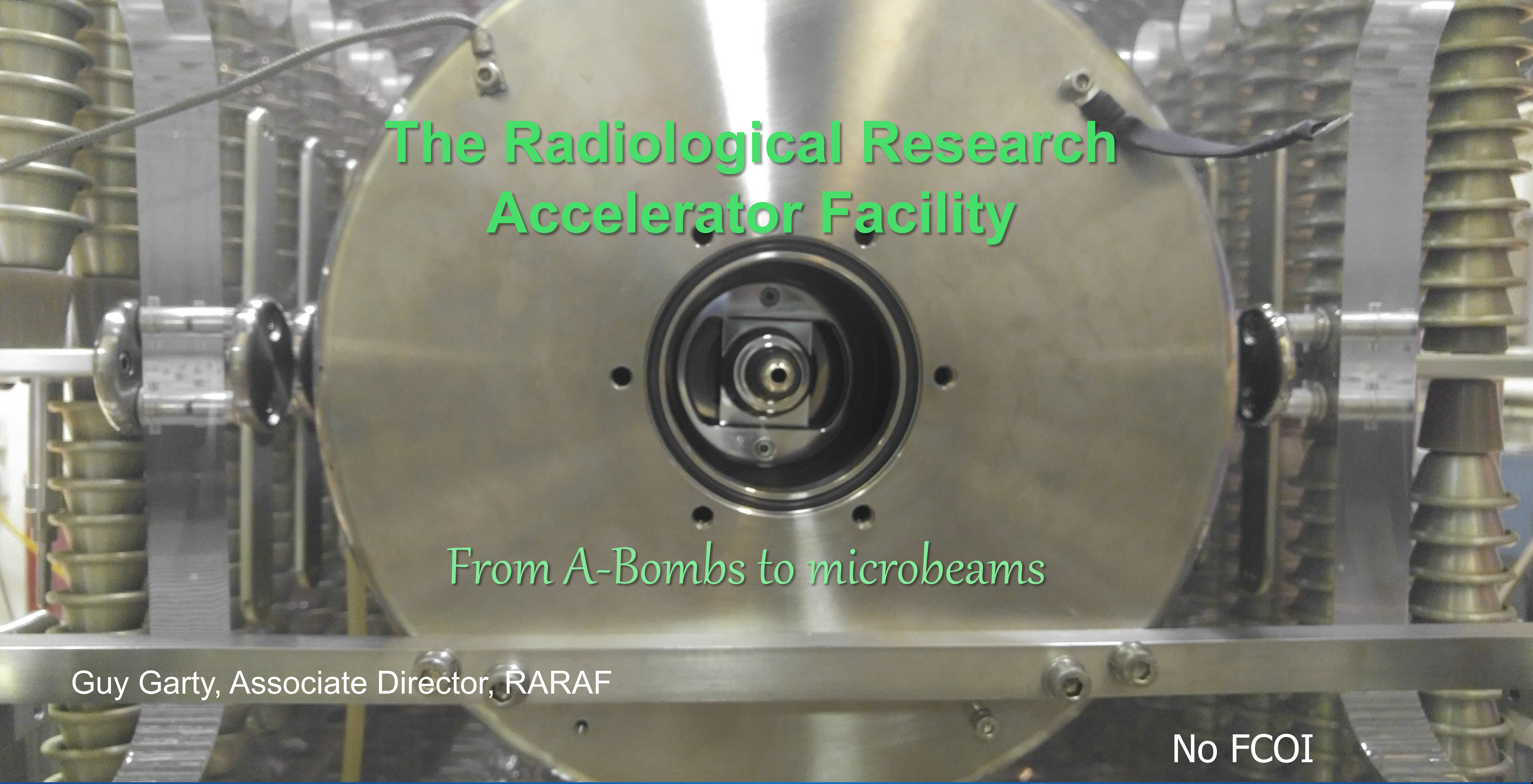


The Radiological Research Accelerator Facility

From A-Bombs to microbeams

Guy Garty, Associate Director, RARAF

No FCOI

Who are we?

- RARAF is a multidisciplinary accelerator facility

  designed for the delivery of known quantities of radiation
  - to biological samples
  - using neutrons and ion beams

- 5 physicists, 3 biologists
- Beam energies much lower than NSRL but

  well suited to radiobiology

Accelerator dedicated to radiobiology
Welcomes outside experimenters!

Our Accelerator

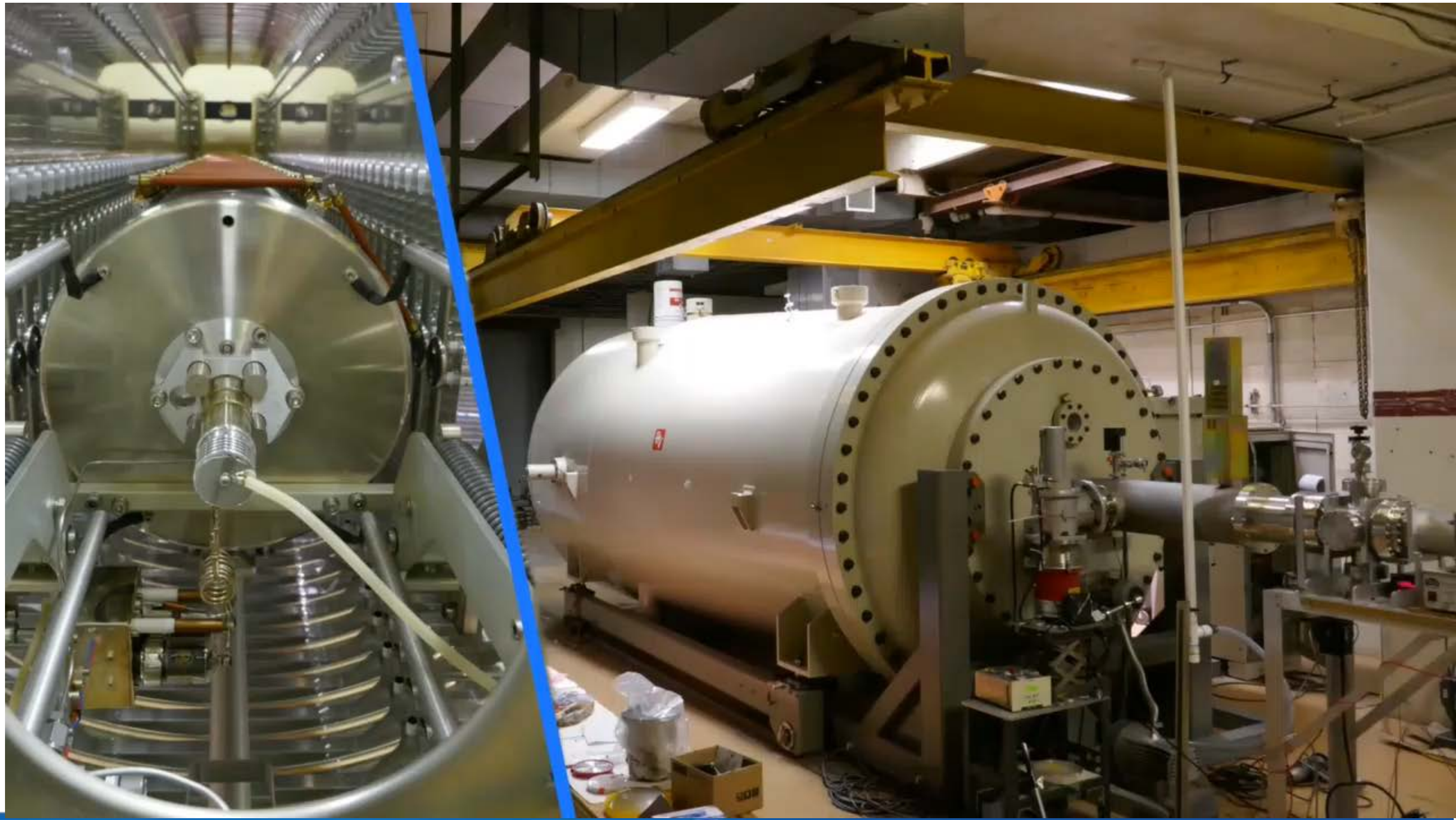
- 5.5 MV Singletron

- Neutrons
- Hydrogen/helium beams

- Broad beams (35 mm)
- Microbeams (1 μm)

- Coming soon:
  - ➢ Heavier ions
  - ➢ Higher energies
  - ➢ High dose rate electrons

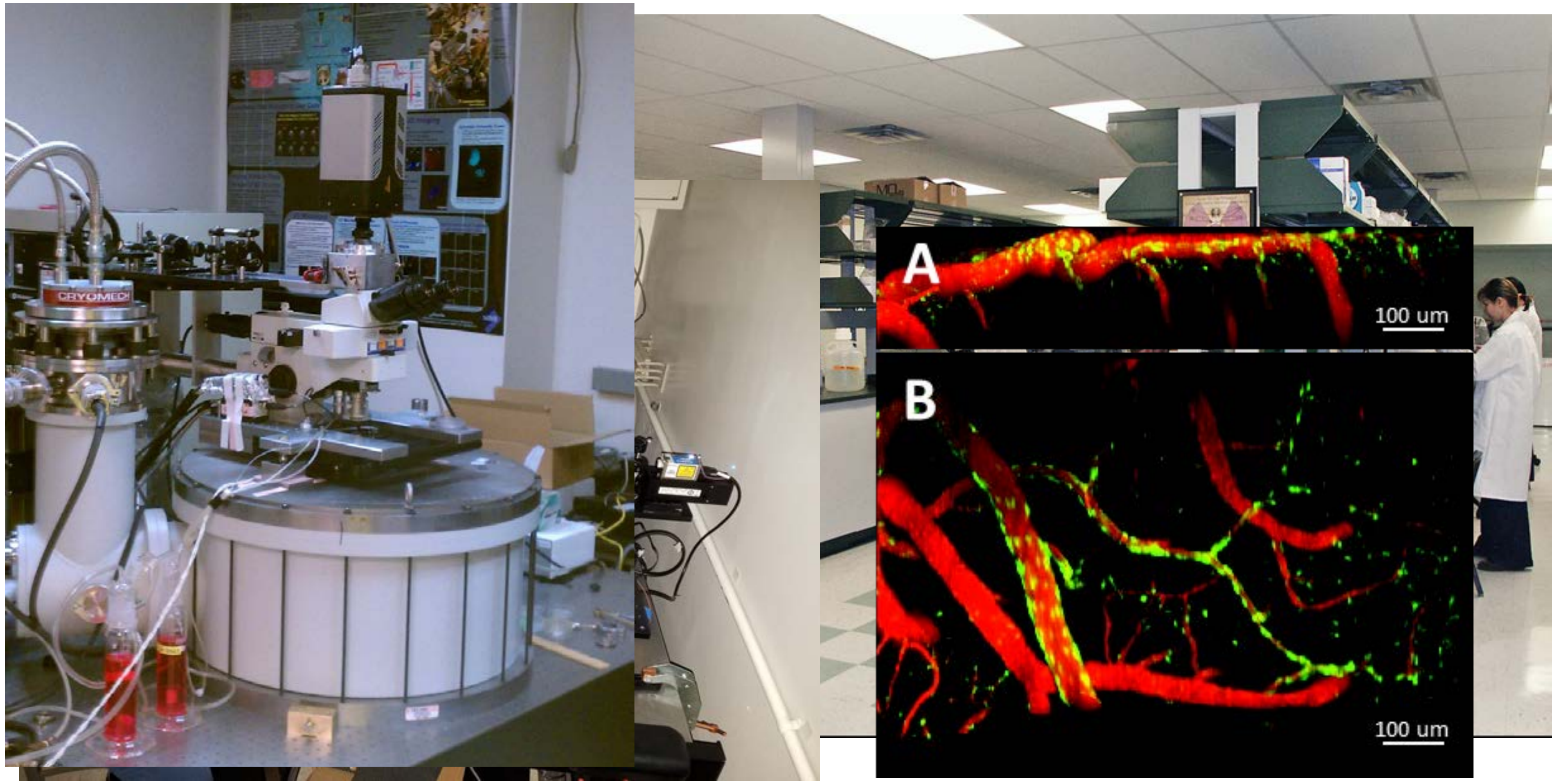
Accelerator dedicated 100% to radiobiology
Welcomes outside experimenters!



