Role of Autonomous PET in Laser-Driven Ion Beam Radiotherapy (L-IBRT)

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Outline

- PET and Autonomous PET

- Lucite Phantom for 62-110 MeV protons

    - depth and lateral profiles for dose and activity (gammas)

-Tissue-Like Target for 200 MeV protons

    - PHITS code simulations
    - depth and lateral profiles for dose and positron emitters

- Lucite Phantom for 293 MeV Carbon
    - depth profiles for dose and activity

-Summary: Role of Autonomous PET in L-IBRT

PMRC: A Consortium of Funding Partners

Key goals: (i) development of laser-driven ion radiotherapy system (L-IBRT)
(ii) establish a multidisciplinary research hub

Typical Physical Proton Dose Distribution: Tissue-Like Target with 200 MeV protons

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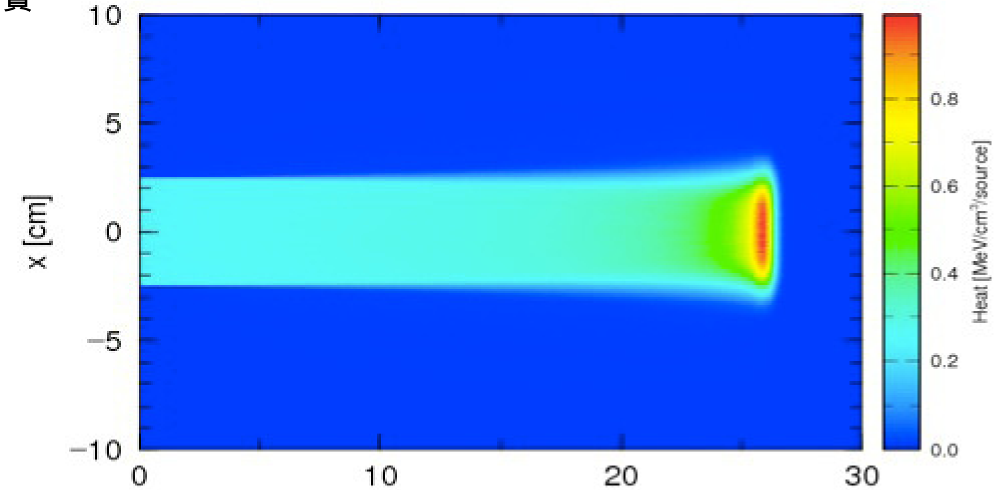

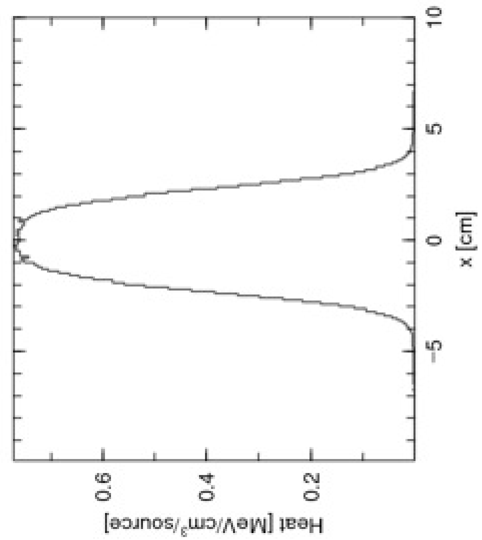

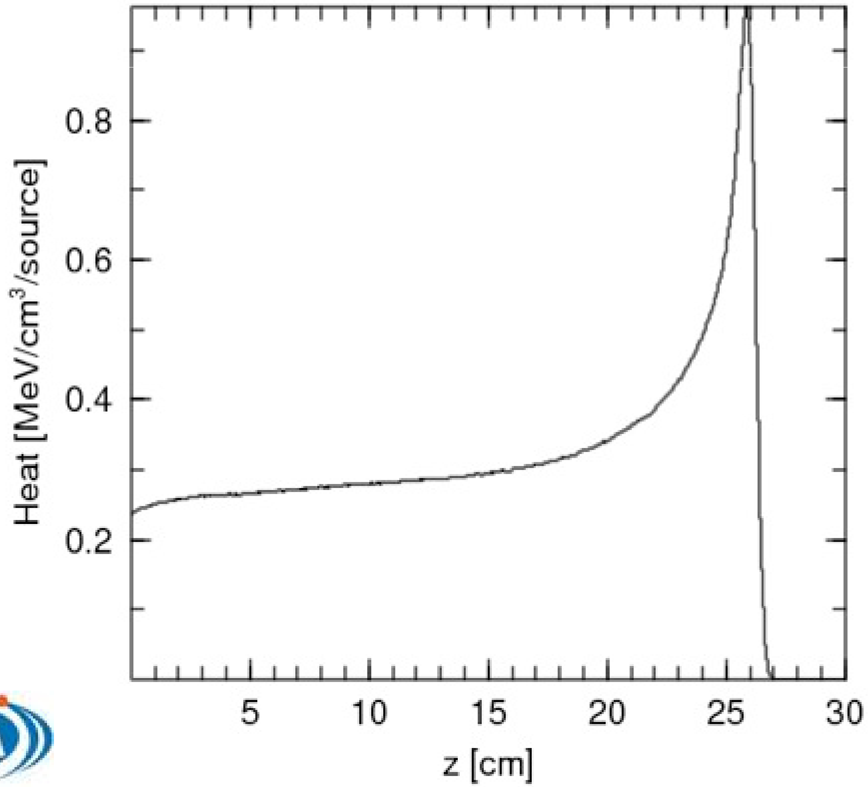

Bragg Peak region: localized volume with
steep dose gradients,
high LET and high RBE

localization capability makes proton beam alignment and control critical

Challenge - online, prompt detection of dose distribution to verify in vivo localization
- more difficult for smaller tumours

explore PET application to this issue

Positron Emission Tomography (PET) – Typical Application

functional/metabolic imaging

injected radiotracers – radioactive isotope incorporated into a carrier such as a metabolically active molecule (eg. FDG – fluorodeoxyglucose is common)

inject typically into blood stream

radiotracers allow PET to image biological paths of compounds that can be radio-labeled like this (typically use relatively short-lived isotopes)

coincident gamma detection - isotope blind

- spatial resolution limited by camera optics and positron displacement prior to annihilation

millions of events - typically poor statistics

Clairvivo – commercial animal PET scanner

Autonomous PET is Different

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not functional/metabolic imaging – no radiotracer injection

ion beam imaging - radioactivity (positron emission and subsequent annihilation)
induced by ion beam (projectile) used for radiotherapy

activity distribution measured by PET (gamma emission) depends on
ion projectile trajectory and is an artifact of:

energy loss distribution of ion projectile
(energy scaling of ion stopping power)

energy dependent cross-sections
for radioactive isotope production

about four distributions:

1. radioactive isotope production & decay (e^+ emission) *

2. e^+ e^- annihilation activity (gamma emission – PET scan) *

3. physical dose (deposited projectile energy)

4. biological dose (RBE x physical dose)

*(* relative displacement between 1 and 2 (~ mm) contributes to overall PET spatial resolution)*

