Online monitoring of ion-beam therapy based on secondary-ion tracking

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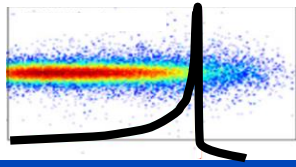
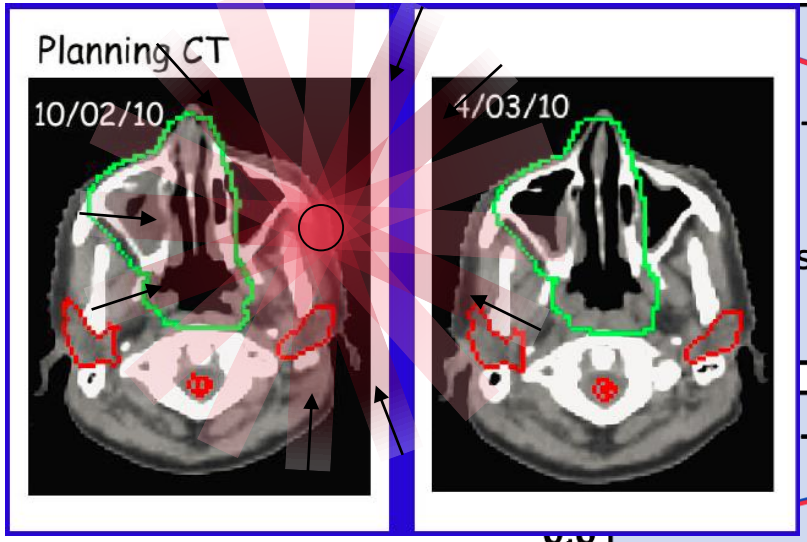
Several slides in courtesy of: Dr. Maria Martisikova, Renato Felix, Laura Ghesquiere

Outline



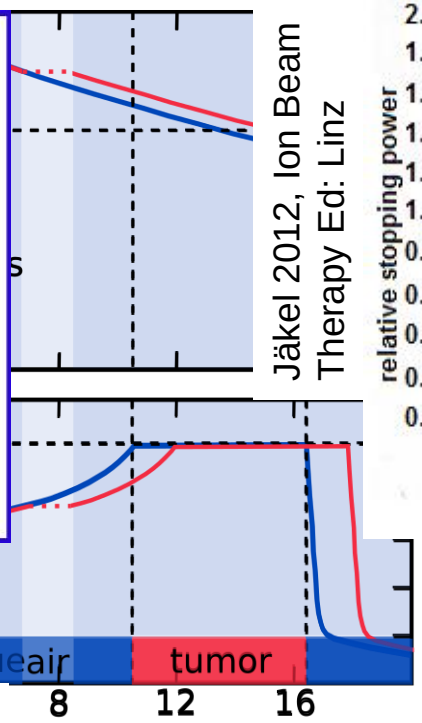
- **The motivation for online monitoring in the field of IBR**
- **Concept of using secondary radiation as treatment monitoring**
- **Material & Methods: HIT facility, detectors, Timepix & Timepix3**
- **Secondary-ion tracking: - results of different set-ups, geometries & reconstructions**

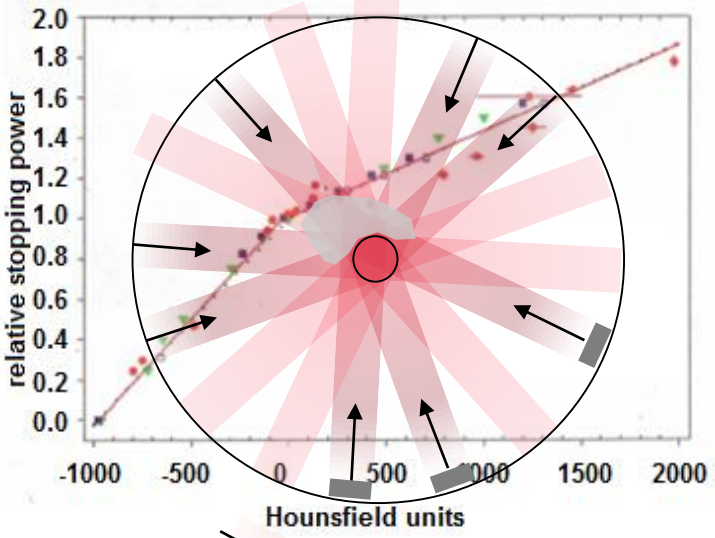
Ion-beam radiotherapy
Advantage and challenge

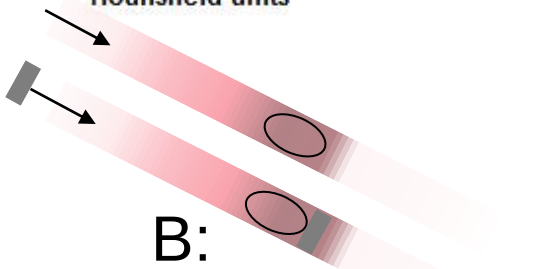


F. Albertini, A. Bolsi,
T. Lomax (PSI)

A







B:

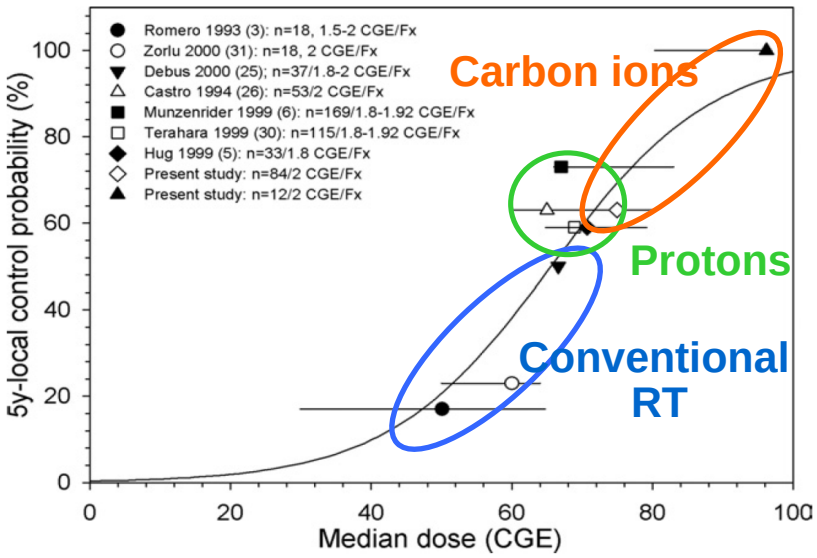
e uncertainties: ~ +3.5% / +1.2 mm

.1); Yang 2012, Phys. Med. Biol. 57(13)]

ious **conversion** from **CT-HU to RSP**

es of anatomy

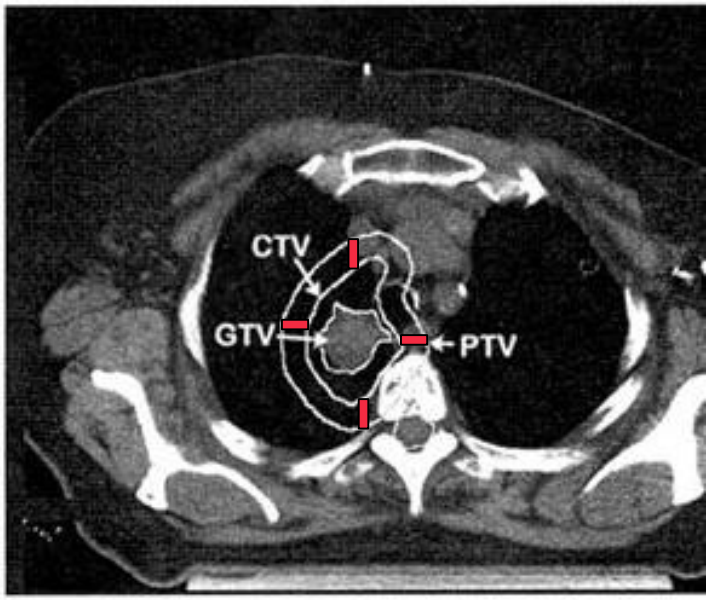
- Typically many beam directions used for protons
- Only 1-6 beam directions for ion-beam therapy.



Motivation
Secondary-ion tracking for IBR

- In clinical practice, a **safety margin including +-3.5 % +-2 mm (PTV)** is treated.
- Reminder: Can be a **substantial fraction** of the total **treated volume.**

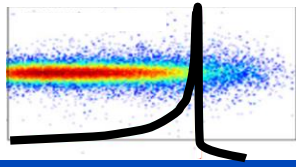
Verellen et al, 2007, *Nature Reviews Cancer* **7,** 949–960



Washington et al, © Elsevier Health Sciences 2015

- **Important** to **see:** any **change** betw. **planning CT** and **treatment.**
- **Monitoring highly desired! Secondary-ion tracking** is a promising method: **In-vivo range monitoring & QA possibilities**

Outline



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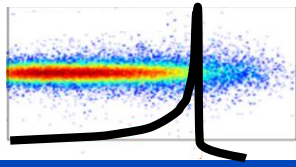
“Online” monitoring methods



Which signal ca

Primary ions **escapes!**

Interactions:

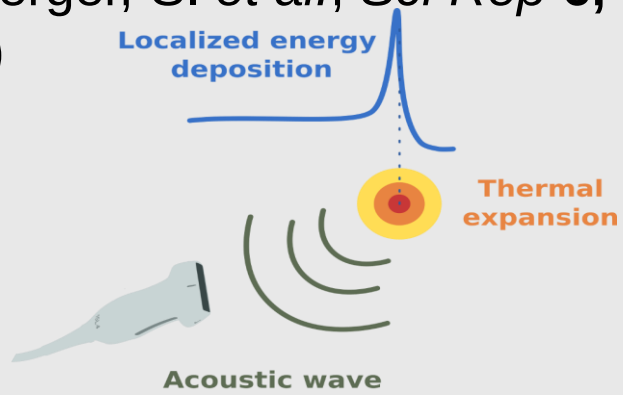
Electromagn

Electromagn

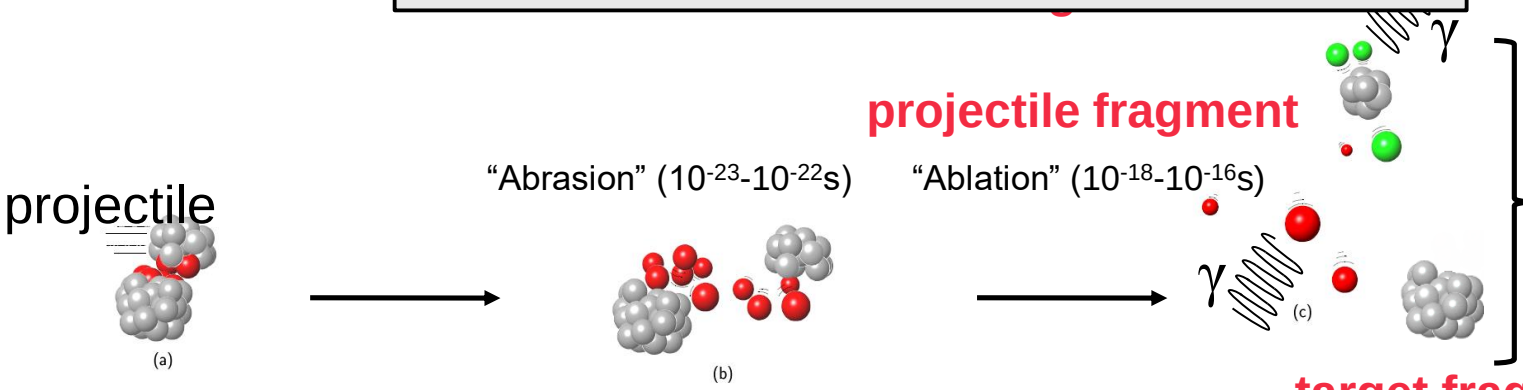
Nuclear inter

“Most”, not all, because there is:

1. Ionoacoustics, e.g. at LMU Munich, (Kellnberger, S. *et al.*; *Sci Rep* **6,** 29305 (2016))



2. PET, exploiting β^+ emitting fragments



Most techniques exploit these products!

