From High Energy Physics to Medical Physics: Detectors for Particle Therapy and Space

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(on behalf of microdosimetry collaboration}
Centre for Medical Radiation Physics , School of Physics, University of Wollongong.

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Acknowledgement of Contributors

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ANU: Prof David Hinde, Prof Mahananda Dasgupta

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SINTEF : Dr Angela Kok, Dr Marco Povoli and 3DMiMiC team

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Meet the CMRP team


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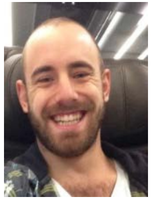
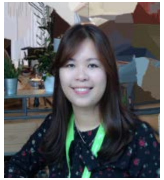

Dr Jeremy Davis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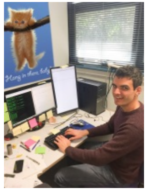
David Bolst

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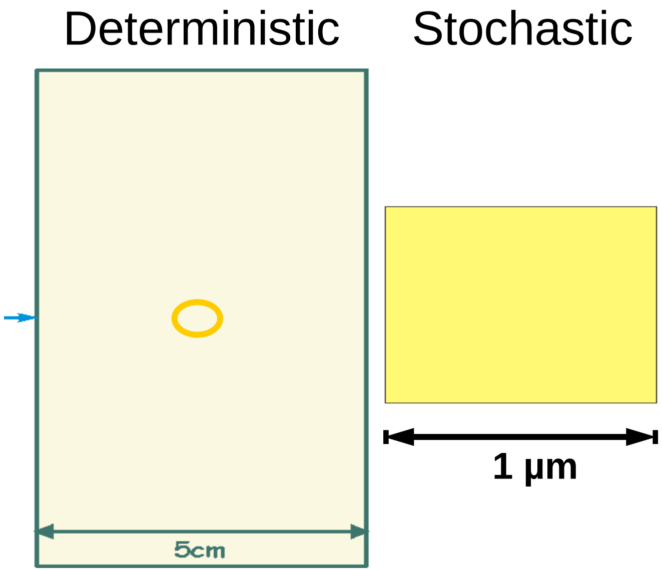
Definition

Microdosimetry quantifies:

- the spatial and temporal energy deposition by ionizing radiation in irradiated material at a scale where the energy deposition is stochastic in nature

- i.e. microdosimetry quantifies the spatial and temporal probability distribution of energy deposition by ionizing radiation in a irradiated volume

Stochastic nature of ionization events



At microscopic scale

- Interactions between radiation and a medium occur in discrete events
- These events occur stochastically around a track

At macroscopic scale:

- The number of these events allows to treat the energy deposition in a volume as a deterministic quantity

Microdosimetry vs. (traditional) dosimetry

	Dosimetry	Microdosimetry
is a	deterministic quantity	stochastic quantity
measures	average energy deposition per unit mass	probability distribution of energy distribution
is expressed as	$D = \frac{\langle E \rangle}{m}$	$f(z)$
where	<*E*> is the average energy deposited in the mass m	*f(z)* is the probability distribution of deposition of the specific energy z

Microdosimetry :Specific Energy

- *Energy imparted ε:* is the energy imparted within a site

$$\varepsilon = \sum_i \varepsilon_i$$

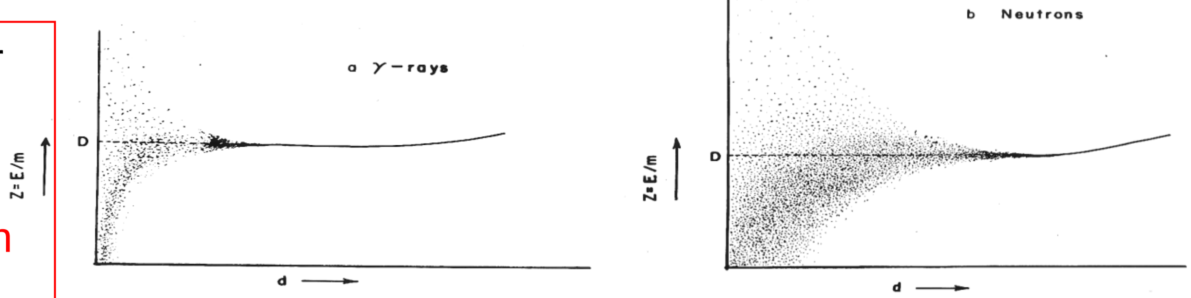
Predictions on the energy imparted can be made based on a probability distributions of energy transfers.

- *Specific energy z:* is defined as the ratio of the imparted energy ε and the site's mass m: $z = \frac{\varepsilon}{m}$
- *Lineal energy y:* is defined as a ratio of the imparted energy and mean chord length

$$y = \frac{\varepsilon}{l} \qquad \overline{y_F} = \int y f(y) dy \qquad \overline{y_D} = \frac{1}{\overline{y_F}} \int y^2 f(y) dy$$

Energy per unit mass vs mass for *constant* dose D.

Reducing of the target size is changing deterministic deposition of energy to stochastic.



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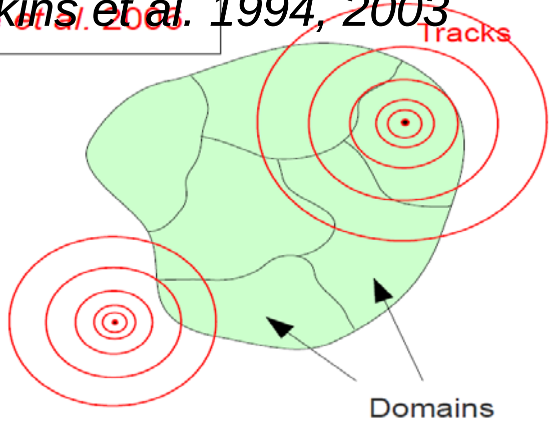
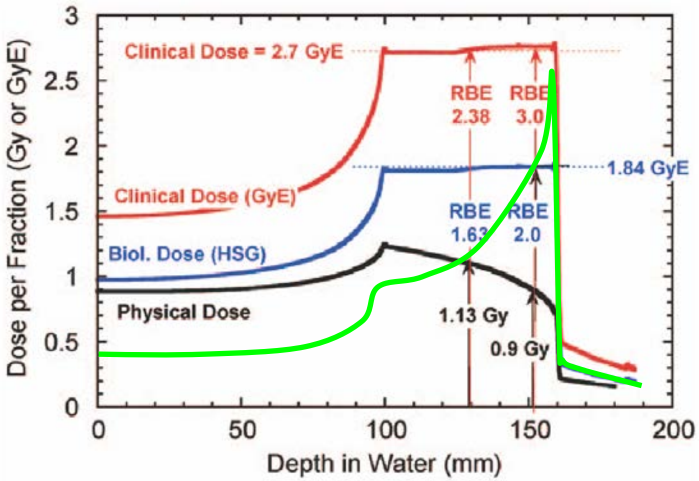
Each type of radiation has their own signature of a single event spectra

Microdosimetric Kinetic Model (MKM)

Hawkins et al. 1994, 2003





Radiobiological Effectiveness (RBE):

$$RBE_{10} = Dose\ that\ gives\ 10\%\ cell\ survival\Big|^{X-rays}_{Radiation} = \frac{\mathbf{D_{10,x}}}{\mathbf{D_{10,ions}}}$$

Biological dose = RBE × D

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CMRP Silicon Microdosimeters

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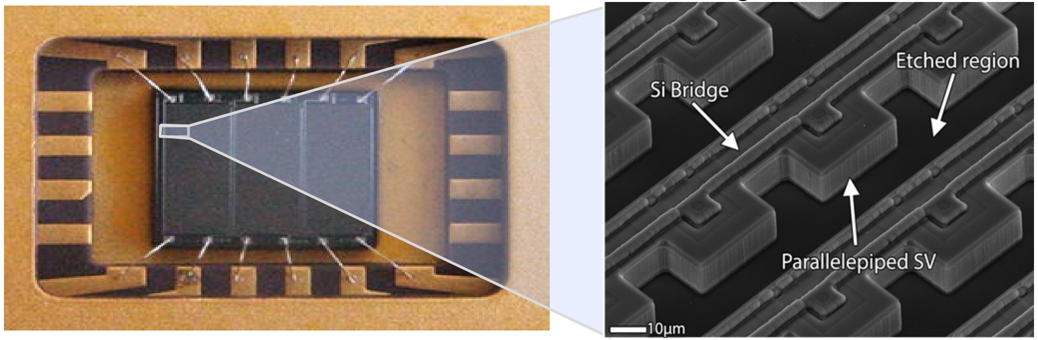
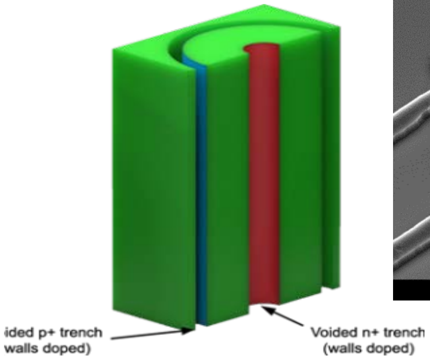
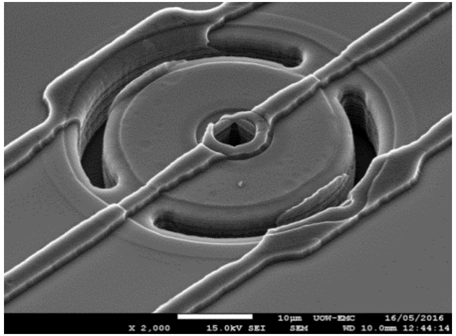
Bridge MD Version 2



