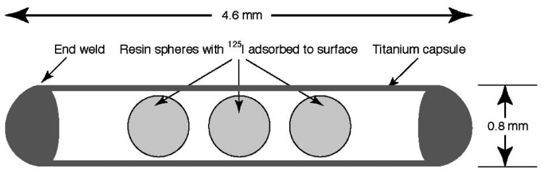
experience in computational microdosimetry

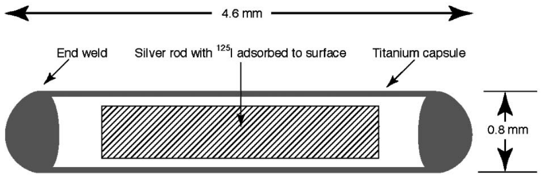
Prof. Dr. B. Reniers

Universiteit Hasselt, Diepenbeek, Belgium

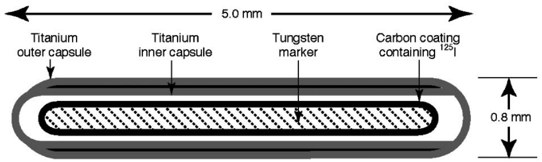
Description of some ^{103}Pd and ^{125}I seeds



Amersham Health model 6702 source



Amersham Health model 6711 source



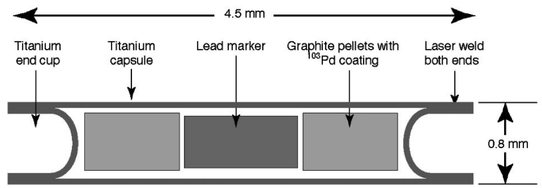
Best model 2301 source

^{103}Pd

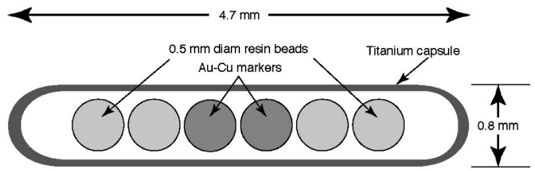
- mean energy : 20.6 keV
- Half-life : 17 days

^{125}I

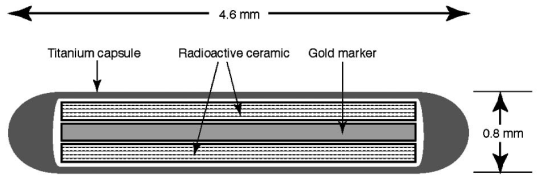
- mean energy : 28.5 keV
- Half-life : 60 days



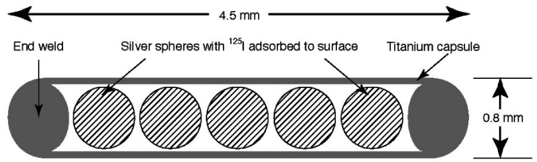
Theragenics model 200 source



NASI model MED3631-A/M or MED3633 source



Bebig model I25.S06 source

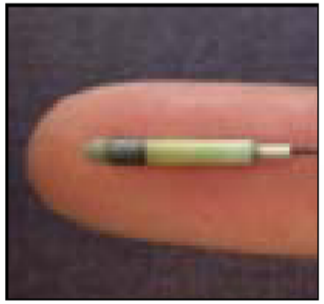


Imagyn model IS-I2501 source

Electronic Brachytherapy source

Xoft AxxentTM

Figure 1. X-Ray Source – Scaled to Size



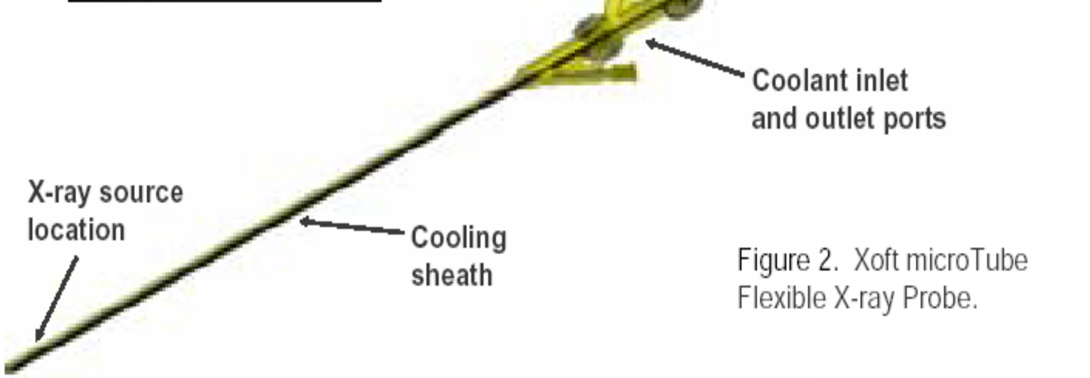
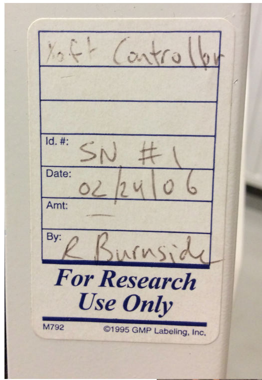
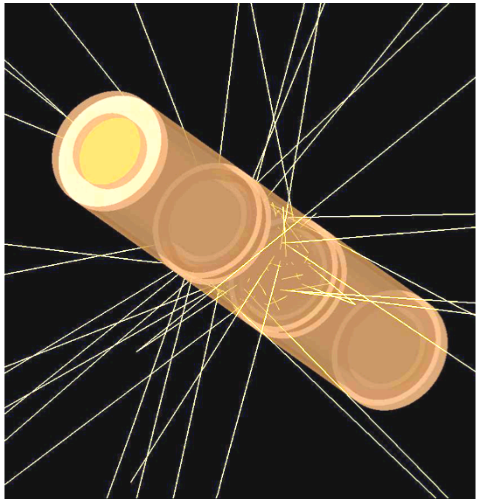


Figure 2. Xoft microTube Flexible X-ray Probe.

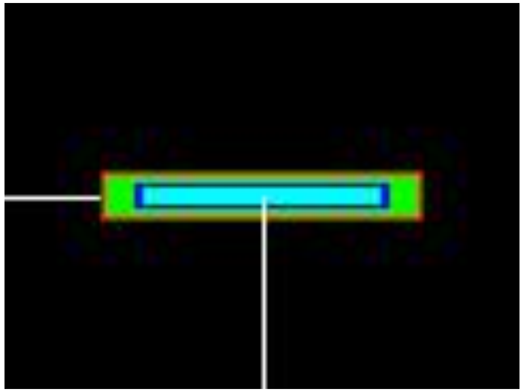


* www.aapm.org/meetings/05SS/program/Radionuclides.pdf and Private communication from Xoft, Inc

