Detectors for high spatial resolution dosimetry and micro-dosimetry in proton and heavy ion therapy

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Outline

- Microdosimetry concept introduction
- Silicon microdosimeters development : state –of-the-art
- Application for RBE studies in proton and heavy ion pencil scanning beam therapy
- Correlation of cell survival with microdosimeter based RBE derivation
- Space applications: radiation shielding evaluation
- Si detectors for ion range verification and PBS

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Definition

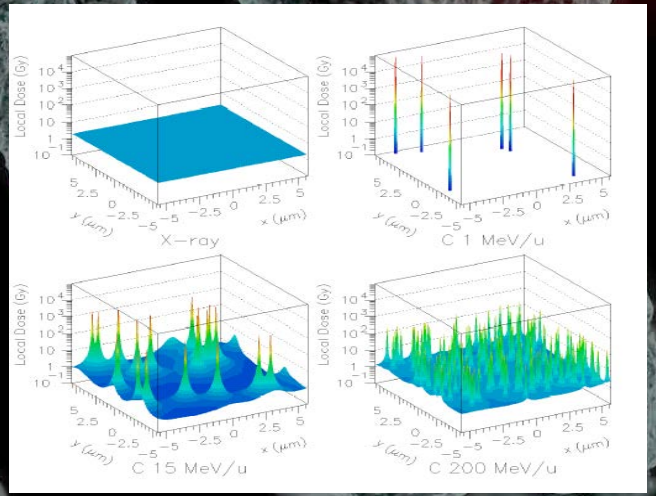
Microdosimetry quantifies:

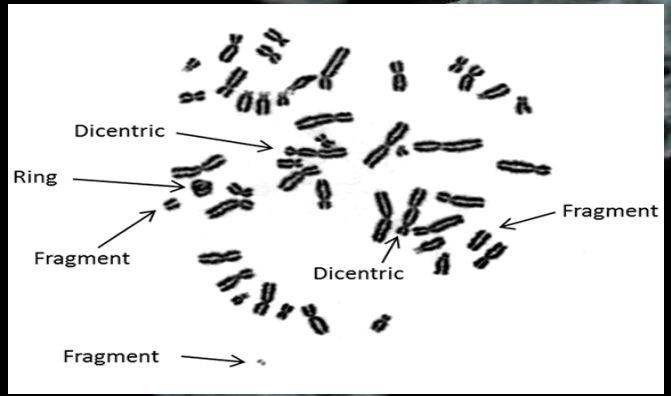
- the spatial and temporal energy deposition by ionizing radiation in irradiated material at a scale where the energy deposition is stochastic in nature

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

Mechanistic understanding

- Chromosomal aberration will be fatal, especially if clustered.
- Energy deposition to the chromosomal size (~µm) is the keystone.
- Spatial energy deposition in **µm scale** is highly dependent on the incident radiation … **Microdosimetry**





Courtesy Scholz (GSI) and Matsufuji (NIRS)

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:

$$z = \frac{\varepsilon}{m}$$

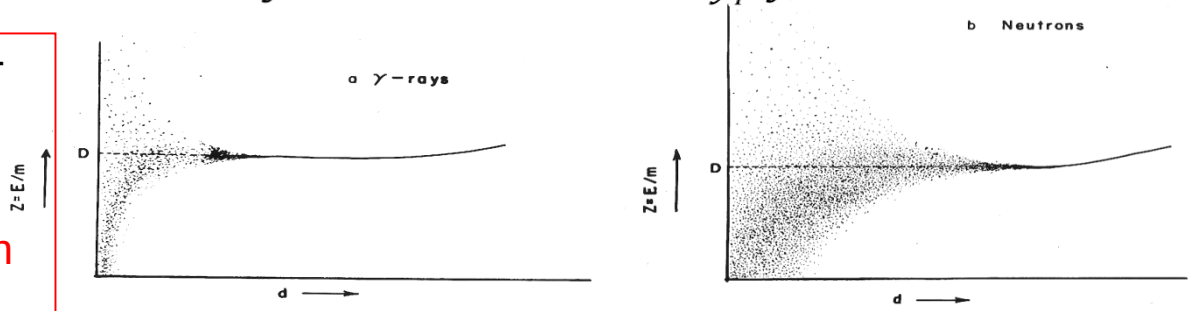
- *Lineal energy y:* is defined as a ratio of the imparted energy and mean chord length

$$y = \frac{\varepsilon}{l}$$

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

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

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



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

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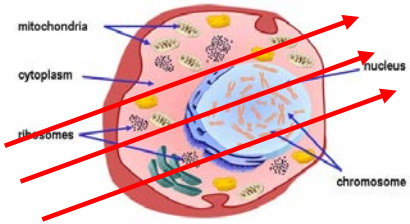
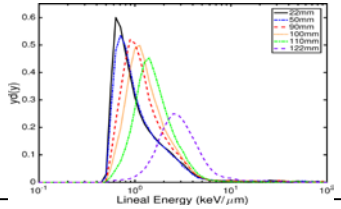
Microdosimetry



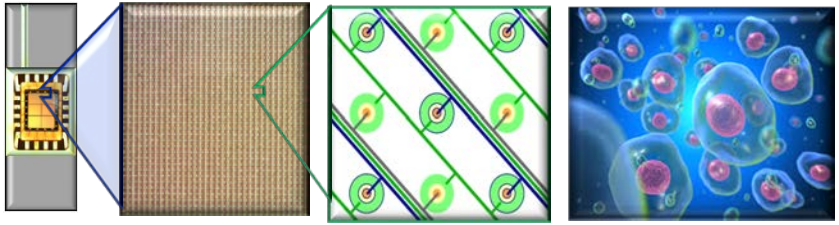
- Study of the distribution of deposited energy in well-defined microscopic volumes
- Aims to relate the type and amount of radiation to a biological effect
- The **basic concept of microdosimetry** is the event , i.e. energy deposited by a single particle (including δ-electrons) in a cell nucleus volume -site
  - Fundamental quantity lineal energy:

$$y = \frac{\epsilon_1}{\bar{l}} \text{ with distribution } f(y)$$

$$y_D = \frac{\int_0^\infty y^2 f(y)dy}{\int_0^\infty y f(y)dy}$$



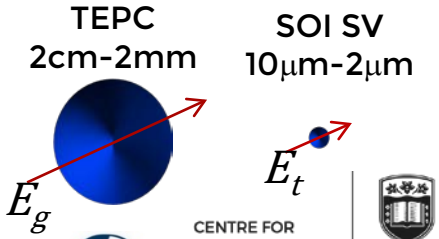
Silicon on insulator (SOI) Microdosimeter



Array of micron sized Si cells

- ✓ Portable
- ✓ Low power
- ✓ High spatial resolution
- ✓ Suitable for routine clinical applications

TEPC



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CMRP Silicon Microdosimeters:18 years of development

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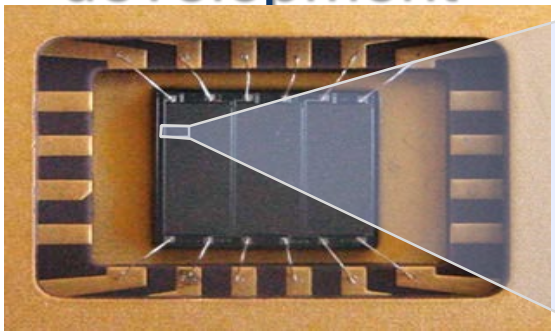
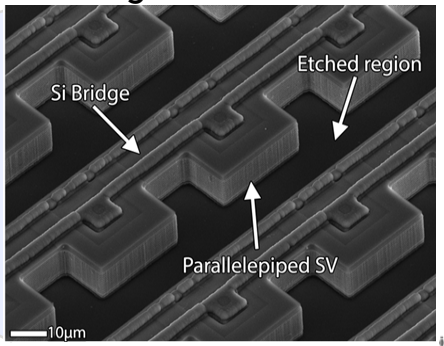
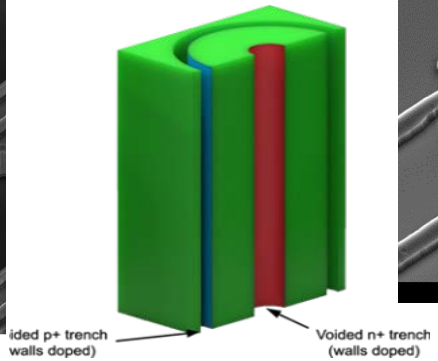
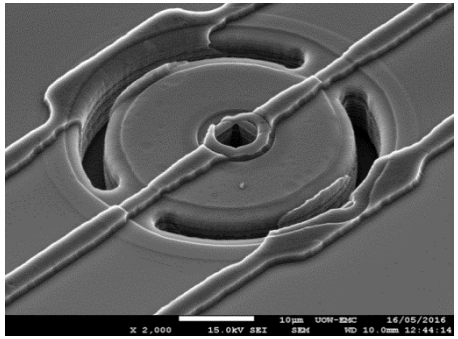