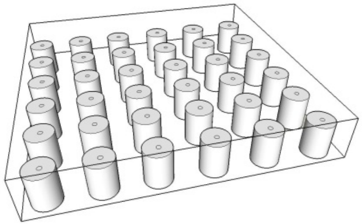




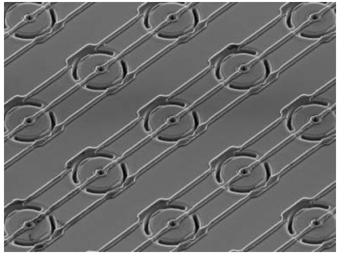
SEM image of Mushrooms

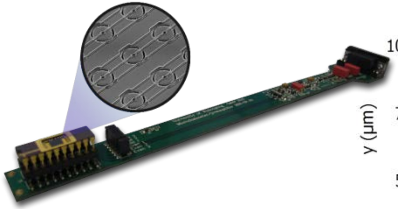
From patent

U.S. Patent No. 8421022
EU Patent, 2019

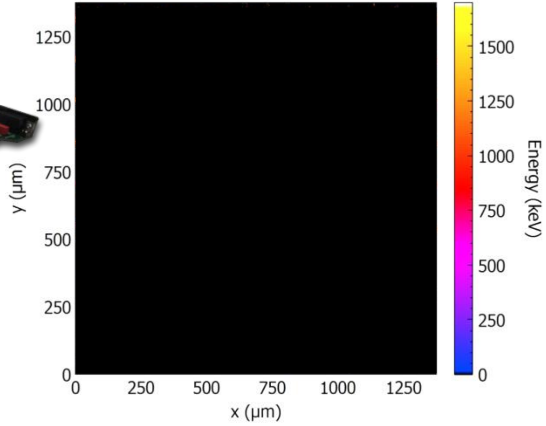


To reality





MicroPlus probe with SOI Mushroom Microdosimeter, and SEM image showing 3D sensitive volumes



Median energy map showing good sensitive volume yield in the Mushroom microdosimeter, biased at -10 V

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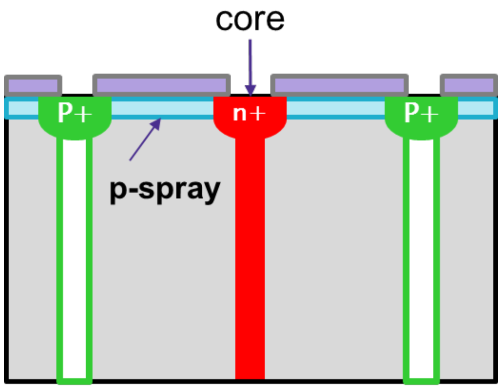
A.Rosenfeld “Novel detectors for silicon based microdosimetry, their concepts and applications”, NIM A, 809, 156-170, 2016

3D Sensitive Volume Array Silicon Microdosimeters: Mushroom

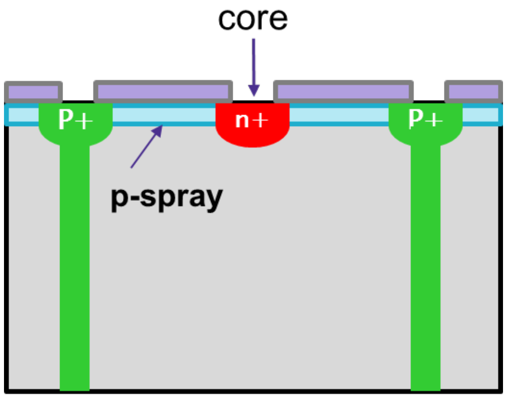
- SOI p-type
- 10µm active layer

- 3D n+ core electrode
- 3D p+ trench electrode filled with air
- P spray on the front

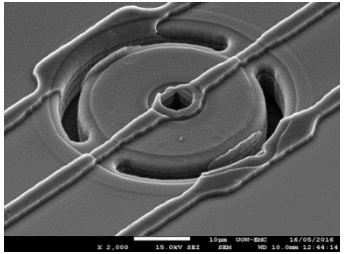
Full 3D *(air-trenched)*



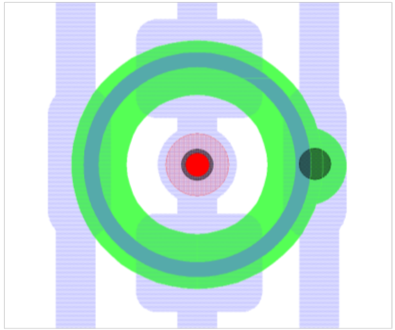
Planar n+ 3D p+ *(poly-trenched)*

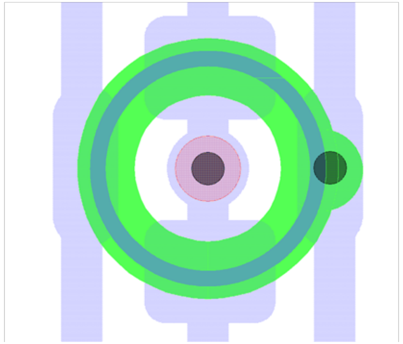


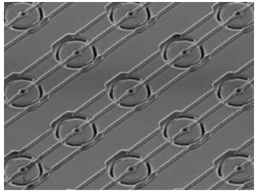
- Planar n+ core electrode
- 3D p+ trench electrode filled with polysilicon
- P spray on the front



SEM image of the Mushroom







The Mushroom Array

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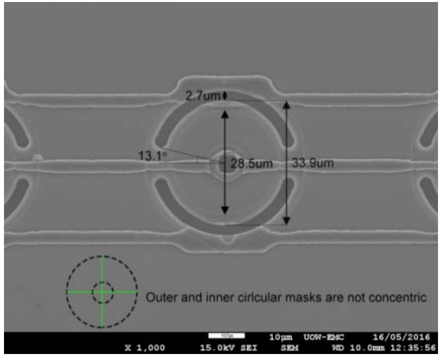
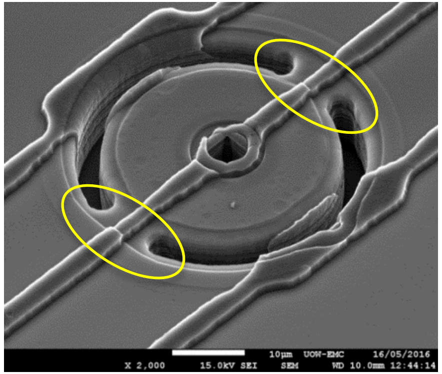
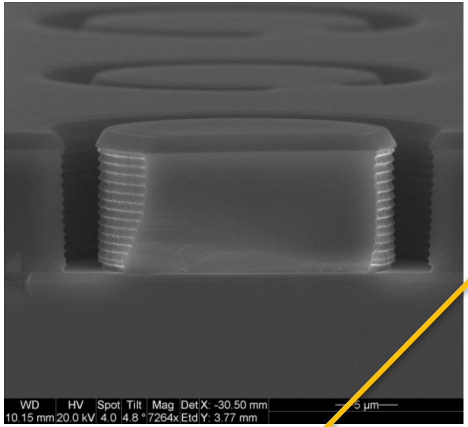
3D Silicon Microdosimeters-Mushrooms *(SEM images)*

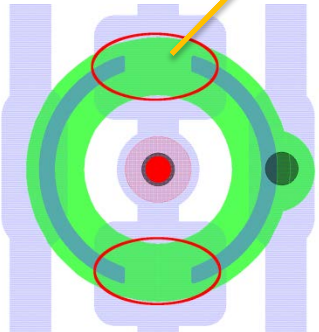
Full 3D *(air-trenched)*

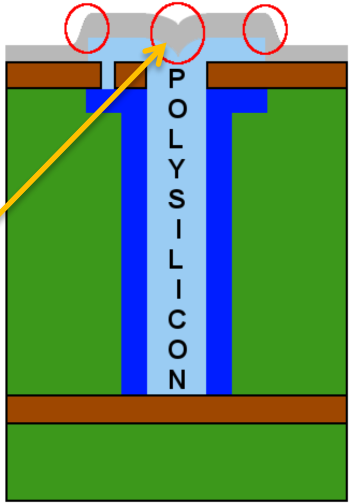




Planar n+ 3D p+ *(poly-trenched)*







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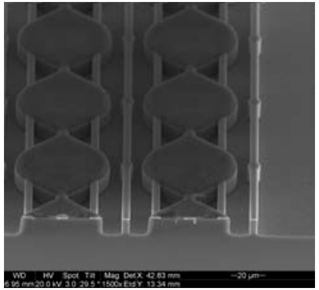
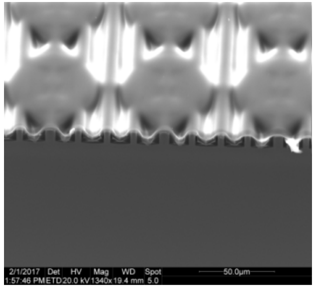
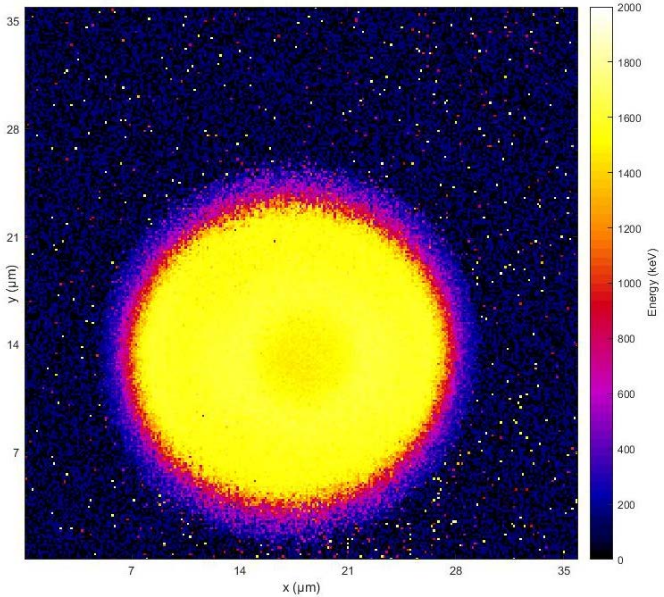
Mushrooms in Polyamide: Tissue Equivalency improvement
Charge Collection study using 5.5 MeV He^{2+} microbeam



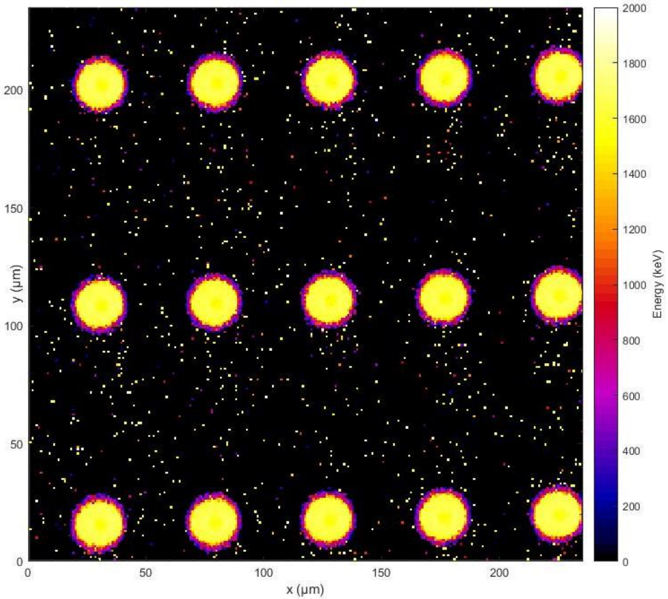
3D mushrooms



PMMA covered



Single Mushroom , 18um diameter



Mushroom Array , 50um pitch

- Median energy maps generated using two different scan sizes, in both cases the detector is biased using 10V
- No cross-talk between adjacent sensitive volumes