LDR seeds MC models

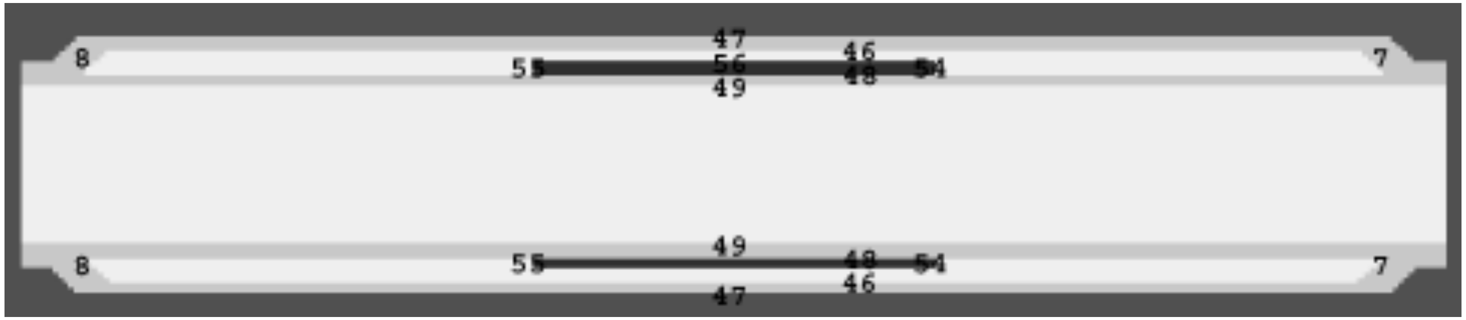


IBt seed EGSnrc



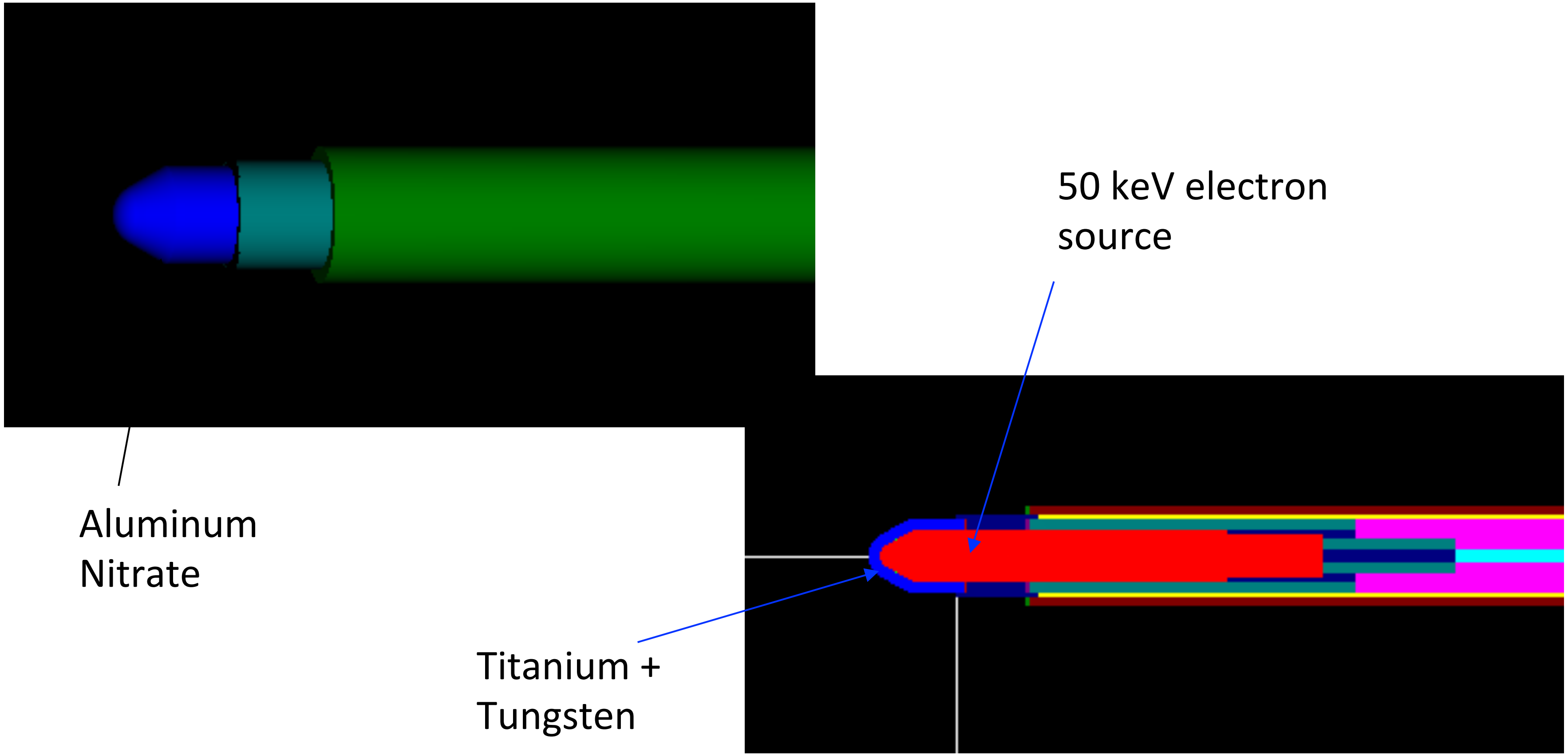
Best EGSnrc++

IBt seed MCNP

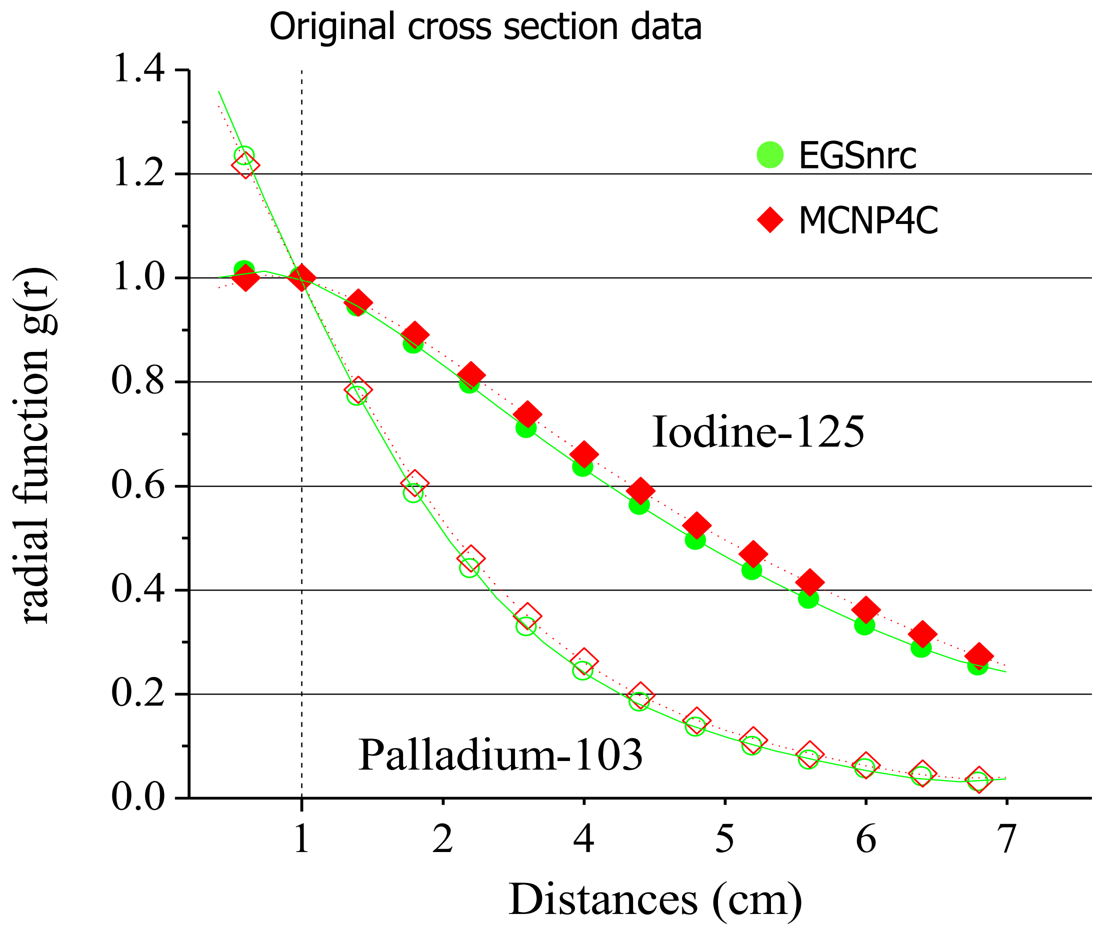


MC Model

- Model of the xoft Axxent probe in EGSnrc++

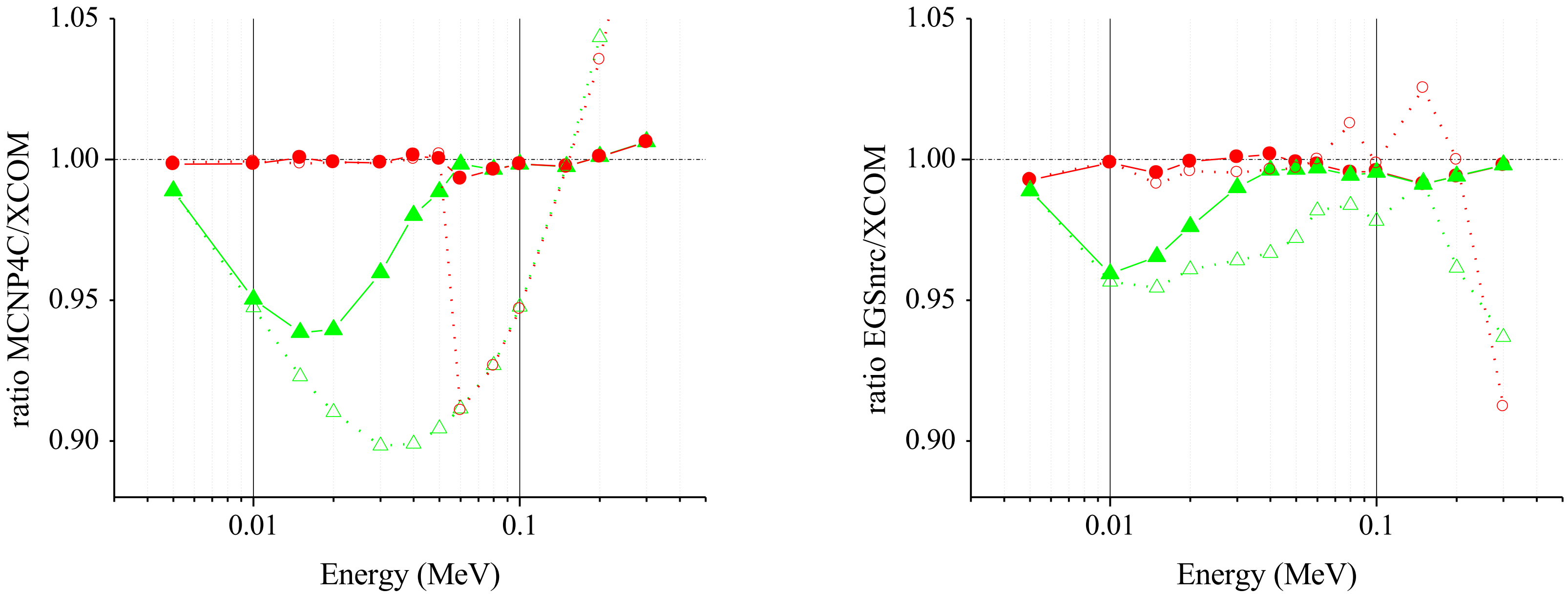


Check basic data!
Example: Photon cross section data



Photon cross section data

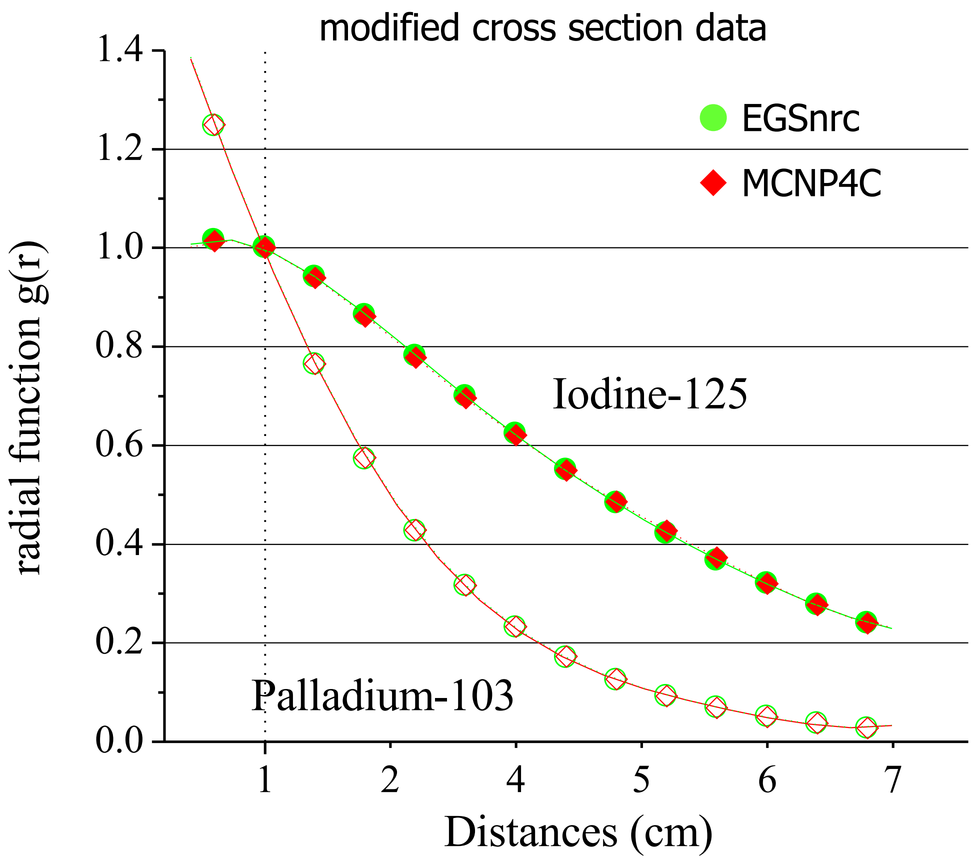
CMK CENTRUM VOOR MILIEUKUNDE UHASSELT



▲ original values of the total attenuation
△ original values of the attenuation coefficients due to photoelectric effect
