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Microdosimetry calculations for monoenergetic electrons using Geant4-DNA combined with a weighted track sampling algorithm

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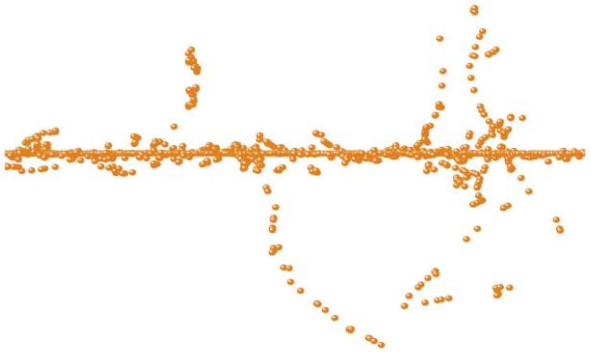
Microdosimetry

- Microdosimetry is the theoretical and experimental investigation of imparted energy probability distributions in a "small" volume of matter that is crossed by a single ionizing particle.

- Analogs to macrodosimetry:
  - D → z
  - LET → y



- When different quantities are compared under identical conditions, the differences in RBE are thought to be related to differences in track structure of the radiation qualities

- Dose mean lineal energy (y_D) is a recommended quantity for the evaluation of radiation quality.

Microdosimetry

Lineal energy:

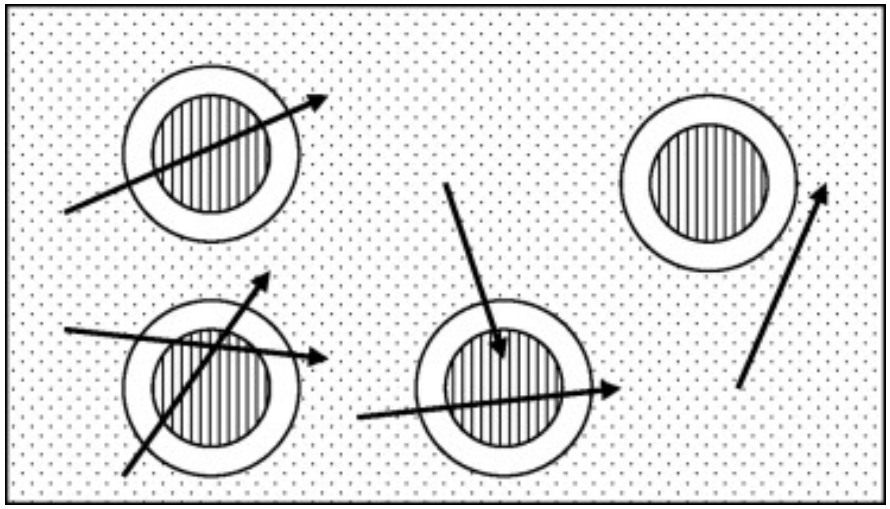
$$y = \frac{\varepsilon}{\bar{l}}$$

Mean chord length (μ-randomness):

Convex volumes: $\bar{l} = \frac{4V}{S}$

Sphere: $\bar{l} = \frac{4}{3}r$

Cylinder: $\bar{l} = \frac{2rh}{r+h}$



Single-event frequency and dose mean lineal energy:

$$\bar{y}_F = \int y\, f(y)\, dy$$

$$\bar{y}_D = \int y\, d(y)\, dy = \frac{\int y^2 f(y)\, dy}{\int y\, f(y)\, dy} = \frac{1}{\bar{y}_F}\int y^2 f(y)\, dy$$

Microdosimetry

- The quantity y varies considerably with the size of the scoring volume
  - Target size is important! (cell nucleus, DNA)

- A SV of 1 μm has typically been used (ease of measurement):
  - Radiation therapy
  - Radiation protection

- Radiation damage at the level of DNA molecule:
  - DNA segment (~ 2 nm)
  - Nucleosome (~ 10 nm)
  - Chromatin fibre (~ 30 nm)
  - Chromatin fibre loop (~ 300 nm)

Issues?

- Recent studies have combined the primary electron spectrum with lineal energy values calculated for monoenergetic electrons.

