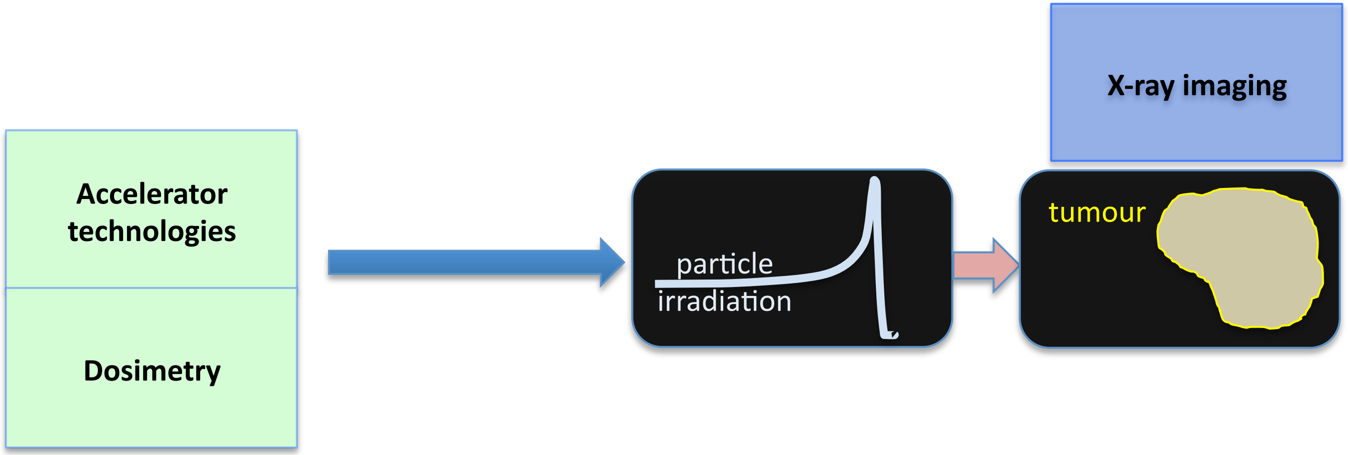
Radiation quality measurements of ion beams: clinical feasibility and possible implementations

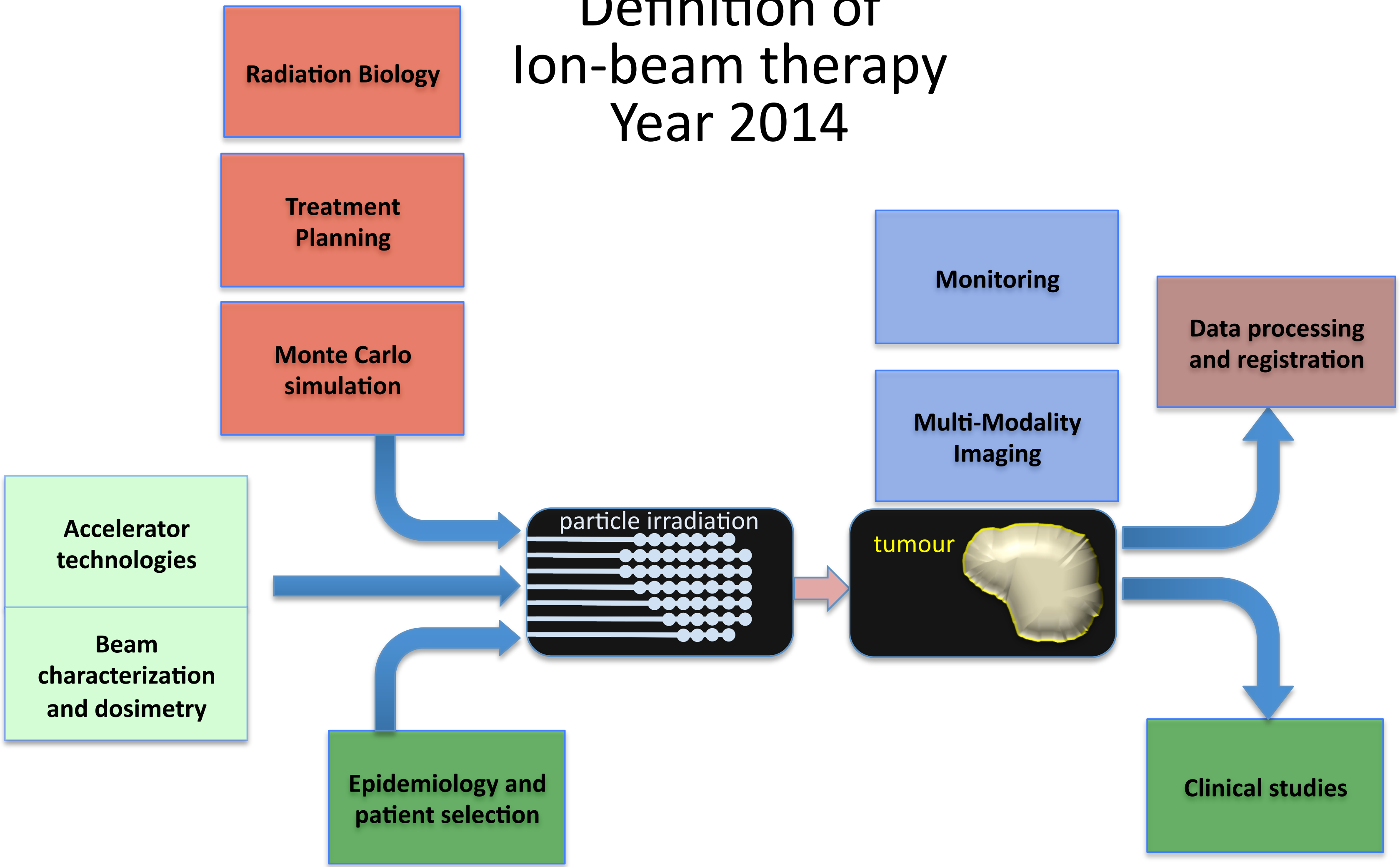
Giulio Magrin, Ramona Mayer

MedAustron, 7 – 9 May 2014
Challenges in micro- and nanodosimetry for ion beam cancer therapy

Definition of Ion-beam therapy Year 1954



Definition of Ion-beam therapy Year 2014



ebg *Med*Austron

What is radiation quality

“Radiation quality is defined by the **type** and **energy spectrum** of the ionizing particles at the point of interest”

Characteristics of ion-beam therapy beams radiation

- Rather well defined particles types (but fragmentation…)
- Rather well defined energies (but straggling and range uncertainty…)
- Rather mono-directional beams (but scattering…)
- High intensities (up to 10^7 protons, $5*10^5$ carbon ions/(s · mm^2)
- Dose from 2 Gy to 36 Gy(RBE) per fraction
- High dose rates (up to tens of Gy/s)

Characteristics of ion-beam therapy beams radiation

- Rather well defined particles types (but fragmentation…)
- Rather well defined energies (but straggling and range uncertainty…)
- Rather mono-directional beams (but scattering…)
- High intensities (up to 10^7 protons, $5*10^5$ carbon ions/(s · mm^2))
- Dose from 2 Gy to 36 Gy(RBE) per fraction
- High dose rates (up to tens of Gy/s)

Why Radiation quality in ion beam therapy

We need a well defined radiation quality because of its **link to RBE**,

and because **RBE changes** virtually in **each voxel** of the cellular targets

ebg MedAustron

The RBE "issues"

Measurements are becoming a key for addressing the RBE issues

- **International recommendations**: ICRU, IAEA recommendations
- **Ion-beam therapy facilities**: converge to common results, unify clinical and biological discrepancies (on RBE)
- **Collective**: multi-disciplinary pressure for rigorous elements in determining the radiation quality.