● corrected values of the total attenuation coefficients (XCOM for EGSnrc and EPDL97 for MCNP4C)*+
○ corrected values of the attenuation coefficients due to photoelectric effect (XCOM for EGSnrc and EPDL97 for MCNP4C)

* Hobeila F., Seuntjens J. P. 2003 proceedings of IAEA-CN-96-17
\+ Bohm T. D et al. Med Phys 30(4) 701-711

Photon cross section data



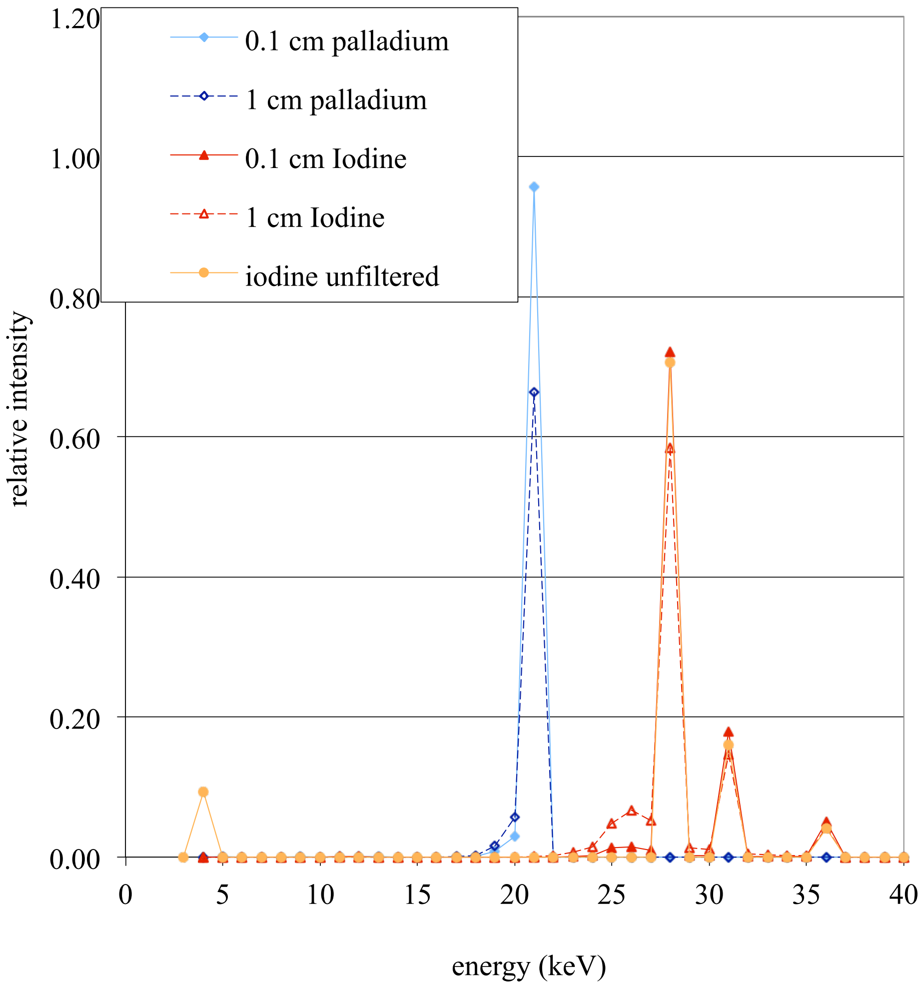
- Use an up-to-date library:
  - EPDL97 (Lawrence Livermore Laboratory)
  - XCOM (NIST)
  - DLC-146 (RSICC)