Bridge MD Version 2



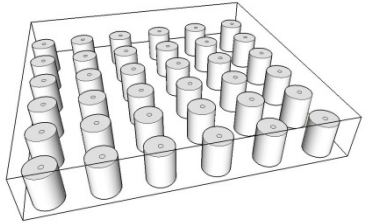




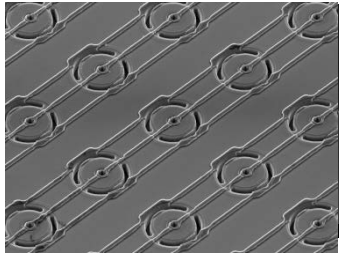
SEM image of Mushrooms

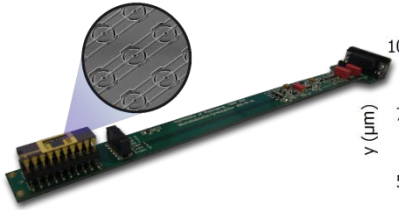
From patent

U.S. Patent No. 8421022
EP 2 102 685 B1

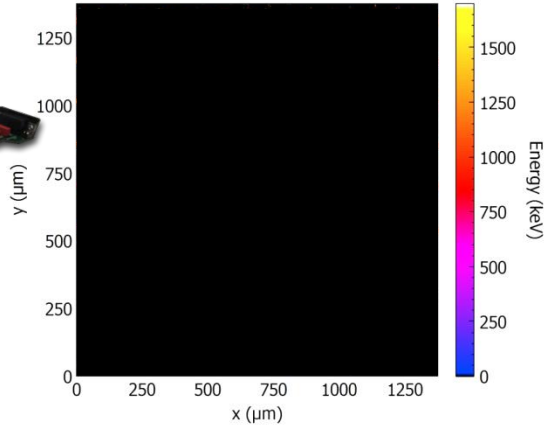


To reality





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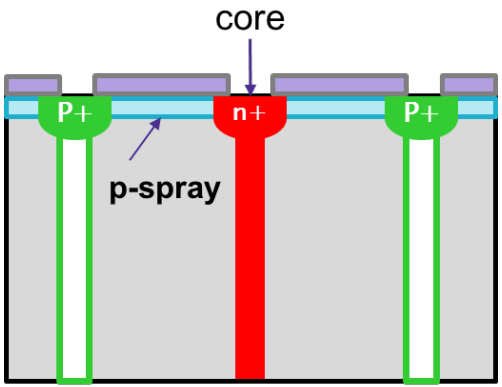
A.Rosenfeld "Novel detectors for silicon based microdosimetry, their concepts and applications", NIM A, 809, 156-170, 2016

3D Sensitive Volume Array Silicon Microdosimeters: Mushroom

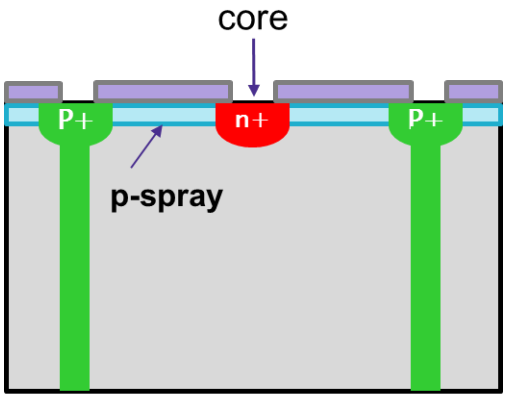
- SOI p-type
- 10µm active layer

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

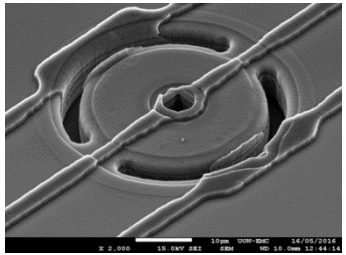
Full 3D *(air-trenched)*



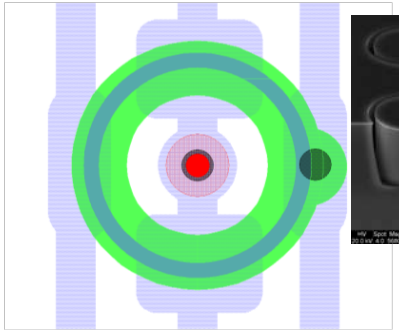
Planar n+ 3D p+ *(poly-trenched)*

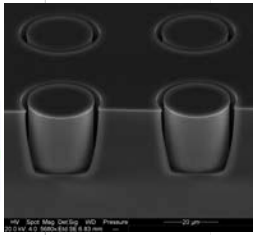


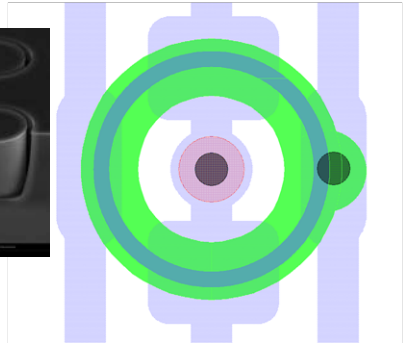
- Planar n+ core electrode
- 3D p+ trench electrode filled with polysilicon
- P spray on the front

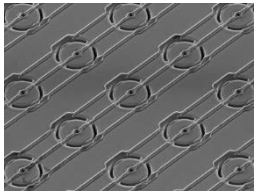


SEM image of the Mushroom









The Mushroom Array

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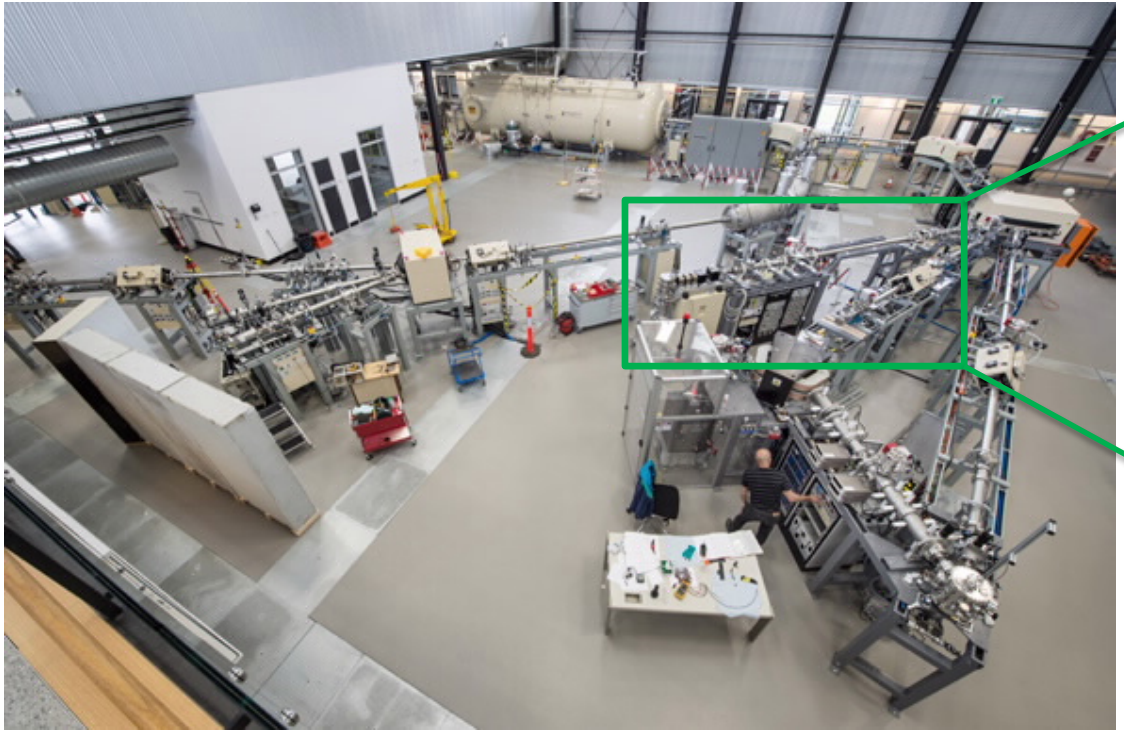
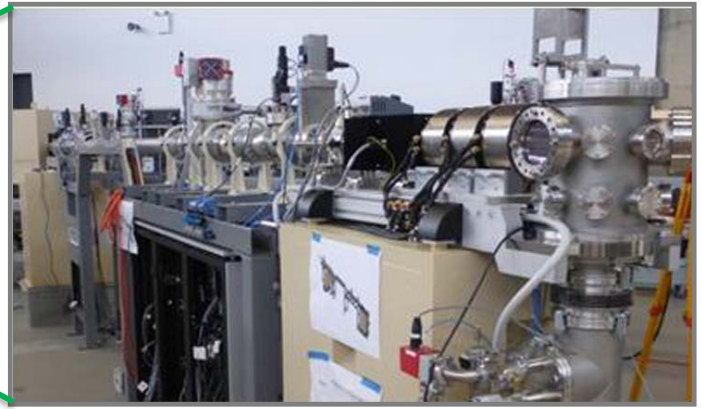
The 6MV SIRIUS Tandem Accelerator, ANSTO for Ion beam induced charge collection (IBIC) study



New nuclear microprobe–Confocal Heavy Ion Micro-Probe (CHIMP)



- **Microbeam spatial resolution:**
- 0.6 μm x 1.5 μm for 3 MeV H^+
- 1.5 μm x 1.5 μm for 6 MeV He^{2+}