Recommendations:(proton)

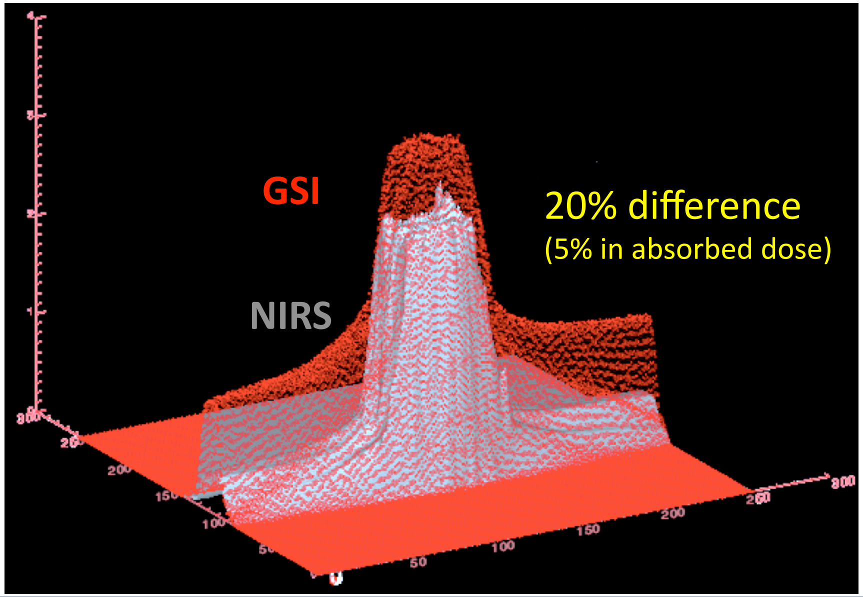
"The microdosimetric characteristics of the proton beam have a **strong influence on the RBE** for each biological system. Linear energy transfer (LET) has been adopted **as an approximation to the microdosimetric** quantity $\bar{y}_{\mathrm{D}}$ (dose mean lineal energy)"

Journal of the ICRU Vol 7 No 2 (2007) Report 78

Ion-beam therapy facilities (carbon ions)

INTER-facility differences of biological effect forecast:

- Local Effect Model
- NIRS Semi-empirical passive scattering model



Distribution of biological-weighted dose. **IAEA-TECDOC-1560** (2007)

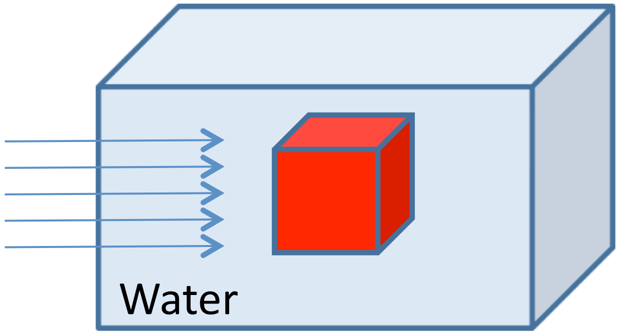
Impossible of sharing directly clinical experience directly

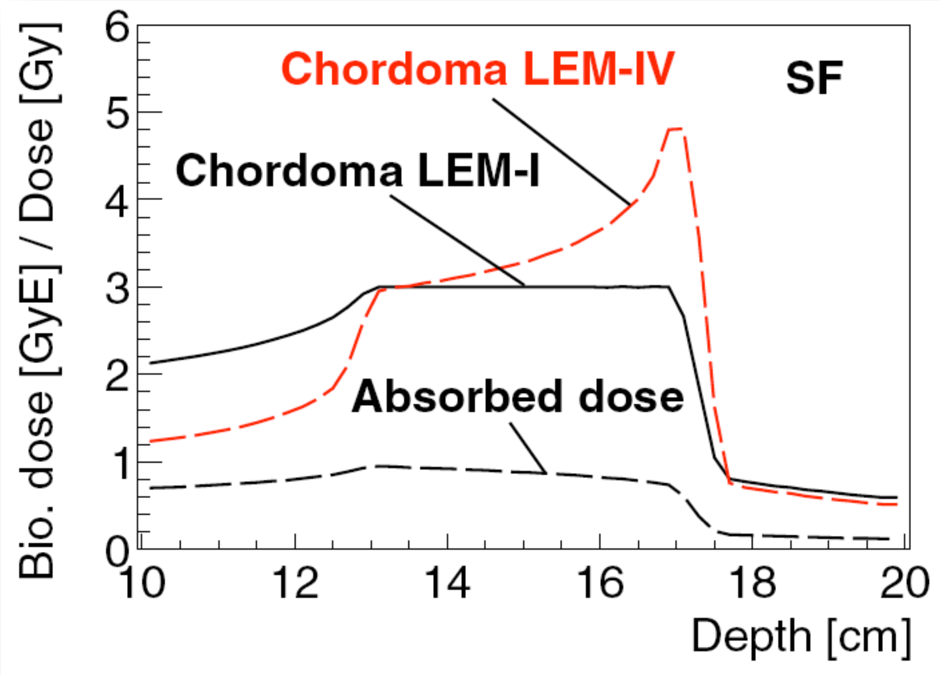
So at the moment biological dosimetry is at RELATIVE level not at ABSOLUTE level

Ion-beam therapy facilities (carbon ions)

Comparison of **2 different versions** of the same model:

- Local Effect Model I
- Local Effect Model IV





Carbon-ion:

- **SHAPE**: cubical 4×4×4 cm^3
- **TYPE**: Chordoma
- **DEPTH**: 15 cm water

Till Boehlen (now MedAustron employee**),**
Phys. Med. Biol. **57** (2012) 7983–8004
Co-authored by Th. Haberer.

Ion-beam therapy facilities

"What level of accuracy is needed, what level of accuracy can we achieve?"

Ideally biological weighted Dose should comply, for ion beam therapy, to the SAME **±2%** dose uncertainty legal requirement of photon radiation therapy

Dosanjh M, Jones B, Myers S. A possible biomedical facility at the European Organization for Nuclear Research (CERN). Br J Radiol 2013;86:20120660.

- Virtually "RBE" with almost zero uncertainty
- The reduction of at least **one order of magnitude** the biological dose discrepancies is it feasible?
- Could we change the reference radiation to decrease the uncertainty and discrepancies (Japanese experience)?

Definition
RBE in Ion Beam Therapy

- The RBE is defined as the ratio of absorbed dose of a reference beam (of photons) to the absorbed dose of any other radiation, notably high LET radiations, to produce the same biological effect.

- As defined, the RBE is a simple concept, however, its apparent simplicity is deceptive (*which means misleading*). The RBE of a given type of radiation will vary with particle type and energy (*this is the def. of radiation quality*), dose, **dose per fraction**, degree of **oxygenation**, cell or tissue type, biological end point, **etc**.

- In the case of (heavier) ion irradiation, the situation is particularly complex and the RBE is a strong function of position within the treatment beam.