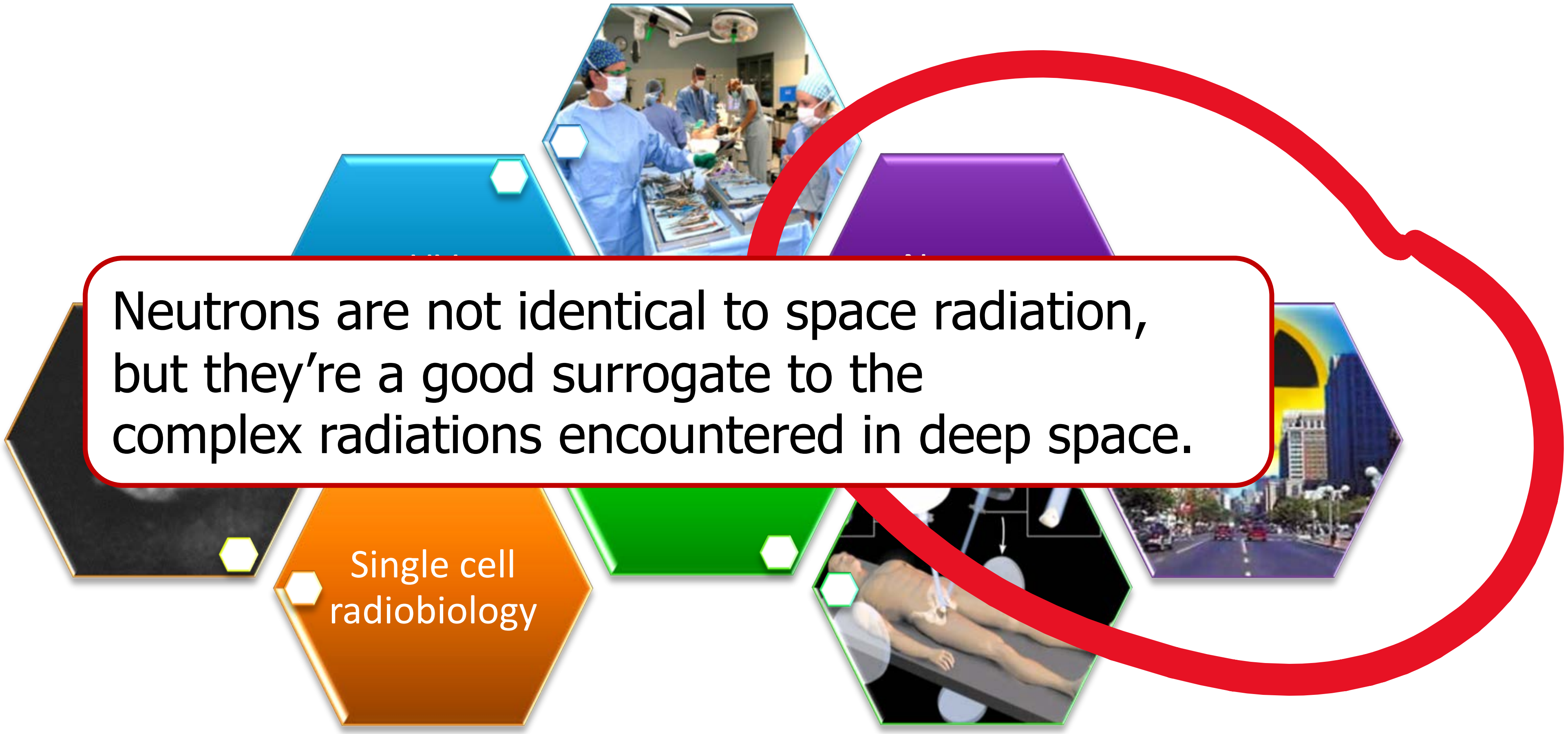
RARAF facilities

- Fully equipped biology lab
- Satellite mouse facility
- High end imaging facilities
  - Regular fluorescence
  - Multiphoton
  - SCAPE microscopy
    - Swept, Confocally-Aligned Planar Excitation
    - 3D in vivo imaging

Accelerator dedicated 100% to radiobiology
Welcomes outside experimenters!



Research at RARAF



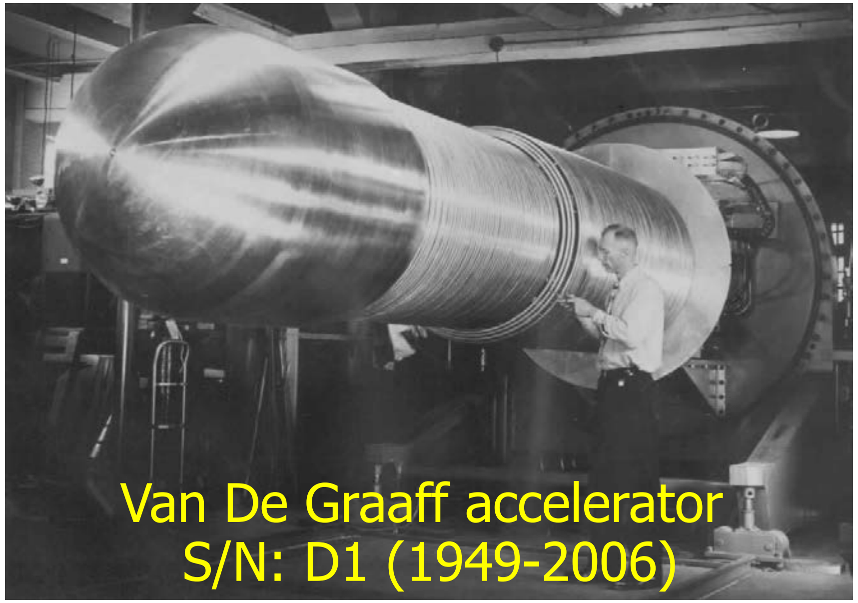
Neutrons are not identical to space radiation, but they're a good surrogate to the complex radiations encountered in deep space.

RARAF50

The Radiological Research Accelerator Facility 1967 – 2017

Need for a dedicated facility for radiobiology and microdosimetry of monoenergetic neutrons

Dr. Harald H. Rossi, Director
Radiological Research Laboratory
Columbia University

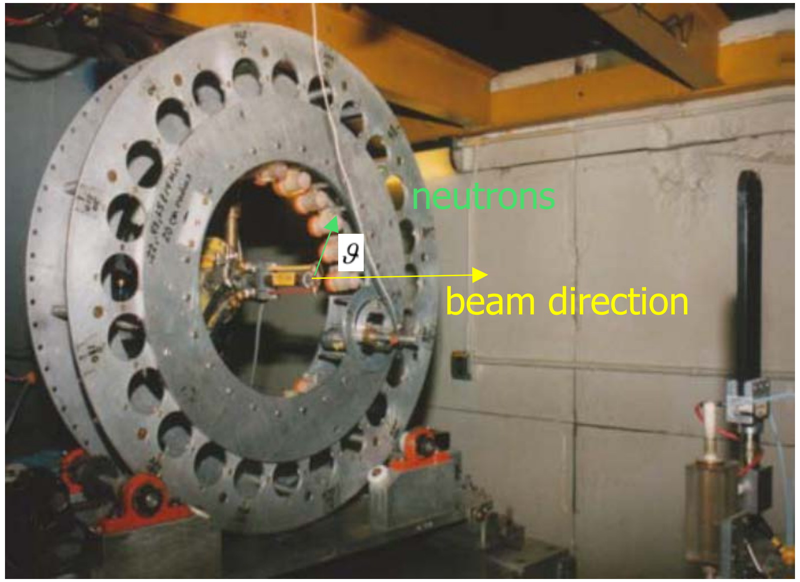


Dr. Victor P. Bond, Associate Director
Brookhaven National Laboratory

Collaboration between Columbia University and Brookhaven National Laboratory (BNL)

Commissioned April 1st,1967 Moved to Nevis labs ~1980

Monoenergetic neutrons



- 0.2 to 14 MeV neutrons generated using
  - ➢ T(p,n), T(d,n) reactions
  - ➢ Adjusting relative energy and angle to target

