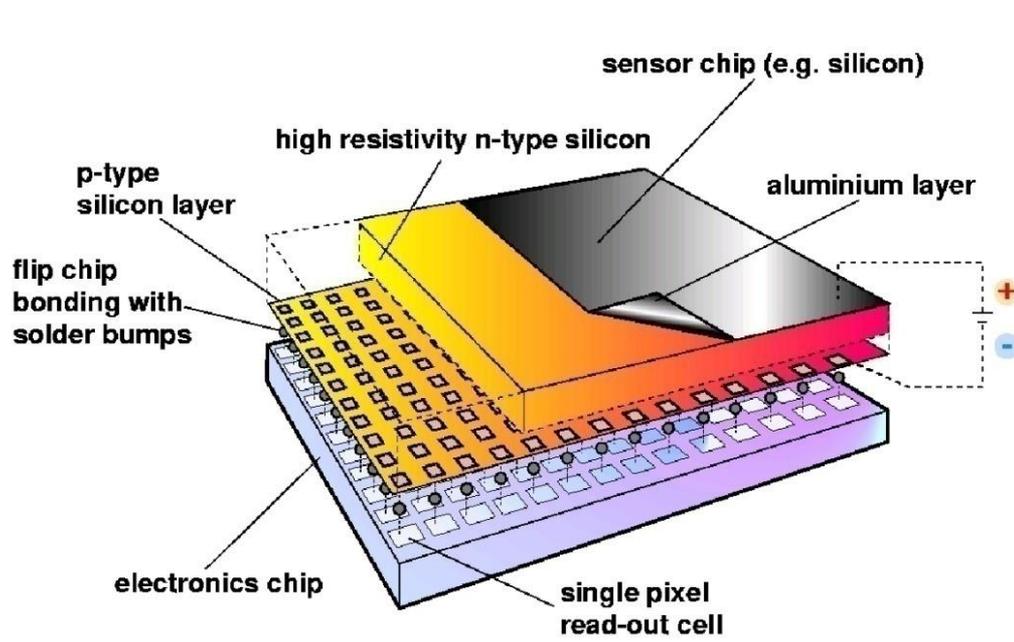


# Outline

- A brief introduction to hybrid pixel detectors
- Timepix
  - Live demonstration of particle detection
  - Some applications in medical imaging
- Particle tracking and detection using Timepix3
- Spectroscopic X-ray imaging using Medipix3
- Conclusions and future work



# Hybrid Silicon Pixel Detectors



Fill factor is 100 % (away from periphery)

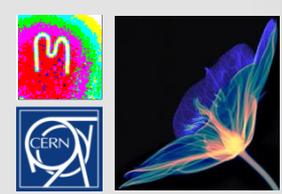
Full depletion of sensor allows prompt charge collection

Extremely high SNR easy to reach

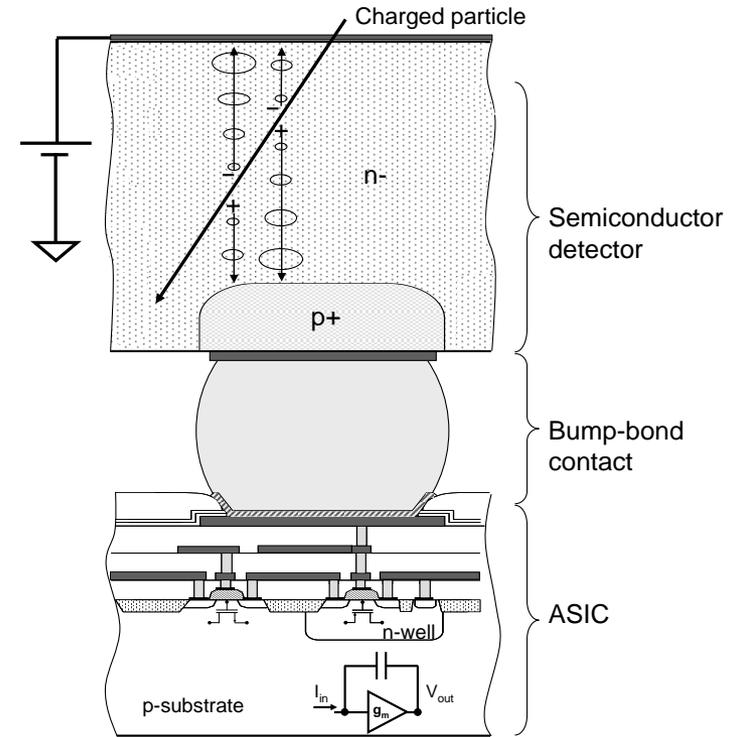
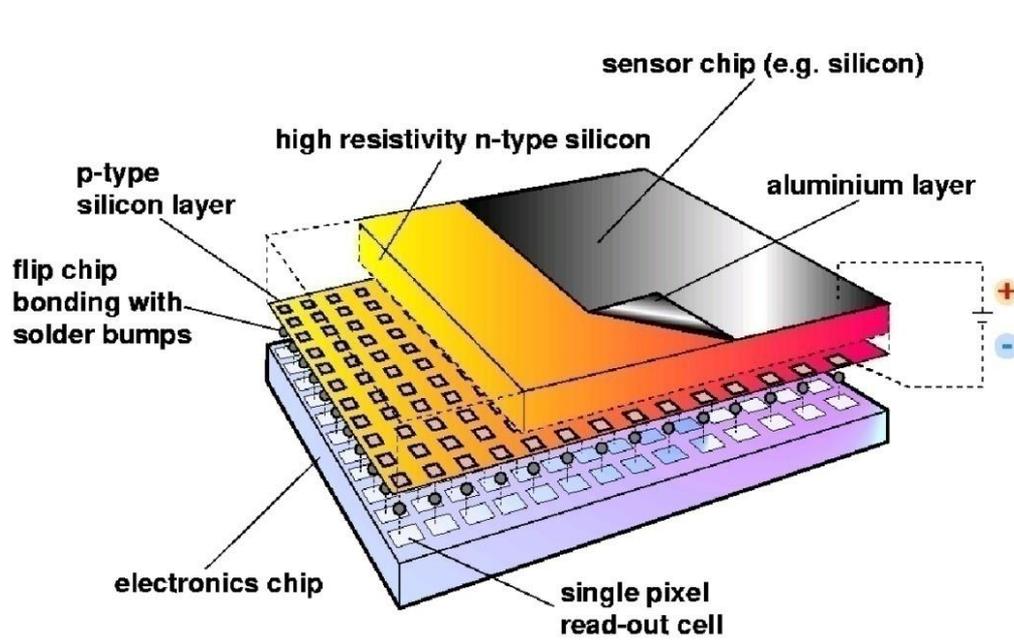
Standard CMOS can be used allowing on-pixel signal processing

Sensor material can be changed (Si, GaAs, CdTe..)

But because of low volumes bump bonding is still expensive



# Hybrid Silicon Pixel Detectors



Fill factor is 100 % (away from periphery)

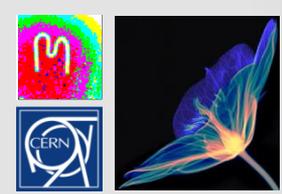
Full depletion of sensor allows prompt charge collection

**Extremely high SNR easy to reach**

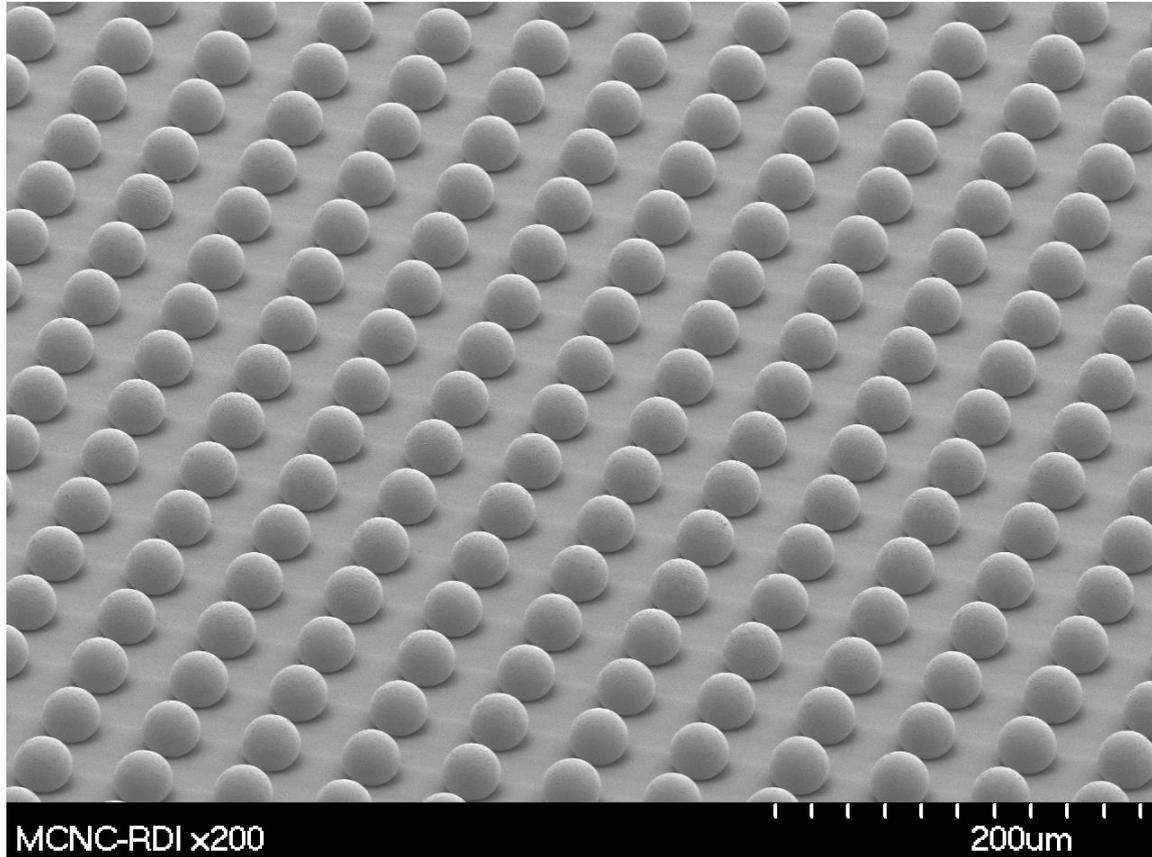
Standard CMOS can be used allowing on-pixel signal processing

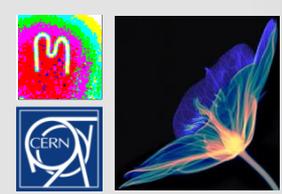
Sensor material can be changed (Si, GaAs, CdTe..)

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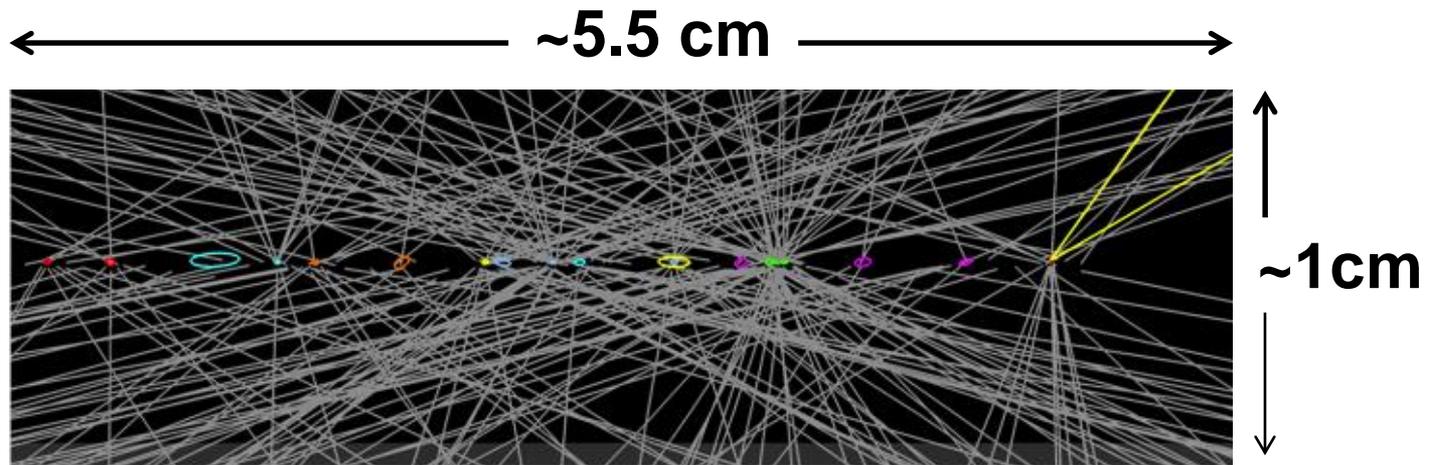


# Solder Bumps on a readout chip

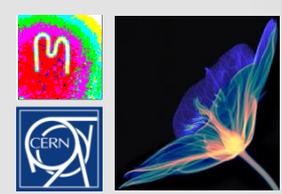




# Reconstruction of one 25ns LHC bunch crossing in the ATLAS pixel detector

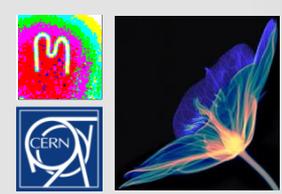


**About  $10^{15}$  events had been accumulated before the Higgs boson discovery was announced, and only some 100's were identified as Higgs boson decays**



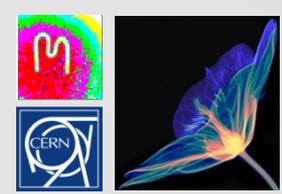
# Hybrid pixel detectors

- Developed initially for LHC
- 3 large scale vertex detector systems operating smoothly
- One large RICH detector system (based on hybrid pixels in a photodetector tube) contributing to LHCb physics
- In the Medipix2 and Medipix3 Collaborations we have taken the technology into many new fields
- This talk will focus on the applications in the medical field



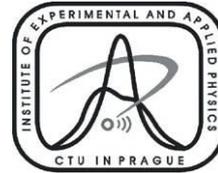
# Medipix2 Collaboration

- Work started in 1999/2000
- 2 chips were developed in 250nm CMOS
- Medipix2 – single photon counting chip. Camera-like logic with window threshold and 14-bit counter per pixel
- Timepix – based on Medipix2. Each pixel can be programmed in counting mode, arrival time mode, or Time-over-Threshold mode.



# Medipix2 Collaboration

- U INFN Cagliari
- CEA-LIST Saclay
- CERN Genève
- U Erlangen
- ESRF Grenoble
- U Freiburg
- U Glasgow
- IFAE Barcelona
- Mitthoegskolan
- MRC-LMB Cambridge
- U INFN Napoli
- NIKHEF Amsterdam
- U INFN Pisa
- FZU CAS Prague
- IEAP CTU in Prague
- SSL Berkeley



ALBERT-LUDWIGS-  
UNIVERSITÄT-FREIBURG



THE ACADEMY  
OF SCIENCES  
OF THE CZECH  
REPUBLIC

Friedrich-Alexander-Universität  
Erlangen-Nürnberg



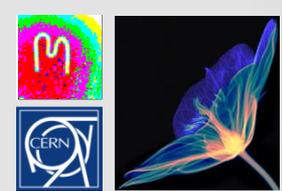
UNIVERSITY  
of  
GLASGOW



MRC

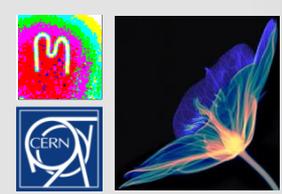
Laboratory of  
Molecular Biology

<http://medipix.web.cern.ch/MEDIPIX/>



# Timepix Specifications

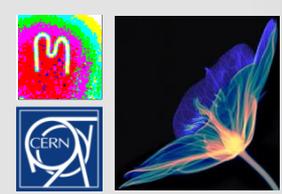
Pixel matrix	256 x 256
Pixel size	55 x 55 $\mu\text{m}^2$
Technology	CMOS 250 nm
Measurement modes	Programmable per pixel: <ul style="list-style-type: none"><li>• Single particle counting</li><li>• Timepix (arrival time wrt shutter)</li><li>• Time over Threshold</li></ul>
# thresholds	1 per 55 $\mu\text{m}$ pixel 4-bit threshold adjustment
Counter depth	1 x 14-bits
Readout type	Frame based <ul style="list-style-type: none"><li>• Sequential R/W</li></ul>
Readout Time	Serial: <100ms at 100MHz Parallel: <300ms @ 100MHz
Minimum threshold	~ 650 e-