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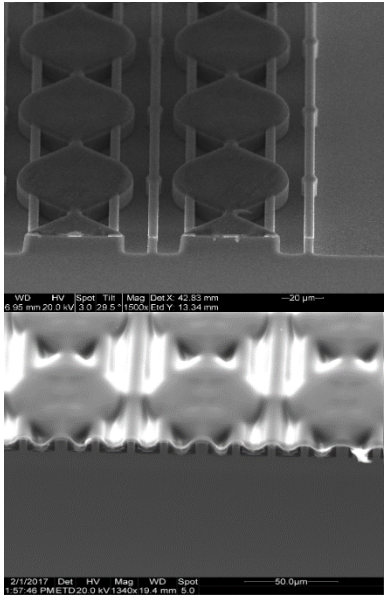
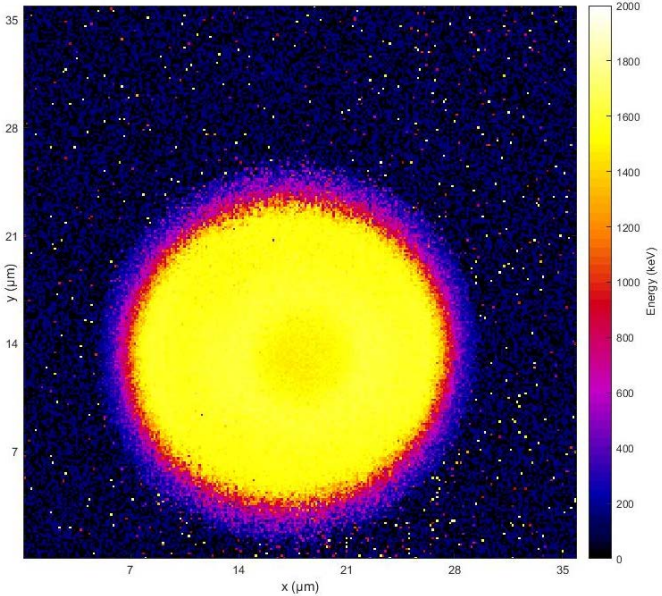
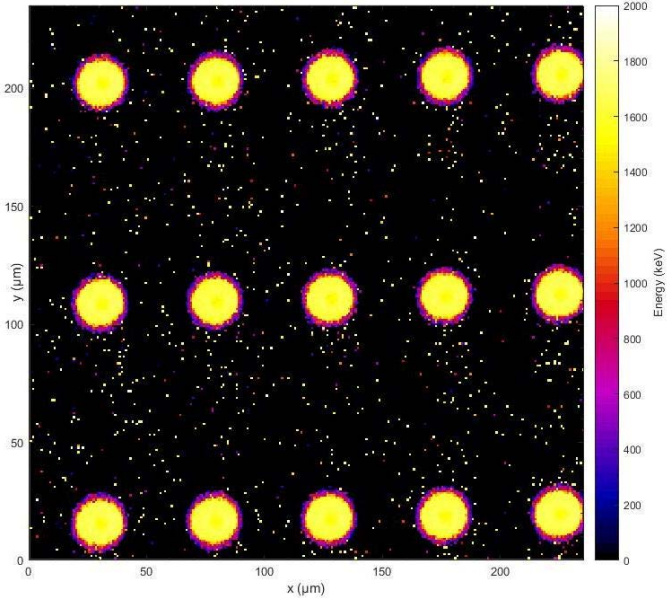
Mushrooms in Polyamide: Tissue Equivalency improvement
Charge Collection study using 5.5 MeV He^{2+} microbeam



3D mushroom microdosimeter



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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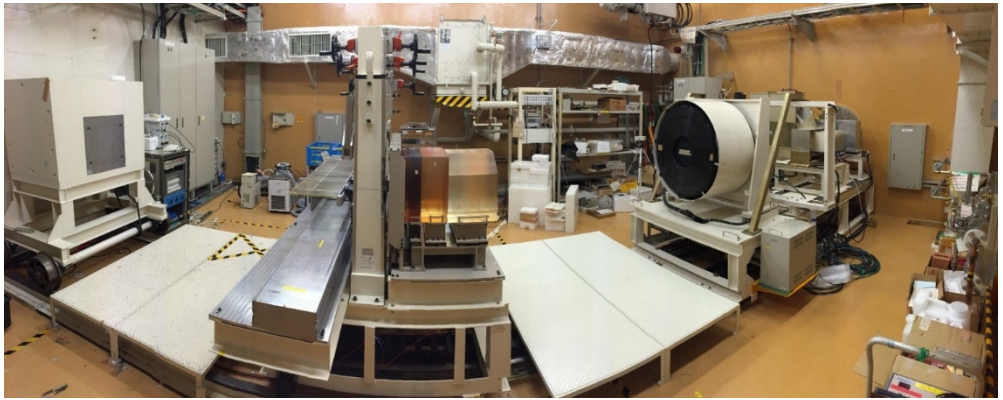
100% CCE and 100% yield in fabrication

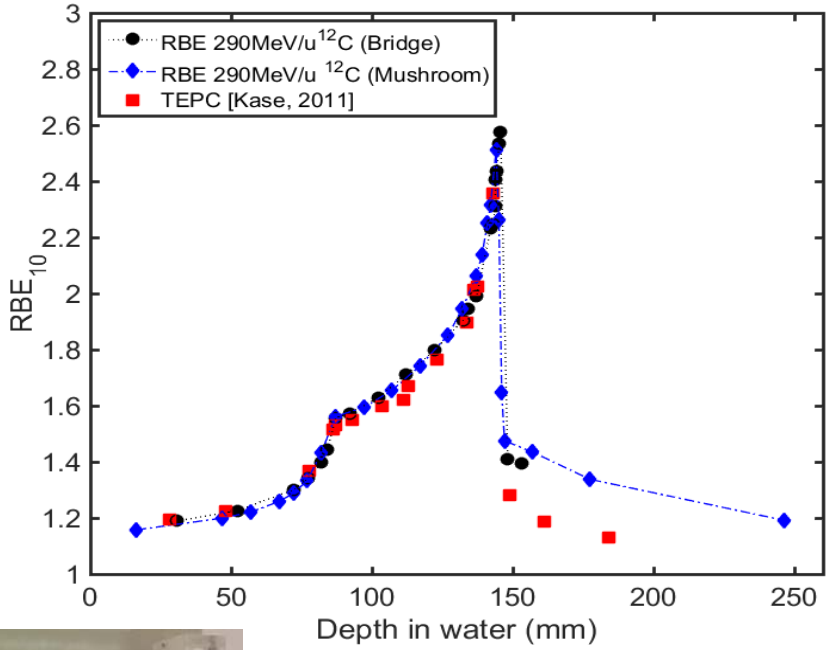
Heavy Ion Medical Accelerator in Chiba

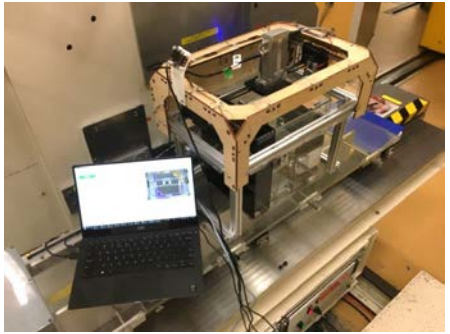
HIMAC, Japan



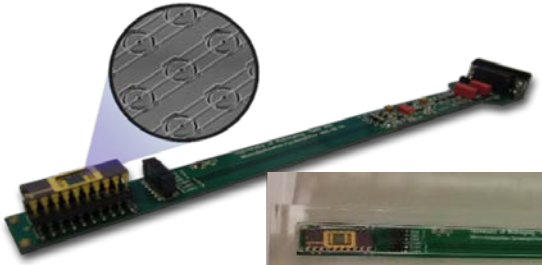
HIMAC Bio-cave beam port with passive scattering delivery

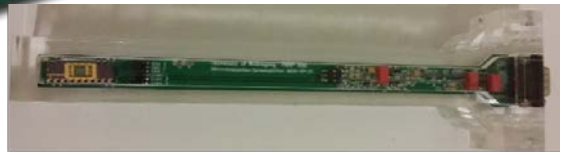
290 MeV/u ^{12}C ion SOBP





MicroPlus probe with XY-movement stage





μ^+ microdosimeter probe in PMMA sheath

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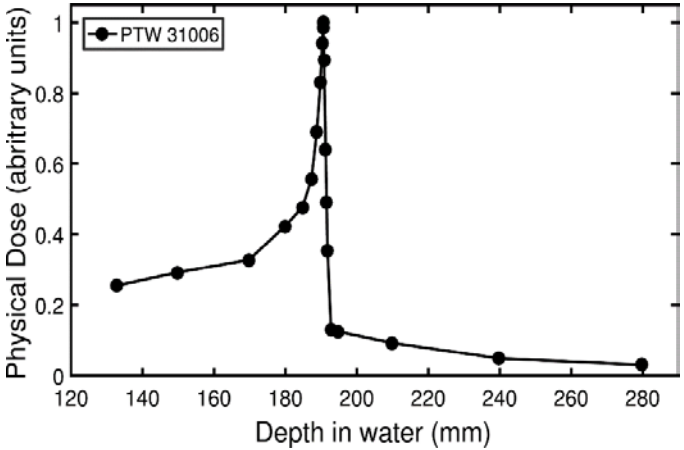
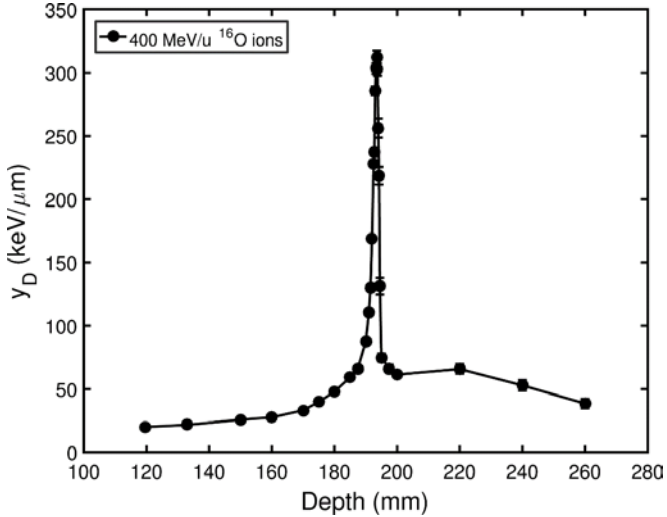
400MeV/u ^{16}O Ion Irradiation