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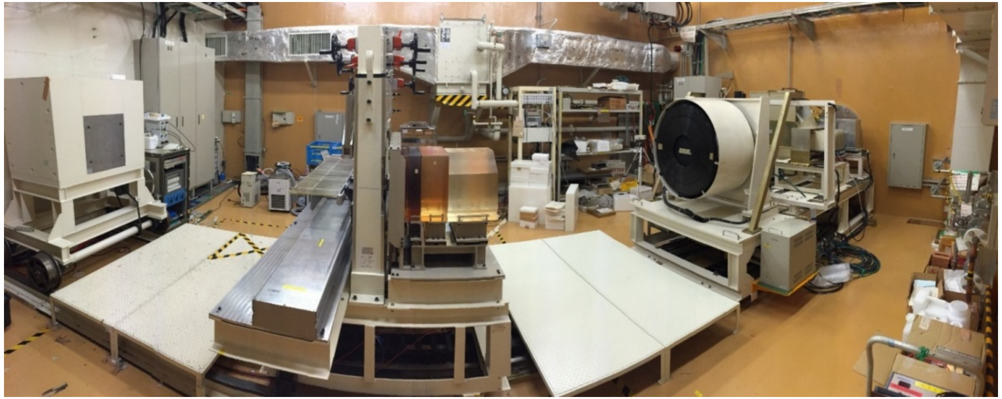
100% CCE and 100% yield in fabrication

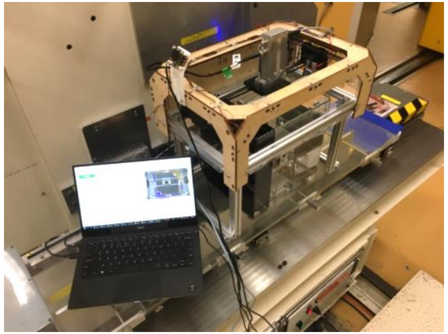
Heavy Ion Medical Accelerator in Chiba

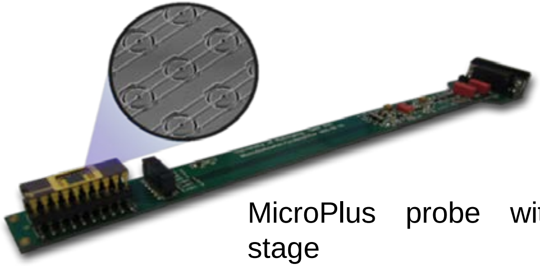
HIMAC, Japan

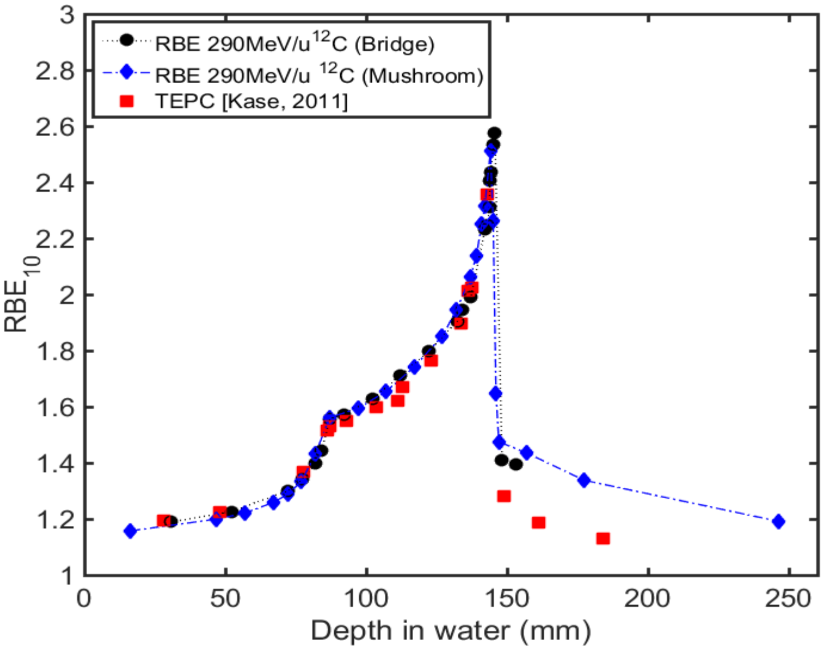
✓ **Ability to match to TEPC**



HIMAC Bio-cave beam port with passive scattering delivery







MicroPlus probe with XY-movement stage

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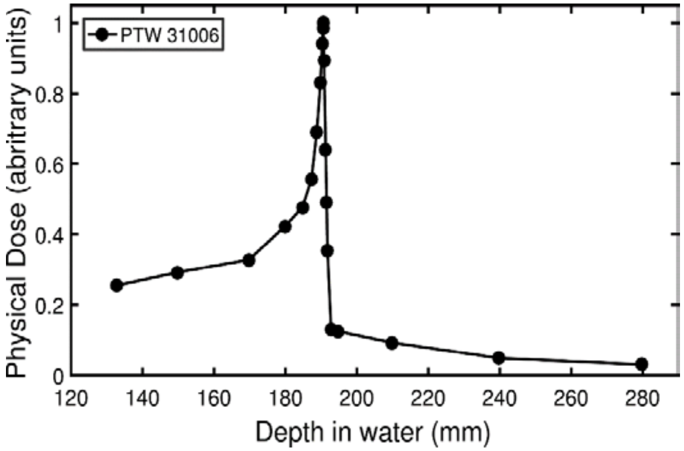
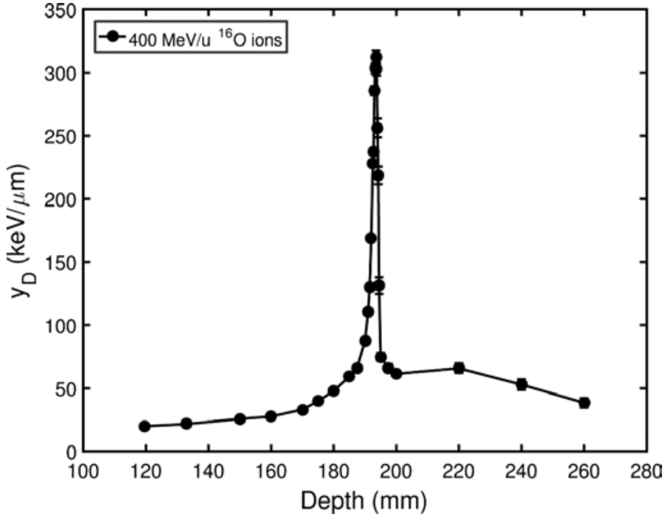
400MeV/u ^{16}O Ion Irradiation

✓ **Ability to measure y_d with submillimeter spatial resolution**

- Parameters measured:
  - Physical dose
  - Dose-mean lineal energy (y_D)
  - Relative Biological Effectiveness (RBE_{10})



Physical dose distribution of 400 MeV/u ^{16}O ions



Dose-mean lineal energy measured for 400 MeV/u ^{16}O ions

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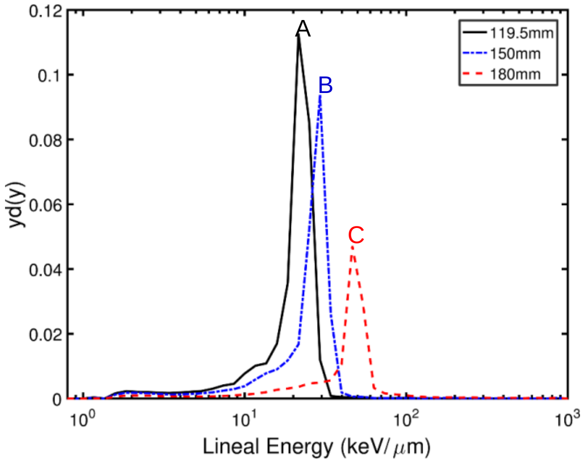
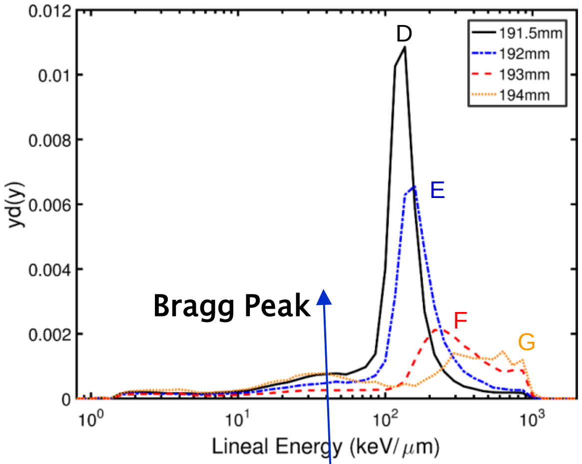
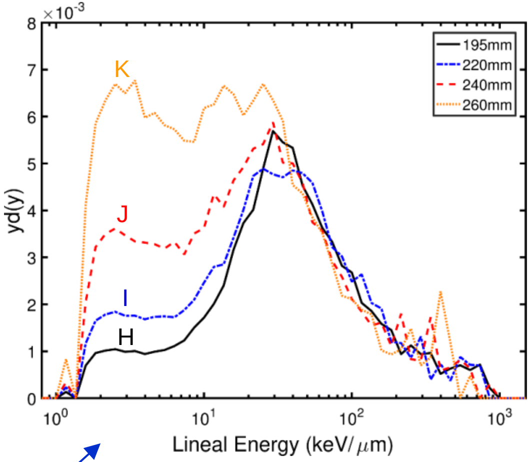