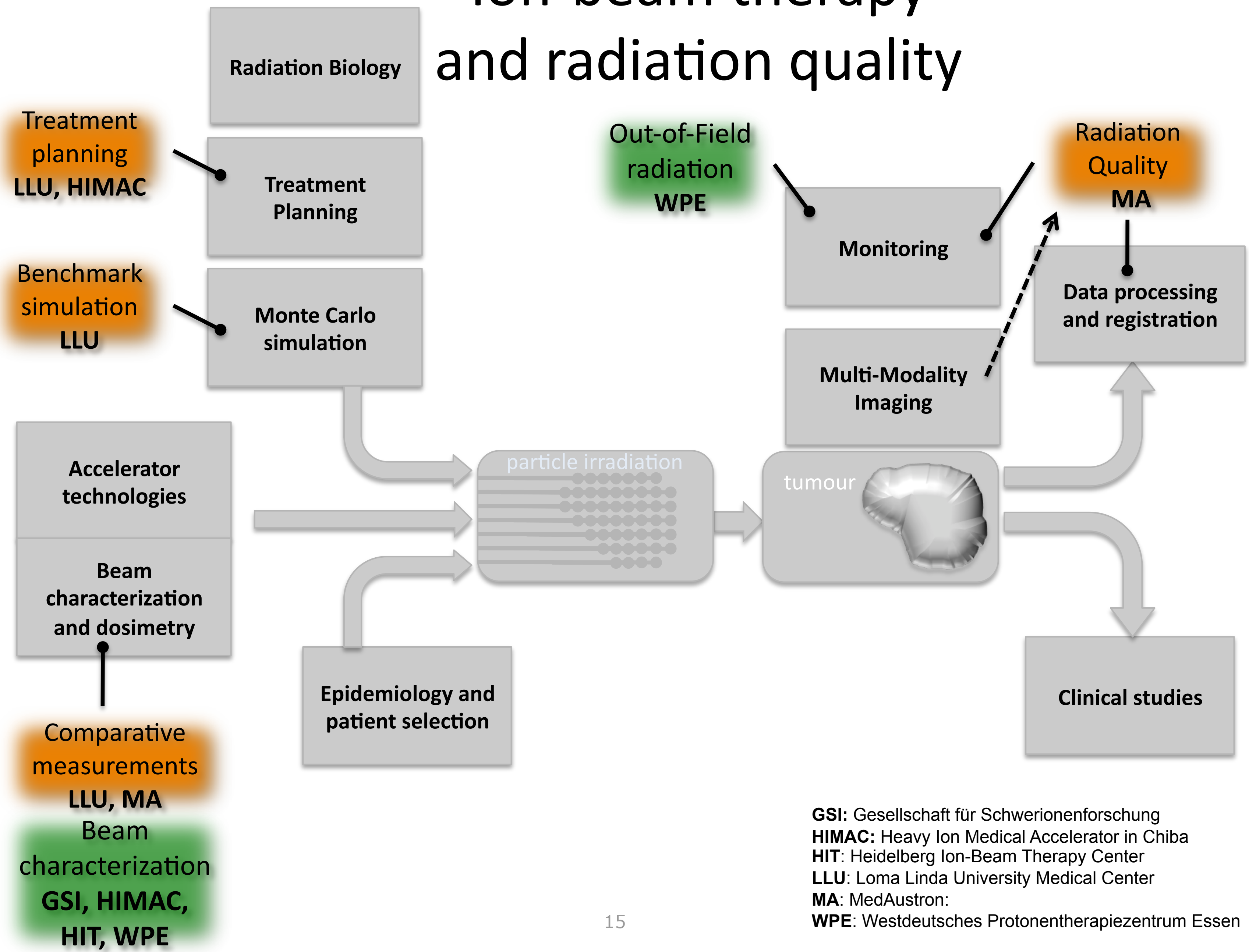
IAEA, Relative Biological Effectiveness in Ion-Beam Therapy,
TRS No. 461, 2008

ebg MedAustron

Particle detectors: which type

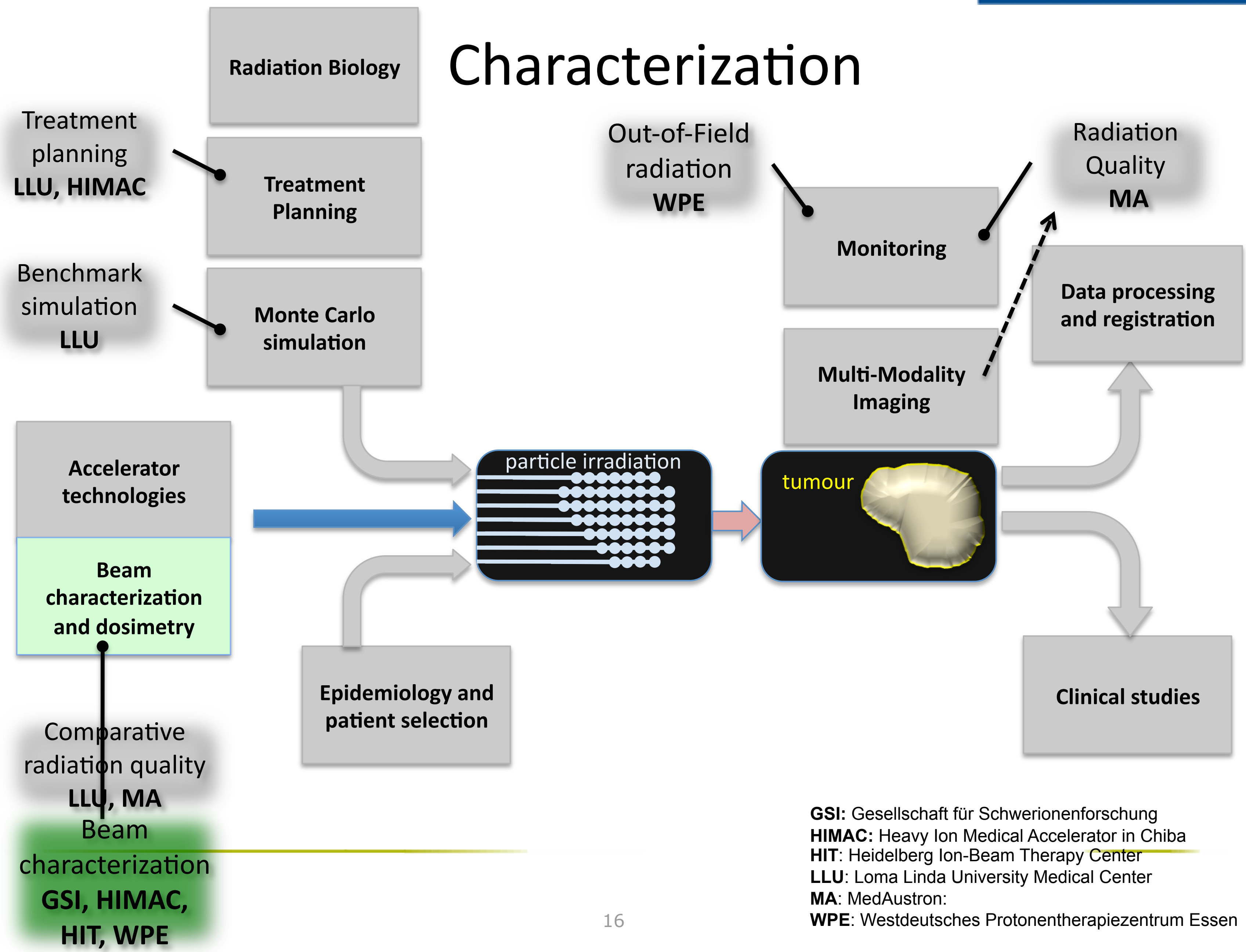
- Tissue Equivalent Proportional Counters, TEPC?
- Solid state?
- Nanodosimeters?
- Reconstructive for prompt gamma?
- Reconstructive from ions/neutron?
- Off-line thermo luminescence devices?
- Off-line track etched detectors?
- Off-line pulsed electron paramagnetic resonance?

Ion-beam therapy and radiation quality



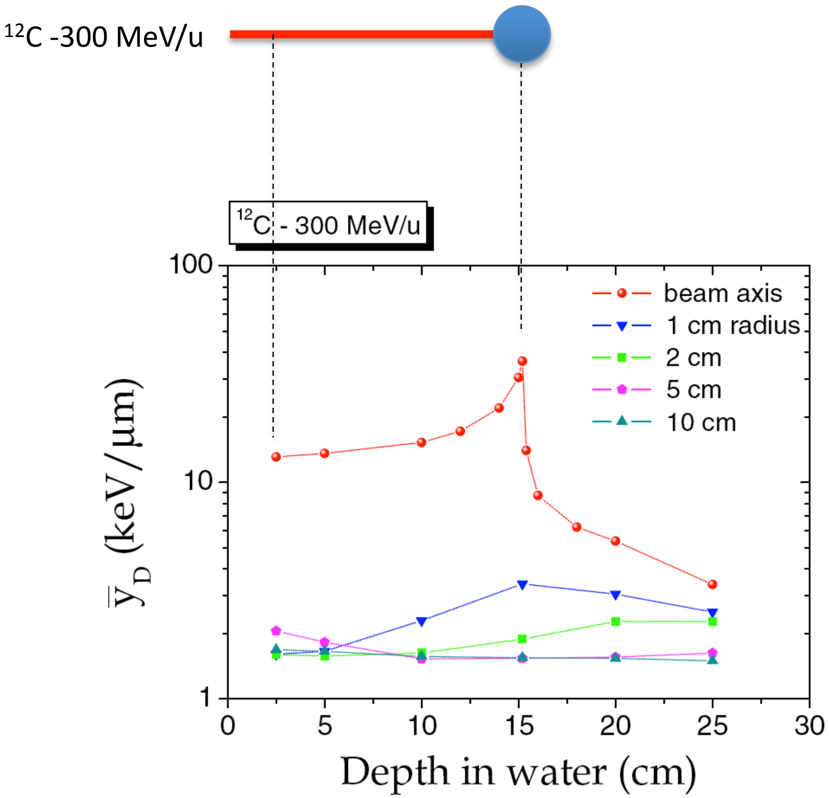
GSI: Gesellschaft für Schwerionenforschung
HIMAC: Heavy Ion Medical Accelerator in Chiba
HIT: Heidelberg Ion-Beam Therapy Center
LLU: Loma Linda University Medical Center
MA: MedAustron:
WPE: Westdeutsches Protonentherapiezentrum Essen

