Ion-beam imaging

(with focus on helium-beam radiography)

aiming at an improved accuracy of ion-beam therapy

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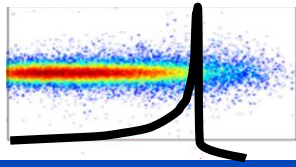
Dept.: Medical Physics in Radiation Oncology (Prof. Dr. Oliver Jäkel)
German Cancer Research Center (*DKFZ)*

Outline



- **Ion-beam radiotherapy (IBR) &**

  the motivation for ion-beam imaging in the field of IBR
- **Basic principle of ion-beam imaging & advantages**

  Applications

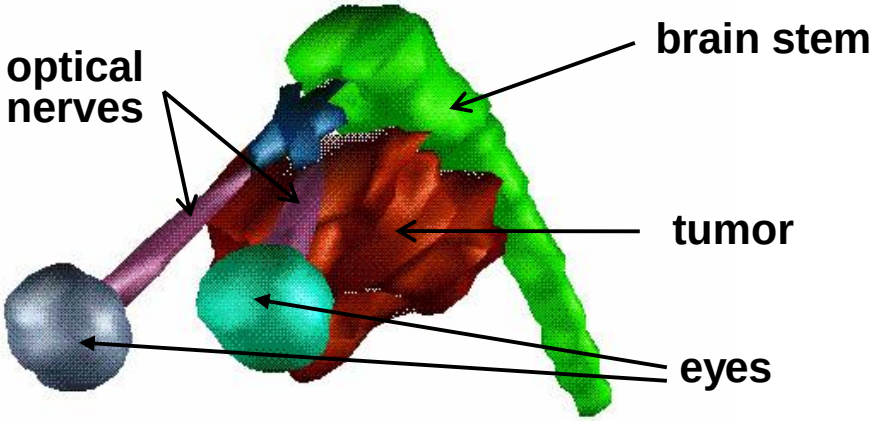
  History & overview of detection systems

Our research of helium-beam radiography

- **Why exactly helium ions? In theory**
- **Where and how do we perfom helium-beam radiography (αRad)?**
- **Experimental comparison between pRAD and αRAD**

Ion-beam radiotherapy
Clinical applications, diff. treatment sites

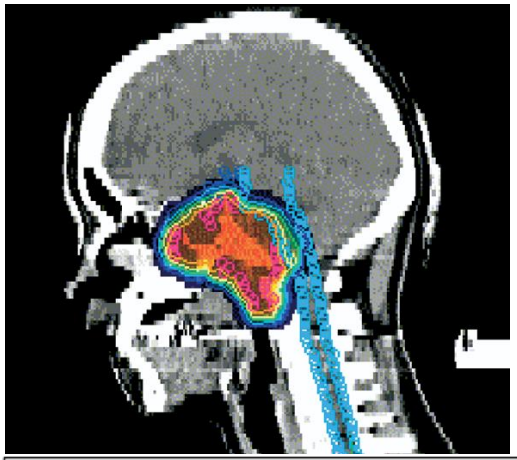
Radioresistent tumors
close to **radiosensitive** organs:

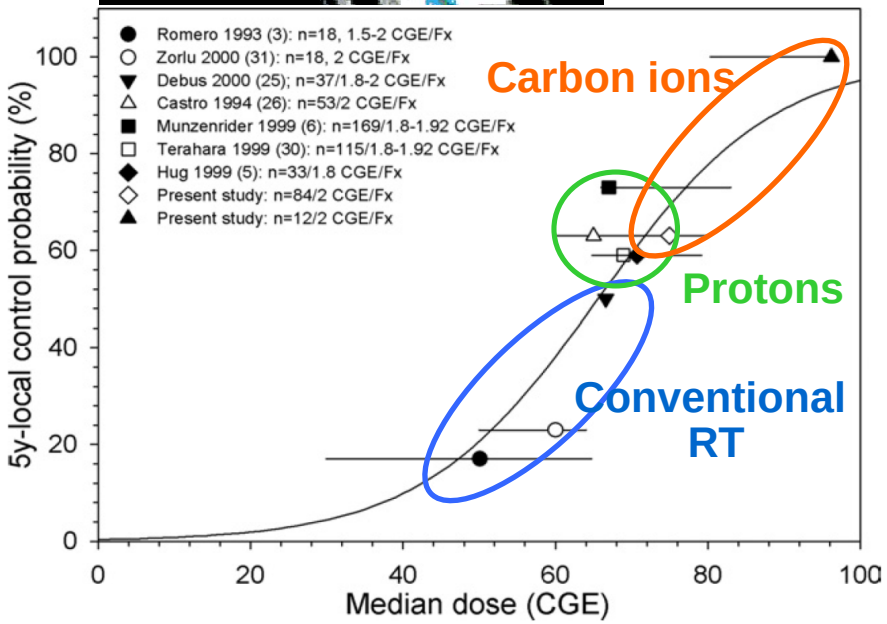


W. Schlegel, A. Mahr: (2007)
3D conformal radiation therapy

- **Central Nervous System (Brain,..)**
- Head and neck cancers (Nasal cavity,)
- Lung
- Prostate

Skull base chordomas

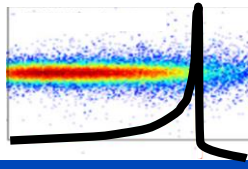


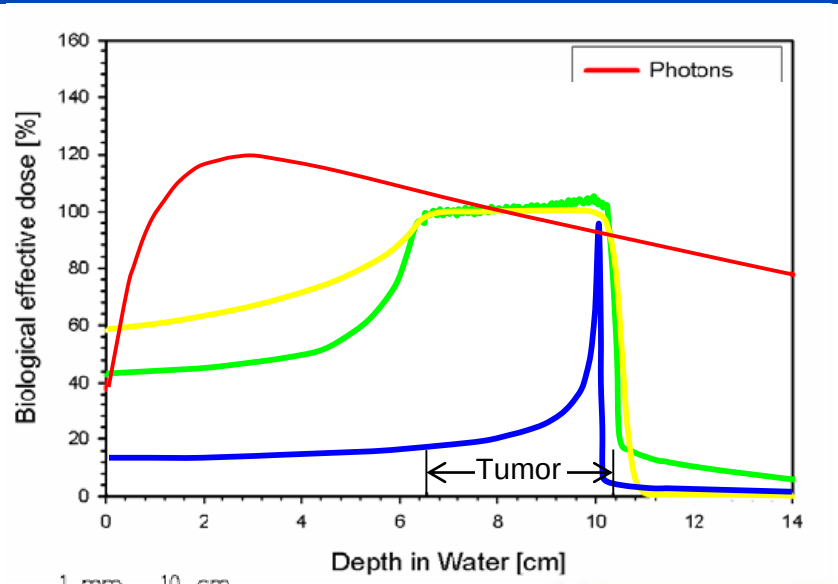


Schulz-Ertner et al. Int. J. ROBP **68** *(2007) 449*

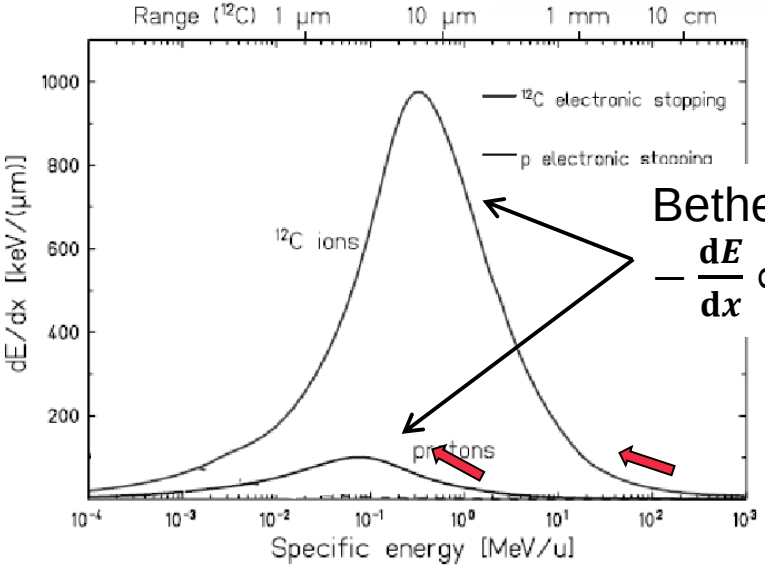
Ion-beam radiotherapy

Physical & biological advantages → Conformal dose





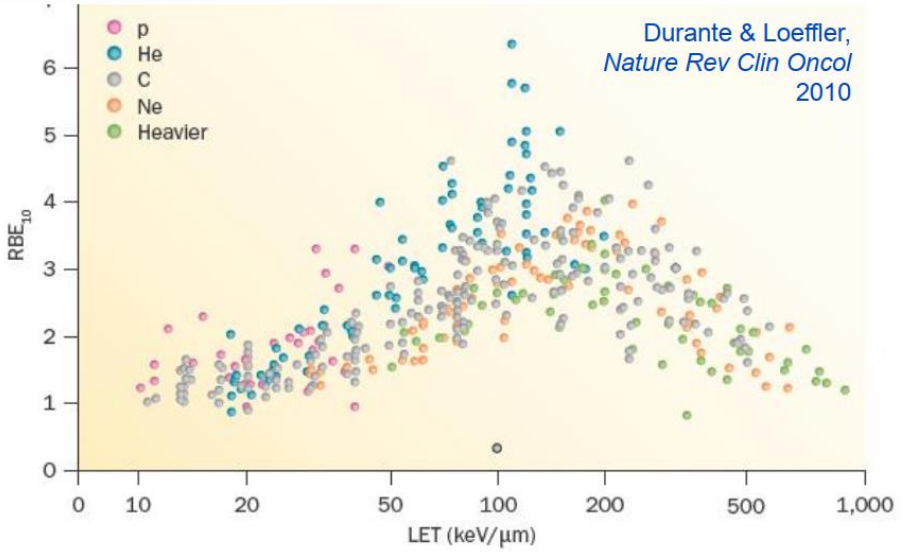
Physical advantage:



Bethe-Bloch:

$$-\frac{dE}{dx} \propto Z^2 \frac{1}{\beta^2}$$

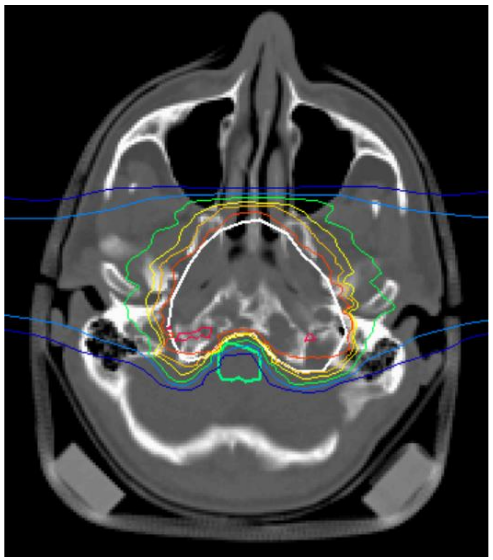
Biological advantage:



Ion-beam radiotherapy

Treatment planning: two important steps

- **X-ray CT for delineating target volume and organs at risk**



- **Converting X-ray CT info (voxel's HU) into ion stopping power (voxel's $RSP = \frac{SP_{mat}}{SP_{H_2O}}$)**