- The shape of SV has varied:
  - Type of radiation
  - Size of SV

- Different scoring techniques:
  - Virtual cell geometry (fixed SV, variable tracks)
  - Random sampling (fixed tracks, variable SV)

- There is a lack of data for low energy electrons.
  - Available data for few energies and SV
  - Low energy cross sections and physics models have been updated

Random sampling and scoring

- Generation of electron tracks:
  - Incident particles: 100 eV - 1 MeV electrons
  - Physics: Geant4-DNA (ionization, excitation, elastic scattering)
  - Electrons tracked down to 10 eV
  - 10^3 tracks (each track sampled 10^3 times) => 10^6 scoring events

- Microdosimetric distributions were calculated by randomly overlaying scoring volumes within the associated volume of the track.
  - Shapes: Sphere, cylinder
  - Size: 2-100 nm

- Associated volume:
  - Volume around a track with a sampling efficiency equal to one.

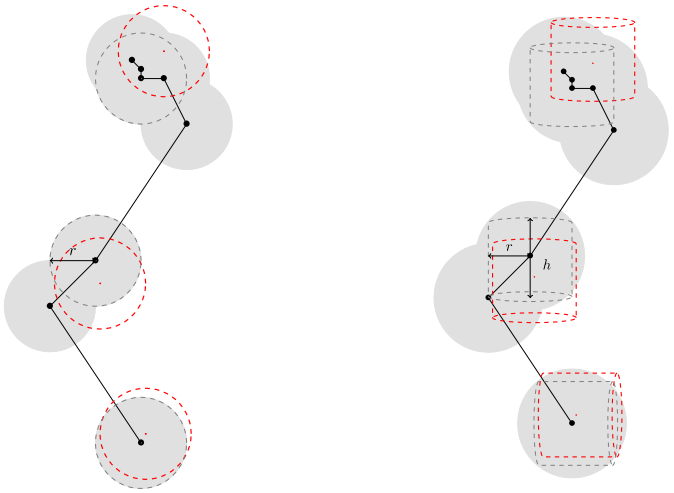
Random sampling and scoring

Random sampling algorithm:

1. Randomly select a transfer point
2. Randomly superimpose a sphere of radius r within a distance r from the transfer point
3. Record energy deposited

Scoring:

- Each event is scored with a weight ω_{tp} inversely proportional to the number of transfer points within the scoring volume
- Each track is scored with a weight ω_{av} which is proportional to the associated volume of the track.