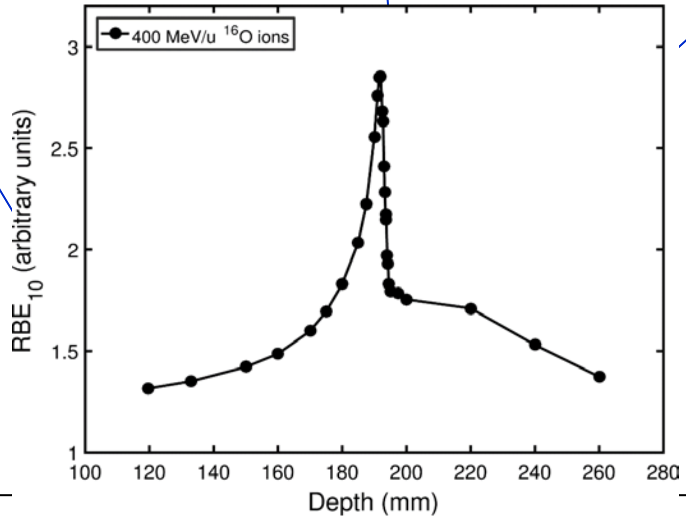




Bragg Peak

Entrance

Downstream



Dose mean lineal energy and RBE_{10} distribution with microdosimetric spectra for each region along the Bragg Peak

400 MeV/u ^{16}O Ions

✓ Ability to derive RBE with submillimeter spatial resolution

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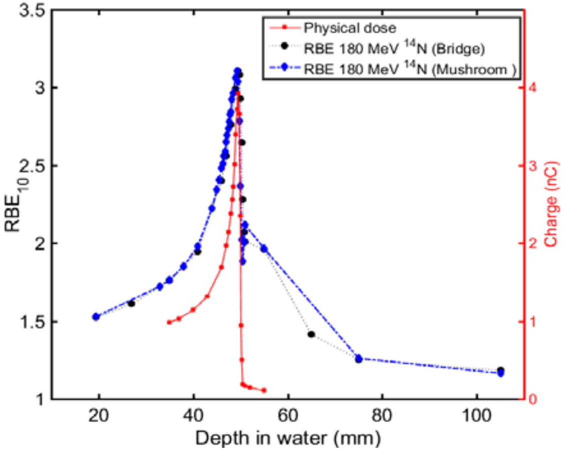
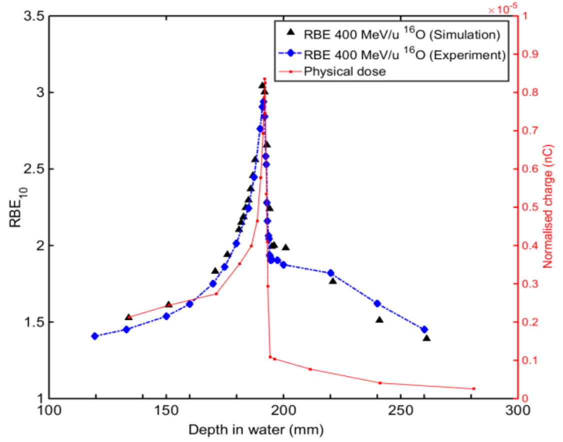
RBE$_{10}$ obtained with SOI microdosimeter in response to pristine BP of *^{14}N, ^{16}O and ^{12}C ion beam*

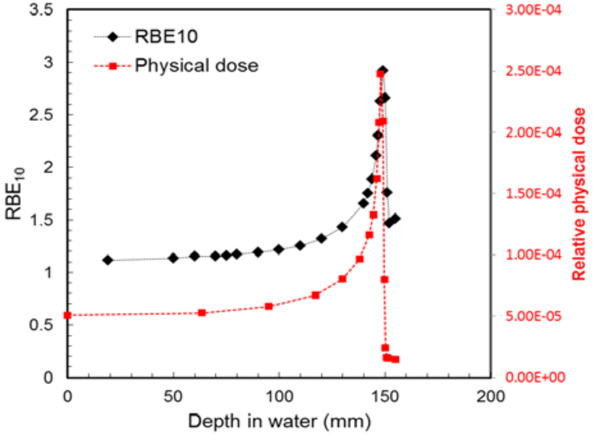
180 MeV/u ^{14}N

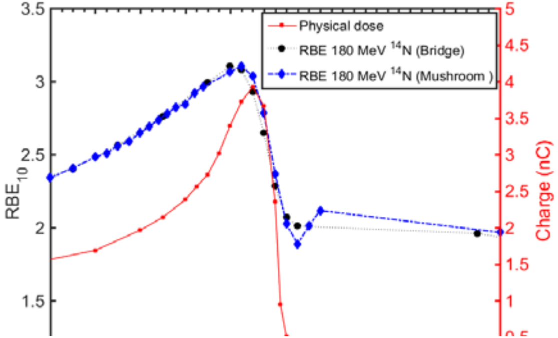
400 MeV/u ^{16}O

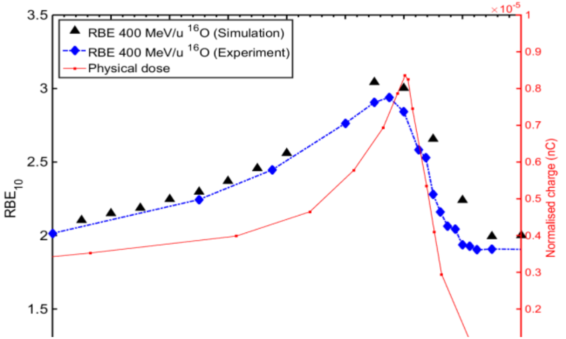
290 MeV/u ^{12}C

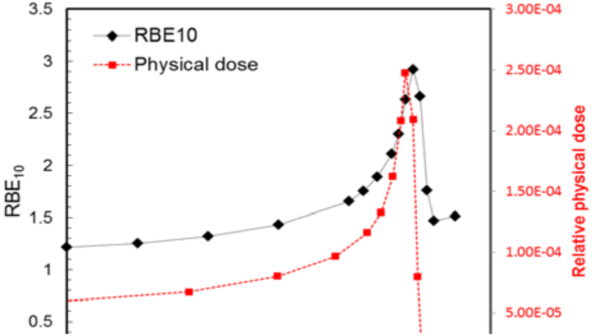












Linh T. Tran, *et. al.*, ***"The relative biological effectiveness for carbon, nitrogen and oxygen ion beams using passive and scanning techniques evaluated with fully 3D silicon microdosimeters"*** Medical Physics, 2018 ,

Proton Beam Scanning Irradiation, Mayo Clinic, Minnesota, USA

MicroPlus operates in clinical PBS with a dose rate 50-100 times higher than during the passive beam treatment delivery

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S. Anderson, K Furutani, L. Tran *et. al*. ***"Microdosimetric measurements of a clinical proton beam with micrometer-sized solid-state detector,"*** Med Phys. 2017 Sep 14. doi: 10.1002/mp.12583.

RBE in proton therapy: Cell survival vs Bridge Microdosimetry

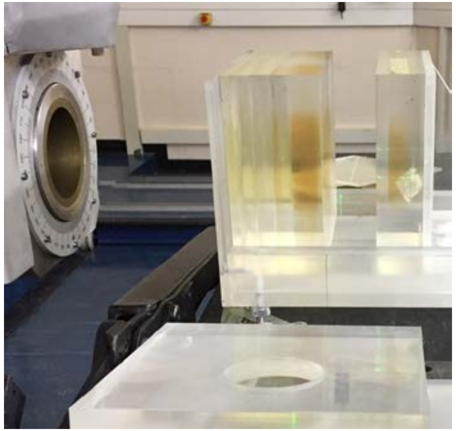


Fig 1: In-vitro radiobiology setup in PMMA phantom. Bridge Microdosimeter was placed at the same depth as cells.

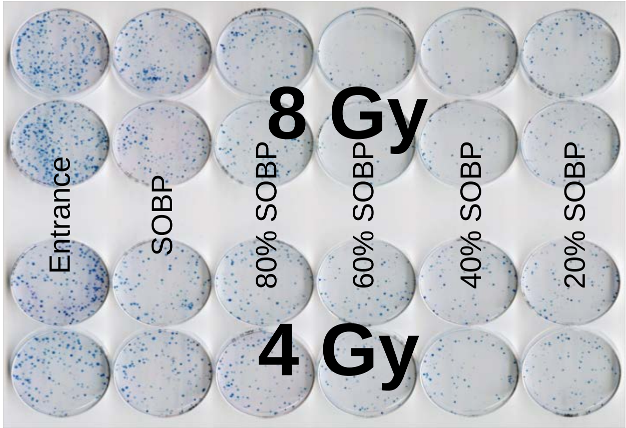
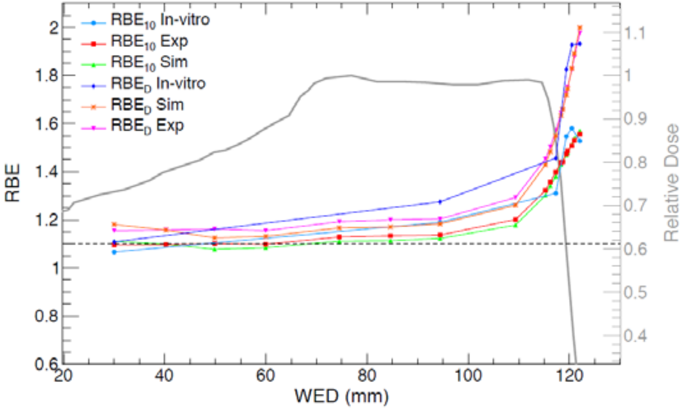


Fig 2: In-vitro CHO-K1 irradiated cells



RBEd : Cells vs Microdosimetry prediction . Good agreement. Dose 2 Gy.