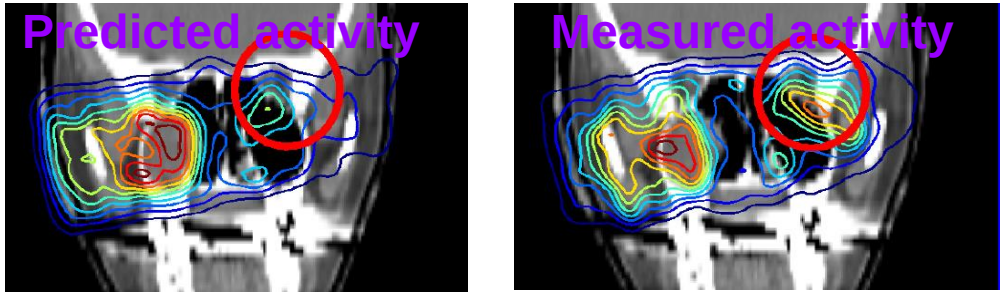
Kraan AC (2015); Front. Oncol. 5:150. doi: 10.3389/fonc.2015.00150

“Online” monitoring methods
PET

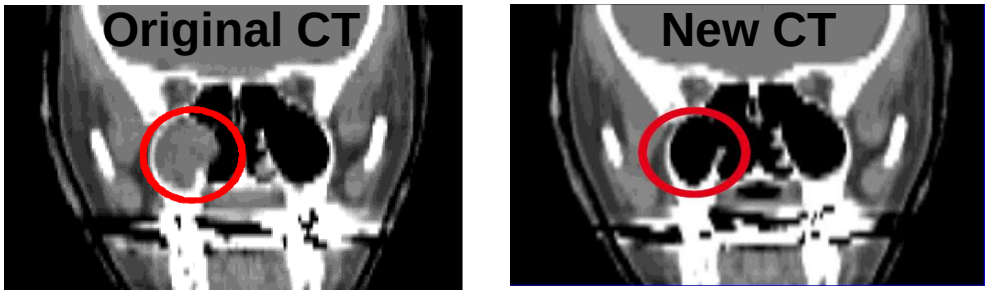
GSI, Darmstadt, Germany

PET-based monitoring:

Detection of ß$^+$ activation by PET scanners



K. Parodi, PhD Thesis 2004, W. Enghardt et al. Radiother. & Oncology 2004



Limitations:

- low induced activities in comparison to diagnostics (lower by at least ~$10^{3\text{-}4}$)
- movement of beam-activated nuclei
  (physiological washout processes; half life of ^{15}O: 2 min, ^{11}C: 20 min)

→ **limited contrast & spatial resolution**

“Online” monitoring methods
Prompt secondary radiation

Monitoring using prompt secondary radiation:

timescale of emission < 10^{-15}s

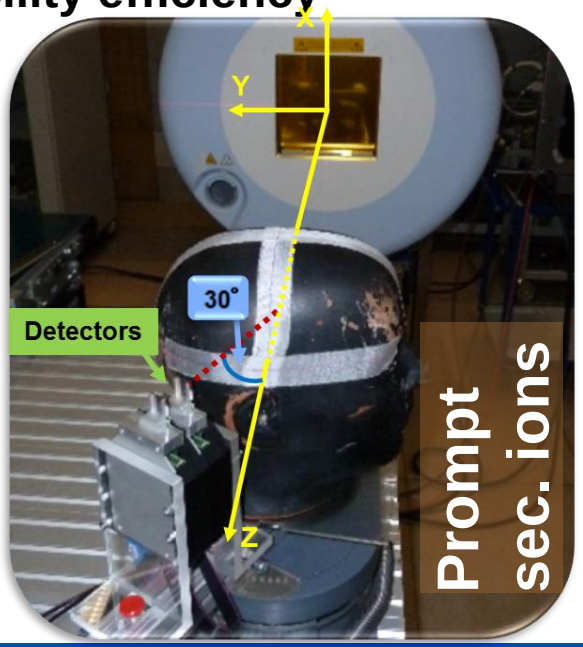
→ elimination of physiological washout of the signal

→ no prolongation of time-on-couch =

reduction of patient discomfort & facility efficiency

→ potential for immediate radiation stop

TEASER for the next lecture by Paulo Martins



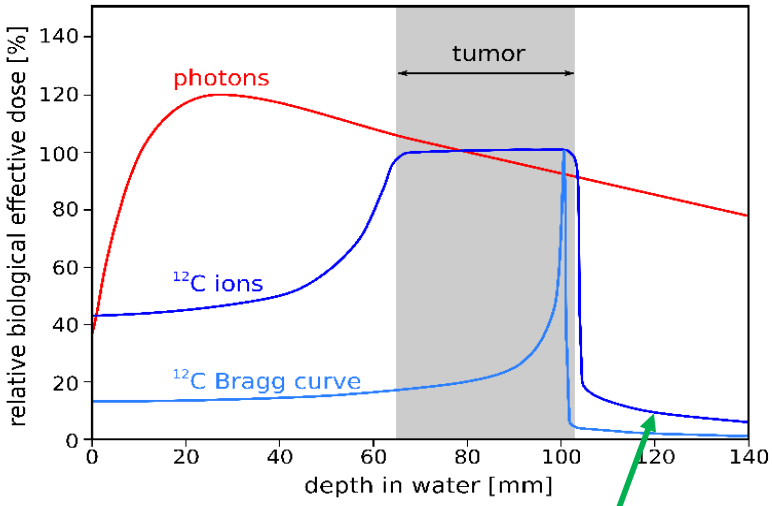
“Online” monitoring methods
Secondary-ion tracking

Secondary ions

Lower Z than $Z_{projectile}$

→ lower dE

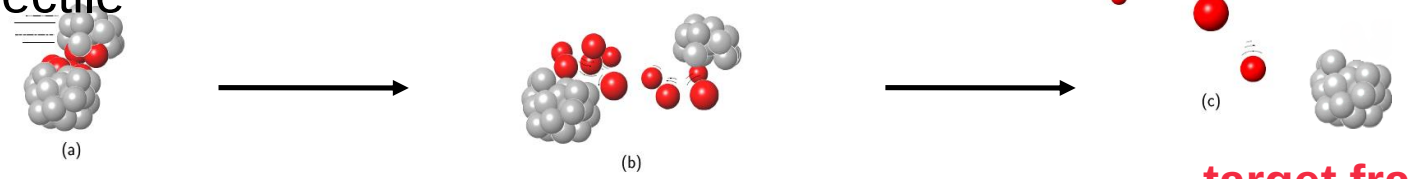
→ range longer than primaries



velocity ≈ primary ions

projectile fragment

projectile



target

target fragment

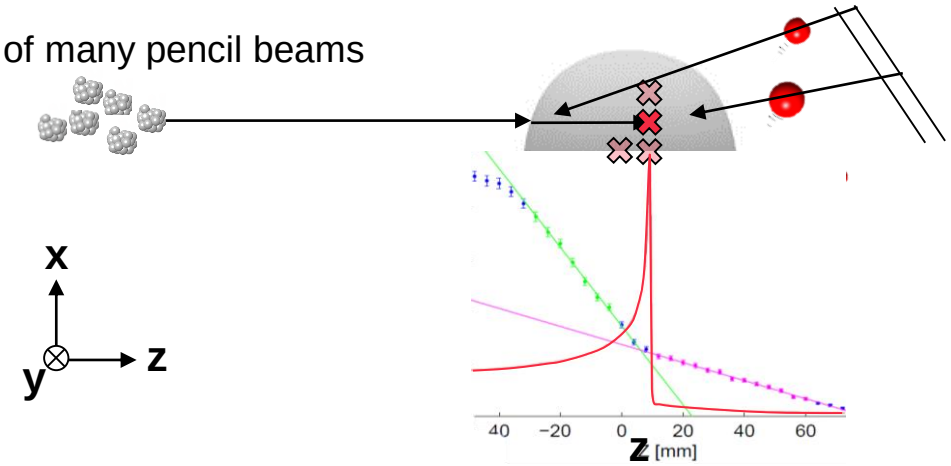
velocity ≈ 0

→ not usable for proton radiotherapy monitoring

Secondary-ion tracking for IBR

Basic principle and motivation

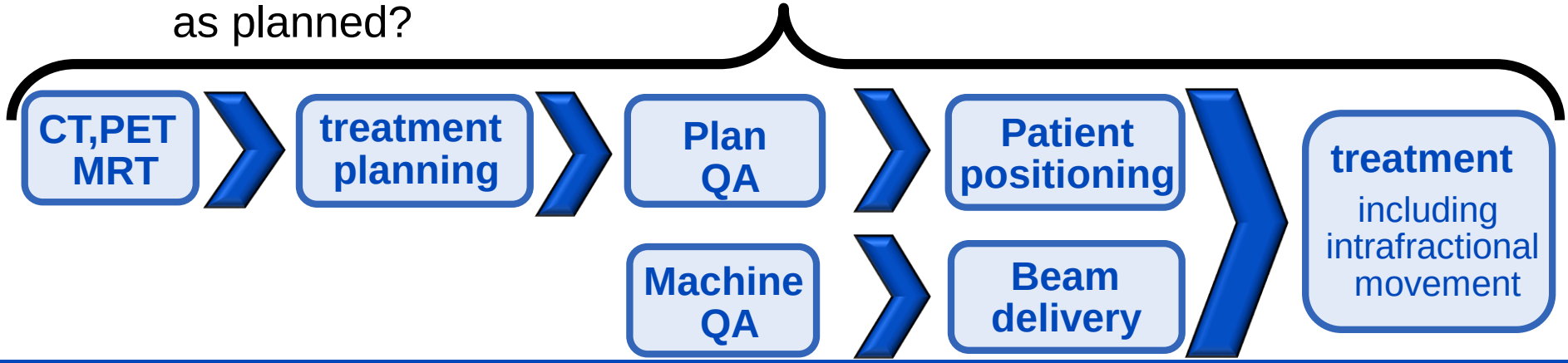
One out of many pencil beams



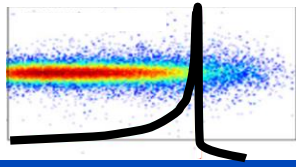
Not only for longitudinal (z) direction,
but also possible for lateral plane (x-y)

Potential of sec.-ion tracking:

- **Online beam monitoring**
- **Independent end-to-end verification**: Was the dose delivered as planned?