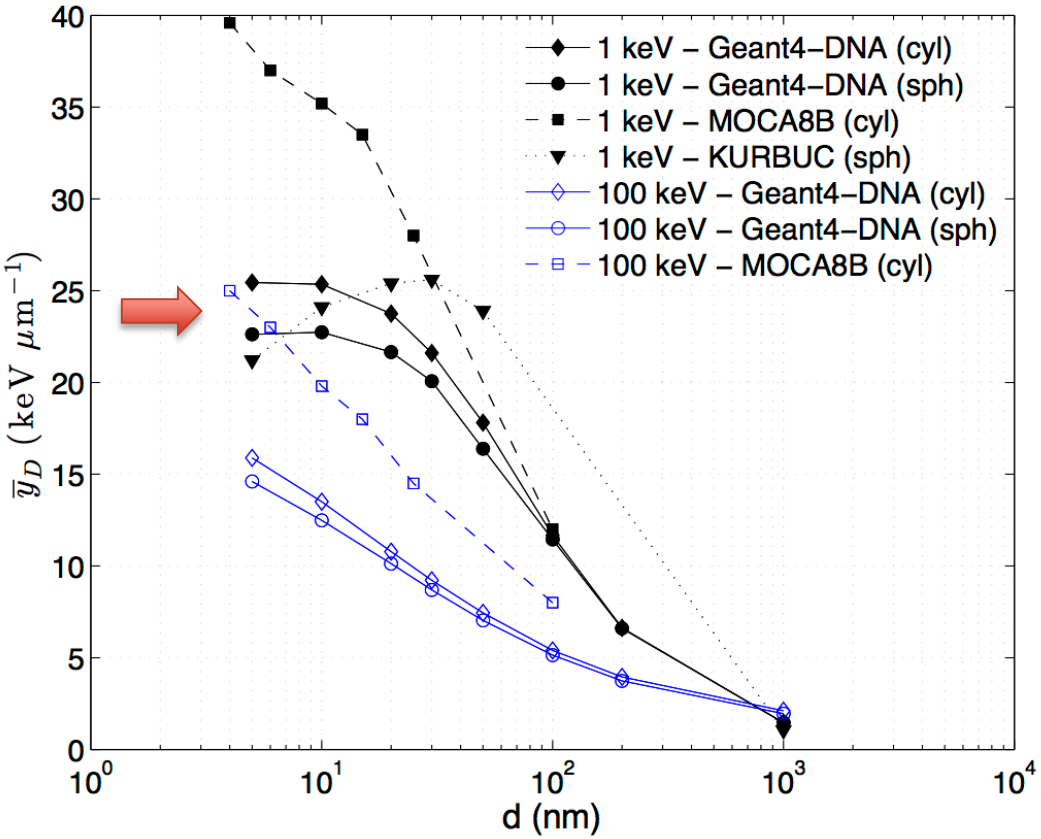
Famulari et al., *Phys Med Biol*, 2017

$$\bar{y}_D = \frac{\sum_{j=1}^{N}\left(\frac{\sum_{i=1}^{M} y_i^{\,2}\,\omega_{tp\,ij}}{\sum_{i=1}^{M}\omega_{tp\,ij}}\right)\frac{\omega_{av\,i}}{\sum_{j=1}^{N}\omega_{av\,j}}}{\sum_{j=1}^{N}\left(\frac{\sum_{i=1}^{M} y_i\,\omega_{tp\,ij}}{\sum_{i=1}^{M}\omega_{tp\,ij}}\right)\frac{\omega_{av\,i}}{\sum_{j=1}^{N}\omega_{av\,j}}}$$

- ✓ Particle track libraries
- ✓ Fast, accurate
- ✓ Simulation geometry does not vary according to SV size and shape

Microdosimetry of electrons

Dose mean lineal energy varies with shape and size of SV.



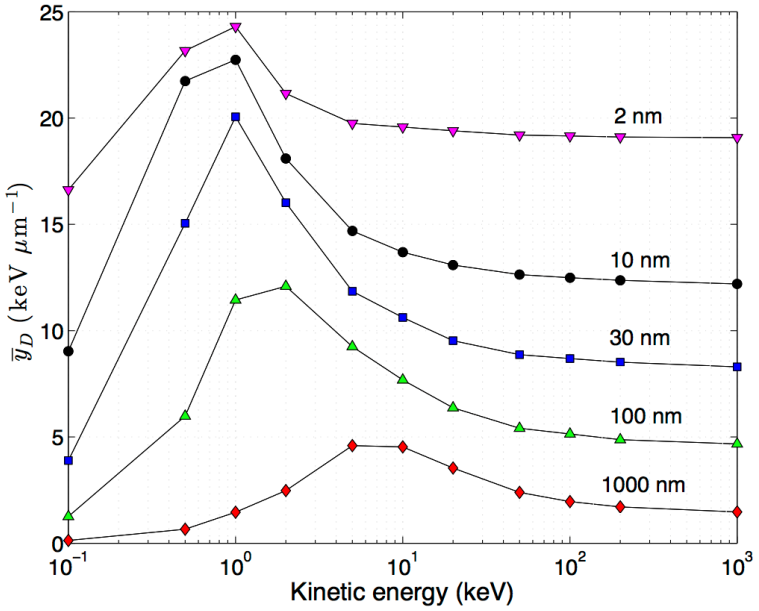
Famulari et al., *Phys Med Biol*, 2017

Microdosimetry of electrons

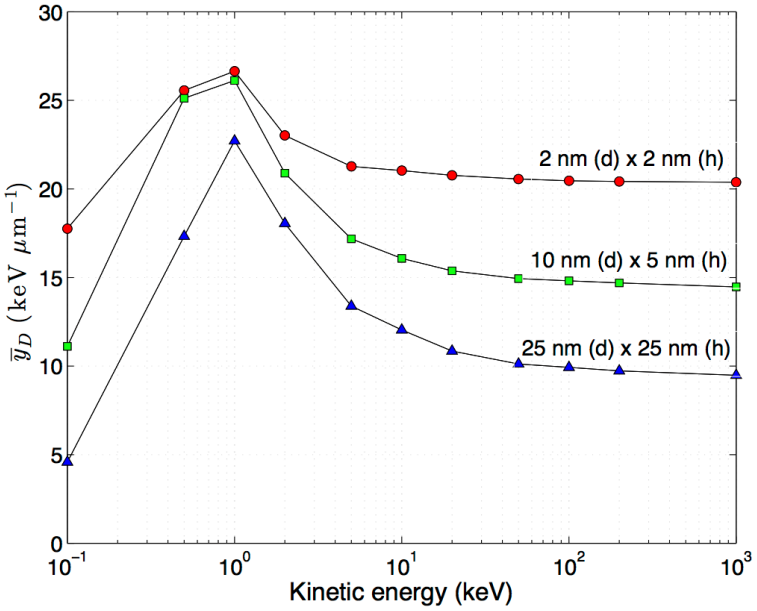
Database of microdosimetric quantities can be combined with secondary electron spectrum for photon sources.