- **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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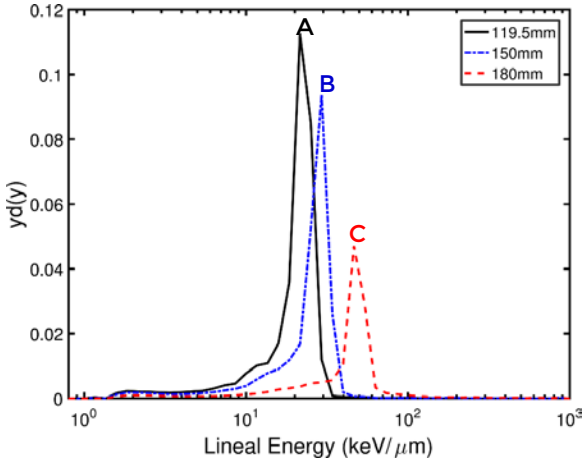
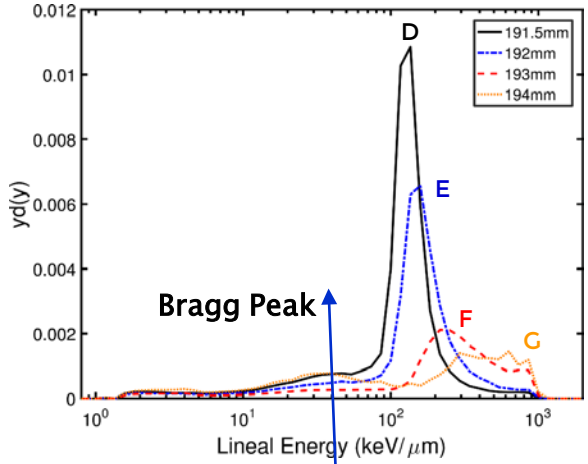
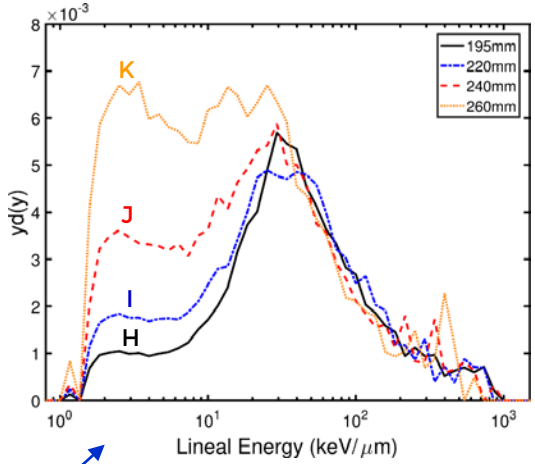
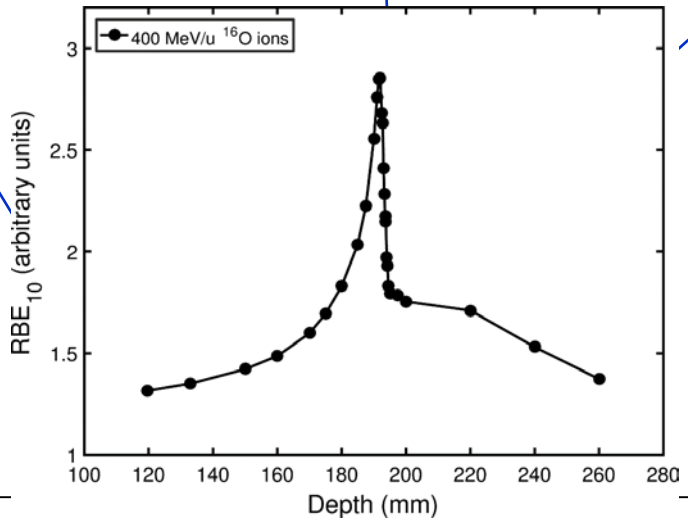






Entrance

Downstream



400 MeV/u ^{16}O Ions

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

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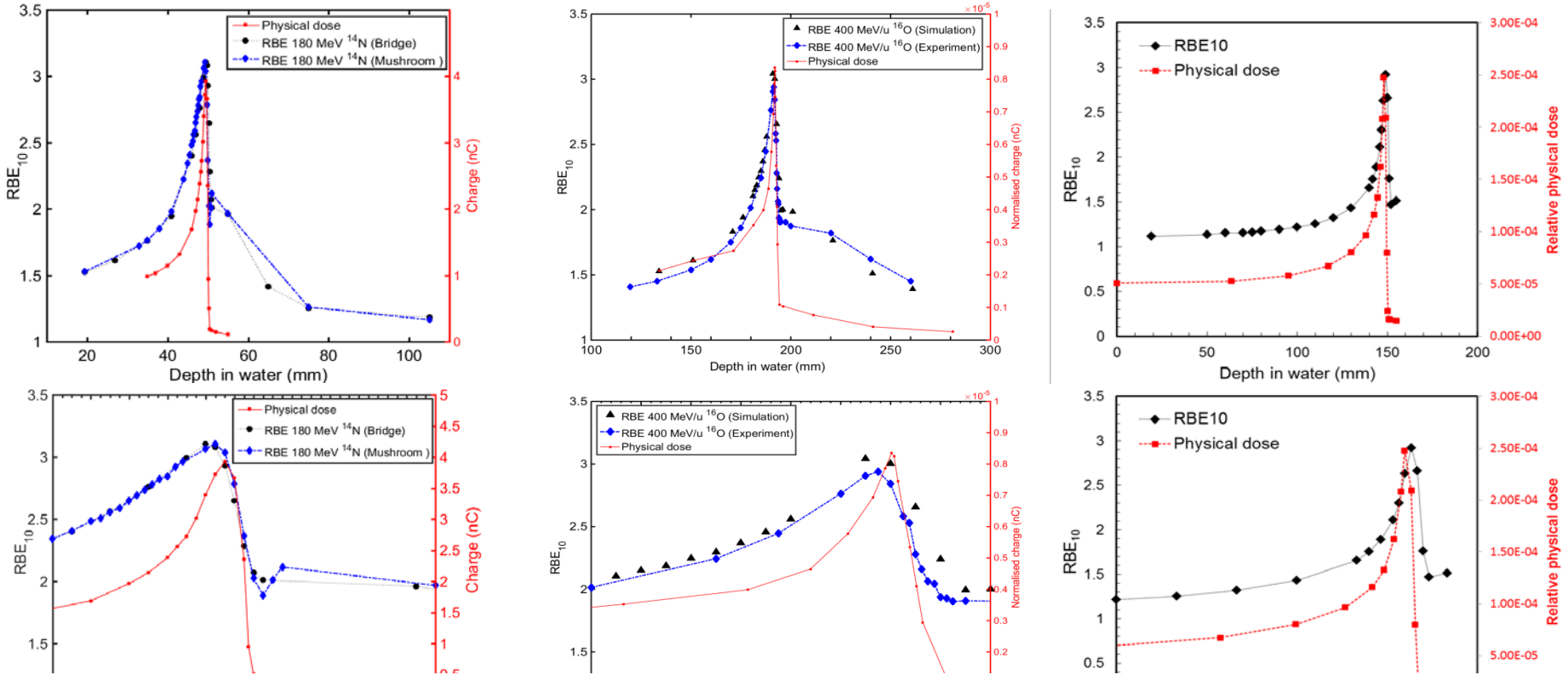
Ability for Multi-ion therapy: RBE_{10} obtained with SOI microdosimeter in response to pristine BP of *^{14}N, ^{16}O and ^{12}C ion beam (HIMAC at NIRS, Japan*

180 MeV/u ^{14}N | 400 MeV/u ^{16}O | 290 MeV/u ^{12}C



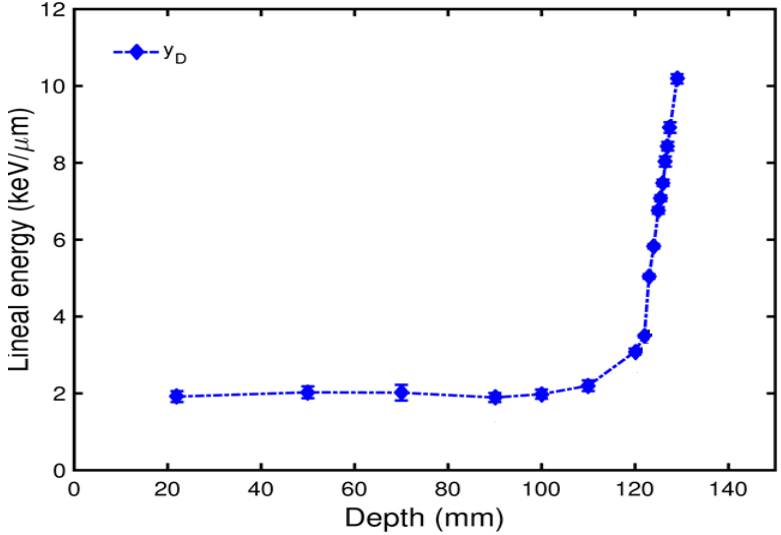
Linh T. Tran, *et. al.*, ***"The relative biological effectiveness for carbon, nitrogen and oxygen ion beams using passive and scanning techniques evaluated with fully 3D silicon microdosimeters"*** Medical Physics, 2018 ,(AAPM Award: The best paper Med .Phys. of 2018)

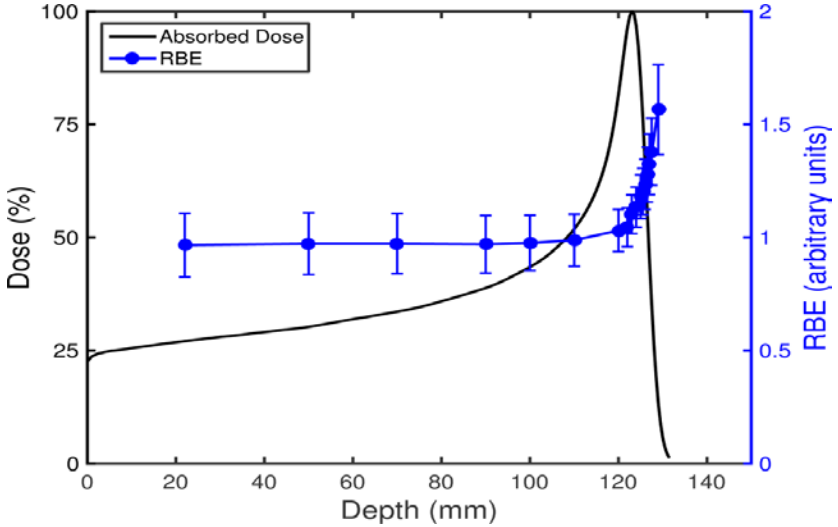
Characterization of Pencil Beam Scanning in Proton therapy

$$RBE = \frac{D_X}{D_p} = \frac{\sqrt{\alpha_X{}^2 + 4\beta_X(\alpha_p D_p + \beta_p D_p{}^2)} - \alpha_X}{2\beta_X D_p}$$