Outline



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- **Material & Methods: HIT facility,**
  detectors, Timepix & Timepix3
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  geometries & reconstructions

HIT facility

Reminder: **Video of the concept of scanned pencil beams**

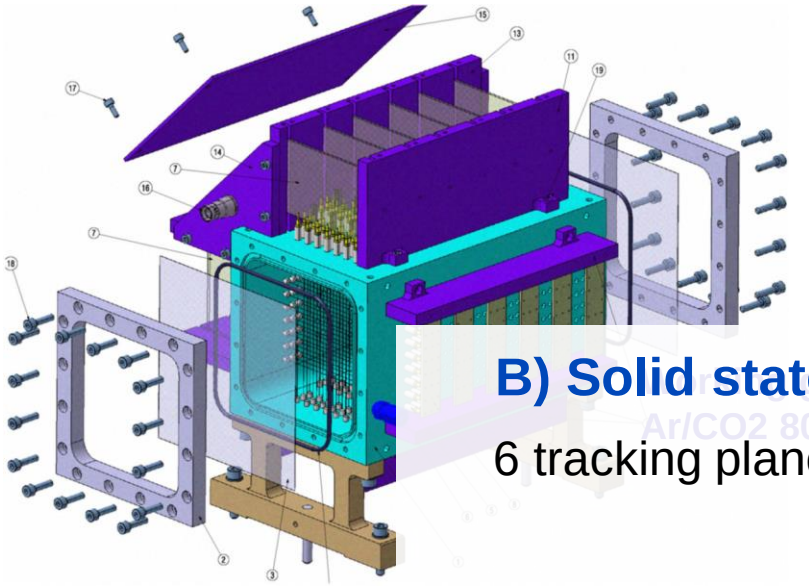
Research beamline

- Treatment of over 4000 patients with p & ^{12}C since 2009
  - Pencil-beam scanning
  - Ion ranges: ~2 – 30 cm (H_2O)

  } lateral, longitud. scanning of target
- Research: ^{4}He & ^{16}O available

Detection systems
For prompt secondary ions

A) Gas based detectors: wire chamber



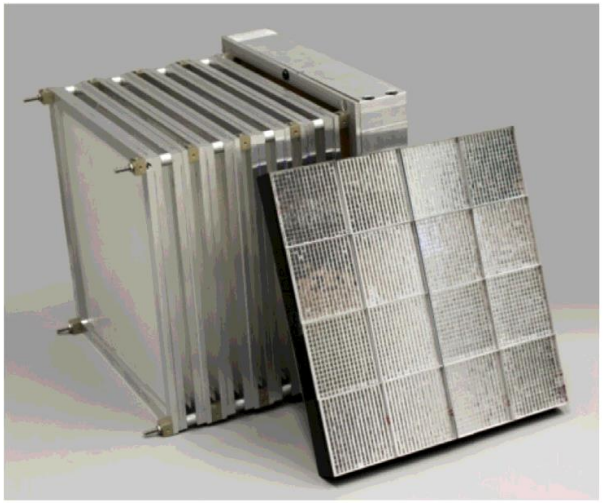
Z. Abou-Haidar et al. in JINST 2012

Low cost
Large experience
Gas filling
High voltage
Curved areas difficult
Bulky

B) Solid state detectors: scintillating fiber tracker

6 tracking planes (each 2 layers of 0.5 x 0.5 mm^2 fibers)

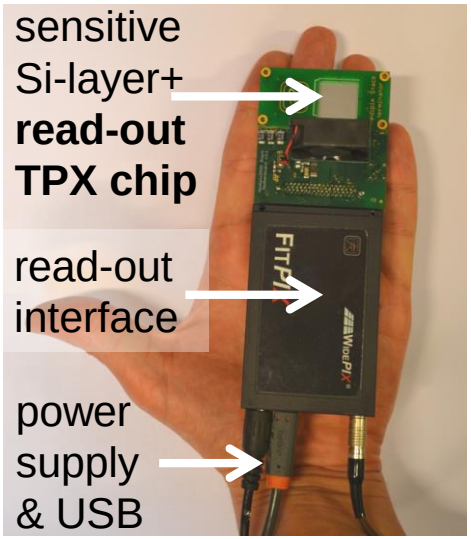
Low cost
Large experience
No gas, no HV
Ambiguities
Material budget



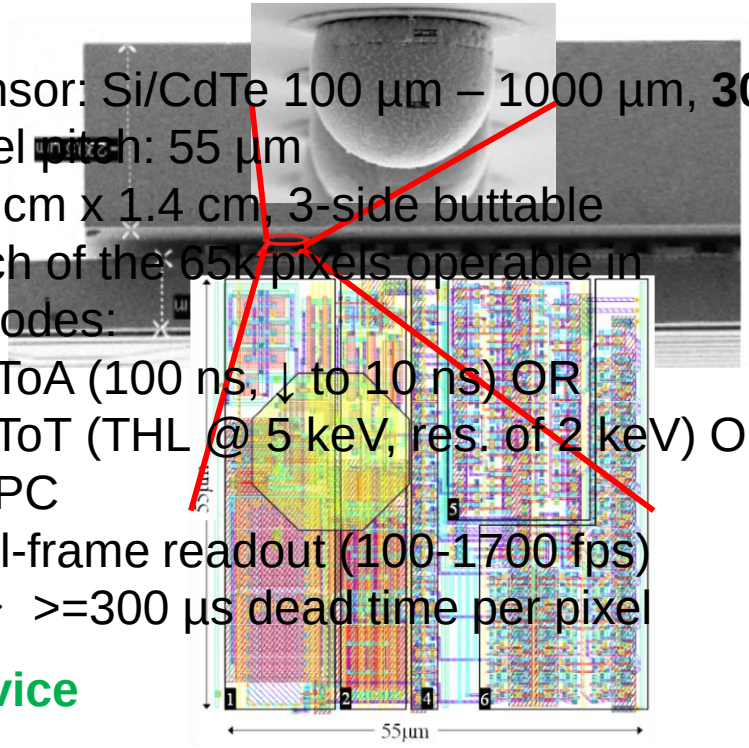
Triani et al. Physica Medica 34 (2017)

Timepix1 detector
For prompt secondary ions

C) Use of the very handy, semiconductor based Timepix detector



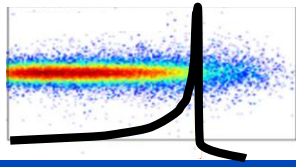
- Sensor: Si/CdTe 100 µm – 1000 µm, **300 µm Si**
- Pixel pitch: 55 µm
- 1.4 cm x 1.4 cm, 3-side buttable
- Each of the 65k pixels operable in 3 modes:
  - →ToA (100 ns, ↓ to 10 ns) OR
  - →ToT (THL @ 5 keV, res. of 2 keV) OR
  - →PC
- Full-frame readout (100-1700 fps)
  - → >=300 µs dead time per pixel

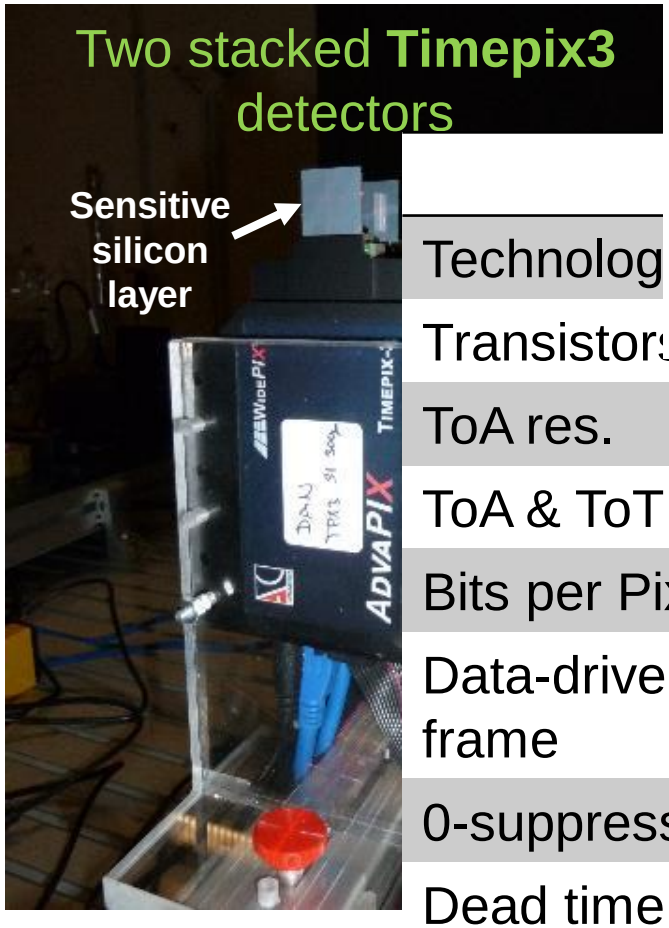


Easy-to-use, versatile device
High spatial resolution
No gas, no HV
Small
Low detection rate (frame-based, dead time)
High costs

Timepix3 detector

For prompt secondary ions





TPX3

Easy-to-use, versatile device

High spatial resolution

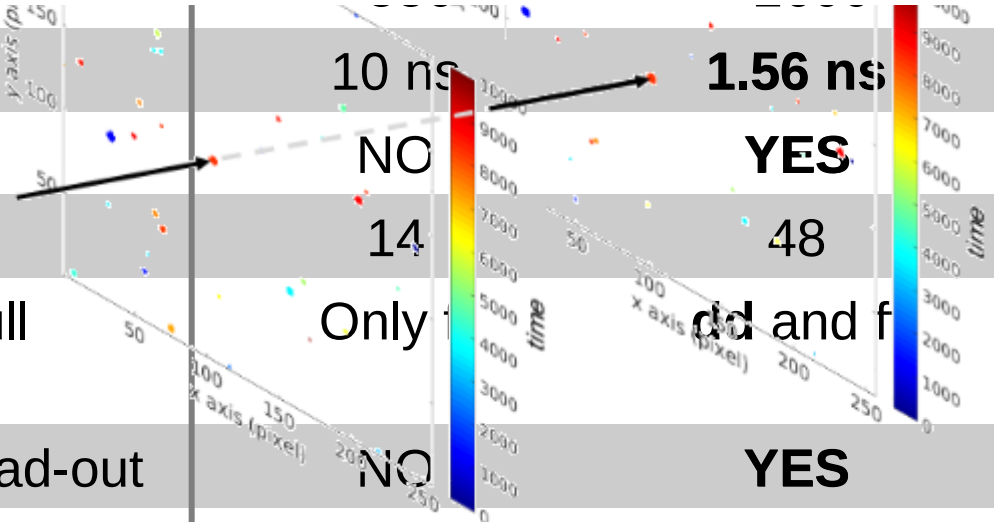
No gas, no HV

Small

High detection rate (contnious, small dead time)

High costs

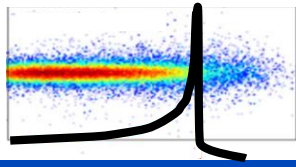
Technolog		
Transistors/px		
ToA res.	10 ns	**1.56 ns**
ToA & ToT	NO	**YES**
Bits per Pixel	14	48
Data-driven or full frame	Only f	**dd** and f
0-suppressed read-out	NO	**YES**
Dead time per px	>=300µs	**>=0.005 µs**
Output bandwidth	<= 3.2 Gbps	<=5.2 Gbps



[C.Brezina et al, 2014, The Timepix3 chip, CERN ESE seminar]

dkfz.