# Medipix2/Timepix photo with Si detector



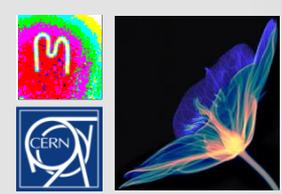
1.4 cm



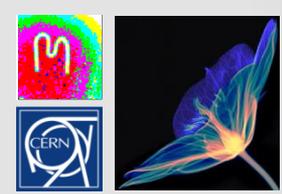
# Timepix miniaturised readout



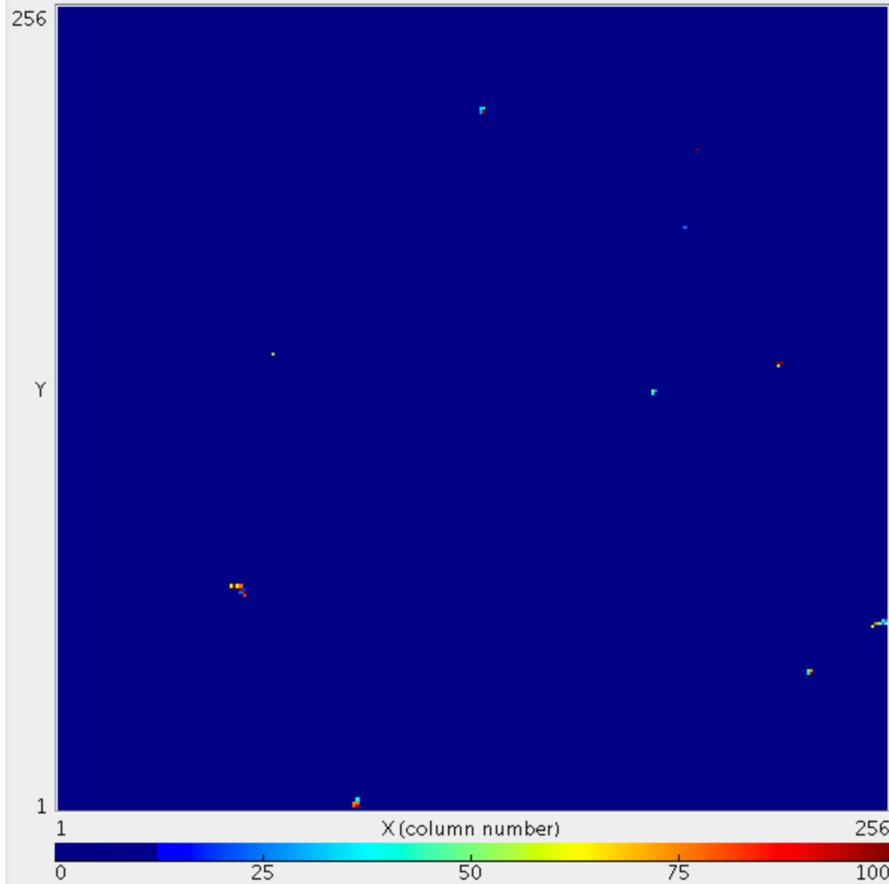
IEAP/CTU, Prague



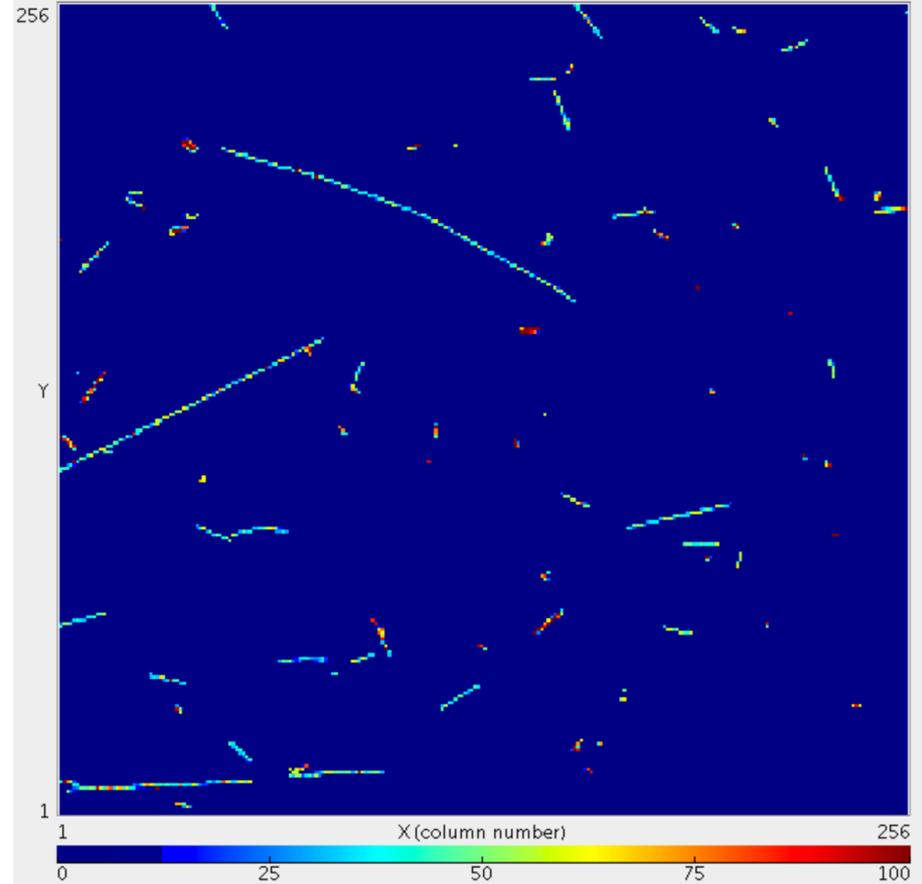
# Timepix demonstration



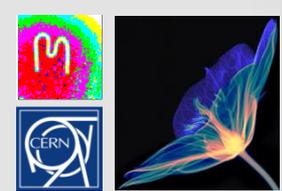
# Timepix chip – 60s exposures



Near sea level



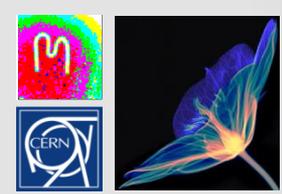
34 000 feet



# CERN@school



Simon Langton School, Canterbury, England



# CERN@school status August 2015



<http://cernatschool.web.cern.ch/participating-institutions>

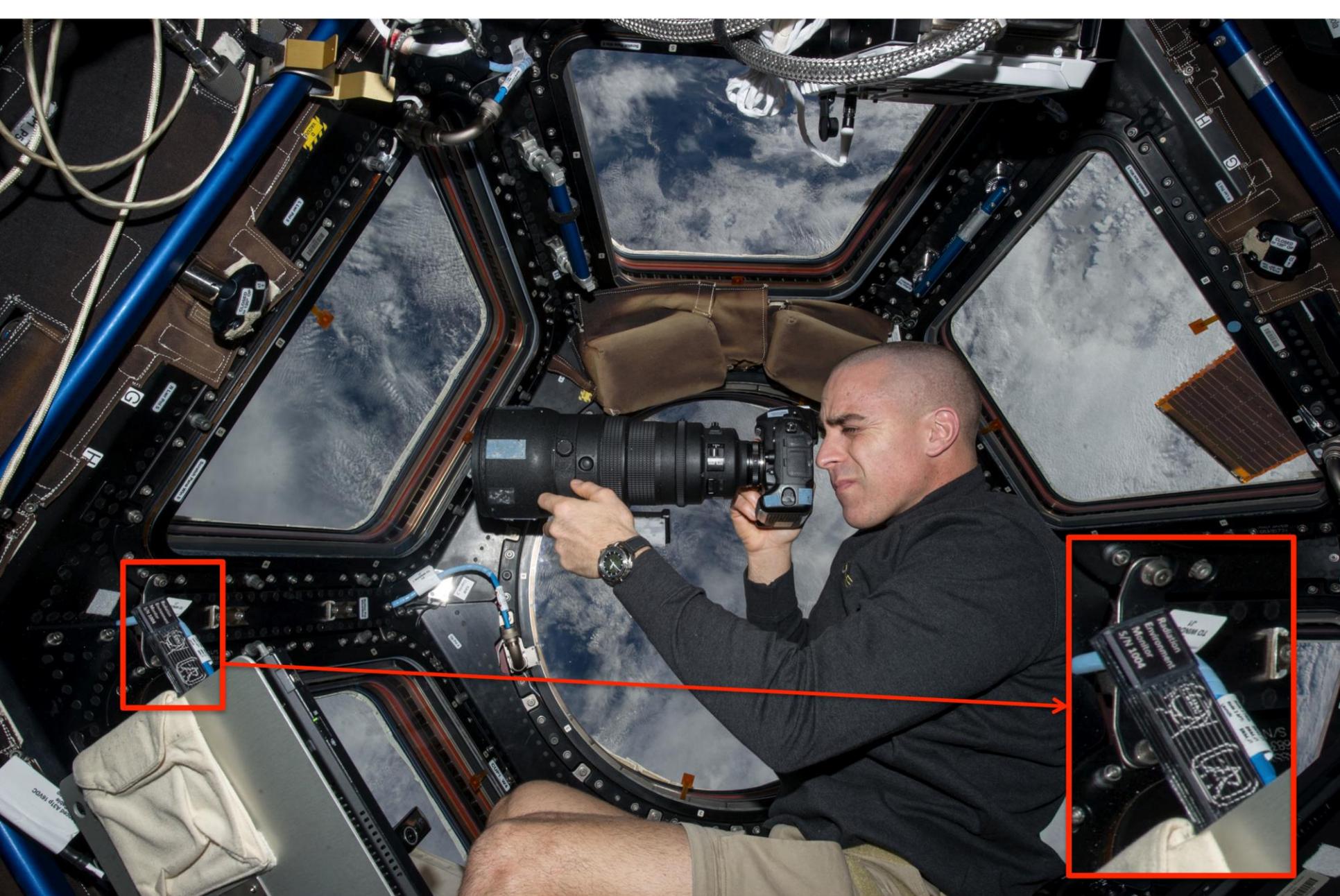
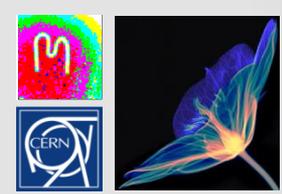
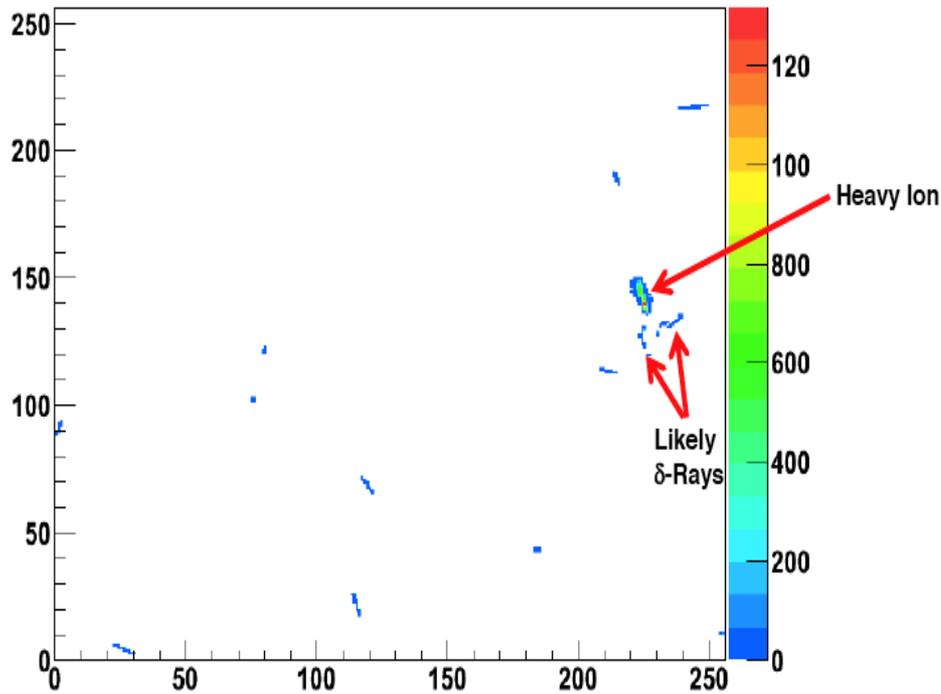


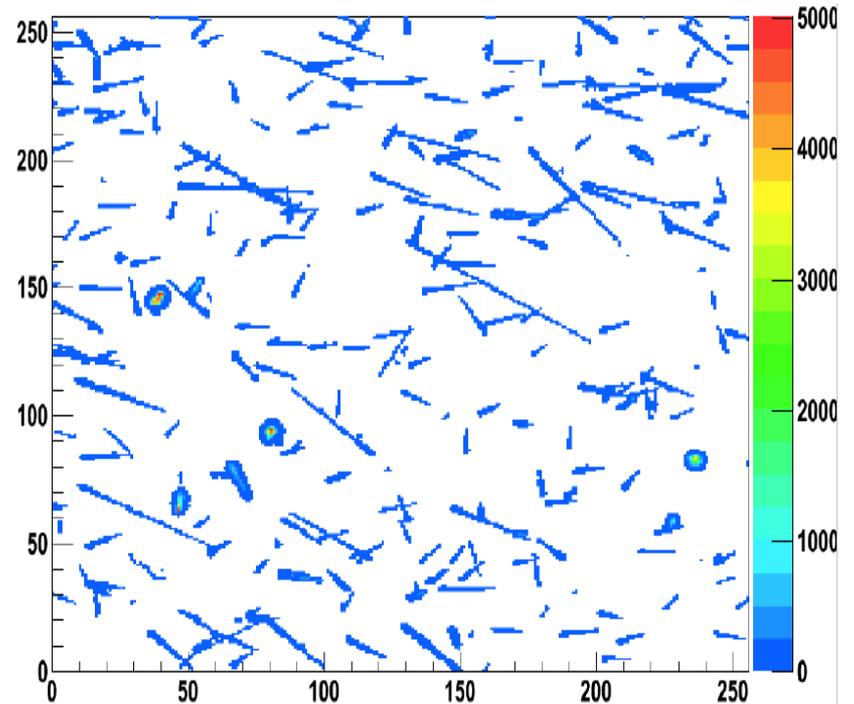
Image of the astronaut Chris Cassidy working near the Timepix USB on the International Space Station (Courtesy of NASA, photo ref. no. iss036e006175)<sup>17</sup>