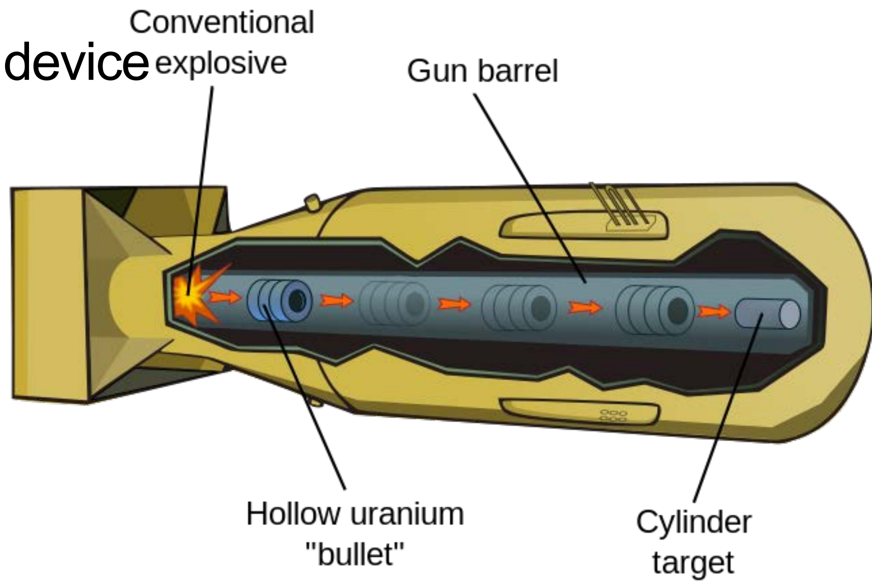
- Today used mainly for physics
  - ➢ Background Calibration for Xe-100 kg

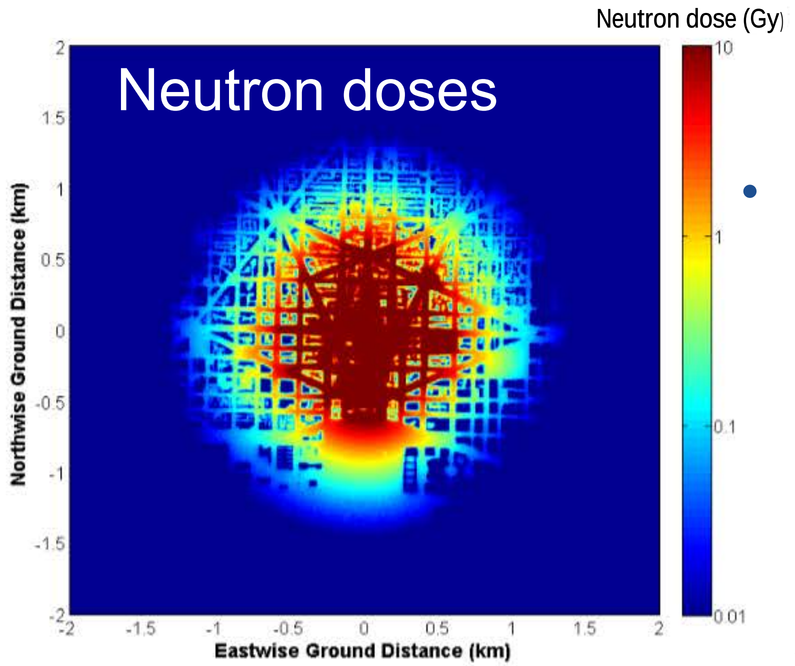
$$E_n = E_p \frac{m_g m_n}{(m_n + m_r)^2}\left\{2\cos^2\vartheta + \frac{m_r(m_r+m_n)}{m_g m_n}\left[\frac{Q}{E_p}+1-\frac{m_g}{m_r}\right] + 2\cos\vartheta\sqrt{\cos^2\vartheta + \frac{m_r(m_r+m_n)}{m_g m_n}\left[\frac{Q}{E_p}+1-\frac{m_g}{m_r}\right]}\right\}$$

- ❖ Bubble detectors
- ❖ Scintillator for Mars Curiosity Rover

CINF: The Columbia IND Neutron Facility

- Designed to model neutron exposures from an improvised nuclear device
  - Gun type device
  - Up to 30% of dose due to MeV neutrons





- Aims
  - Irradiate Mice/blood/cells
  - To develop biodosimetry assays
  - To test radiation countermeasures

Kramer et al, Monte-Carlo Modeling of the Initial Radiation Emitted by a Nuclear Device in the National Capital Region DTRA-TR-13-045 (R1)

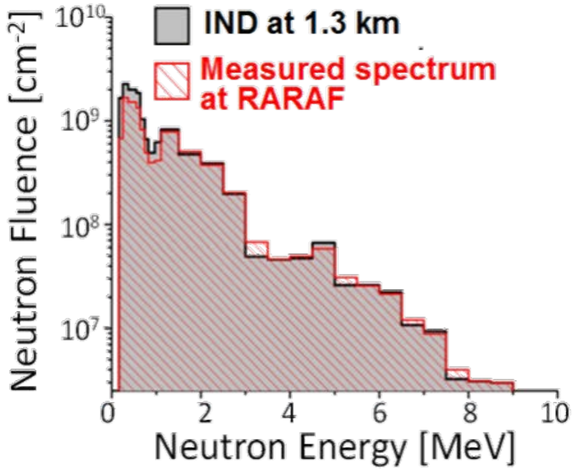
CINF: The Columbia IND Neutron Facility

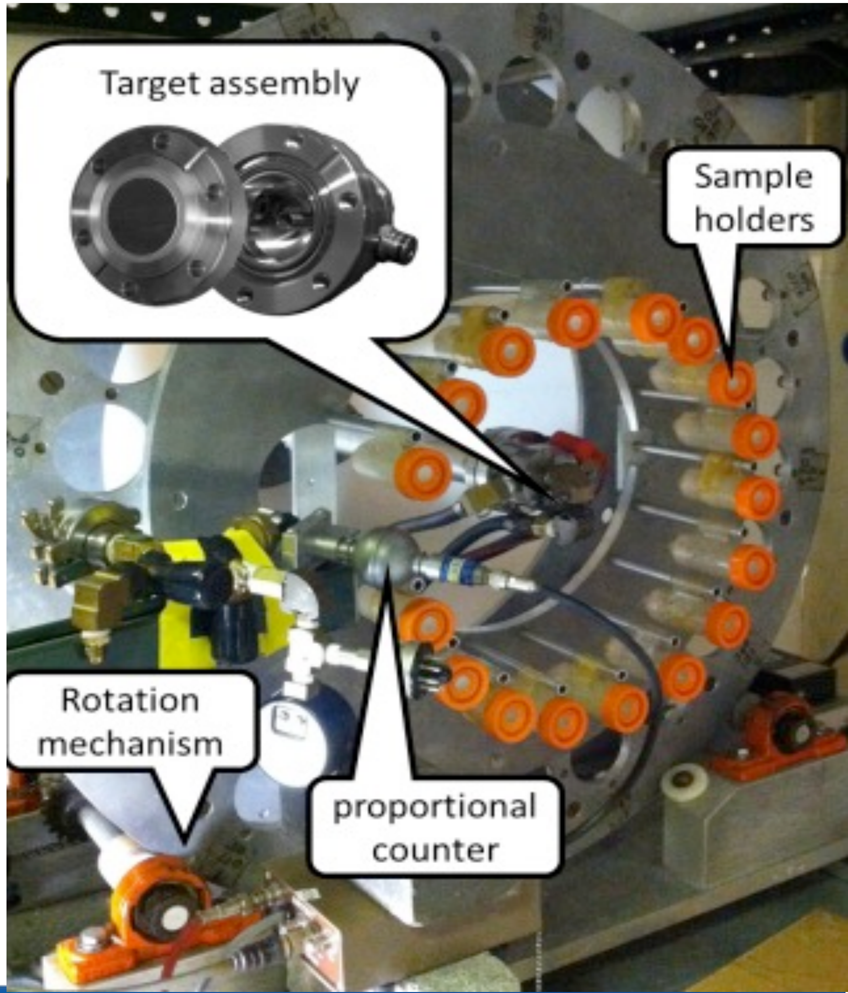
- How we do it?
  - Samples are mounted on a rotating irradiation fixture
  - Generate neutrons by H^+/D^+ on Beryllium
  - Using multiple simultaneous reactions

$^9Be(p,n)$ & $^9Be(d,n)$

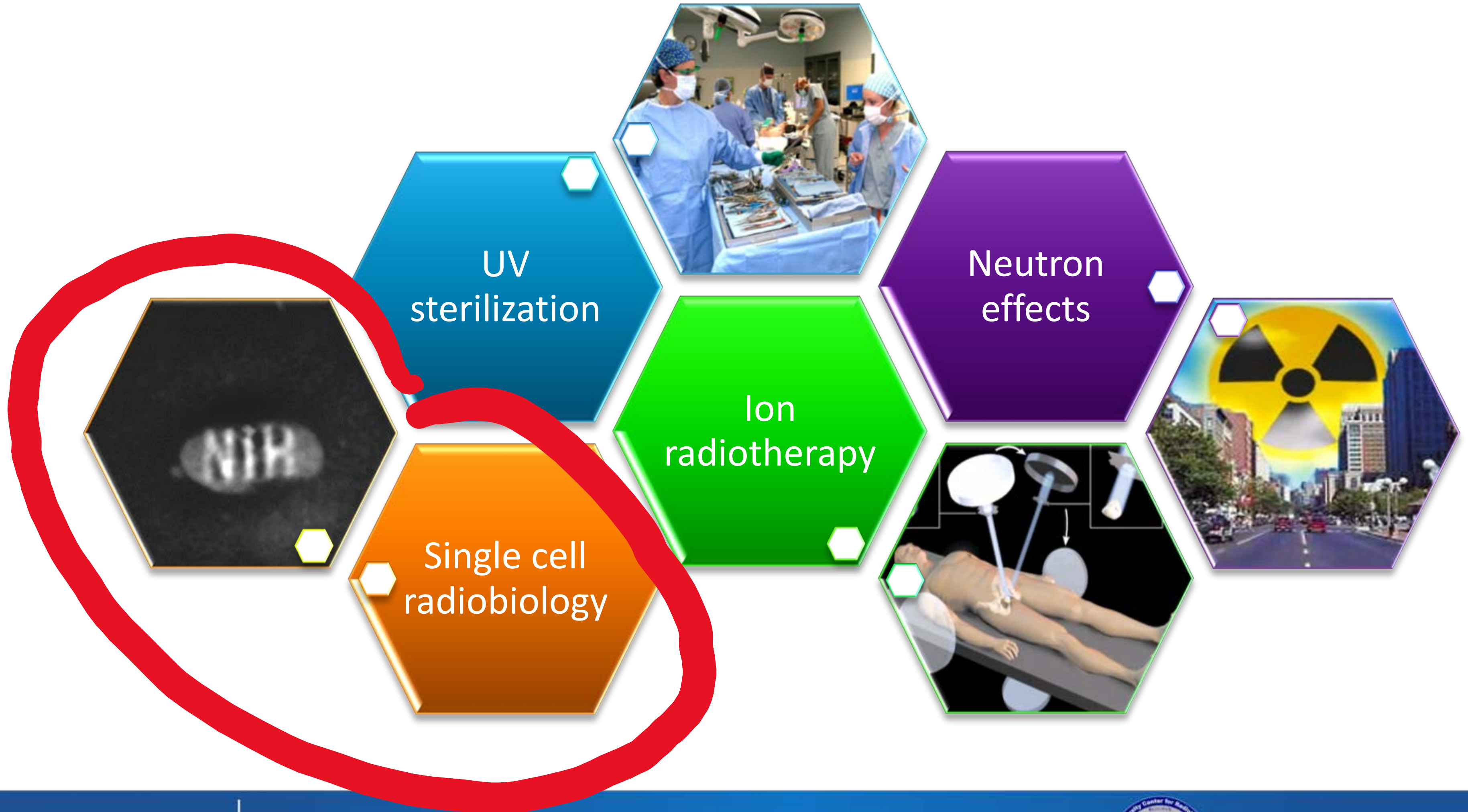
Low energy ⮰ ⮱ High energy

- Spectrum approximates hiroshima
- Dose rate > 5cGy/min (3 Gy/h)
- Can also simulate microgravity
- Daily traceable dosimetry