MicroPlus probe predicts RBE_d and RBE_{10} in agreement the CHO-K1 cell line

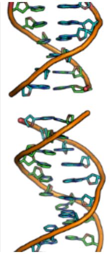
✓ **Ability to replace time consuming radiobiological RBE experiments**

SCK•CEN STUDIECENTRUM VOOR KERNENERGIE CENTRE D'ETUDE DE L'ENERGIE NUCLÉAIRE | dkfz. | NRF National Research Foundation | iThemba LABS Laboratory for Accelerator Based Sciences | CENTRE FOR MEDICAL RADIATION PHYSICS | UNIVERSITY OF WOLLONGONG AUSTRALIA

E Debrot, L Tran, L Chartier *et. al.* SOI microdosimetry and modified MKM for evaluation of relative biological effectiveness for a passive proton therapy radiation field, PMB , 2018,

Effects of Cosmic Radiation

Radiobiological effect

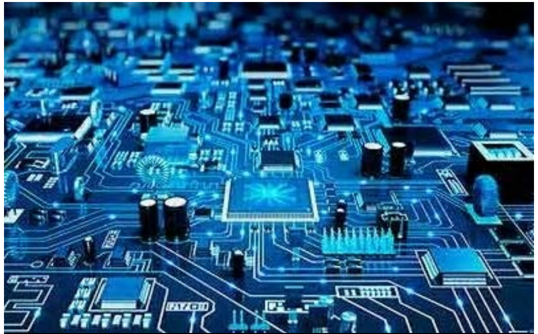


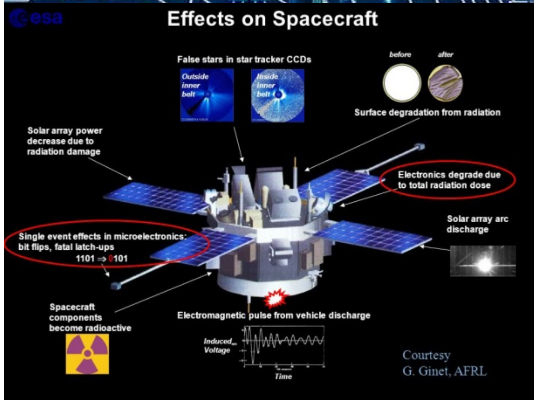
- Potentially fatal radiation sickness
  Much higher risk of cancer later in life.
  > 2000mSv

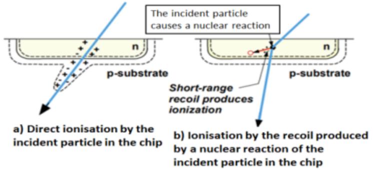
- No immediate symptom. Increased risk of serious illness later in life.
  100mSv to 1000 mSv

- No symptom. No detectable increased risk of cancer.
  < 20 mSv

Single Event Upset







- High energy charged particles or photons can result in neutron mixed field radiation
- Production of neutrons via nuclear interactions with high energy charged particles or spontaneous fission of isotopes
- Dosimetry for radiation protection in high energy mixed radiation fields is a challenging task

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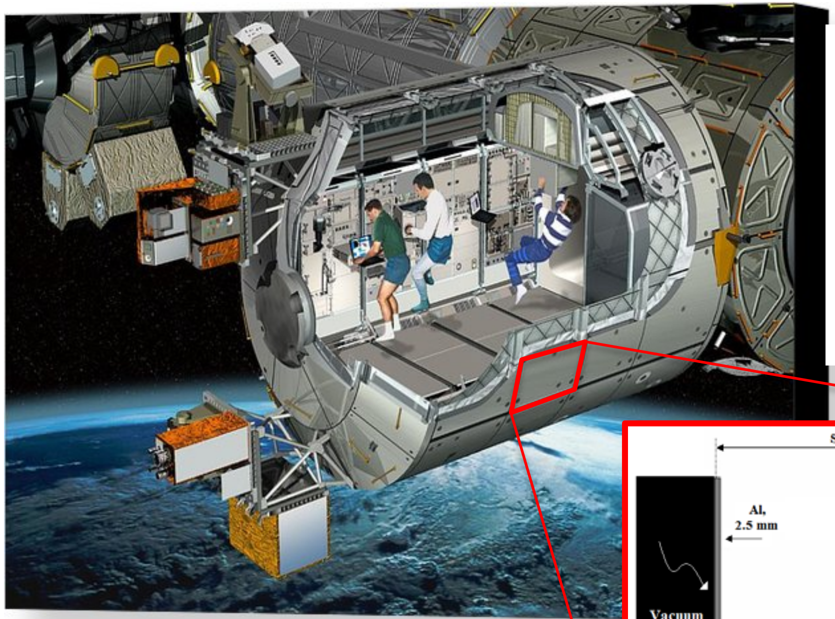
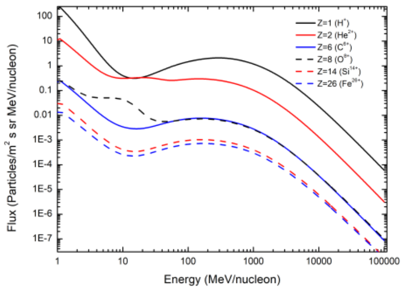
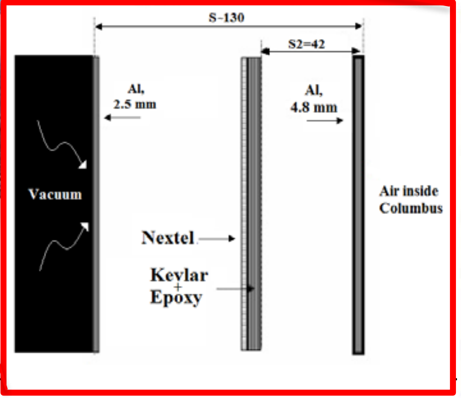
Columbus ISS space module: wall shielding properties optimization



GCR: Heavy Charged Particles





Layout of the Columbus debris shield configuration [R. Destefanis *et. al.*]

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Ions Fe-56 , energy 500MeV/u

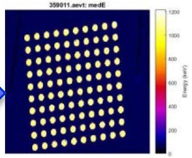
Aims: Modelling of radiation environment inside of the Columbus module

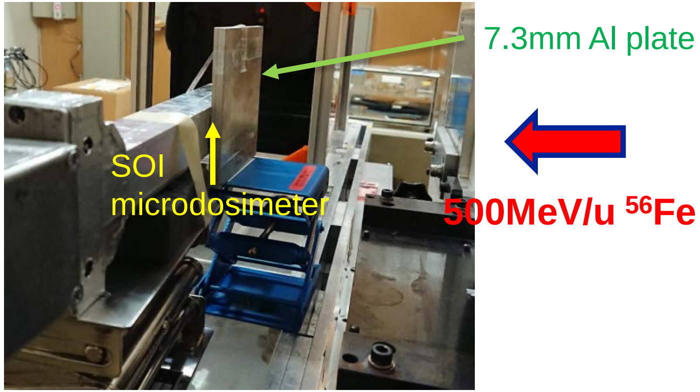
Effect of the THIN and THICK Aluminium wall (7.3 mm and 36 mm.)

0.07 mm PMMA slab in front of MicroPlus

10mm PMMA converter in n front of MicroPlus

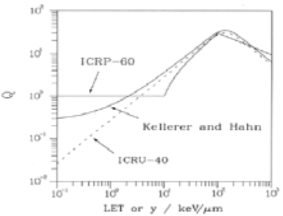
Mushroom 10um | $2x2mm^2$ | 18um diameter | 50um pitch

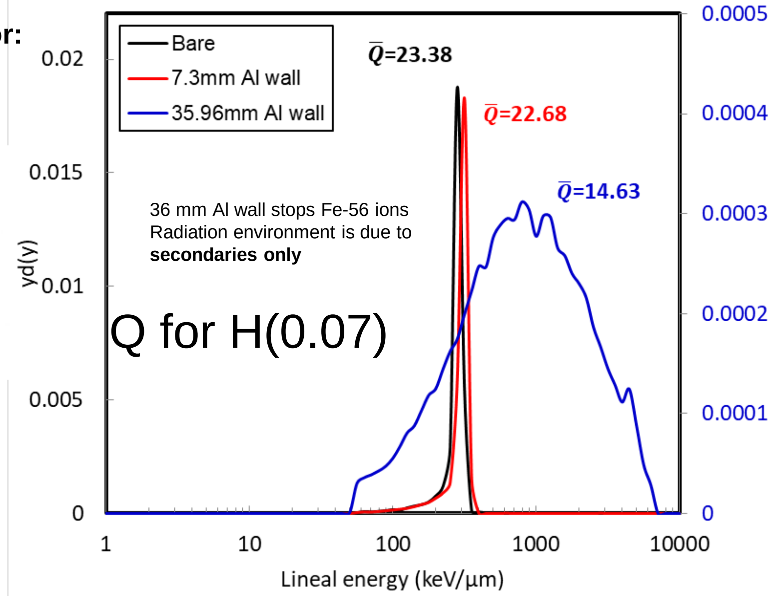


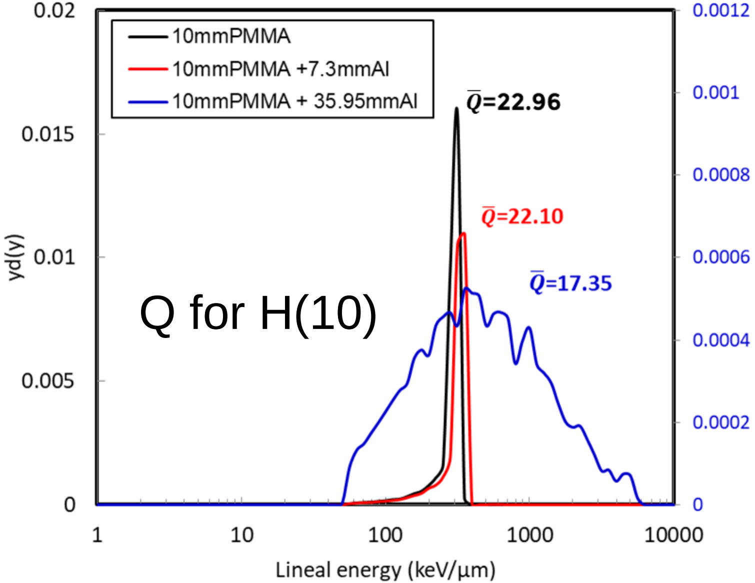


Average quality factor:

$$\bar{Q} = \int_0^\infty Q(y)d(y)dy$$







Water Phantom: Ions Fe-56, energy 500 MeV/n

Aims: Modelling of radiation environment inside of the Columbus module

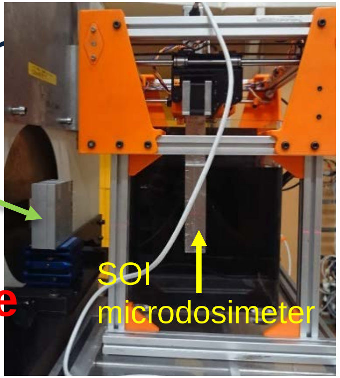
- Energy deposition (with/without 7.3mm Al wall)
- Quality coefficient vs depth in water