$\alpha_x = 0.13\ Gy^{-1}$

$\beta = 0.05\ Gy^{-2}$. *HSG cells*





a) $\overline{y_D}$ obtained using Bridge microdosimeter obtained with Bridge μ+ **probe** in water for spot PBS (MGH), σ=12 mm

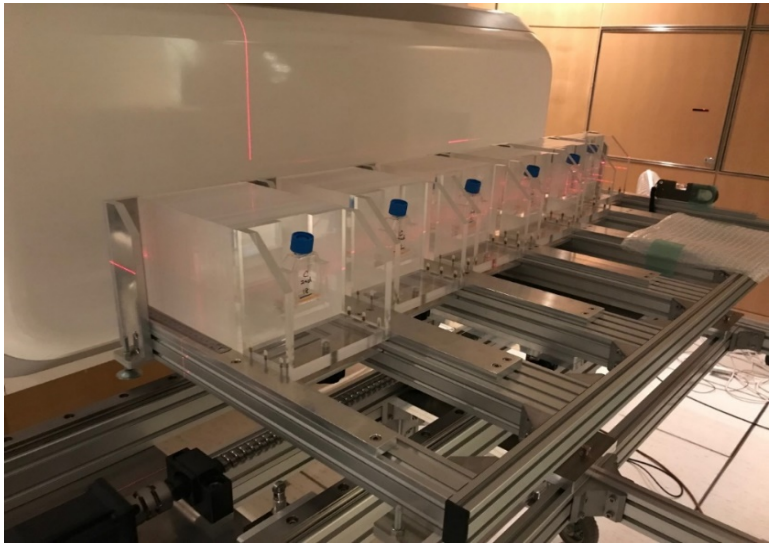
b) Depth dose distribution and RBE for PBS spot for dose in BP 2Gy. (MGH), σ=12 mm

Good agreement with Cell experiement at Prague PT centre ., see Kevin Prise et al , IJROBP , 2017

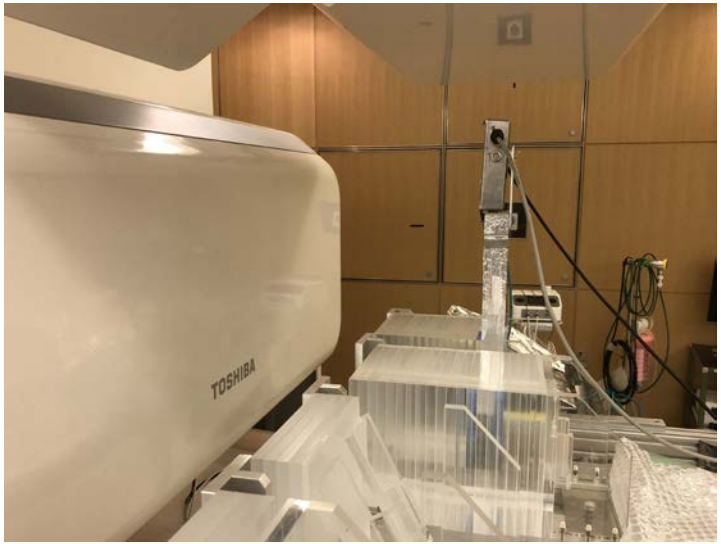
S.Anderson *et al* ., Med. Phys., 2017 and L.Tran *et al* ., Med.Phys., Sept., 2017 ,doi: 10.1002/mp.12563

Validation of MK model in MIT

We made treatment plans with (He + O) or (C + Ne) beams to make 10% survival of HSG or MiaPaca cells at SOBP.



Cell flasks were setup behind PMMA slabs of different thicknesses.



Measurements with MicroPlus probe

Courtesy of T. Inaniwa

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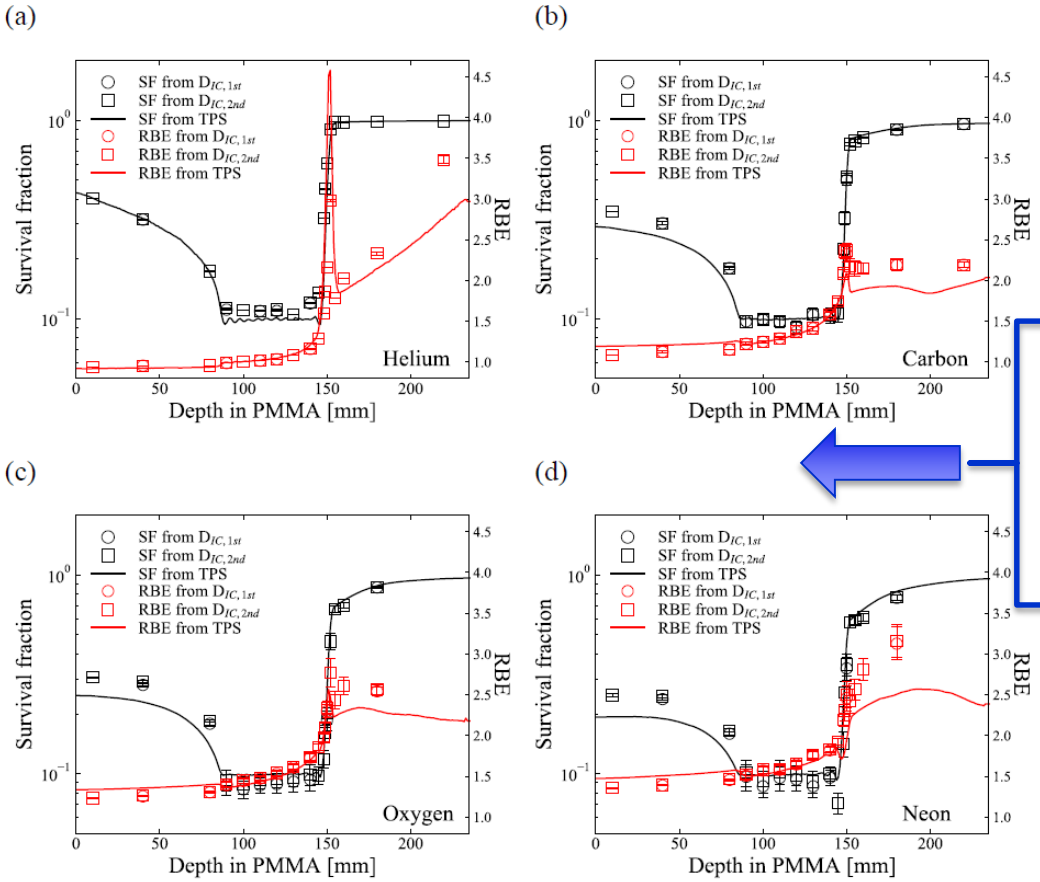
SF: MicroPlus predicted vs TPS in SOBP



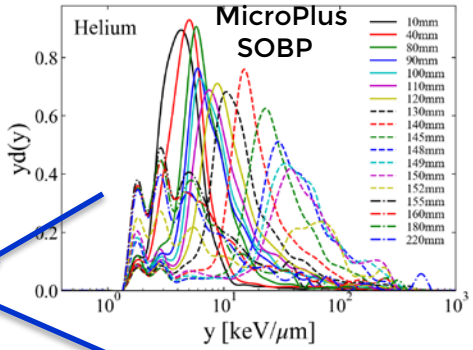
TPS: RBE_{10}xD
10x10x6 cm^3

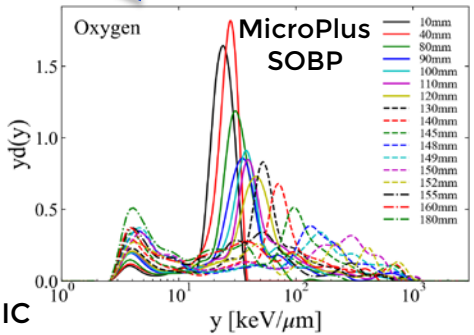
$$\alpha = \alpha_o + \frac{\beta}{\rho \pi r_d^2} y^*$$

Linear Quadratic Model

$SF(D) = \exp[-\alpha D - \beta D^2]$

Dose in SOBP measured by Markus IC





Good prediction of SF

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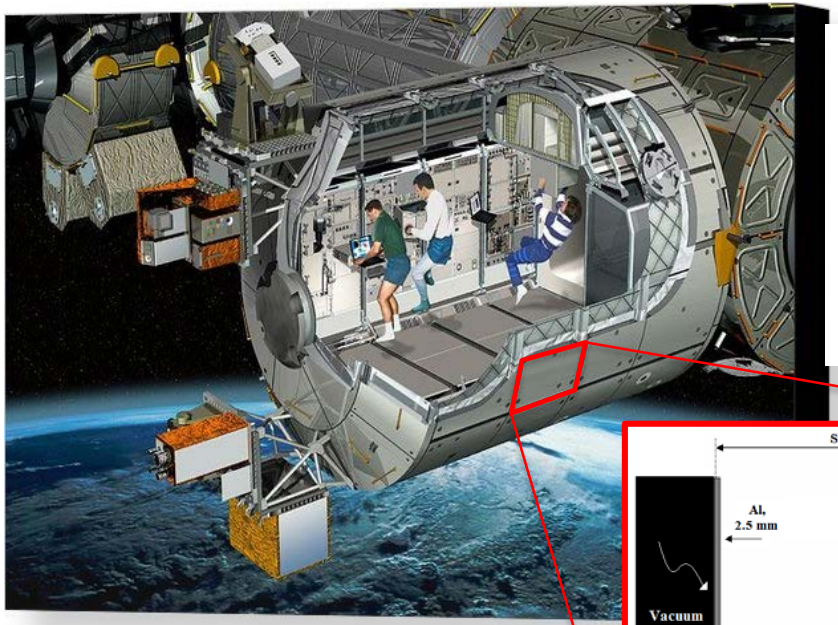
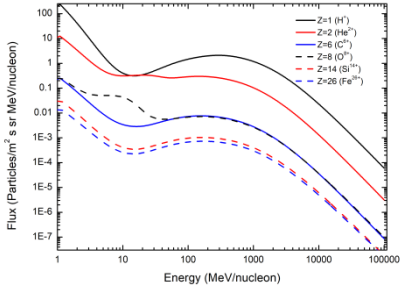
Y.H.Lee , T.Inaniwa, D.Bolst , L.Tran, A.Rosenfeld et al «Estimation of the biological effect of He, C, O , Ne ion beams using 3D silicon microdosimetry», PMB, 2021 (accepted December , 2020)