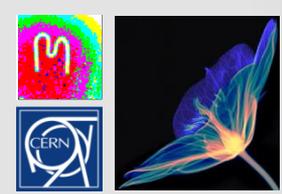
# Timepix - 4s exposures



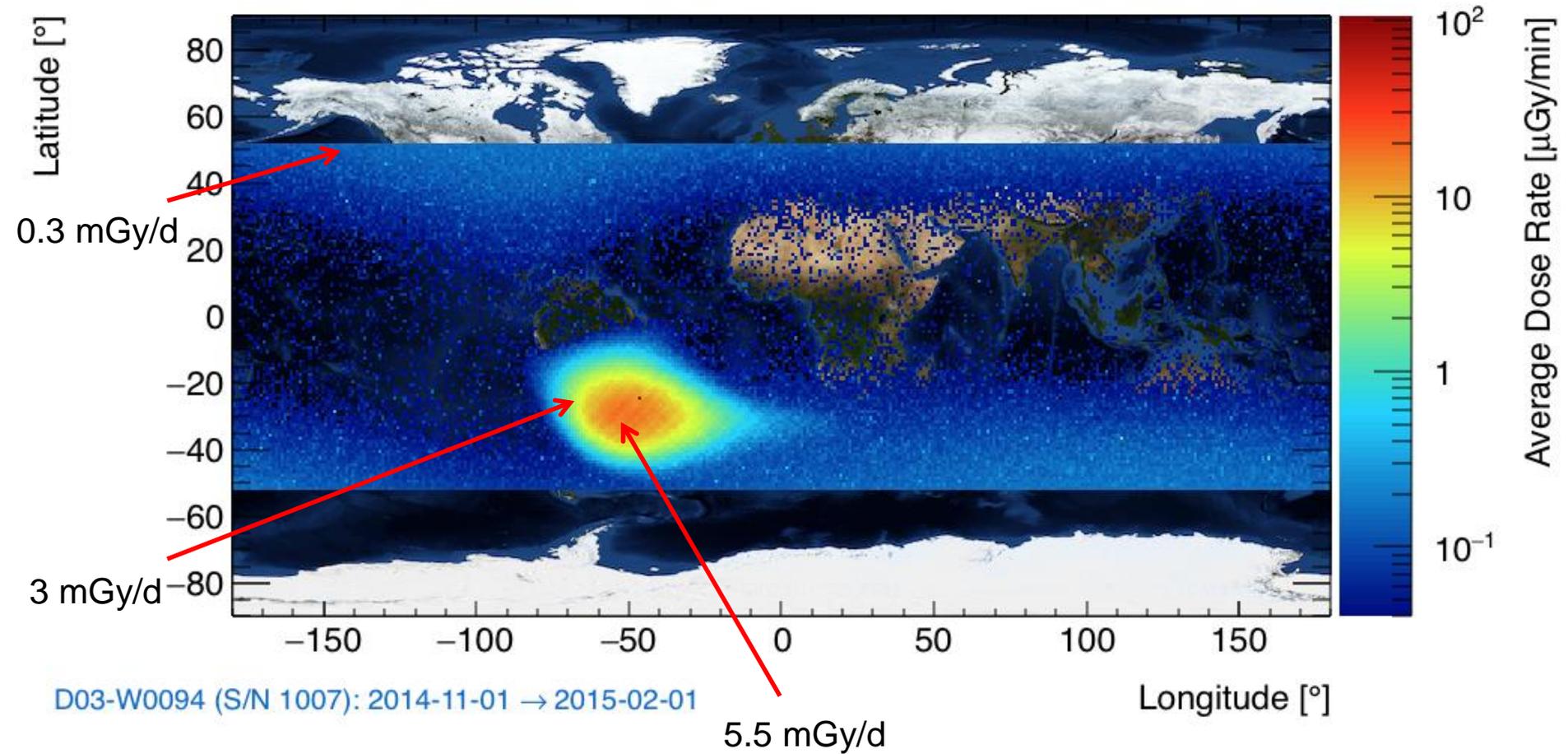
South China Sea



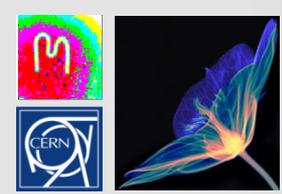
South Atlantic Anomaly



# REM Dose Rate Data ( $\mu\text{G}/\text{min}$ )

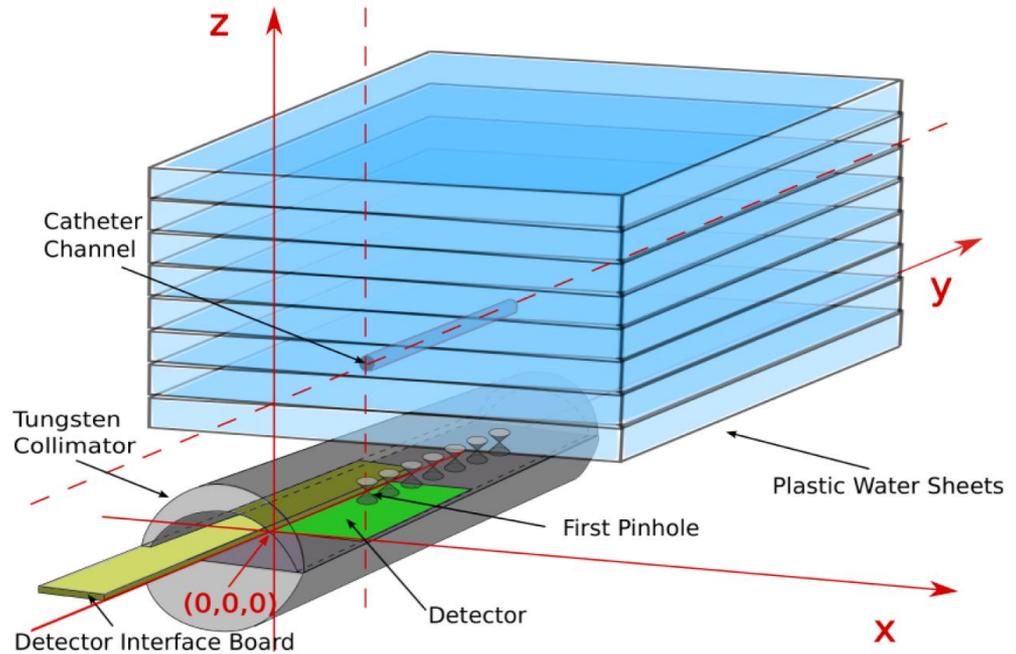
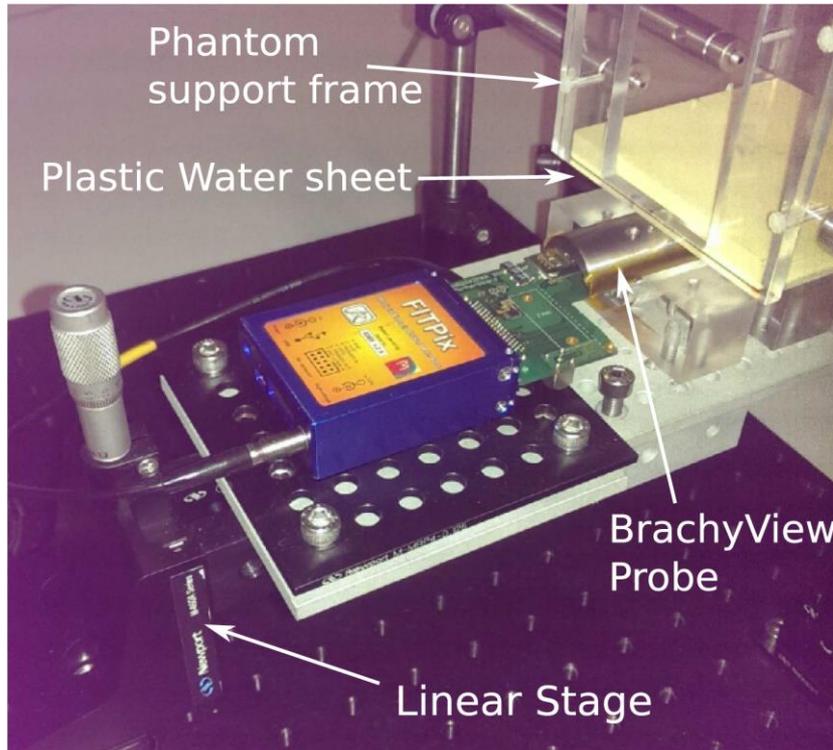


University of Houston, IEAP Prague, NASA



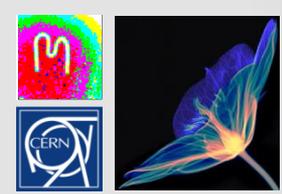
# High Dose Rate BrachyView

On-line monitoring of  $^{125}\text{I}$  prostate implants



3 x Timepix readout chips, Si detector, multiple pinholes in W sheet

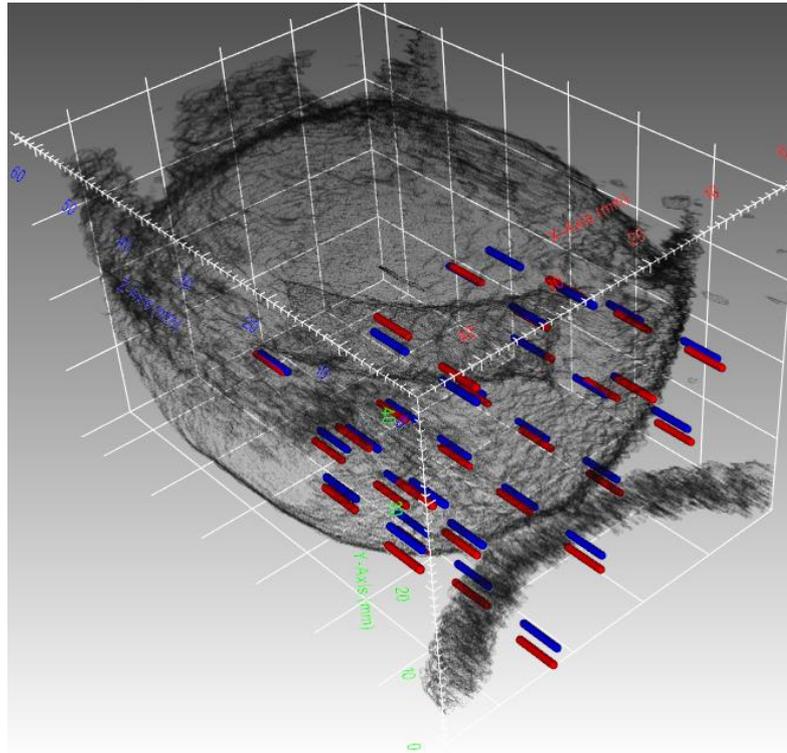
Slide courtesy of A. Rozenfeld, Centre for Medical Radiation Physics, University of Wollongong, Wollongong 2522, Australia



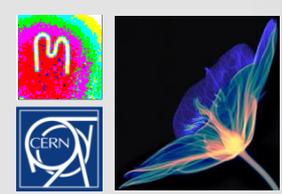
# High Dose Rate BrachyView

Comparison of HDR BrachyView position measurements with CT measurements

Very good agreement (<1mm mostly, 1.3mm worst case)

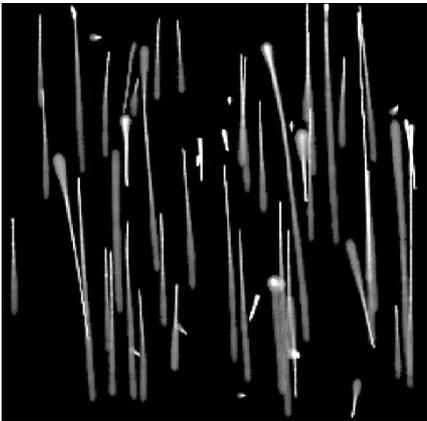


Slide courtesy of A. Rozenfeld, Centre for Medical Radiation Physics, University of Wollongong, Wollongong 2522, Australia



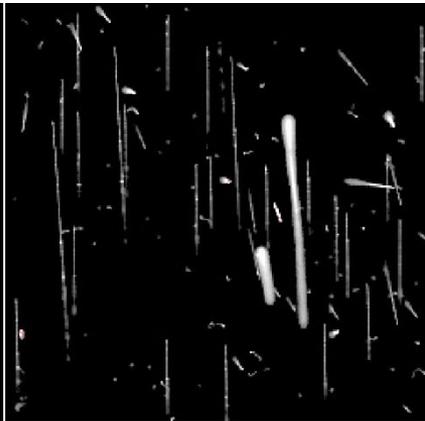
# In-line images of a Hadron Therapy Beam

Protons 48 MeV



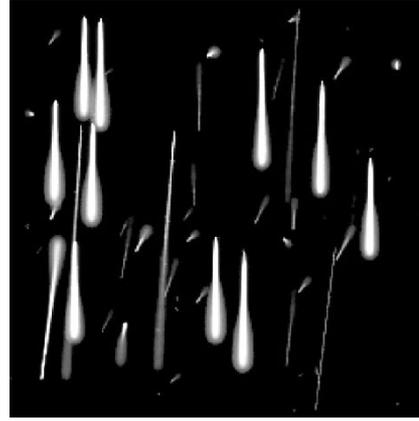
Only protons and their scattering, no secondaries.

Protons 221 MeV



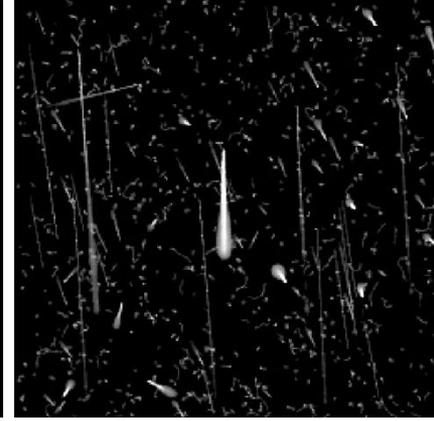
Many secondaries, (delta electrons fragments).

Carbons 89 MeV/u



Carbons and protons and their scattering, no secondaries.

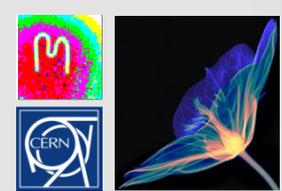
Carbons 430 MeV/u



Carbons and many secondaries.

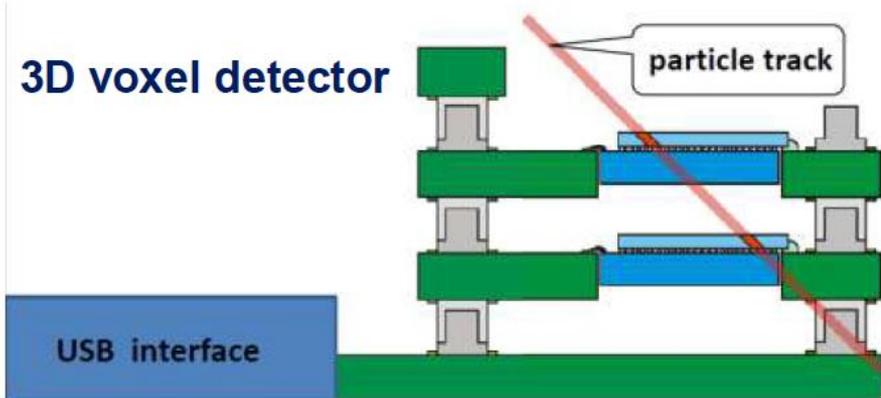
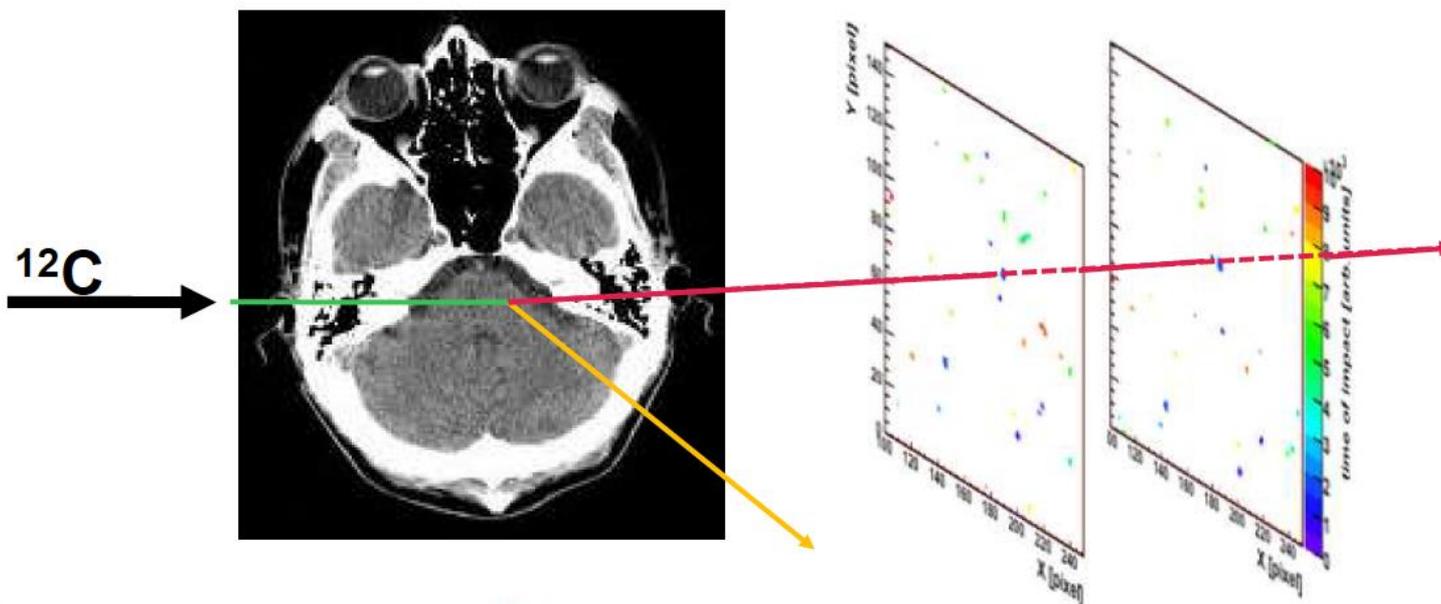
Timepix chip combined with Si detector

Jan Jakůbek  
IEAP, Prague



# Carbon Therapy beam monitoring

## Secondary Ion Tracking in 3D

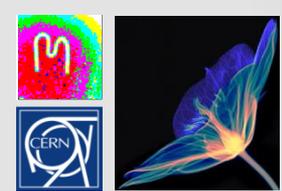


1. Measurement of ion impact time in the **time-of-arrival mode**
2. Correlation of the particle hits in all layers (coincidence)

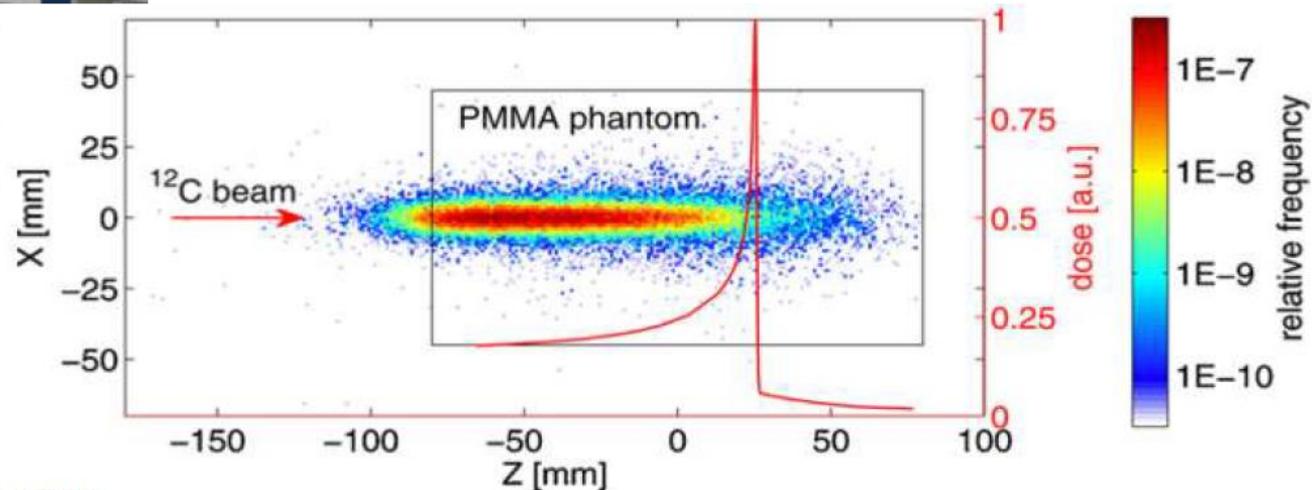
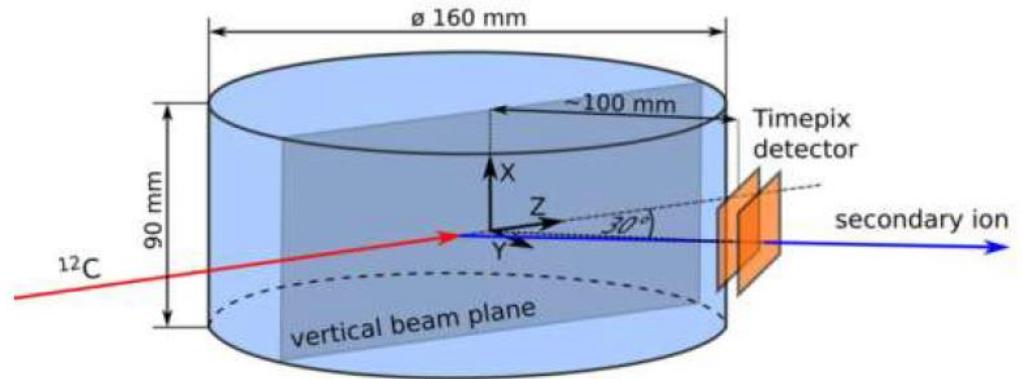
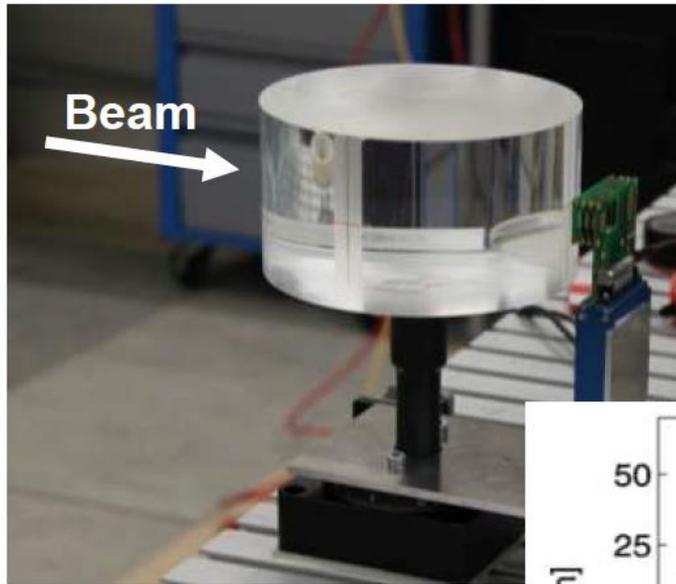
3. **Particle direction** *J. Jakubek et al. 2011 JINST 6 C12010*