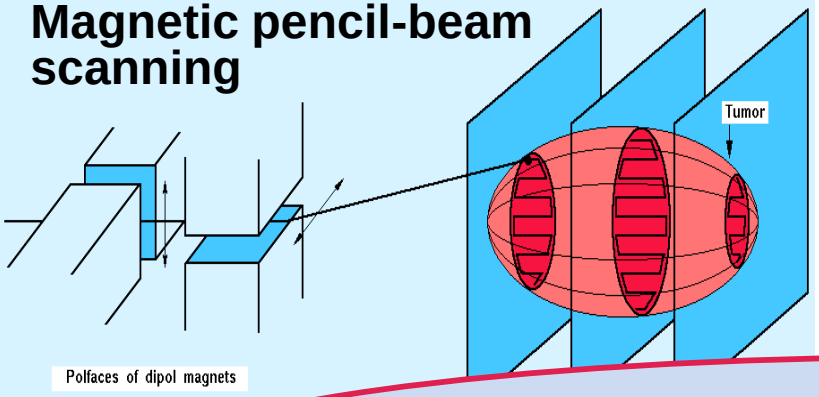
- $RSP = \frac{SP_{mat}}{SP_{H_2O}}$

- $WET = \int_{\text{entr.}}^{\text{exit}} RSP(z)\,\mathrm{d}z$

Hounsfield units

Ion-beam radiotherapy
Technology for beam delivery

Magnetic pencil-beam scanning



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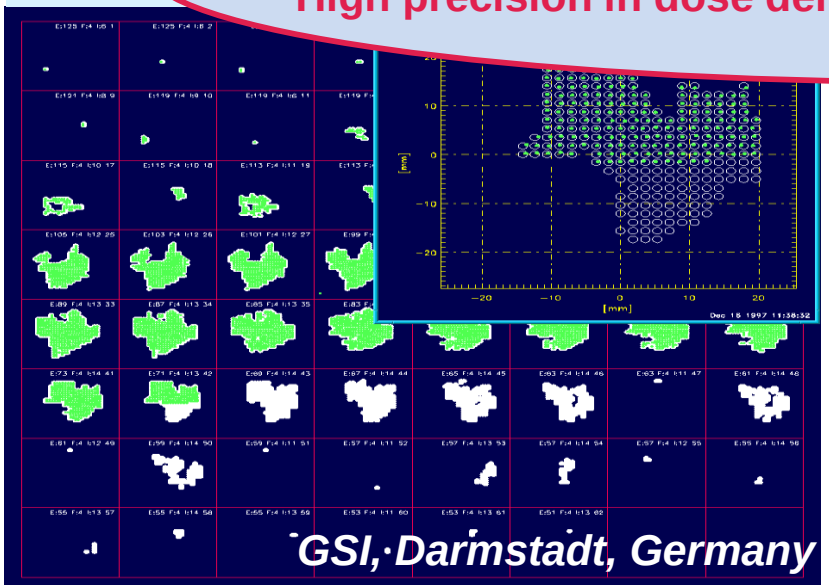
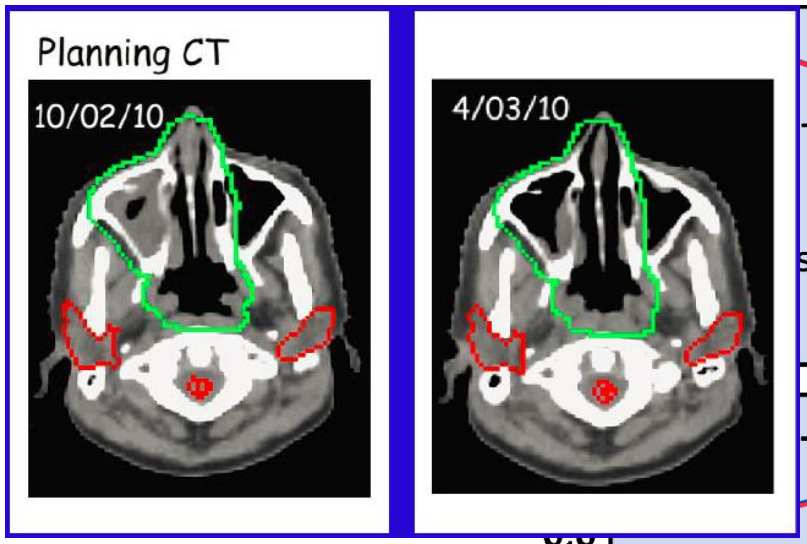
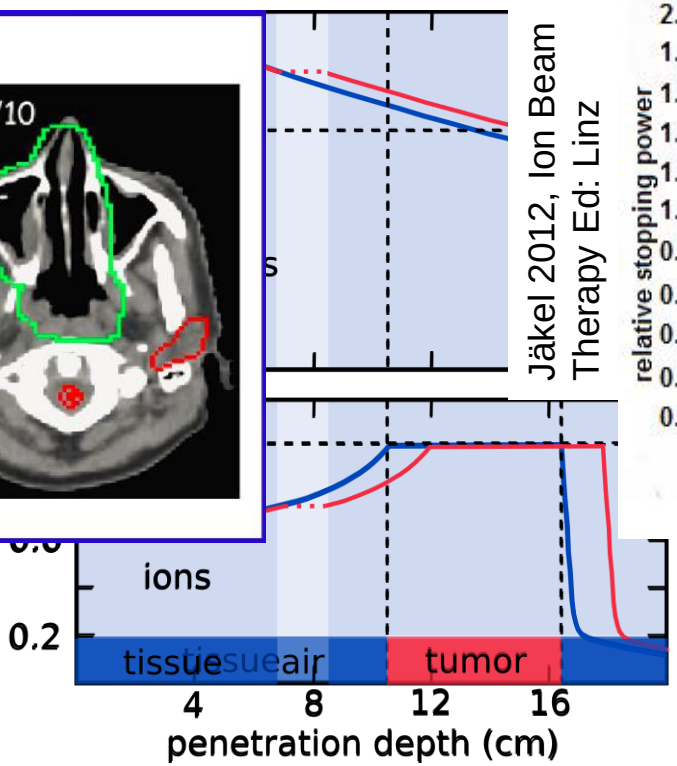
Conformal dose distributions +
High precision in dose delivery to arbitrarily shaped volumes

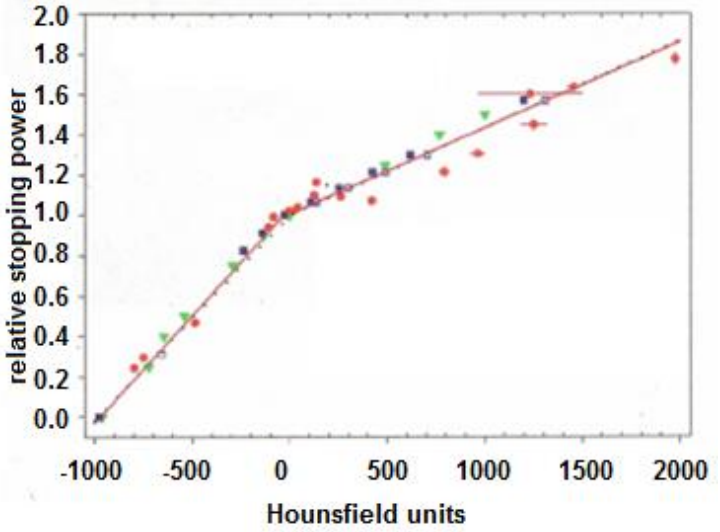


Ion-beam radiotherapy
Advantage and challenge



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





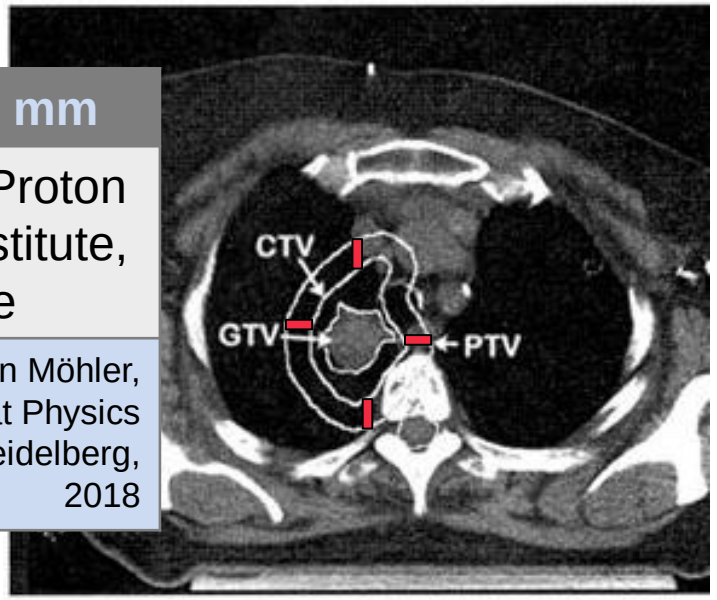
- Currently, overall **range uncertainties: ~ +-3.5 % +- 1.2 mm**
  [Paganetti 2012, Phys. Med. Biol. 57(11); Yang 2012, Phys. Med. Biol. 57(13)]
- Main reason: ambiguous **conversion** from **CT-HU to RSP**

Motivation

Ion-beam imaging for ion-beam therapy

3.5 % + 3 mm	3.5 % + 1 mm	2.5 % + 1.5 mm
MD Anderson Proton Therapy Center, Houston	MGH Proton Beam Therapy Center, Boston	UF Health Proton Therapy Institute, Jacksonville
Loma Linda University Medical Center		

From: Christian Möhler, Dissertation at Physics Faculty Heidelberg, 2018

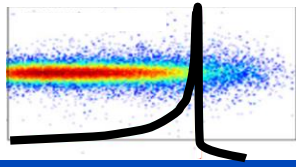


Washington et al, © Elsevier Health Sciences 2015

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

- **Important** to **see/avoid:** any **change/conversion error** betw. **planning CT** and **treatment.**
- **Ion-beam imaging** could be a promising method.

Outline



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- **Basic principle of ion-beam imaging & advantages**
  Applications
  History & overview of detection systems

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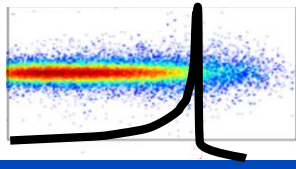
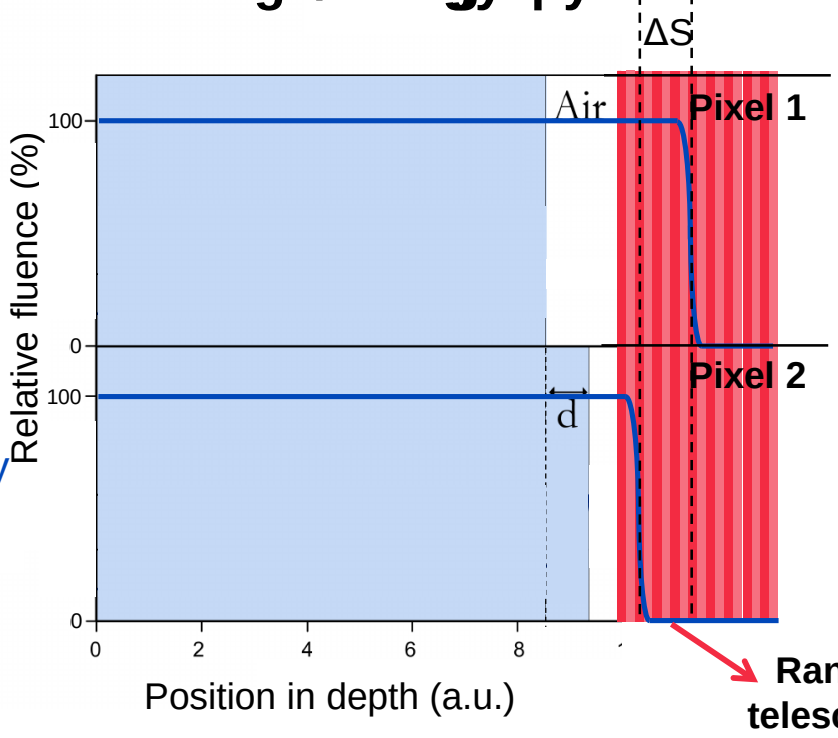
Ion-beam imaging: iRad/iCT

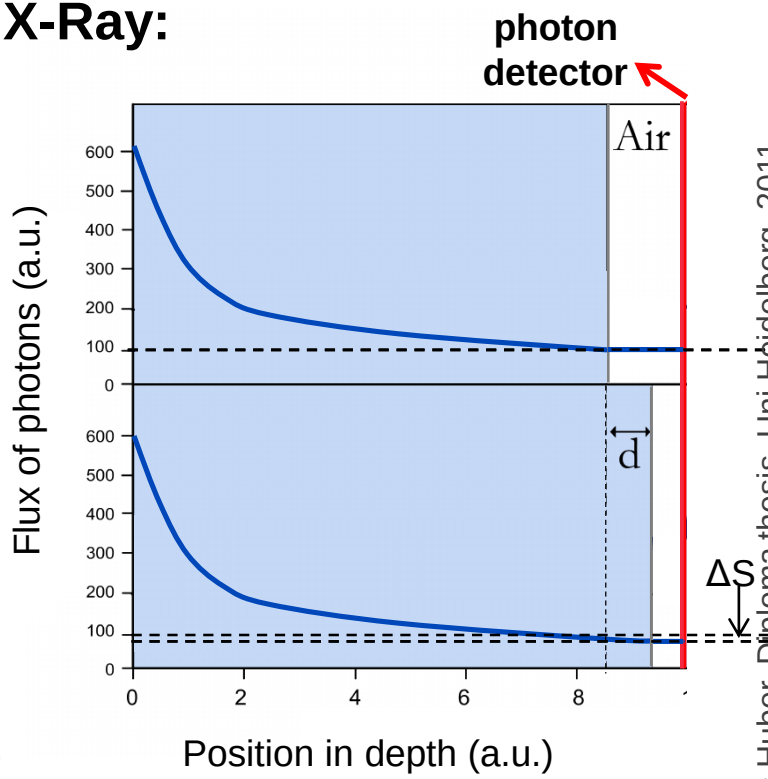
Basic principle and advantages



- Ion Beam Radiography measurement:
- X-Ray:

Ion beam @ high energy





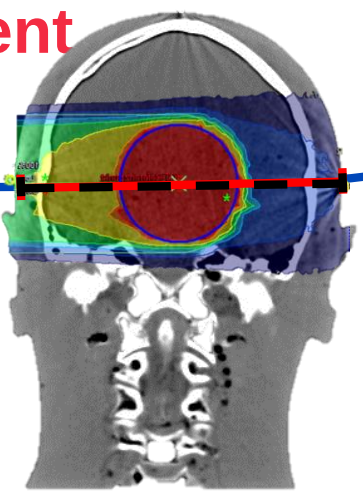
- **Low radiation exposure:**
  ~10 times less than for x-ray @ same density resolution [3,4]
- **Direct measurement of stopping power :**
  No error-prone conversion: HU (phot)→ stopping power (ions)
- **No metal artifacts**

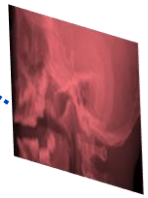
[2] modified from Lucas Huber, Diploma thesis, Uni Heidelberg, 2011
[3] R. Schulte, 2005, Med. Phys. 32: 1035-1046.
[4] Collins-Fekete et al 2020, PMB. 65 08501.

iRad/iCT
Potential clinical applications

- **iRad @ day of treatment**

^{4}He
@ high energy



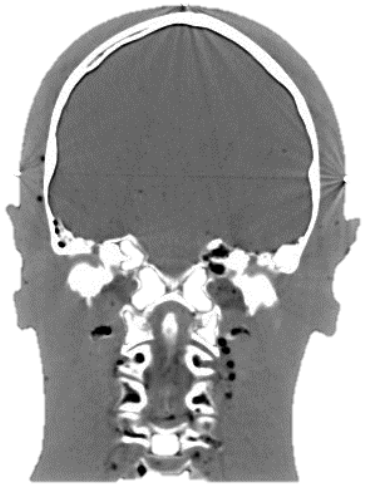


$WET_{meas} \stackrel{?}{=} WET_{CT}$

Verification of 2D WET-map from the planning CT in treatment position

- **Planning iCT**

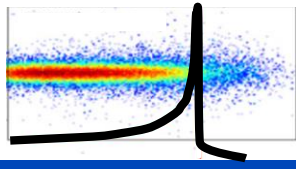
Ion beam
@ high energy



Range telescope

Technical feasibility ?