Characterization



GSI: Gesellschaft für Schwerionenforschung
HIMAC: Heavy Ion Medical Accelerator in Chiba
HIT: Heidelberg Ion-Beam Therapy Center
LLU: Loma Linda University Medical Center
MA: MedAustron:
WPE: Westdeutsches Protonentherapiezentrum Essen

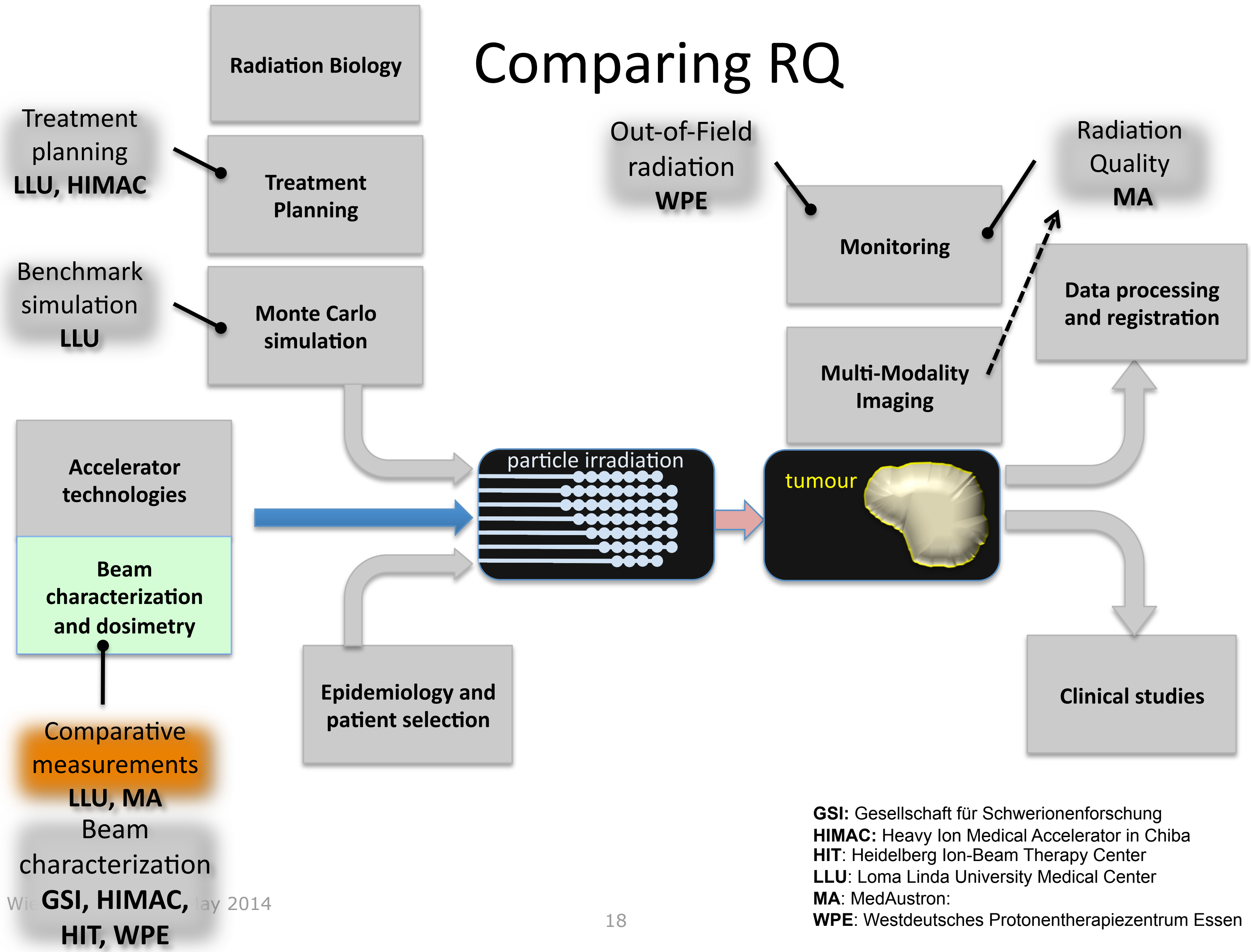
Beam characterization



The microdosimetric characterization of the carbon-ion beam allows to see the transversal decrease of the radiation quality due to the different contribution of primary ions and fragments.
The important therapy consequence is that voxel pitch must be kept small

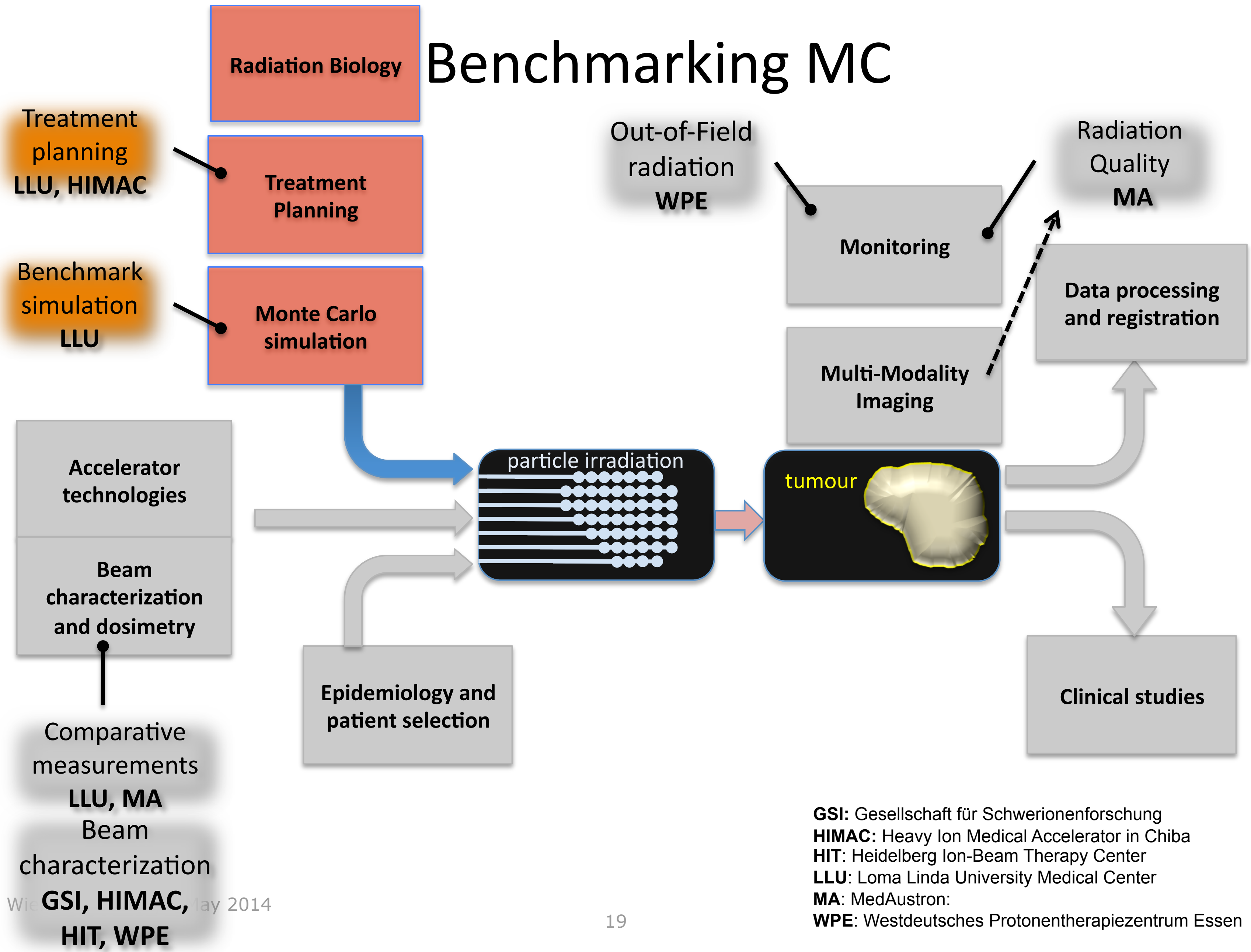
G Martino, M Durante and D Schardt, Phys. Med. Biol. 55 (2010) 3441–3449