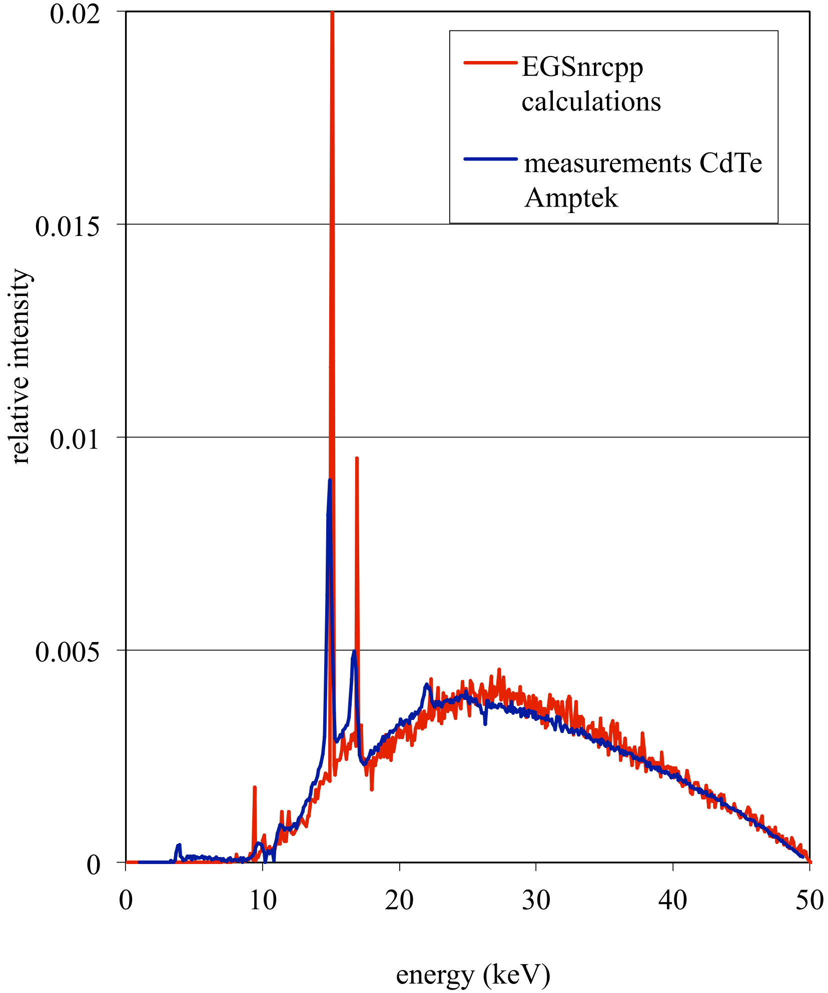
Calculation of the microdosimetric spectra

- Impossible to use the same MC codes as for dosimetry.
  - Need of an « event-by-event » code for the electron transport
  - Need to transport the electron down to 13 eV ⇨Limitation due the cross section range in classical codes (often minimum of 1keV)
- Microdosimetric MC code used : TRION*
  - Event-by-event code capable of following the electrons generated during a single collision by monoenergetic electrons, photons and ions ($Z \leq 10$) down to energies of 13 eV in water vapour (d=1)
  - Calculation of the distributions of energy imparted and lineal energy in spherical volumes (0.01-1μm).
- Input for this code: photon spectra calculated with a classical code.

*Lappa AV *et al*. 1993 TRION code for radiation action calculations and its application in microdosimetry and radiobiology. *Radiat. Environ. Biophys.* **31**, 1-19.

Photon spectra





Microdosimetric spectra in 1μm sphere

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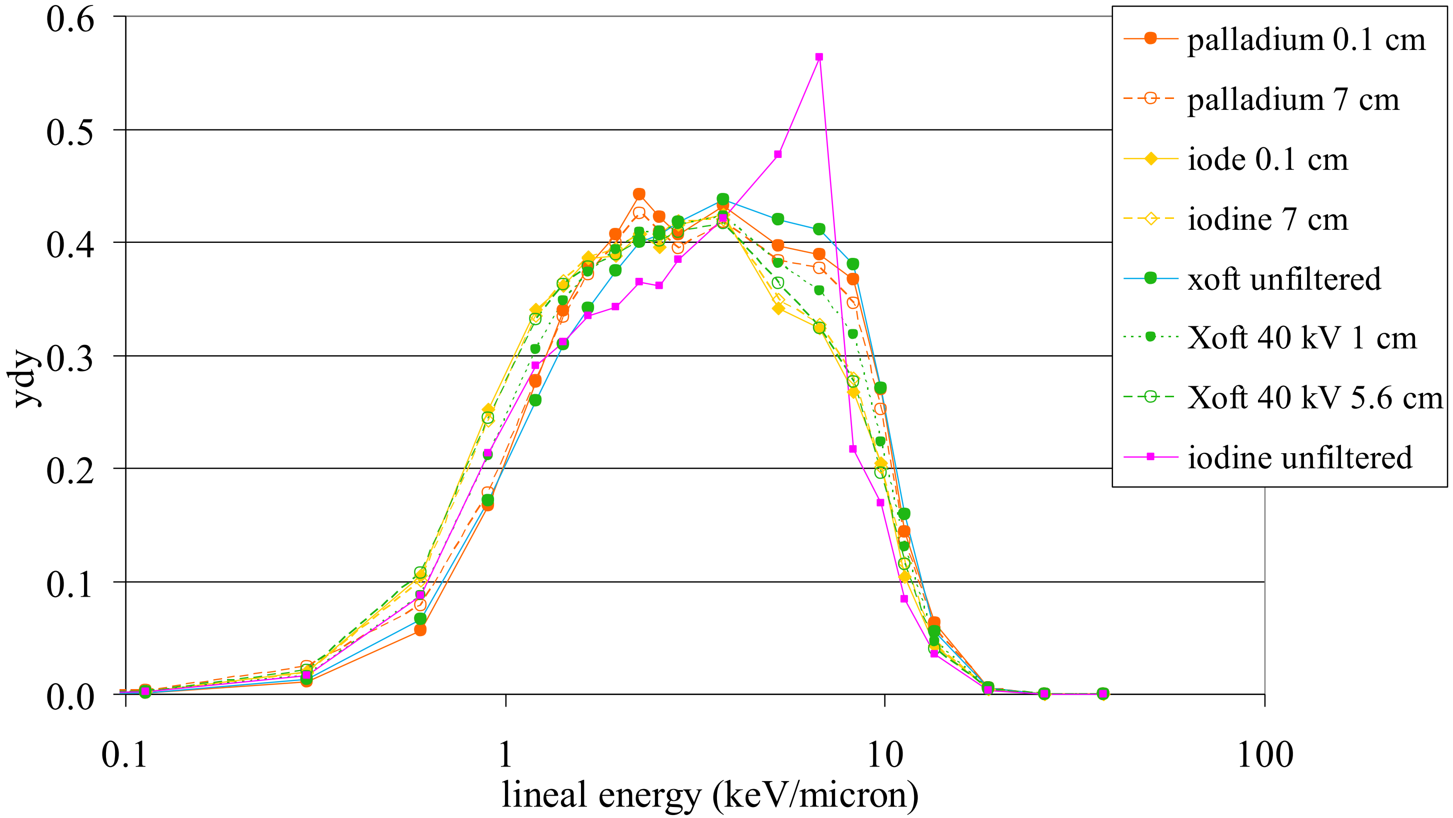
UHASSELT