Basic principle of iRad/iCT
& integrating detection systems



Firstly mentioned by Nobel prize winner (CT) in 1963

A. M. CORMACK

Physics Department, Tufts University, Medford, Massachusetts

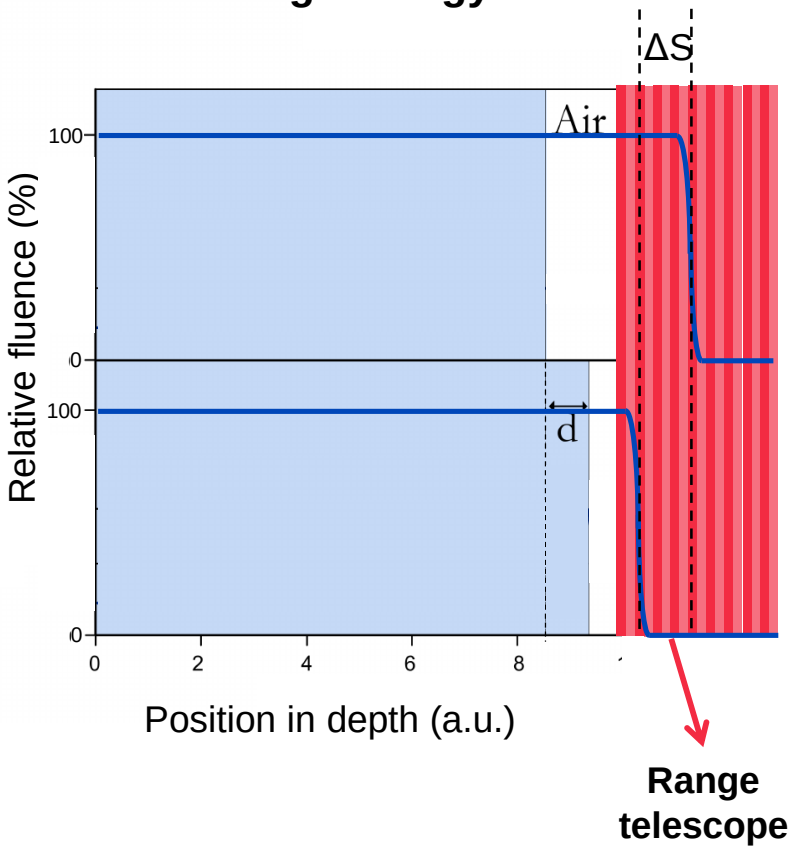
(Received 28 January 1963; in final form 26 April 1963)

••• the problem is the same as the [redacted] for x rays, •••

if a fine beam of protons pa[redacted] energies incident on, and emergent from, D are known, the number of g/cm² of material along L can be found from the range-energy relation for the material. •••

Ion beam
@ high energy

Residual range/energy measurement:



- **Integrating detection systems**: **one detector behind** the object measures residual energy or range **beam-wise** (not single ions)

Integrating detection systems (history)

My sketch of the first experimental set-up for proton radiography (Koehler, 1968, *Science*)

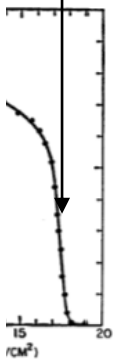
- **High WET-resolution at low doses!**
- **Limitation: Low spatial resolution** due to multiple Coulomb scattering (MCS) of protons

A. M. KOEHLER
Cyclotron Laboratory,
Harvard University,
Cambridge, Massachusetts

15 January 1968
Science

Proton Radiography

Abstract. *Energetic protons from an accelerator may be used to produce radiographs showing unusually high contrast but relatively poor spatial resolution.*



...on of depth ...ling portion of the curve near 18 g/cm² is used to obtain the high contrast of Fig. 1.

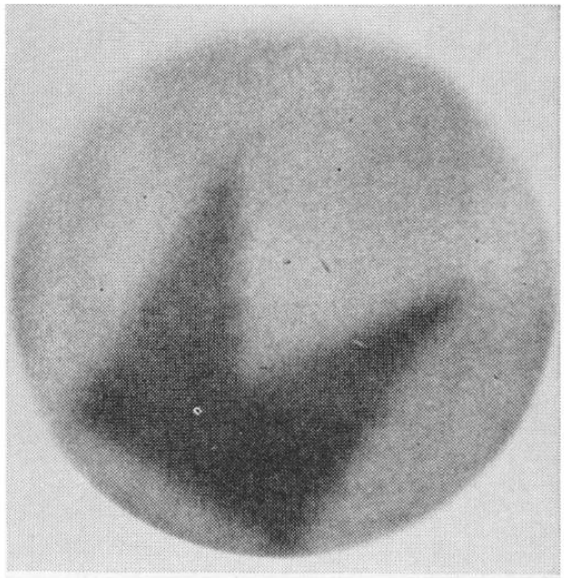
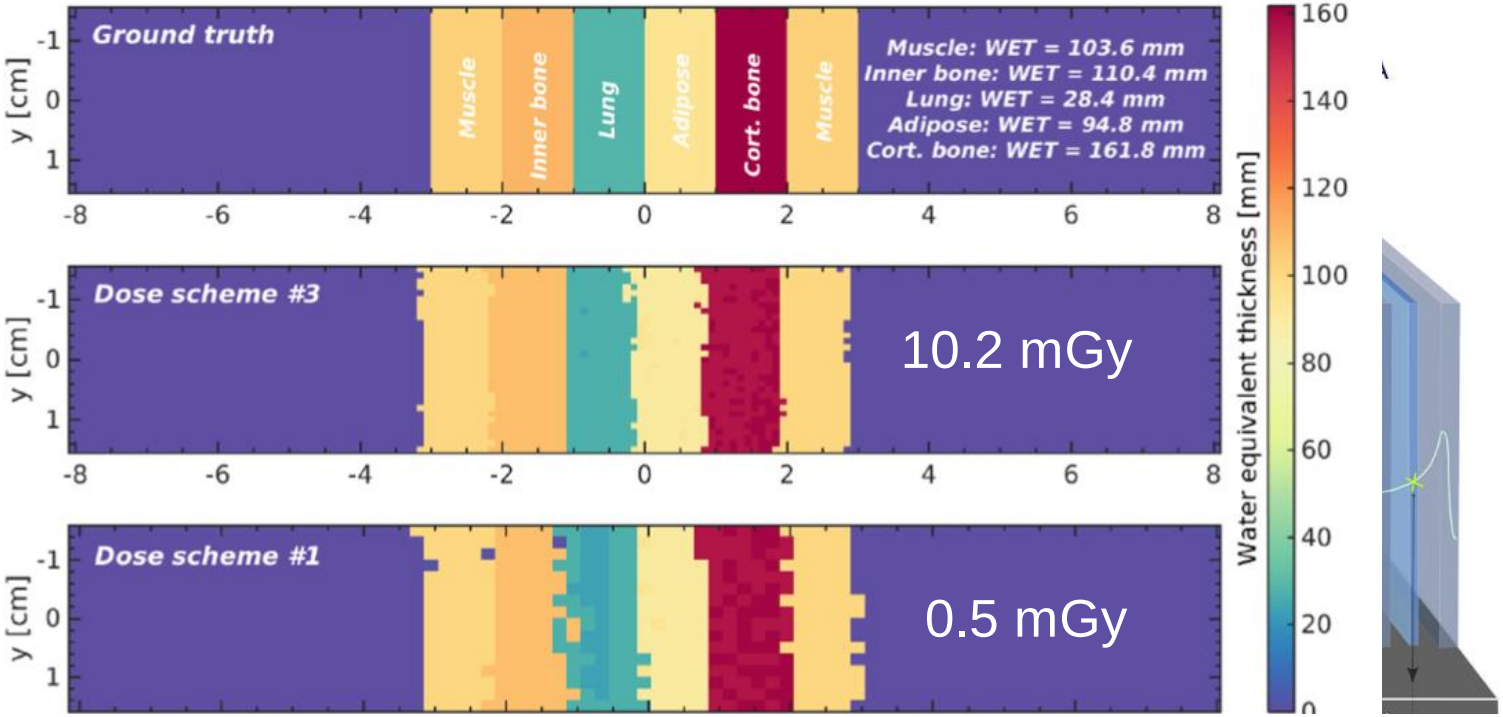


Fig. 1. Proton radiograph of aluminum absorber 7 cm in diameter and 18 g/cm² thick, with an additional thickness of 0.035-g/cm² aluminum foil, cut in the shape of a pennant, inserted at a depth of 9 g/cm². The addition of 0.2 percent to the total thickness produces a substantially darker area on the film.

Integrating detection systems (nowadays)

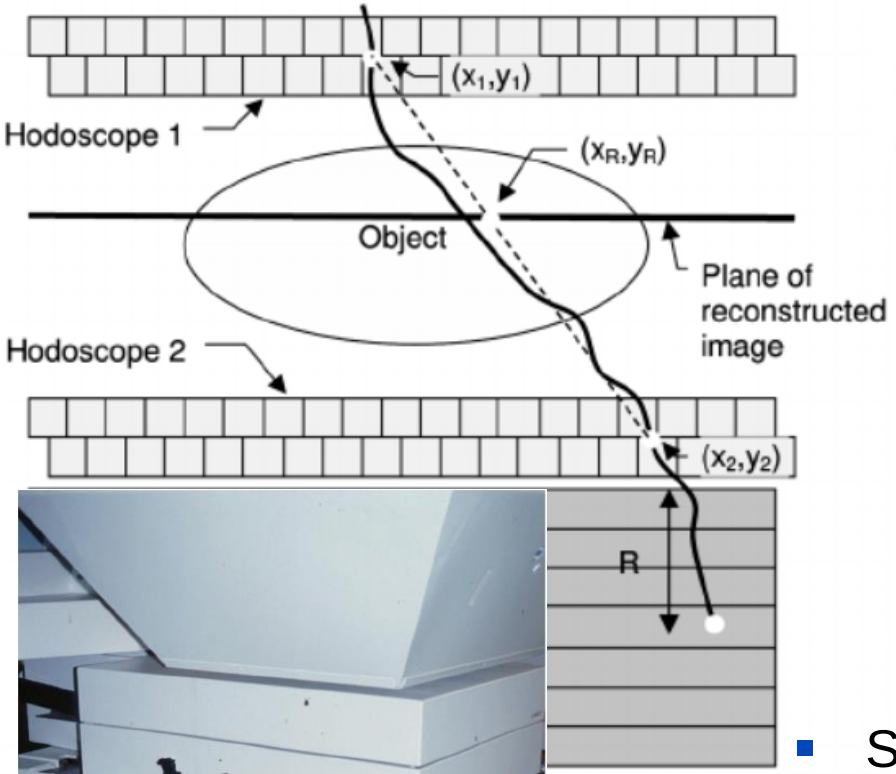
- I Rinaldi et al 2013: Phys. Med. Biol. 58 413
- L. M
  Rad
- B. K

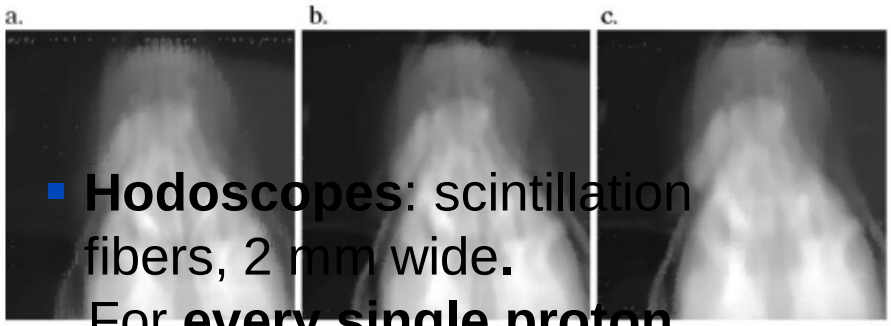


- Imaging of a **wide WET range->much closer to application.** (WET resolution at certain dose might be a bit compromised)
- Even a **bigger challenge for spatial resolution,** but luckily there are ^{12}C-ions.

