8th ECMP, Athens
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Fluorescent nuclear track detectors as a tool for ion-beam therapy research

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GERMAN CANCER RESEARCH CENTER IN THE HELMHOLTZ ASSOCIATION

50 Years – Research for A Life Without Cancer

Photons or charged particles?

Conventional radiotherapy

← ? →

Particle therapy

Conventional radiotherapy:

- *cost:* € 3 million
- *space:* 500 m³
- *staff:* 3 employees

Particle therapy:

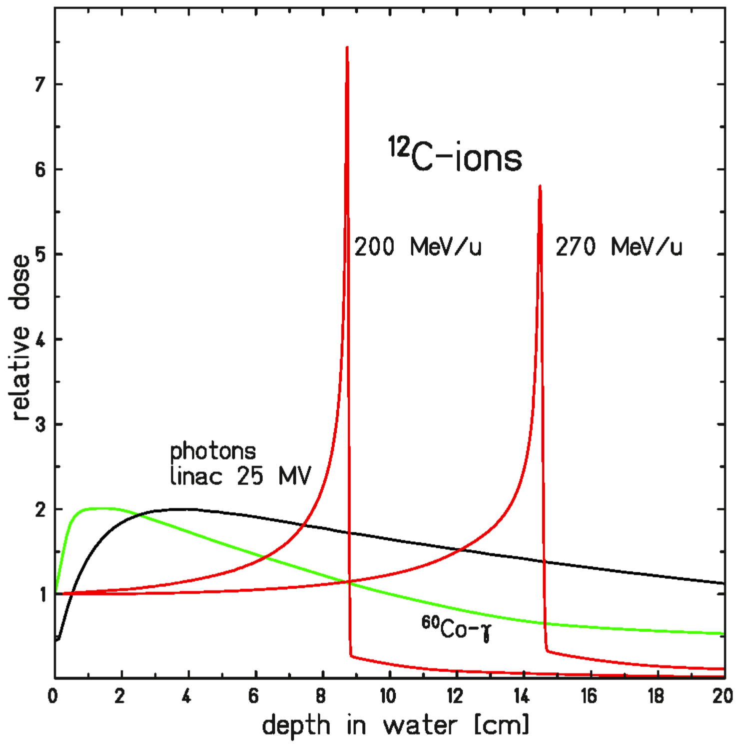
- *cost:* € 120 million
- *space:* 50,000 m³
- *staff:* 40 employees

Carbon ion radiotherapy

Main characteristics

- inverse depth-dose profile (Bragg peak)

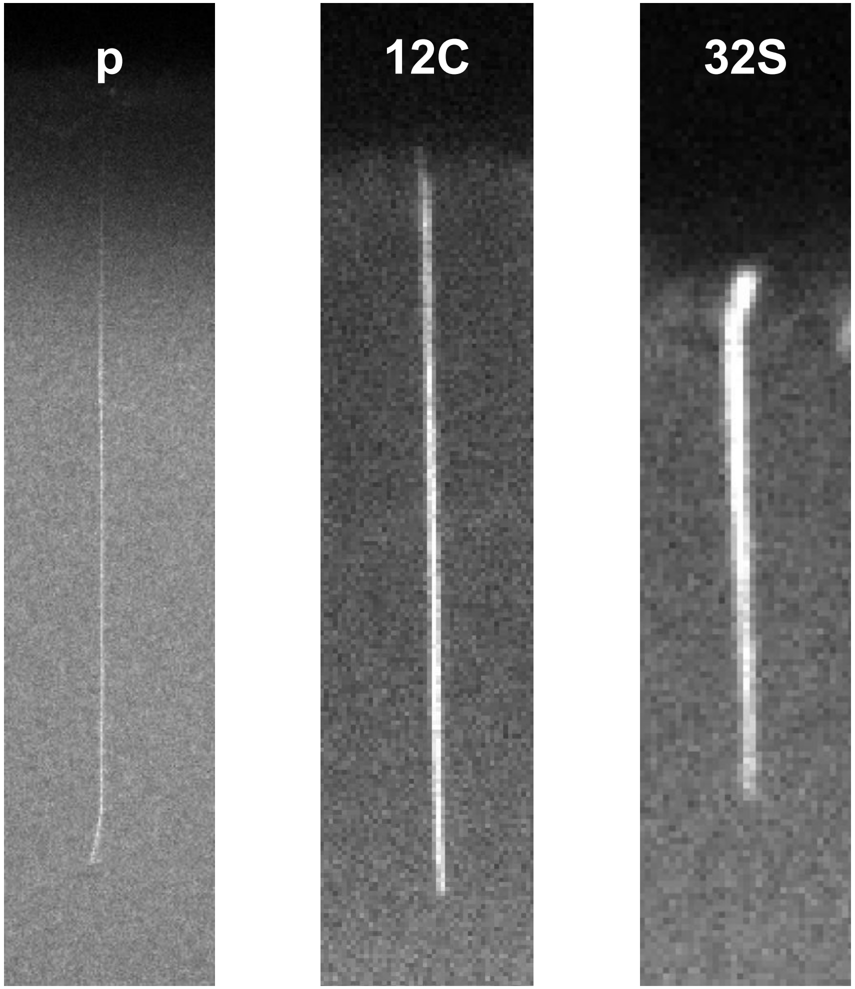
[Schardt et al., Rev. Mod. Phys. 82, 2010]



Carbon ion radiotherapy

Main characteristics

- inverse depth-dose profile (Bragg peak)
- high ionization density (LET)

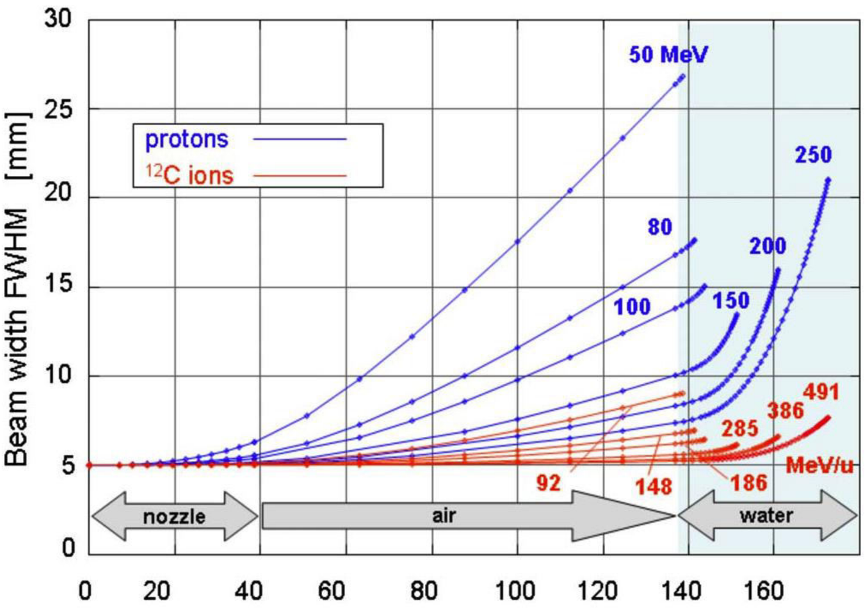


Carbon ion radiotherapy

Main characteristics

- inverse depth-dose profile (Bragg peak)
- high ionization density (LET)
- reduced lateral scattering

[Schardt et al., Rev. Mod. Phys. 82, 2010]

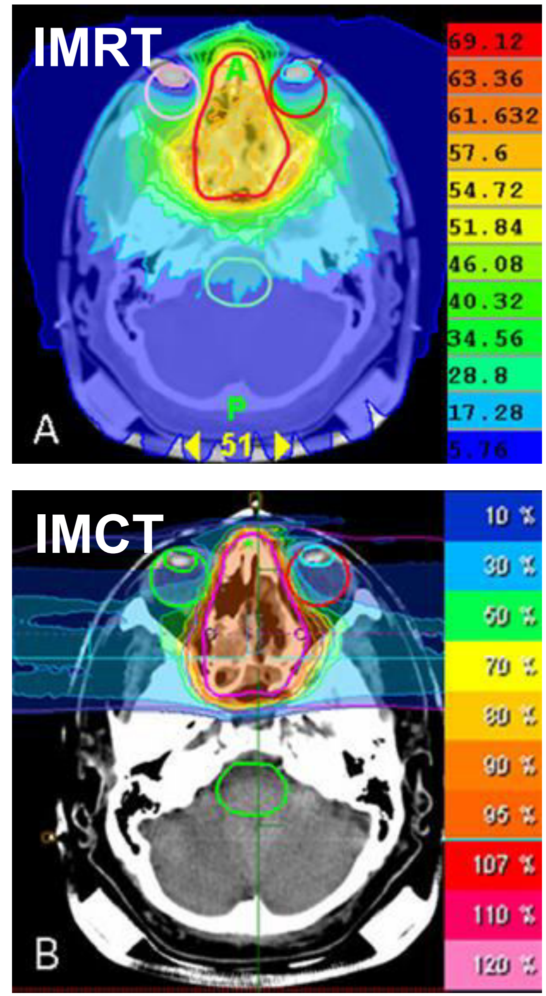


Carbon ion radiotherapy

[Kosaki et al., Radiat. Oncol. 7, 2012]

Main characteristics

- inverse depth-dose profile (Bragg peak)
- high ionization density (LET)
- reduced lateral scattering



Consequences

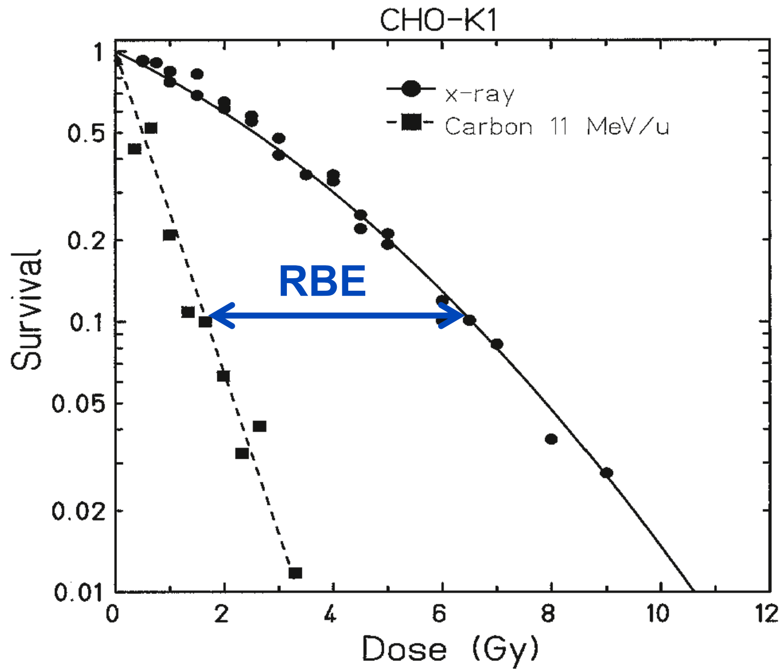
- superior dose conformity

Carbon ion radiotherapy

Main characteristics

- inverse depth-dose profile (Bragg peak)
- high ionization density (LET)
- reduced lateral scattering

[Weyrather et al., Radiother. Oncol. 73, 2004]



Consequences

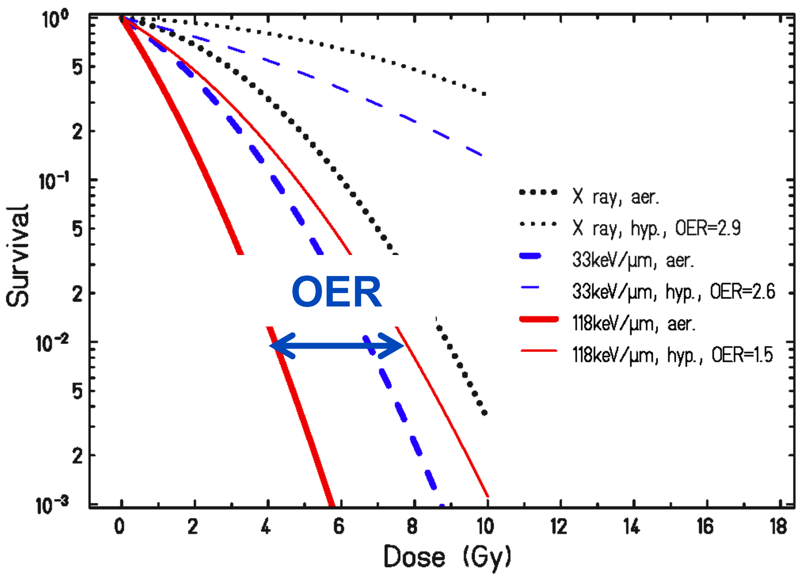
- superior dose conformity
- enhanced relative biological effectiveness (RBE)