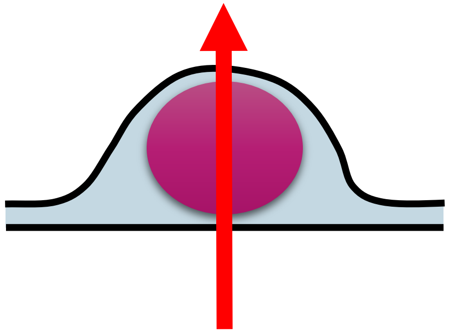


Research at RARAF



What is a Single-Cell Microbeam?

A single-cell microbeam can deposit ionizing radiation damage in micrometer or sub-micrometer sized regions of cells



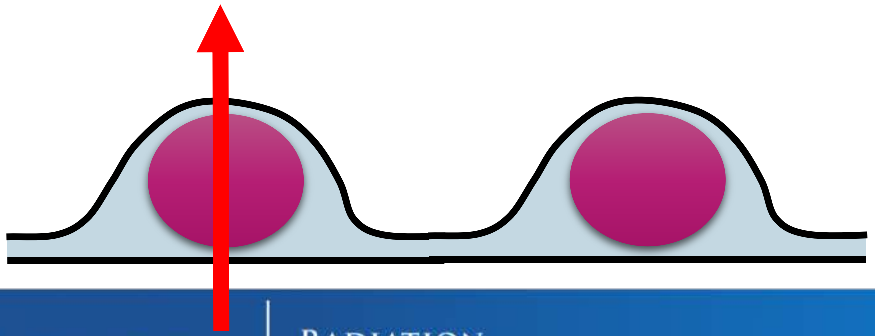
What is a Single-Cell Microbeam?

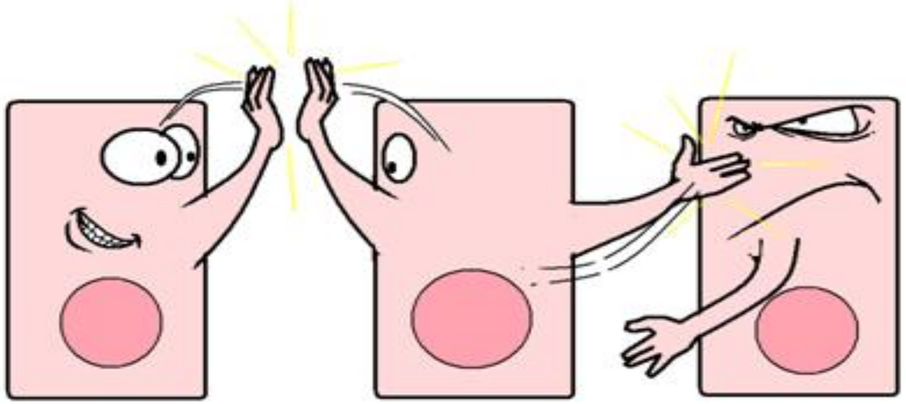
A single-cell microbeam can deposit ionizing radiation damage in micrometer or sub-micrometer sized regions of cells

Allows investigation of single-particle effects

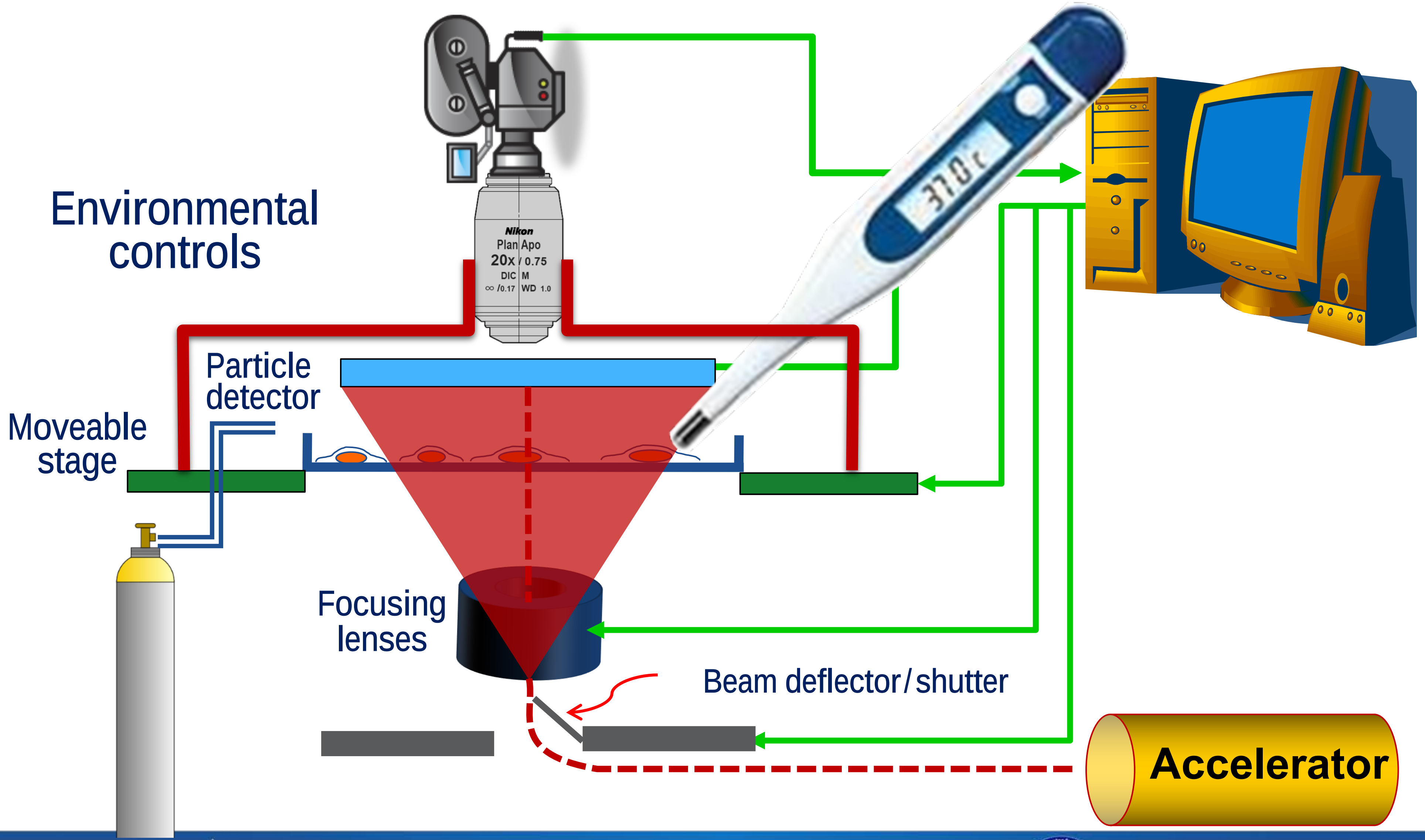
Allows investigation of various intra-cellular targets