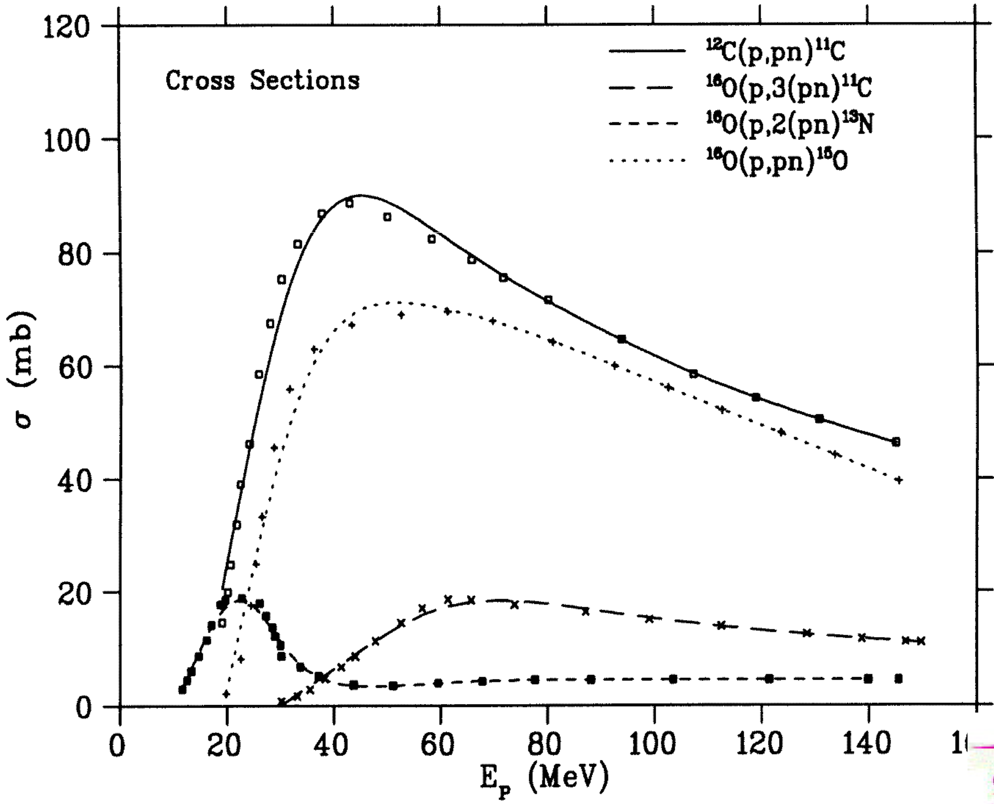
Phantom Targets Afford Controlled Investigations With Better Known Density Distributions: Simulations and Measurements with a Lucite Phantom

^{12}C (p,pn) ^{11}C (dominant); & ^{16}O (p, 3(pn)) ^{11}C ;
^{11}C lifetime ~ 20.4 minutes
(activation threshold ~ 20.6 MeV) (activation threshold ~ 27.5 MeV)

^{16}O (p, pn) ^{15}O (dominant) ;
^{15}O lifetime ~ 2.0 minutes
(activation threshold ~ 16.8 MeV)

^{16}O (p, 2(pn)) ^{13}N ;
^{13}N lifetime ~ 10.0 minutes
(activation threshold ~ 5.7 MeV)

lucite - $C_5 H_8 O_2$
density ~ 1.18 gm/cm³ :
well-known ^{12}C (p,pn) ^{11}C
and ^{16}O (p, pn) ^{15}O
cross-sections dominate



(U. Oelfke et al Phys. Med. Biol. 41, 177 (1996).

Autonomous PET Studies at HIBMC Using ~ 74 MeV Protons in Phantom Targets (Lucite…)

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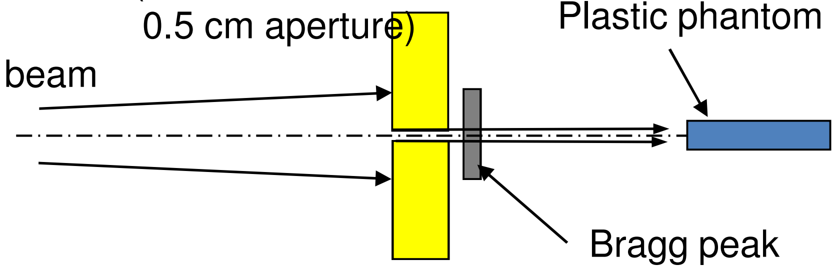
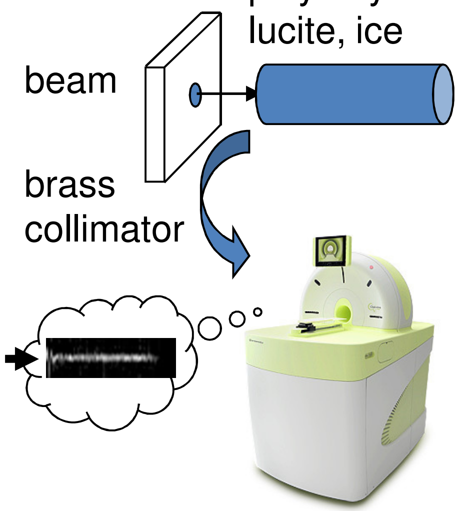
early results from Hyogo Ion Beam Medical Center:

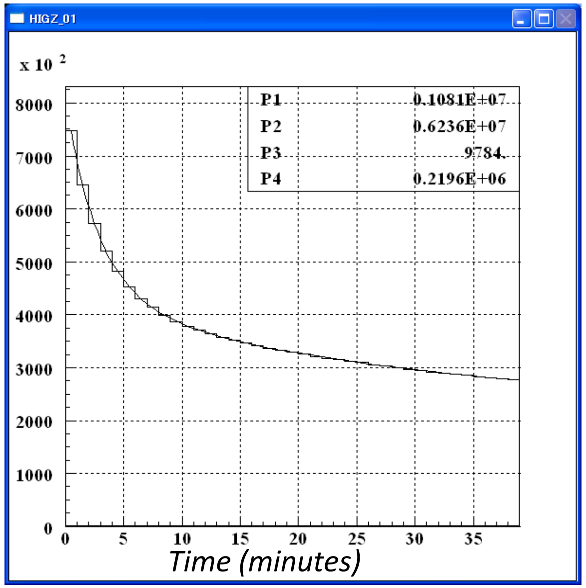
- 1.6 pulses /sec
- ~ 10^8 - 10^{10} protons
- ~ 74 MeV
- 5 mm pencil beam





high resolution, efficient PET scanner: Clairvivo

Lucite:



N(^{15}O)=1.08×10^6
N(^{11}C)=6.24×10^6
N(^{10}C)= 9.8×10^3
B.G.=2.20×10^5

(irradiation by ~ 10^{10} protons)

JAEA · SPring-8 · APR · KPSI Kansai Photon Science Institute · PMRC photo medical research center

Activity Depth Profile vs Dose Depth Profile in Lucite for 74 MeV Protons

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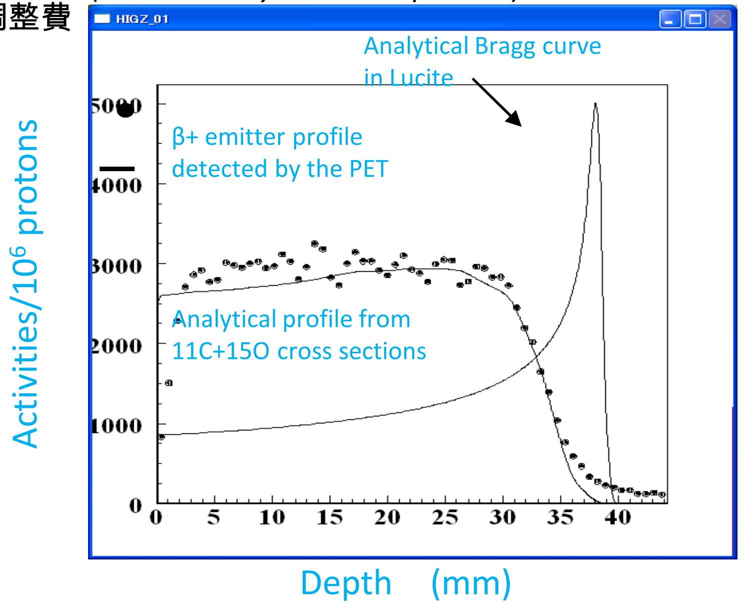
(irradiation by 1.6 x 10^{10} protons)



Activity (gamma emission) Depth Profile:

- ~ flat top
- less penetration than Bragg peak by few mm
- attribute to (i) energy dependence of ^{11}C and ^{15}O production cross-sections
  (ii) inverse energy dependence of proton stopping power
  (iii) proton number reduction with increasing depth

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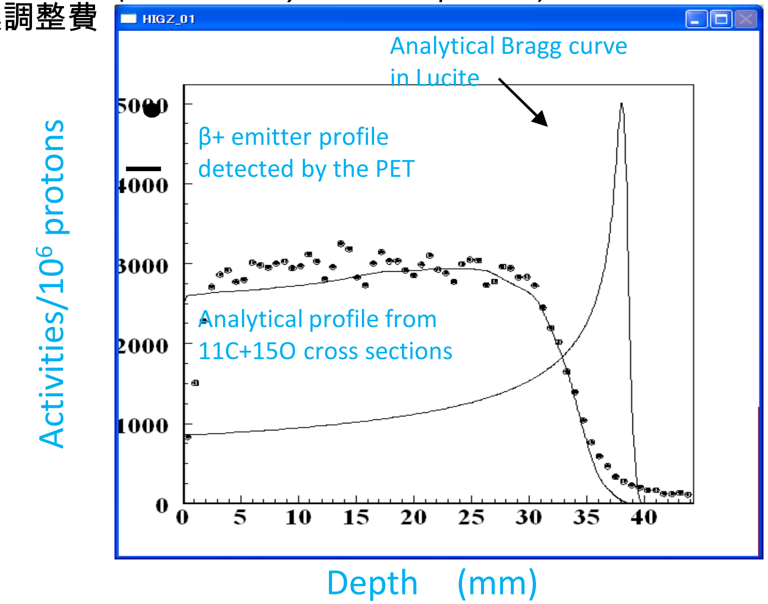