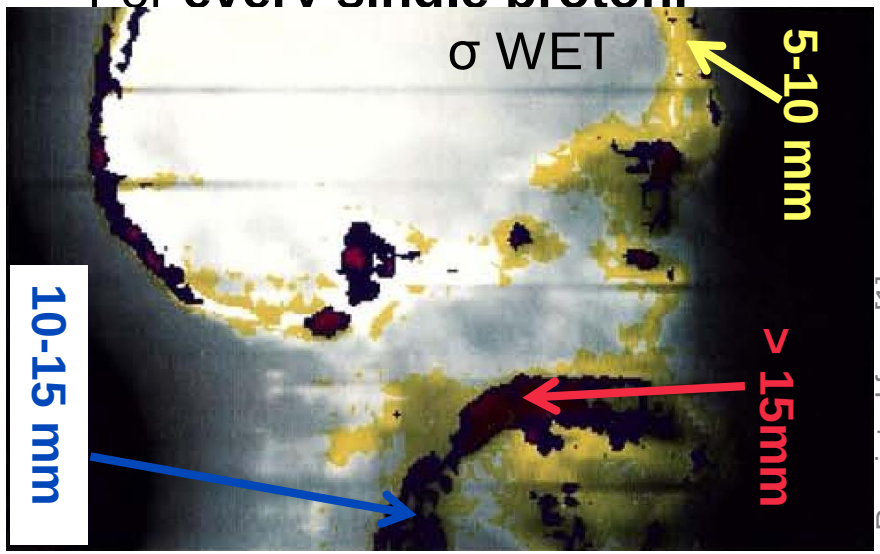
Tracking detection systems (history)

- **U. Schneider et al 2004, First proton radiography of an animal patient; Med. Phys., 31: 1046-1051**





- **Hodoscopes**: scintillation fibers, 2 mm wide**.**
  For **every single proton**,

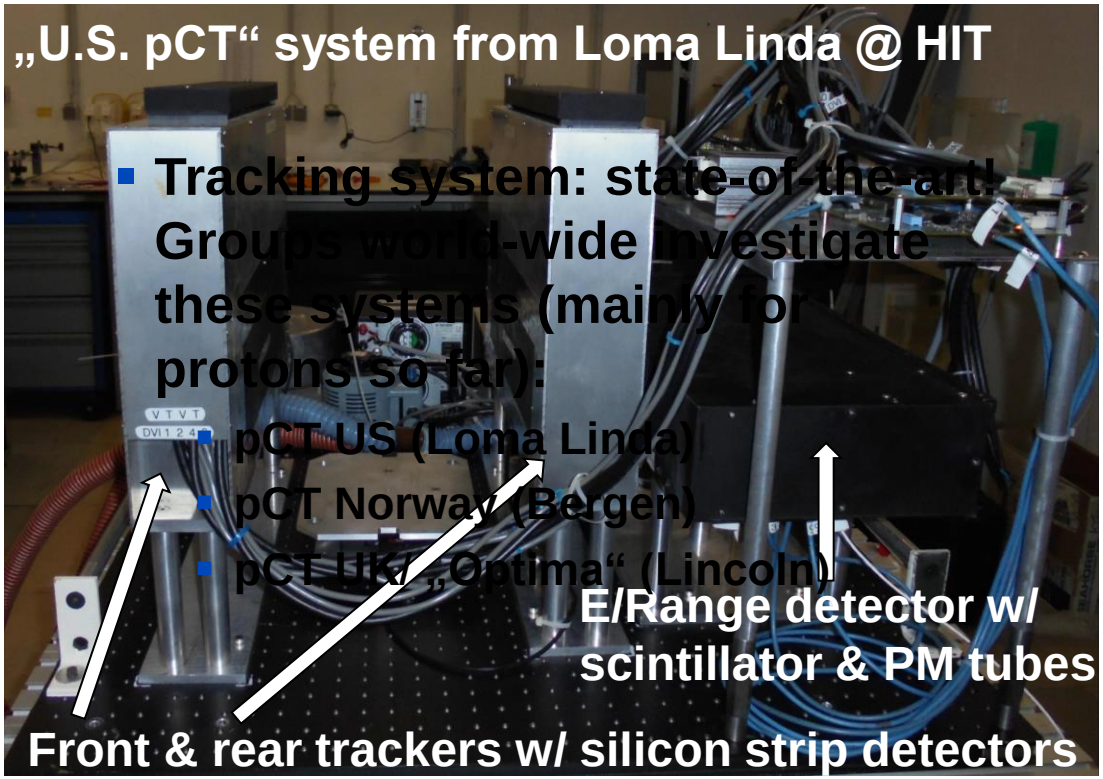


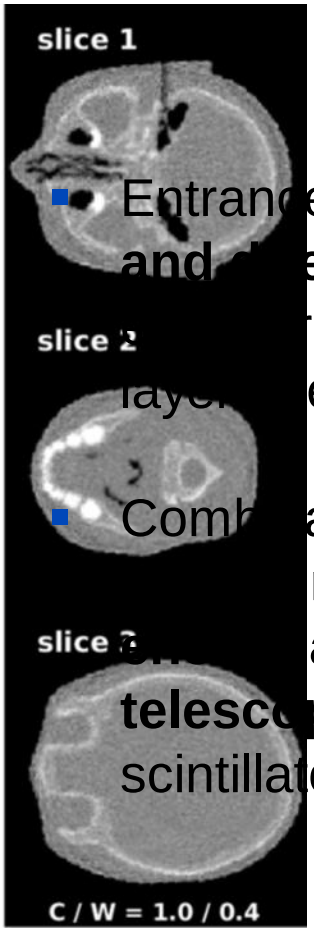
Reprinted from [1]

- Single-ion tracking: potentially high WET res. at low doses: 0.03 mGy.
- Improved spatial resolution! σ_{PSF}<2mm (clinically still challenging?!)

Tracking detection systems (nowadays) State of the art!

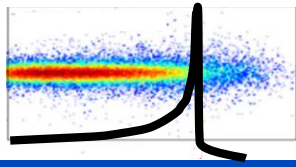
- R. Schulte et al. 2012; Trans. Am. Nucl. Soc 106:59–62
- R. Johnson et al. 2015; IEEE Trans. Nucl. Sci. 63:52–60
- J Dickmann et al 2019 Phys. Med. Biol. 64 145016





- Entrance/exit **position and direction** of proton (4 det. layer tracker)
- Combination of tracking **residual and range telescope**; 3 scintillator stages.
- **Close to** clinically-required SR: $\sigma_{res} \approx 1$mm
- WET precision **< 1 %** for **low doses** (whole CT @ **0.9 mGy**!)

Outline



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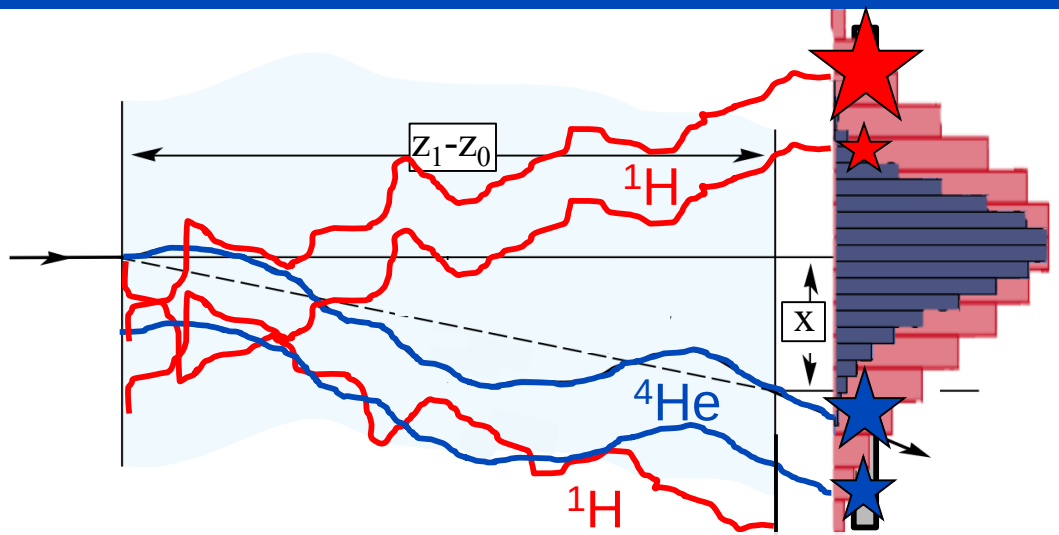
Why exactly helium ions? Theory



- **Multiple Scattering (MCS)**

  reduced by a factor of 2 for ^{4}He w.r.t. ^{1}H

→ **Better spatial resolution**

- Energy loss straggling

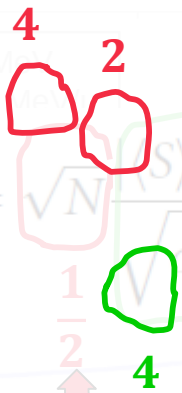
  reduced by a factor of 2 H

→ Better contrast-to-noise r

$$\int_{z_0}^{z_1} \frac{(z_1 - z)^2}{\beta^2(z)c^2 p^2(z)} \frac{\mathrm{d}z}{X_0}$$

1 16

Schulte et al 2008



erial

n and charge of incident ion

- Energy loss

  Increased by a factor of 4

→ Increased dose

more detailed in:
Gehrke *et al* 2018 *Phys. Med. Biol.* **63** 035037

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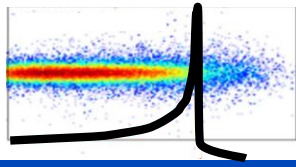

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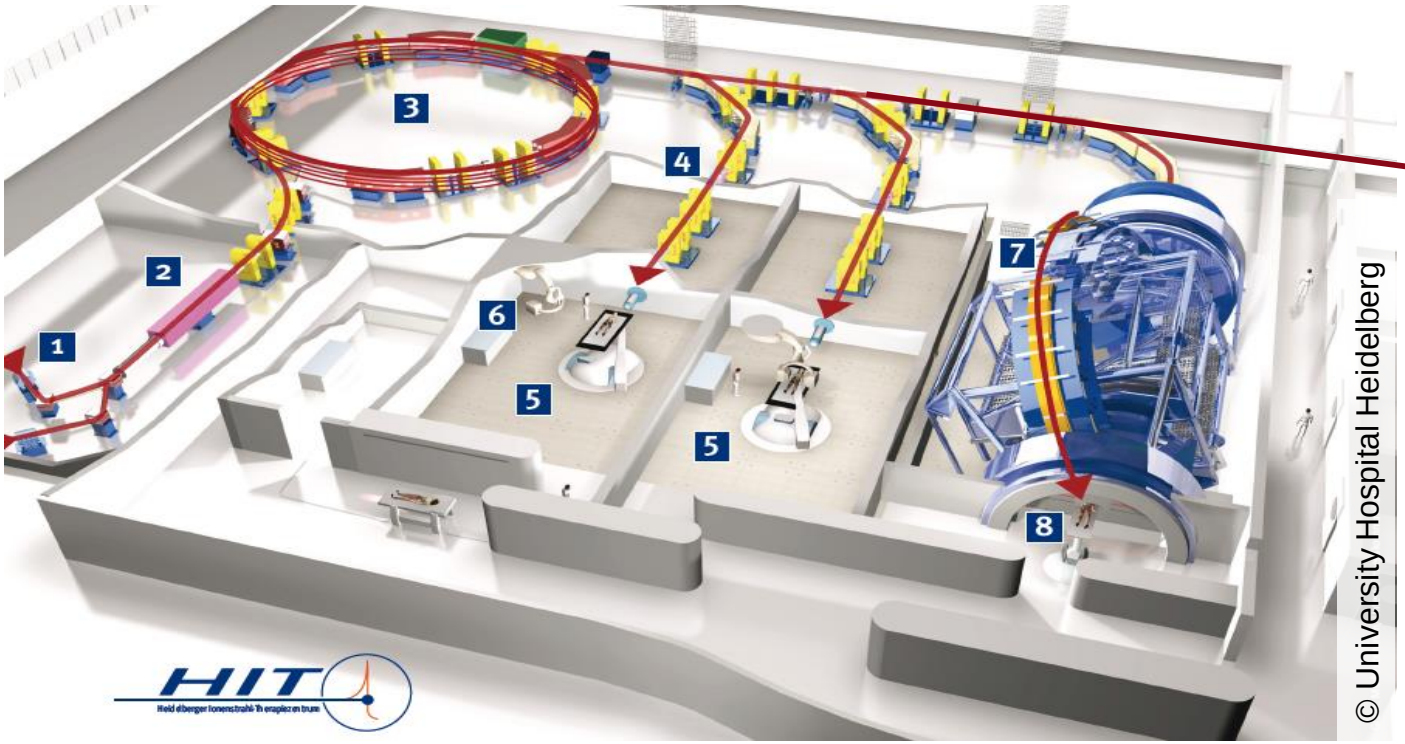
HIT facility

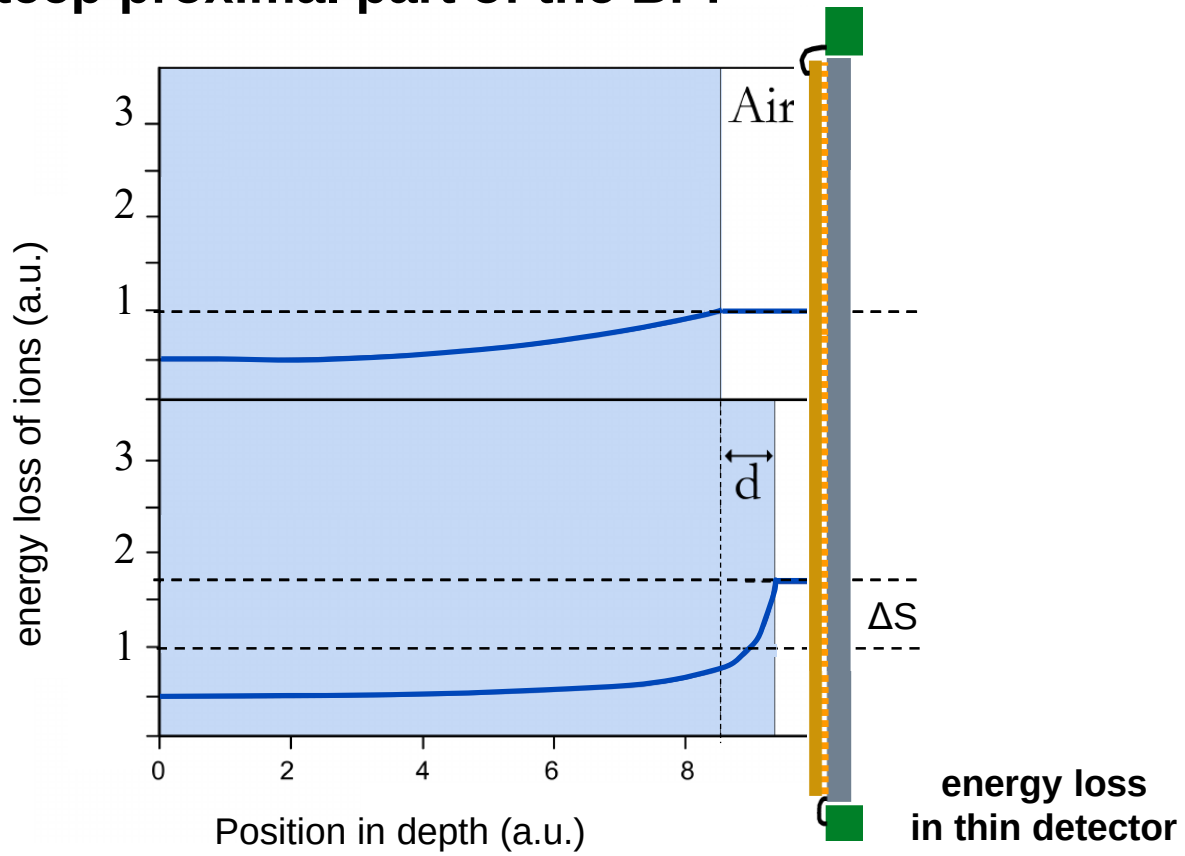


- Treatment of over 4000 patients with p & ^{12}C since 2009
  - Pencil-beam scanning
  - Ion ranges: ~2 – 30 cm (H_2O)