$$\bar{y}_D = \frac{\int_0^\infty \phi(E) \left(\frac{S(E)}{\rho}\right) \bar{y}_D(E)\, dE}{\int_0^\infty \phi(E) \left(\frac{S(E)}{\rho}\right) dE}$$

Sphere



Cylinder



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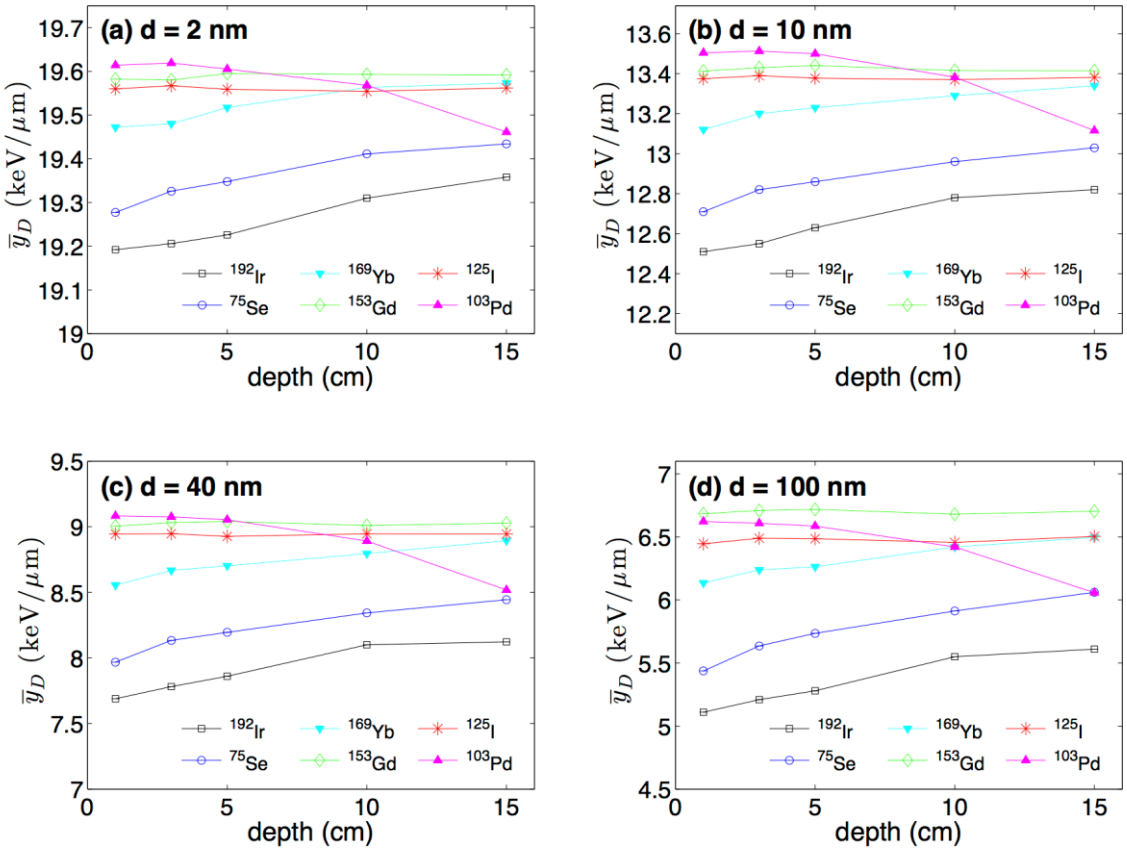
Applications to brachytherapy