Carbon ion radiotherapy

Main characteristics

- inverse depth-dose profile (Bragg peak)
- high ionization density (LET)
- reduced lateral scattering

[data: Blakely et al., Radiat. Res. 80, 1979]
[plot: Schardt et al., Rev. Mod. Phys. 82, 2010]



Consequences

- superior dose conformity
- enhanced relative biological effectiveness (RBE)
- reduced oxygen enhancement ratio (OER)

Carbon ion radiotherapy

Main characteristics

- inverse depth-dose profile (Bragg peak)
- high ionization density (LET)
- reduced lateral scattering

Consequences

- superior dose conformity
- enhanced relative biological effectiveness (RBE)
- reduced oxygen enhancement ratio (OER)

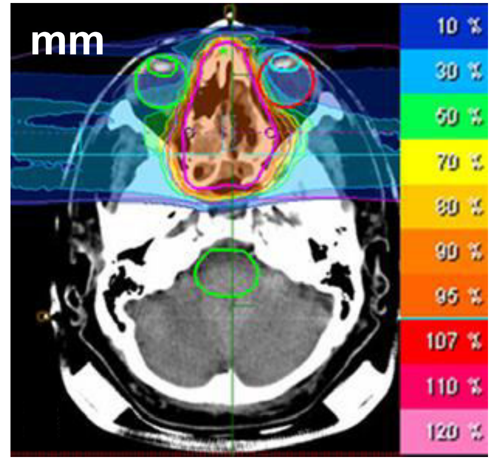
Expected clinical benefits

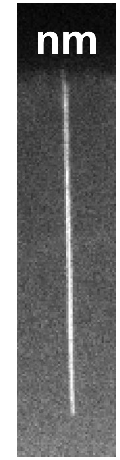
- sparing of critical structures
- higher local control for
  - (a) radioresistant, slow-growing tumors
  - (b) hypoxic tumors

Gradients in energy deposition

Main characteristics

- inverse depth-dose profile (Bragg peak)
- high ionization density (LET)
- reduced lateral scattering





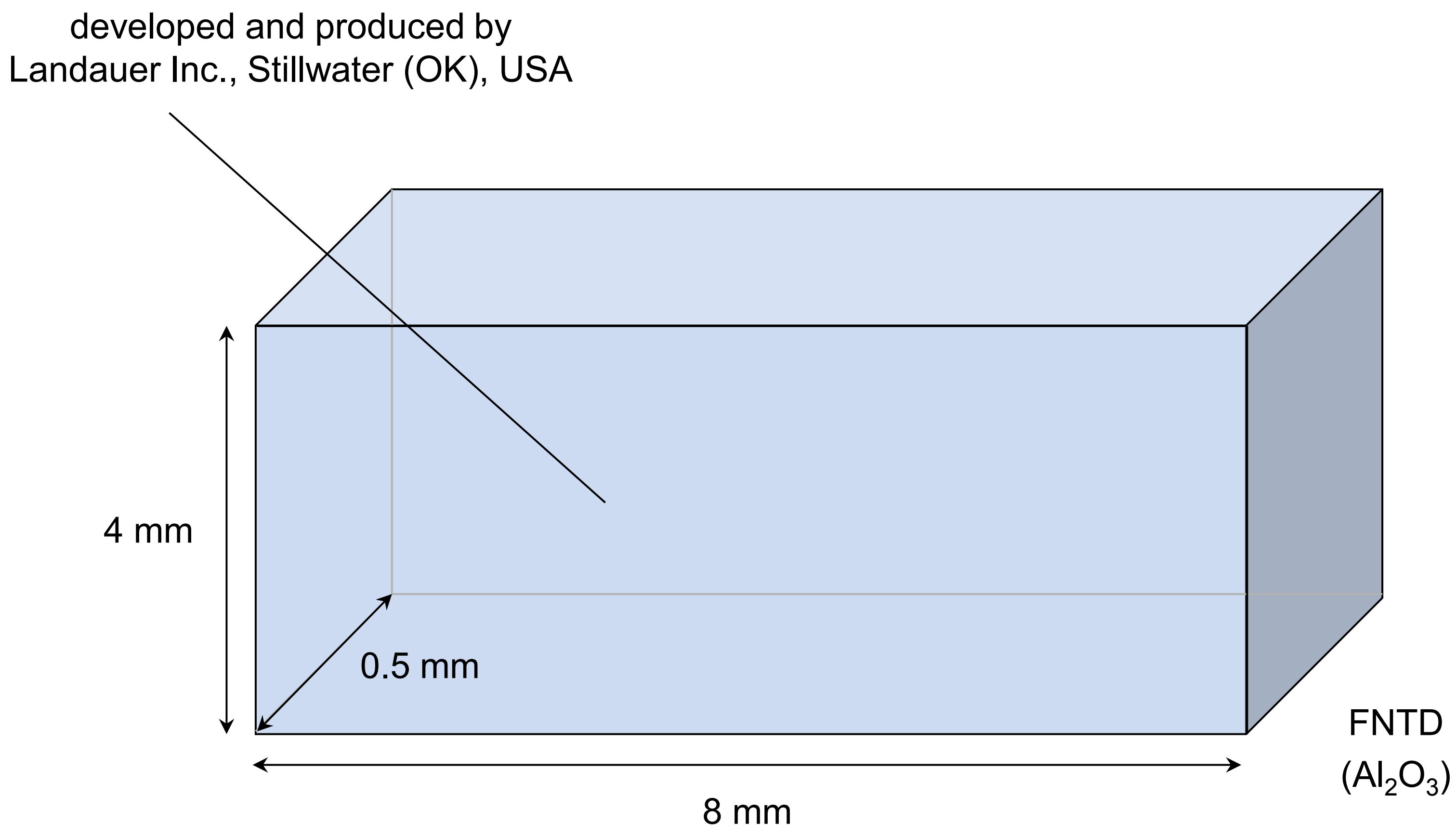
Large dose gradients on mm and nm scale

Ion-beam therapy research requires detectors that function on both scales.