Allows investigation of inter-cellular mechanisms of stress response

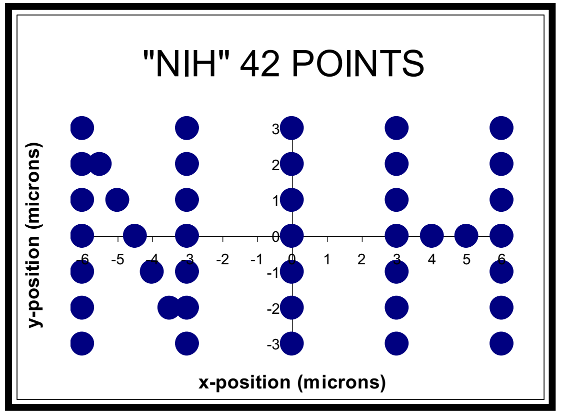


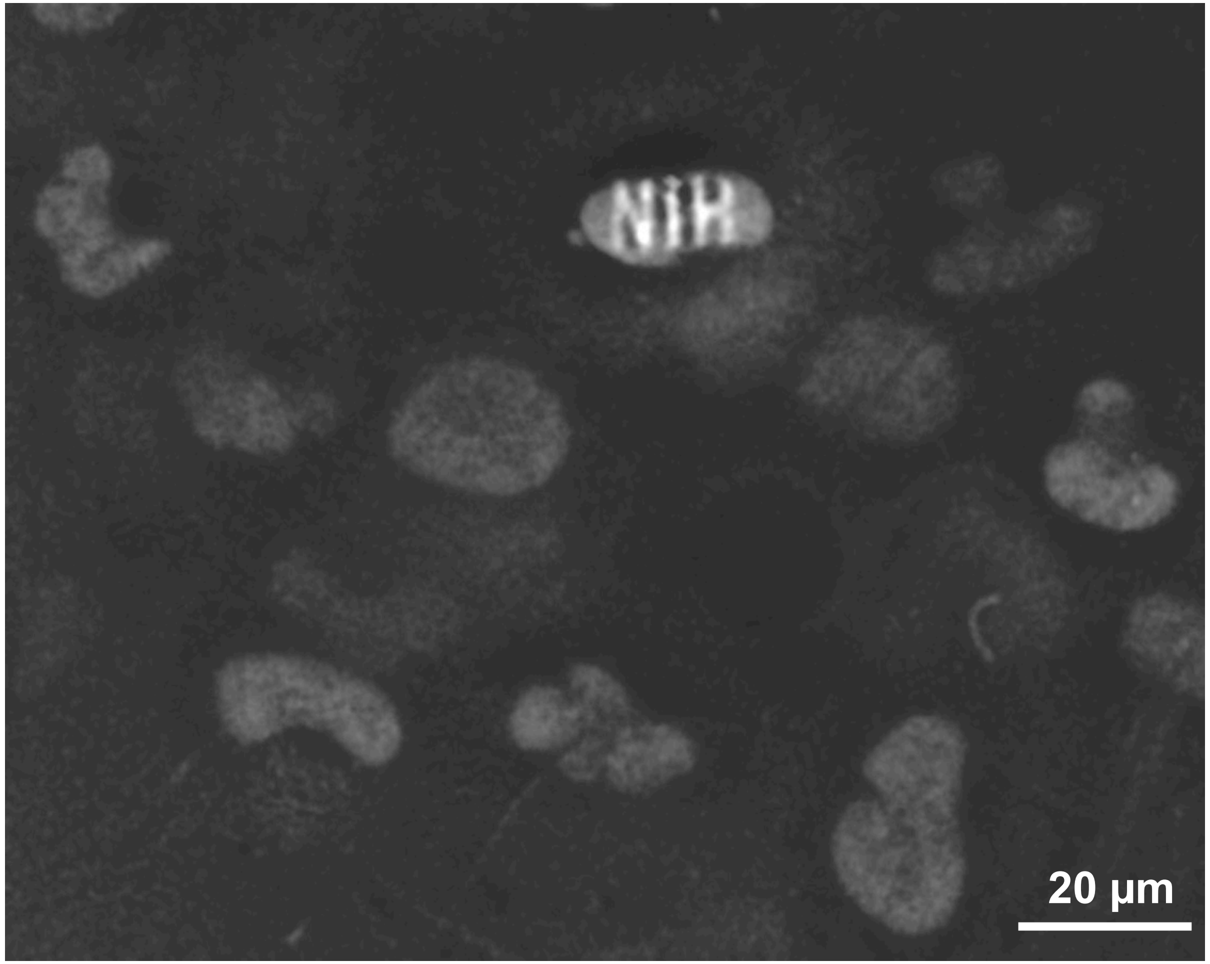


How to make a microbeam?



And if you do it right:

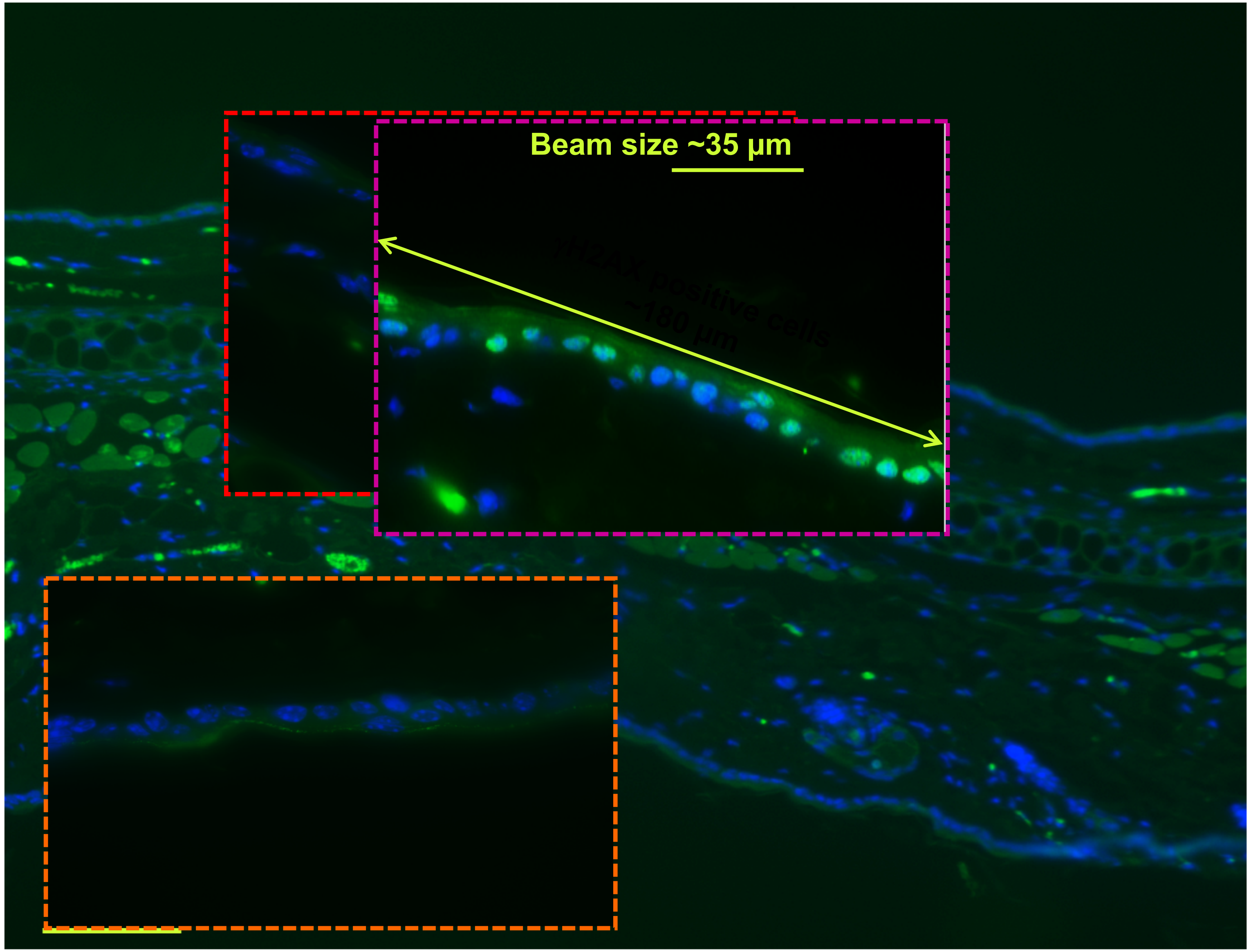




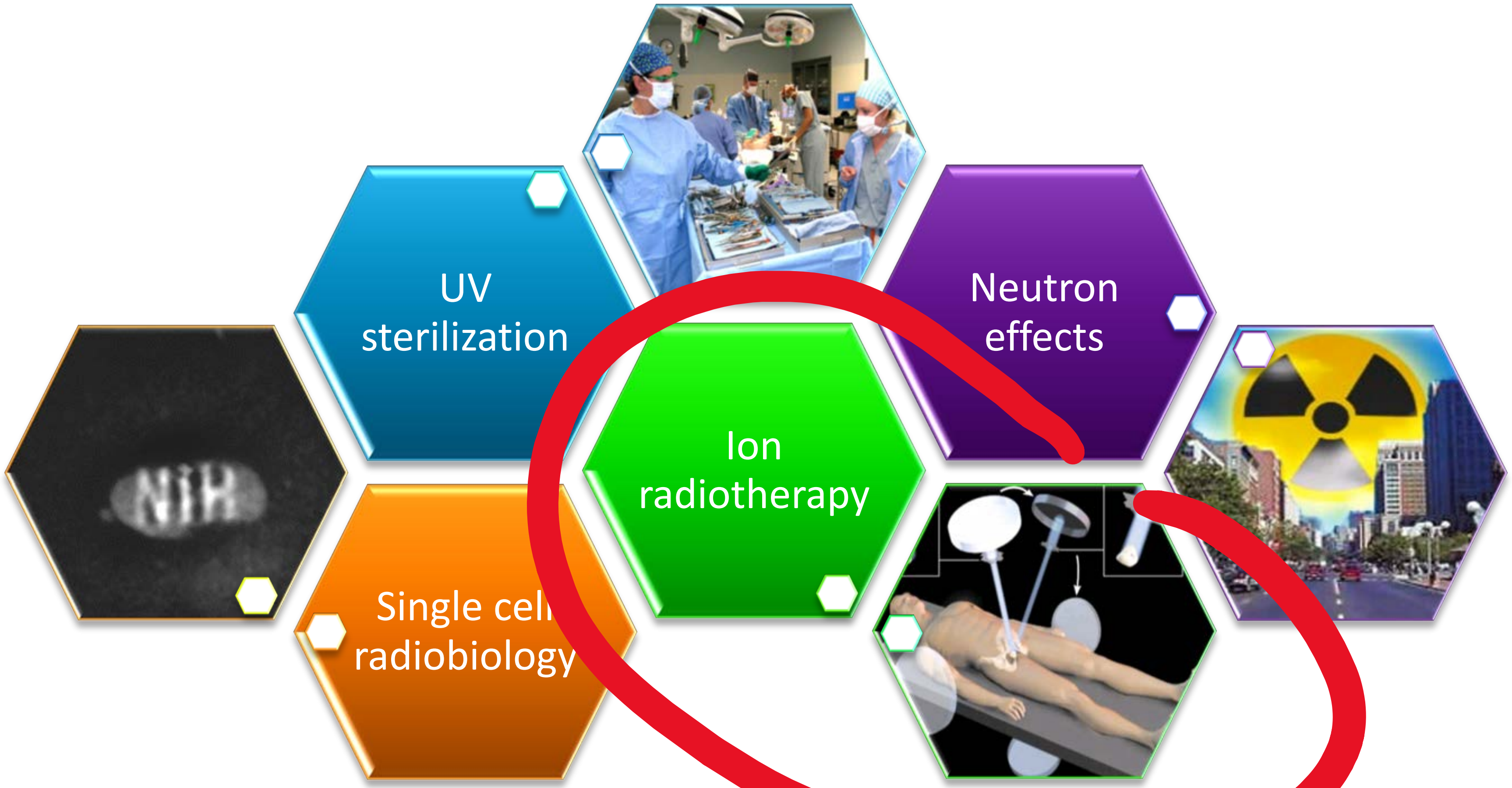
Painting "NIH" on a cell nucleus

- **GFP-tagged XRCC1 SSB repair foci**
- **0.6 μm microbeam**

Proton microbeam-irradiated mouse ear - γ-H2AX

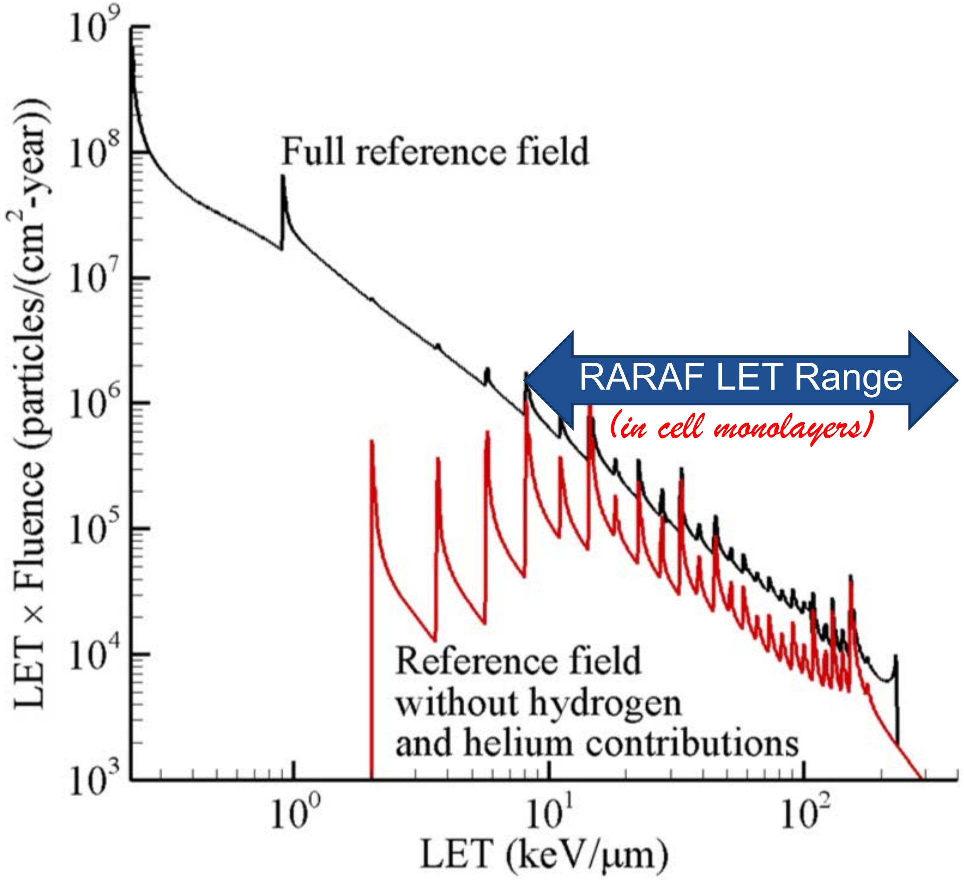


Research at RARAF



Why heavy ions

- High LET
  - Much higher Relative Biological Effectiveness compared to standard modalities
  - Encouraging results from Japan using Carbon ion RT
    - Indications of immune-mediated tumor killing
  - Also relevant for space radiation
    - End of track and secondaries

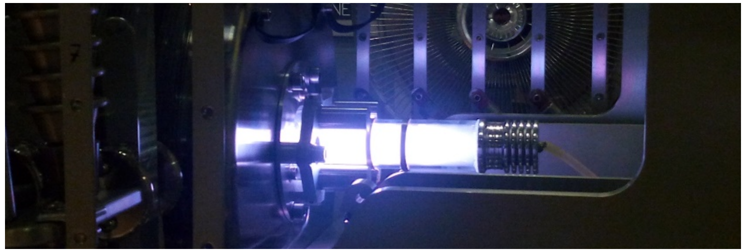


- Is Carbon the best option?
  - Mechanisms not well understood
  - Very expensive question
    - Would helium be enough?

A Flexible Platform for Pre-Clinical Studies in Support of Heavy-Ion Radiotherapy

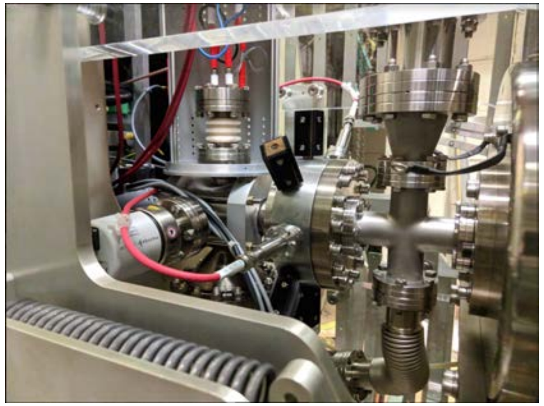
Presently, we can produce

- protons (low LET 8 – 25 kev/μm),
- deuterons (intermediate LET 15 – 40 keV/μm)
- helium ions (high LET 50-160 keV/μm)



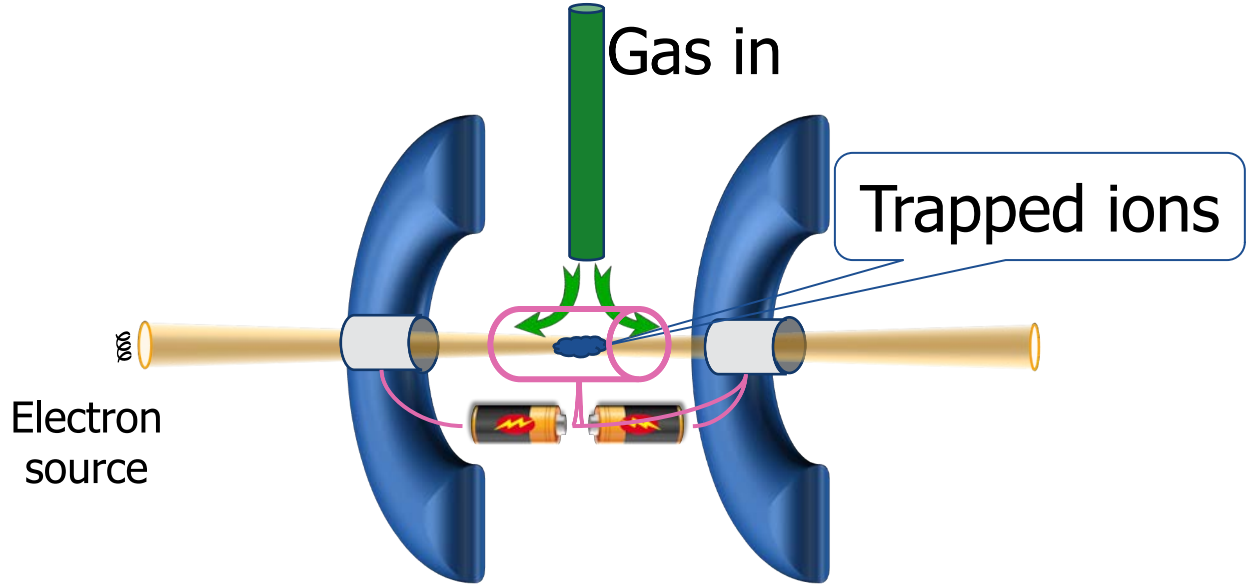
Coming soon: Heavy Ions

- C,B,N, Be/Li (very high LET 200 – 900 keV/μm)



DREEBIT
Electron & Ion Beam Technologies

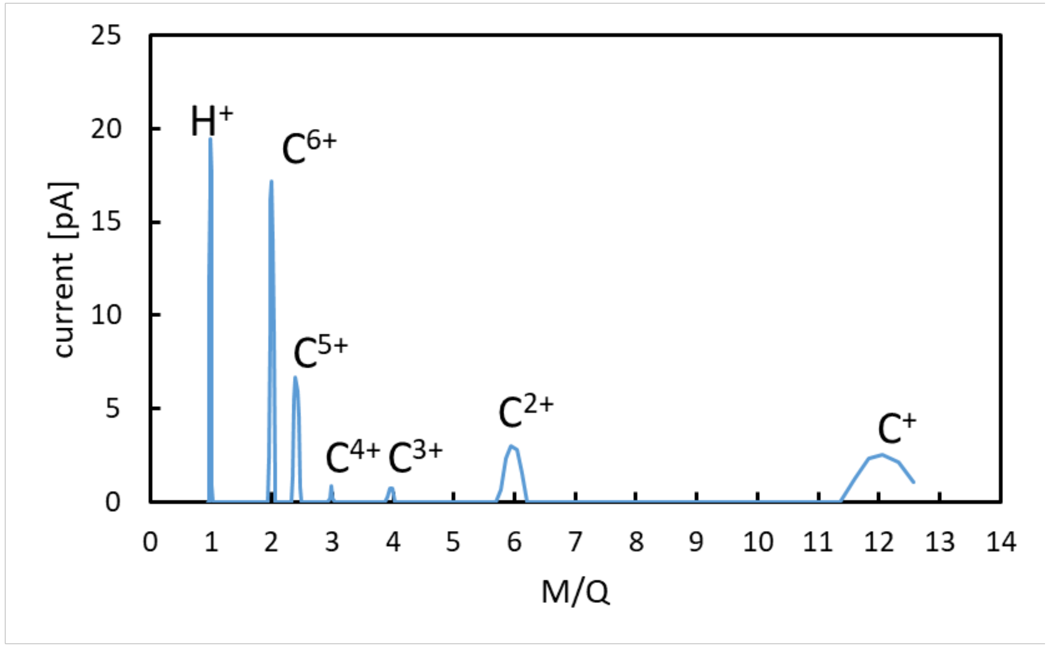
Operation of DREEBIT ion source

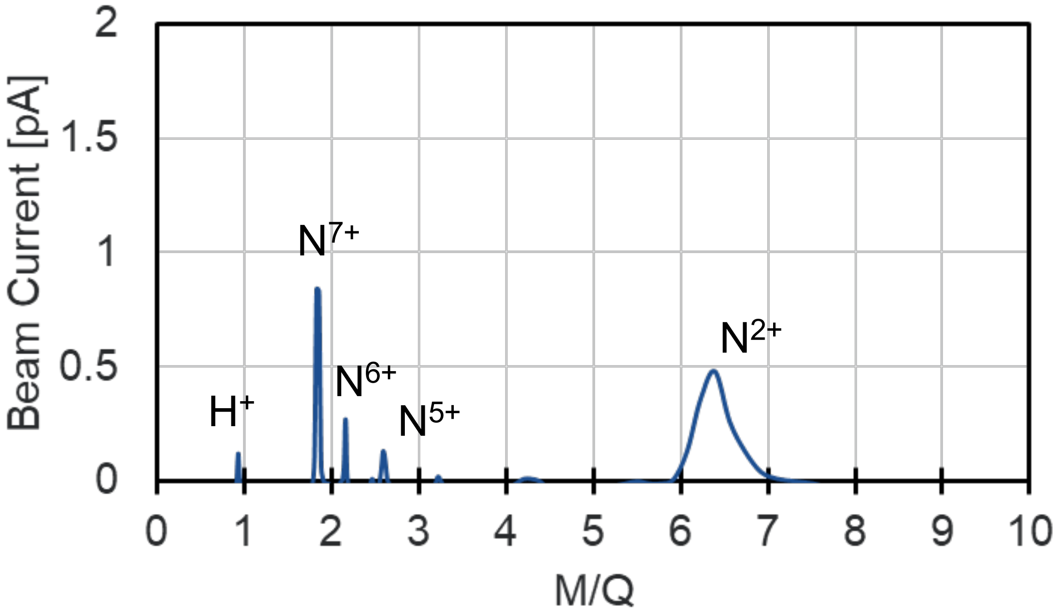


- Gas introduced into ion source
- Electron beam ionizes gas
- Ions trapped in magnetic trap
- Electron beam further ionizes ions
- Trap opened to release stripped ions