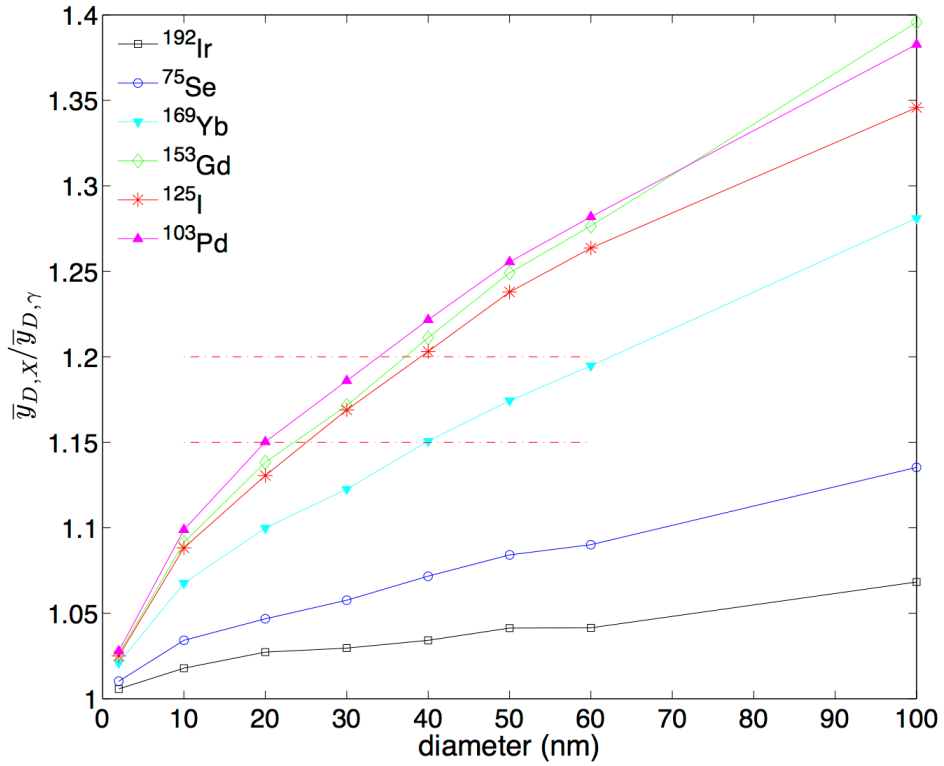
Dose mean lineal energy varies with distance from the source.



Famulari et al., *Int J Radiat Oncol Biol Phys*, 2017 (accepted)

Applications to brachytherapy

The characteristic diameter is in the range of 25-40 nm.



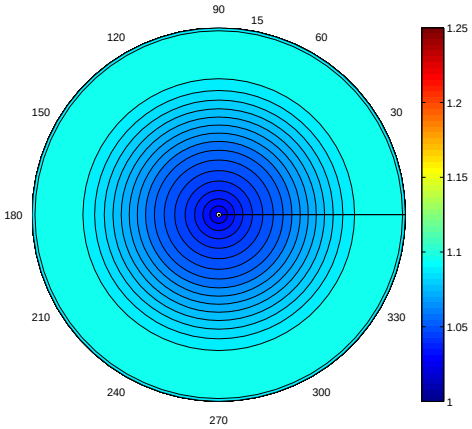
Famulari et al., *Int J Radiat Oncol Biol Phys*, 2017 (accepted)

Applications to brachytherapy

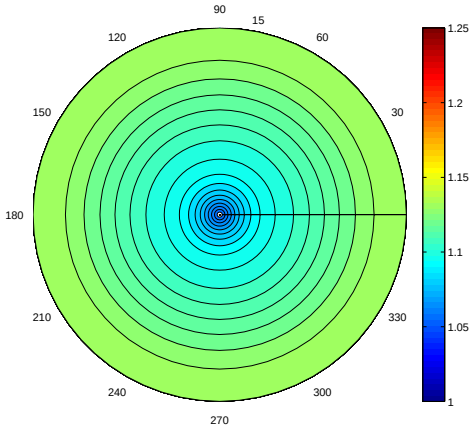
- Prescription doses for HDR brachytherapy can vary based on many factors and is primarily a clinical decision.
- The DVH constraints are established based on an accumulation of treatment outcome studies to avoid radiation-induced toxicity.
- Goal for alternative HDR sources:
  - Ensure the same biologically effective dose is given to target and OARs.
- Two options:
  - Modify dose according to single RBE value (simple)
  - RBE-weighted dose maps (complex)