NuTeC
Nucleair Technologisch Centrum
KU LEUVEN
universiteit hasselt
UHASSELT

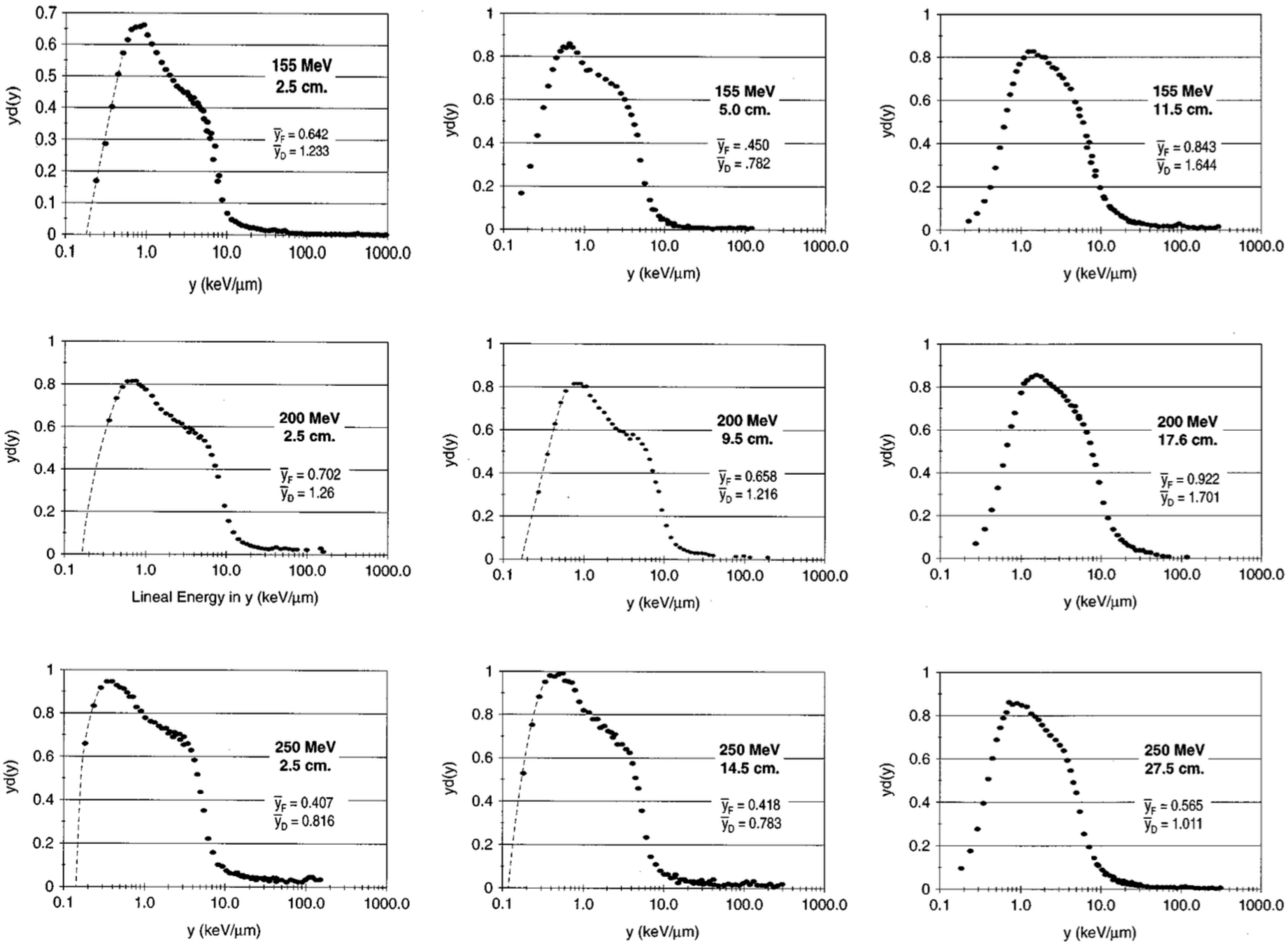


FIG. 7. Spectra taken at three energies and three depths in the proton beam.

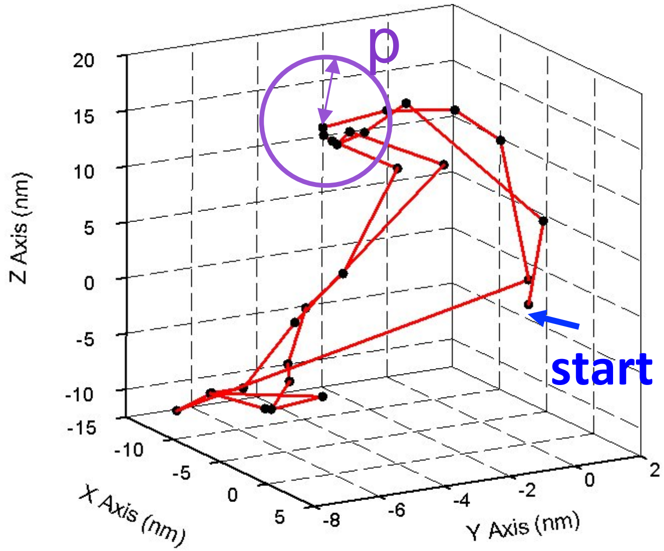
Conclusion microdosimetry

y_D	unfiltered	0.1 cm	1 cm	2 cm	3 cm	5 cm	6 cm	7 cm
palladium	4.05	4.05	4.04	4.05	4.05	4.03	3.99	3.89
iodine	3.79	3.52	3.54	3.56	3.56	3.57	3.57	3.57
Xoft 40 kV	4.13		3.78		3.61	3.54		

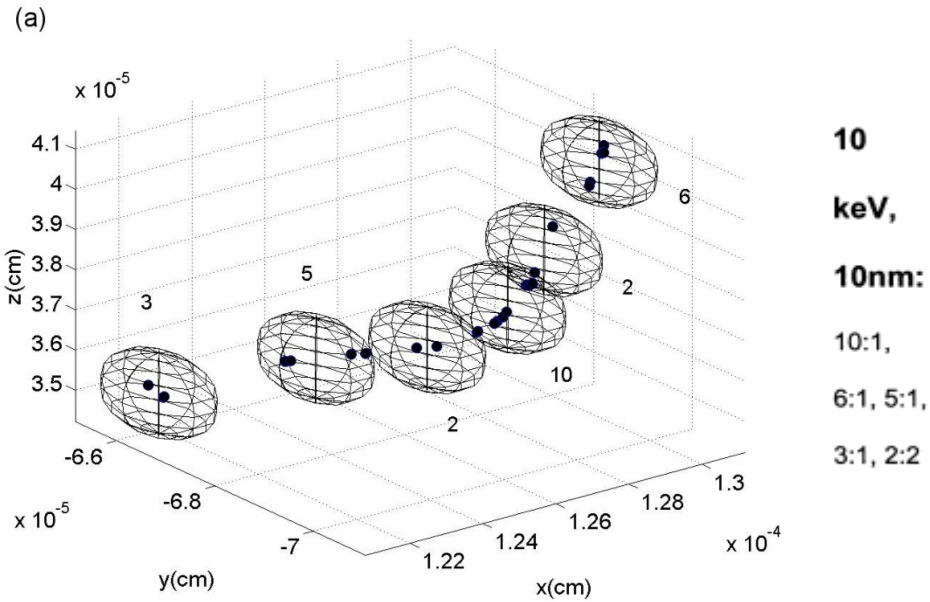
Q (ICRP40)	unfiltered	0.1 cm	1 cm	2 cm	3 cm	5 cm	6 cm	7 cm
palladium	1.14	1.14	1.14	1.14	1.14	1.14	1.12	1.10
iodine	1.07	0.99	1.00	1.00	1.00	1.00	1.00	1.00
Xoft 40 kV	1.12		1.06		1.02	0.998		