Mushroom 10um | $2x2mm^2$ | 18um diameter | 50um pitch

Average quality factor:
$\bar{Q} = \int_0^\infty Q(y)d(y)dy$

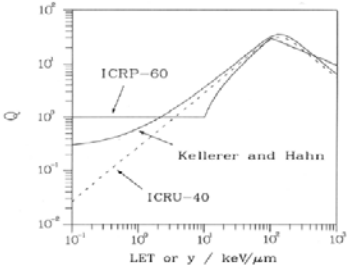
7.3mm Al plate

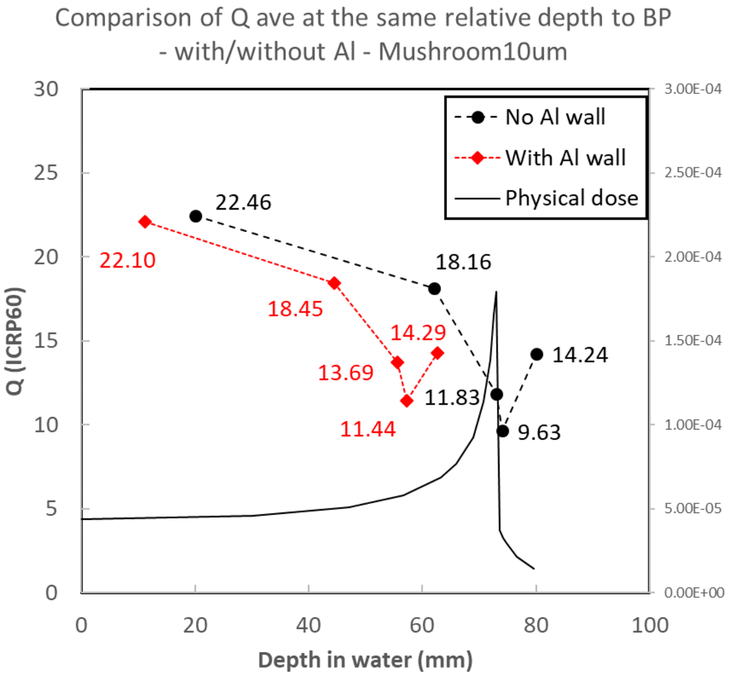
500MeV/u ^{56}Fe

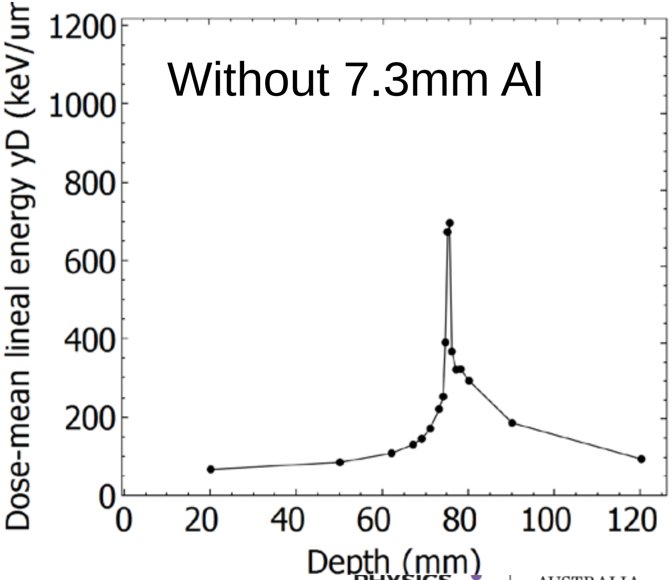


Average quality factor:

$$\bar{Q} = \int_0^\infty Q(y)d(y)dy$$





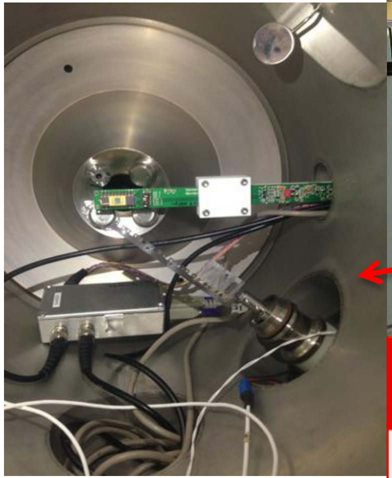


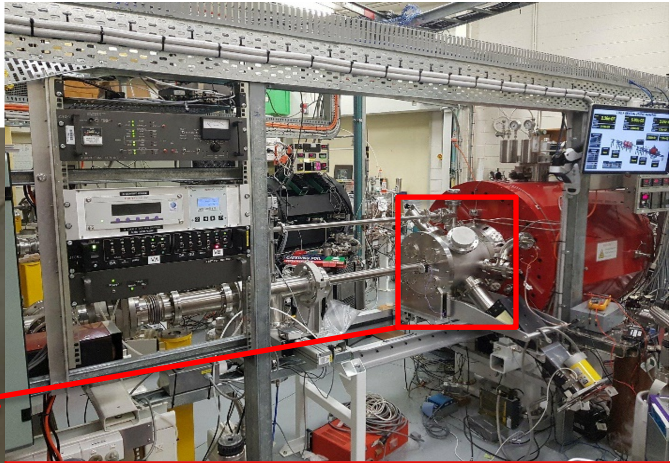
✓ Ability to evaluate Q and dose equivalent in GCR environment for shielding optimization

ANU Low Energy Ions Microdosimetric Studies :SEU in microeletronics

Experiment in collaboration with the Nuclear Sciences Department of the Australian National University (ANU)

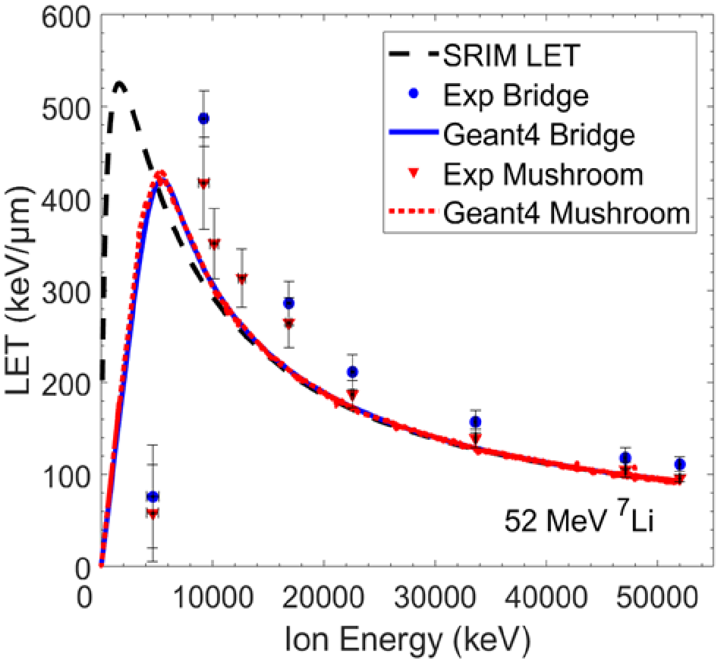
- Low energy ion (high LET) microdosimetric studies using ANU heavy ion accelerator
- **Aim:** verification of the Bethe-Bloch formula and GEANT 4 low energy ions typical for
- **Ions:** ^{12}C, ^{16}O, ^{6}Li and ^{48}Ti
- Modelling of the distal part of the BP for RBE studies with high spatial resolution



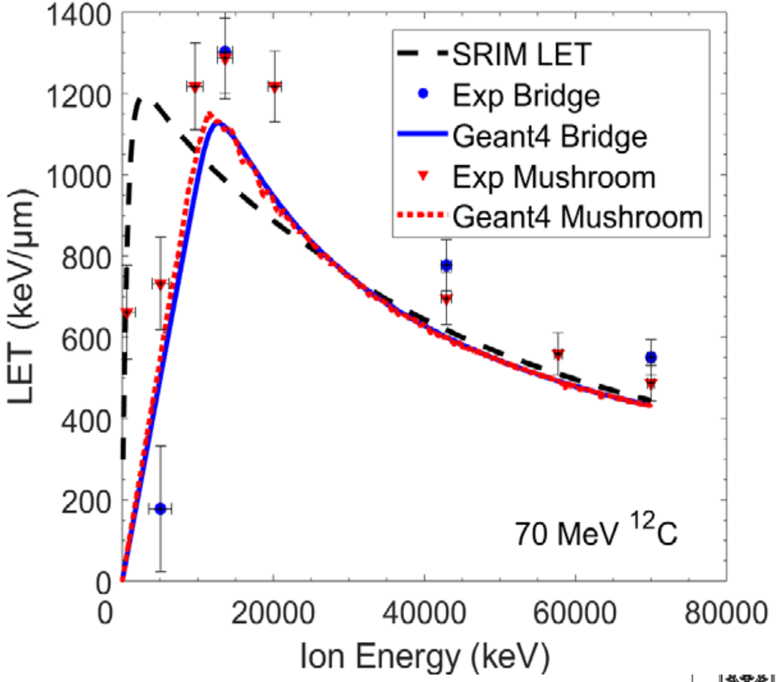


Ion	LET in Si (keV/µm)	Range in Si (µm)
70MeV C-12	444	103
52MeV Li-6	92	331
118MeV O-16	642	121
170MeV Ti-48	5061	34.85

Ion's LET measured by mushroom microdosimeter covered with different thicknesses of polyethylene (PE): comparison with SRIM and Geant4