*P. Soukup et al. 2011 JINST 6 C01060*

Slide courtesy of M. Martisikova, German Cancer Research Centre, Heidelberg

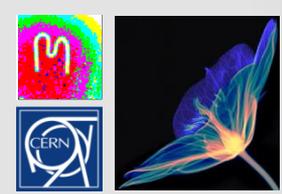


# Carbon Therapy beam monitoring

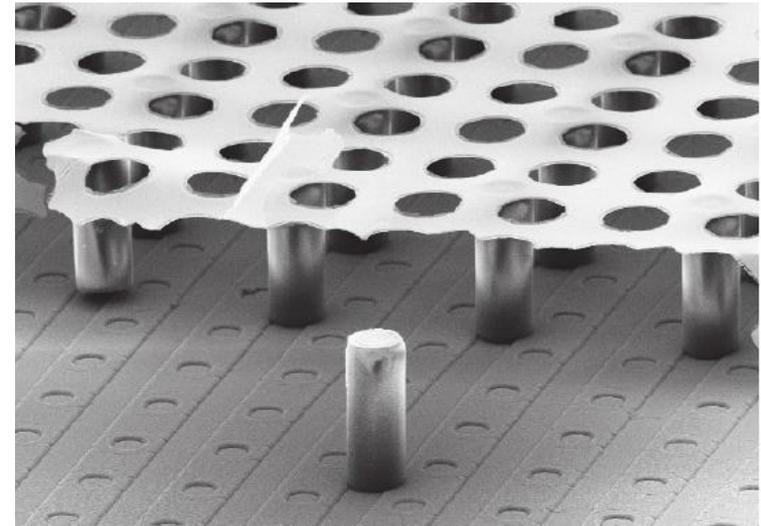
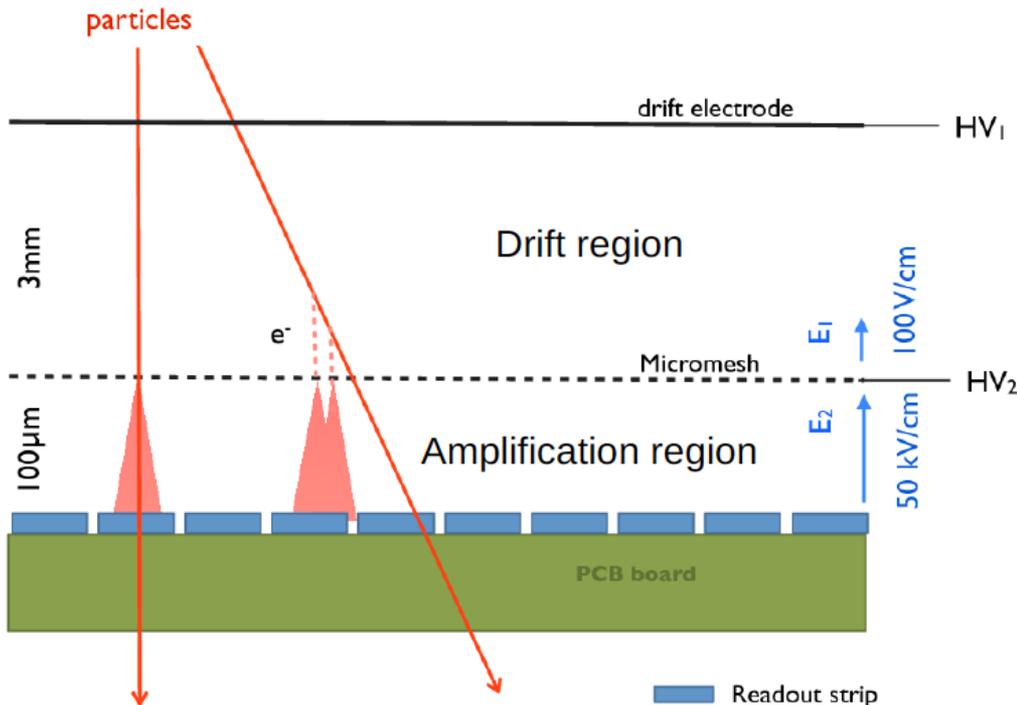


Gwosch et al.: PMB 58 (2013) 3755

Slide courtesy of M. Martisikova, German Cancer Research Centre, Heidelberg



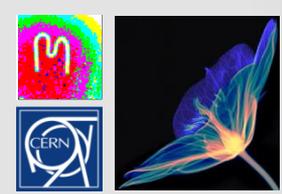
# Gas detector readout - InGrid



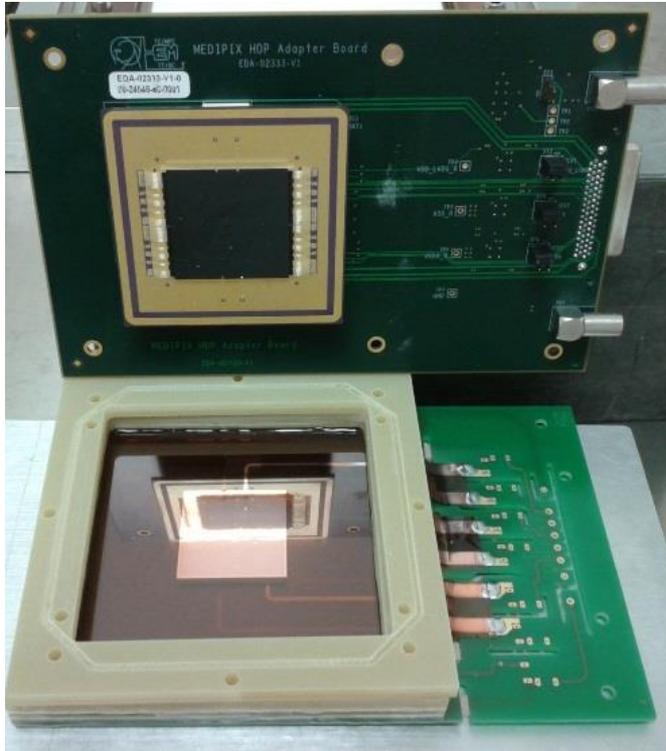
Semiconductor detector is replaced with charge amplification grid  
Permits lower energy events to be detected

NB: GEM foils may be used in place of the InGrid foils

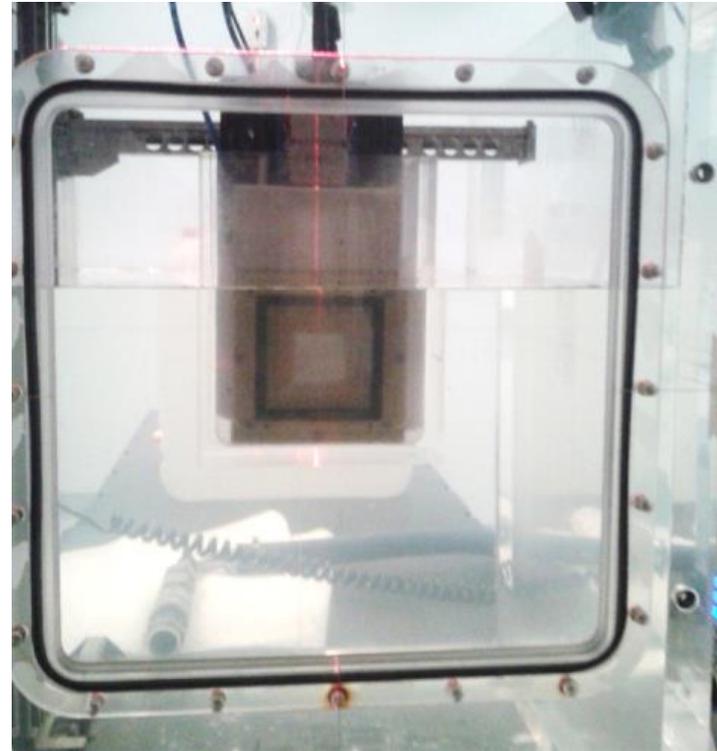
Slide courtesy of H. Van der Graaf, Nikhef, NL



# GEMPix for Hadron Therapy

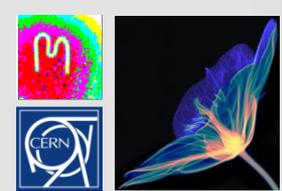


GEMPix detector: 2 x 2 Timepix chips combined with gas detector  
8 cm<sup>2</sup> GEM detector read by 55x55 $\mu$ m pixels, 262 000 channels



GEMPix placed in phantom

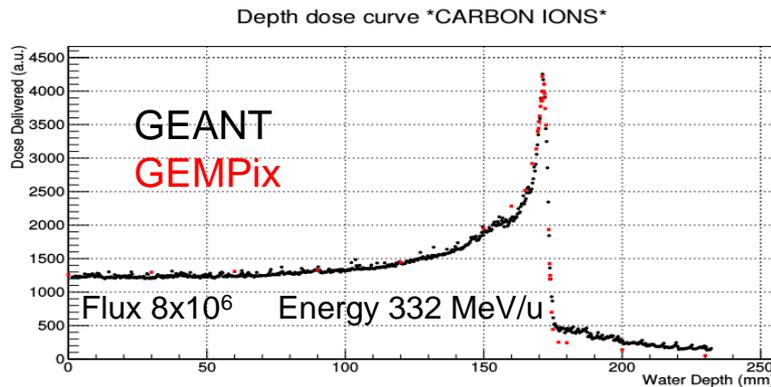
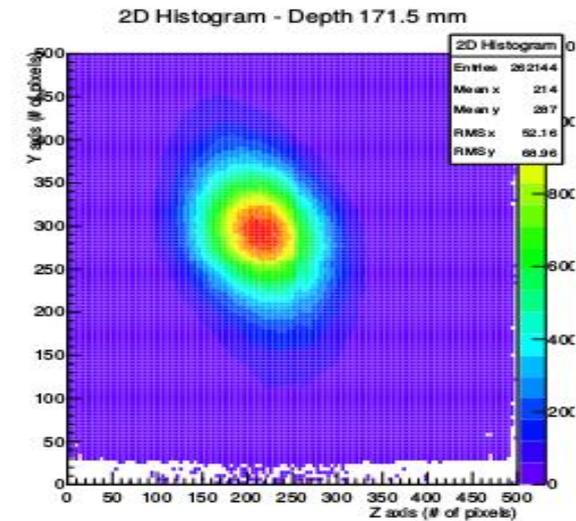
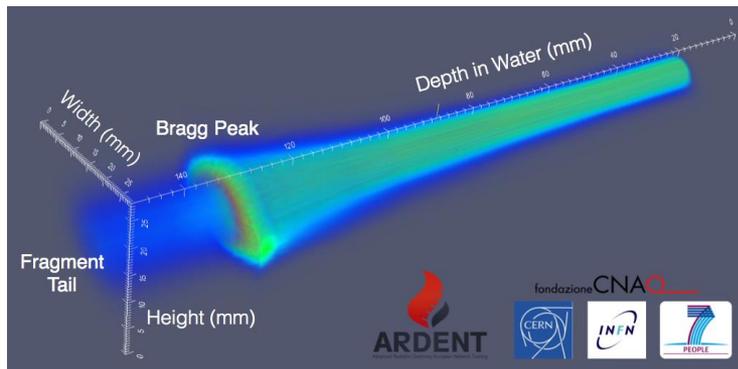
F. Murtas , M. Silari, S. George,  
A. Rimoldi, A. Tamborini,  
M. Ciocca and A. Mirandola  
CERN, INFN, UNIPV, CNAO



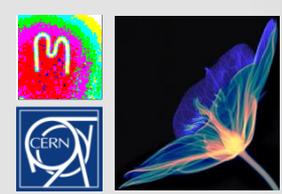
# GEMPix for Hadron Therapy



- **3D measurements** of energy released in water phantom in hadrontherapy treatment facility (CNAO Pavia)

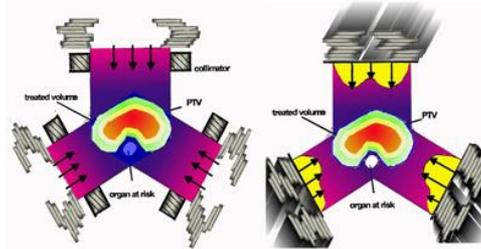
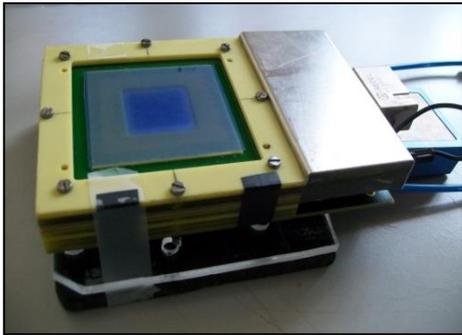


F. Murtas , M. Silari, S. George,  
A. Rimoldi, A. Tamborini,  
M. Ciocca and A. Mirandola  
CERN, INFN, UNIPV, CNAO

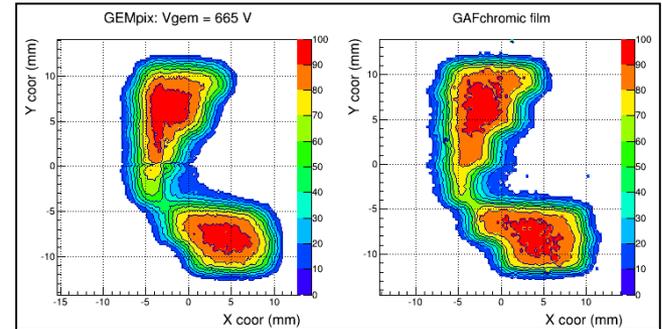
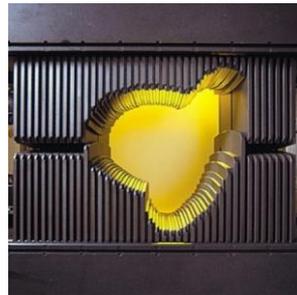
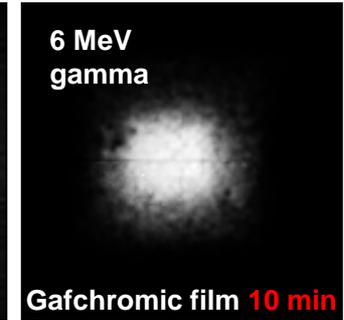
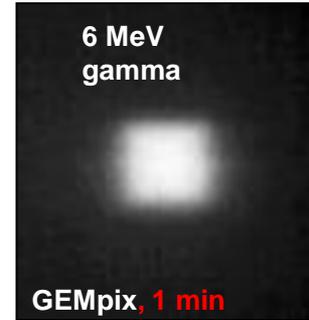


# GEMPix for Radiotherapy

GEMPix detector (8cm<sup>2</sup> GEM detector read by 55x55µm pixels, 262 000 channels )  
 - **2D measurements** of energy released in IMRT (Policlinico Tor Vergata Roma)

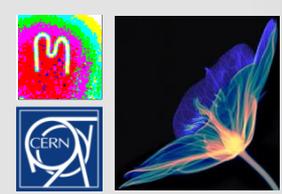


**Intensity Modulated Radiation Therapy (IMRT)**

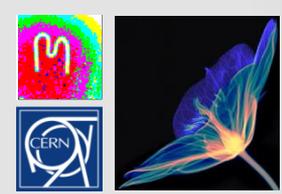


F. Murtas , G. Claps, D. Falco  
 CERN, INFN, PTV

An optimal agreement between GEMPix and gafchromic film is obtained  
 Real-time measurements with GEMPix allows fast Quality Assurance procedure

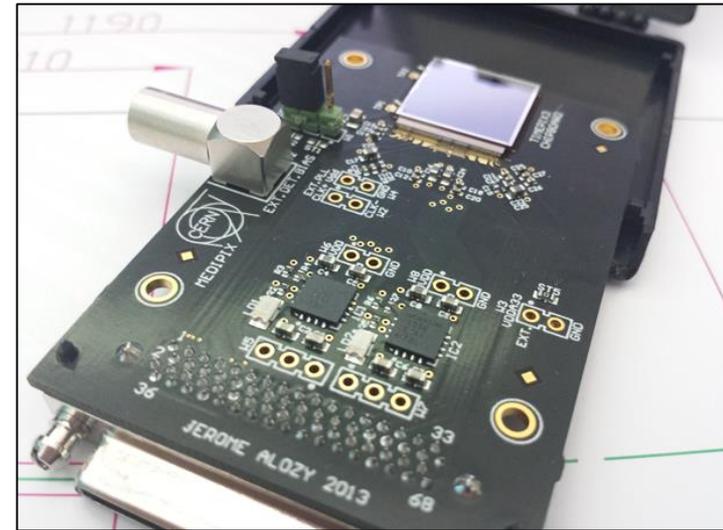


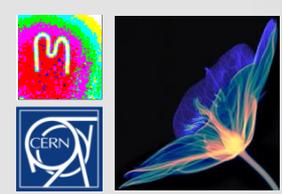
For more information on GEMpix in hadron therapy please see the presentation of **Fabrizio Murtas** on Friday morning



# Timepix3

- Timepix3 is a multi purpose hybrid pixel detector developed within the Medipix3 collaboration
- Designed for particle tracking with simultaneously time of arrival (TOA) and energy measurement (TOT)
- Data driven read out mode
- 1.56 ns TOA precision
- 130 nm CMOS





# The Medipix3 Collaboration

University of Canterbury, Christchurch, New Zealand

CEA, Paris, France

CERN, Geneva, Switzerland,

DESY-Hamburg, Germany

Albert-Ludwigs-Universität Freiburg, Germany

University of Glasgow, Scotland, UK

Leiden University, The Netherlands

NIKHEF, Amsterdam, The Netherlands

Mid Sweden University, Sundsvall, Sweden

IEAP, Czech Technical University, Prague, Czech Republic

ESRF, Grenoble, France

Universität Erlangen-Nürnberg, Erlangen, Germany

University of California, Berkeley, USA

VTT, Information Technology, Espoo, Finland

KIT/ANKA, Forschungszentrum Karlsruhe, Germany

University of Houston, USA

Diamond Light Source, Oxfordshire, England, UK

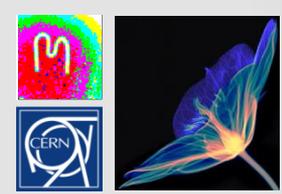
Universidad de los Andes, Bogota, Colombia

University of Bonn, Germany

AMOLF, Amsterdam, The Netherlands

Technical University of Munich, Germany

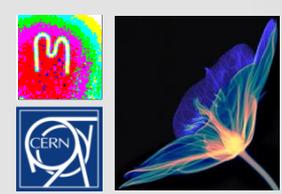
Brazilian Light Source, Campinas, Brazil