Comparing RQ



GSI: Gesellschaft für Schwerionenforschung
HIMAC: Heavy Ion Medical Accelerator in Chiba
HIT: Heidelberg Ion-Beam Therapy Center
LLU: Loma Linda University Medical Center
MA: MedAustron:
WPE: Westdeutsches Protonentherapiezentrum Essen

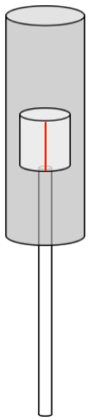
Benchmarking MC



GSI: Gesellschaft für Schwerionenforschung
HIMAC: Heavy Ion Medical Accelerator in Chiba
HIT: Heidelberg Ion-Beam Therapy Center
LLU: Loma Linda University Medical Center
MA: MedAustron:
WPE: Westdeutsches Protonentherapiezentrum Essen

Chiba - RBE and MKM

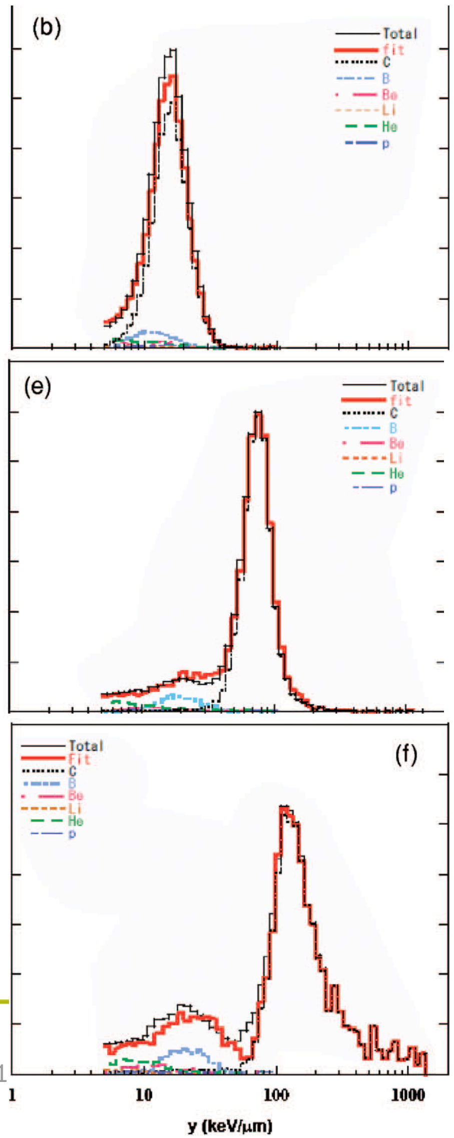
TEPC



Plateau

Distal edge

Tail



Concept presented by
H. Tsujii

Spectra from
S. Endo et al. Med. Phys.
32, 12 (2005) 3843

The microdosimeter collects the energy of each single particle independently and represents it in a distribution.

Microdosimetric spectrum

MKM

RBE$_{biological}$

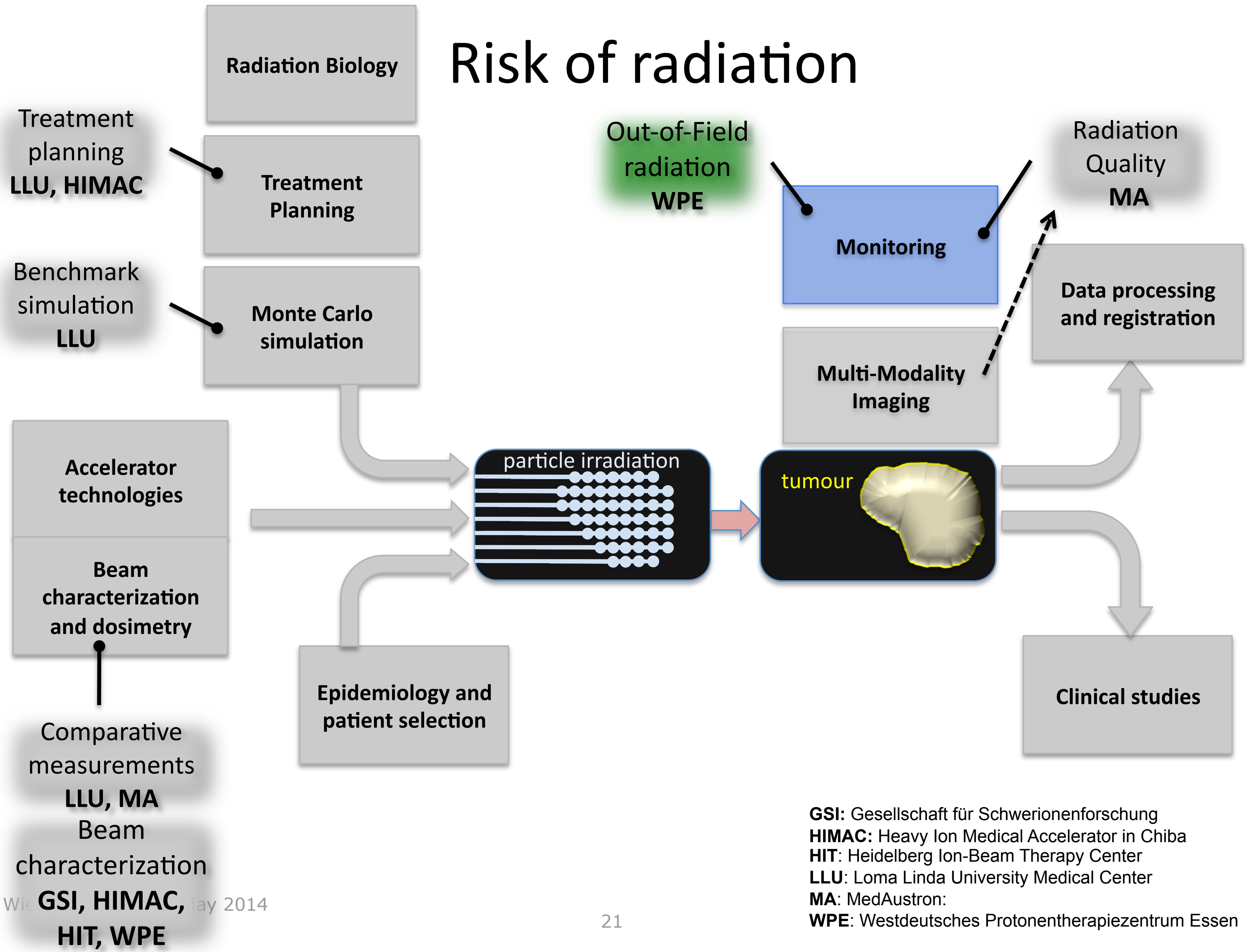
x 1.43

RBE$_{clinical}$

Absorbed dose, D

$D_{clinical}$ = **RBE**$_{clinical}$ x **D**

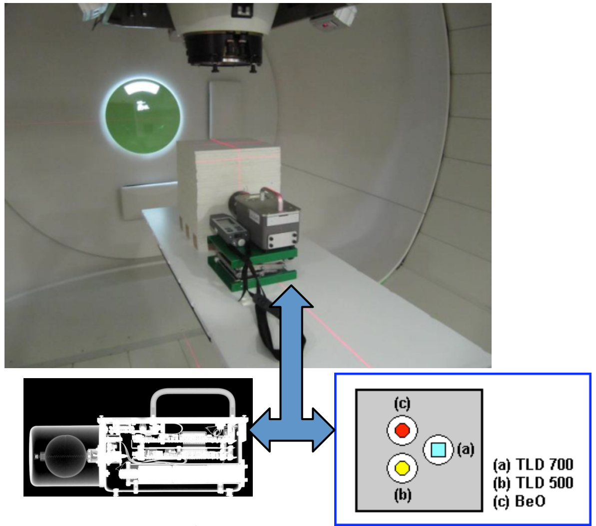
Risk of radiation



GSI: Gesellschaft für Schwerionenforschung
HIMAC: Heavy Ion Medical Accelerator in Chiba
HIT: Heidelberg Ion-Beam Therapy Center
LLU: Loma Linda University Medical Center
MA: MedAustron:
WPE: Westdeutsches Protonentherapiezentrum Essen