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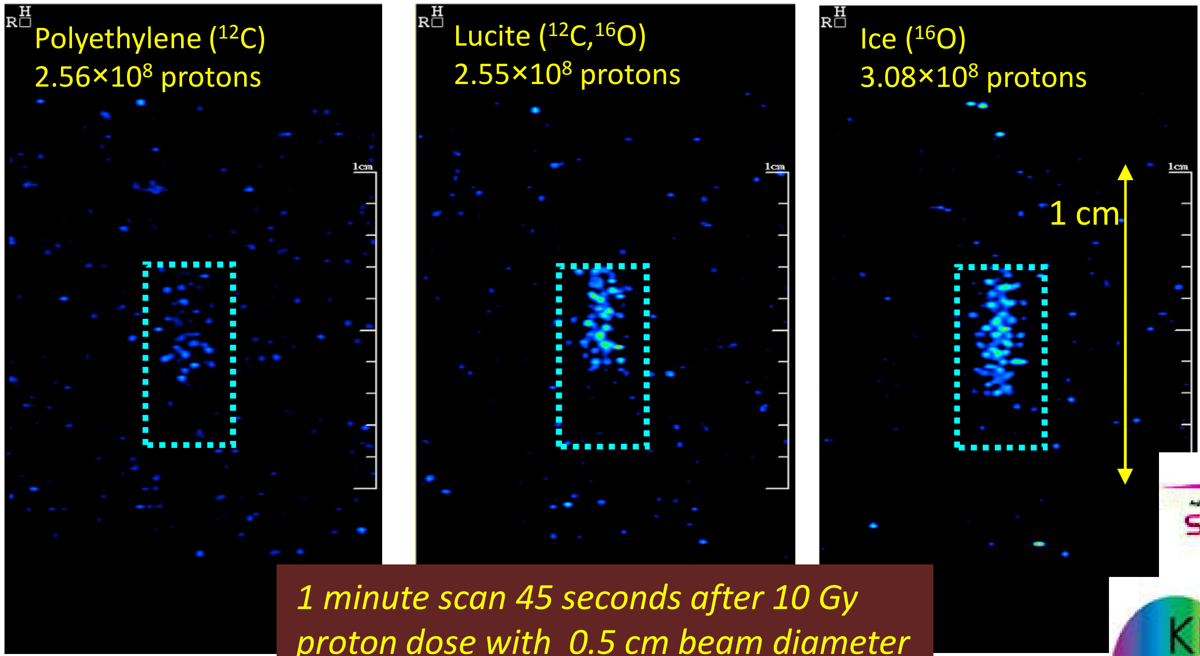
  (iii) proton number reduction with increasing depth
- profile edges resolution limited

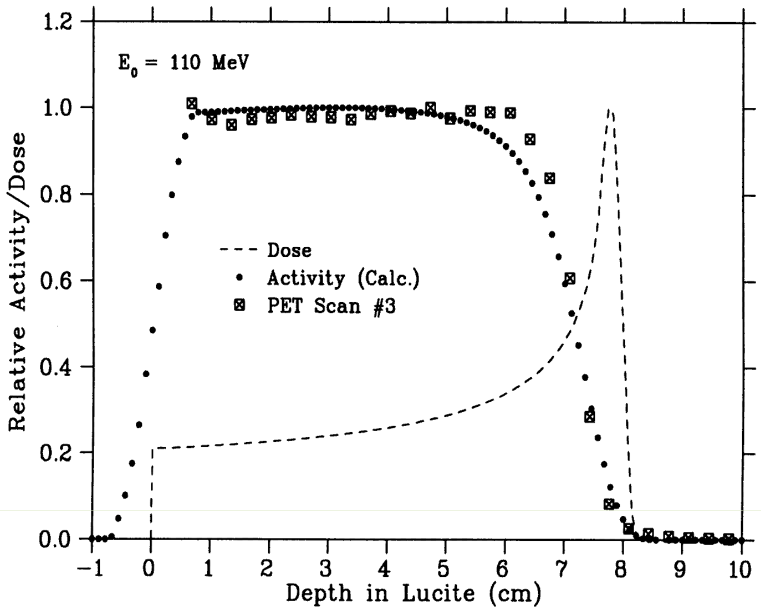
Prompt detection of activity with short scan time from 10 GY irradiation :
spatial resolution ~ 2 mm



1 minute scan 45 seconds after 10 Gy proton dose with 0.5 cm beam diameter

Comparing Activity (Gamma Emission) Depth Profile and Dose Depth Profile for 62 and 110 MeV Protons in Lucite

(early results from TRIUMF /UBC study)



RBP result at 110 MeV (~ 1% spread) similar to HIBMC observation (PET scans taken 20-40 minutes after proton irradiation lasting ~ 3 -26 minutes @ ~ nA)

U. Oelfke et al Phys. Med. Biol. 41, 177 (1996)

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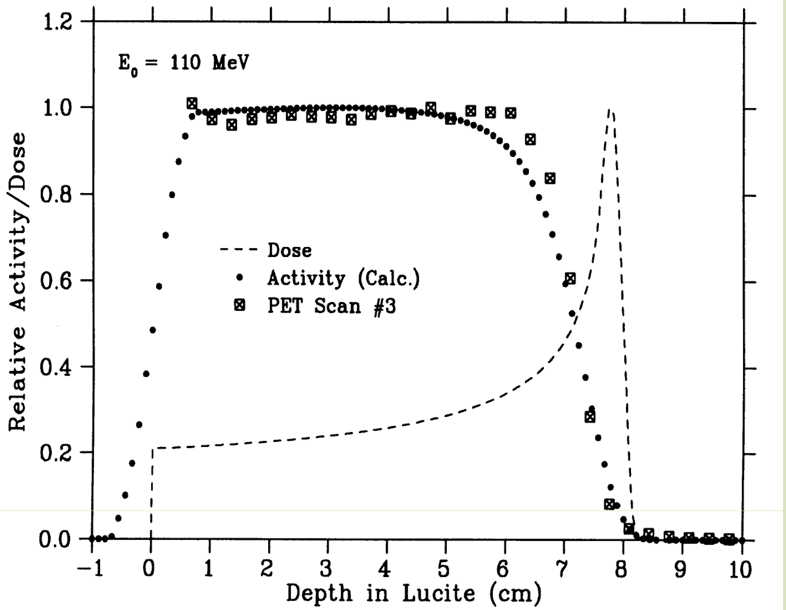