# Specifications

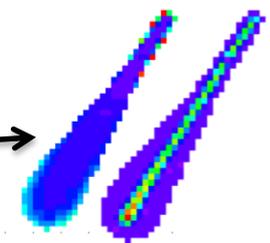
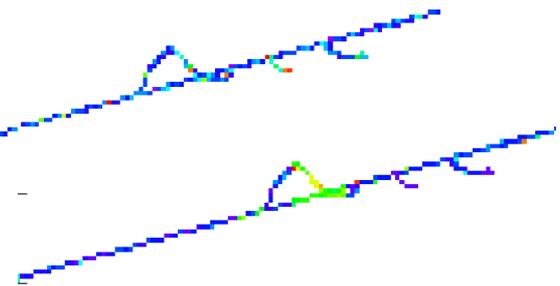
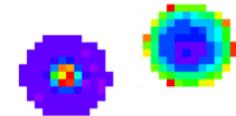
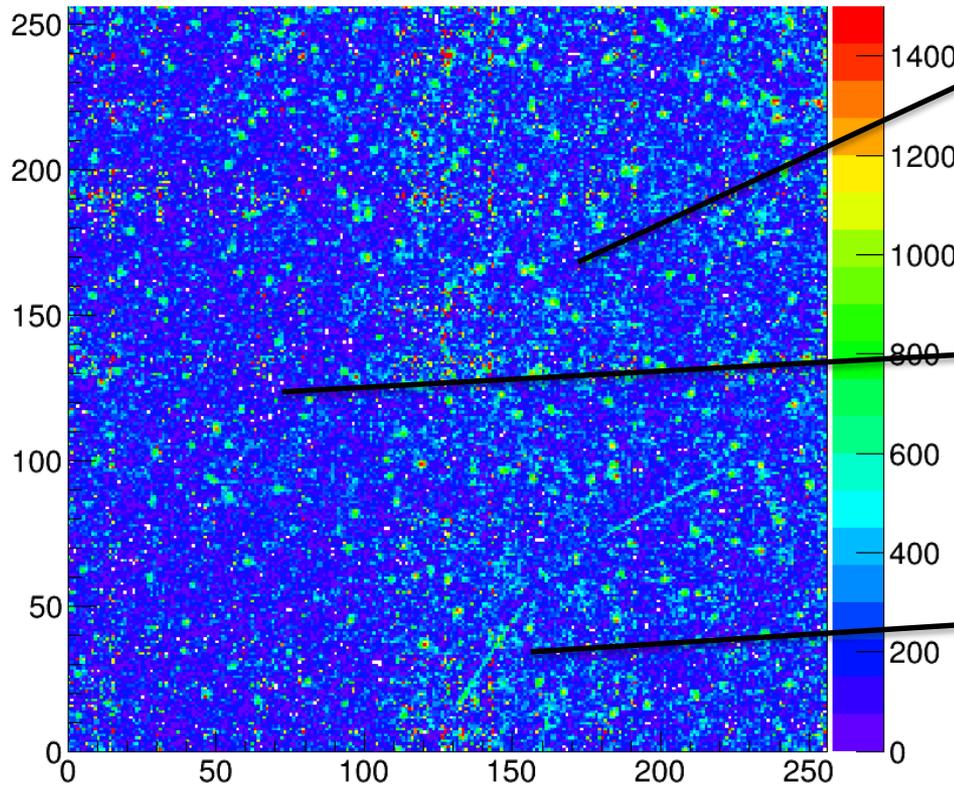
## Timepix3

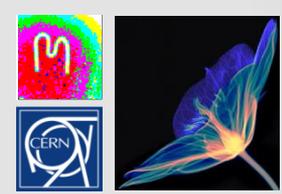
Pixel matrix	256 x 256
Pixel size	55 x 55 $\mu\text{m}^2$
Technology	CMOS 130 nm
Measurement modes	<ul style="list-style-type: none"><li>• Simultaneous 10 bit TOT and 14 + 4 bit TOA</li><li>• 14 + 4 bit TOA only</li><li>• 10 bit PC and 14 bit integral TOT</li></ul>
Readout type	<ul style="list-style-type: none"><li>• Data driven</li><li>• Frame based (both modes with zero suppression)</li></ul>
Dead time (pixel, data driven)	>475 ns (pulse processing + packet transfer)
Output bandwidth	40 Mbits/s – 5.12 Gbits/s
Maximum count rate	0.4 Mhits/mm <sup>2</sup> /s (data driven mode)
TOA Precision	1.56 ns
Front end noise	60e- RMS
Minimum threshold	~500 e-



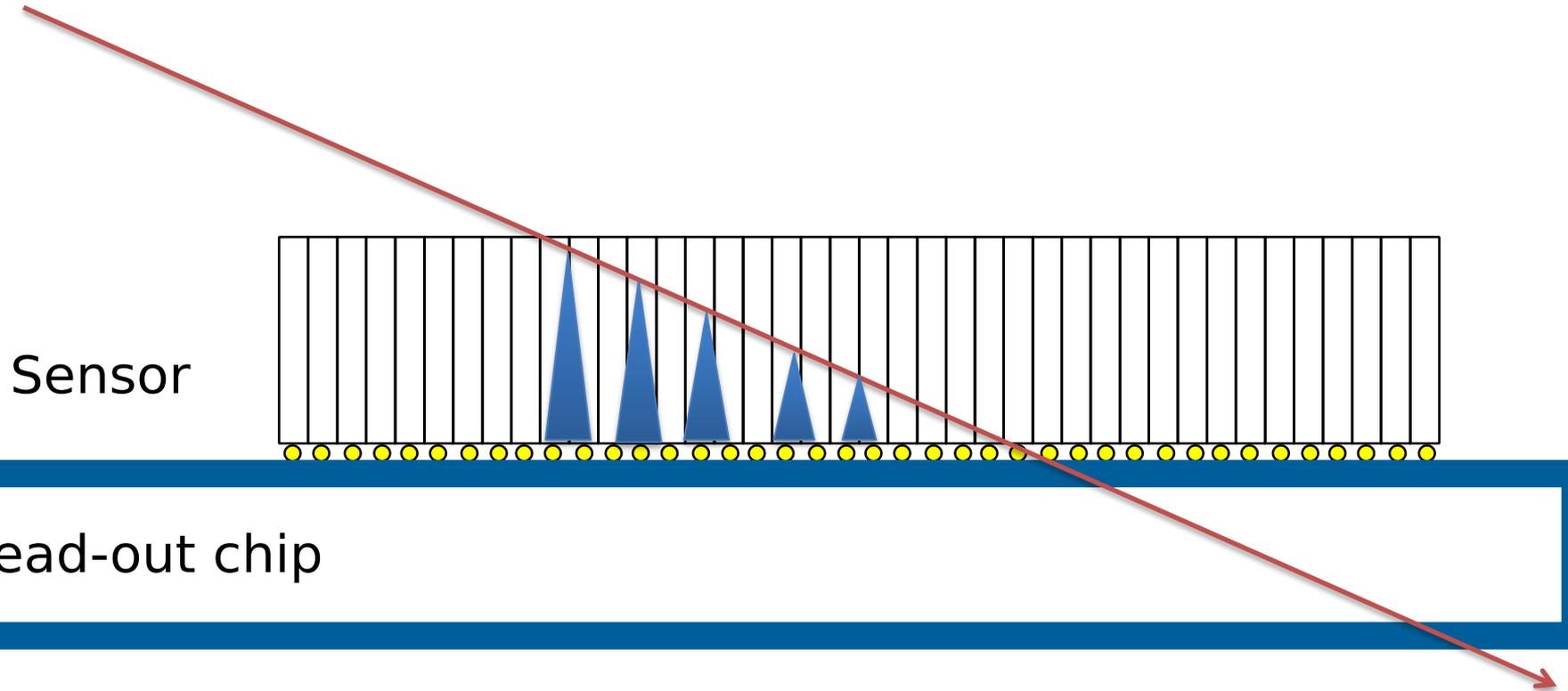
# Energy and time measurements with cosmic particles

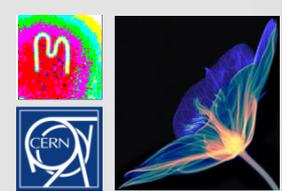
Integral frame ~ 72h





# Energy and time measurements with cosmic particles

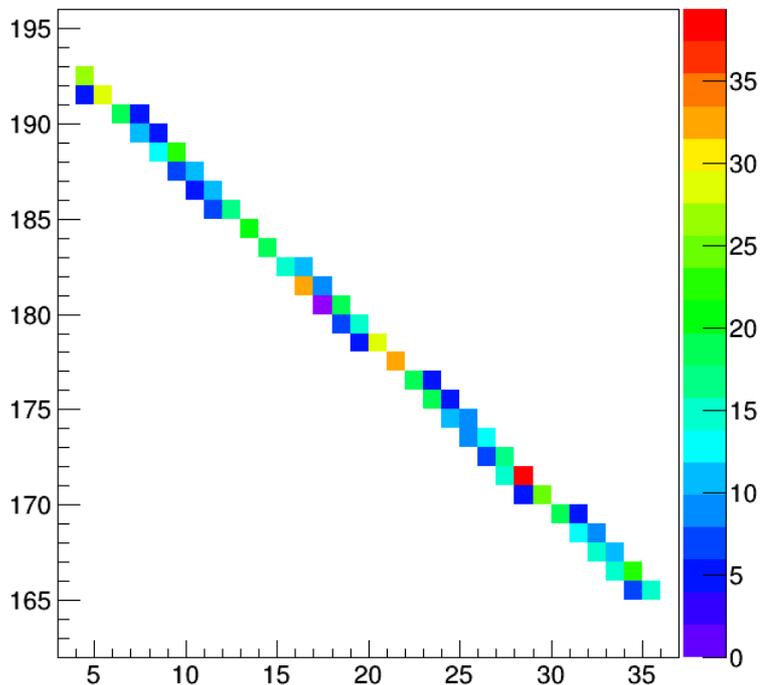




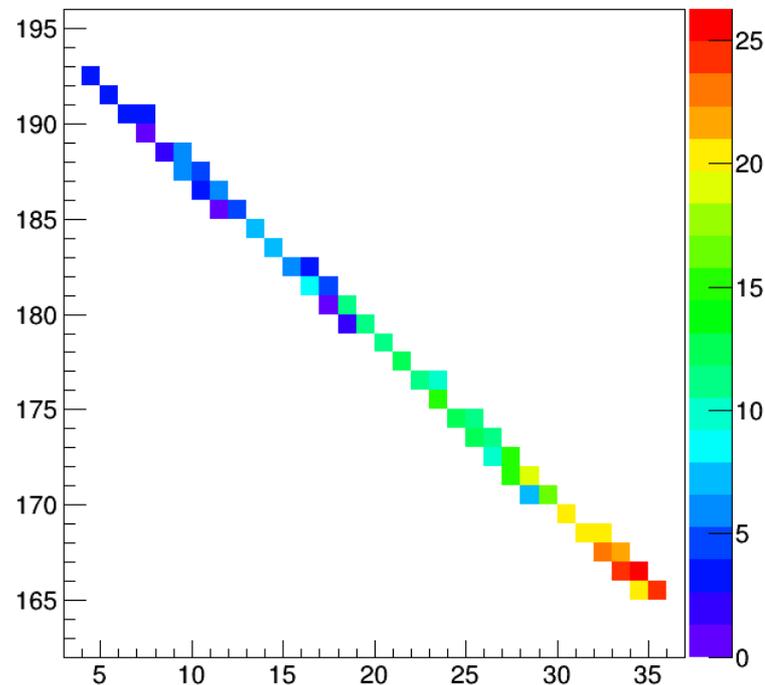
# Cosmic ray in Timepix3 - measurement



Energy (keV)

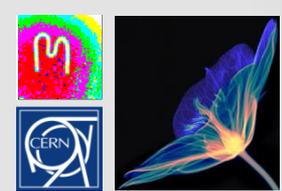


Time (ns)

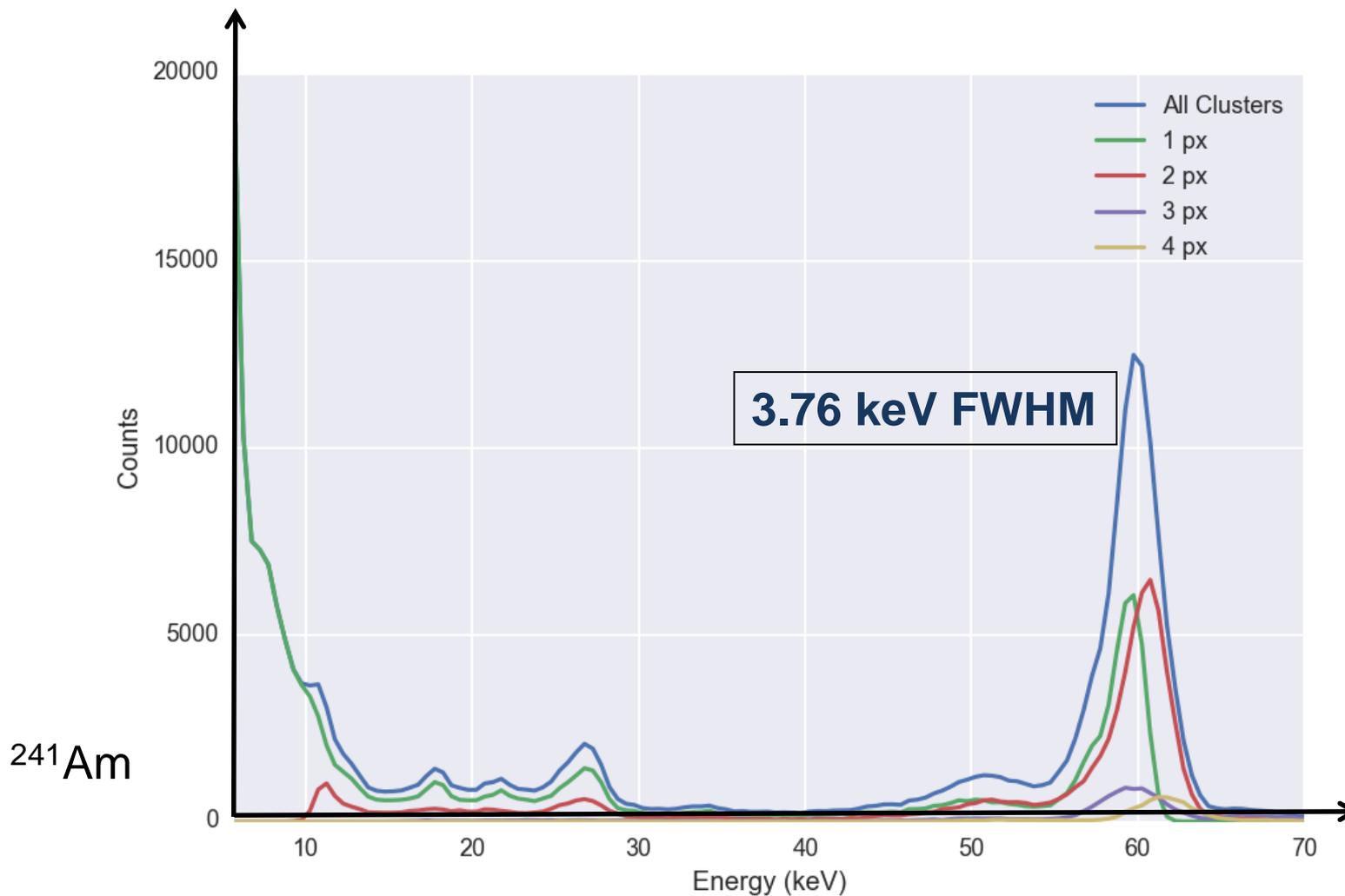


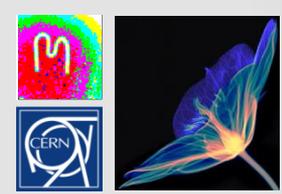
**Precise arrival time information (1.6ns steps) provides depth of interaction within the sensor layer**

Bias 100V, Ikrum 5, **with** time walk correction



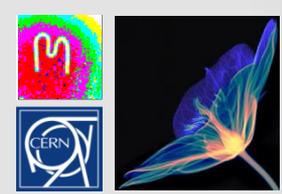
# Timepix3 Spectrum(Si 55 $\mu\text{m}$ /300 $\mu\text{m}$ )





# But what if you need to work at really high fluxes e.g. CT?

On-pixel or inter-pixel event processing becomes essential



# Medipix3 Motivation

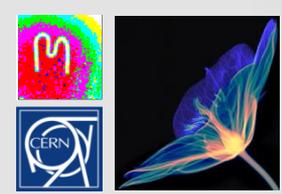
Access to spectroscopic information opens a new dimension in X-ray imaging

Retaining the energy information in X-ray radiography extracts more information from a given deposited dose