Essen, proton detector: during commissioning and during therapy

Out of Field radiation estimation and risk of secondary cancer



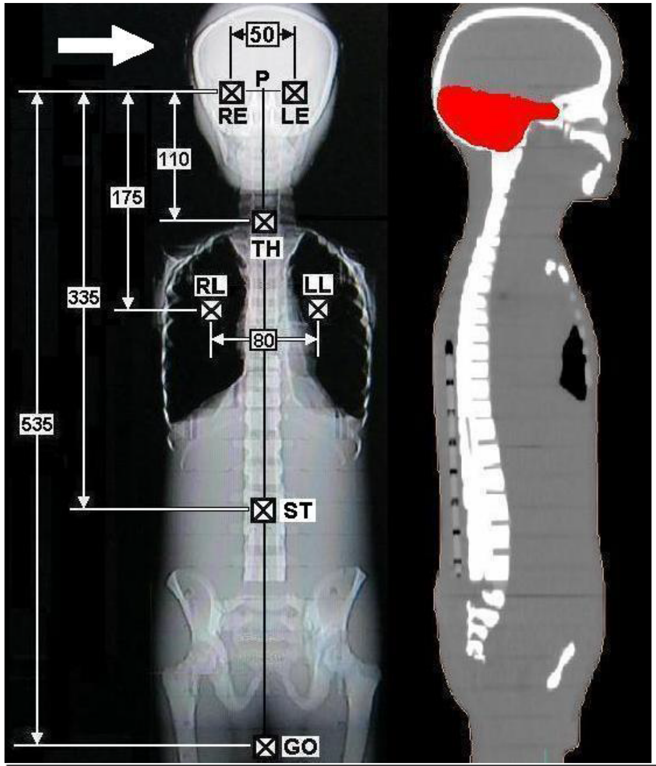
Far West Tech.
REM 500 TEPC

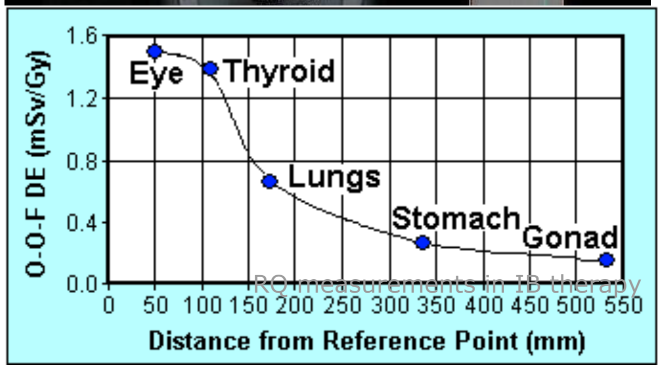
TLD chips

Exposed to secondary particles produced by irradiating a poly-styrene phantom with high-protons of various energies.

Out of Field radiation estimation and risk of secondary cancer

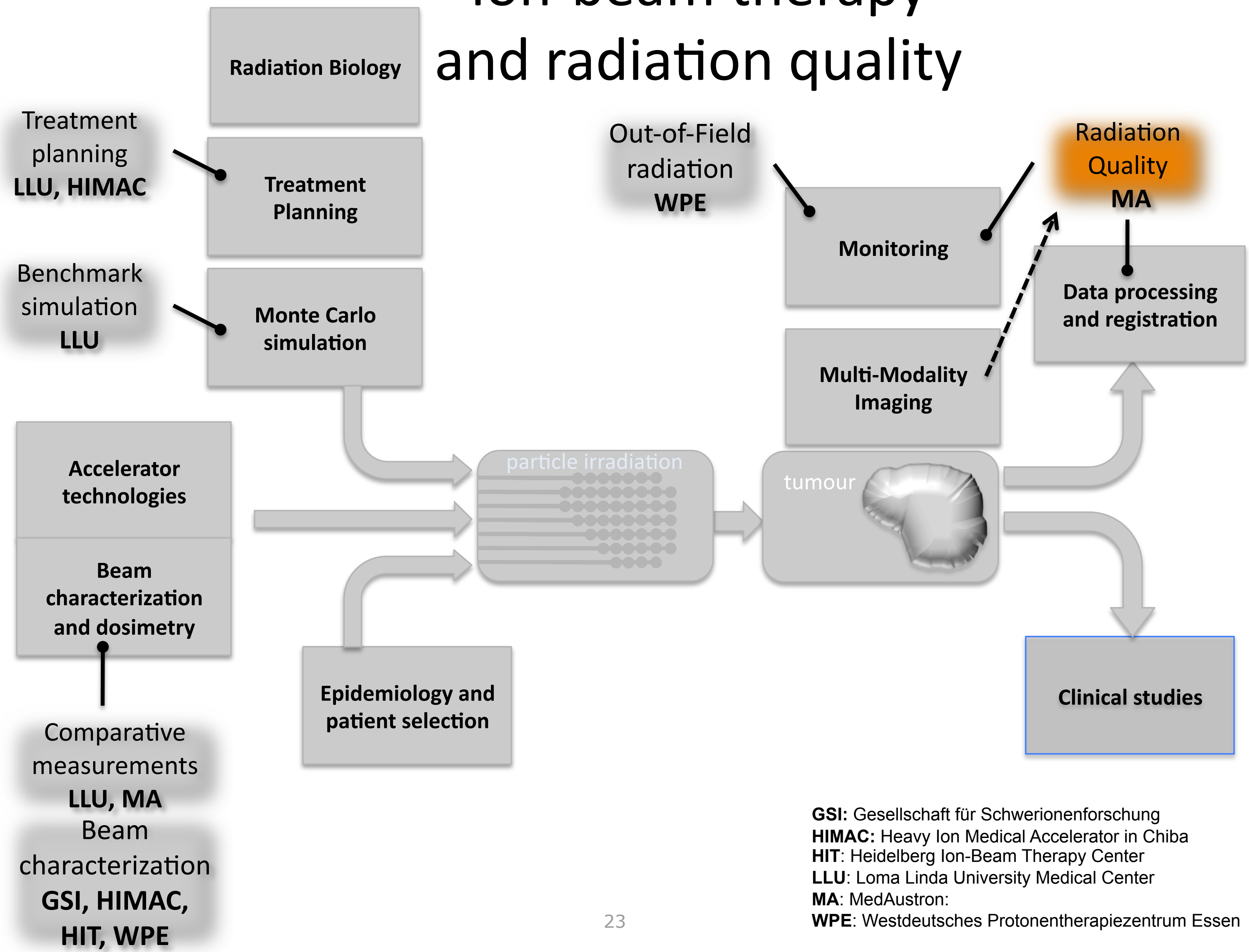
The device was used at WPE for the explicit estimation of out-of-field neutron and gamma dose equivalents, average LET and QF, in **phantoms** and **patients**





Courtesy of Bhaskar Mukherjee, WPEssen

Ion-beam therapy and radiation quality



GSI: Gesellschaft für Schwerionenforschung
HIMAC: Heavy Ion Medical Accelerator in Chiba
HIT: Heidelberg Ion-Beam Therapy Center
LLU: Loma Linda University Medical Center
MA: MedAustron:
WPE: Westdeutsches Protonentherapiezentrum Essen