52 MeV ^{6}Li



70 MeV ^{12}C

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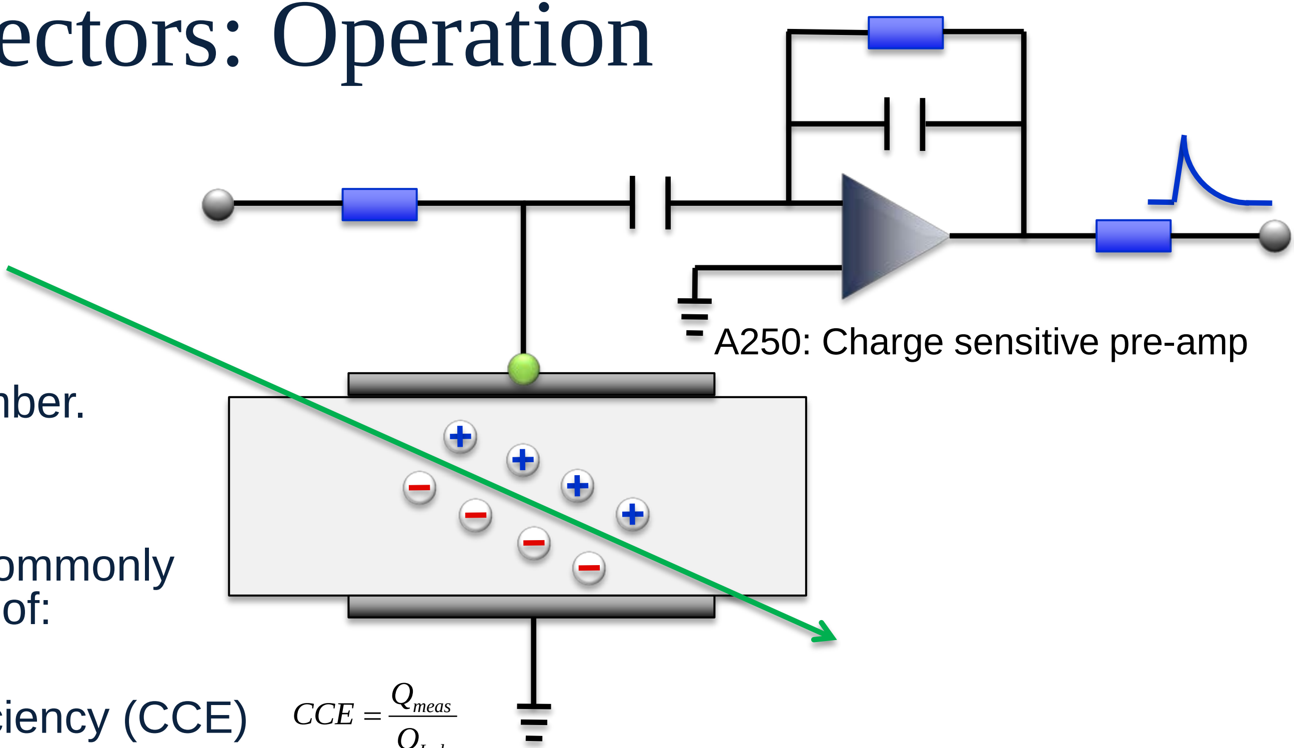
Diamond Detectors: Operation



Solid state ionisation chamber.

- $E_{e/h}$=13eV

Detector performance is commonly characterised in terms of:

- Charge Collection Efficiency (CCE)
- Charge Collection Distance (CCD)

$$CCE = \frac{Q_{meas}}{Q_{Ind}}$$

$$CCD = CCD \times d$$

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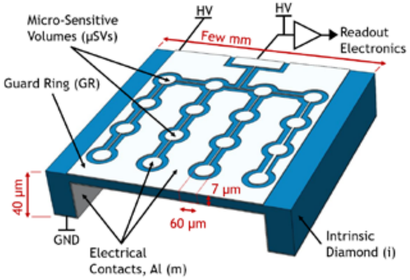
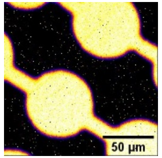
Thin membrane structures

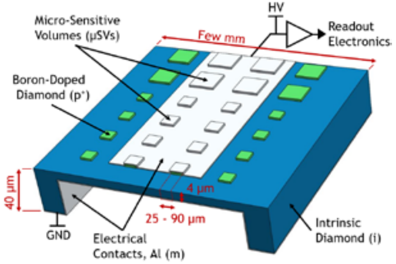
Collaboration CMRP CEA ANSTO
Izabella Zahradnik, CEA
Samuel Saada, CEA
Michael Pomorski, CEA
Jeremy Davis, CMRP
Dale Prokopovich , Zeljko Paustovic , ANSTO
Anatoly Rozenfeld, CMRP

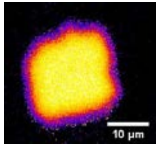
DIAμDOS guard-ring (external-biased 7 μm)

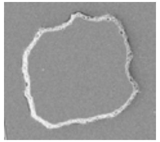




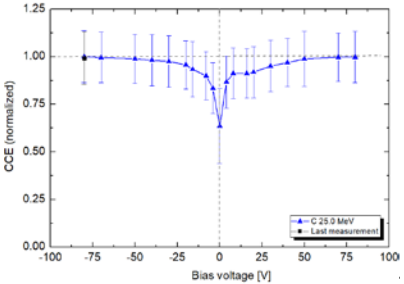
DIAμDOS p^+ (self-biased 4 μm)



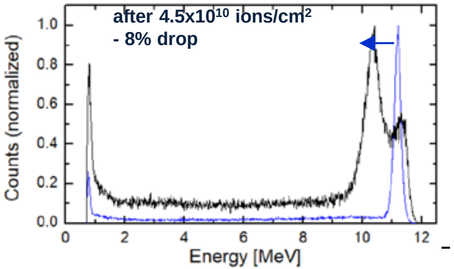




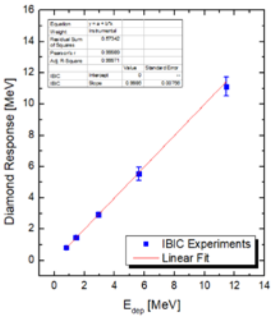
CCE vs. bias study

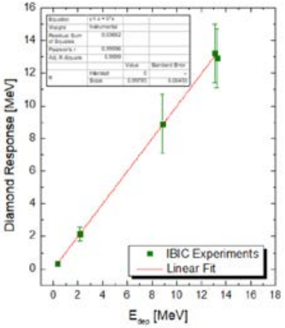


Radiation damage effects



Linearity for stopping and crossing ions





Australian Government
ANSTO
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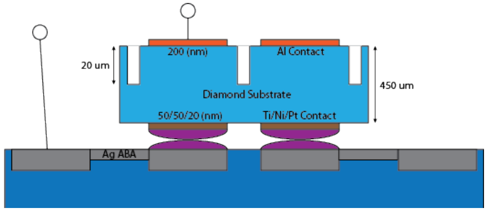
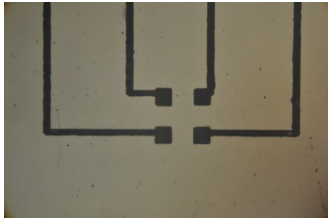
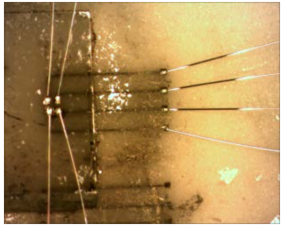
list cea tech

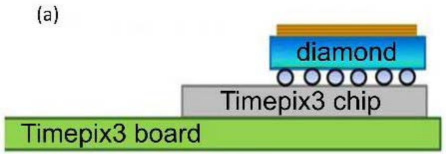
Pixelated diamond detectors

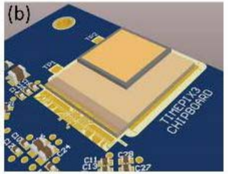






1st iteration of a diamond pixelated detector with mirrored contacts with semi-isolated sensitive volumes (2015). This concept will be extended upon in order to improve spatial resolution of ‘DiamondPix’ for particle tracking applications.



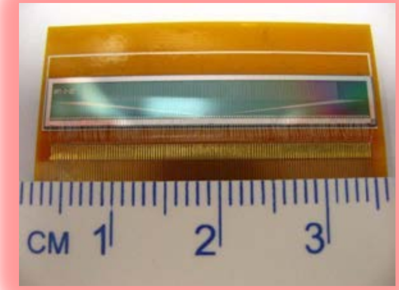


Sketch of Diamondpix. (a) CVD diamond layer is bump bonded on the Timepix3 chip which is fixed on a (b) standard Timepix readout board. Figure reproduced from Claps, et al, 2018.

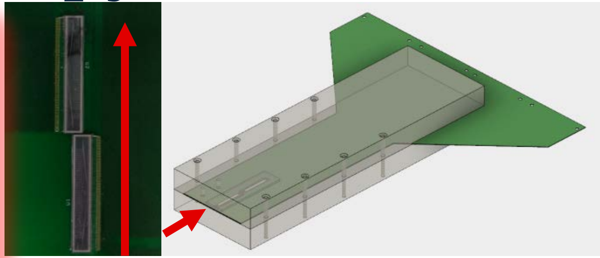
G. Claps, et al, *IEEE Trans. Nucl. Sci.*, vol. 65(10), 2018.

sDMG: Proton and C-12 Beam therapy: Range Verification QA

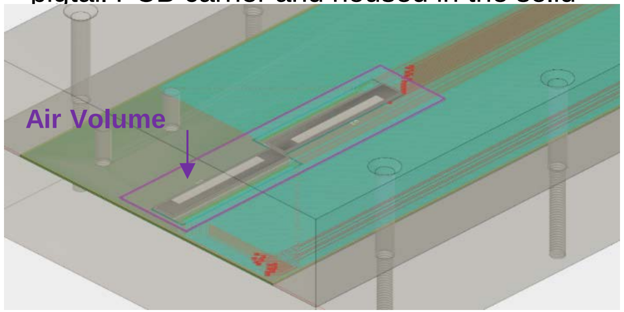
- sDMG: Miniature multi-strip silicon detector **designed by the Centre for Medical Radiation Physics** (CMRP), University of Wollongong
  - Two linear silicon diode arrays – 128 sensitive silicon strips in each.
  - Pitch:0.2mm
  - Strip size: 2x0.02 mm2
- **sDMG** housed in solid water phantom (GAMMEX, WI, USA)
  - Small air volume surrounds the silicon to prevent damage of Si detector



Si strip detector-DMG.



(Left): Photograph of sDMG linear array of detectors. An arrow indicates the direction of the axis of detection.
(Right): Schematic of sDMG mounted on a pigtail PCB carrier and housed in the solid



Close up schematic of sDMG.

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Experimental Methodology – C-12

- The detection axis is aligned **parallel** to the direction of the C-12 beam.
- **C-12** ion beam, energy **290 MeV/u** and **10x10cm^2** square field.
  - **PBP** (pristine Bragg peak)
- **Depth Dose Profiles: PBP** measurements conducted with increasing depth in PMMA (+/- 1mm).