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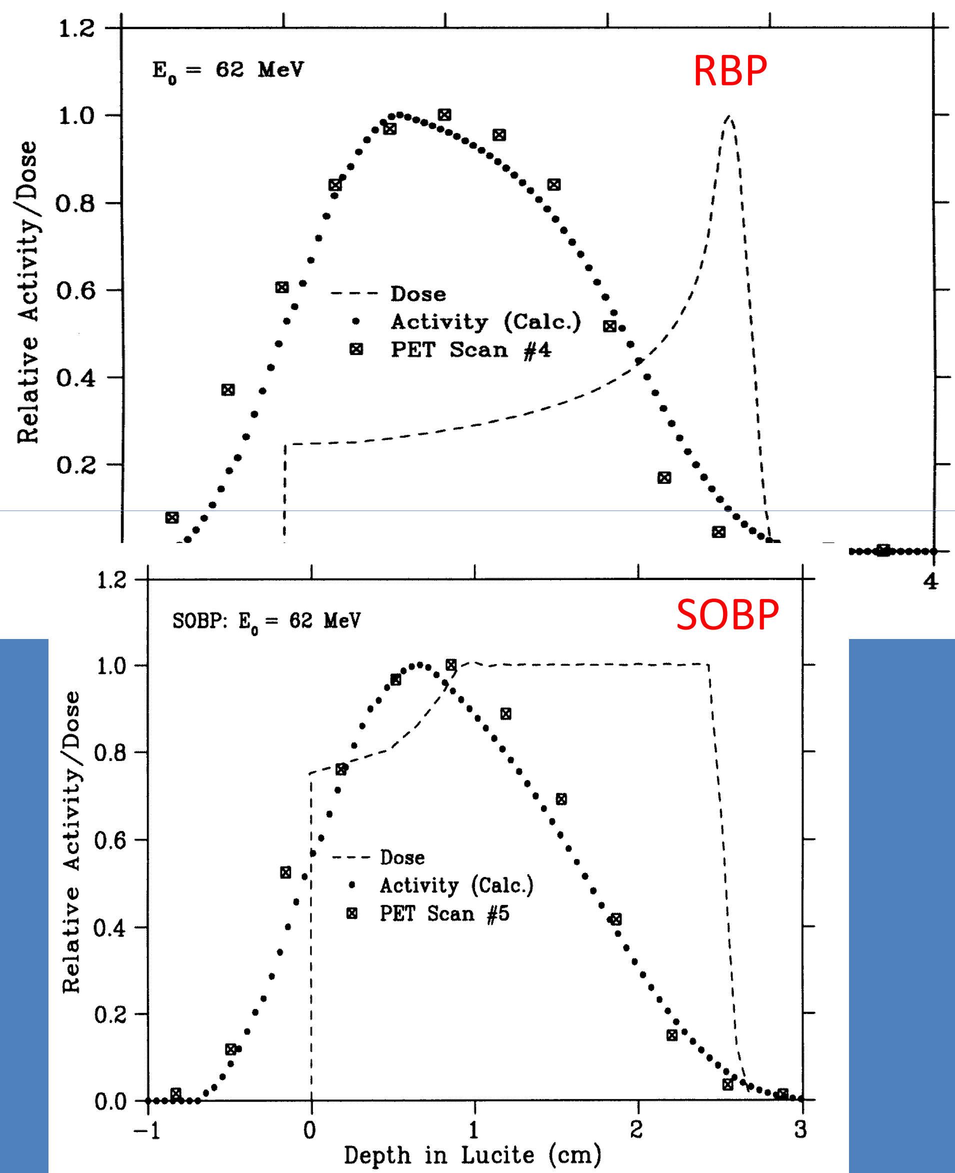
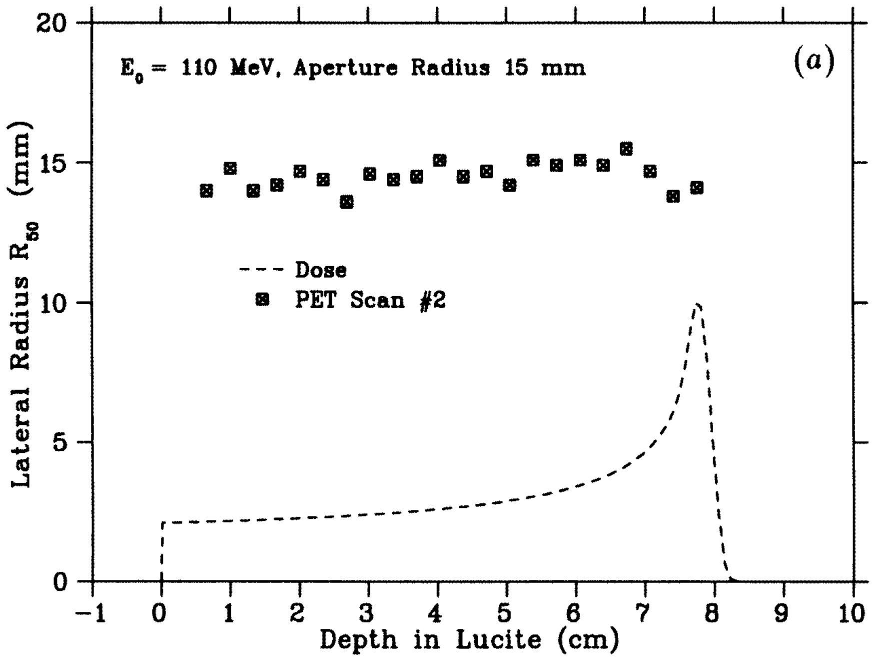


Activity depth profile is relatively unaltered for RBP and SOBP cases; indicates insensitivity to dose profile

U. Oelfke et al Phys. Med. Biol. 41, 177 (1996)

Correlation of Lateral Activity and Dose Profiles for 110 MeV Protons:
50 % Isoactivity Radius Correlates to 50 % Isodose Radius



U. Oelfke et al Phys. Med. Biol. *<u>41</u>, 177 (1996)*

PHITS Simulations with a Tissue-like Target

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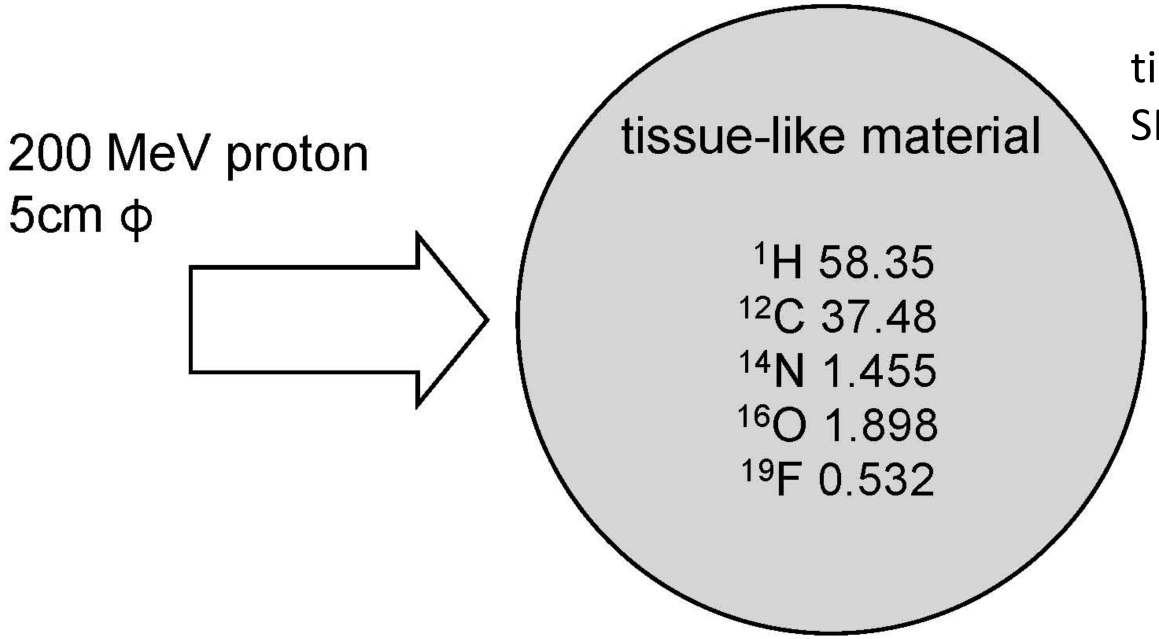
calculation geometry



tissue equivalent plastic:
SRIM code

$$a_I^{E_0}(r,t) = \sum_T \rho_T(r)\varphi^{E_0}(r,t)\sigma_{TI}(E(r))f(t)$$

- $a_I^{E_0}(r,t)$: isotope, I activity profile
- $\rho_T(r)$: density of target nuclei, T
- $\varphi^{E_0}(r,t)$: proton flux
- $\sigma_{TI}(E(r))$: isotope production cross-section