	y_D	Q
implant outside calc	3.55	1.00
implant in calc	3.71	1.04

Link to biology?
analysis of microscopic ionization clusters



Ionization track for a 1 keV electron at nanometer scale



Ionization cluster sizes linked to DNA damage

Frank Verhaegen

Ionization cluster frequency for ^{125}I and ^{103}Pd

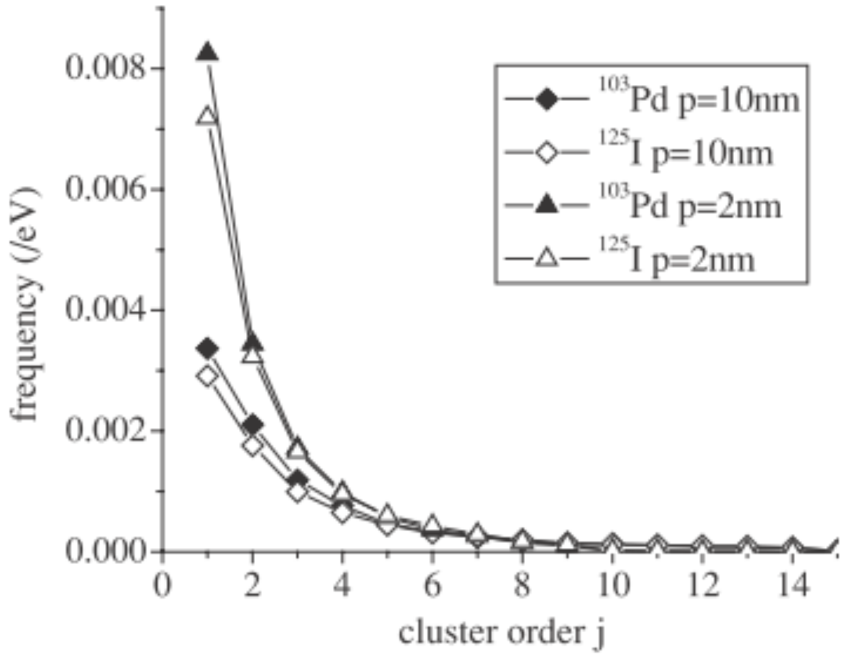


Figure 11. Distributions of the number of clusters of order between 1 and 14 of a radius of 10 nm and 2 nm for ^{125}I and ^{103}Pd per eV deposited energy.

^{103}Pd has higher number of ionization clusters than ^{125}I
⇨ higher RBE

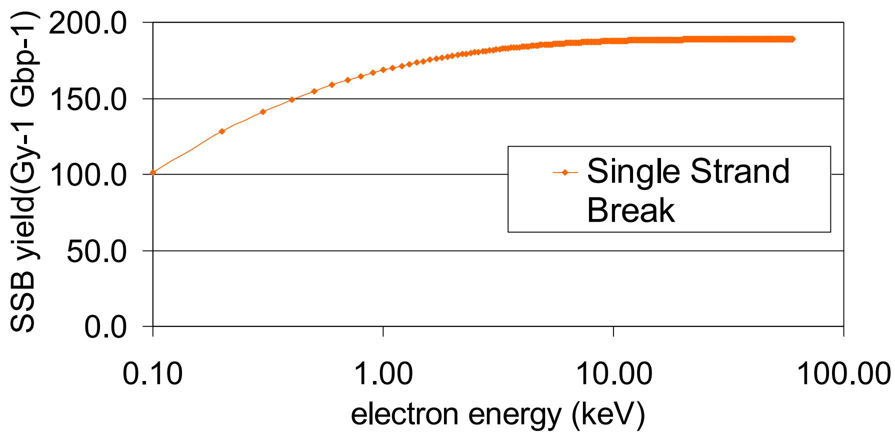
Link to biology?
MC Damage Simulator

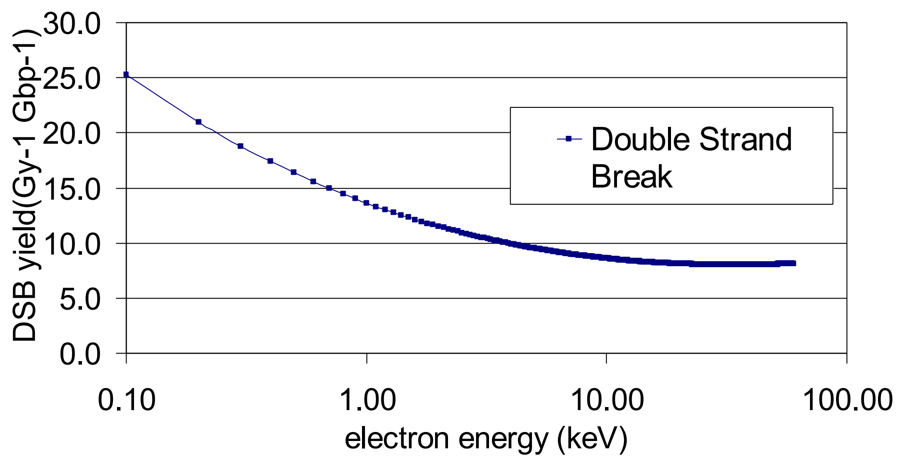
Monte Carlo Damage simulator (*MCDS*): MC tool for calculating the spectrum of biological damage to a cell by estimating DSB and other types of damage for charged particles

Two steps:

1. randomly distribute in a DNA segment the expected number of lesions coming from detailed MC simulations based on track-structure calculations.

2. subdivide the lesions in the segment into clusters





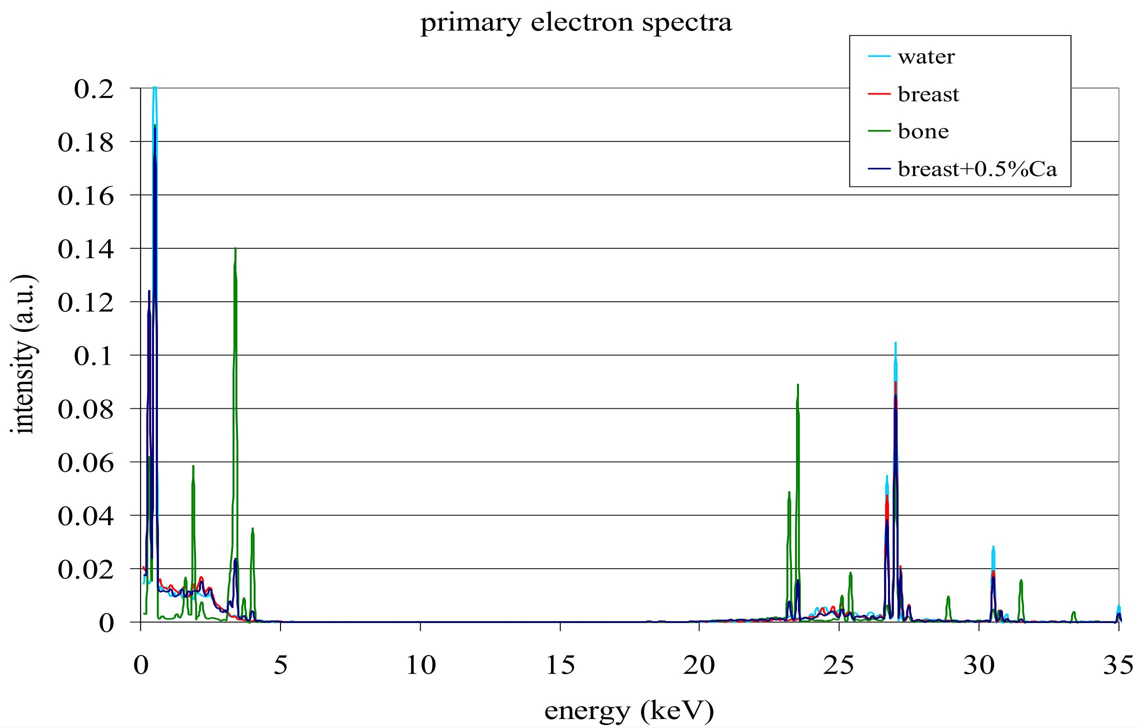
(*Semenenko et al., PMB* **51** 2006)

Primary electron spectra

- Primary electron spectra in different materials calculated using EGSnrc++
- Problem for the Auger electrons: generated only if above 1keV.