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

How do we perform it?
Operating principle

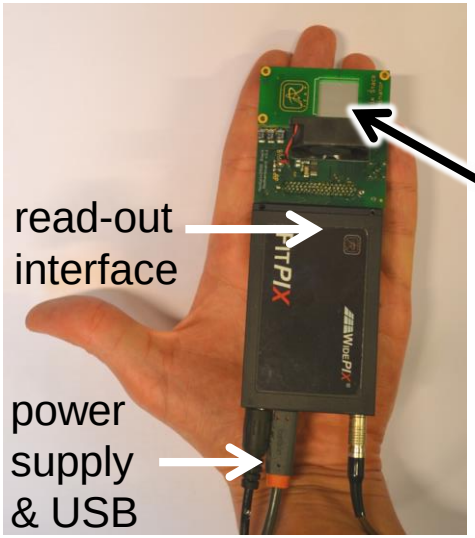
- **Energy loss measurement in the steep proximal part of the BP:**

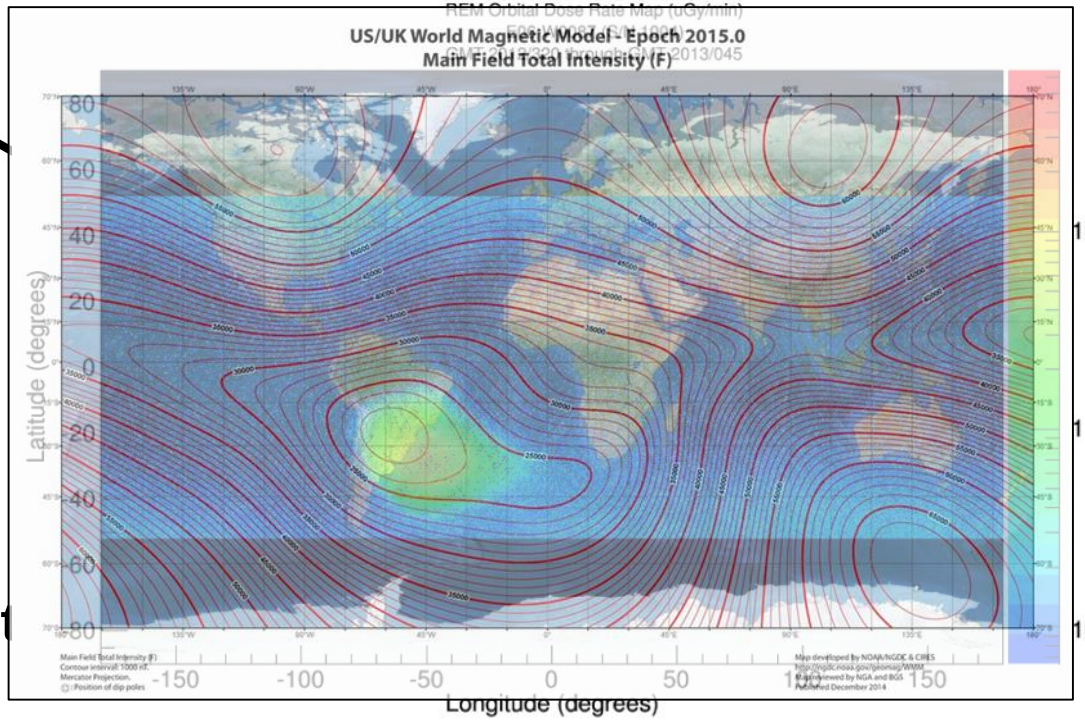


How do we want to implement αRad?

Timepix detector

Utilization of the very **compact, semiconductor based Timepix detector**



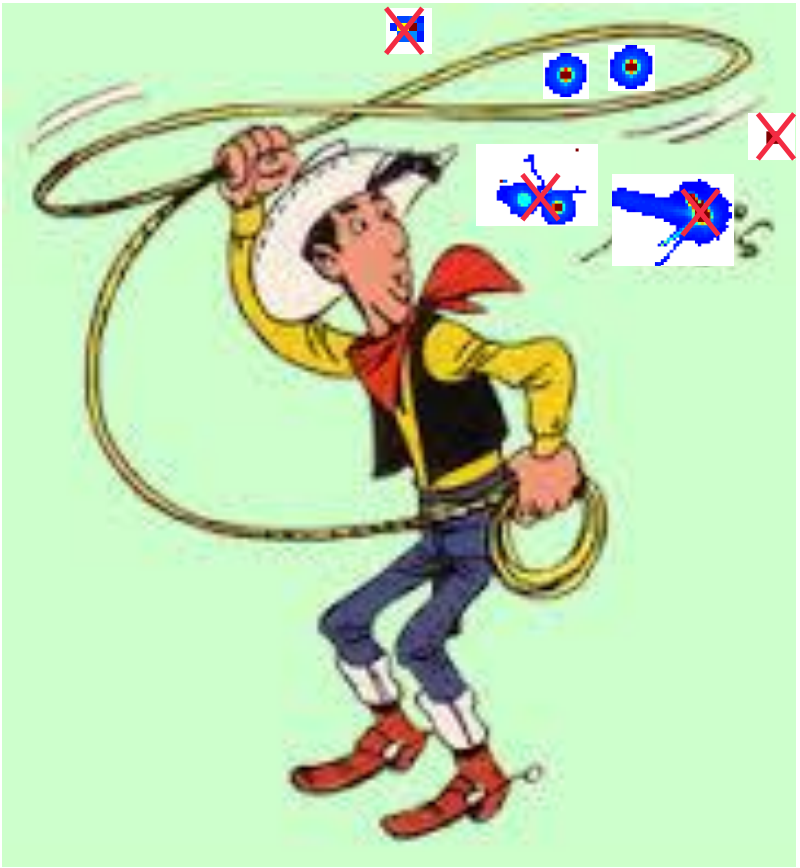


Single ion detect

- **ion type** [5]
- **Direction** [6]

[5] B. Hartmann et al., NSSMIC, 2012 IEEE, p. 4076-4079
[6] P. Soukup et al., JINST p.C01060, 2011
Initial Report on ISS Radiation Environment Monitor Perf., 2016

Ion identification



Ion identification

Timepix detector – particle identification

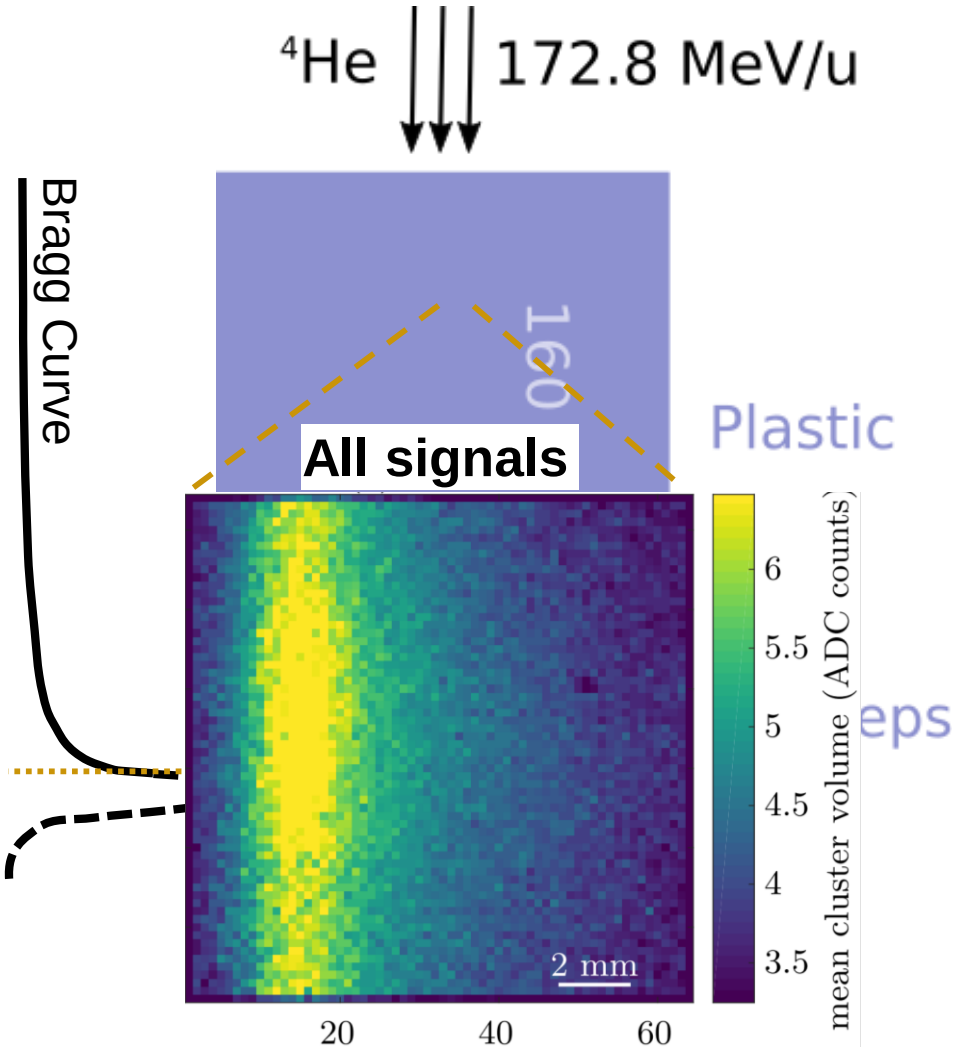
α heavy ions

β

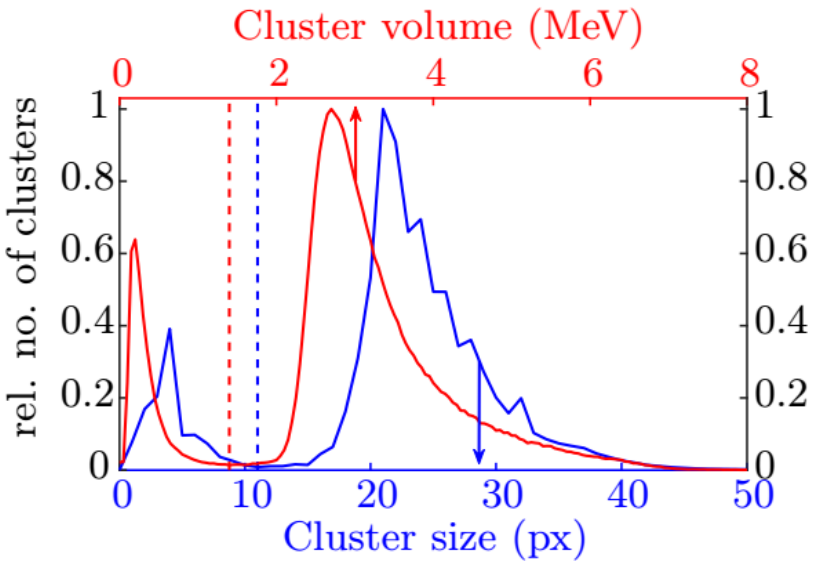
μ

X

Ion identification
Experimental set-up



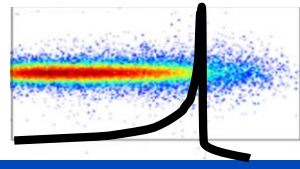
Ion identification
Selection method



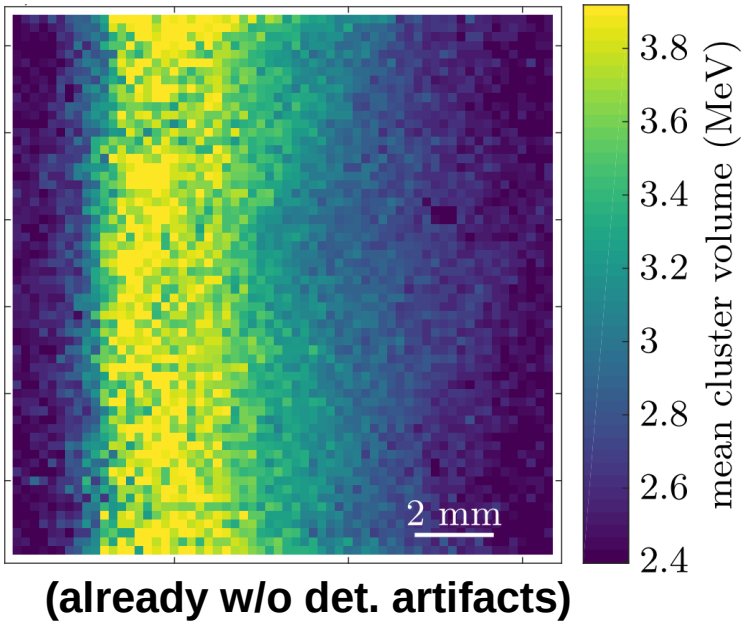
- Unambigious separation between primary and secondary ions

[Gehrke *et al* 2018, Med. Phys., 45: 817-829]