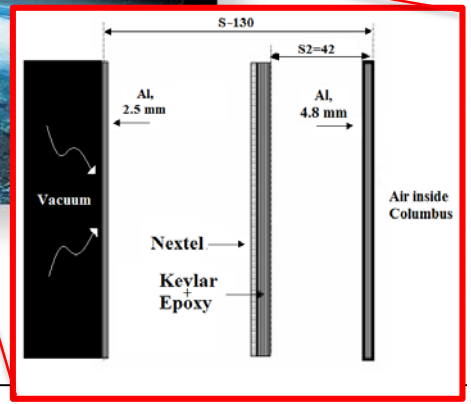
Radiobiological shielding optimization, astronaut personal dosimetry and SEU prediction



GCR: Heavy Charged Particles



ISS Columbus Module



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

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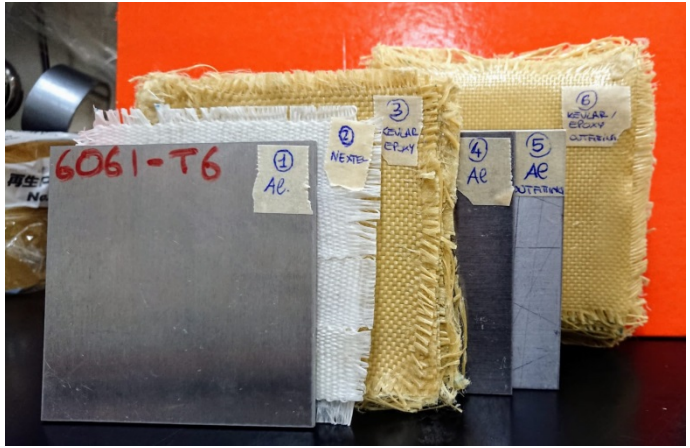
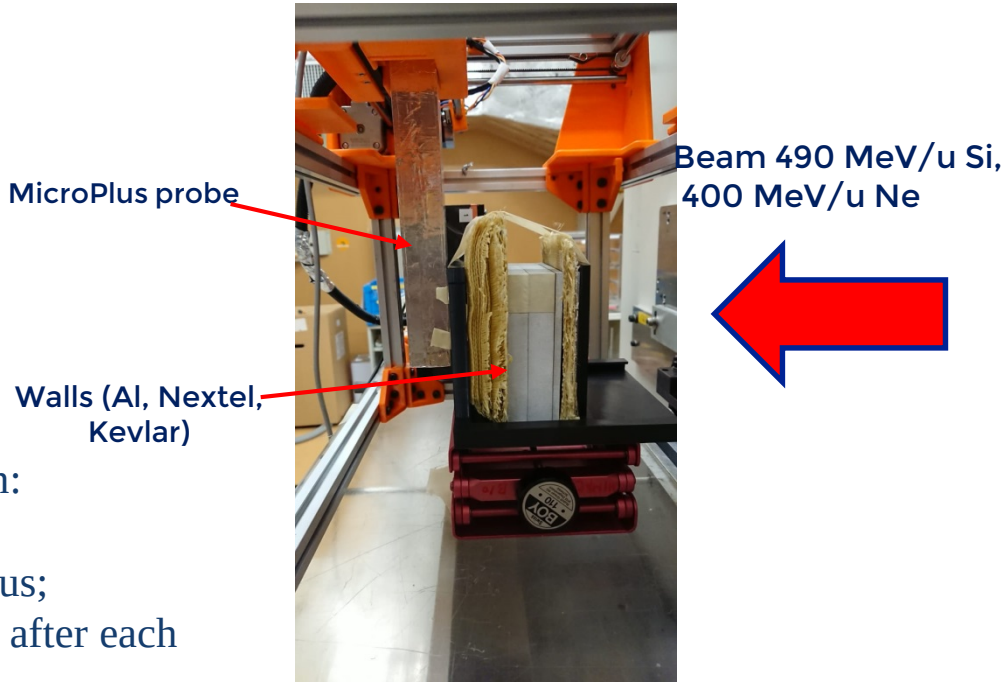
S.Peracchi *et al* 'Modelling of SOI microdosimeters response at ISS for rad. prot. of astronauts " in press , 2019

Study the shielding properties of component materials of the ISS/Columbus





Experiment carried out last week at HIMAC, Japan:

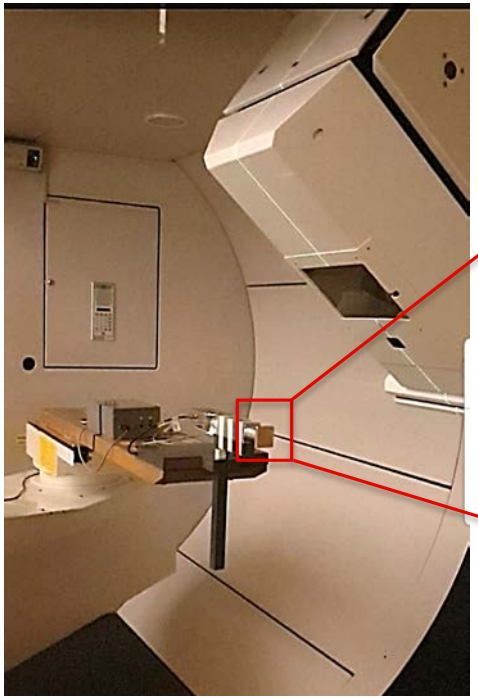
- Assemble a realistic sample of the ISS/Columbus;
- Measure microdosimetric spectra, Q and H(10) after each layer;
- Use different order configuration of layers and new materials.
- Mimicking measurements inside/outside of ISS

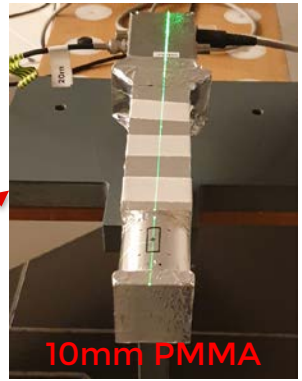
Sample layers of the ISS/Columbus build at CMRP./ANSTO

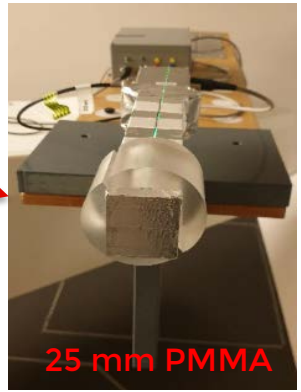
Materials composition, thicknesses, and properties have been considered the same as found in the literature and provided by Alenia and Thales space companies

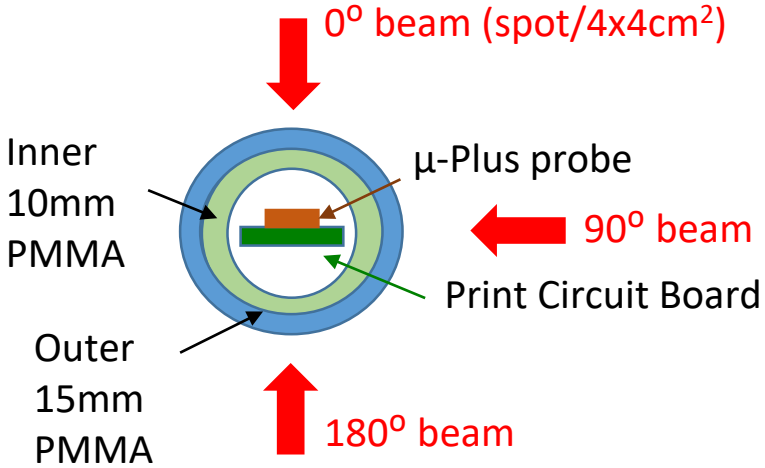
PhD student Stefania Peracchi *et al* (CMRP)

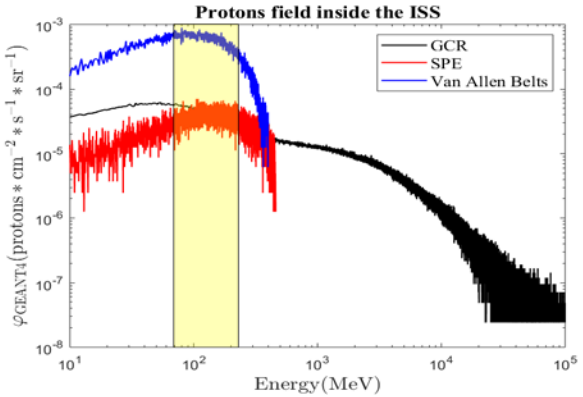
Isotropic proton irradiation at Paul Sherrer Institute (PSI)