where

$$f(t) = (1 - e^{-\beta_I t}) \; for\; t < t_R$$

$$f(t) = (1 - e^{-\beta_I t_R})e^{-\beta_I(t-t_R)} \; for\; t > t_R$$

$\beta_I \equiv isotope\ decay\ constant$ & $t_R \equiv irradiation\ time$

PHITS overview

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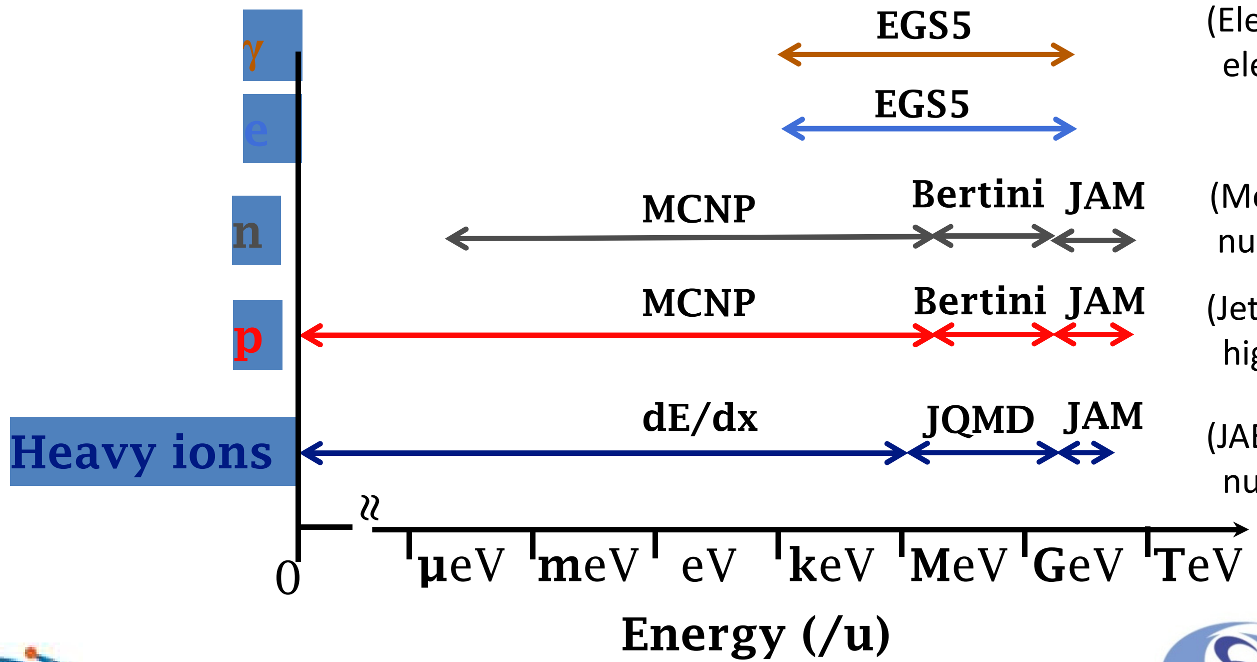
- One of world famous **general-purpose** Monte-Carlo codes
  FLUKA, MCNPX, GEANT4, MARS, HETC-HEDS, SHIELD-HIT, **PHITS**, ...
- Simulates particles and heavy ions **transport in matter** and **nuclear reactions**
- a parameter-free package of **reliable physical models** and XS data
- **User friendly** input/output interfaces (easy use)
  CT-data support, 3D geometry, various tally functions, web-interface

Particles and available energies by PHITS



(Electron Gamma Shower –
electron, photon transport)

(Monte Carlo N-Particle code –
nucleus, electron , photon transport)

(Jet AA Microscopic Transport Model –
high energy nuclear model)

(JAERI Quantum Molecular Dynamics –
nuclear model

PMRC photo medical research center

JAEA

APR SPring-8

KPSI Kansai Photon Science Institute

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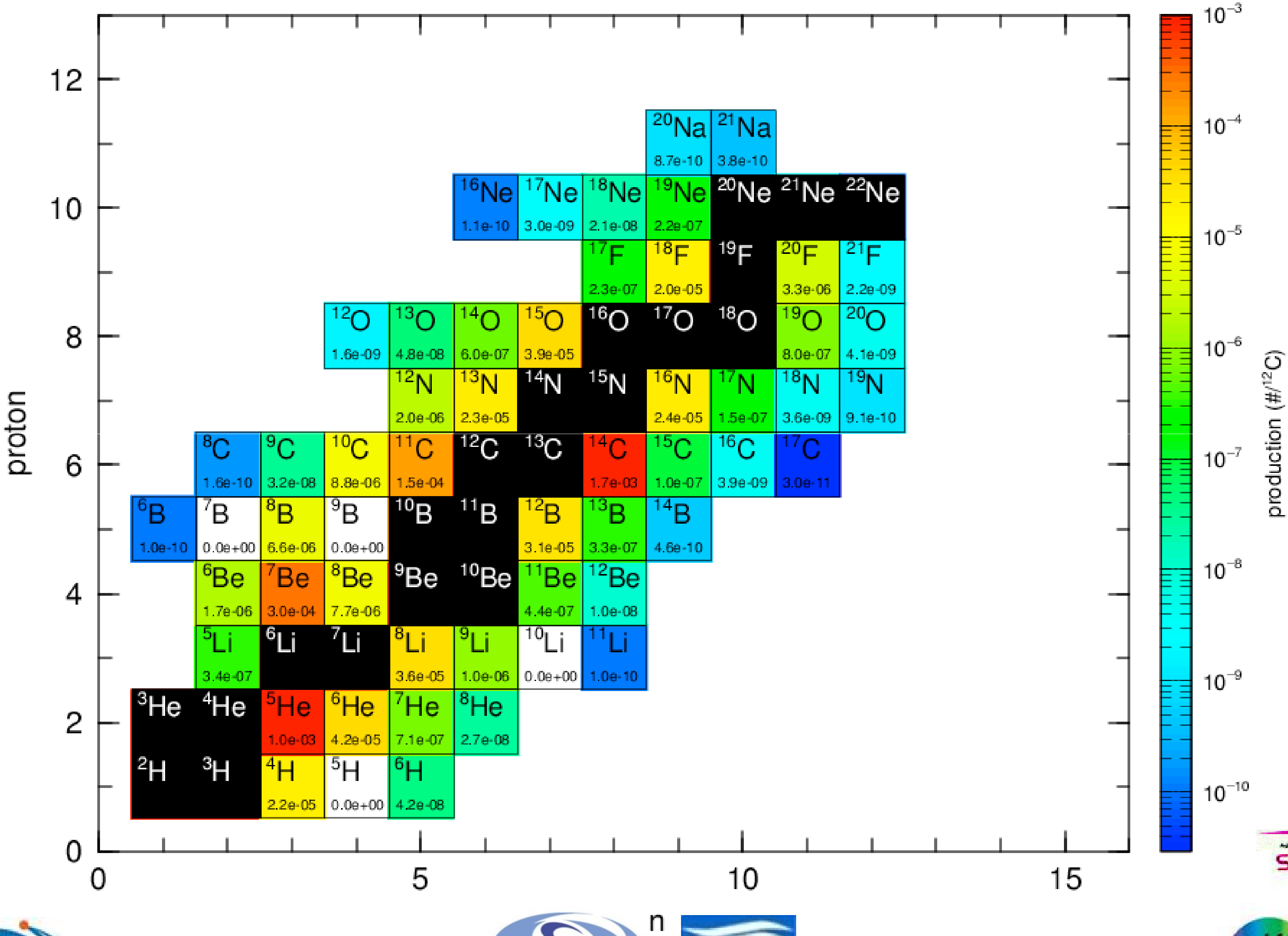
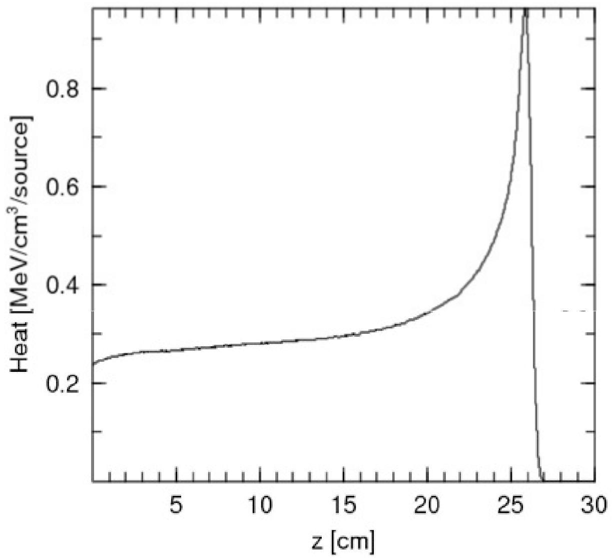
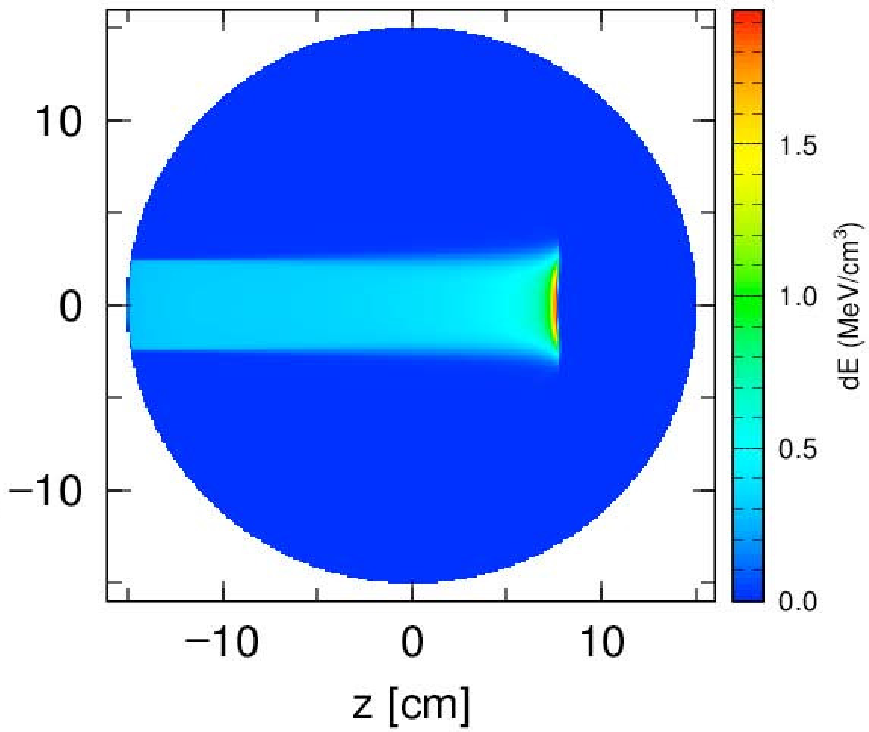
200 MeV proton induced radioactive nuclei in tissue-like material