Ion identification
Comparison

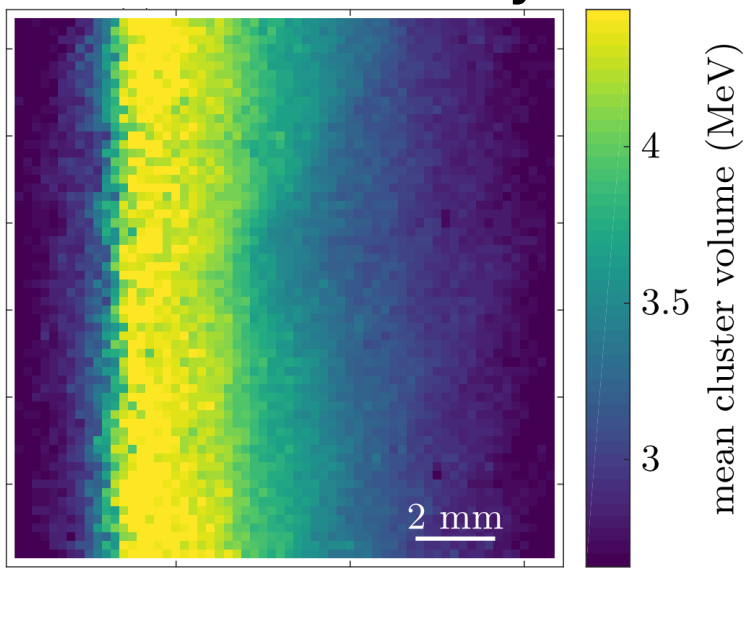


All Ions

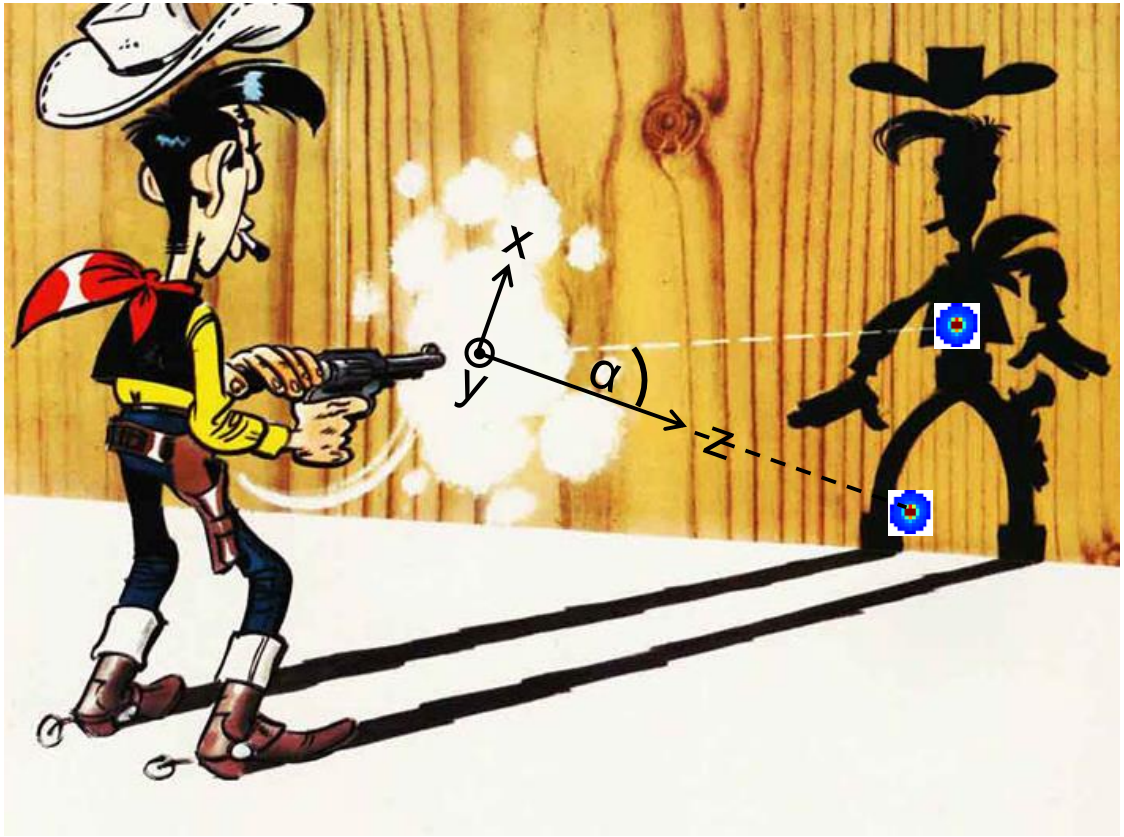


(already w/o det. artifacts)

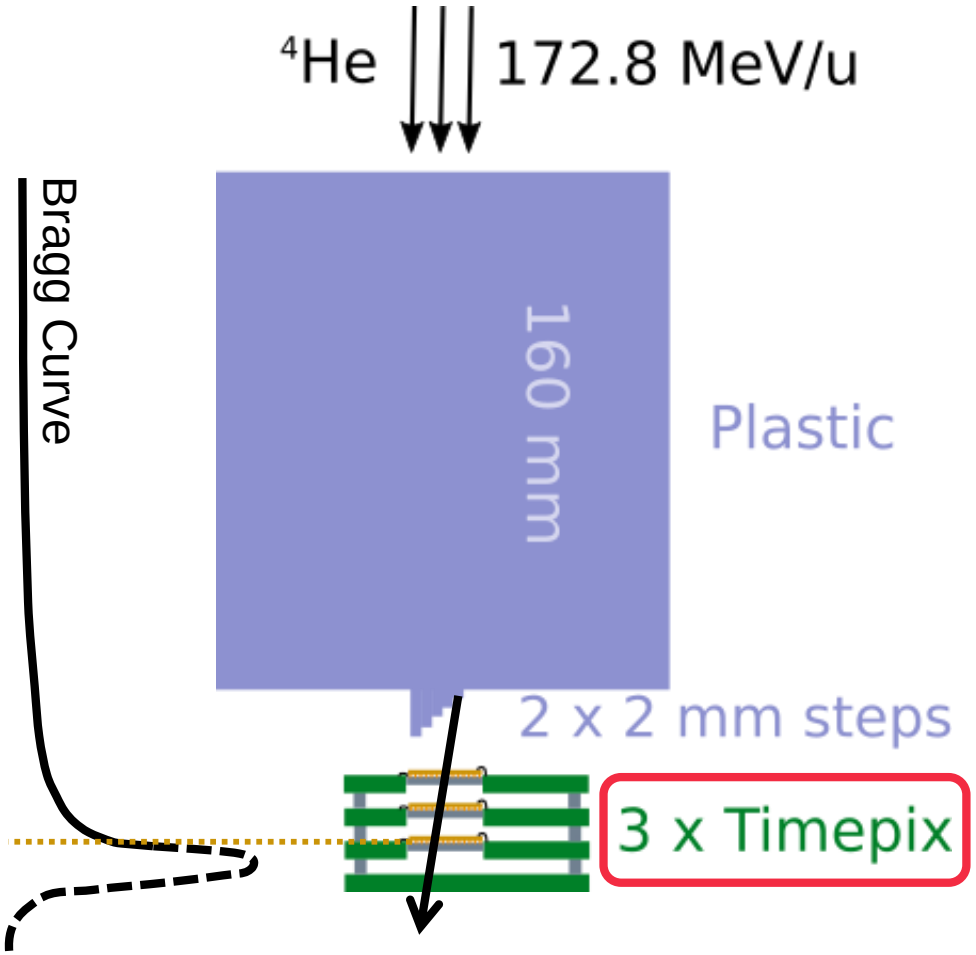
Helium ions only



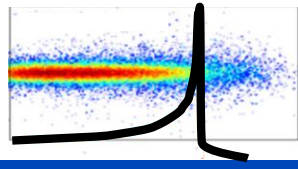
Ion tracking



Ion tracking
Experimental set-up



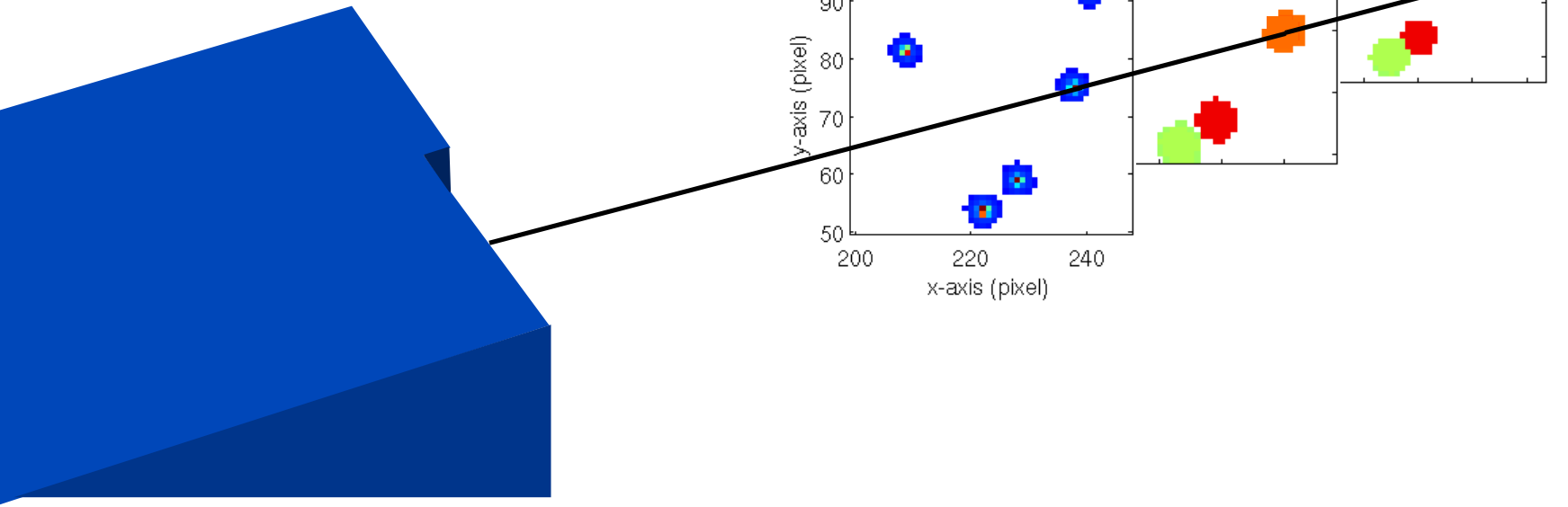
Ion tracking
Procedure



Time mode

Time mode

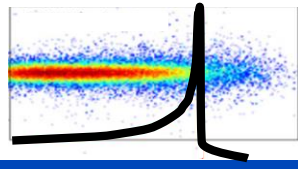
Energy mode

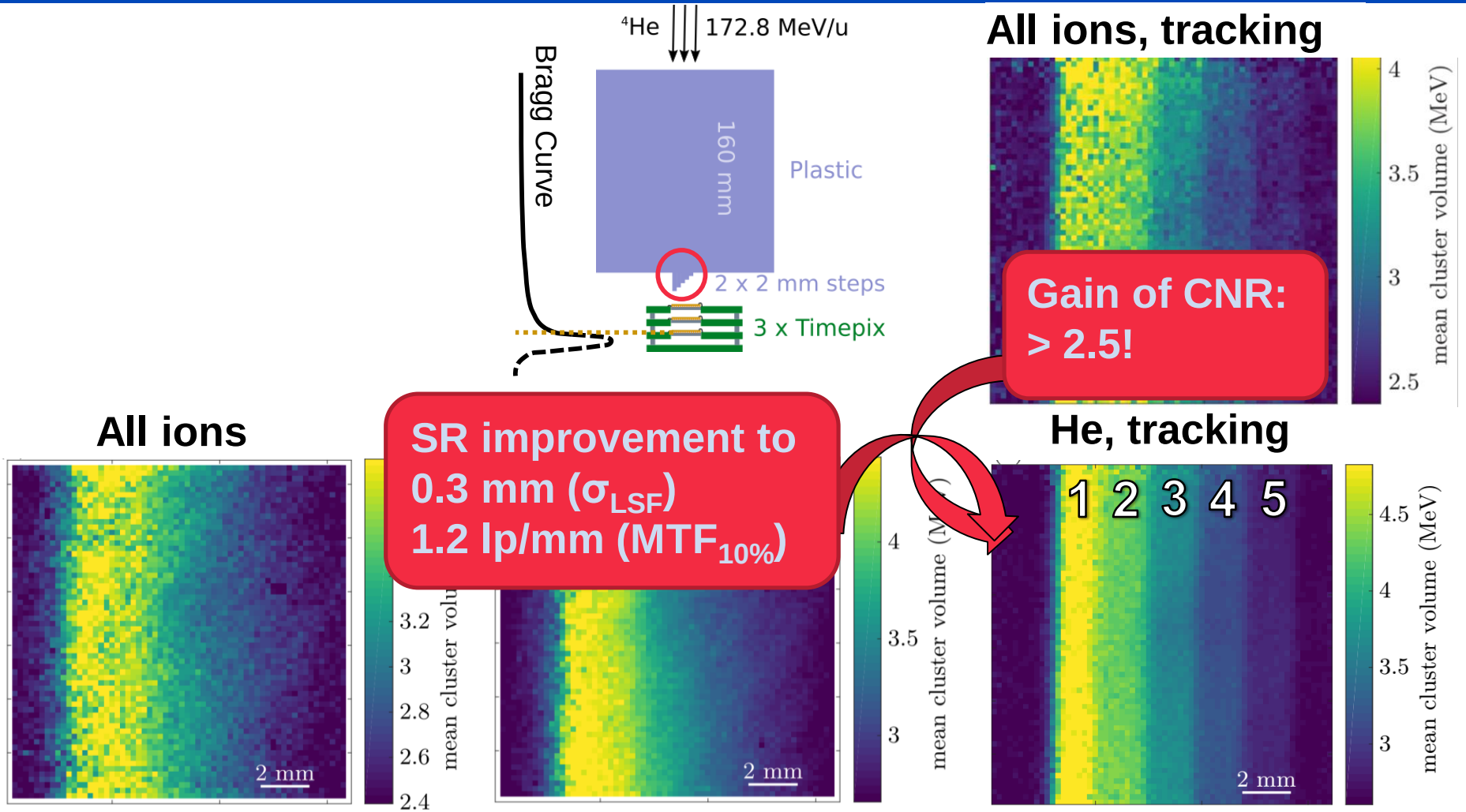


dkfz.

