Fluorescent nuclear track detectors as a tool for ion-beam therapy research

Grischa M. Klimpki\textsuperscript{1,2}, J.-M. Osinga\textsuperscript{1,3}, M. Niklas\textsuperscript{1}, H. Mescher\textsuperscript{1,2}, O. Jäkel\textsuperscript{1}, S. Greilich\textsuperscript{1}

\textsuperscript{1} German Cancer Research Center, Heidelberg, Germany
\textsuperscript{2} University of Heidelberg, Department of Physics and Astronomy, Heidelberg, Germany
\textsuperscript{3} Physikalisch-Technische Bundesanstalt (PTB), Braunschweig, Germany
Photons or charged particles?

Conventional radiotherapy

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

Particle therapy

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

- inverse depth-dose profile (Bragg peak)

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

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

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

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

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

Consequences

- superior dose conformity
Main characteristics

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

Consequences

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

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

[data: Blakely et al., Radiat. Res. 80, 1979]
[plot: Schardt et al., Rev. Mod. Phys. 82, 2010]
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
developed and produced by Landauer Inc., Stillwater (OK), USA

FNTD (Al$_2$O$_3$)

8 mm

4 mm

0.5 mm
FNTD technology

untransformed color center

secondary electron

heavy charged particle

FNTD (Al$_2$O$_3$)
FNTD technology

untransformed color center ($\lambda = 520 \text{ nm}$)

transformed color center ($\lambda = 750 \text{ nm}$)

FNTD ($\text{Al}_2\text{O}_3$)
• 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
Unidirectional field

12C irradiation
(entrance channel)

12C track core

δ electron

FNTD readout
(Zeiss LSM 710)

30 µm
1st APPLICATION

Particle counter

project of J.-M. Osinga
Quality assurance and verification

Ionization chamber

Dose to water:

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

~ 3% uncertainty for carbon ions
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
Novel fluence-based dosimetry approach

\[ \Delta = \frac{D_{IC} - D_{FNTD}}{D_{IC}} \]

- protons: \( \Delta_p = +2.4\% \)
- carbons: \( \Delta_C = +4.5\% \)

\[ k_Q \text{ uncertainty?} \]

Water calorimetry (primary standard)

\[ D_{WC} = \Delta T \ c_p \ \prod_{i} k_i \]
Direct determination of $k_Q$

Water calorimetry (primary standard)

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

$$k_{Q,Q_0} = \frac{D_{WC}}{M_{Q,k_i} \times N_{D,Q_0}}$$
2nd APPLICATION

In vivo dosimeter

project of G. Klimpki
with fluorescent nuclear track detectors (FNTDs):

- measure dose *in vivo*
- estimate biological effect

*measured quantities:*

\[ D_{\text{biol}} = f(\Phi, S, Z) \]

- **particle fluence** $\Phi$
  - calculated from
  - normalized particle number $N/A_L$

- **stopping power** $S$
  - calculated from
  - track intensity $I$

- **atomic number** $Z$
  - attributed to
  - track intensity distribution
\[ D_{\text{biol}} = f(\Phi, S, Z) \]

(a) particle fluence $\Phi$

(b) stopping power $S$

(c) atomic number $Z$
12C irradiation
(Bragg peak)

FNTD readout
(Zeiss LSM 710)
Irradiation
Heidelberg Ion-Beam Therapy Center

1 detector under 6 angles:
($\theta = 0^\circ, 15^\circ, 30^\circ, 45^\circ, 60^\circ, 75^\circ$)

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

Readout
Zeiss LSM 710 microscope (30 min)
Angular distribution

\[ \Phi / \Phi_{ref} = (95.8 \pm 5.8)\% \]

reference fluence: \[ \Phi_{ref} = \frac{N}{A_\perp} = 1.2 \times 10^6 \text{ cm}^{-2} \]
\[ D_{\text{biol}} = f(\Phi, S, Z) \]

- (a) particle fluence \( \Phi \)
- (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

$I \sim S$ plot
based on 28 irradiations

 averged over 3 detectors

$I \sim \log(S)$

[H. Mescher, Bachelor’s Thesis, DKFZ, 2014]
Sensitivity correction

\[ \sigma_{rel}(I) = f(S, Z, ...) \]

track intensity \( I \)

depth \( z \)

\( \mu(I) \)

\( 2 \sigma(I) \)

track information \( \mu(I) \) and \( \sigma(I) \)

FNTD
Relative intensity straggling

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

based on 31 irradiations

$\sigma_{rel}(I) \sim 1/S$
\[ D_{\text{biol}} = f(\Phi, S, Z) \]

- (a) particle fluence \( \Phi \)
- (b) stopping power \( S \)
- (c) atomic number \( Z \)
1. correlate $Z$ and track width

information on track width lost during confocal readout

2. attribute Z to intensity spectrum

- **fragments**
  - e.g. p

- **fragments**
  - e.g. He

- **primaries**
  - 12C

FNTD placed in mixed heavy ion field

![Graph showing track intensity](image)
2. attribute $Z$ to intensity spectrum

The image shows a histogram of mean track intensity [MHz] against the number of detected tracks. The histogram is divided into three sections:

- **Fragments**: e.g., $p$
- **Fragments**: e.g., He
- **Primaries**: $^{12}\text{C}$

The attribution is feasible if knowledge on the primary beam is available.
3rd APPLICATION

Hybrid detector

project of M. Niklas
radiotherapy with carbon ions

is based on

physical energy deposition

calls for

advanced treatment planning

requires knowledge on

macroscopic level:
e.g. D, LET, RBE, ...
CLINICAL OUTCOME

differential biological response

microscopic level:
e.g. energy loss, Z, ...
SINGLE CELL FATE
A549 cell layer
- tightly packed
- monolayer
- immobilization
- little overlap

[Niklas et al., Radiat. Oncol. 8, 2013]
A549 cell layer
- tightly packed
- monolayer
- immobilization
- little overlap

DSB sequence in single cell nucleus

track signature

FNTD
\((\text{Al}_2\text{O}_3)\)

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