Tissue-Like Target: Monoenergetic Physical Dose

200 MeV proton induced dE distribution





2 x 10^9 protons

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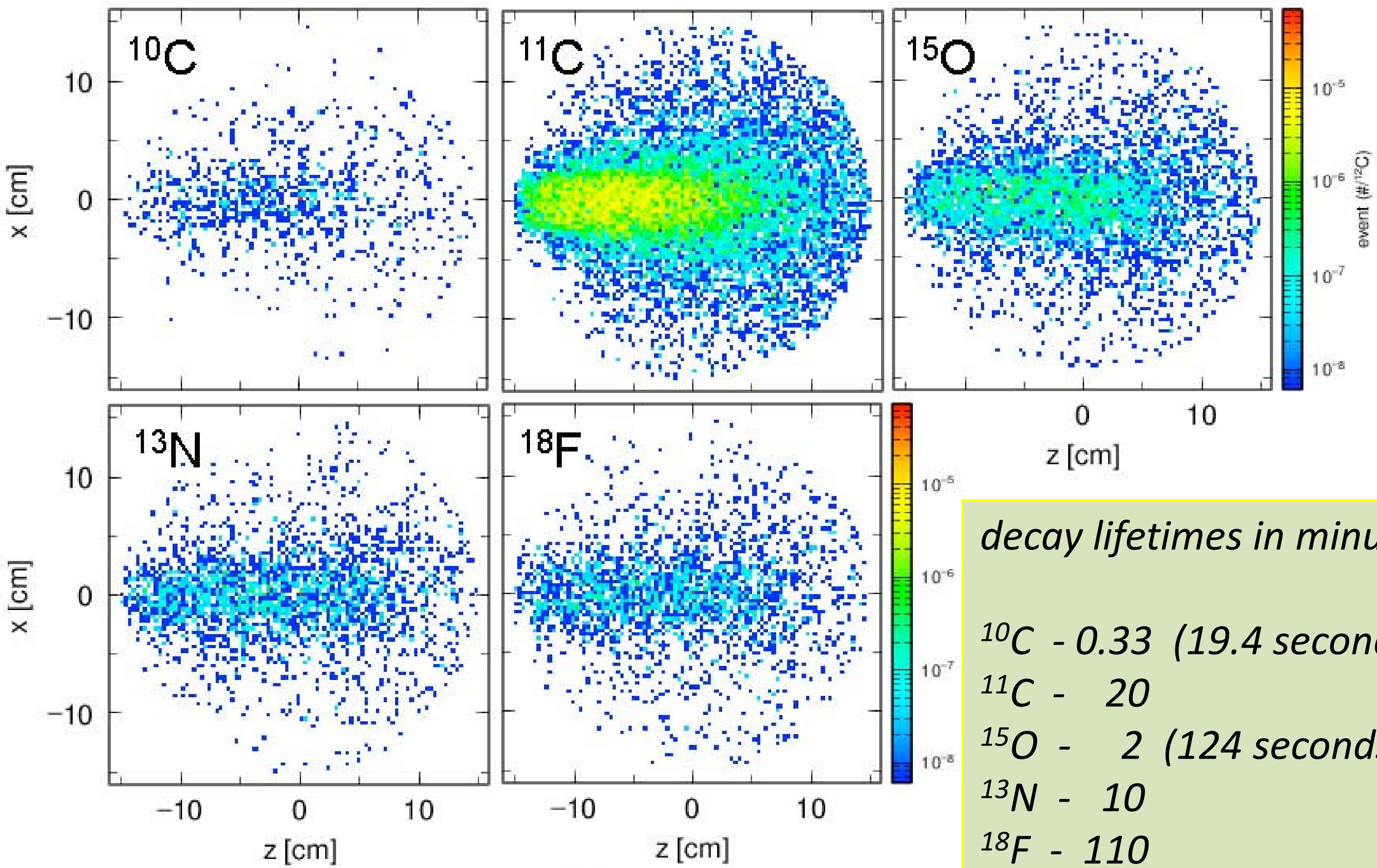
Tissue-Like Target: Radioactive Isotope Distribution

200 MeV proton induced positron emitters



decay lifetimes in minutes:

^{10}C - 0.33 (19.4 seconds)
^{11}C - 20
^{15}O - 2 (124 seconds)
^{13}N - 10
^{18}F - 110

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Radio Isotope (Positron Emitter) Distribution and Dose Distribution for 200 MeV Protons in Tissue-Like Target

activity depth is significantly less than Bragg Peak depth (resolution limited)

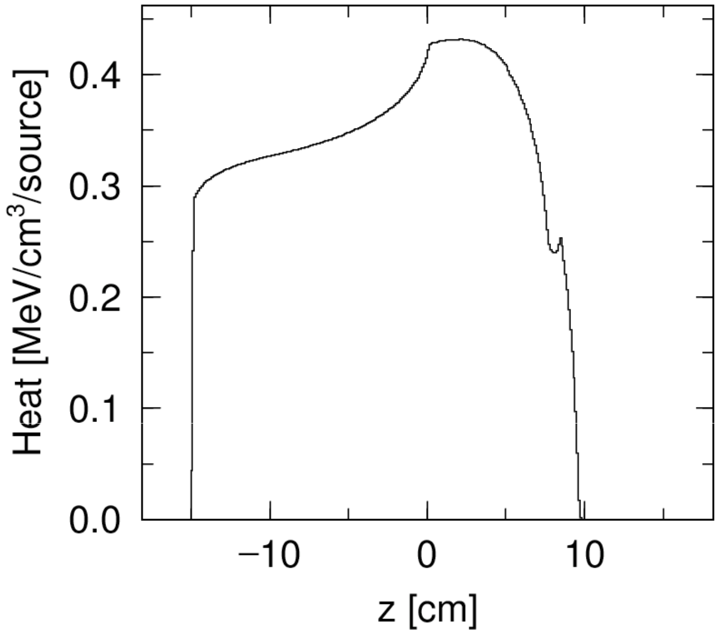
- attribute to activation threshold energy for isotope production