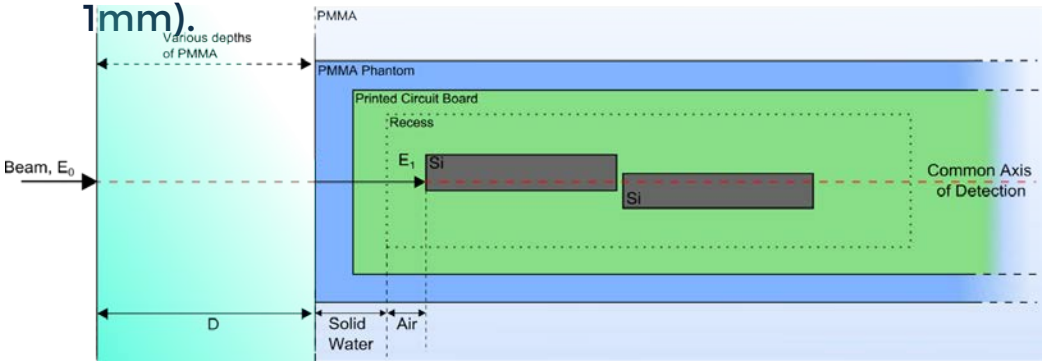


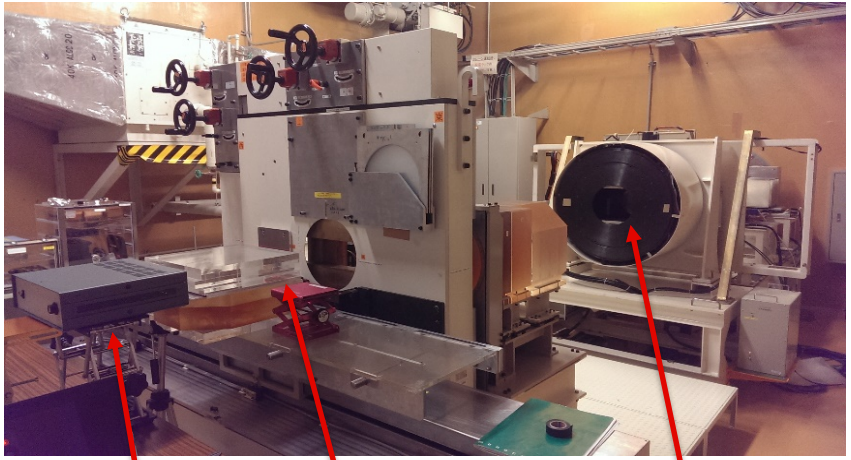




Ion Range Meter: new, accurate and fast approach – C-12, HIMAC

- The detection axis is aligned **parallel** to the direction of the C-12 beam.
- **C-12** ion beam, energy **290 MeV/u** and **10x10cm²** square field.
  - **PBP** (pristine Bragg peak)
- **Depth Dose Profiles: PBP** measurements conducted with increasing depth in PMMA (+/- 1mm).





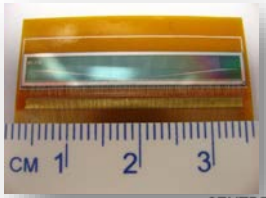


Figure – Schematic of experiment, beam energy E_0 is modified along trajectory through materials & detector to deposit PBP in sensitive volumes for measurement.

E.Debrot et al , Med Phys , 45(2), 953-962, 2018

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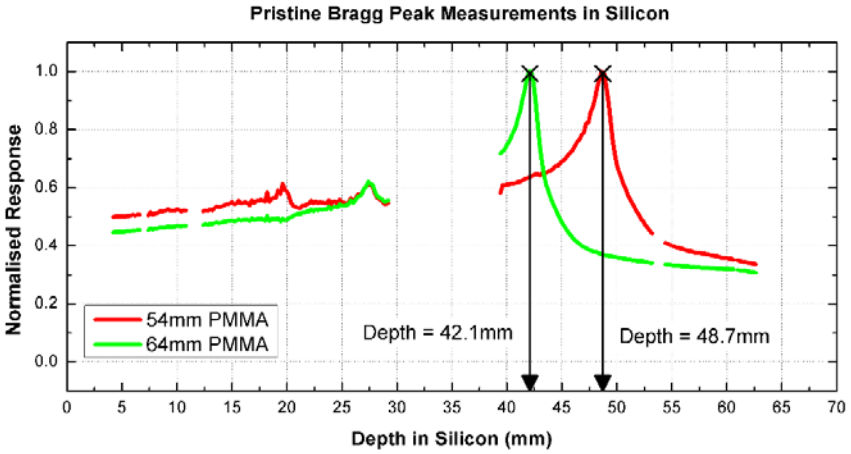
Results: Energy Reconstruction for Heavy-Ions



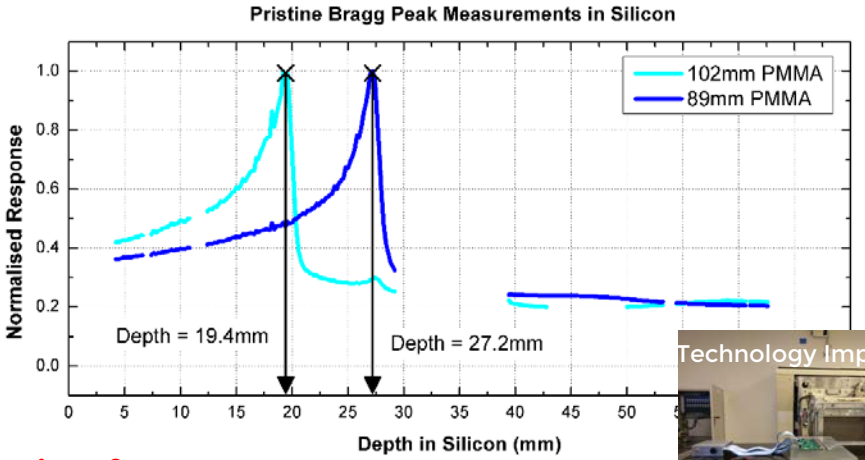
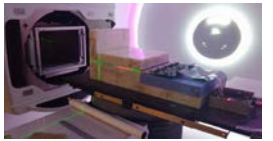


Table III – Energy Reconstruction for C-12.

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

Mayo Clinic, MN



MGH, Boston

- 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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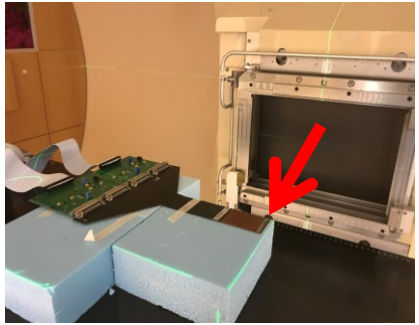
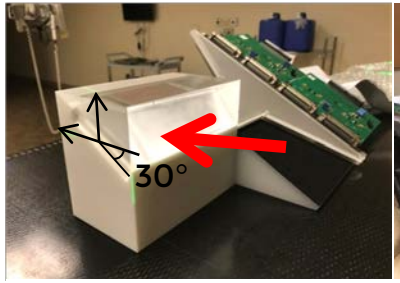
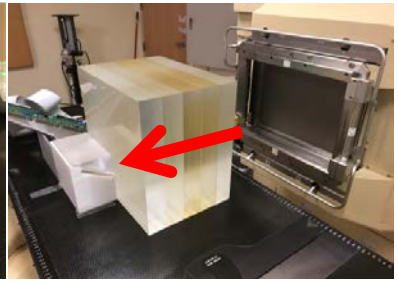
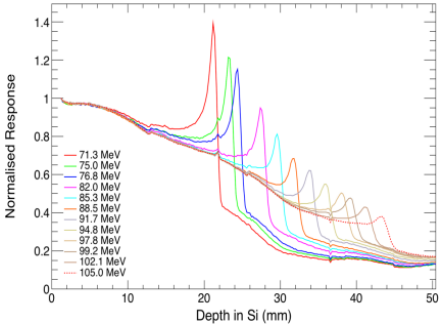
DMG-256 for range verification in spot-scanning proton therapy: Mayo collaboration

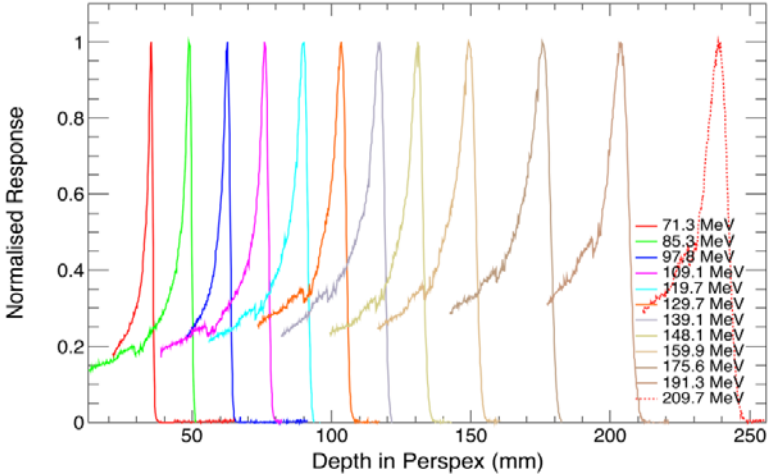




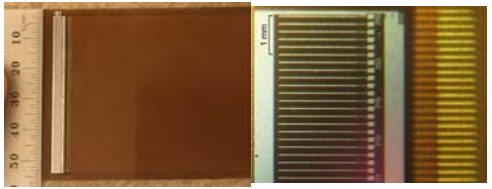


DUO-DMG: Range Spot Beam





DMG : Range PBS beam, field 5x5 cm²



CMRP and Mayo Clinic collaboration

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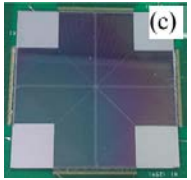
Proton Beam Experiment – PBS Spot Profile (MGH)