Outline
(follow-up on HighRR talk on Nov 6th)



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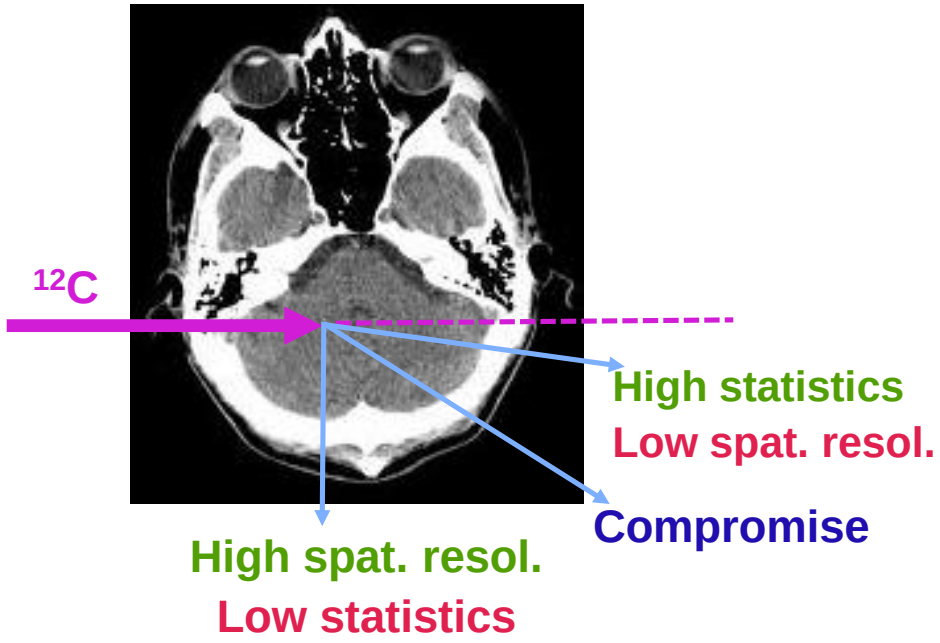
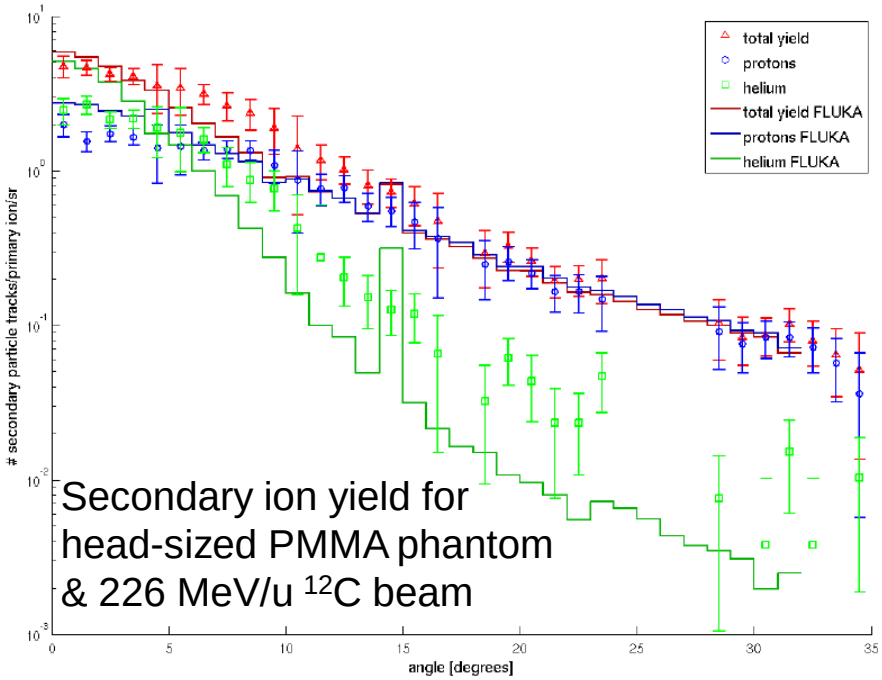
Prompt secondary ions
Yield and consequences for set-ups

Secondary ions:



Angular distribution strongly forward peaked!

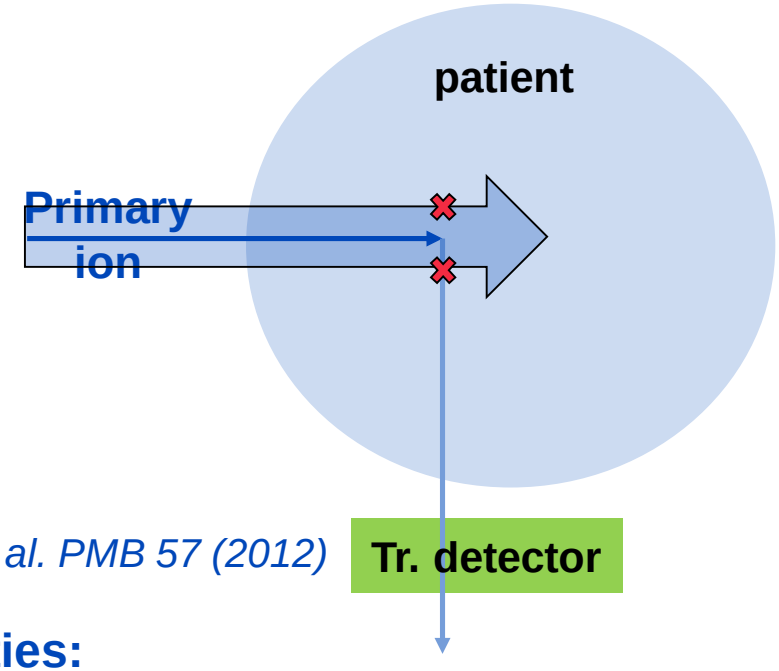


20-35°: 0.1 secondary ion / primary ^{12}C

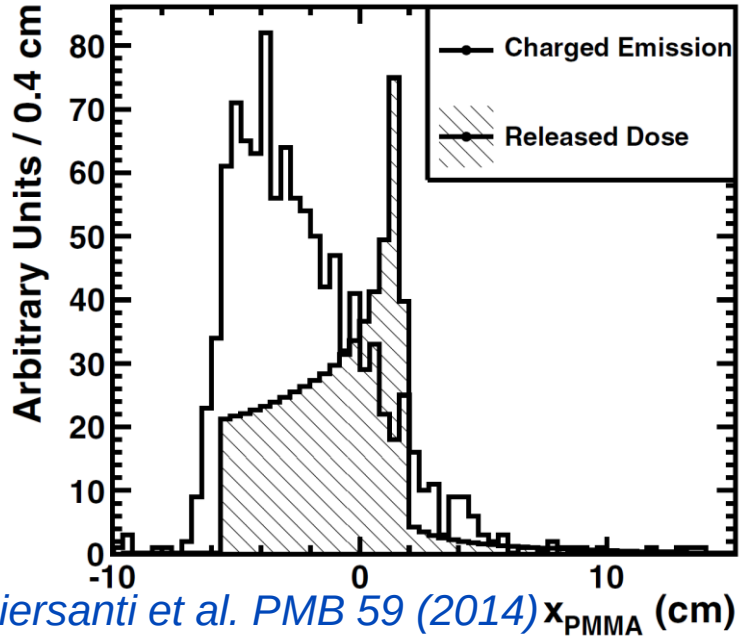
Merle Reinhart, Master thesis (2015)

Prompt secondary ions
Reconstruction strategies (I)

A) Back-projection at 90°



Agodi et al. PMB 57 (2012)



Piersanti et al. PMB 59 (2014)

Properties:

Sensitivity to the Bragg-peak position, beam width

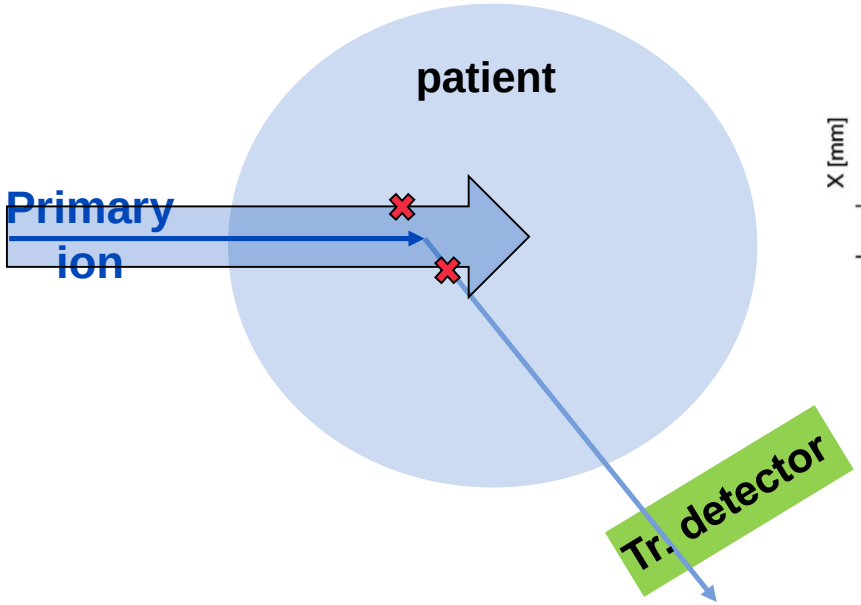
Finite width of primary beams does not introduce uncertainties on long. Info

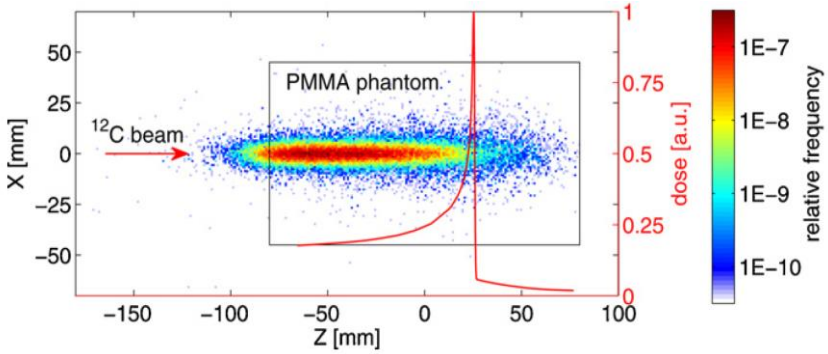
No lateral beam position

Ions predominantly forward peaked → low ion yield

Prompt secondary ions
Reconstruction strategies (II)

B) Back-projection at 10-60º





Gwosch et al.: PMB 58 (2013)

Properties:

Sensitivity to the Bragg-peak position, lateral beam pos, beam width.

Much higher ion yield!

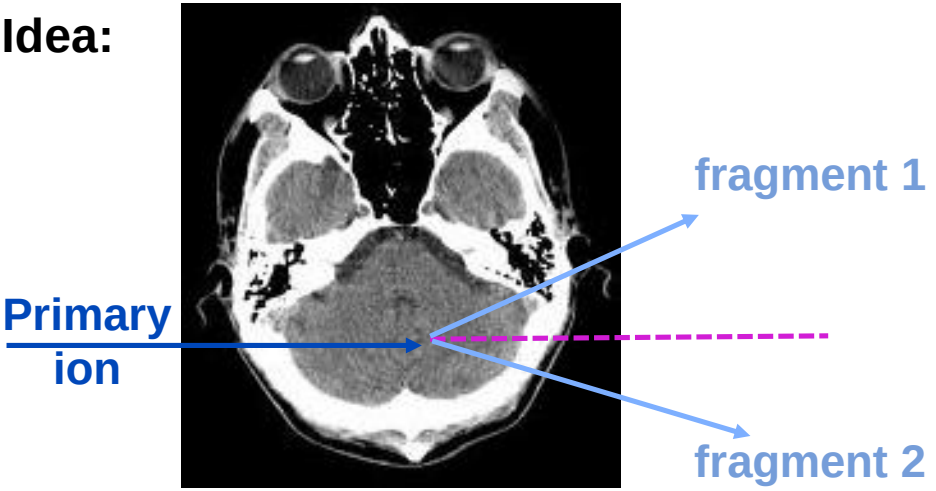
Higher uncertainties on longitudinal information

Prompt secondary ions
Reconstruction strategies (III)