DREEBIT Electron & Ion Beam Technologies

Bench tests of new ion source

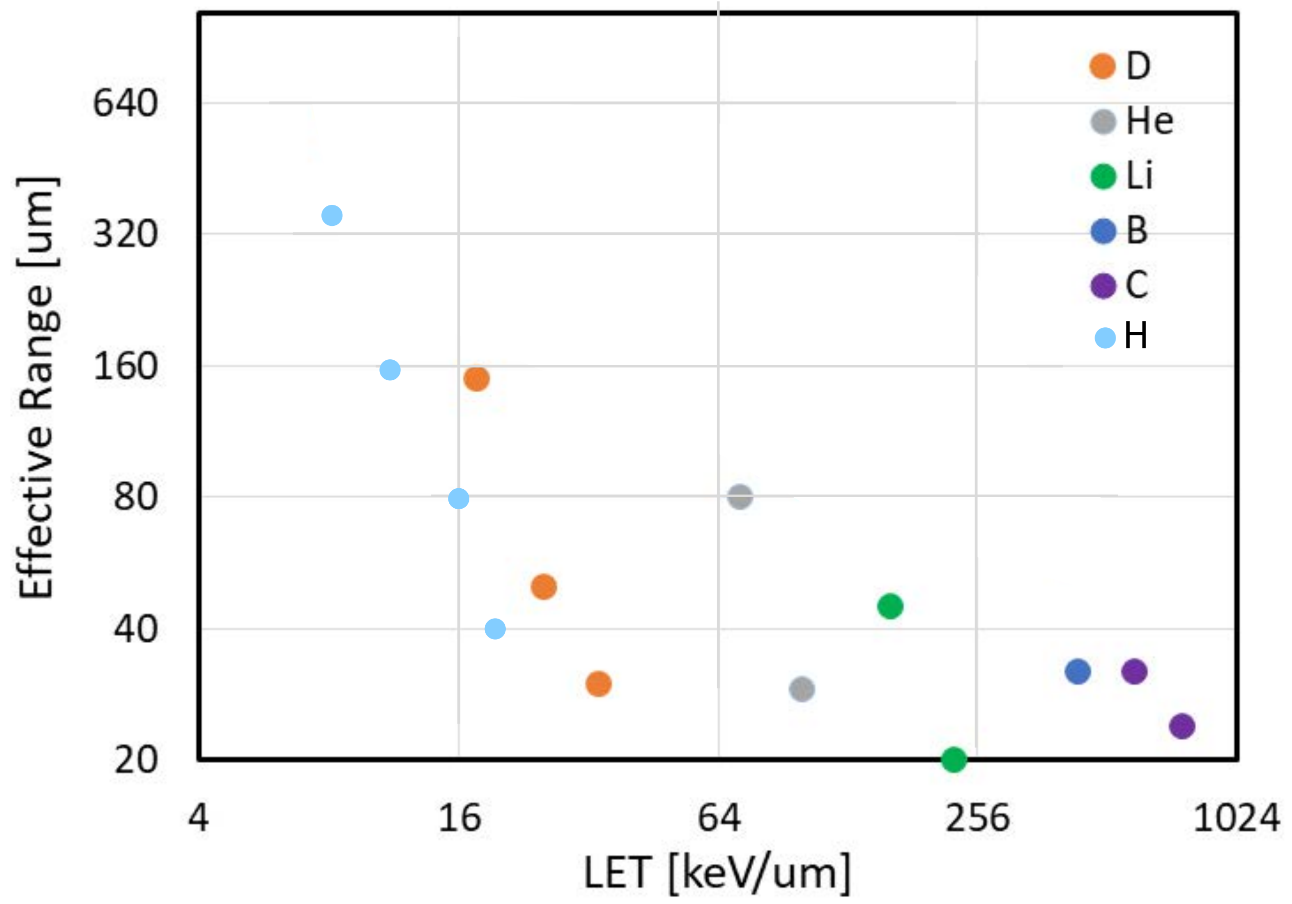




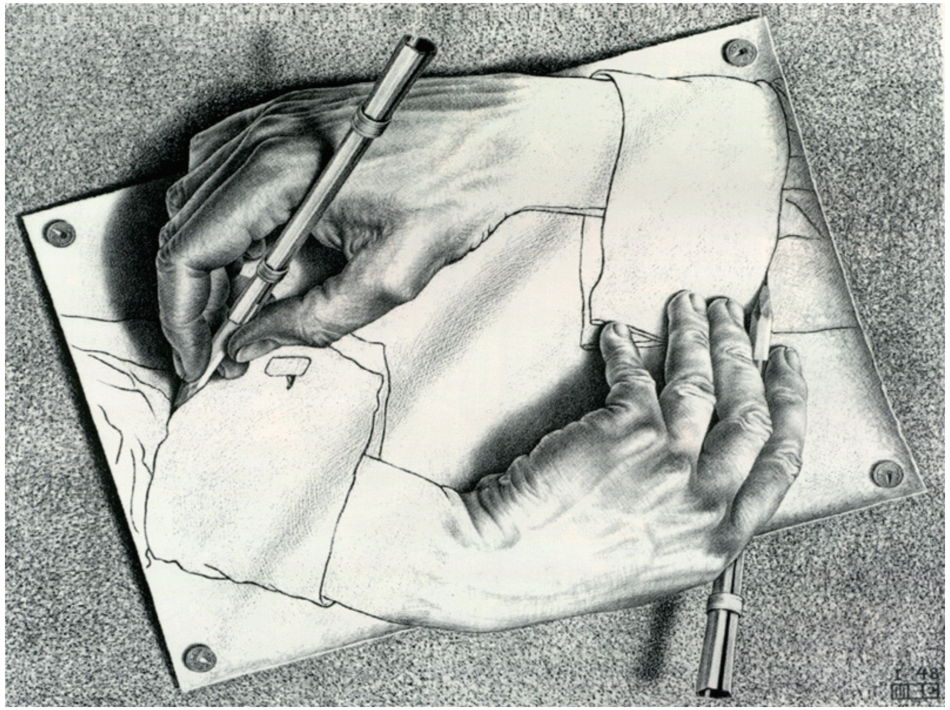
- Can generate fully stripped C,N ions
- Working on other ions between He and C

Available beams

Using our existing 5.5 MeV (2.75 MeV/AMU) accelerator we can only deliver high LET radiation to cell monolayers