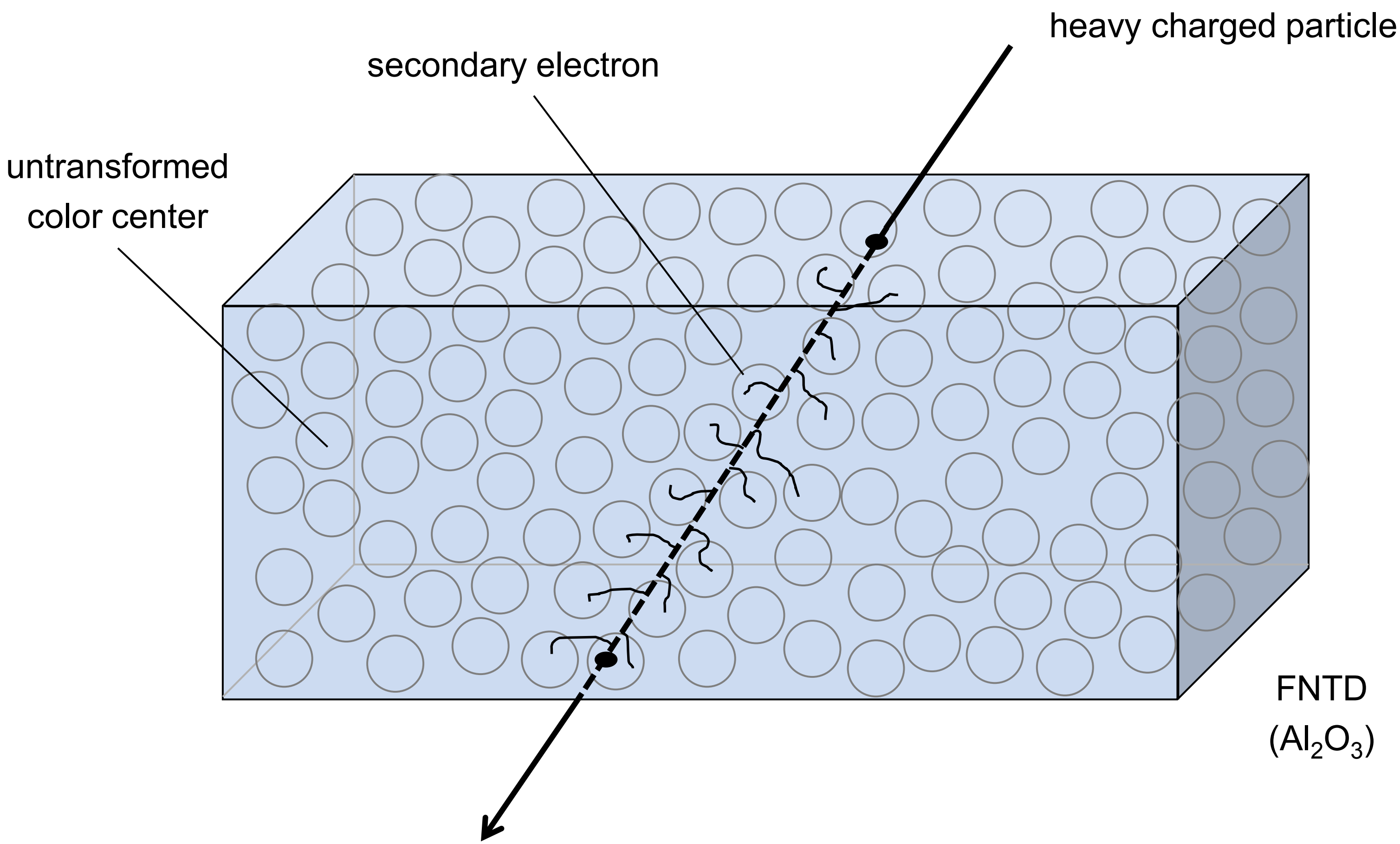
INTRODUCTION

Detector principle

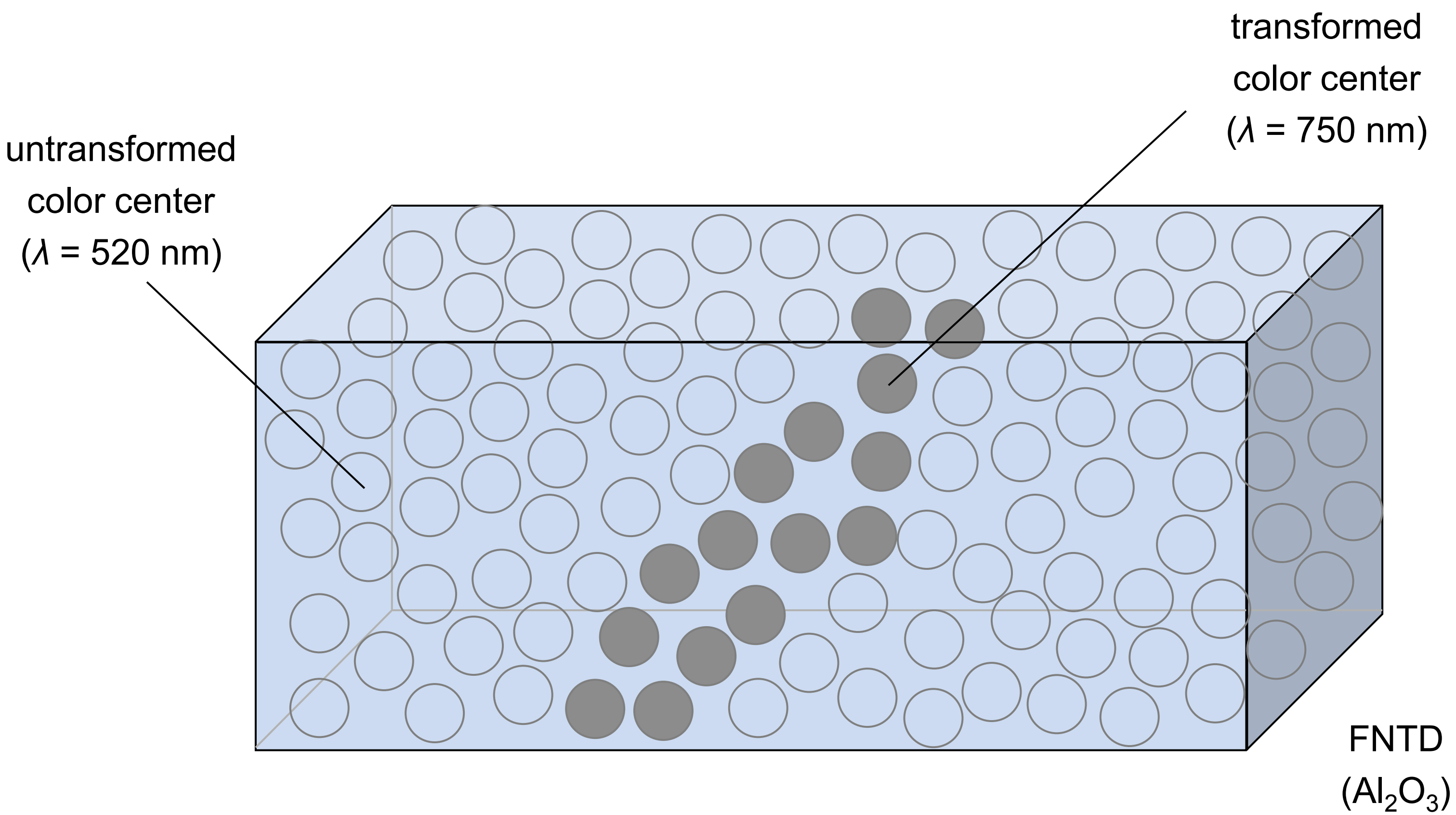
FNTD technology



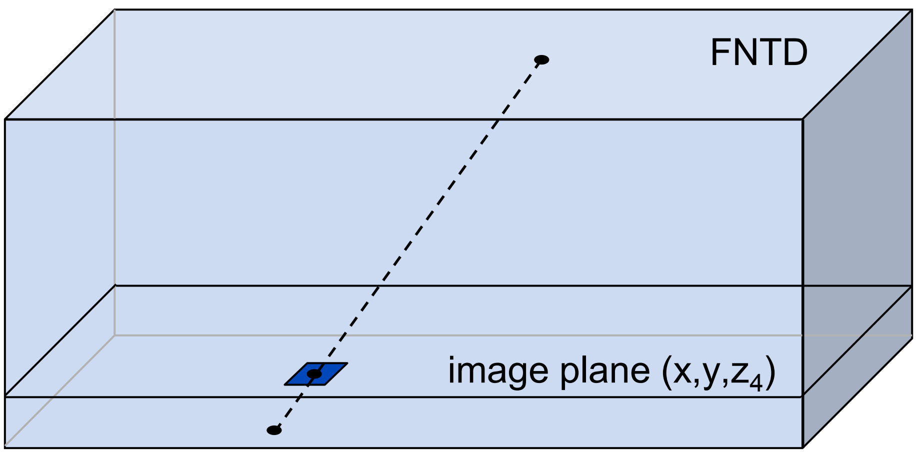
FNTD technology



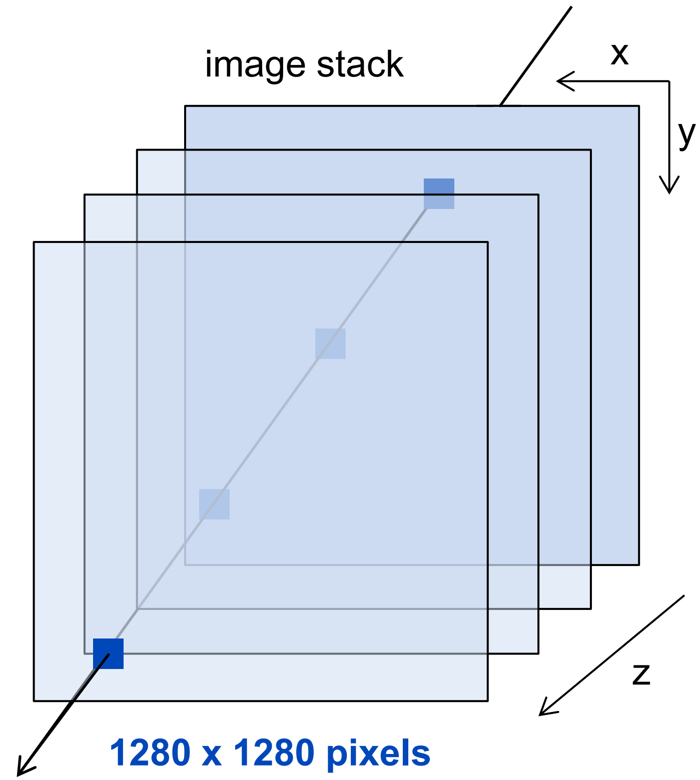
FNTD technology



Readout principle



- detector stores trajectory information of traversing ions
- access information via confocal microscopy
  - scan focus plane laterally
  - change focus depth
- image stack contains full 3D information on individual ion tracks

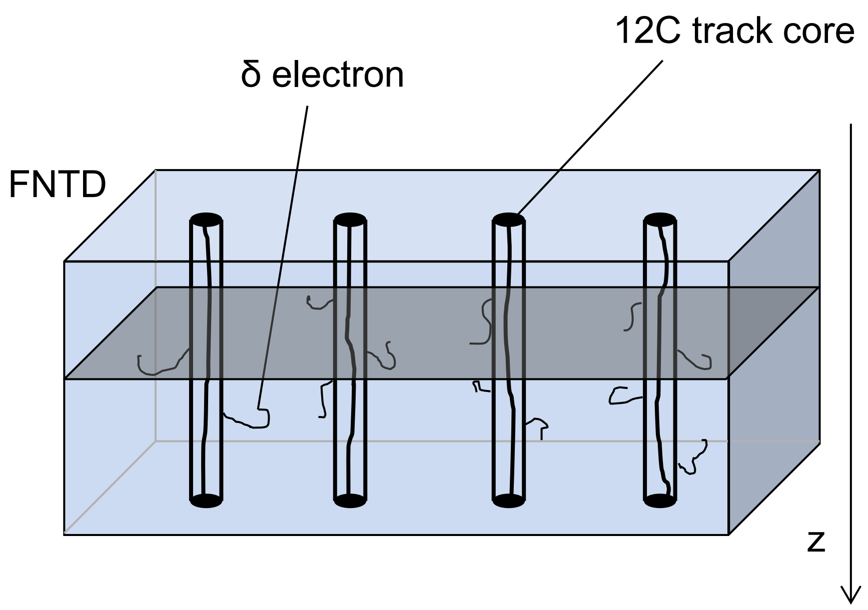


1280 x 1280 pixels
135 x 135 µm²
21 slices (Δz = 2 µm)

Unidirectional field

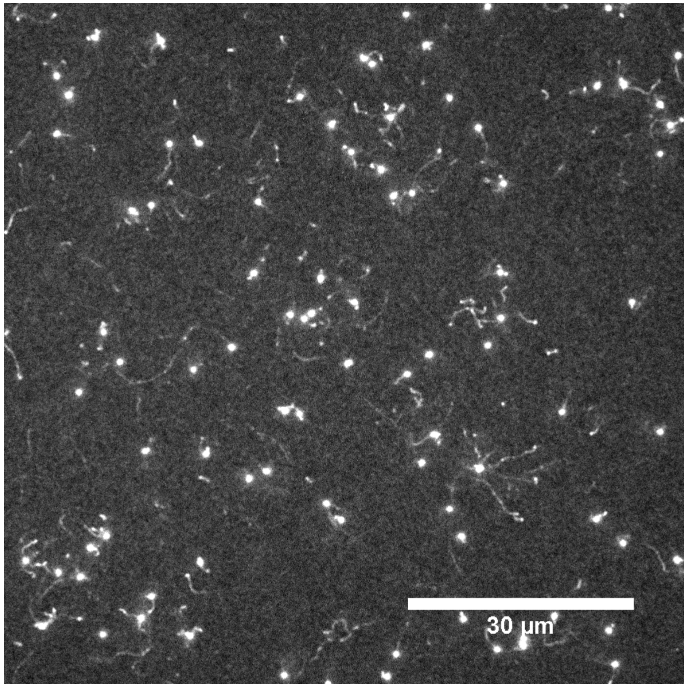
12C irradiation

(entrance channel)



FNTD readout

(Zeiss LSM 710)



I

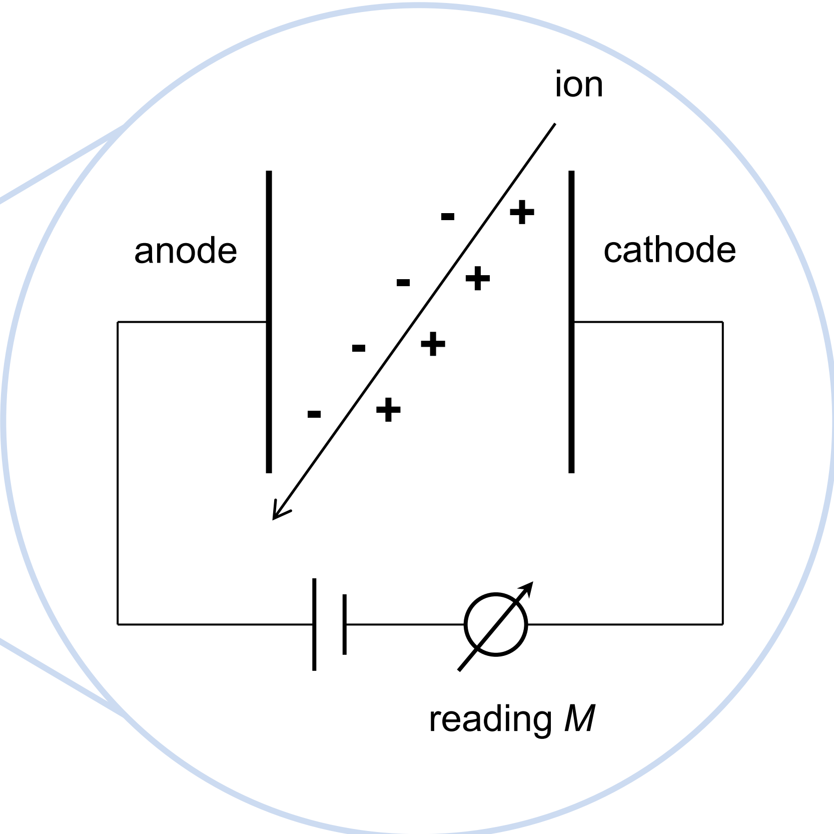
1st APPLICATION

Particle counter

project of J.-M. Osinga

Quality assurance and verification

ionization chamber



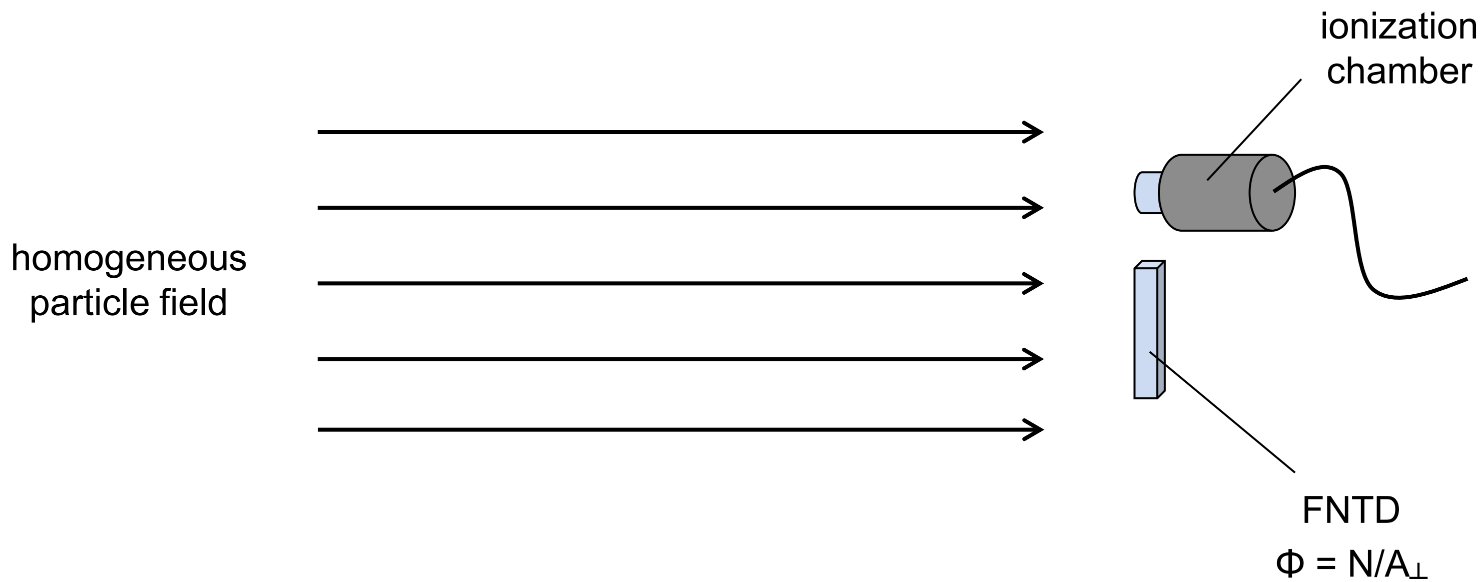
dose to water:

$$D_{IC} = \underbrace{M_{Q,k_i}}_{\text{reading}} \times \underbrace{N_{D,Q_0}}_{\text{calibration}} \times \underbrace{\boldsymbol{k_{Q,Q_0}}}_{\text{correction}}$$