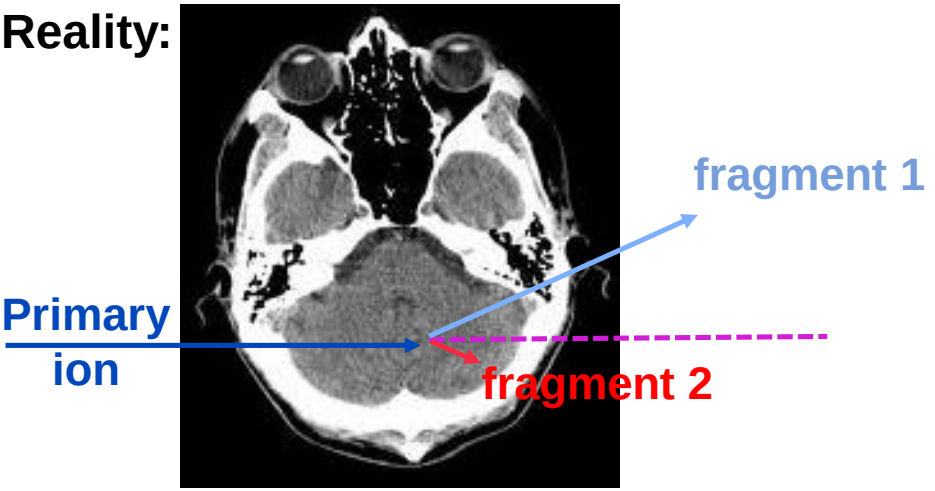
C) Interaction vertex imaging

Henriquet et al. PMB 2012

Idea:



Reality:



Properties:

Method from particle physics - elegant

Straight forward data reconstruction

3D distributions

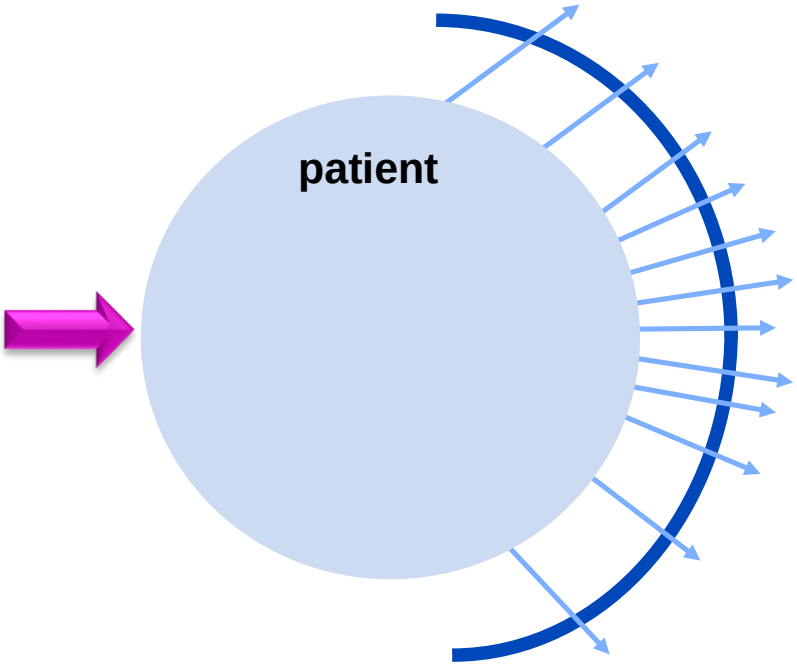
Low statistics:

fragment stopping &

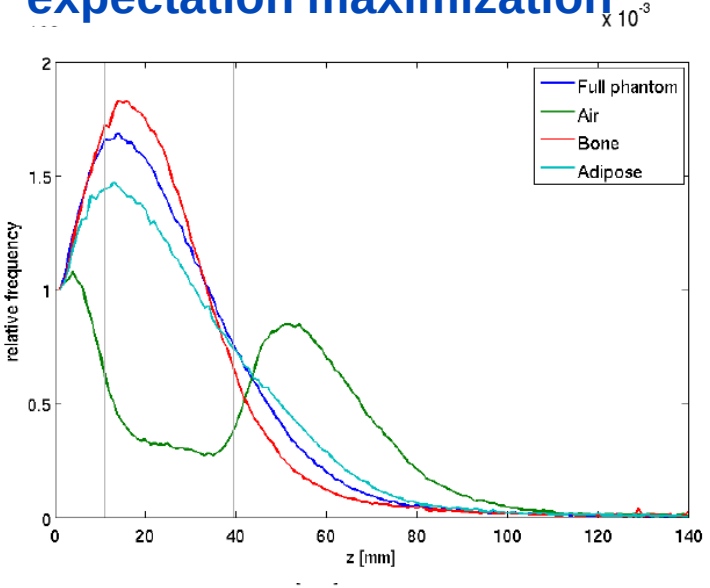
limited geometrical acceptance

D) Iterative, 3D image reconstruction

Merle Reinhart et al. PMB (2017)

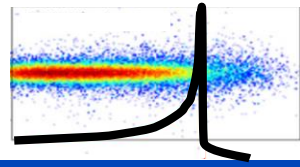


Maximum likelihood expectation maximization

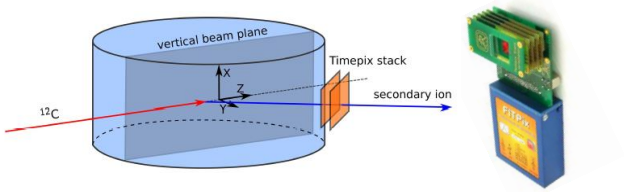


3D information
No assumptions on plane of backprojection
Large detection areas needed
Development at the beginning

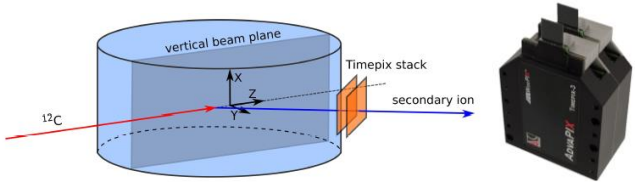
Results on backprojection at 30 °
(discussed in the following slides)



- An **initial study** using homogeneous PMMA phantom + TPX (K. Gwosch, 2013)



- Using **homogeneous PMMA** phantom + **TPX3** (M. Reimold, 2018)

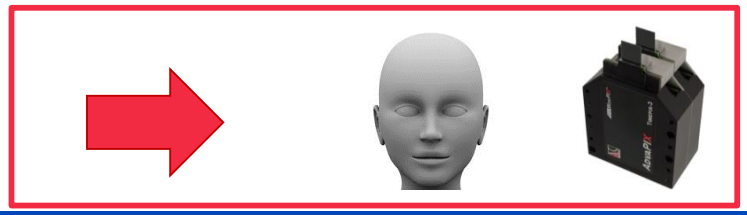


- Using **anthropomorphic head phantom** + **TPX** (R. Félix Bautista, 2017)

not presented here

Increasing complexity of set-ups

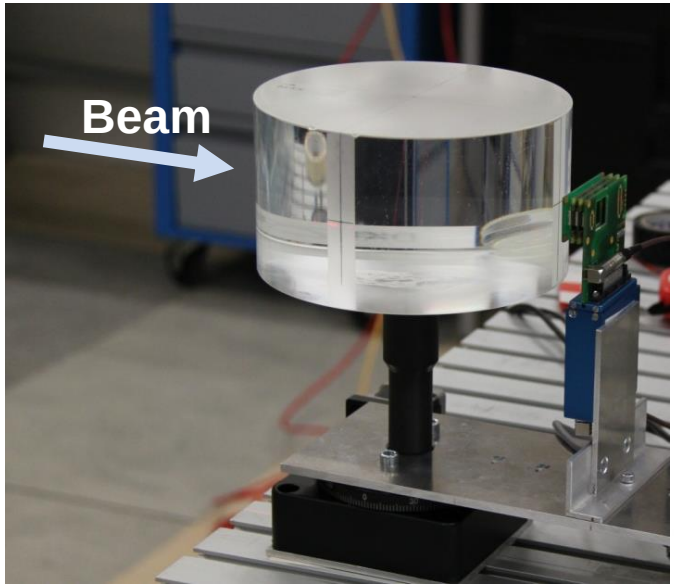
- Using **anthropomorphic head phantom + TPX3** (Work in progress: Ghesquiere, Bautista, Gehrke, Martisikova)



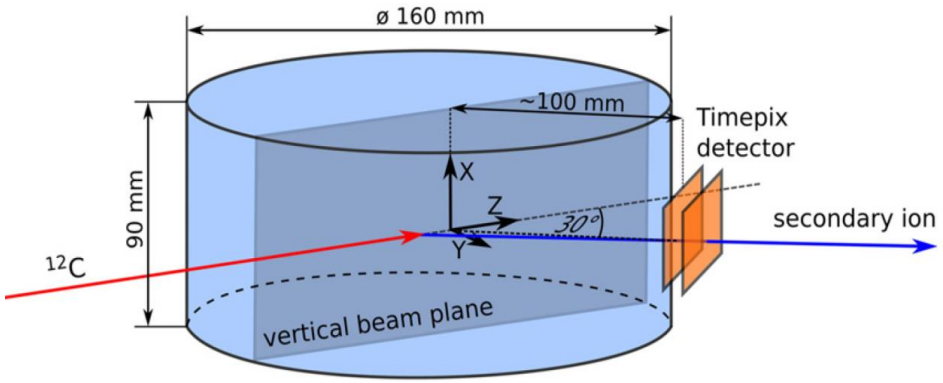
Secondary-ion backprojection

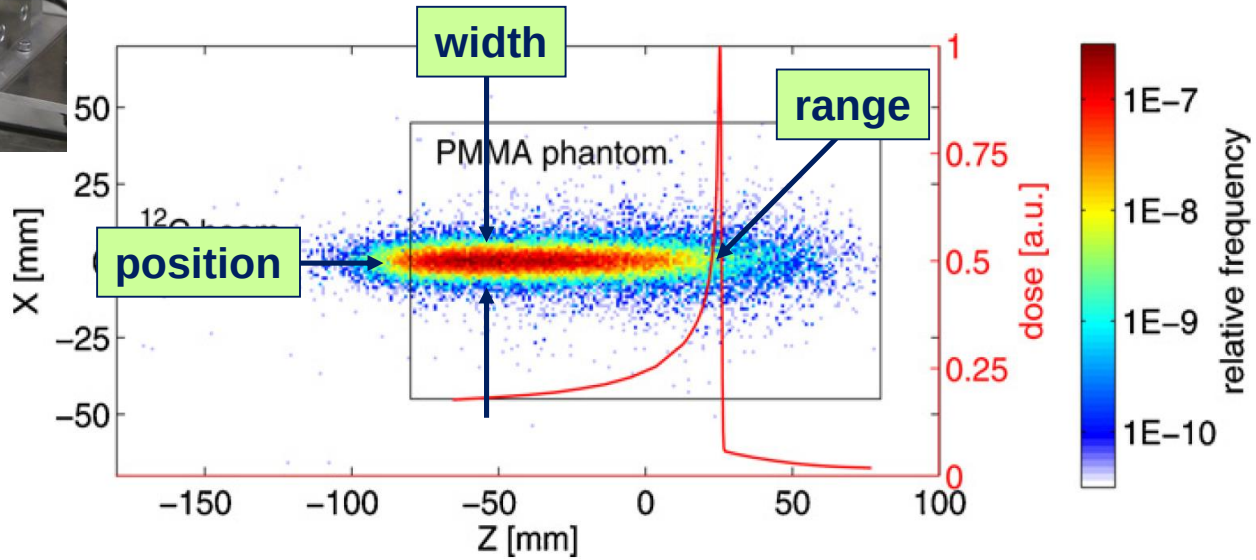
Results @ 30 ˚, PMMA cylinder + TPX1 (I)

Secondary ion distribution ↔ beam properties?