the interesting biology happens in 3D systems



From 2D to 3D

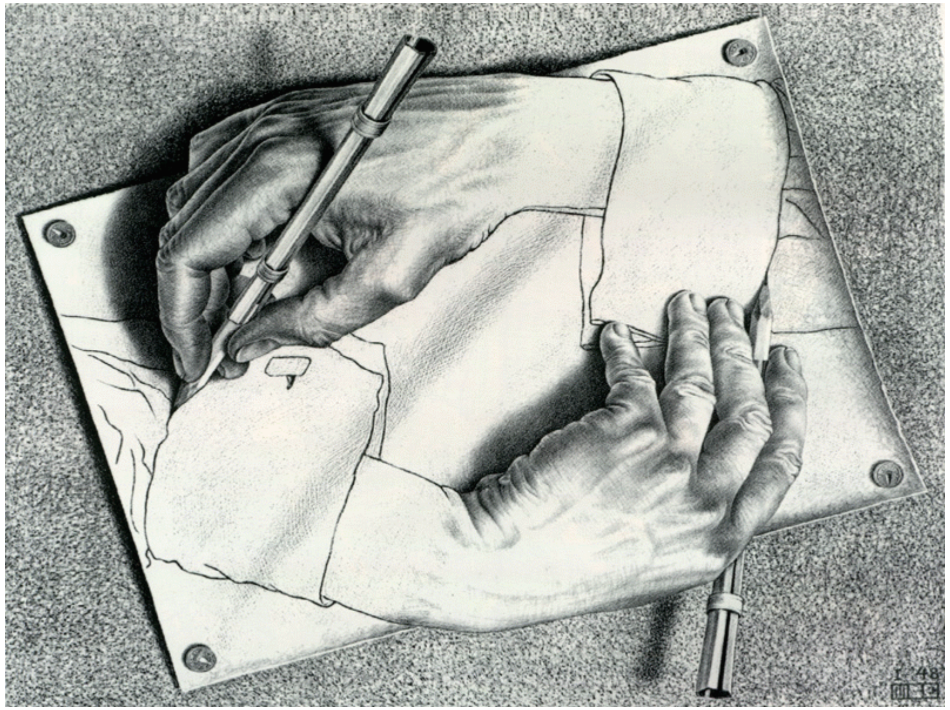
We want to irradiate tumors

Need to at least double beam penetration

Need higher energy

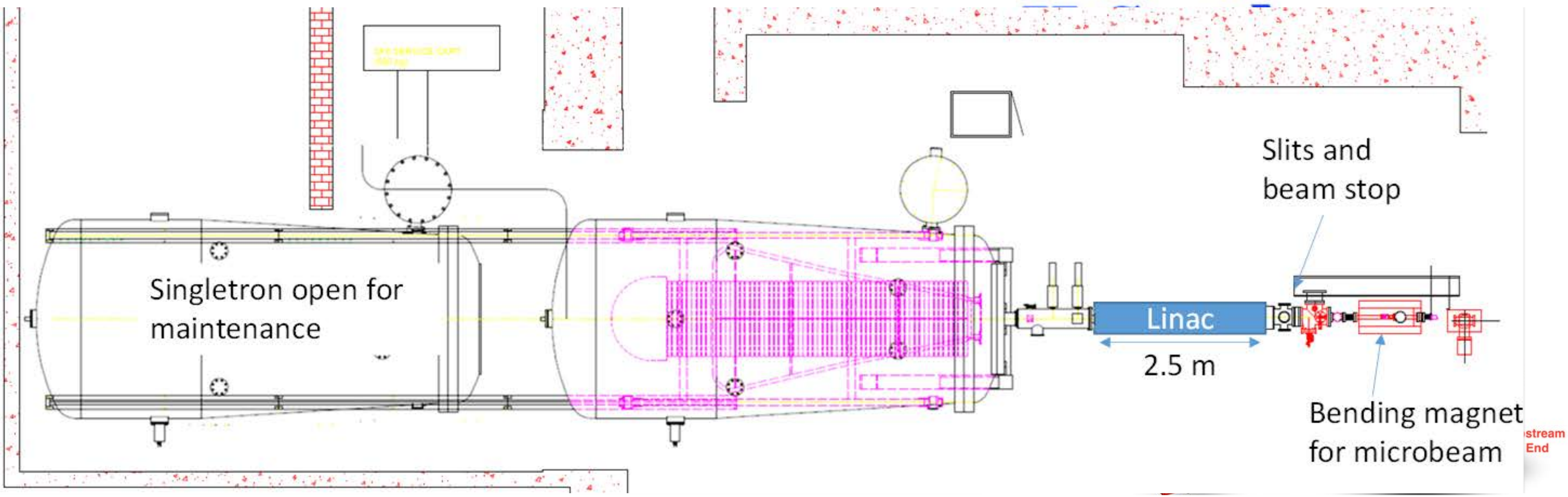
Add a second accelerator in line with our singletron

the interesting biology happens in 3D systems



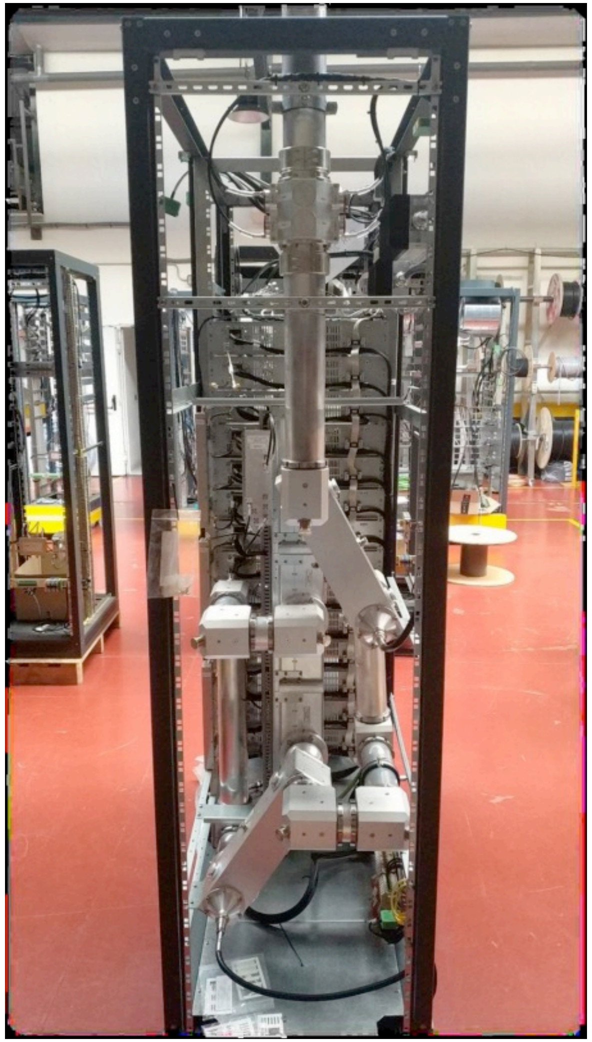
We need more energy

- A Linac booster will get our ion energy up to 5.5 MeV/amu
  - Alternating field accelerates bunches of ions as they pass between the rings.



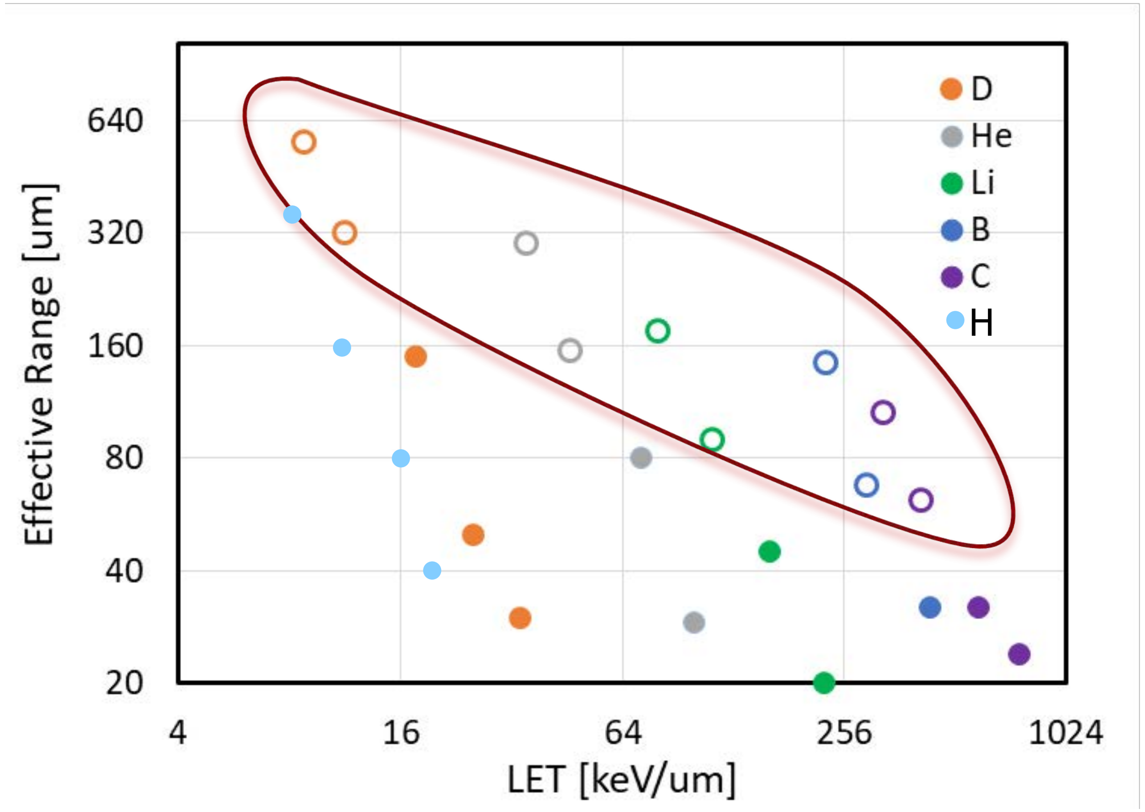
Last pre-COVID photos of linac

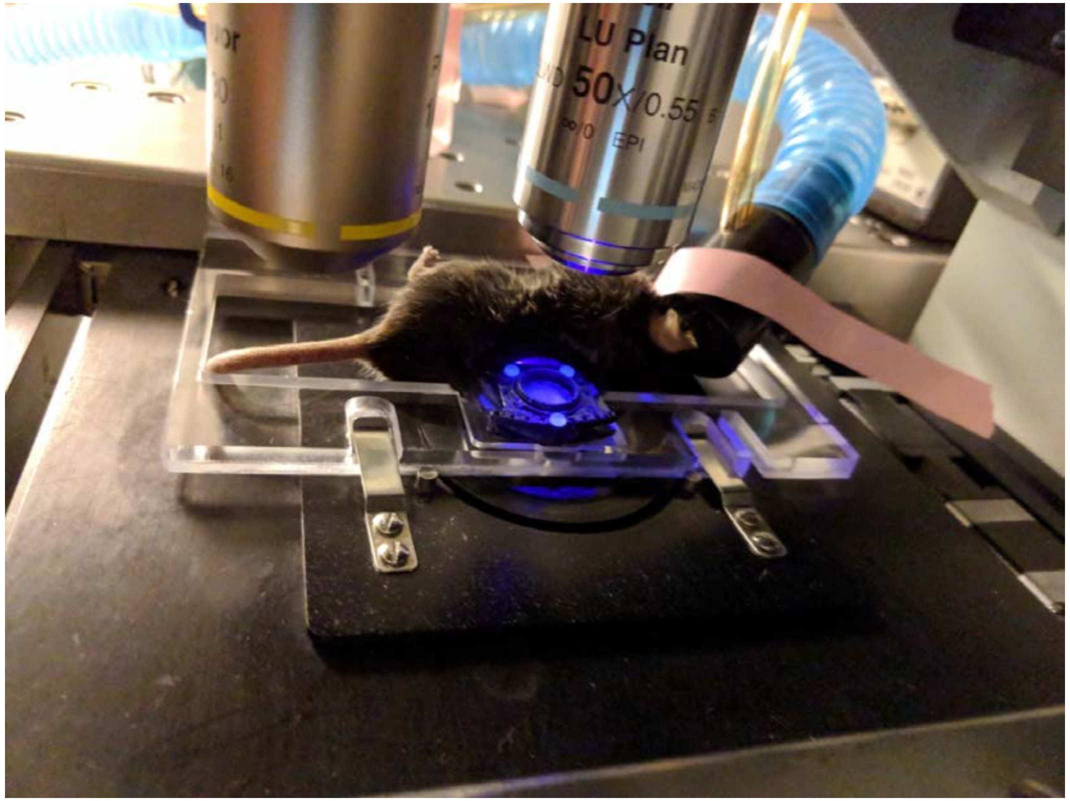
- Mostly manufactured – expected delivery this summer.



Available beams with linac booster

- Will allow irradiation of thin tissues
- Window tumors





Summary

- RARAF is a dedicated radiobiological accelerator facility
- We provide:

	Neutrons	H+/D+	He	Heavy Ions	High dose rate
Cell Monolayers	Now			Summer	Protons now
Thin Tissues			End of 2020		Electrons this Summer
Mice					

- Experiments typically scheduled month by month
  - ➢ contact me or RARAF@columbia.edu
  - ➢ Fill out beam time application at www.raraf.org

Funding: NIH National Institute of Allergy and Infectious Diseases; NIH NATIONAL CANCER INSTITUTE; NIH National Institute of Biomedical Imaging and Bioengineering