~ 3% uncertainty for carbon ions

Comparison experiment

Novel fluence-based dosimetry approach



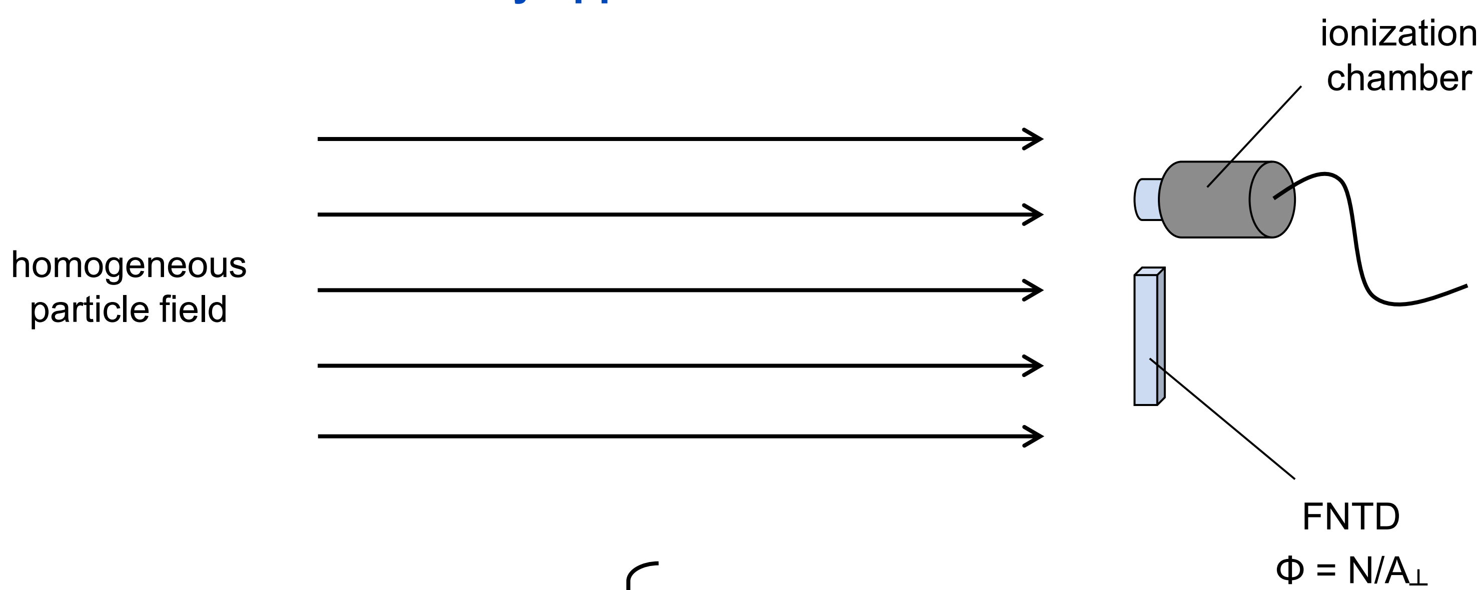
$$D_{FNTD} = \frac{1}{\rho}\,\Phi\,S_{eff}$$

nuclear interactions:

- **protons:** energy straggling and target fragmentation
- **carbon ions:** projectile fragmentation; build-up of lower-*Z* secondary ions

Comparison experiment

Novel fluence-based dosimetry approach



$$\Delta = \frac{D_{IC} - D_{FNTD}}{D_{IC}}$$

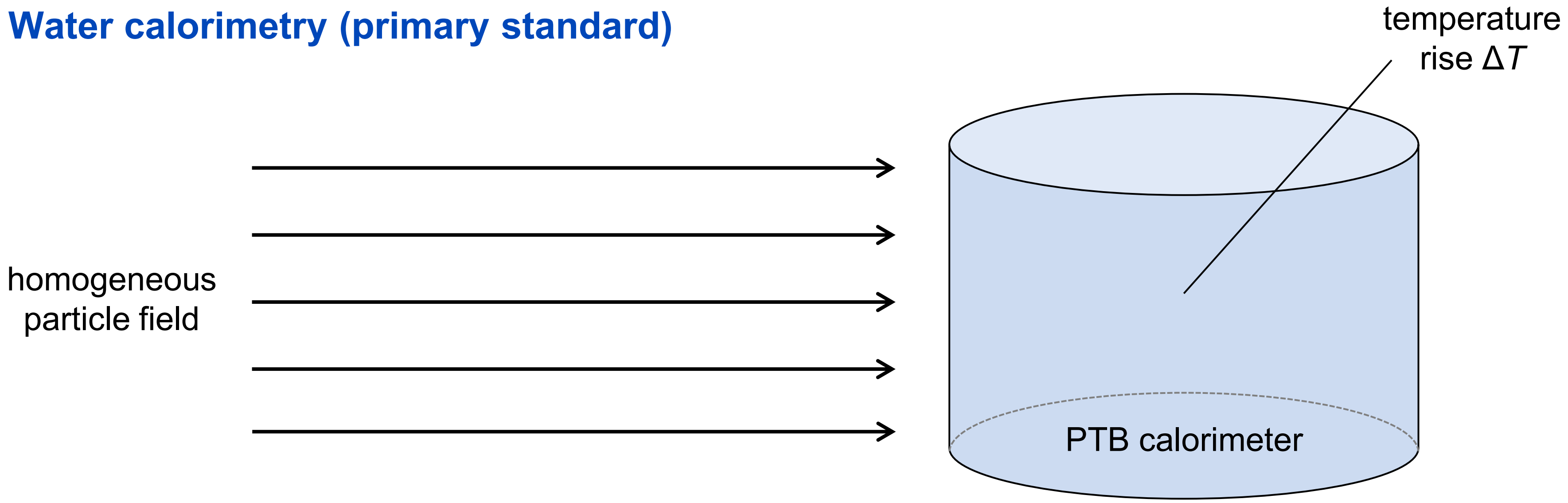
- **protons:** $\Delta_p = +2.4\%$
- **carbons:** $\Delta_C = +4.5\%$

k_Q uncertainty?

[Osinga et al., Radiat. Prot. Dosim., 2014]

Direct determination of k_Q

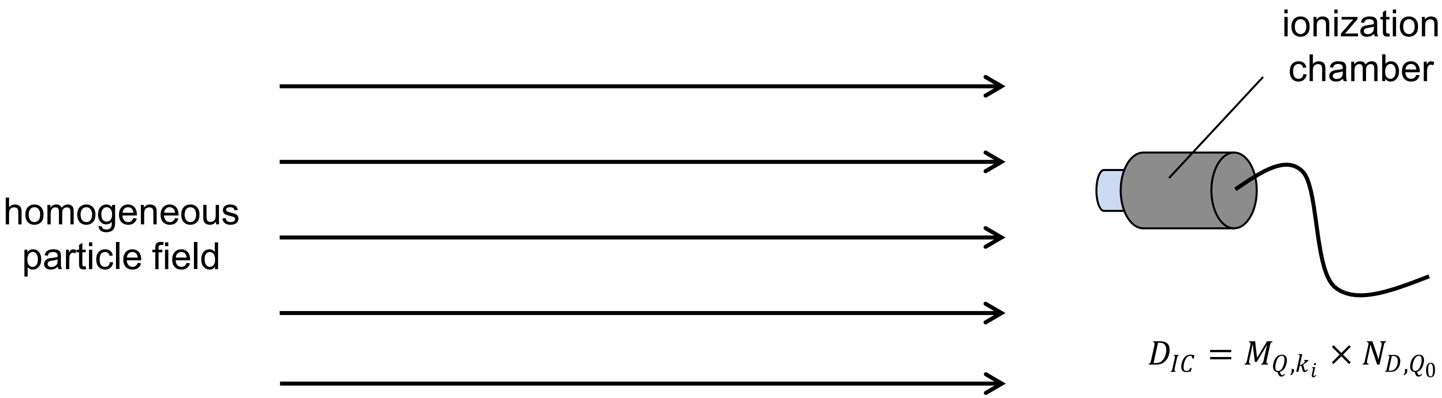
Water calorimetry (primary standard)



$$D_{WC} = \Delta T \, c_P \, \prod_i k_i$$

Direct determination of k_Q

Water calorimetry (primary standard)



$$D_{IC} = M_{Q,k_i} \times N_{D,Q_0} \times k_{Q,Q_0}$$

$$D_{WC} = \Delta T \; c_P \; \prod_i k_i = D_{IC}$$

$$k_{Q,Q_0} = \frac{D_{WC}}{M_{Q,k_i} \times N_{D,Q_0}}$$

II

2nd APPLICATION

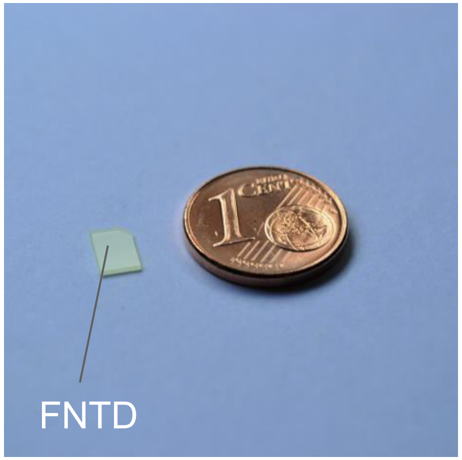
In vivo dosimeter

project of G. Klimpki

Measurement principle

with fluorescent nuclear track detectors (FNTDs):