Gwosch et al.: PMB 58 (2013)

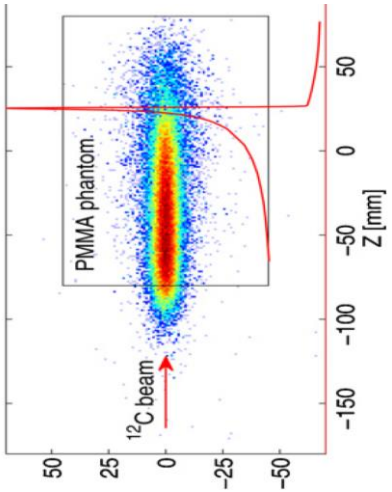


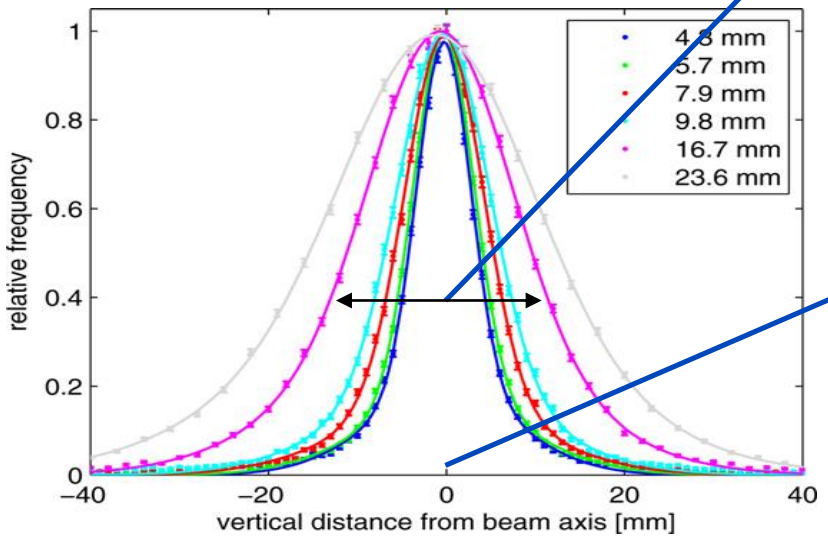


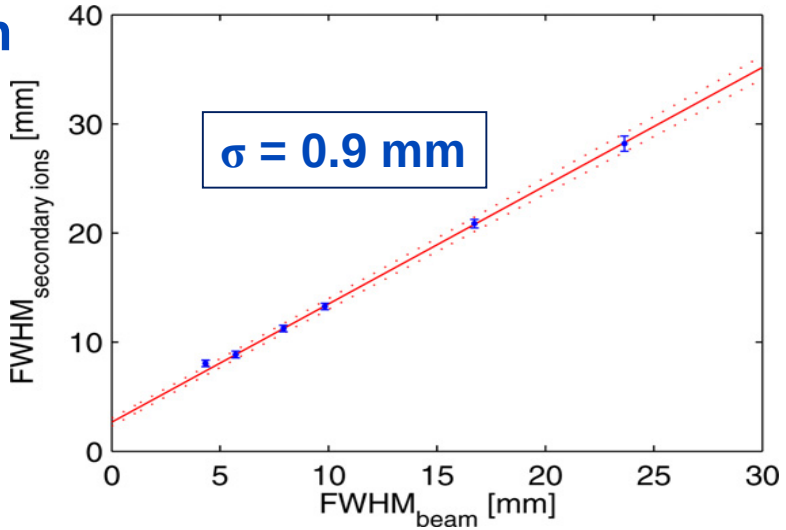
Secondary-ion backprojection

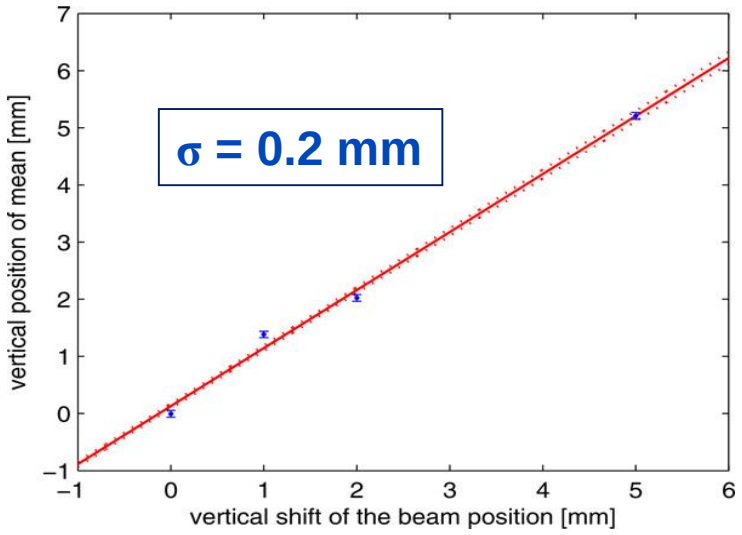
Results @ 30 °, PMMA cylinder + TPX1 (II)

Sensitivity to beam position & width







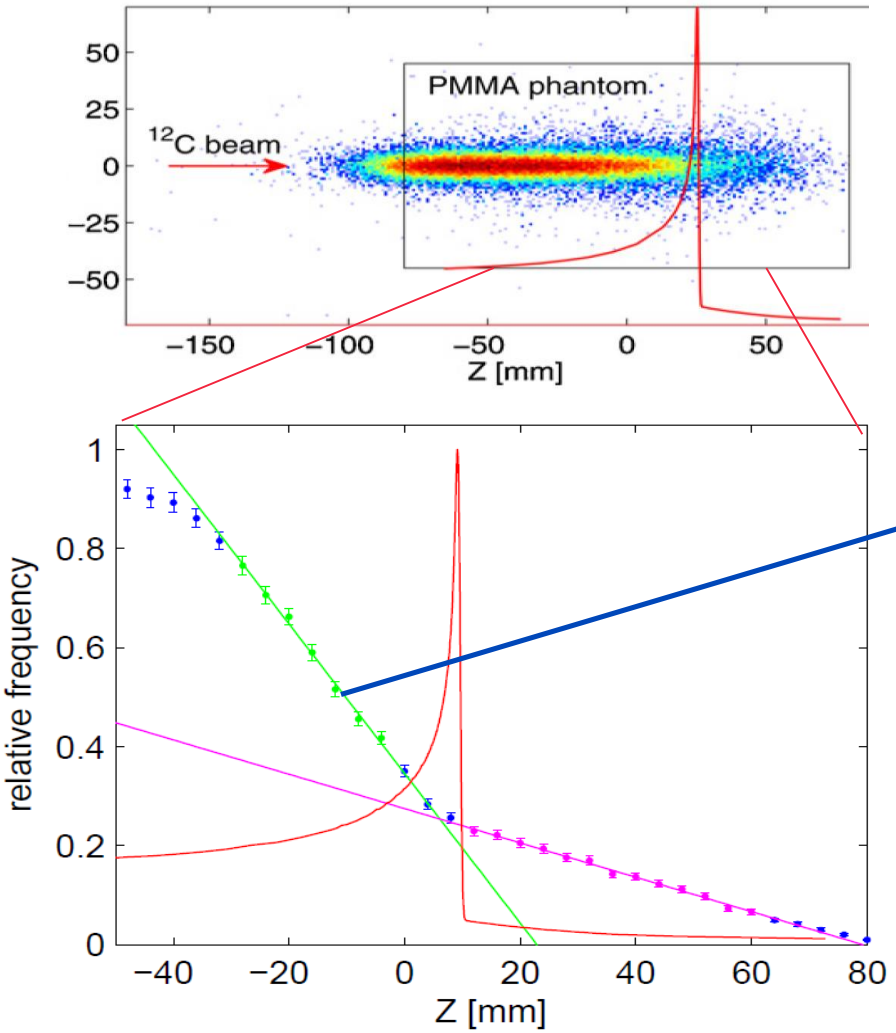


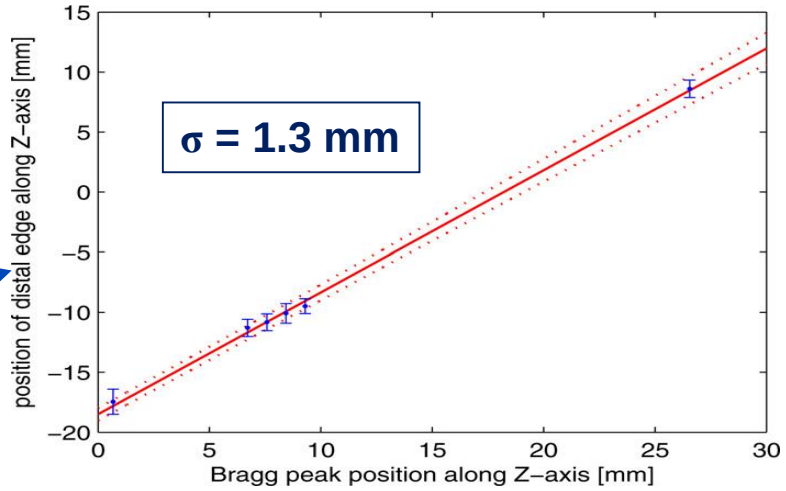
Gwosch et al.: PMB 58 (2013)

Secondary-ion backprojection

Results @ 30 ˚, PMMA cylinder + TPX1 (III)

Sensitivity to beam range





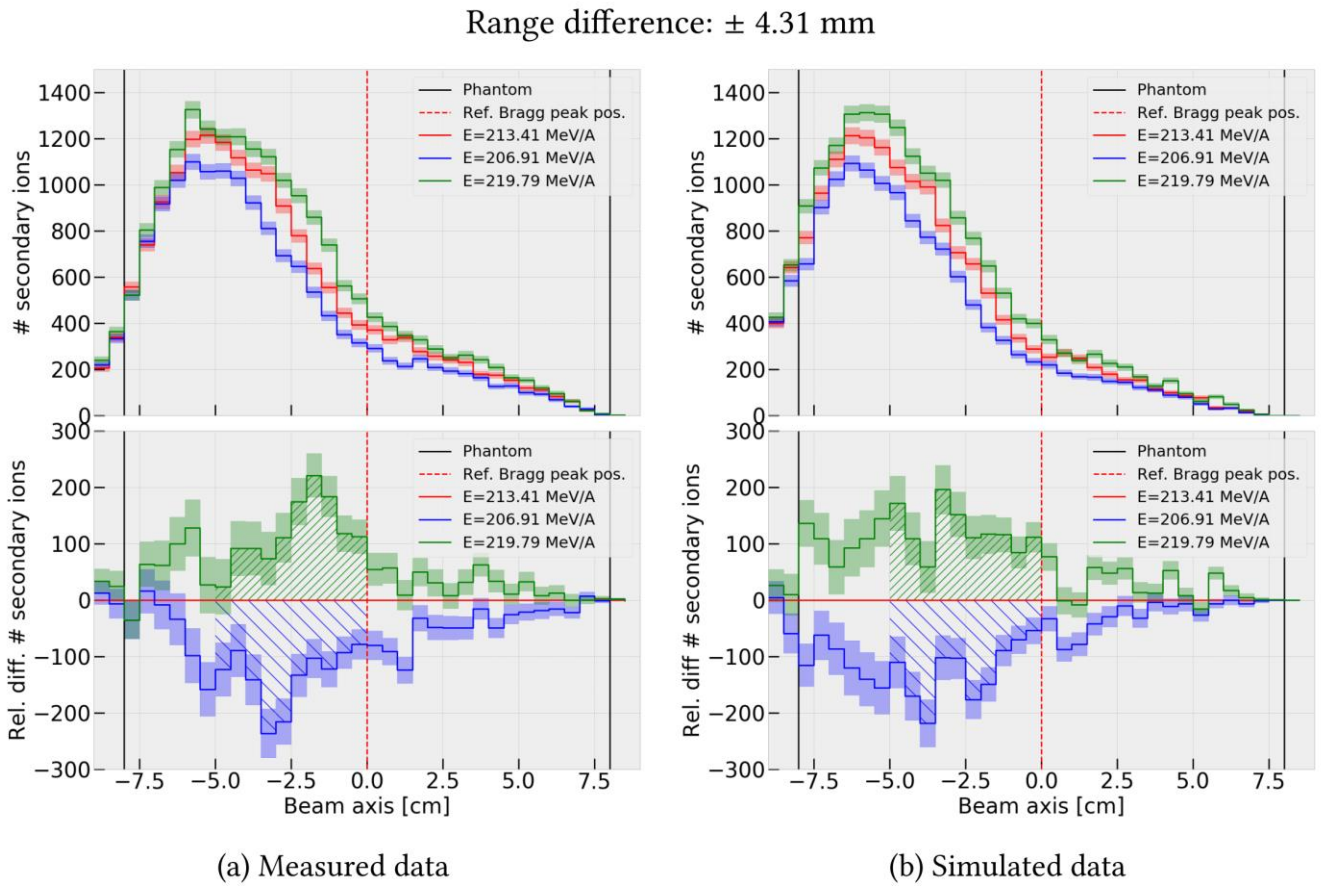
But: Much higher fluence than in treatment (2E9 primaries for one pencil beam)