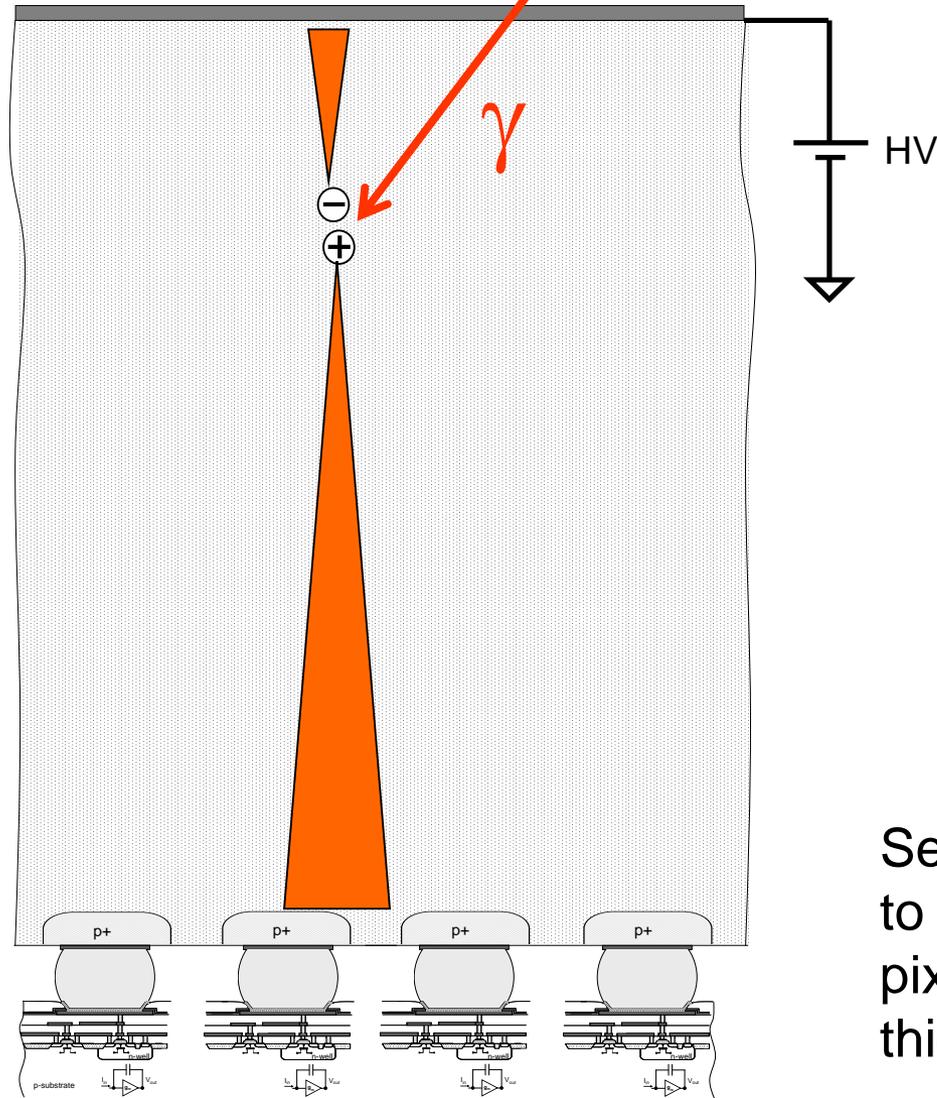
Contrast agents (with metal nanoparticles) attached to bio markers could open the field of functional imaging using X-rays

But several technical challenges remain:

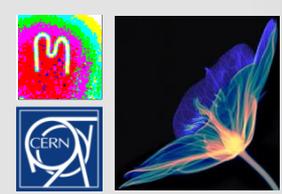
- Charges sharing in the sensor reduces (or destroys) spectral fidelity
- High photon fluxes prohibit the use of data driven architectures



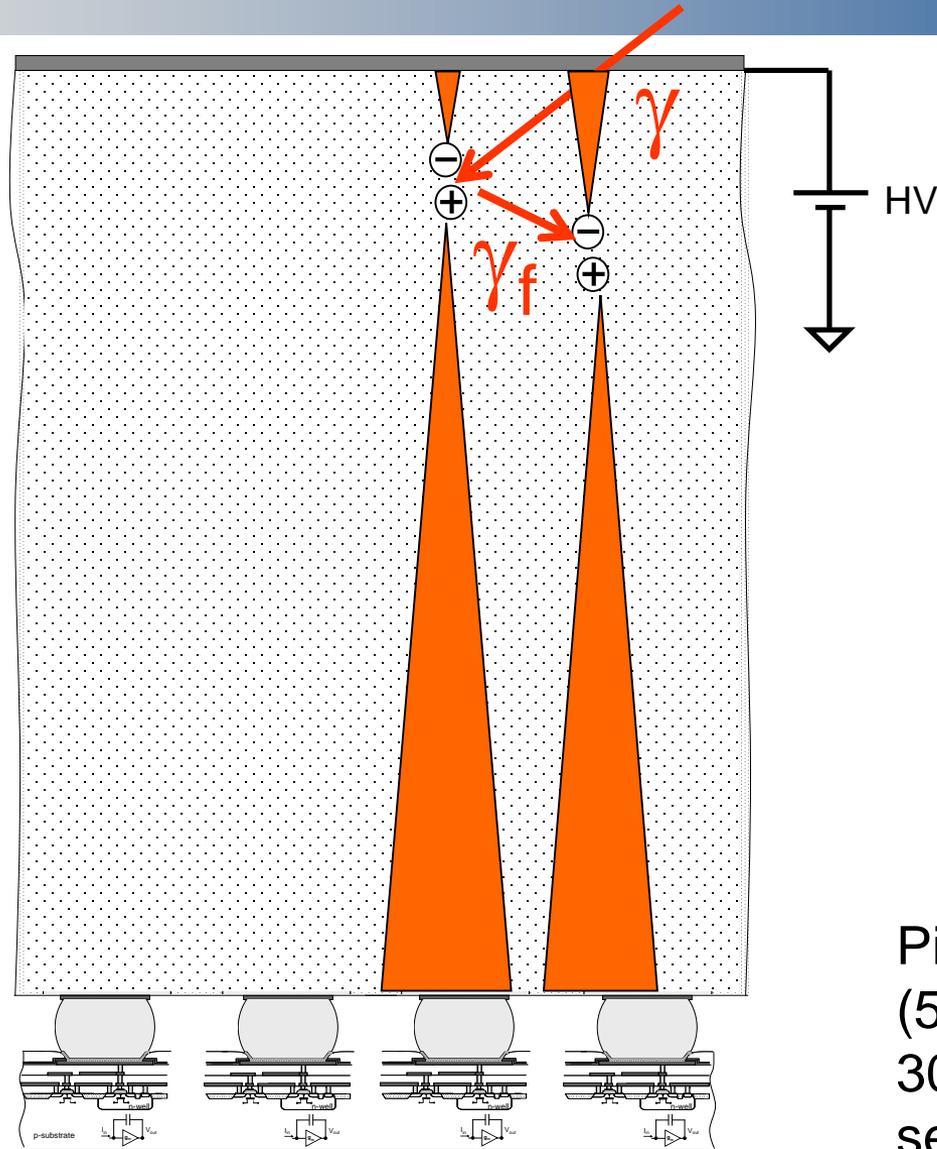
# Cross section of a Hybrid Pixel Detector system (X-ray photon energy deposition)



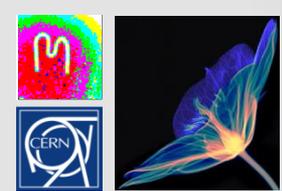
Sensor dimensions  
to scale ( $55\mu\text{m}$   
pixel pitch,  $300\mu\text{m}$   
thick sensor)



# Fluorescence in high-Z materials



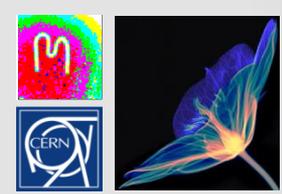
Picture to scale  
(55 $\mu\text{m}$  pixel pitch,  
300 $\mu\text{m}$  thick  
sensor)



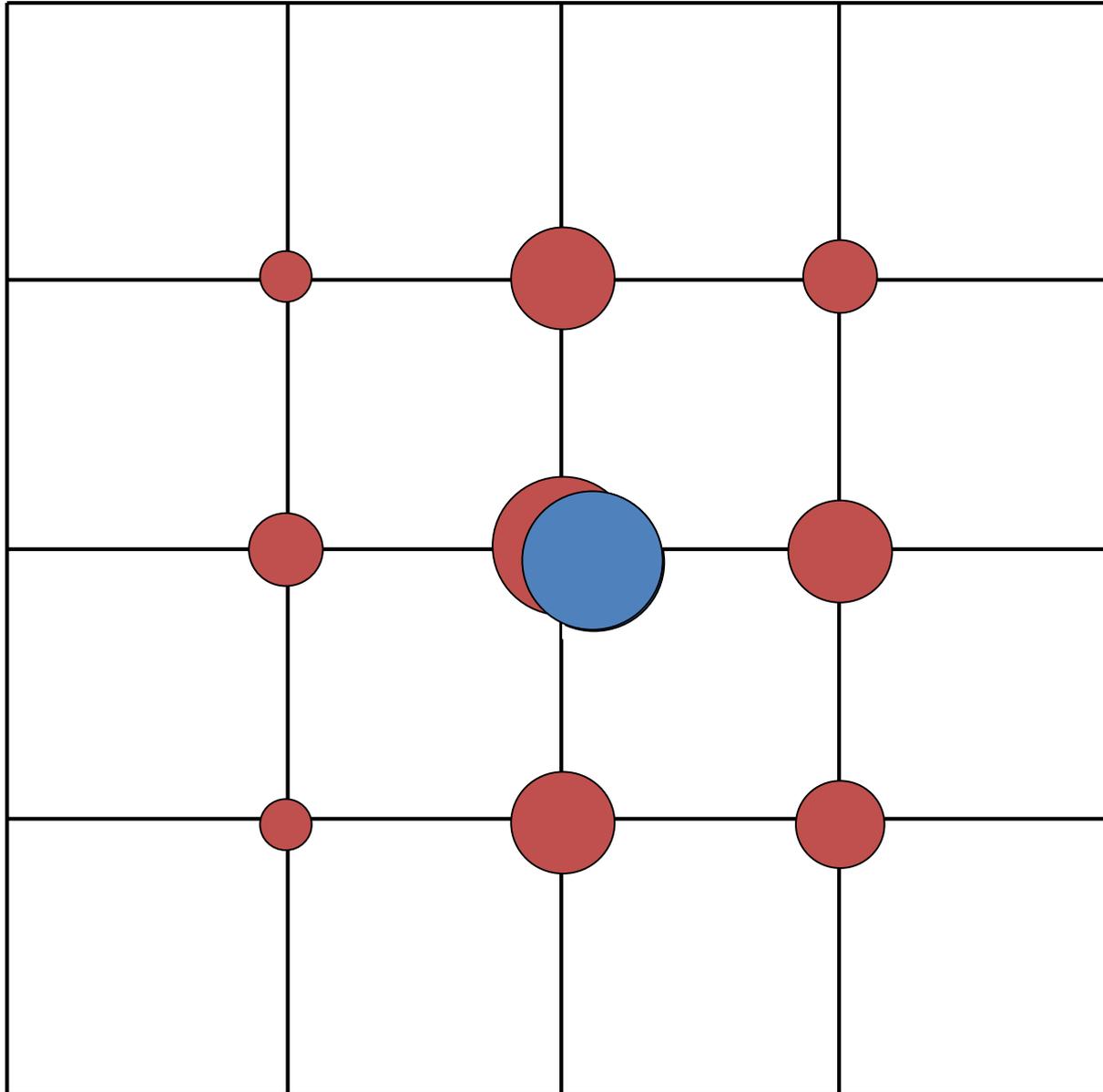
# Fluorescence in high-Z detectors

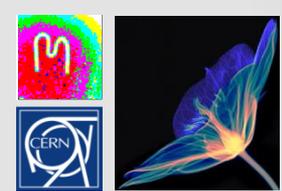
	<b>N</b>	<b>k-edge (keV)</b>	<b>K<math>\alpha</math> energy (keV)</b>	<b>d<math>\alpha</math> (<math>\mu</math>m)</b>	<b><math>\eta</math> [%]</b>
<b>Si</b>	14	1.84	1.74	12	5
<b>Ge</b>	32	11.11	9.89	51	55
<b>GaAs:</b>					
<b>Ga</b>	31	10.38	9.25	42	51
<b>As</b>	33	11.87	10.54	16	57
<b>CdTe:</b>					
<b>Cd</b>	48	26.73	23.17	128	84
<b>Te</b>	52	31.82	27.47	64	87

Journal of Instrumentation Volume 6 June 2011  
 D Pennicard and H Graafsma 2011 *JINST* **6** P06007  
 doi:10.1088/1748-0221/6/06/P06007



# The algorithm for charge reconstruction and hit allocation: Charge Summing Mode

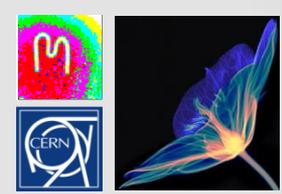




# Medipix3 Specifications

Suitable for low-Z  
 detectors such  
 as SiTe, GaAs

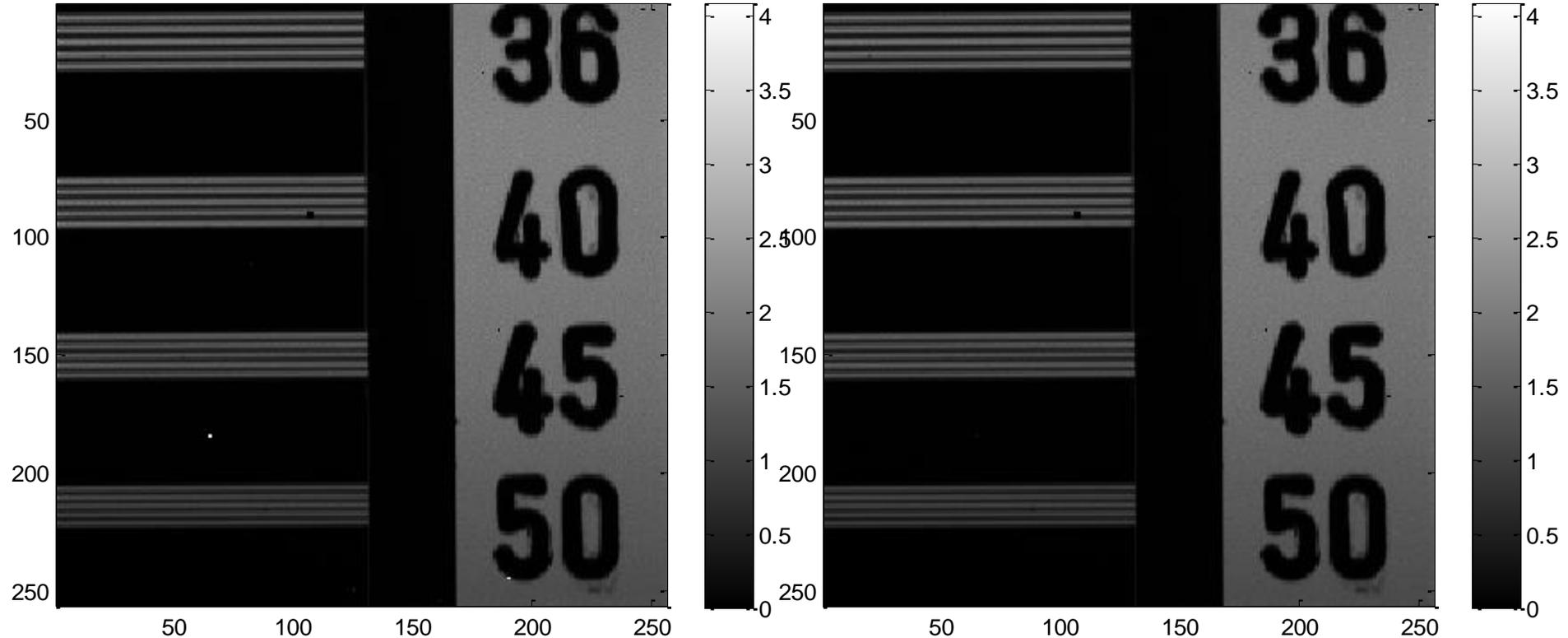
<b>Pixel matrix</b>	<b>256 x 256</b>
Pixel size	55 x 55 $\mu\text{m}^2$ or 110 x 110 $\mu\text{m}^2$
Technology	CMOS 130 nm
Measurement modes	<ul style="list-style-type: none"> <li>• Single pixel (SPM)</li> <li>• Charge summing (CSM)</li> </ul>
Gain modes	<ul style="list-style-type: none"> <li>• Super low gain mode</li> <li>• Low gain mode</li> <li>• High gain mode</li> <li>• Super high gain mode</li> </ul>
# thresholds	<ul style="list-style-type: none"> <li>• 2 per 55 <math>\mu\text{m}</math> pixel</li> <li>• 8 per 110 <math>\mu\text{m}</math> pixel</li> </ul>
Programmable counter depths	<ul style="list-style-type: none"> <li>• 2 x 1-bit</li> <li>• 2 x 6-bit</li> <li>• 2 x 12-bit</li> <li>• 1 x 24-bit</li> </ul>
Readout type	Frame based <ul style="list-style-type: none"> <li>• Sequential R/W</li> <li>• Simultaneous R/W</li> </ul>
Readout Time	Depends on counter depth used
Minimum threshold	~ 500 e-



# Imaging a LPPM phantom (Si 55 $\mu\text{m}/300\mu\text{m}$ )

## Single Pixel Mode (SPM)

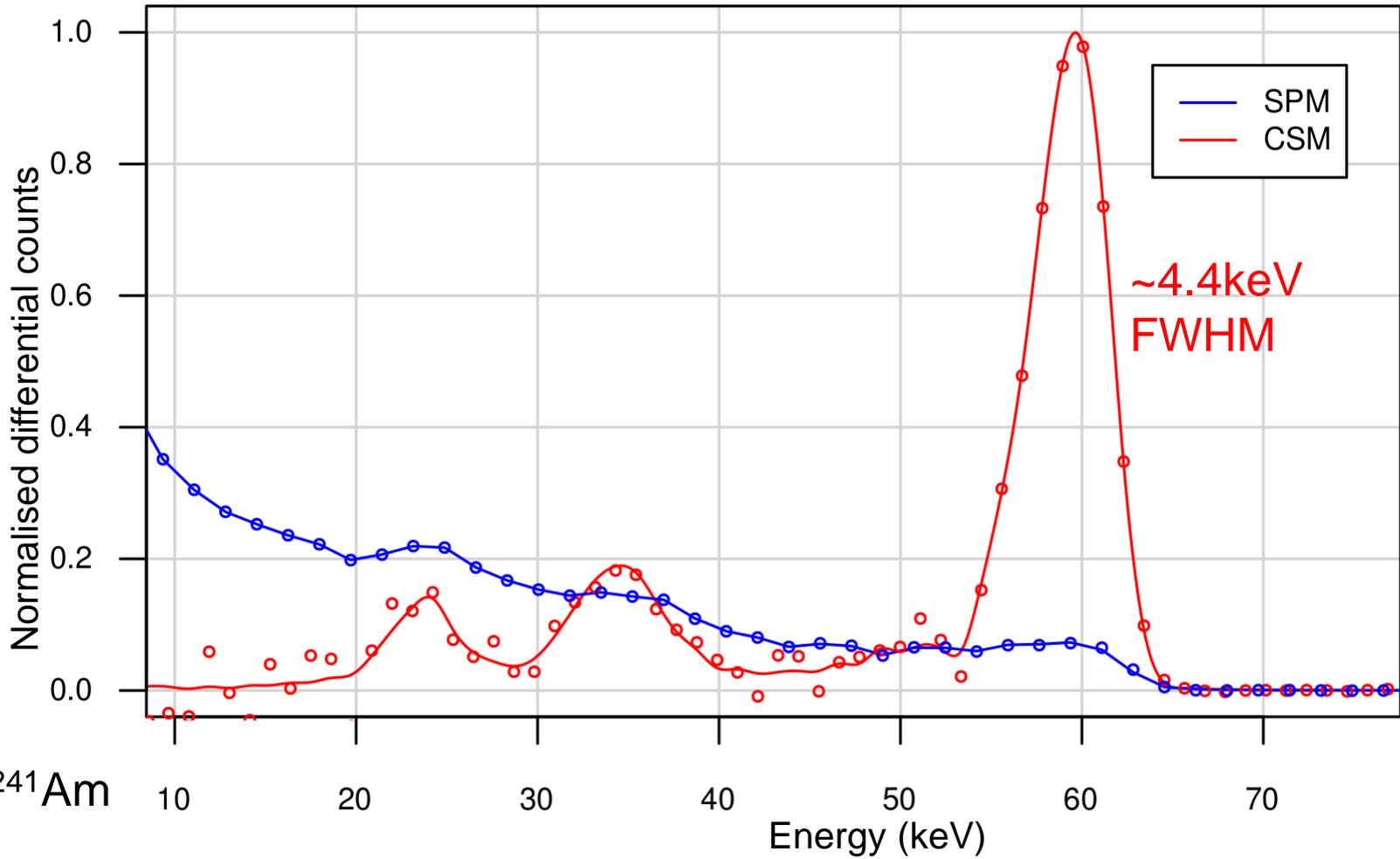
## Charge Summing Mode (CSM)