- measure dose *in vivo*
- estimate biological effect



measured quantities: $D_{biol} = f(\Phi, S, Z)$

particle fluence Φ

calculated from

normalized particle number $N/A_\perp$

stopping power *S*

calculated from

track intensity *I*

atomic number *Z*

attributed to

track intensity distribution

$$D_{biol} = f(\Phi, S, Z)$$

(a) particle fluence Φ

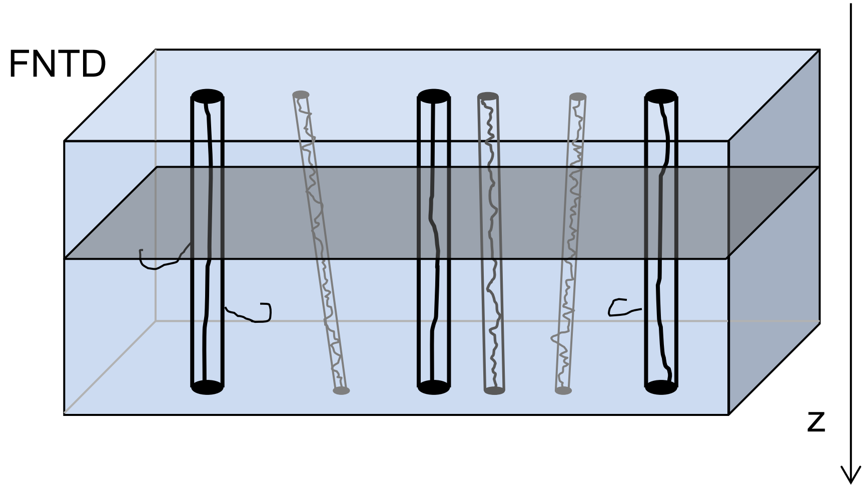
(b) stopping power S

(c) atomic number Z

Multidirectional field

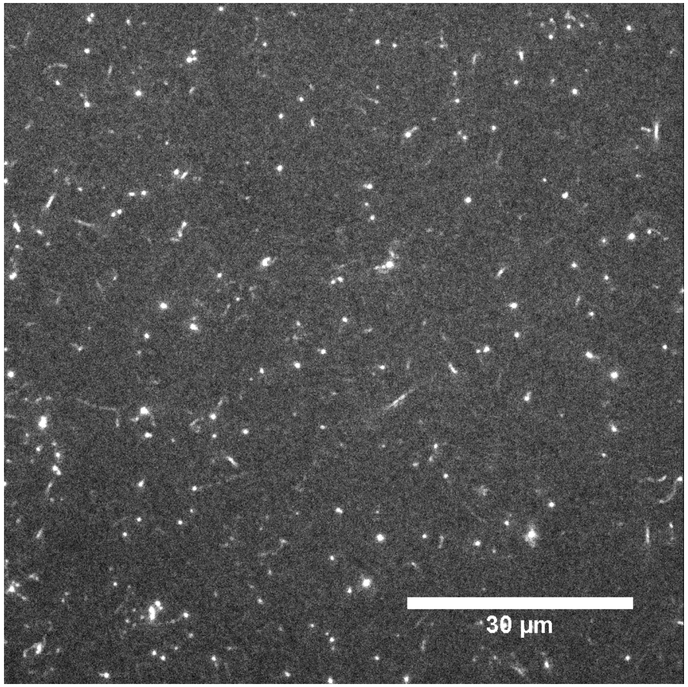
12C irradiation

(Bragg peak)



FNTD readout

(Zeiss LSM 710)



Proof of principle

Irradiation

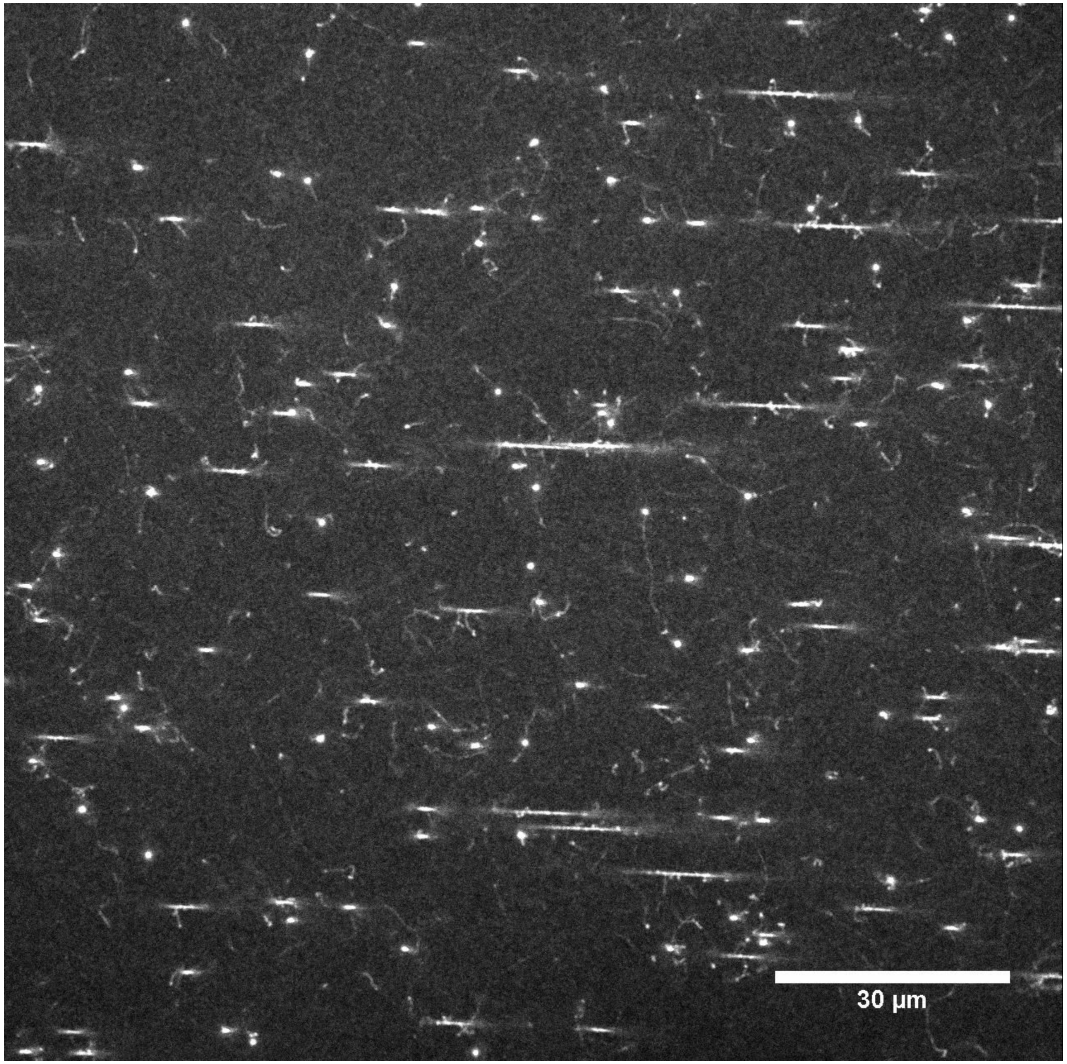
Heidelberg Ion-Beam Therapy Center

1 detector under 6 angles:
(ϑ = 0°, 15°, 30°, 45°, 60°, 75°)

- ion type: 12C
- energy: 90 MeV/u
- total fluence:
  1.2×10^6 cm^{-2}

Readout

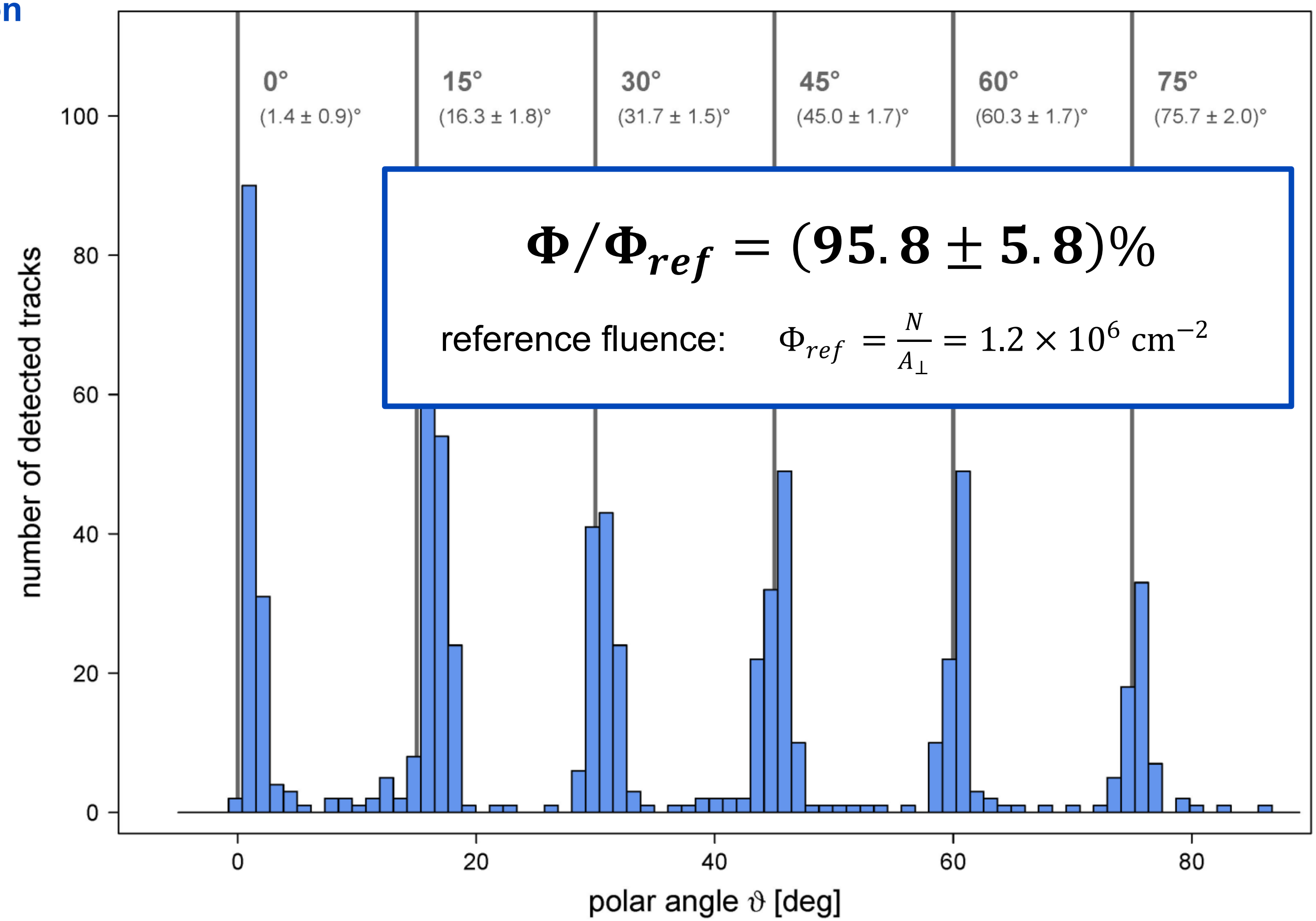
Zeiss LSM 710 microscope (30 min)



Angular distribution

ϑ histogram

701 carbon ion trajectories



$$\boldsymbol{\Phi/\Phi_{ref} = (95.8 \pm 5.8)\%}$$

reference fluence: $\Phi_{ref} = \frac{N}{A_\perp} = 1.2 \times 10^6\ \mathrm{cm}^{-2}$

$$D_{biol} = f(\boldsymbol{\Phi}, S, Z)$$

(a) particle fluence Φ

(b) stopping power S

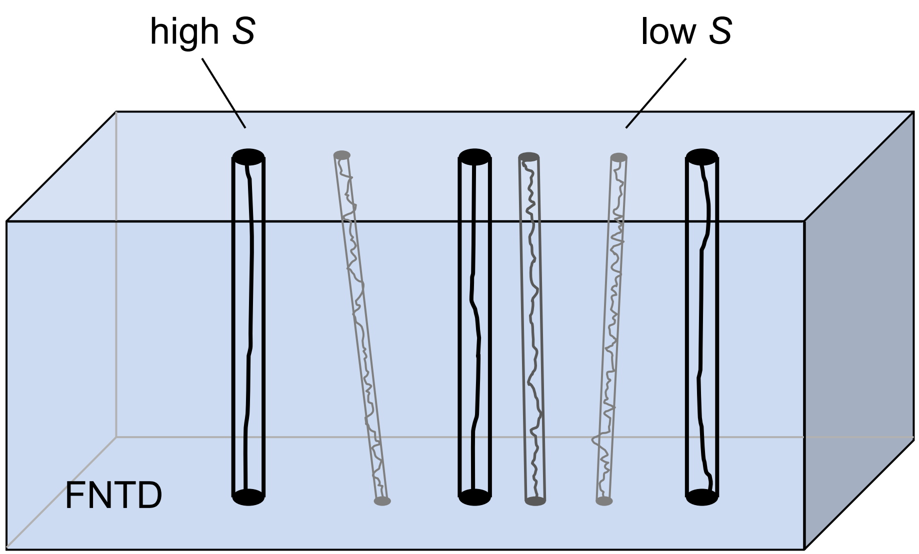
(c) atomic number Z

Stopping power determination

FNTD in mixed field

- high linear stopping power
- large number of secondary electrons
- large number of transformed color centers
- high local track intensity