Gwosch et al.: PMB 58 (2013)

Secondary-ion backprojection

Results @ 30 ˚, PMMA cylinder + TPX3 (I)

Sensitivity to beam range: Fluence like in treatment (4E5 primaries) x 18 = 1E7 (assuming detector ring @ 30 ˚ , 18 pairs)



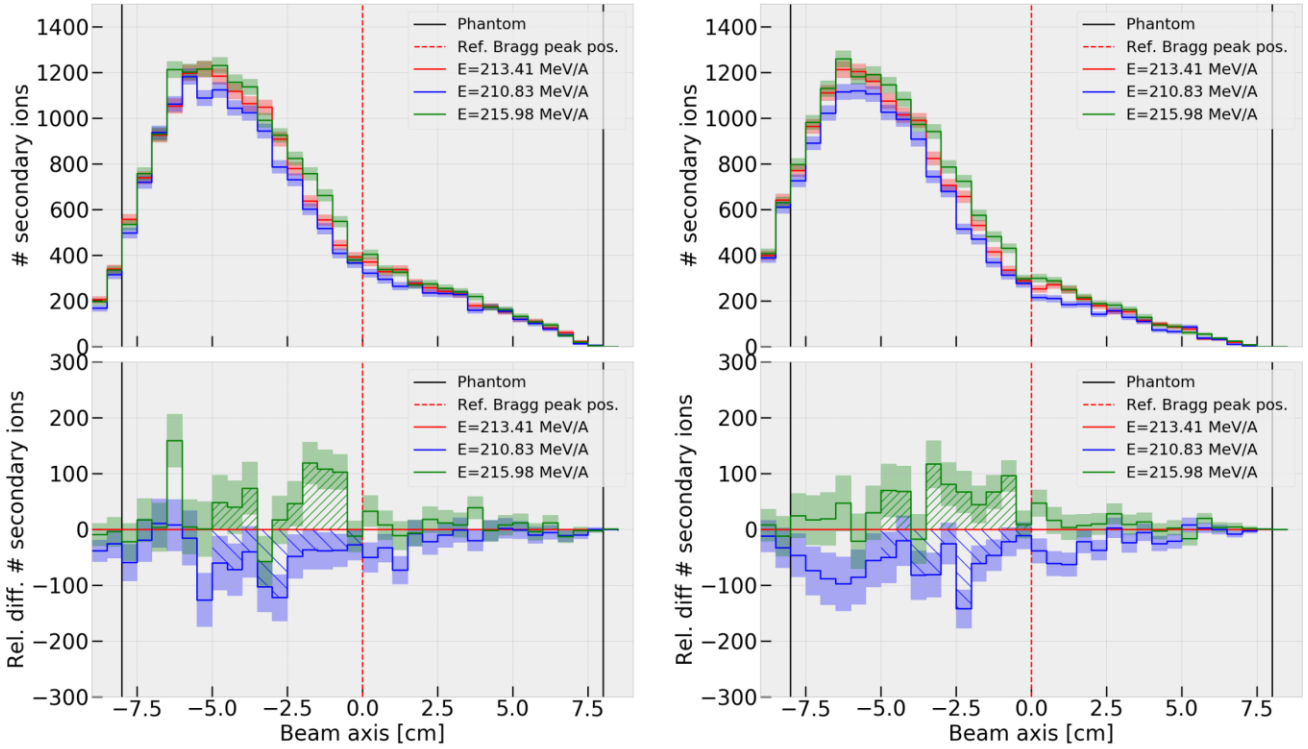
Marvin Reimold.: Master thesis (2018)

Secondary-ion backprojection

Results @ 30 ˚, PMMA cylinder + TPX3 (II)

Sensitivity to beam range: Fluence like in treatment (4E5 primaries) x 18 = 1E7 (assuming detector ring @ 30 ˚ , 18 pairs)

Range difference: ± 1.72 mm



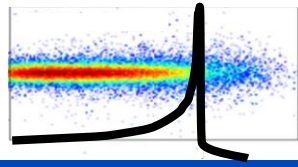
(a) Measured data

(b) Simulated data

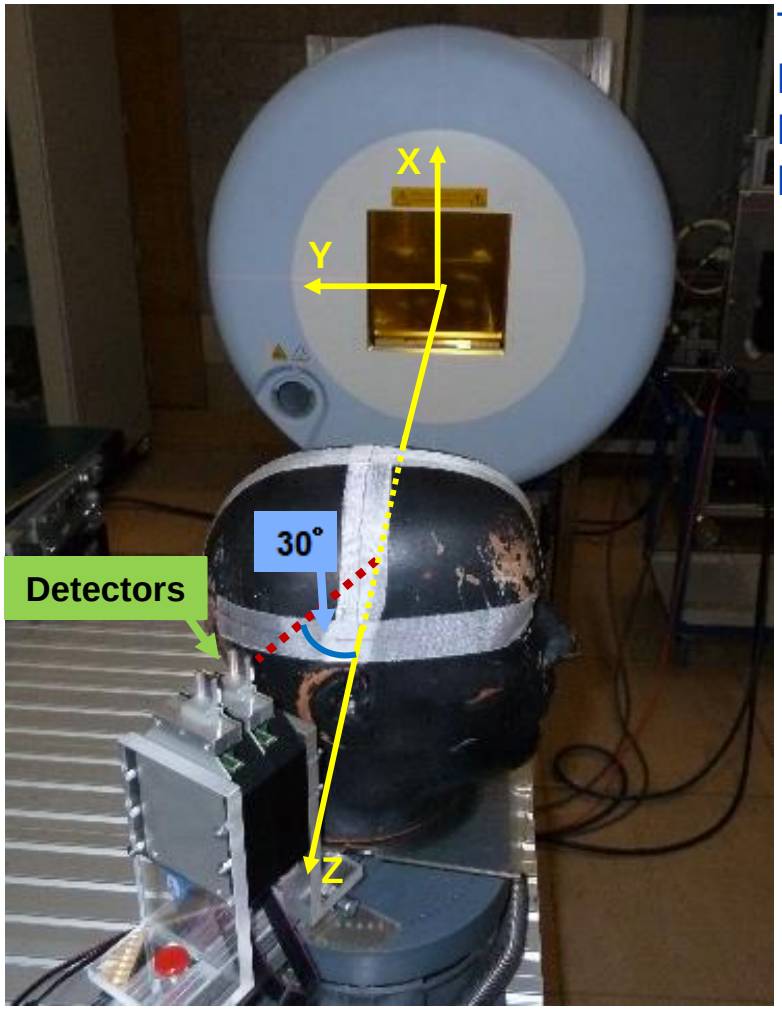
Marvin Reimold.: Master thesis (2018)

Secondary-ion backprojection

Head phantom, real treatment + TPX3, laterally (I)

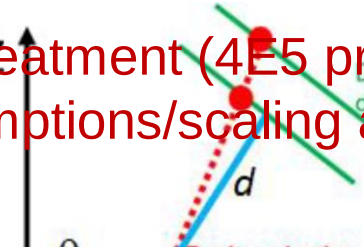


Treatment-like situation: treatment of the Alderson phantom

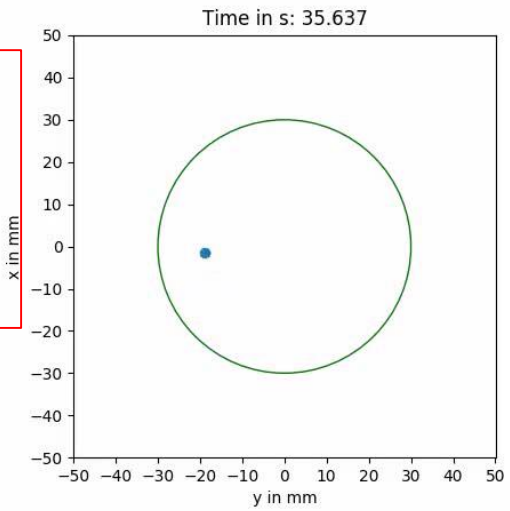


Tumor: 100 cm^3
Prescribed dose: 3 Gy(RBE)
Lateral scanning: 2 mm
Energy layers: 22, spacing: 3 mm

Fluence like in treatment (4E5 primaries) x 1
= 4E5 (no assumptions/scaling at all!!!)



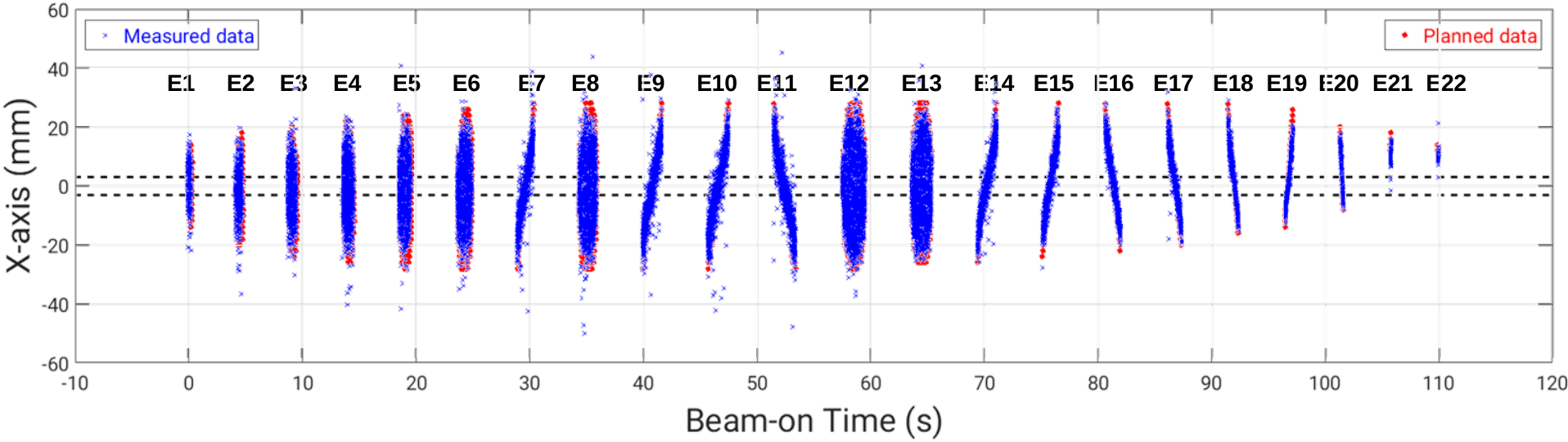
First time-resolved ^{12}C beam monitoring