Ion tracking + selection

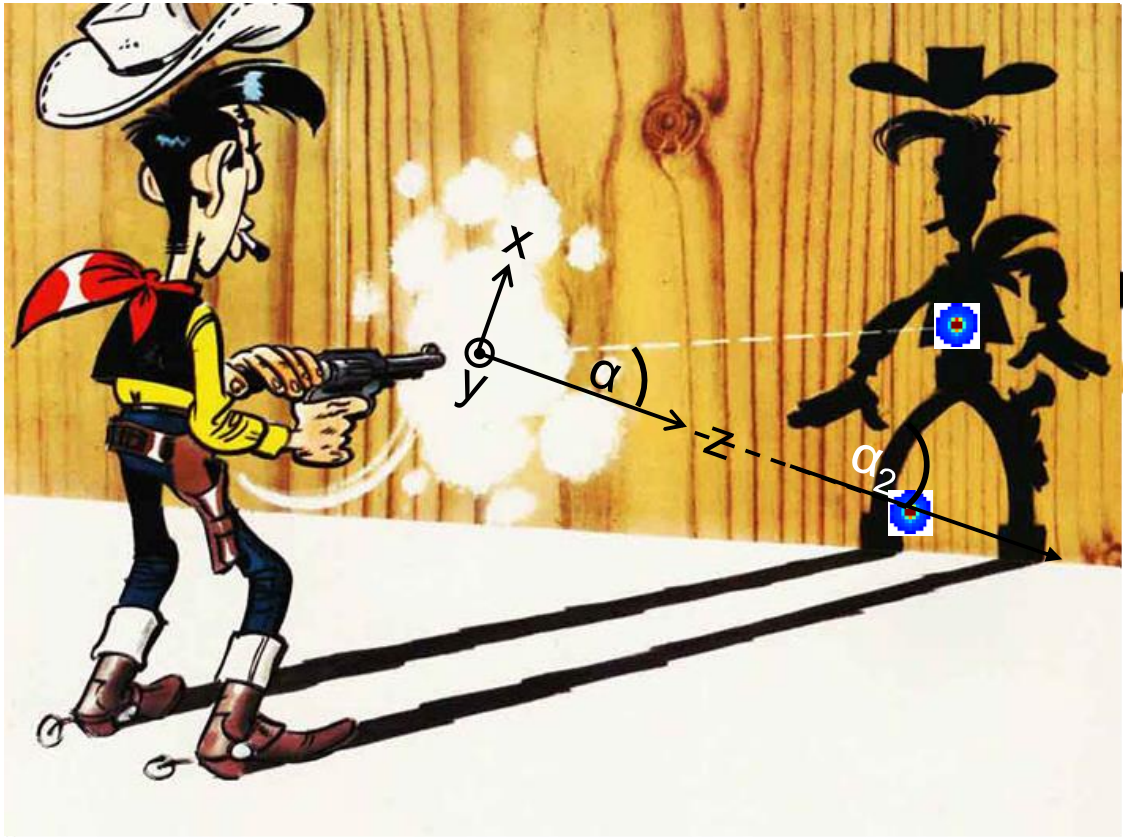
Comparison of αRads



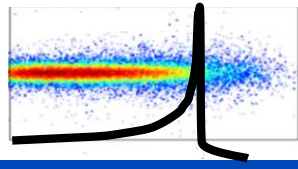


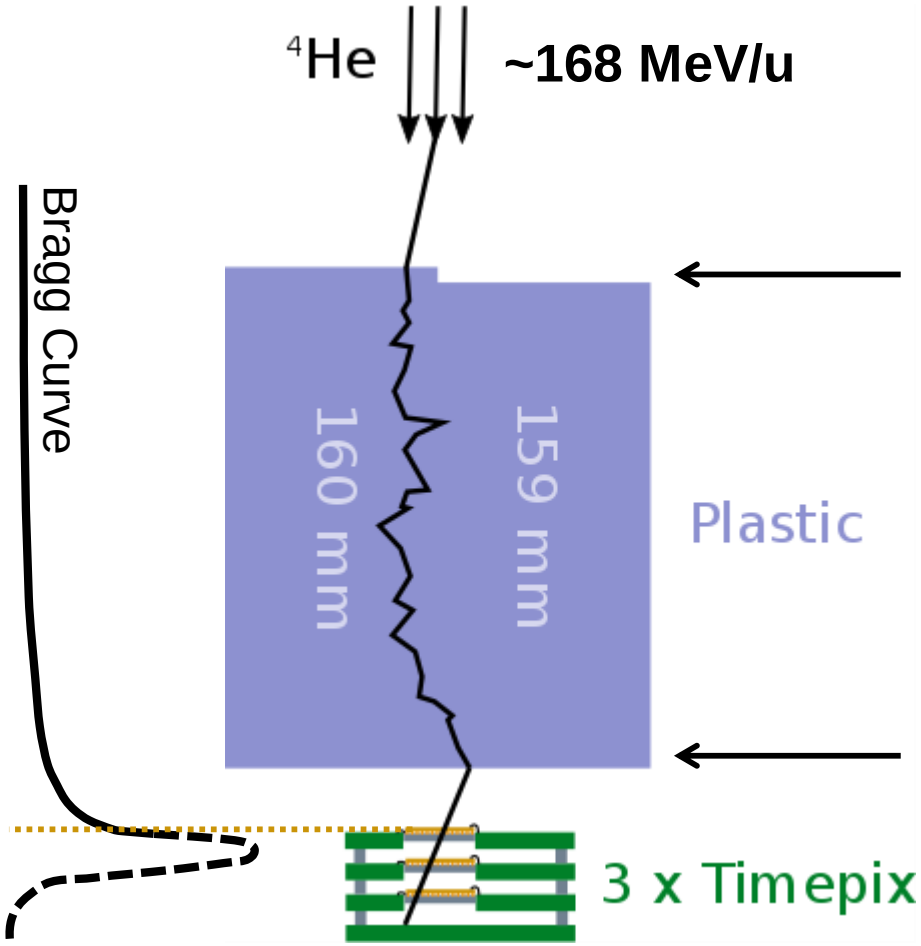
WET resolution ~1 % at clinical dose levels
+ clinically useful spatial resolution

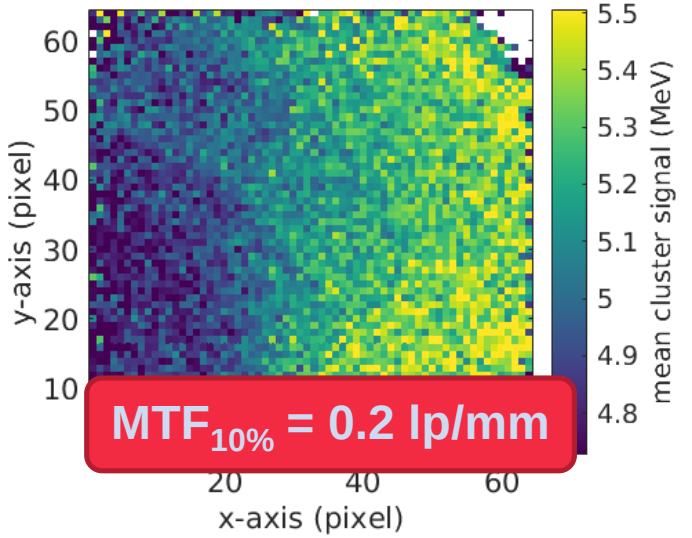
Ion tracking (Part II)

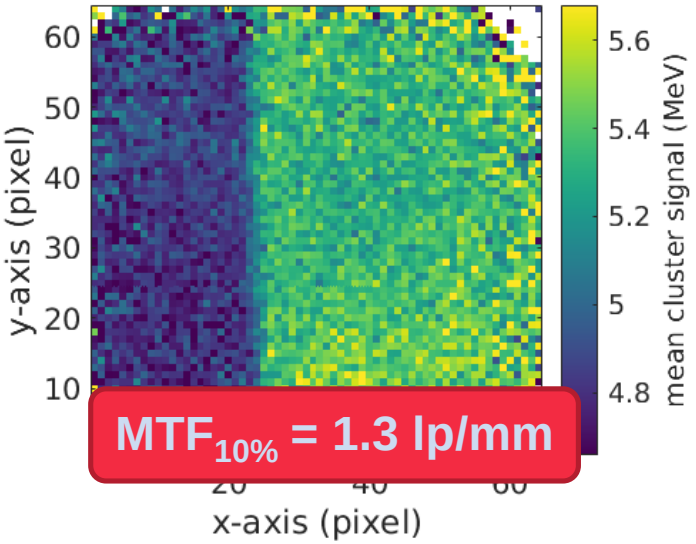


Ion Tracking (Part II)
Challenge



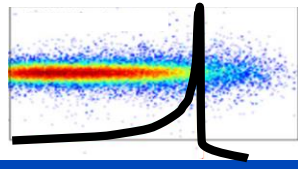


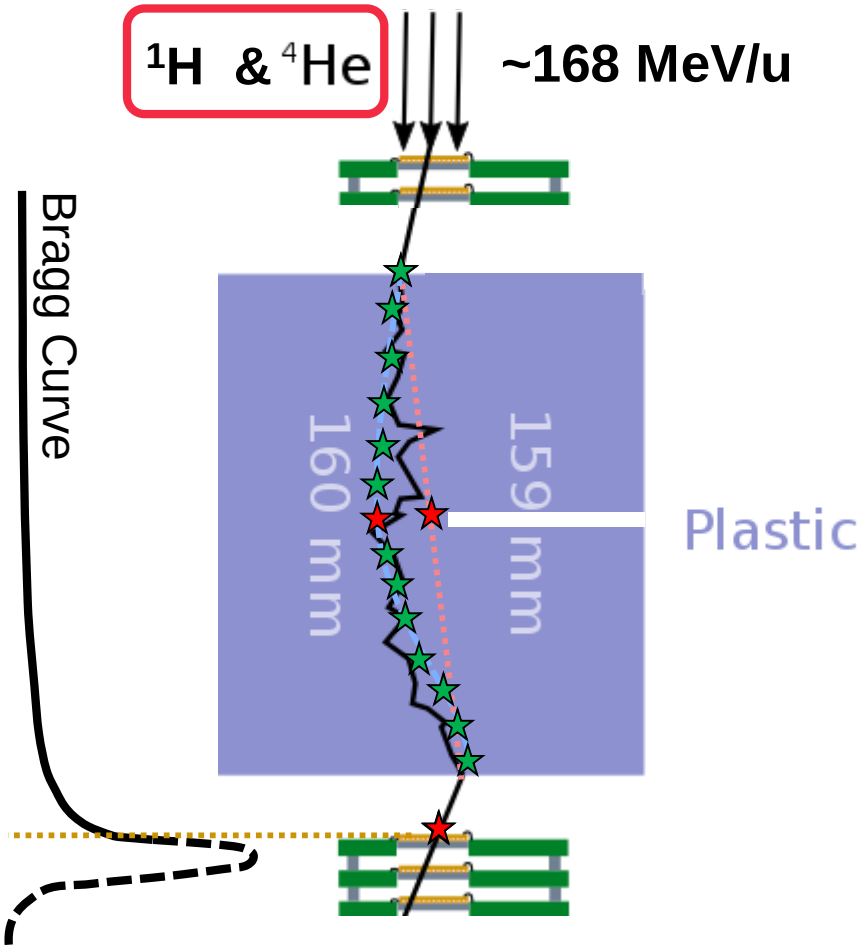




Ion Tracking (Part II) + ion comparison

Experimental set-up



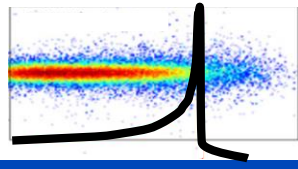


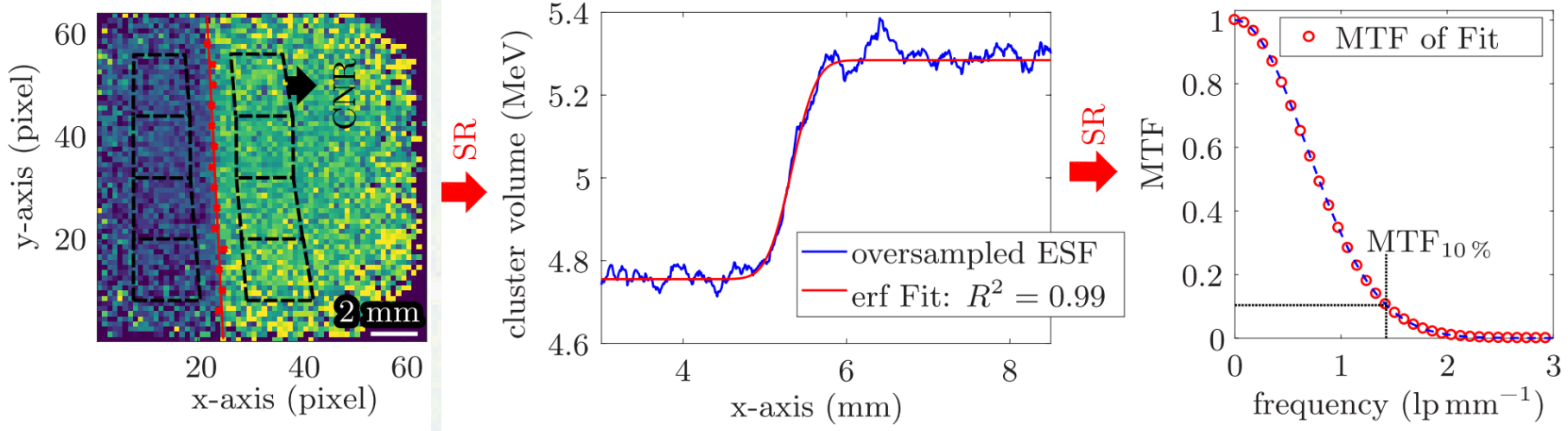
- **Position** and **energy loss**:
  linked via **timing meas.**
- **Middle pos.**
  by linear interpolation (SLP) or
  by cubic spline path (CSP) or
  by along-path reconstr. (APR)
- **Also performed with ^{1}H**
  for comparison

idea of measuring entrance- and exit-vectors: H.F.-W. Sadrozinski et al, 2004
measuring entrance- and exit-vectors: R.P. Johnson et al, 2014
Cubic spline path algorithm: C-A C Fekete et al, 2015 and 2017