[Sykora et al., Radiat. Meas. 43, 2008]



correlate stopping power and intensity

list of limitations:

- **FNTD:** detector sensitivity fluctuations; …
- **PHYSICS:** stochastic energy deposition; intensity loss of angular tracks; intensity measurements itself (maximum, Gauss peak, mean); …
- **MICROSCOPE:** flat field correction; spherical aberration; …

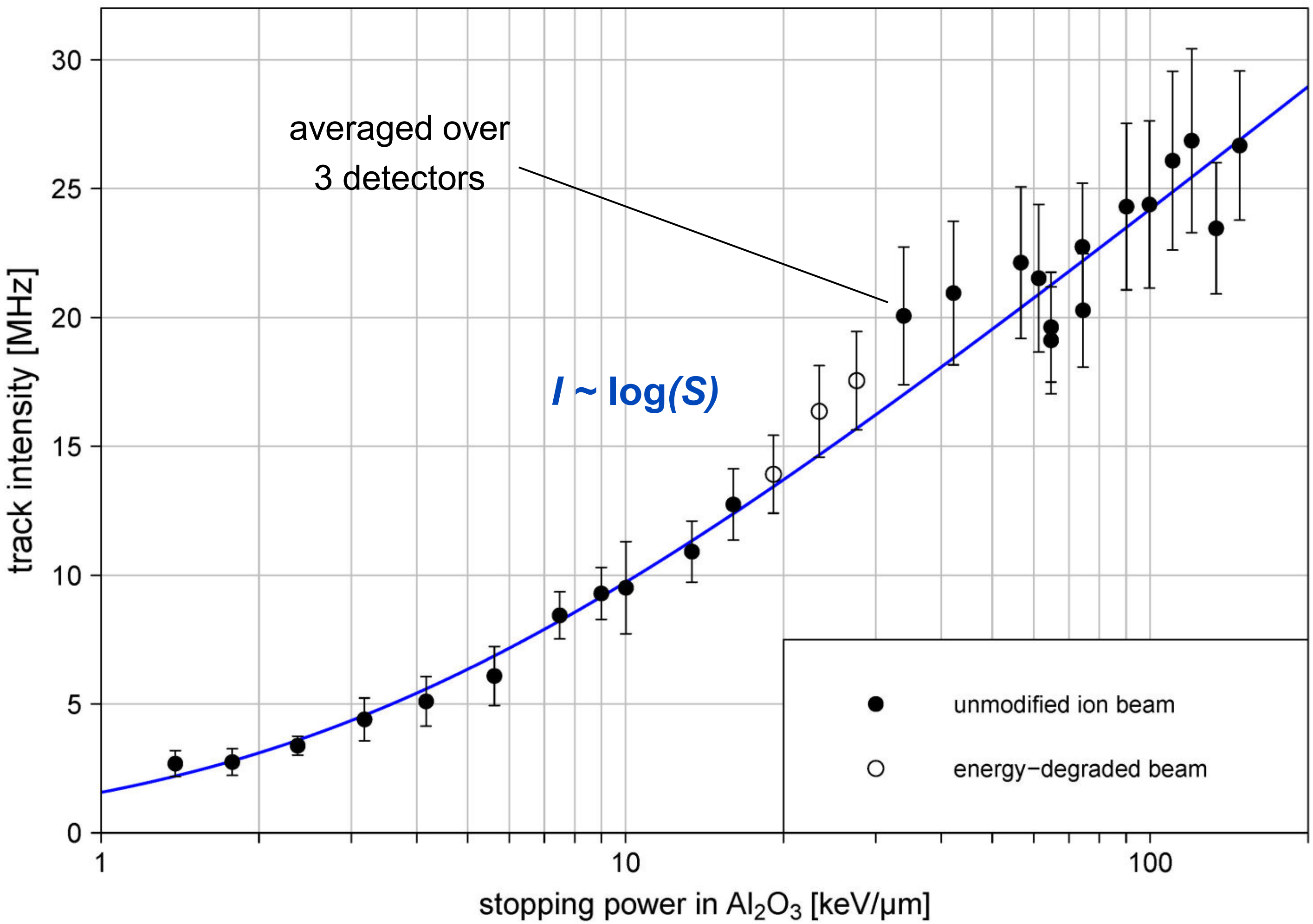
Calibration curve

dkfz.
50 Years – Research for A Life Without Cancer

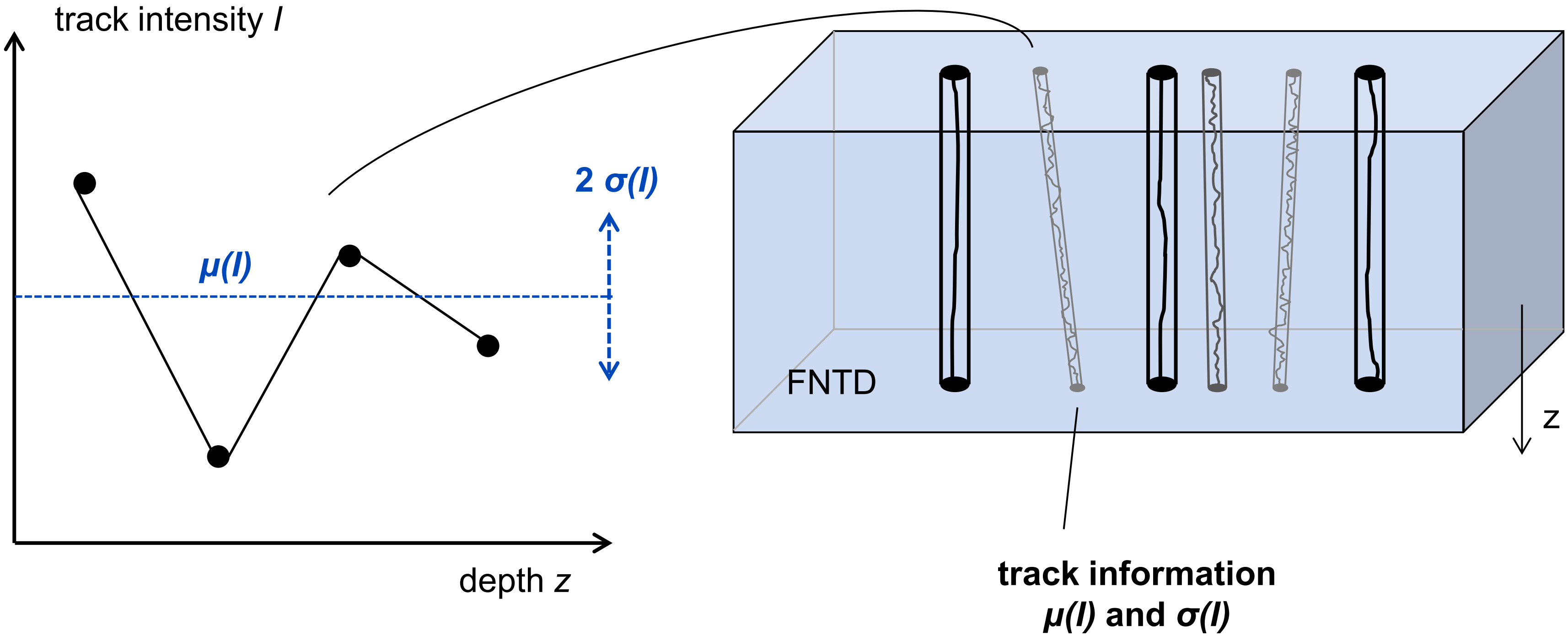
***I* ~ *S* plot**

based on 28 irradiations

[H. Mescher, Bachelor's Thesis, DKFZ, 2014]