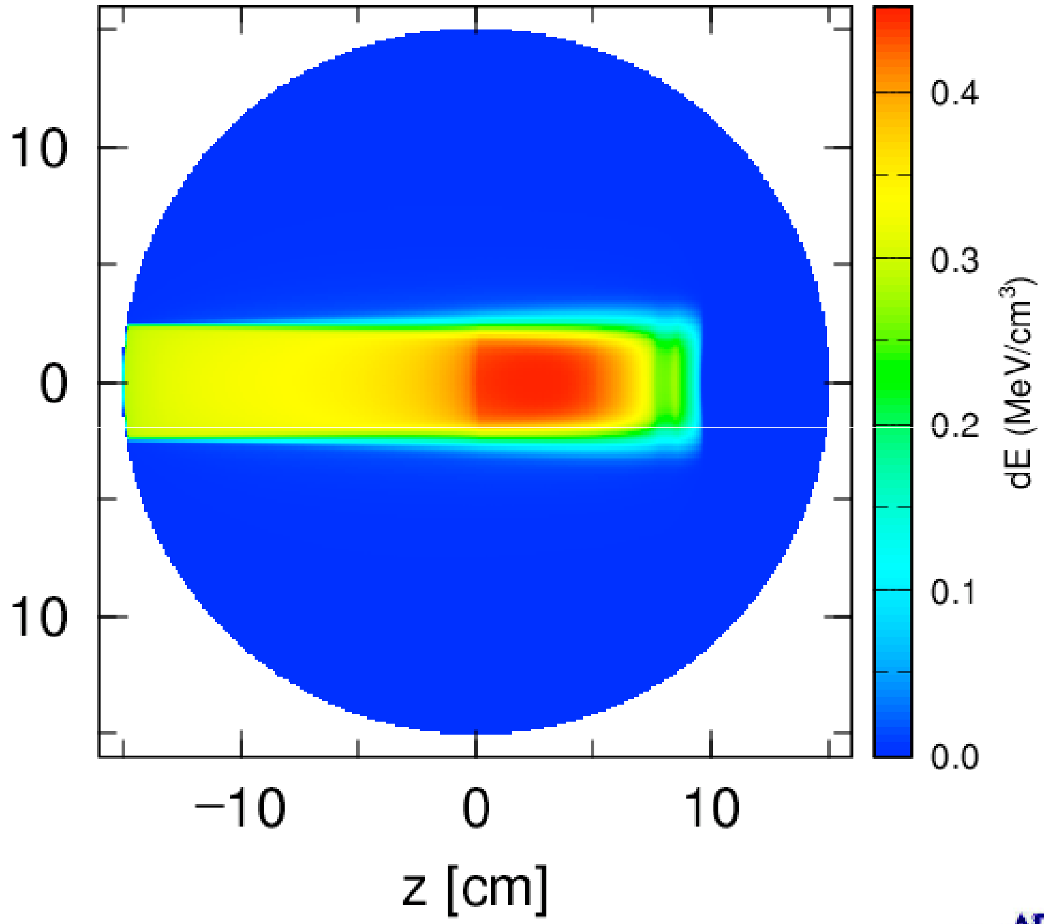
- tumour location can be downstream

- no correlation between activity and dose depth profiles

- dose and activity lateral profiles are correlated

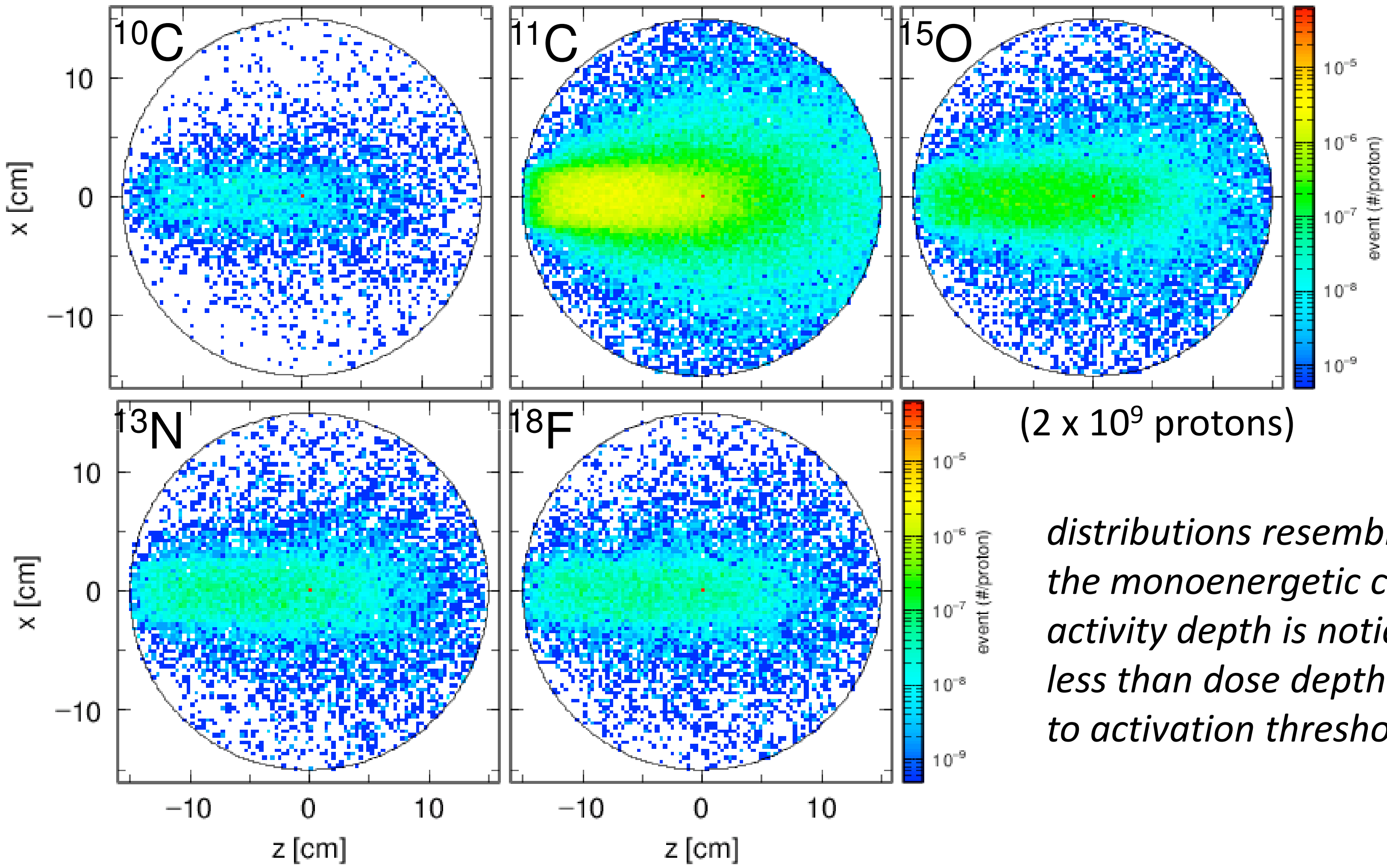
Tissue-Like Target: Spread Out Bragg Peak (SOBP) Physical Dos





2 x 10^9 protons
158 – 208 MeV

Radioactive Isotope Distribution: SOBP
200 MeV Proton- Induced Positron Emitters

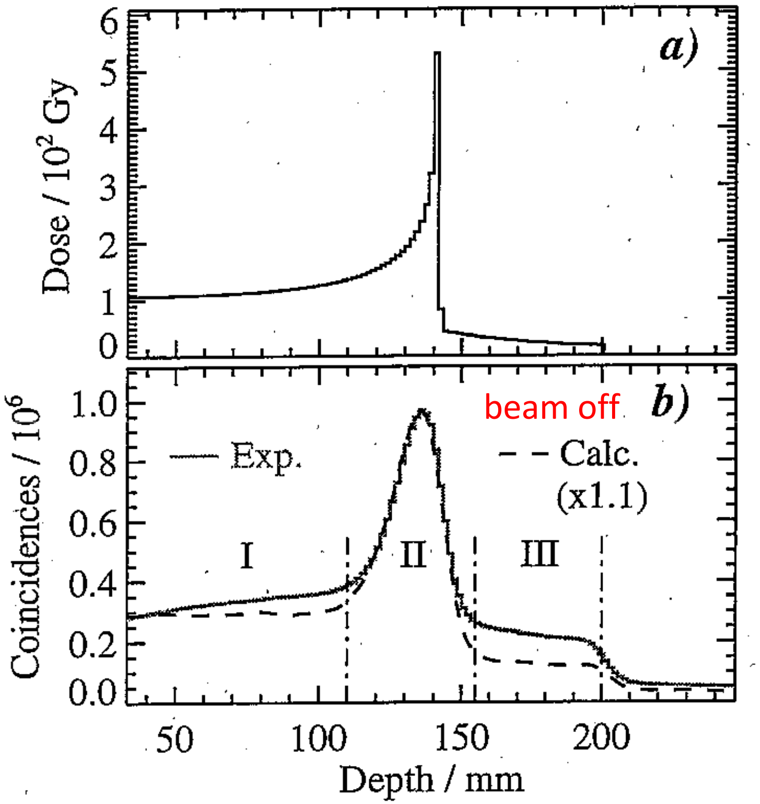


(2 x 10^9 protons)