- Auger that cannot be simulated:
  - in water: Auger from O at 500 eV
  - In tissues : Auger from C at 300 eV, N at 400 eV and O at 500 eV

-> very high probability and very damaging for DNA



Damage yield

^{125}I					
with Auger	**DSB ($Gbp^{-1}.Gy^{-1}$)**	**RBE_{DSB}**	**without Auger**	**DSB ($Gbp^{-1}.Gy^{-1}$)**	**RBE_{DSB}**
water	15.59	1.48	**water**	14.68	1.40
breast	16.15	1.54	**breast**	14.97	1.43
breast+0.5%Ca	16.06	1.53	**breast+0.5%Ca**	14.83	1.41
prostate	15.74	1.50	**prostate**	14.74	1.40
prostate+0.5%Ca	15.67	1.49	**prostate+0.5%Ca**	14.69	1.40
bone	14.77	1.40	**bone**	12.25	1.17
calc in prostate	15.07	1.43	**calc in prostate**	12.69	1.21
implant			**implant**		
in calc	14.94	1.42	**in calc**	13.09	1.25
no calc	15.72	1.49	**no calc**	14.13	1.35
water	15.59	1.48	**water**	14.68	1.40

^{125}I Afsharpour (Geant4) ^{125}I	**SSB ($Gbp^{-1}.Gy^{-1}$)**	**DSB ($Gbp^{-1}.Gy^{-1}$)**
water	158	15.5

Damage yield

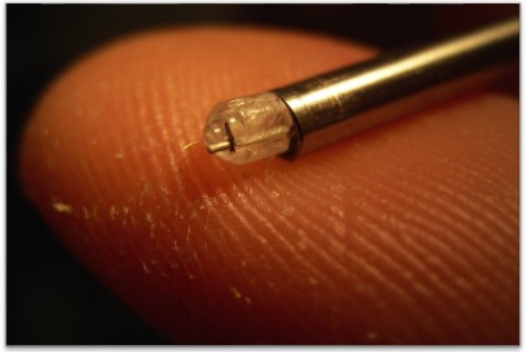
Xoft					
with Auger	DSB ($Gbp^{-1}.Gy^{-1}$)	RBE_{DSB}	without Auger	DSB ($Gbp^{-1}.Gy^{-1}$)	RBE_{DSB}
water	15.62	1.48	water	13.78	1.31
breast	16.19	1.54	breast	14.64	1.39
breast+0.5%Ca	16.09	1.53	breast+0.5%Ca	14.55	1.39
prostate	15.76	1.50	prostate	14.55	1.39
prostate+0.5%Ca	15.66	1.49	prostate+0.5%Ca	14.39	1.37
bone	14.65	1.39	bone	12.29	1.17
calc in prostate	14.98	1.43	calc in prostate	12.53	1.19

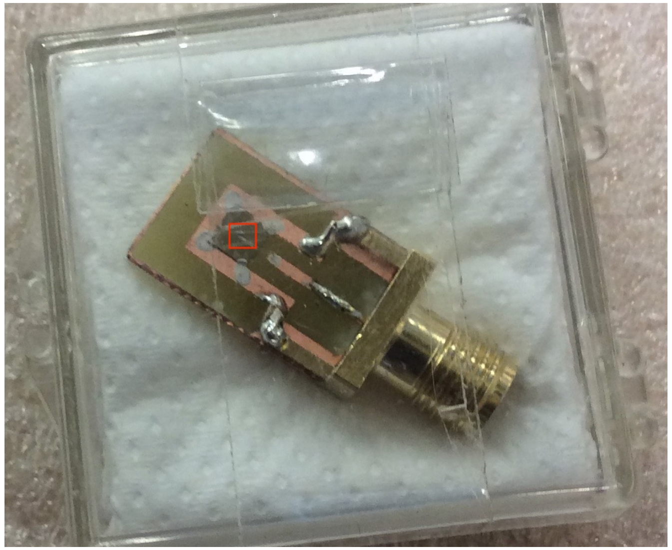
Radiobiological experiment in tumours in mouse: RBE between 1.4 and 1.5

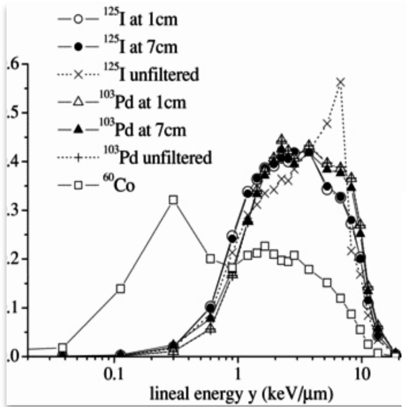
Lehnert et al. IJROBP 63(1) pp 224-229 (2005)

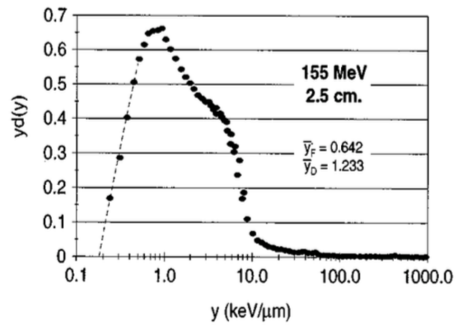
Validation!
Experimental microdosimetry:

- Diamond
- Mini-TEPC (collaboration Hasselt – SCK – LNL-INFN)





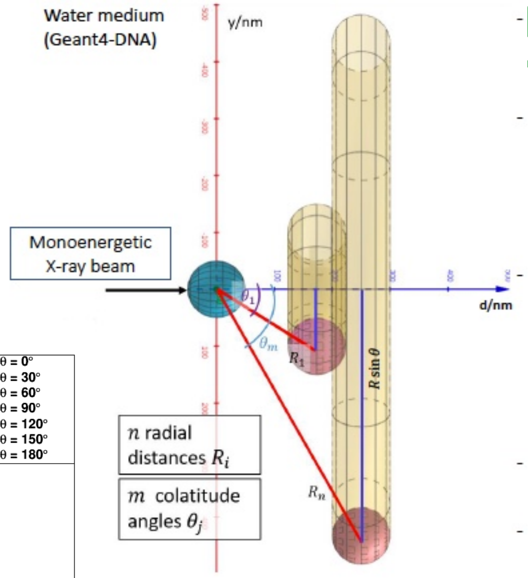


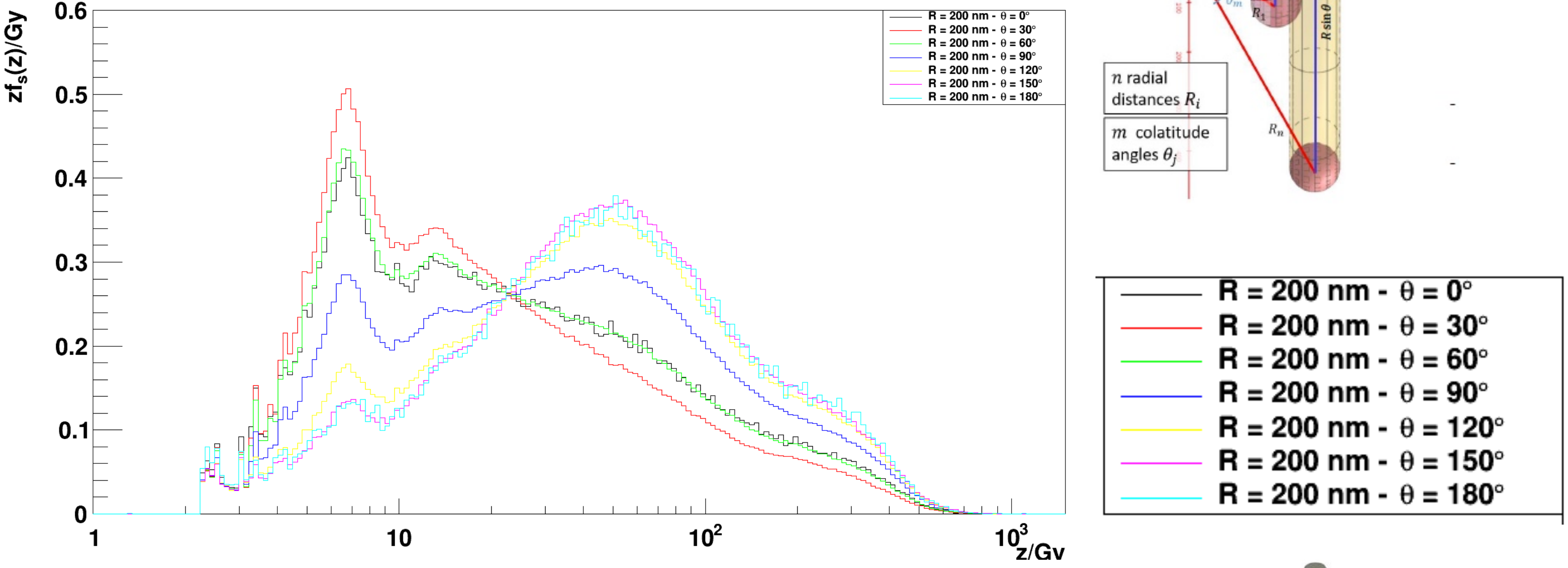


New developments

- Codes such as Geant-DNA

Jonathan Derrien PhD student: 50-nm-radius Gold nanoparticle hit by 150 keV X-ray at 200 nm for different θ angles. Detector radius of 50 nm.