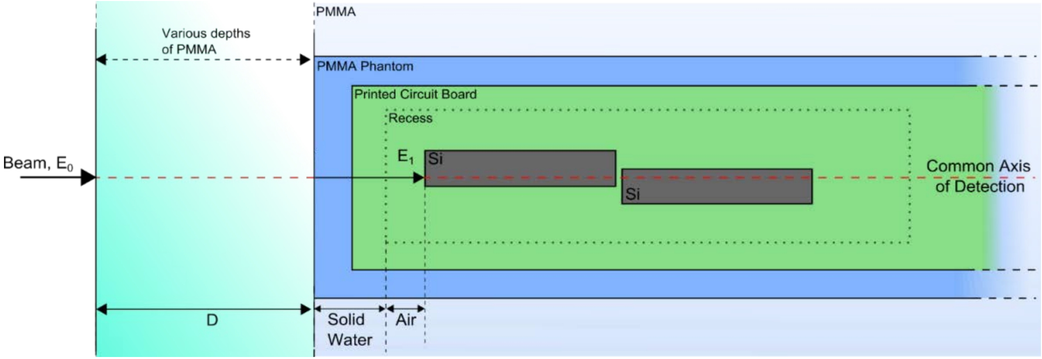
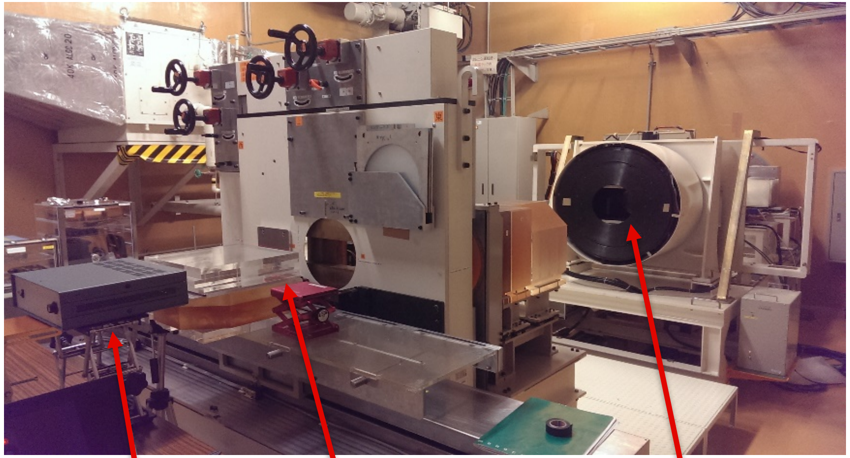


Figure – Schematic of experiment, beam energy E_0 is modified along trajectory through materials & detector to deposit PBP in sensitive volumes for measurement.



Data Acquisition System

sDMG detector in PMMA

C-12 beam

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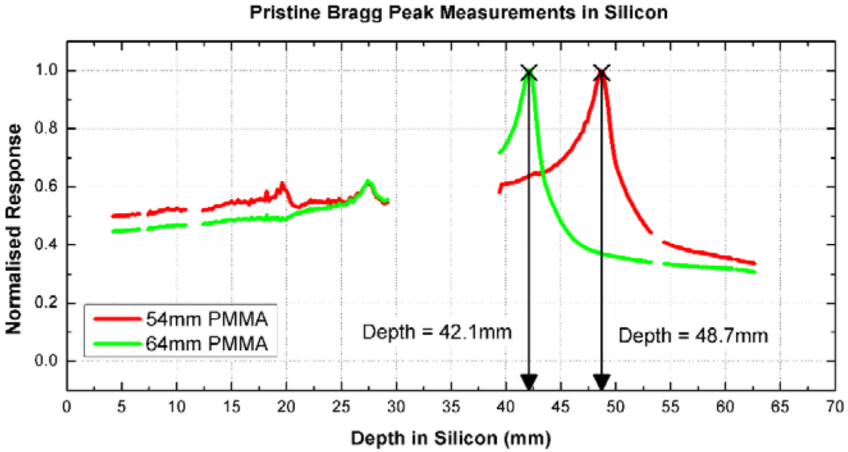
Results: Energy Reconstruction for Heavy-Ions



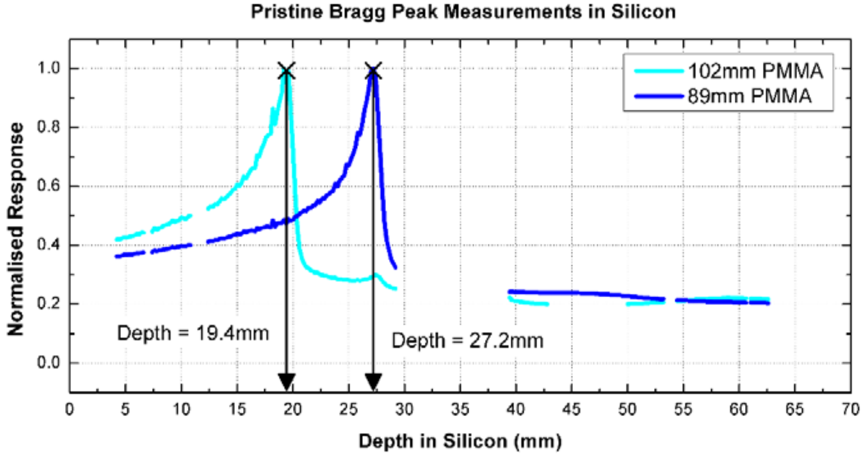


Table III – Energy Reconstruction for C-12.

Depth in PMMA (mm), (+/- 1 mm)	Measured Peak Location in Silicon (mm), (+/-0.4mm)	Reconstructed Energy, E_1 (MeV/u), (+/-3MeV/u)	Simulated Energy (MeV/u), (+/-0.1%)	Reconstructed Residual Energy, E_0, (MeV/u), (+/-3MeV/u)	Percentage Difference to Monte-Carlo (%)
102	19.4	118	121	279	1.62
89	27.2	143	147	277	1.25
64	42.1	186	190	277	0.93
54	48.7	203	206	278	1.30

- E_0 determined by Monte-Carlo simulation to be **275 MeV/u +/- 0.01%,**
- E_0 determined by detector reconstruction to be (**278 +/- 1) MeV/u**

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Conclusion

- Solid State SOI microdosimetry concept has been developed
- Optimized geometry of 3D SVs and simple conversion to tissue equivalency
- SOI microdosimeters using 3D detector technology have been fabricated
- SOI microdosimeter in mixed radiation fields is matching to TEPC
- Unique submillimetre spatial resolution in proton and heavy ion fields
- Ability of microdosimetry in a wide range of LET (0.15-10000) keV/um
- Ability to operate in PBS particle therapy without pile up
- Ability to predict cell survival (RBE) based on measured y_d and MKM model
- Ability to operate as a QA tool in particle therapy for RBE based TPS
- Ability operate in GCR environment and low energy ion fields

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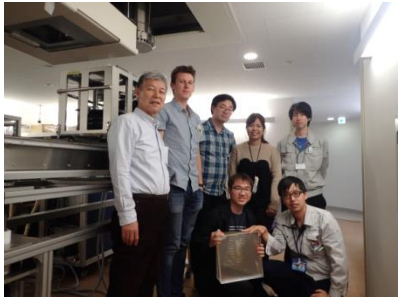
Hadron Therapy Collaboration

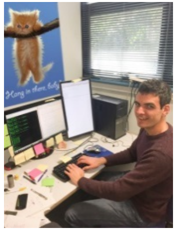
Thanks to CMRP particle therapy PhD students:

BNCT: Kyoto Reactor



HIT: Gunma Uni

HIT: NIRS

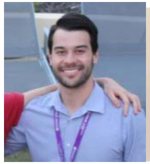


David Bolst

Ben James

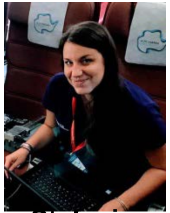
Lachlan Chartier

Emily Debrot



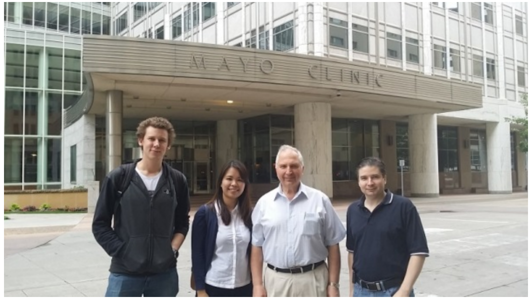
James Vohradsky

Aaron Merchant



Stefania

PT: MGH



PT: Mayo Clinic

FNT and PT: IThemba

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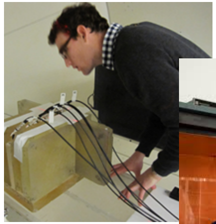
Education and Training in particle therapy at CMRP

11 PhDs trained in Particle Therapy research and graduated by CMRP

Peter Bradley 1999 AINSE Gold Medal

Greg Kaplan 1999-2001



Scott Penfold Cancer Inst NSW Award,

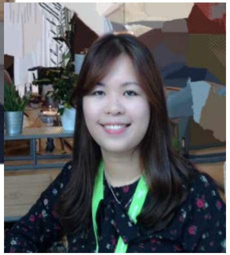
Dale Prokopovich 2011

Iwan Cornelius 2005 AINSE Gold Medal

Jayde Livingston 2013

Nicolas Depauw 2014

Linh Tran



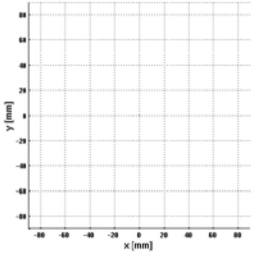
Linh Tran 2014

AIP Best Thesis Award

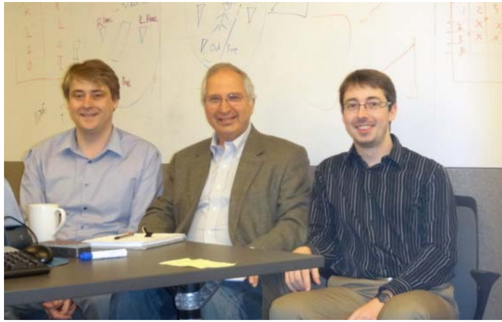
Ben Clasie 2006 University Gold Medal

Andrew Wroe 2007 AINSE Gold Medal

Stephen Dowdell 2011



courtesy A. Trofimov, MGH



MGH: Learning never end… especially when you are learning from your former students

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