Comparison between pRad and αRad

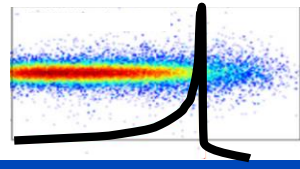
Examples of images & their evaluation

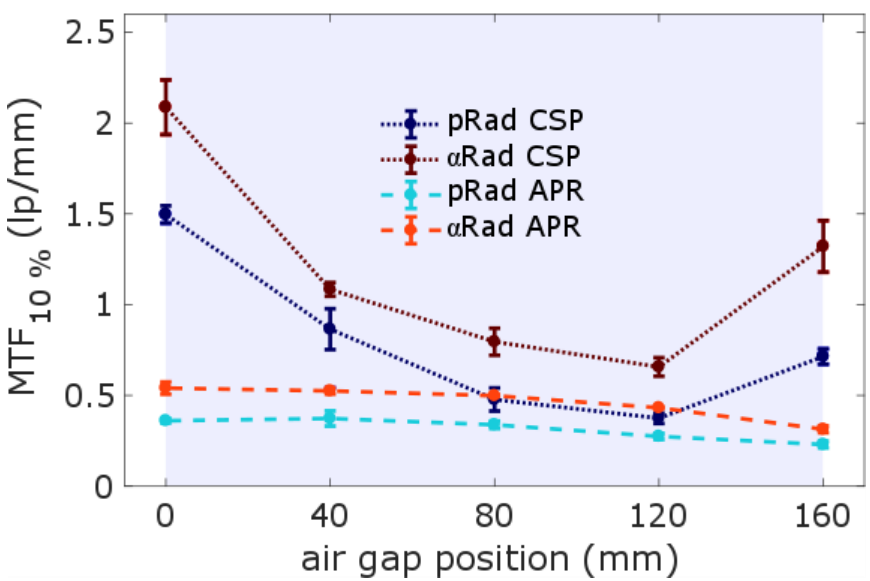


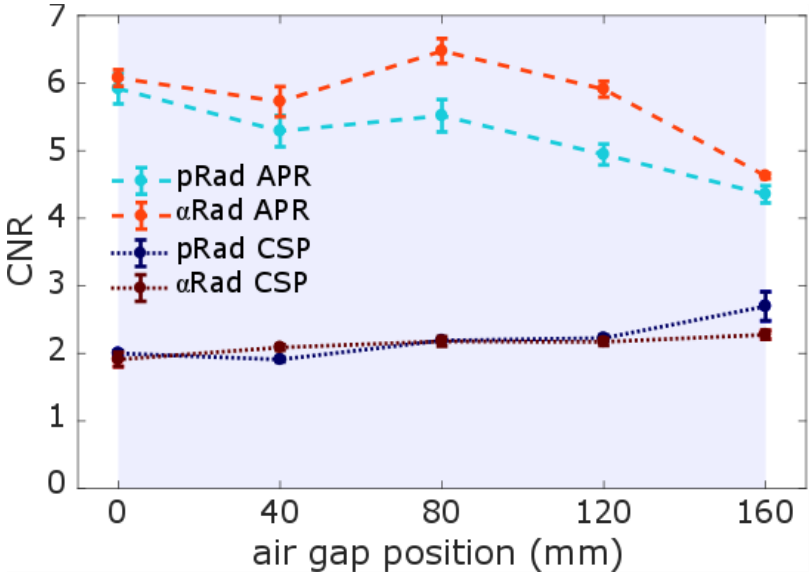


[Gehrke et al 2018 Phys. Med. Biol. 63 035037]

Comparison between pRad and αRad
Results

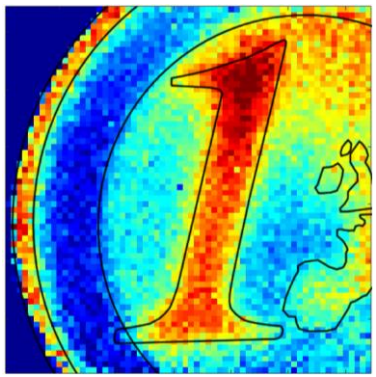






- **αRAD improves SR** compared to pRAD on average **by 55 %.**
  $MTF_{10\%,avg}$=0.46 lp/mm(worst case: 0.31 lp/mm) @ phantom‘s WET≈190 mm.
- $CNR_{\alpha Rad}=CNR_{pRad}$ @ the same clinical doses.

Conclusion on ion-beam imaging & on our research about αRad



- Implemented clinically, **iRad (& iCT)** have the **potential** to **improve accuracy** of ion-beam therapy
- **Research** on detection systems for iRad/iCT still **ongoing** to fulfill simultaneously requirements of **spat. res. & WET res. & acquisition speed.**
- At least 1 detection system, which is **very close to clinical application**

Results from our study on αRAD:

- **Ion identification** crucial for αRAD & developed method successful**:**

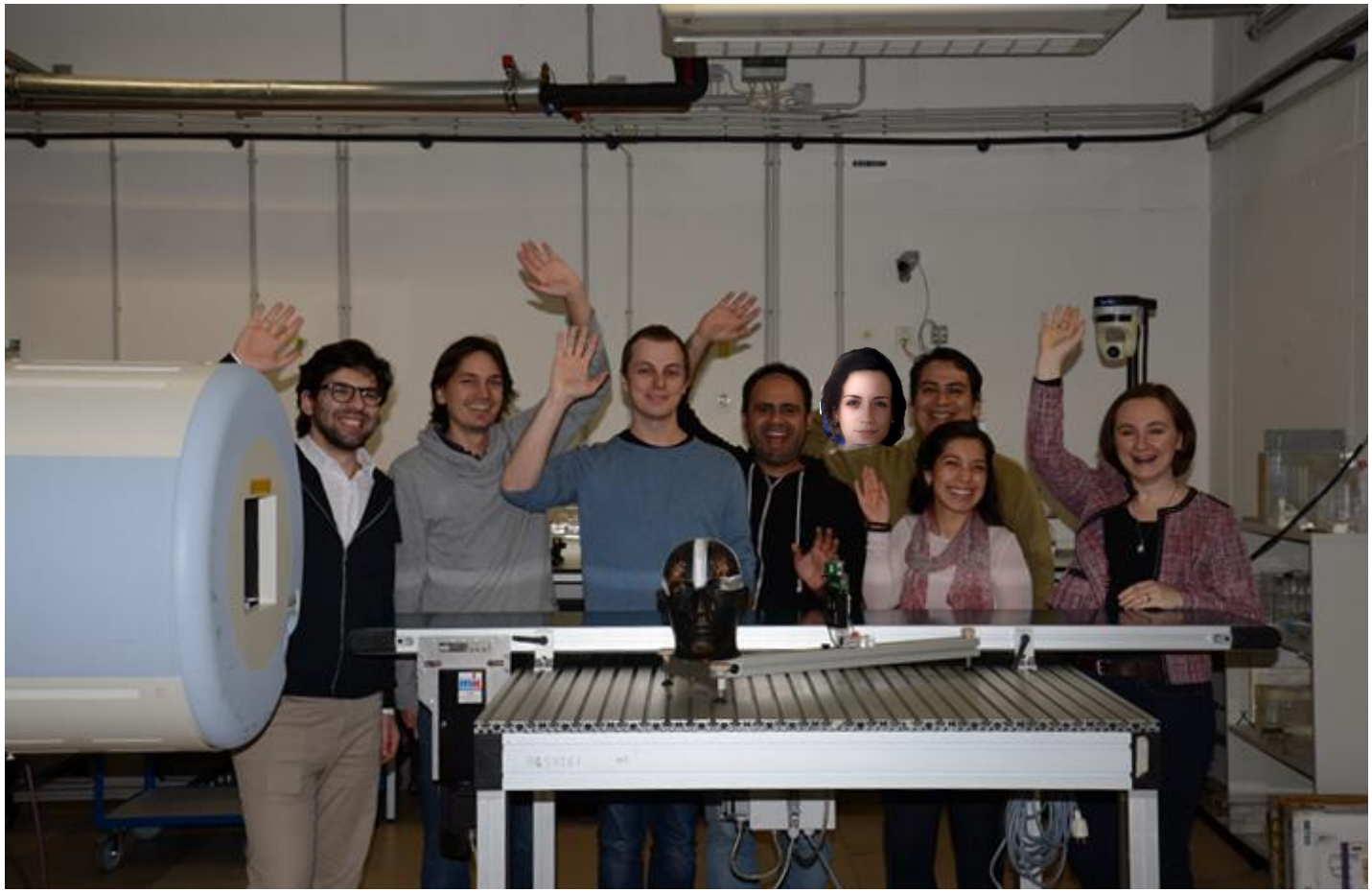
  CNR: ↑ 2.5-times
- **WET resolution <1 %** achieved at dose levels for diagn. X-rays (~350 µGy)
- **αRAD improves the SR** compared to pRAD **by ~55 %,**

  without any disadvantages in terms of imaging dose or CNR. SR of

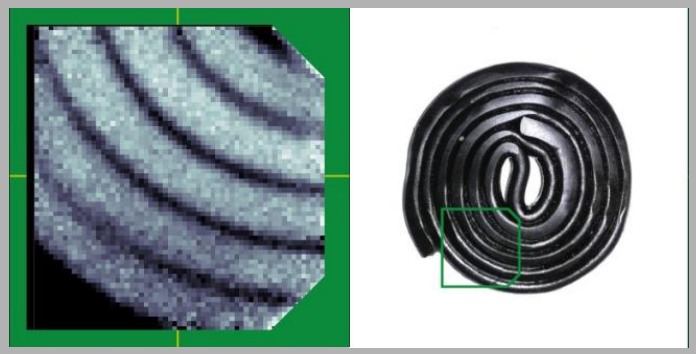
  $MTF_{10\%,\,avg}$=0.46 lp/mm for head-sized objects.

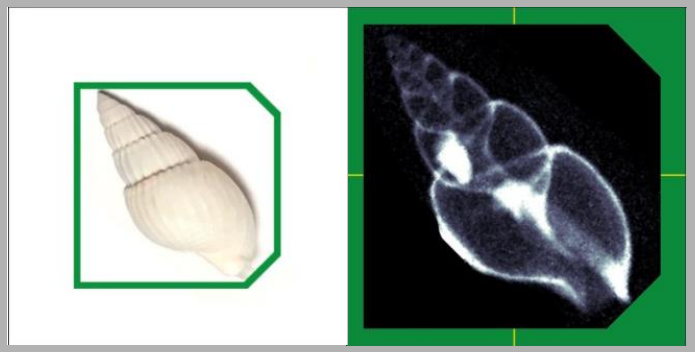
Thank you for your attention!

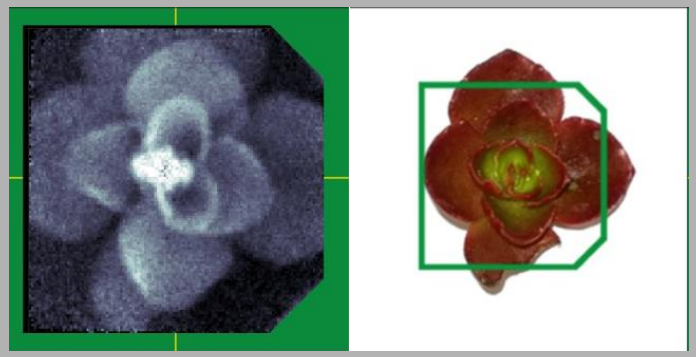
If you are interested in a Master project in this topic, please contact Maria Martisikova m.martisikova@dkfz.de or me t.gehrke@dkfz.de



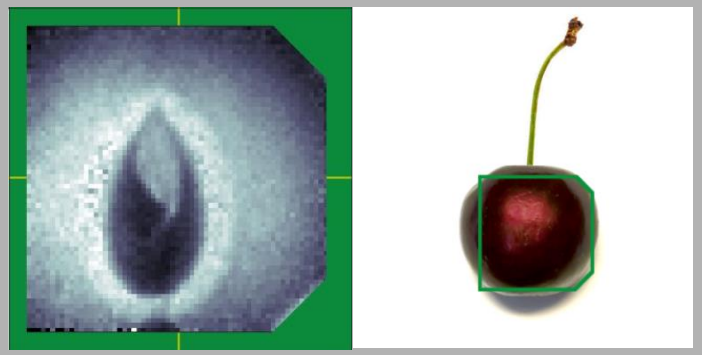
This is the end

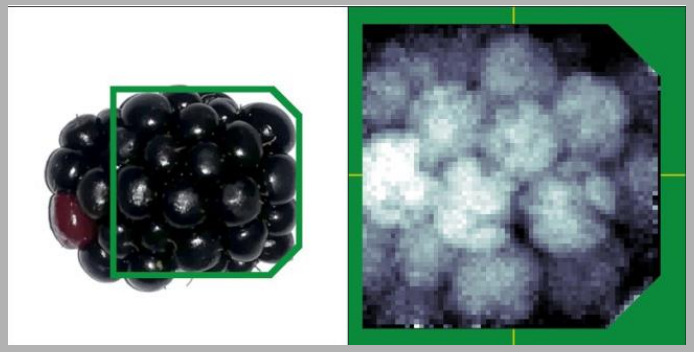






Are there any questions?





Images: C. Amato, L. Ghesquiere, R. Felix-Bautista, T. Gehrke, M. Martisikova