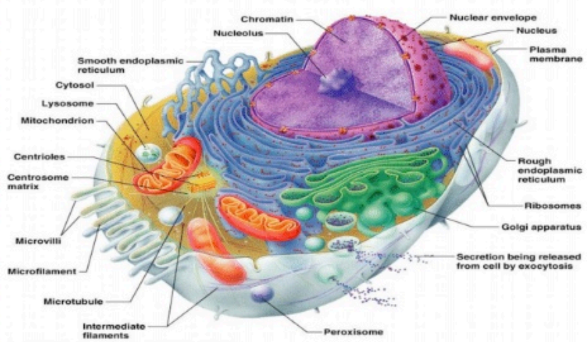
Specific energy z (Gy)

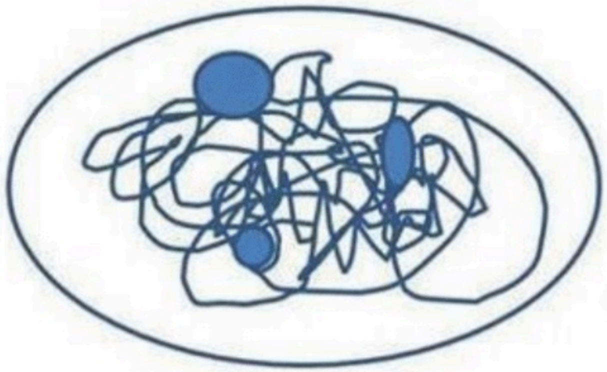
Topas n-bio?

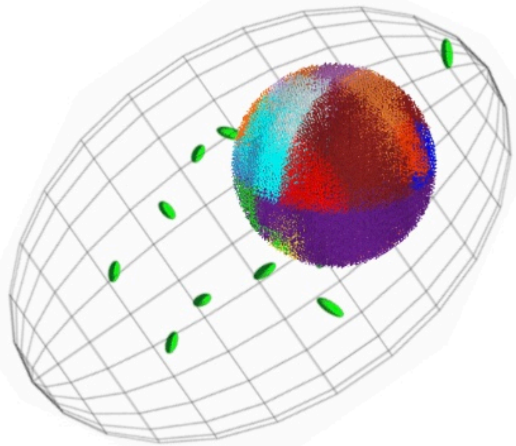
Cell scale

Structure of a generalized cell
as seen by:

cell image from @LoversScience

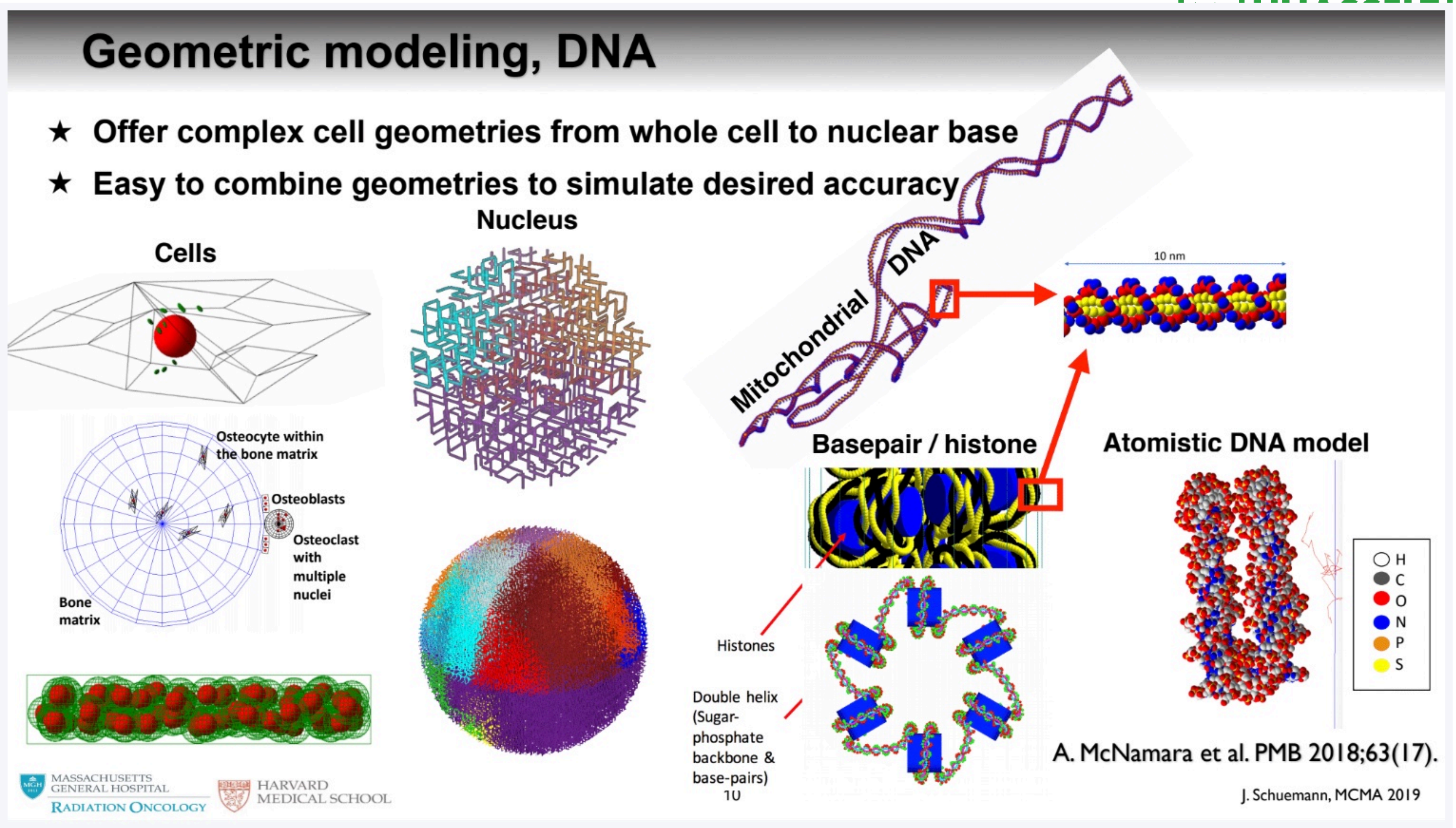






a biologist **a chemist** **a physicist**

Topas n-bio


Geometric modeling, DNA
★ Offer complex cell geometries from whole cell to nuclear base
★ Easy to combine geometries to simulate desired accuracy
Cells
Nucleus
Mitochondrial DNA
10 nm
Osteocyte within the bone matrix
Osteoblasts
Osteoclast with multiple nuclei
Bone matrix
Basepair / histone
Atomistic DNA model
H
C
O
N
P
S
Histones
Double helix (Sugar-phosphate backbone & base-pairs)
10
MASSACHUSETTS GENERAL HOSPITAL
RADIATION ONCOLOGY
HARVARD MEDICAL SCHOOL
A. McNamara et al. PMB 2018;63(17).
J. Schuemann, MCMA 2019