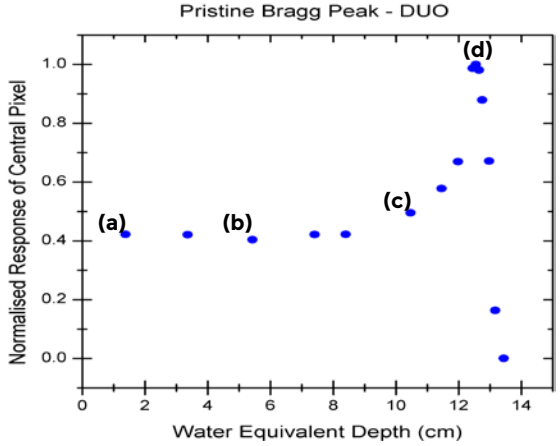
PBS "Golden" data obtaining

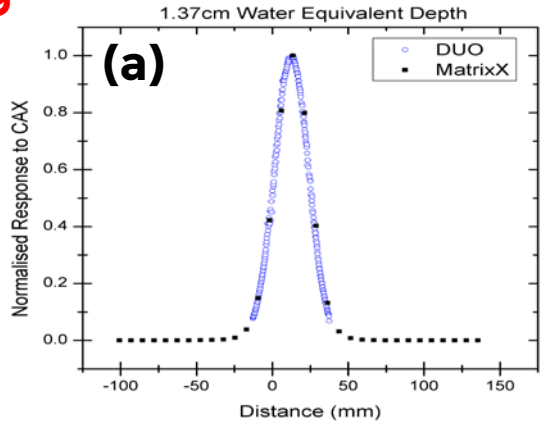
DUO

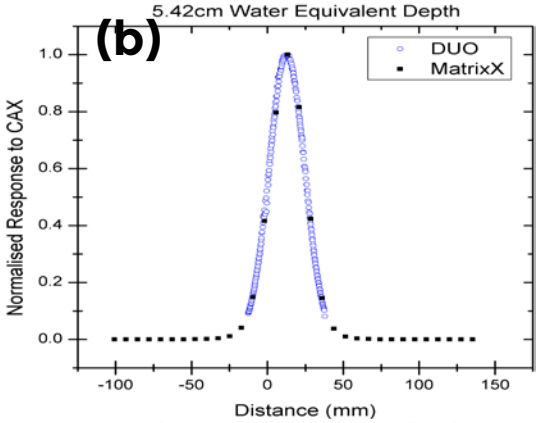


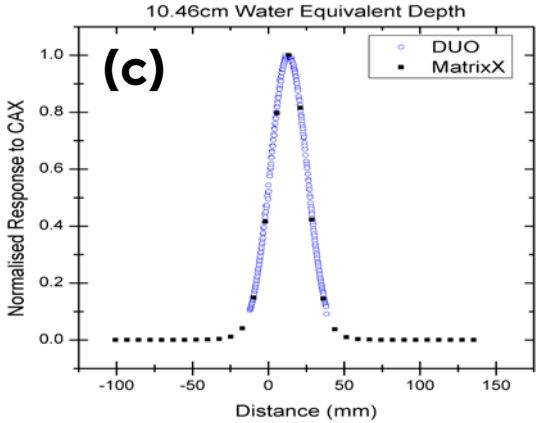
Profiles compared between **DUO** and **MatrixX** at each depth investigated.

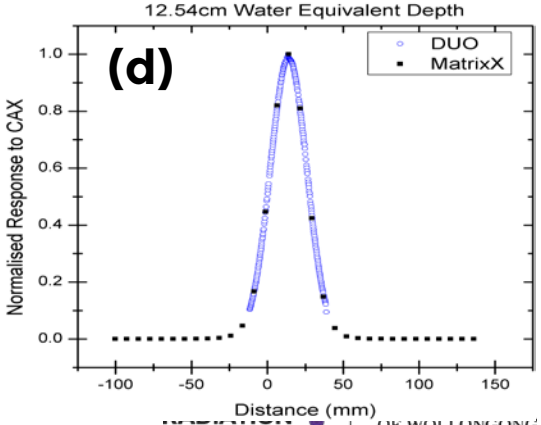
A sample of the measurements taken is shown.





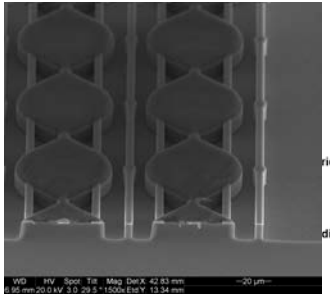


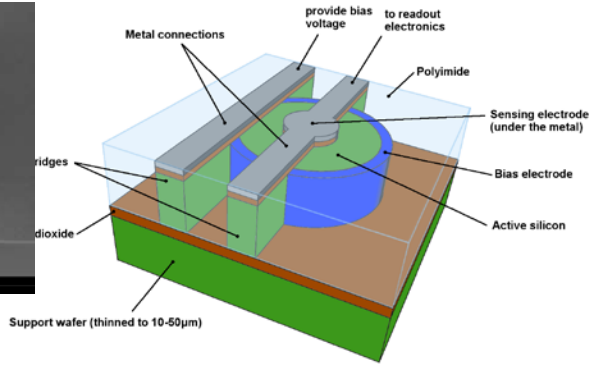




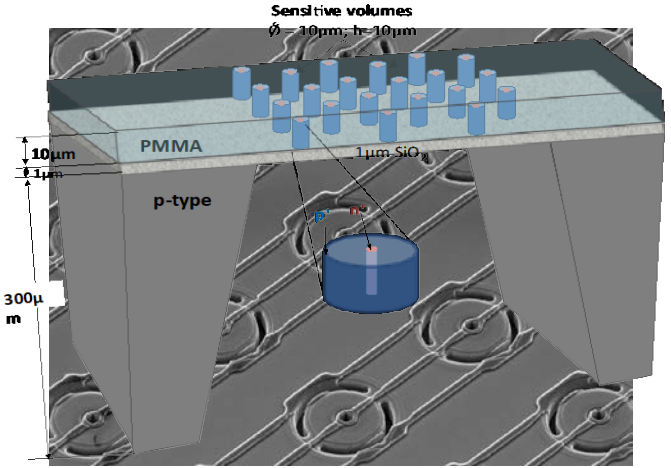
Conclusions

- New SOI microdosimeter utilizing 3D detector technology was introduced for particle therapy QA
- PT and HIT provide directional radiation that require using mean average path rather then average chord for TE conversion.
- Microdosimetric properties and RBE of passive ^{14}N, ^{16}O and pencil scanning beam of ^{12}C , and effect of organ motion on RBE has been studied. RBE can be essentially different to planned.
- MicroPlus Probe with Bridge and Mushroom Microdosimeters have extremely high spatial resolution
- Next version: of Mushroom 2 microdosimeter will be with silicon etched out and filled with PMMA to increase tissue equivalence by avoiding secondaries production from silicon.

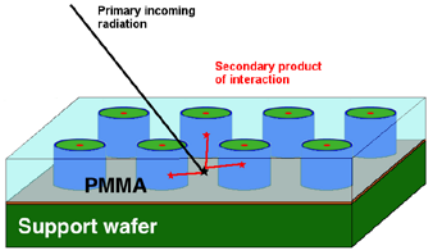


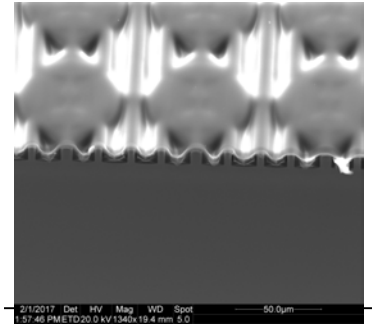


Mushroom 2



Mushroom 1





Mushroom 3

Patented by UOW in USA, Europe

SINTEF

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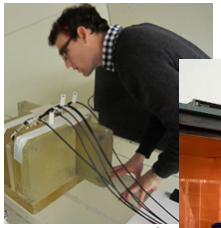
Education and Training in particle therapy at CMRP

14 PhDs trained in Particle Therapy and Space research at different medical accelerators

Peter Bradley 1999 AINSE Gold Medal

Greg Kaplan 1999-2001

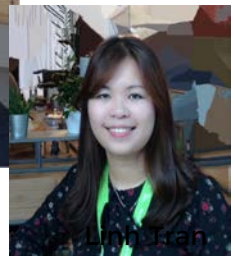


Scott Penfold Cancer Inst NSW Award,

Dale Prokopovich 2011

Jayde Livingston 2013

Nicolas Depauw 2014



Linh Tran

Linh Tran 2014

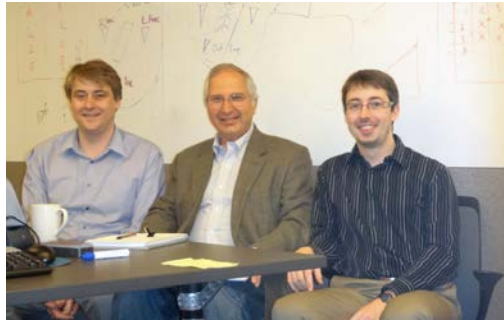
AIP Best Thesis Award
AAPM Award

Iwan Cornelius 2005 AINSE Gold Medal

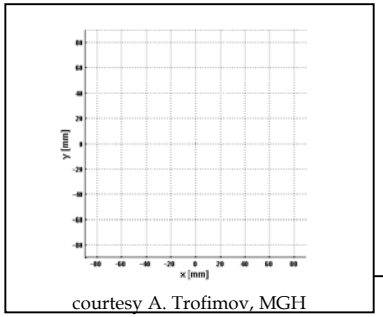
Ben Clasie 2006 University Gold Medal

Andrew Wroe 2007 AINSE Gold Medal

Stephen Dowdell 2011



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



courtesy A. Trofimov, MGH

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