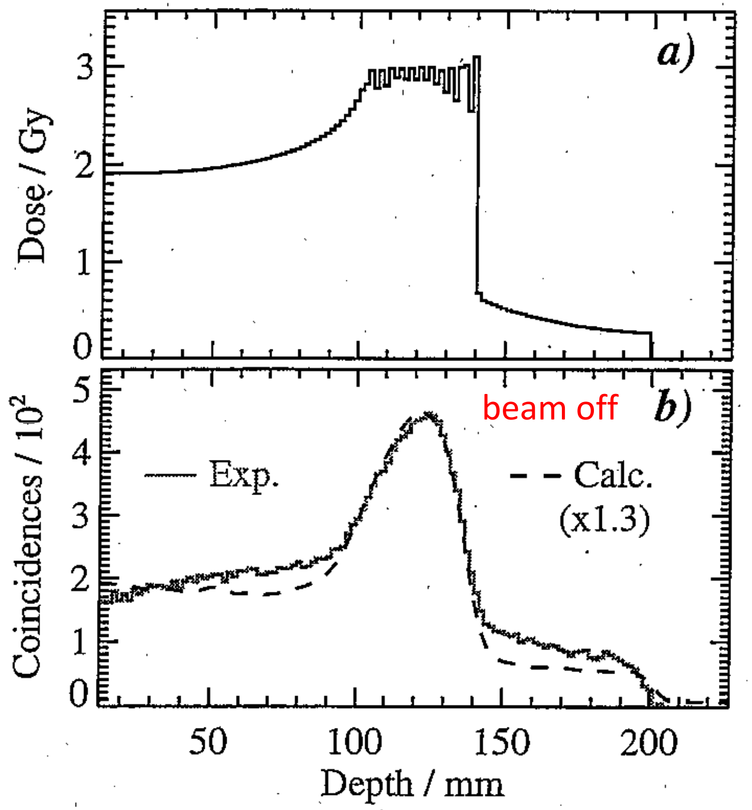
distributions resemble the monoenergetic case: activity depth is noticeably less than dose depth & due to activation threshold

Depth Profiles: Activity (Gamma Emission) and Dose for 293 MeV Carbon in PMMA Target

Carbon RBP



Carbon SOBP



for Carbon Depth Profiles: activity is relatively insensitive to dose (similar for SOBP and RBP)

(^{10}C, ^{11}C, ^{13}N, ^{15}O)

- broad activity peak (in II) – projectile fragmentation
- plateau (in I and III) – target fragmentation
- (activity is the only measured quantity)

J. Pawelke et al IEEE Trans. Nucl. Sci. 44[4], 1492 (1997)

Summary: Role of Autonomous PET in L-IBRT : Protons

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Consider activity profiles of dominant positron emitters, ^{11}C and ^{15}O:

Spatial correlation - no unique correlation with dose depth profile
- lateral profile correlation (beam position and diameter)

Dynamically - concerning short treatment times and dynamics of spot scanning, decay rates are too low (half life: 20 minutes for ^{11}C and 2 minutes for ^{15}O) to 'track' activity profile changes or dose accumulation that would be needed for prompt online monitoring or feedback

Treatment Planning Issue - more readily infer activity profile from dose profile
(much harder to infer dose profile from activity profile - insensitive/not unique)

The Challenge – What is the Role of Autonomous PET *with prominent e+ emitters* ?

- post irradiation integration as verification of lateral profile (beam diameter and lateral steering)
- check of body composition (density distribution) as given by CT scan by comparing modeled and observed activity distributions (assuming reliable cross-sections and ion beam information)

Faster emitters needed for prompt online activity profile detection (^{9}C or ^{12}N ?)

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PHITS calculation

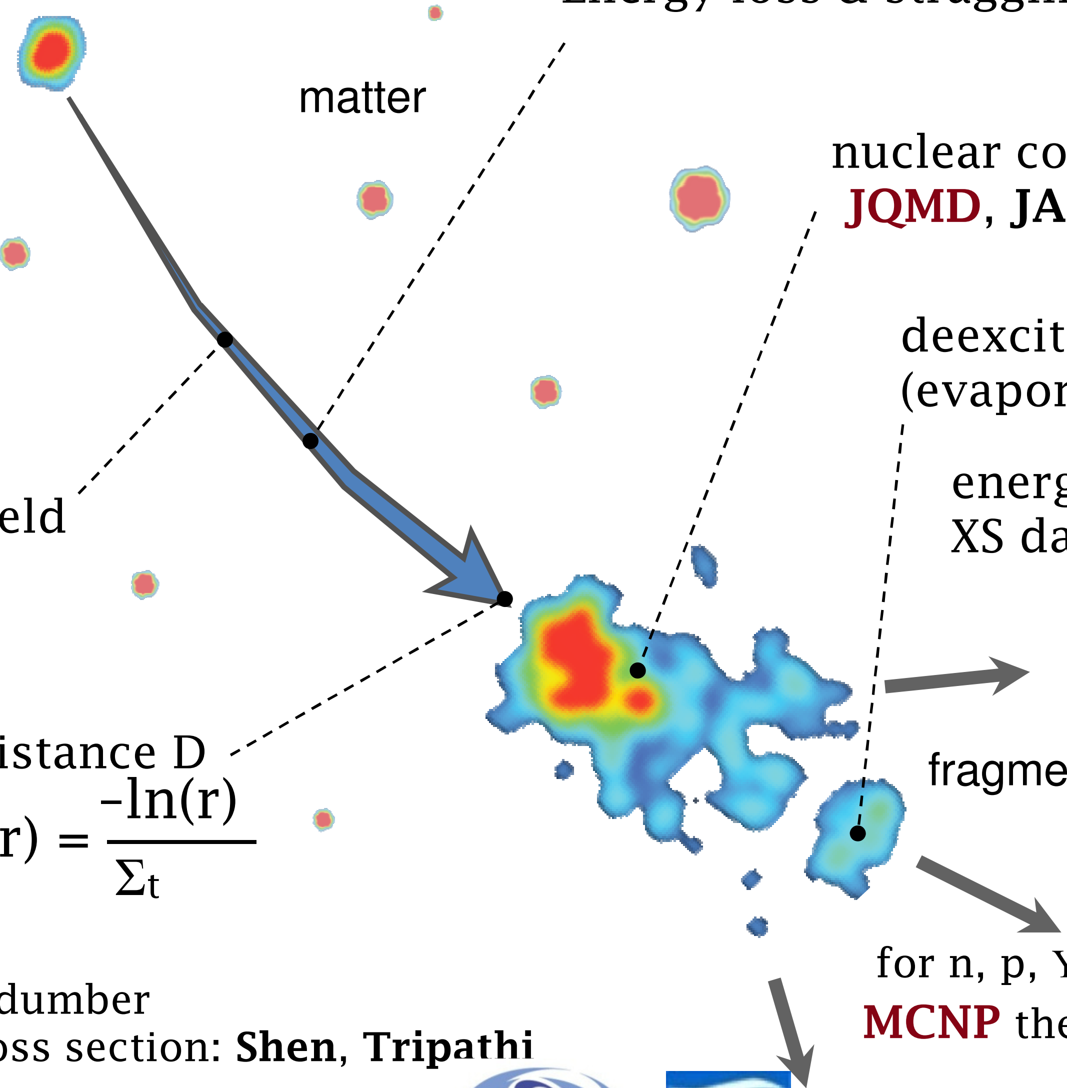
- Example of “Nucleus transport in matter” by PHITS

Energy loss & straggling: **ATIMA**, **SPAR** (determines dE/dx)

nuclear collisions: **JQMD**, **JAM**, **Bertini**

deexcitation: **GEM** (evaporation & fission)

energy conservation after XS data use: **Event-generator**



magnetic field
gravity

collision distance D

$$D = \lambda \cdot -\ln(r) = \frac{-\ln(r)}{\Sigma_t}$$

for n, p, Y below 20 MeV use **MCNP** the world standard MC

r: random dumber

Σ_t: total cross section: **Shen**, **Tripathi**