Applications to brachytherapy

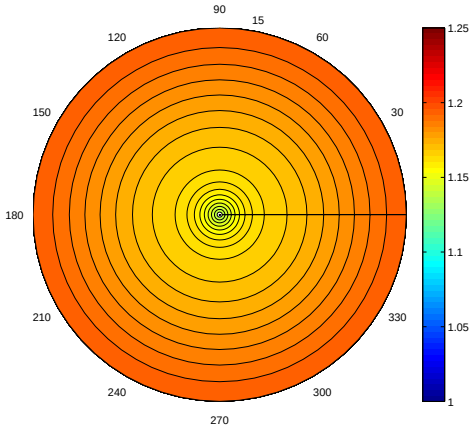
(a) ^{192}Ir



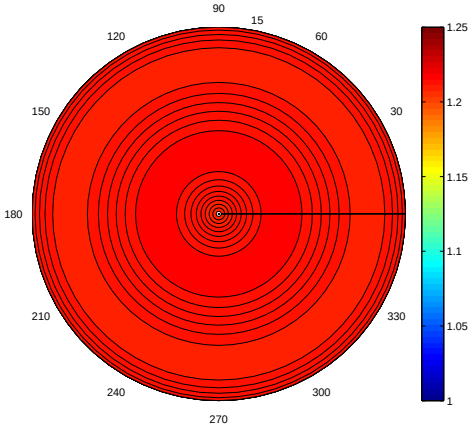
(b) ^{75}Se



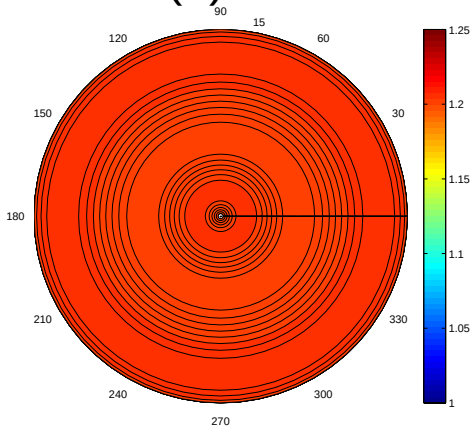
(c) ^{169}Yb



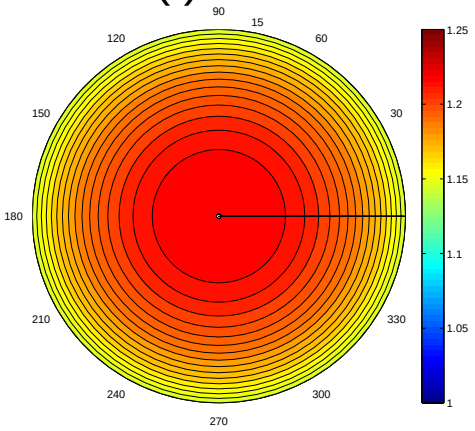
(d) ^{153}Gd



(e) ^{125}I



(f) ^{103}Pd



15 cm

Conclusions

- Microdosimetry can be used as a tool to evaluate radiation quality.
  - Radiation damage at level of DNA predicts biological effect
- Database of microdosimetric quantities for electrons
  - Variety of scoring volume size and shape
- Application to brachytherapy:
  - Quantify RBE between alternative sources
- Additional data is needed to provide clinically relevant RBE values (radiobiology, DSB yields, microdosimetry, nanodosimetry, LET)

Acknowledgements

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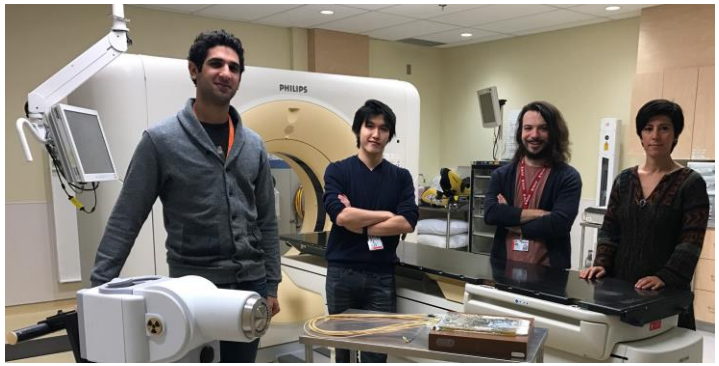

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