Sensitivity correction

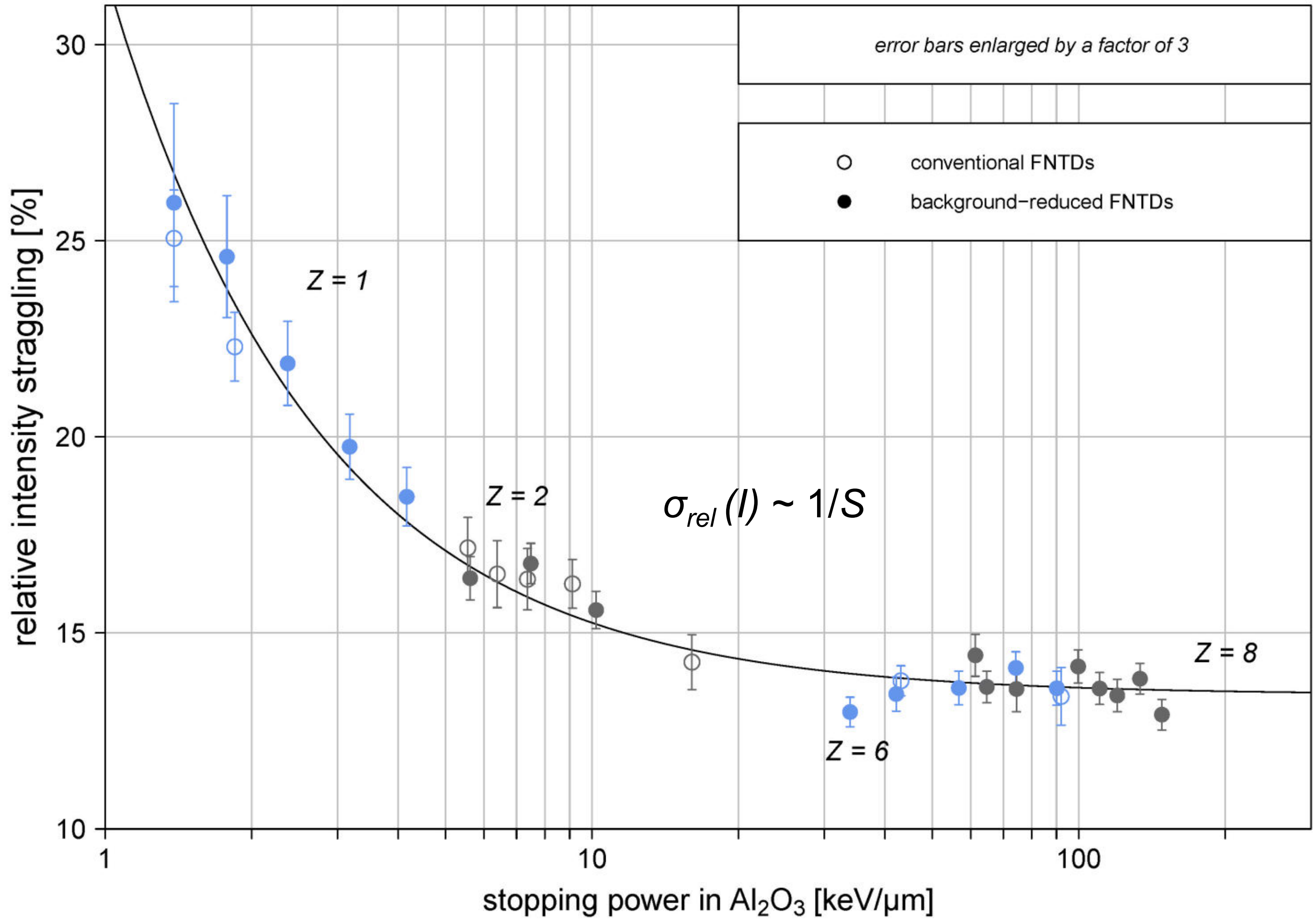


$$\sigma_{rel}(I) = f(S, Z, \ldots)?$$

Relative intensity straggling

$\sigma_{rel}(I) \sim S$ plot

based on 31 irradiations



$$D_{biol} = f(\Phi, S, Z)$$

(a) particle fluence Φ

(b) stopping power S

(c) atomic number Z

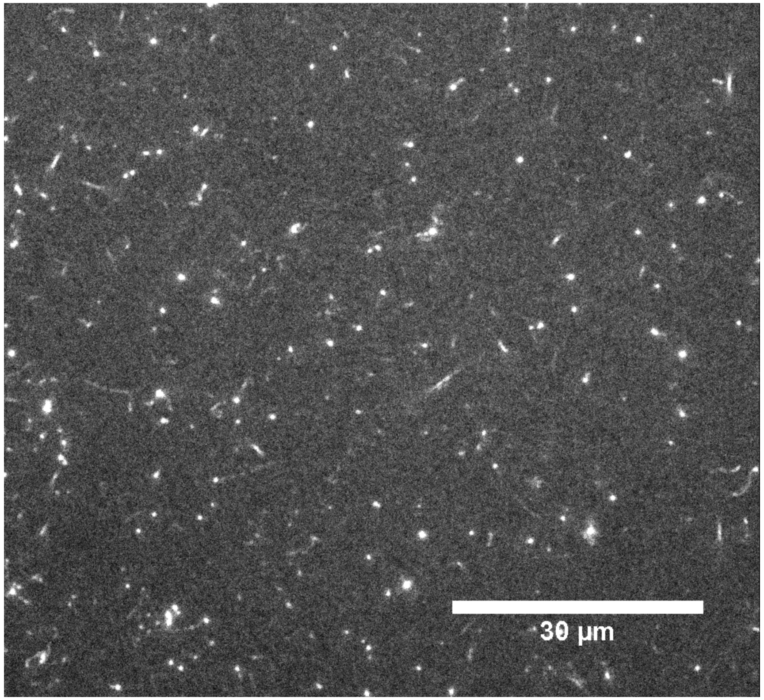
Charge spectroscopy

1. correlate *Z* and track width

↓

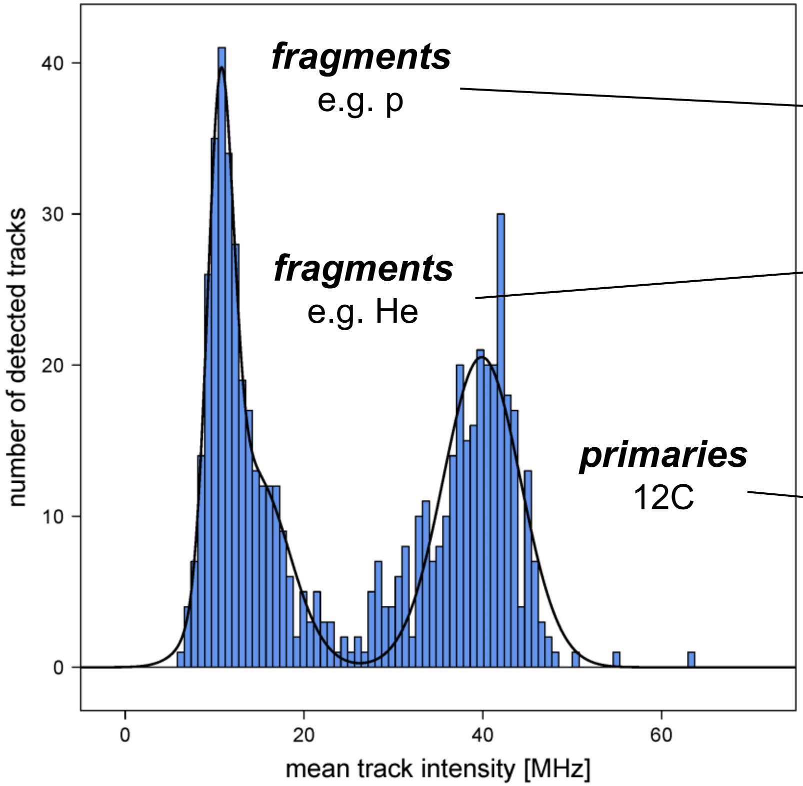
information on track width lost
during confocal readout
[Niklas et al., Radiat. Meas. 56, 2013]

FNTD placed in mixed heavy ion field

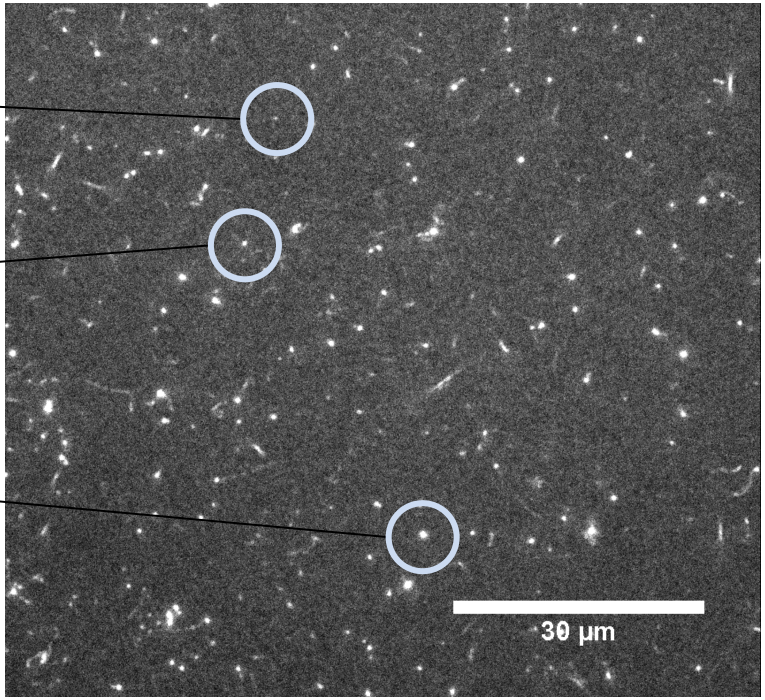


Charge spectroscopy

2. attribute *Z* to intensity spectrum



FNTD placed in mixed heavy ion field



Charge spectroscopy

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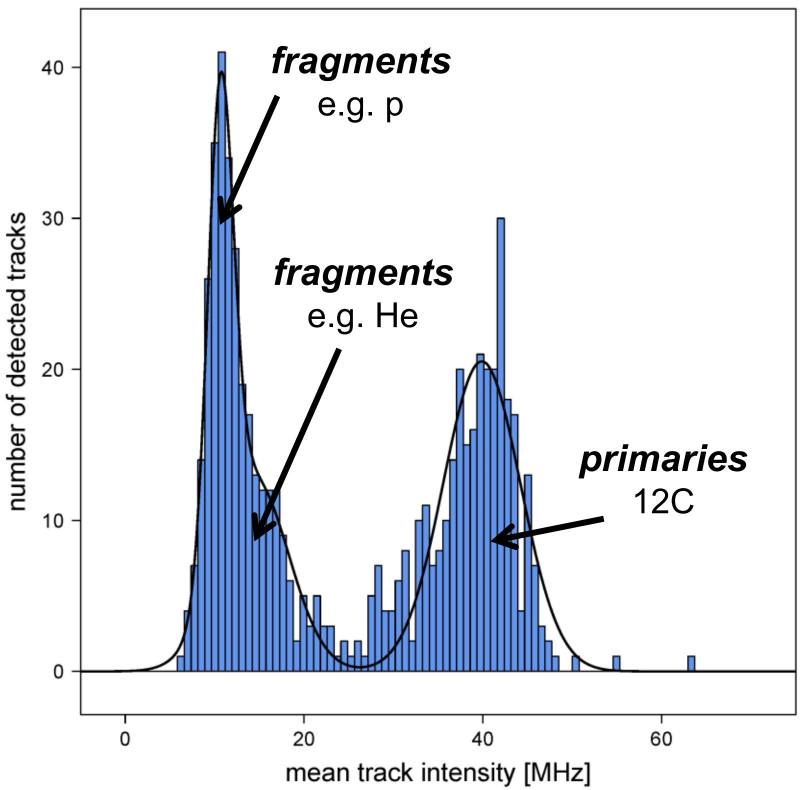
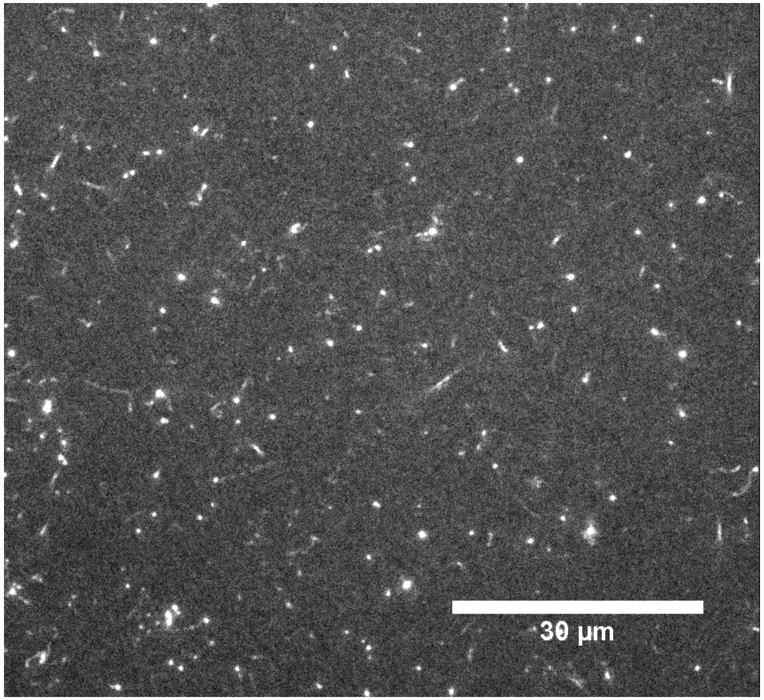