**LPPM phantom** Tube voltage: 15 kV, Tube current: 5mA, Al filtering, 1s acquisition

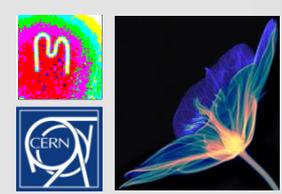
**RAW DATA**

# Energy Response Function (CdTe 110 $\mu\text{m}/2\text{mm}$ )

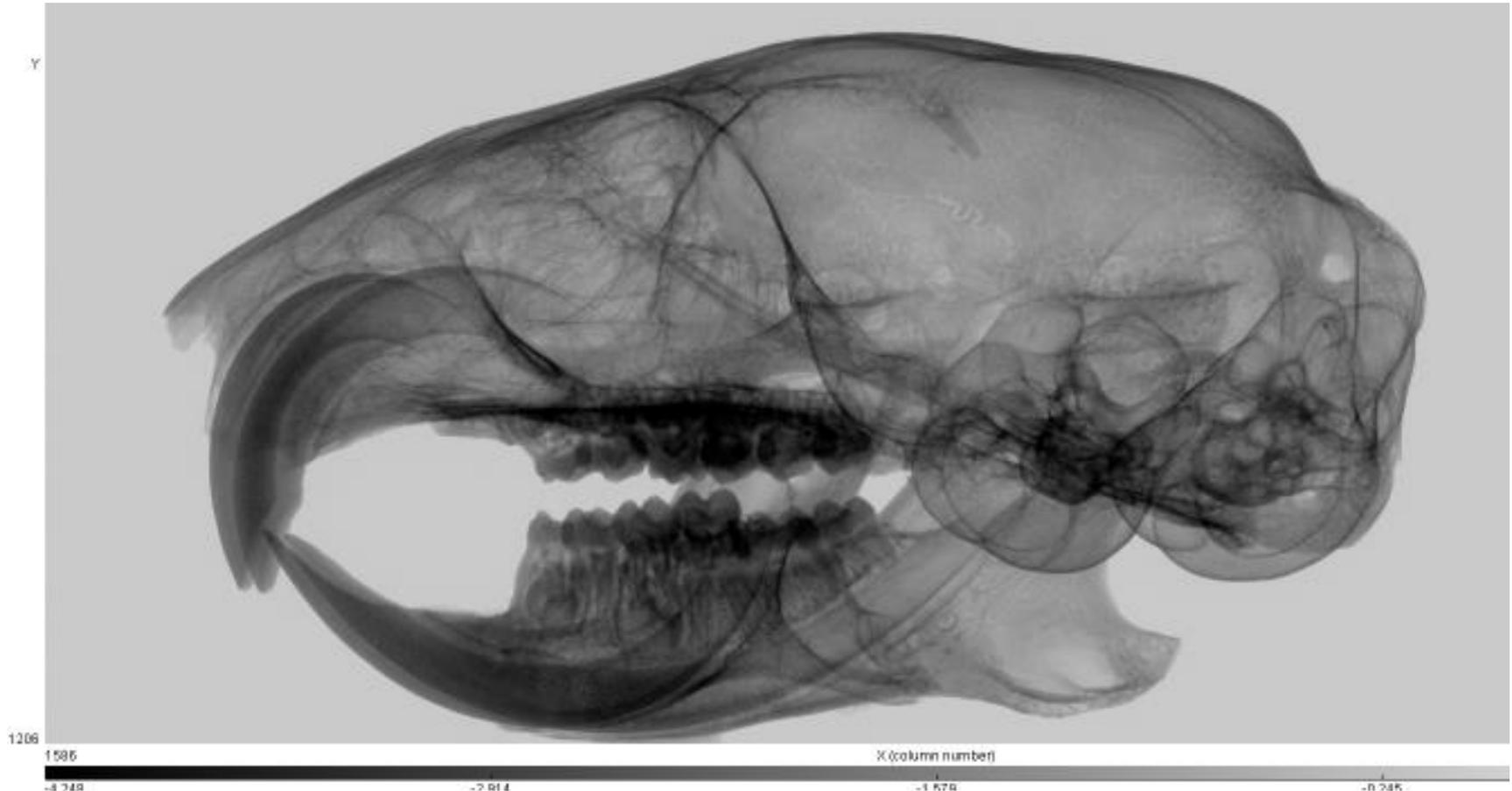


Slide courtesy of T. Koenig, KIT

Charge Summing in Spectroscopic X-Ray Detectors With High-Z Sensors; TNS  
Dec. 2013 4713-4718

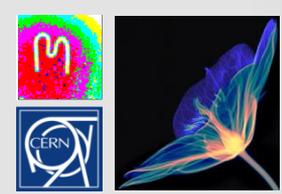


# Medipix3 Image (GaAs $55\mu\text{m}/500\mu\text{m}$ )

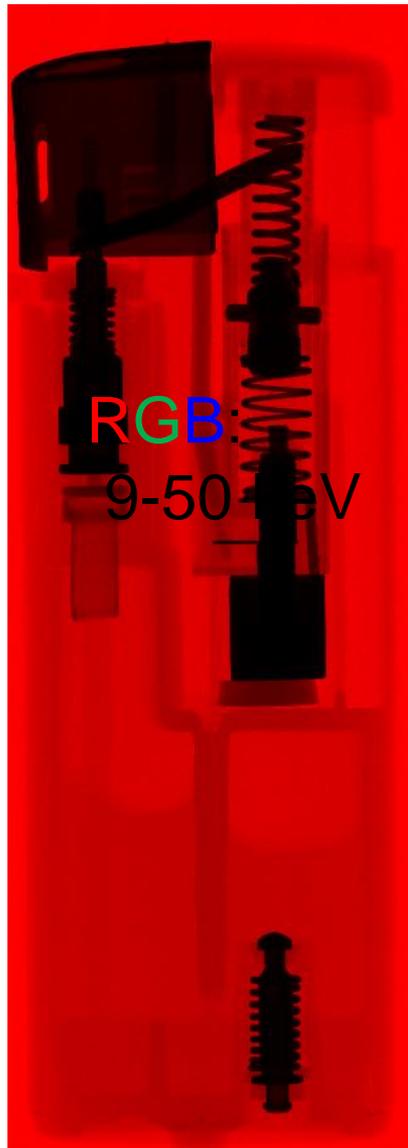


A tiled X-ray image of a mouse skull.

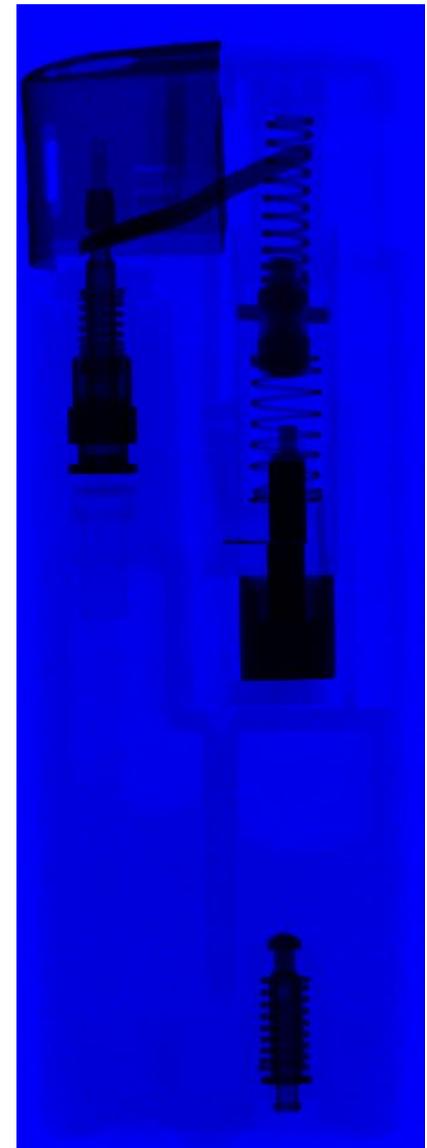
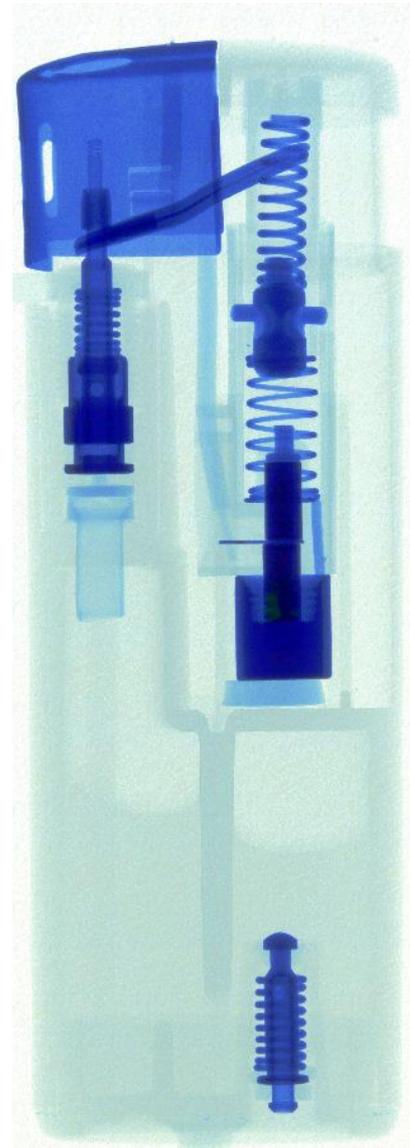
Courtesy S. Procz

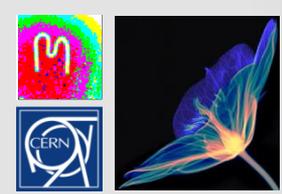


# Colour x-ray of a lighter



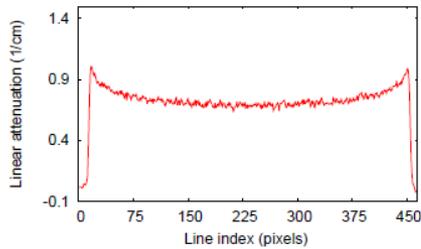
RGB:  
9-50 keV



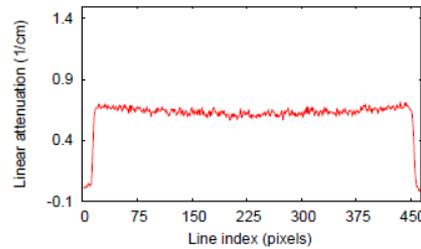


# Spectral imaging of Joints

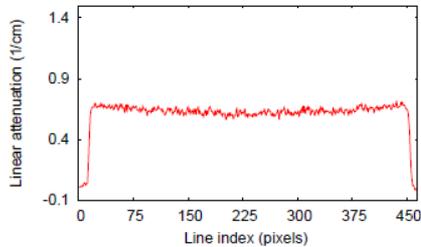
## Removal of beam hardening artifacts



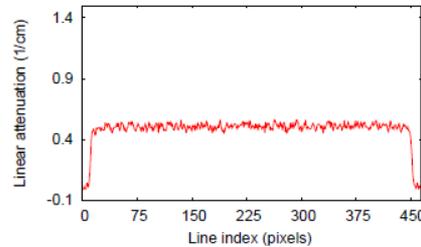
(a) 15 to 120 keV



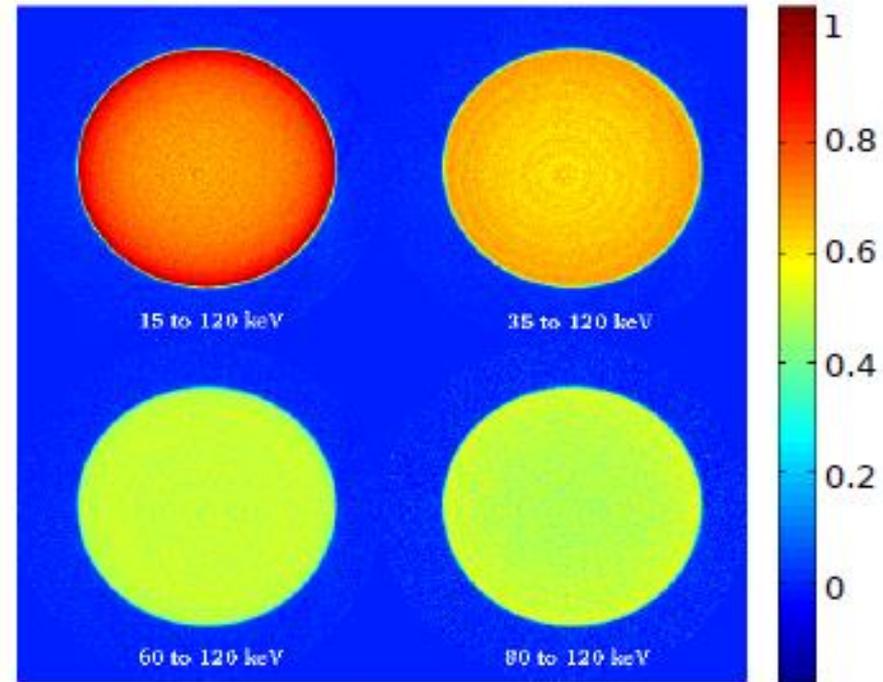
(b) 35 to 120 keV



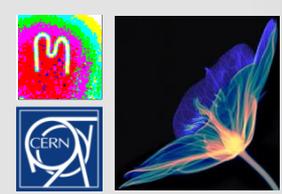
(c) 60 to 120 keV



(d) 80 to 120 keV

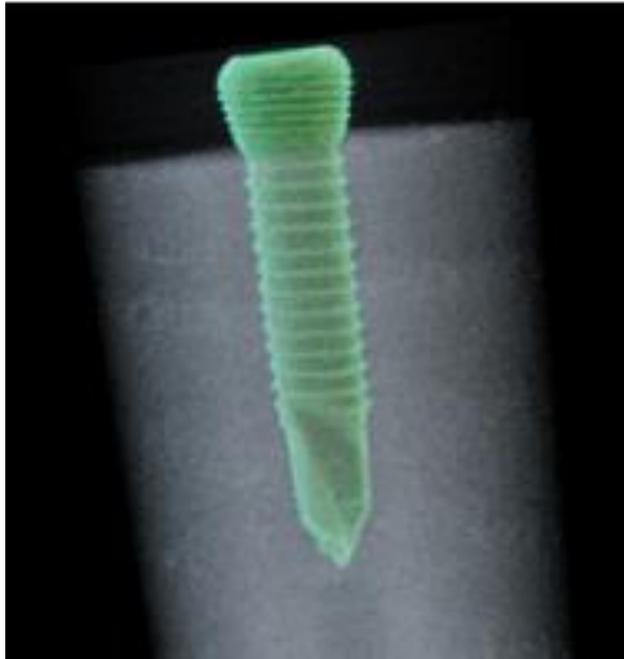


Slide courtesy of A. Butler, University of Otago, New Zealand and MARS Bio-Imaging