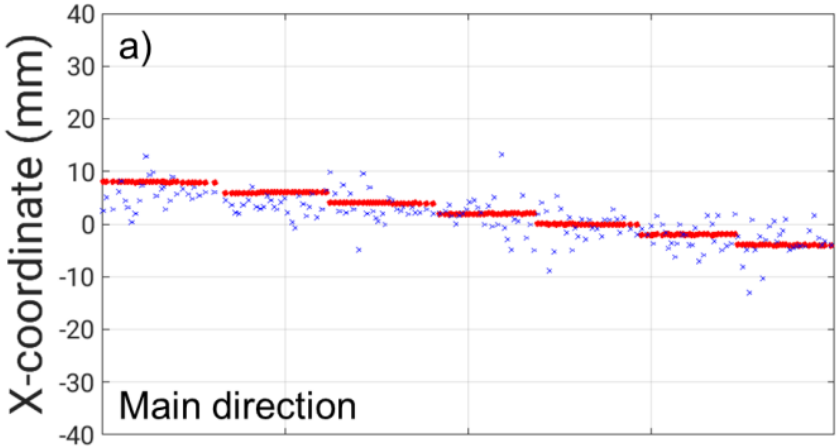


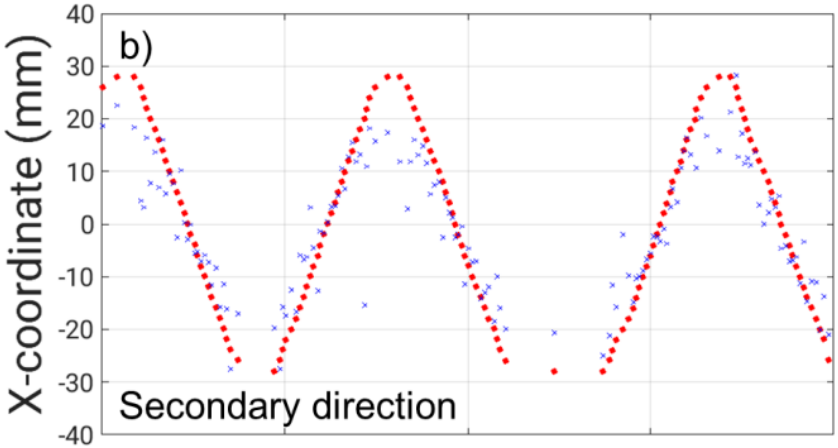
Prompt secondary ions

Head phantom, real treatment, laterally (III)

Measurements of the lateral beam position:



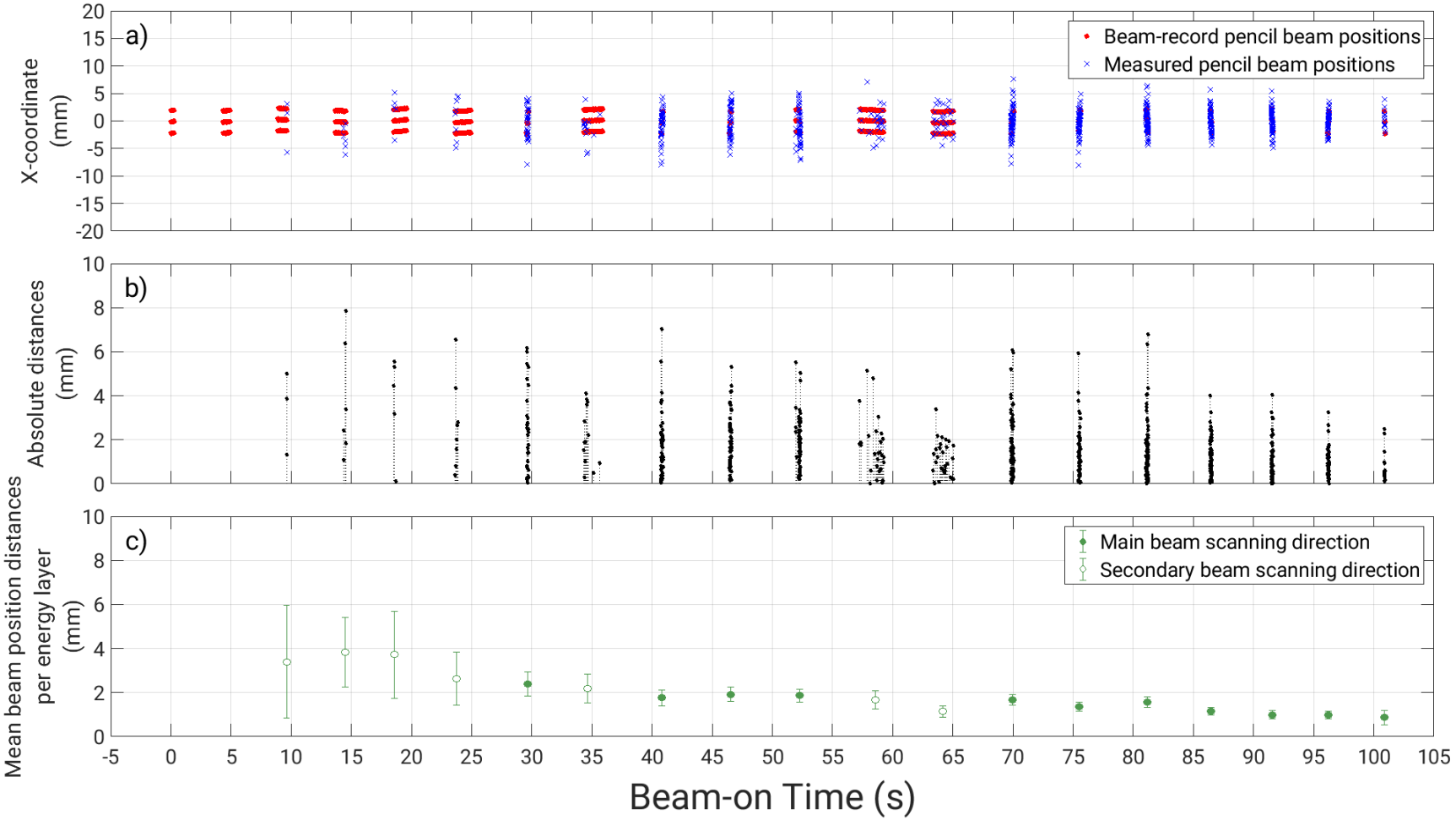




Secondary-ion backprojection

Head phantom, real treatment + TPX3, laterally (II)

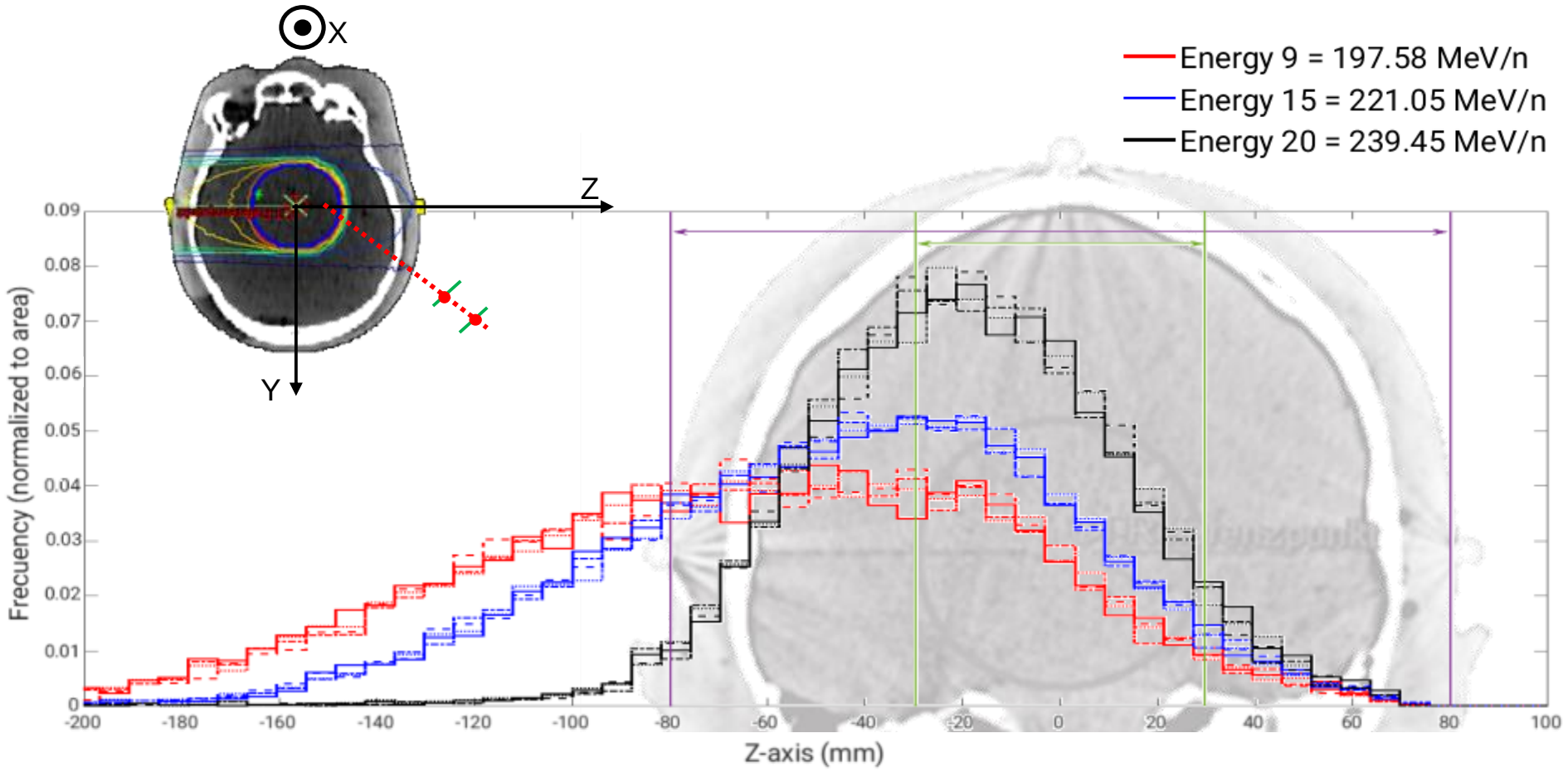
Measurements of the lateral beam position:



Prompt secondary ions

Head phantom, real treatment + TPX3, longitudinally

Detection of range differences between the energy layers

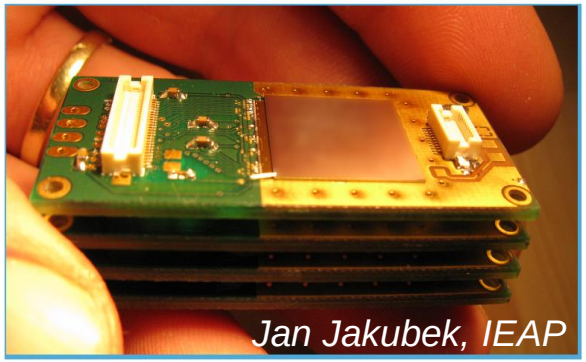


Renato Bautista, Master thesis, DKFZ 2017, further investigations by Laura Ghesquiere and Laurent Kelleter

Conclusions for prompt secondary ions

- **Secondary ions: interesting candidate for monitoring of the deposited dose**

  Prompt → potential for “real-time”!



- **Method currently rather at the beginning**

  Investigated:

  - Suitable detectors: completely different from photon detectors
  - Detection geometry
  - Data reconstruction methods

- **Gain of therapy-relevant information experimentally demonstrated**

  - e.g. measurement of the lateral pencil-beam scanning in clinic-like situation

- **Exciting research field!**

Thank you for your attention!

If you are interested in a Master project in this topic, please contact Maria Martisikova m.martisikova@dkfz.de or me t.gehrke@dkfz.de