FNTD placed in mixed heavy ion field



⇨ attribution feasible if knowledge on primary beam is available

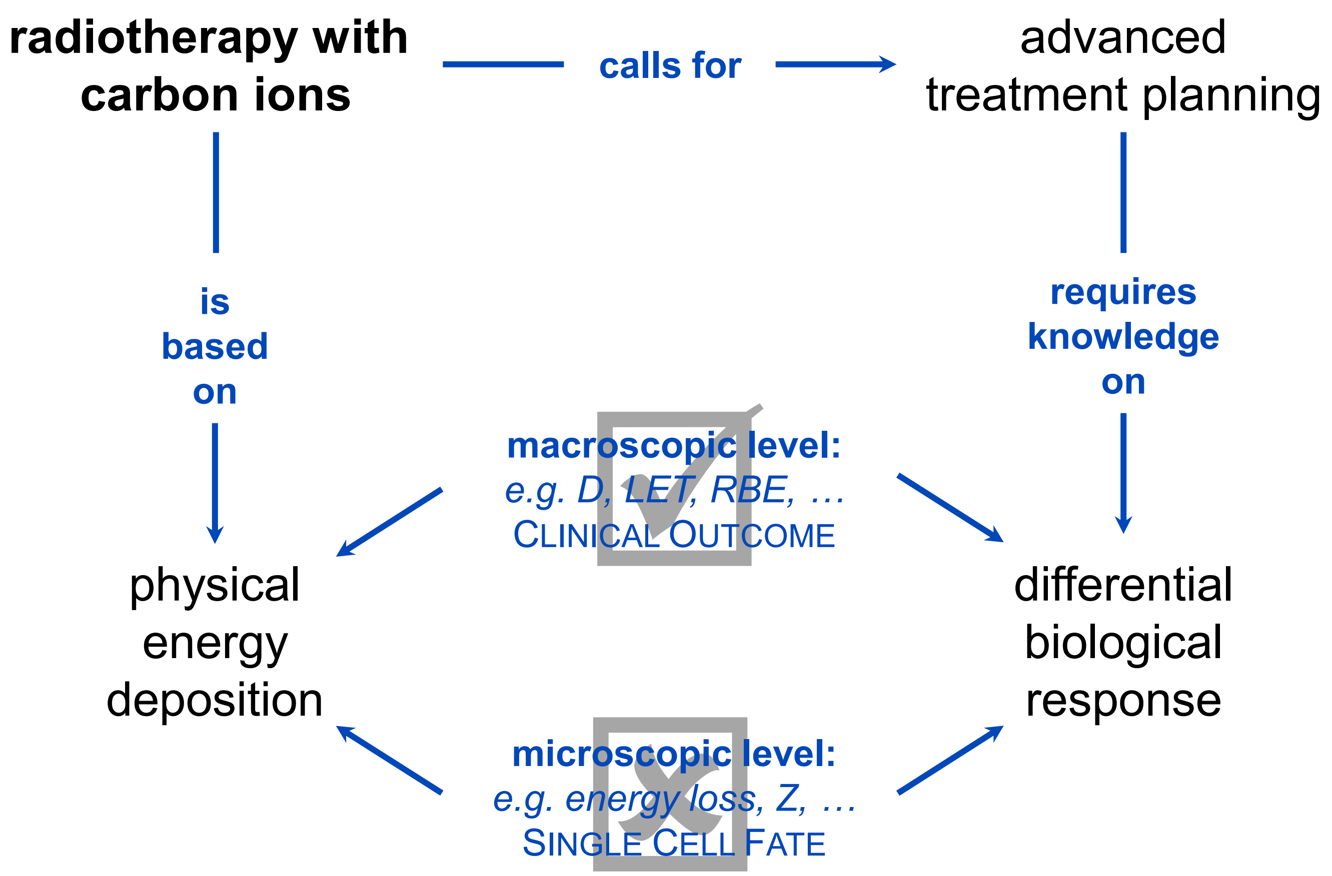
III

3^{rd} APPLICATION

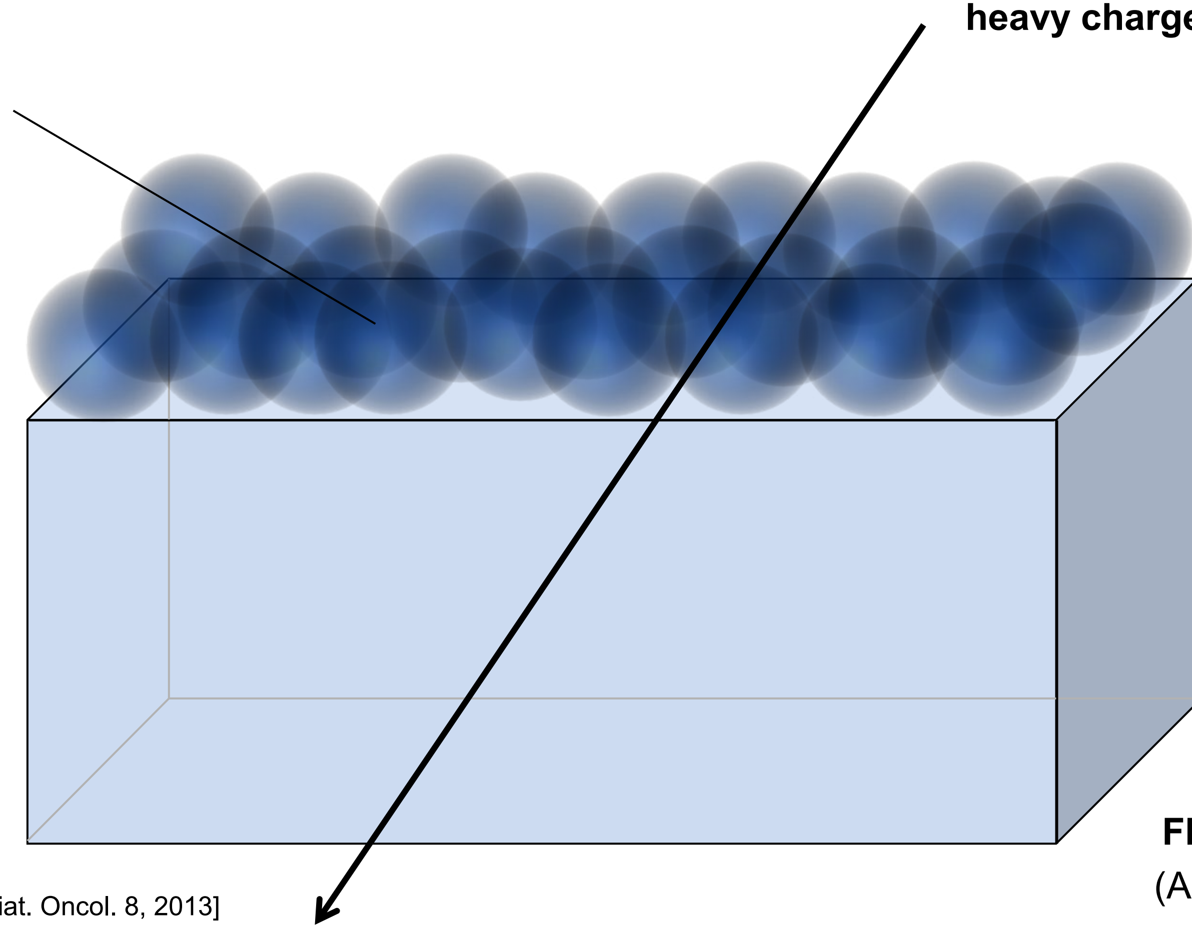
Hybrid detector

project of M. Niklas

Fundamental principle of ion RT

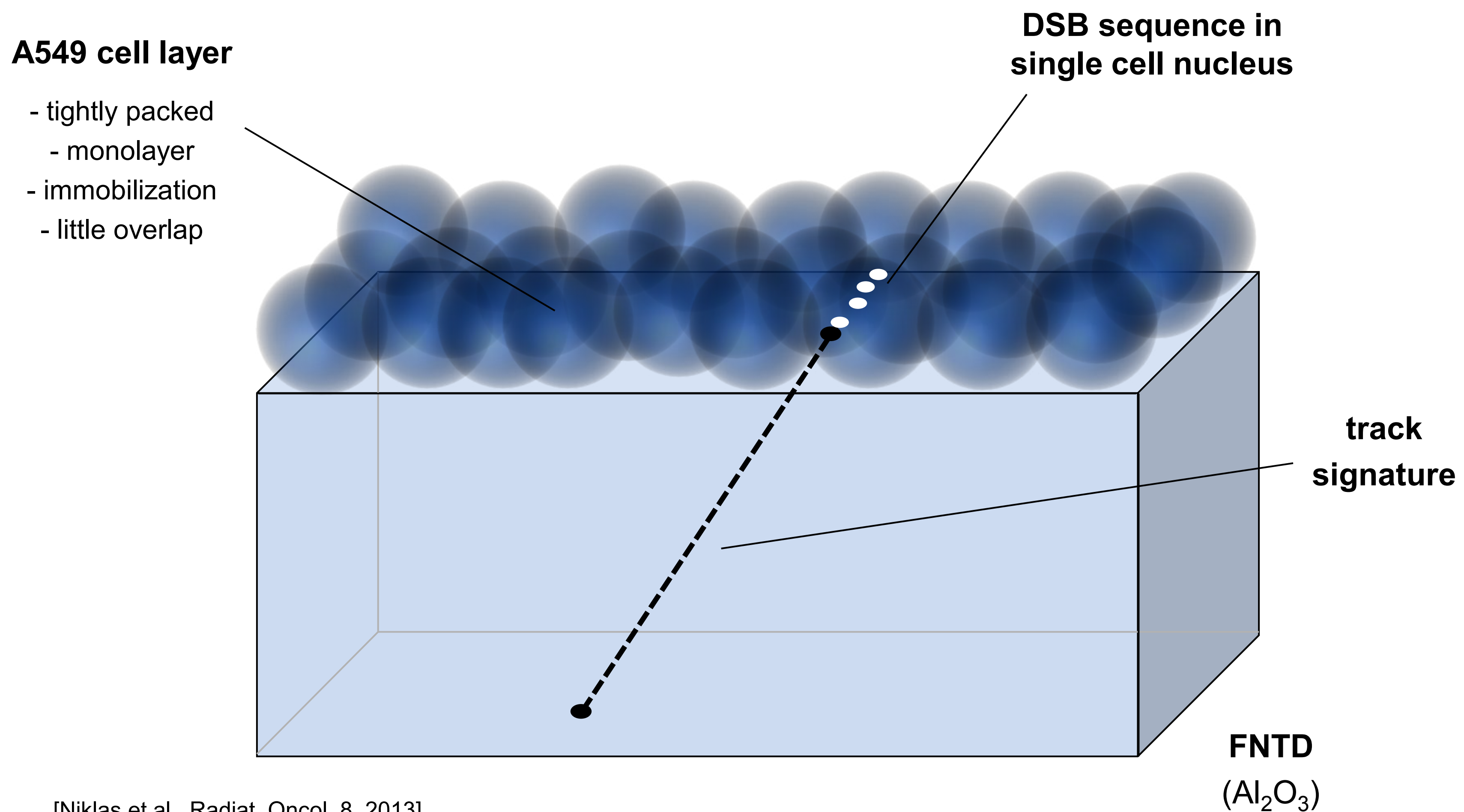


Hybrid detector system



[Niklas et al., Radiat. Oncol. 8, 2013]

Hybrid detector system



[Niklas et al., Radiat. Oncol. 8, 2013]

Detected DSB sequences

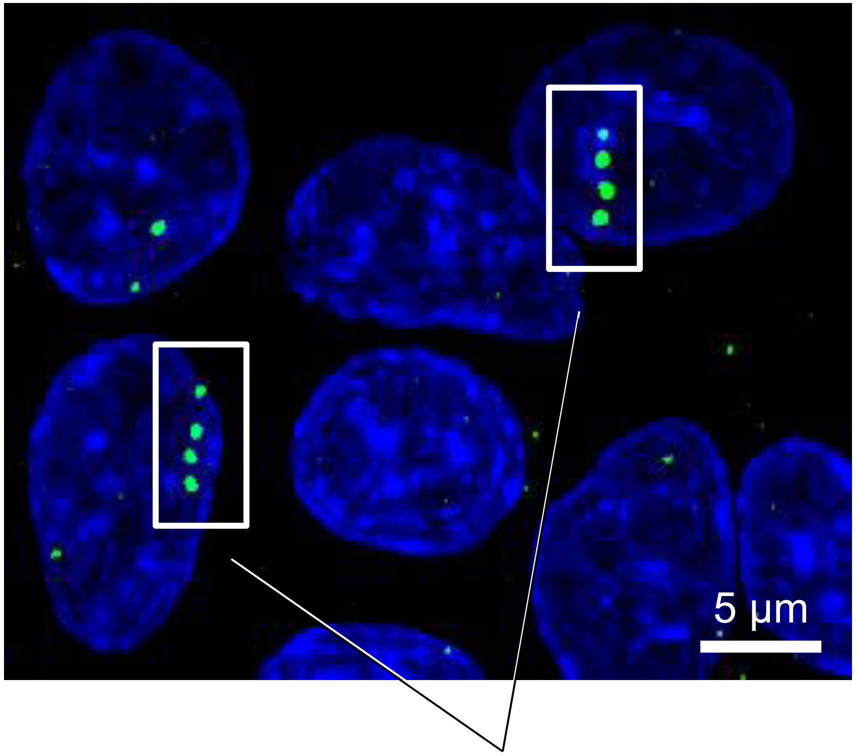
Experiment overview

- irradiation with 270 MeV/u carbon ions
- 360 analyzed cells
- 100 detected nucleus hits
- 16 DSB sequences

↓

correlation of all DSB sequences to ion tracks

[Niklas et al., Int. J. Radiat. Oncol. 87, 2013]



SUMMARY

and outlook

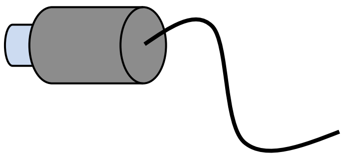
Summary

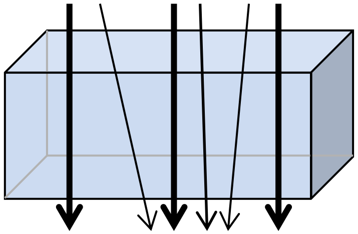
I

1st APPLICATION

FNTDs as particle counters

J.-M. Osinga





II

2nd APPLICATION

FNTDs as in vivo dosimeters

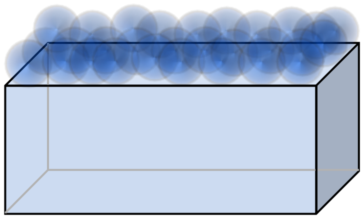
G. Klimpki

III

3rd APPLICATION

FNTDs as hybrid detectors

M. Niklas



Thank you for your attention!

dkfz. GERMAN CANCER RESEARCH CENTER IN THE HELMHOLTZ ASSOCIATION

50 Years – Research for A Life Without Cancer