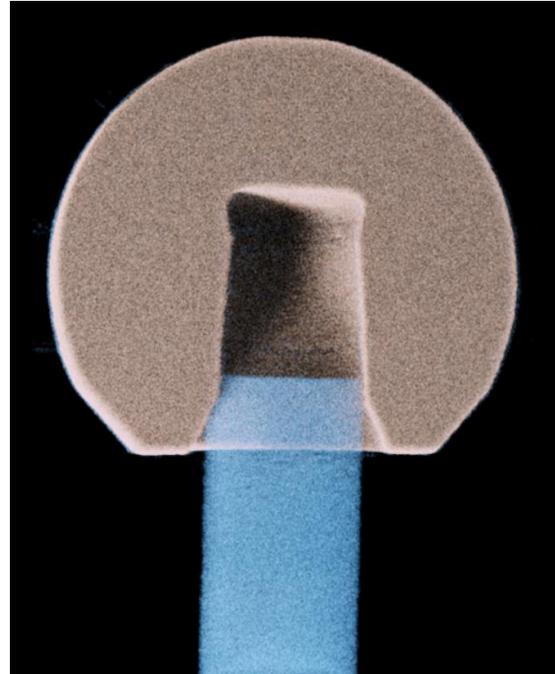


# Spectral imaging of Joints

## Removal of beam hardening artifacts



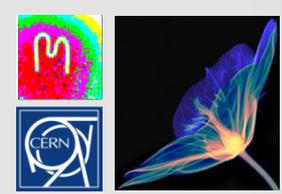
Titanium screw in PMMA



CoCr femoral head with PMMA shaft

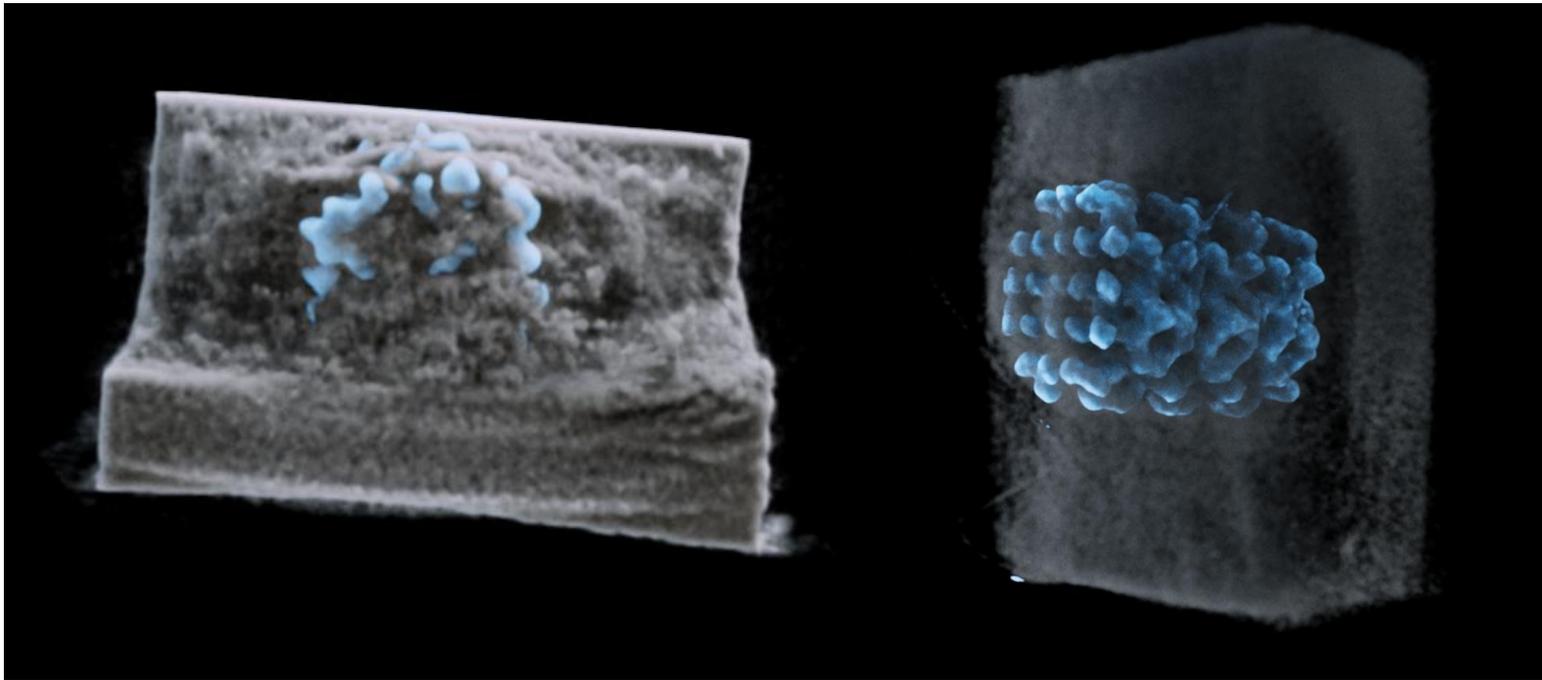


Slide courtesy of A. Butler, University of Otago, New Zealand and MARS Bio-Imaging



# Spectral imaging of Joints

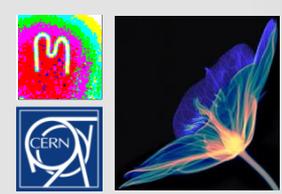
Titanium implant in sheep bone



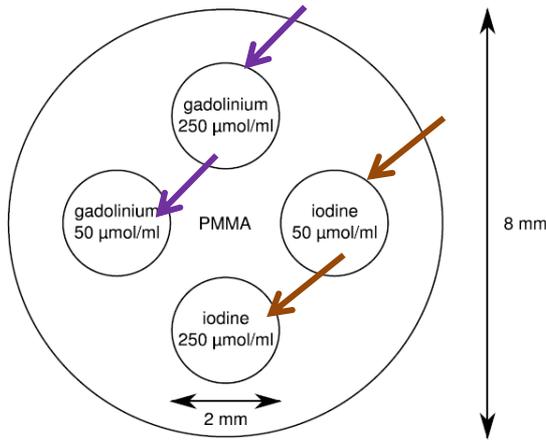
Enables better understanding of

- process of bone ingrowth
- bone / implant interface

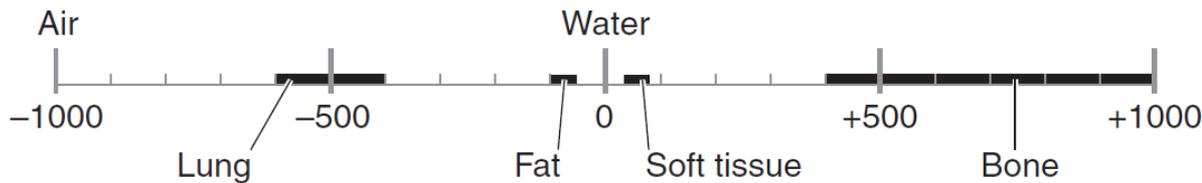
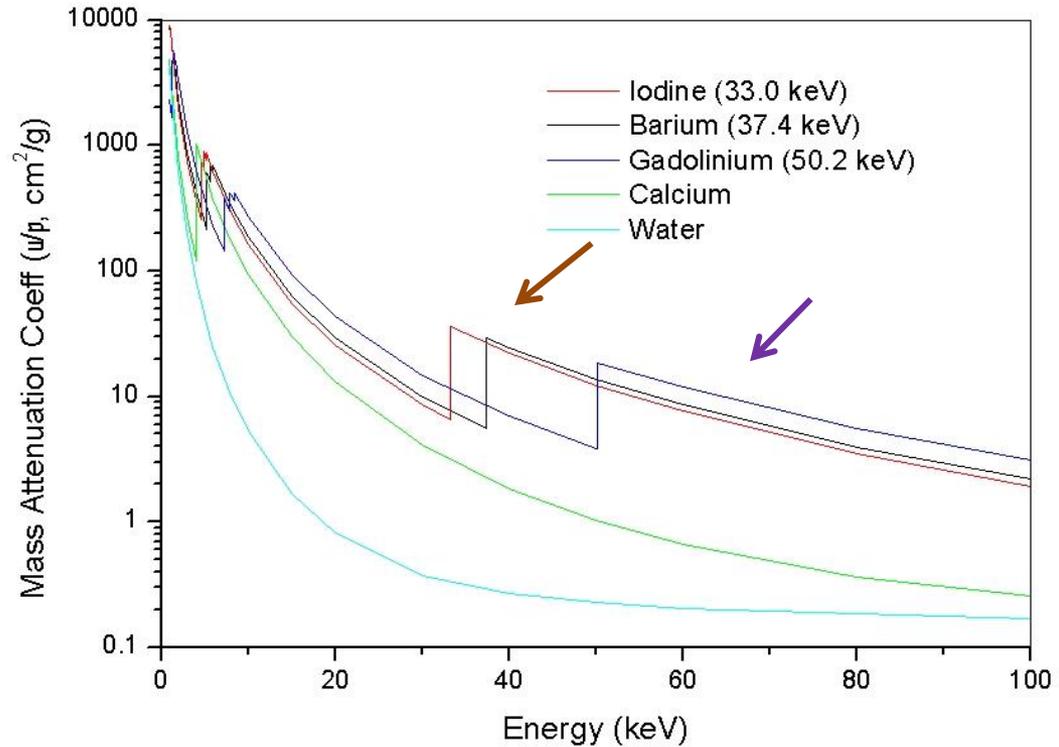
Slide courtesy of A. Butler, University of Otago, New Zealand and MARS Bio-Imaging



# Distinguishing Iodine and Gadolinium

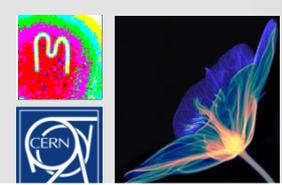


CT of a phantom  
0.15s acquisition  
720 projections

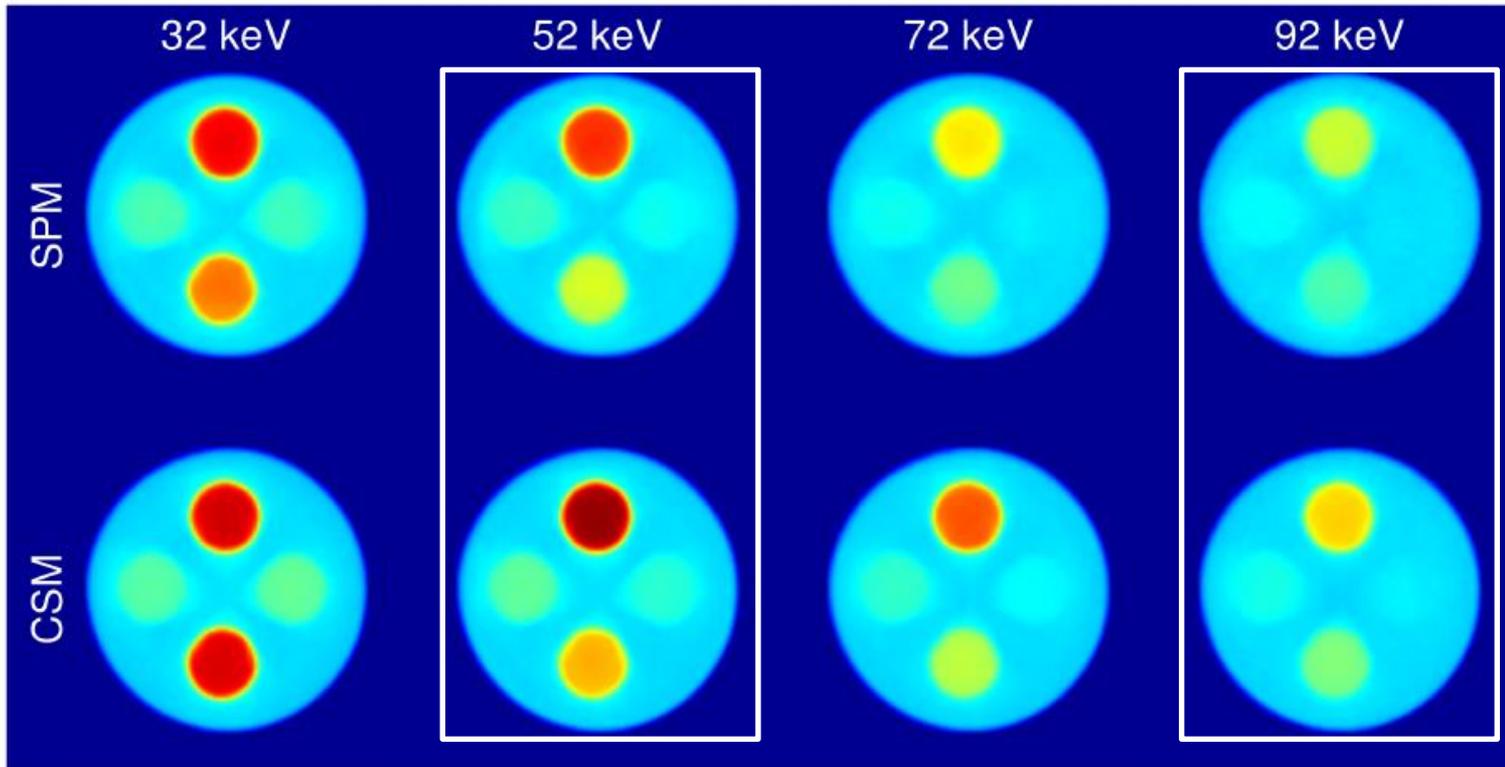


$$HU = 1000 \times \frac{\mu_X - \mu_{water}}{\mu_{water}}$$

Courtesy, T. Koenig, KIT



# Distinguishing Iodine and Gadolinium



Gd K-edge only visible in Charge Summing Mode

DQE better for Charge Summing Mode

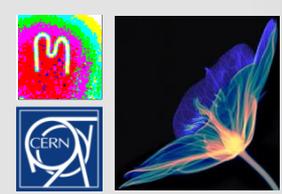
Courtesy, T. Koenig, KIT<sub>52</sub>



Workshop on  
Medical Applications of Spectroscopic X-ray Detectors  
CERN, 20-23 April 2015

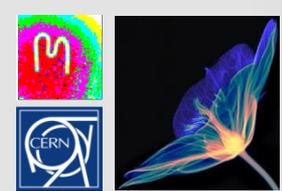


- 113 invited participants of which ~50 were from industry
- Large delegations from GE, Philips, Siemens and Toshiba
- Also major research institutes present :Johns Hopkins, University of Massachusetts, Mayo Clinic, Royal Marsden, TU Munich etc



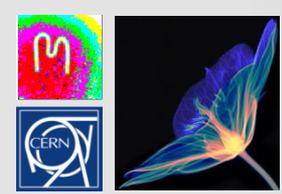
# What's next?

- A new Collaboration called Medipix4 is in formation
- Chips to be fully tile-able on 4-sides
- 2 chips development are foreseen (65nm CMOS)
- Medipix4 Photon counting spectrometric chip
  - Will use charge summing and allocation scheme
  - Multiple thresholds
  - Pixel pitch varied to match sensor material
  - Better high count rate performance (aimed at human CT)
- Timepix4
  - Smaller pixel pitch
  - Better timing resolution (sub-ns)
  - Better high count rate performance (TSV)

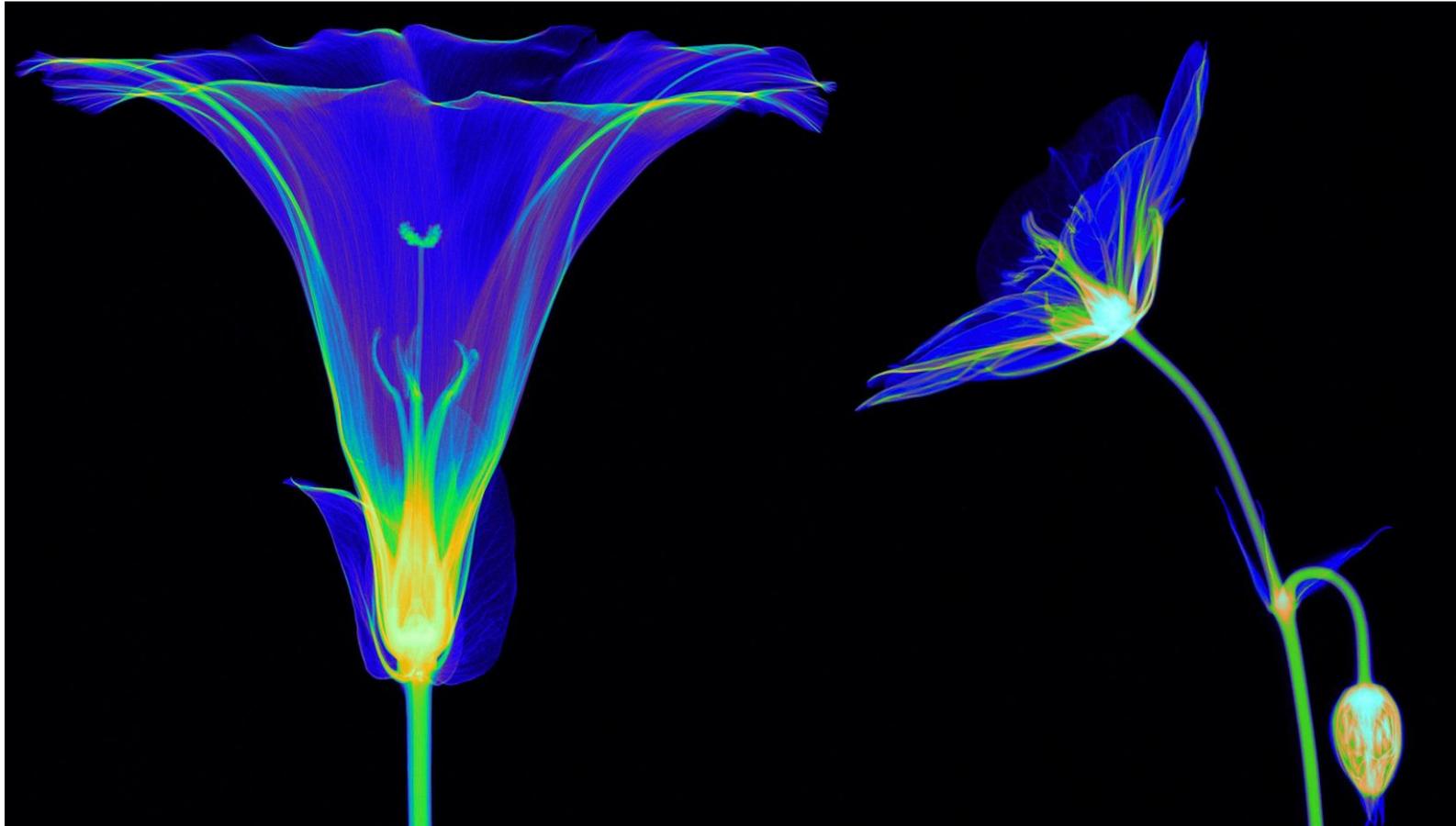


# Summary

- Hybrid pixel detectors were developed to respond to a need at the LHC – particle tracking in high rate environments
- Medipix2/Timepix proved the versatility of the technology for multiple other applications including in the medical applications sphere
- Timepix3 demonstrates particle tracking in a single semiconductor layer permits spectroscopic imaging at moderate fluxes
- Medipix3 demonstrated how spectral fidelity can be maintained even at relatively high X-ray fluxes
- The Medipix4 Collaboration (which is in formation) will fully explore the design of 4-side tile-able devices for the first time enabling larger areas to be covered seamlessly



# Thank you for your attention!



Medipix3RX images: S. Procz et al.