Understanding the need of users

- Have a **feedback** of the radiation
- **Decrease the uncertainty** on the biological weighted dose
- Create radiation description **independent from the facility** (a single detector type)
- Obtain "direct" values of **clinical biological effects** (coupling radiation quality to molecular imaging)

One answer is to develop measuring devices for assessing quantity (dose) and quality of the radiation, voxel by voxel

The ideal detector should have:

- Simulated volume (thickness) from 10 nm to 10 µm
- Spherical sensitive volume
- Surface detection (minimal shielding of few µm)
- Operation at 2 Gy (cross section of 100µm x100µm)

But most of all:

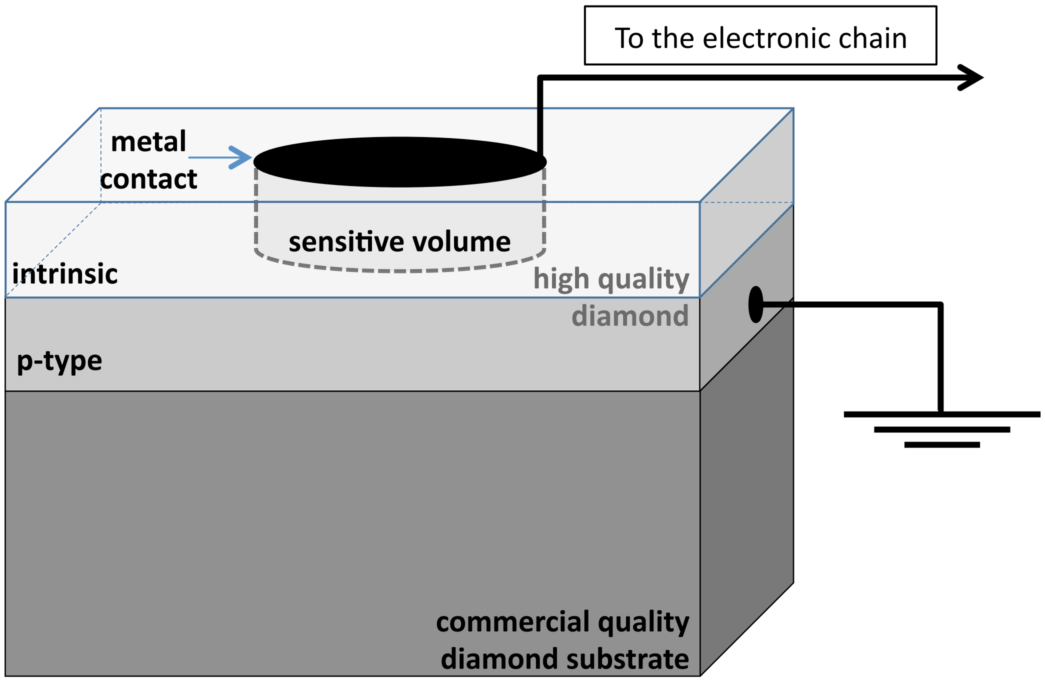
- Minimal interaction with the treatment procedure
- Safe
- Easy in operation, one switch ON/OFF
- Small

Particle detectors: location

A significant location in the **distal border of the tumour:**
• Radiation quality (energy spectra vary drastically in the last millimeters) • Tumour-health tissue interaction (competition between tumor cells searching for oxygen and nutrients and healthy tissue immunologic activity) • Therapy (high range, high uncertainty)

Prostate cancer seems to be a good candidate

The prototypes



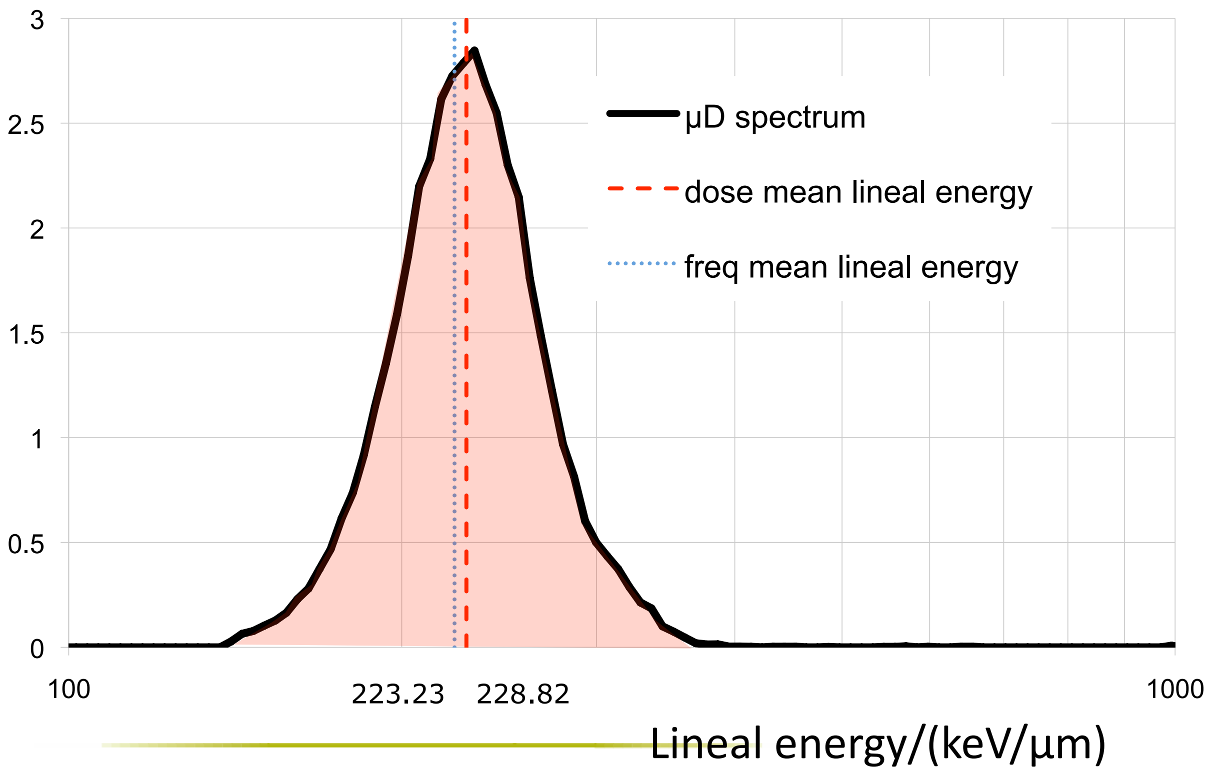
The preferred candidate
(Rollet, IEEE Transactions on Nuclear Science, VOL. 59, NO. 5, 2012):
Access to technologies thanks to international common effort.
MedAustron is collaborating with Austrian Institute of Technology, Tor Vergata university, Enea, INFN Legnaro and Mitra project, Ruđer Bošković Institute.

1. General studies
   1. funnelling,
   2. channelling
   3. radiation hardness
2. Geometrical sizes
   1. Thickness (tested down to 300 nm)
   2. Orientation in respect of incident beam
   3. Transversal diameter
3. Compatibility
   1. with MRI measurements
   2. with biological tissues

Dose and radiation quality for range estimation

ebg MedAustron

This spectrum is the response of a Chemical Vapor Deposition Diamond μ-spectrometer to 110 000 alpha particles (241-Am)



Simultaneously

dose, *D*

area of the spectrum

in this case, 1.51Gy (factor 3.47)

radiation quality, $\overline{y}_D$

mean value of the spectrum

In this case 229keV/μm

CVD-diamond μdosimeter:

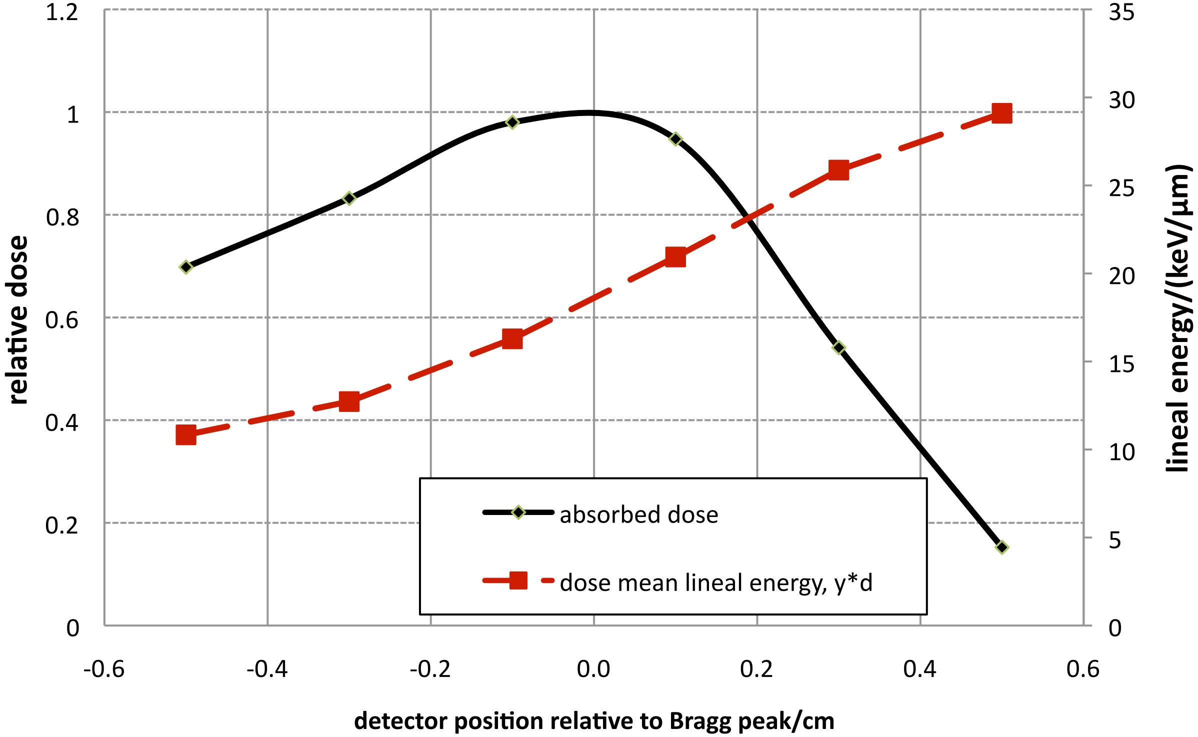
~ 1μm in thickness

~ 10μm in cross diameter

~ 100μm total detector size

Dose and radiation quality for range estimation

ebg MedAustron



Simulation (Gate-Geant4) of proton beam on a 2µm thick carbon detector in water phantom

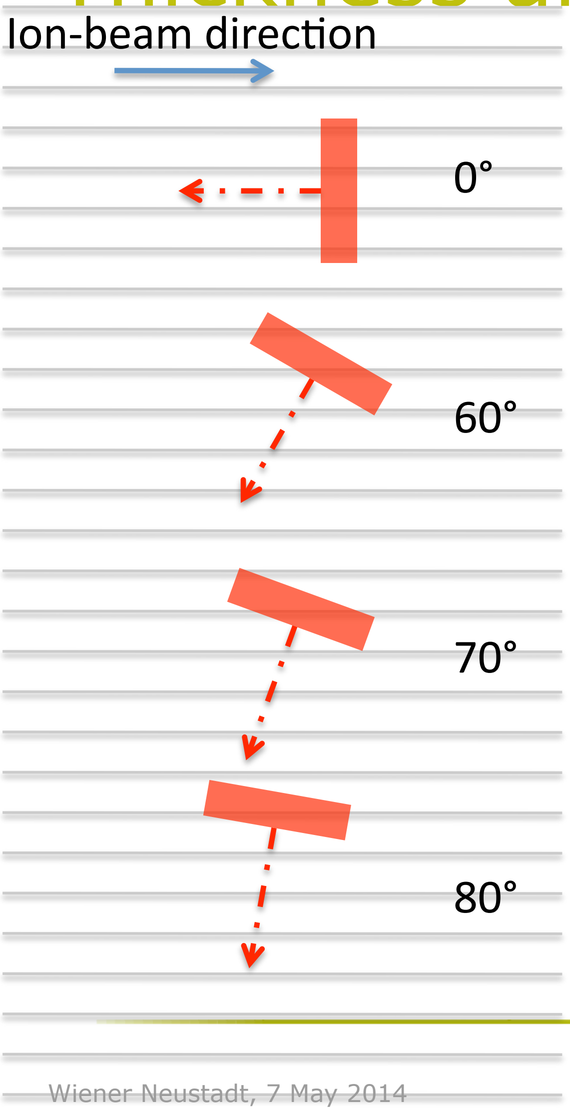
Dose and radiation quality have independent correlation to range:

Bragg peak

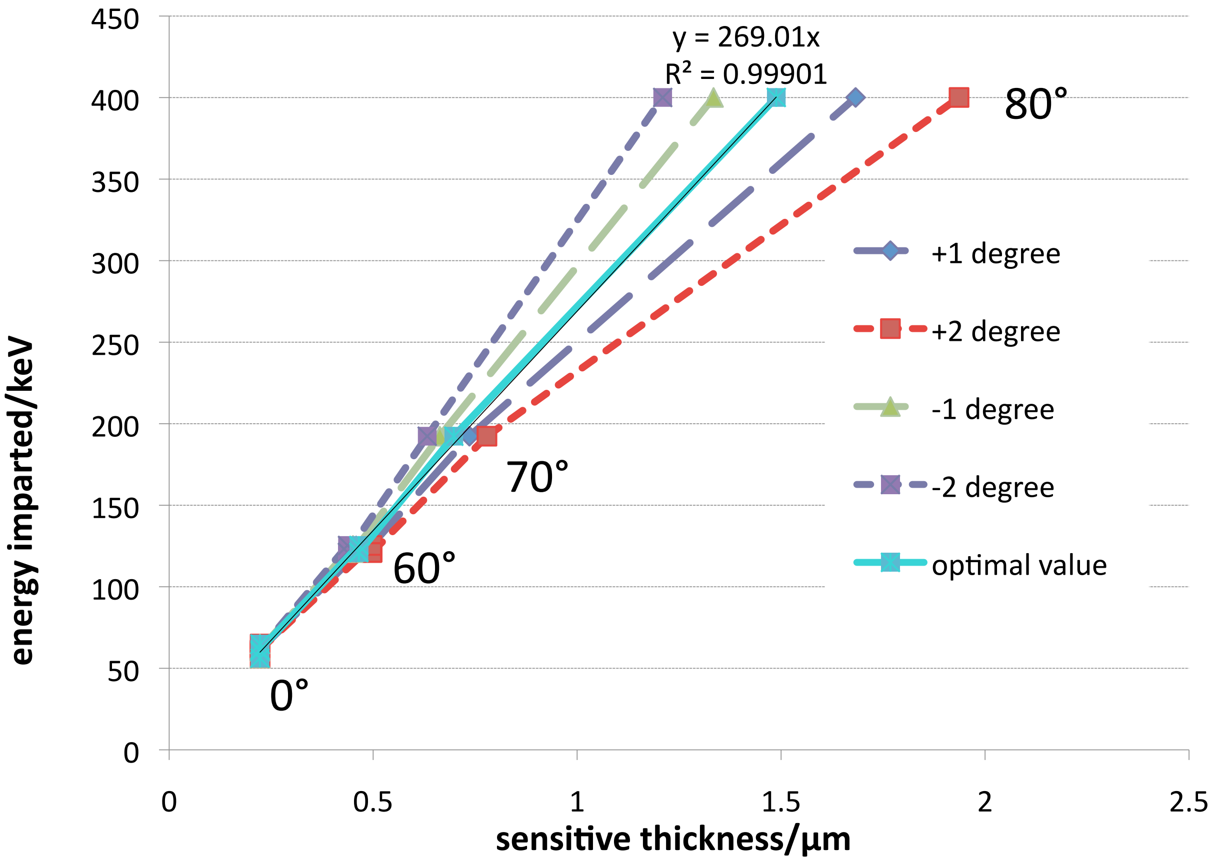
Radiation quality increase at end of the path

Two variables for a robust determination of the range.

Thickness and orientation

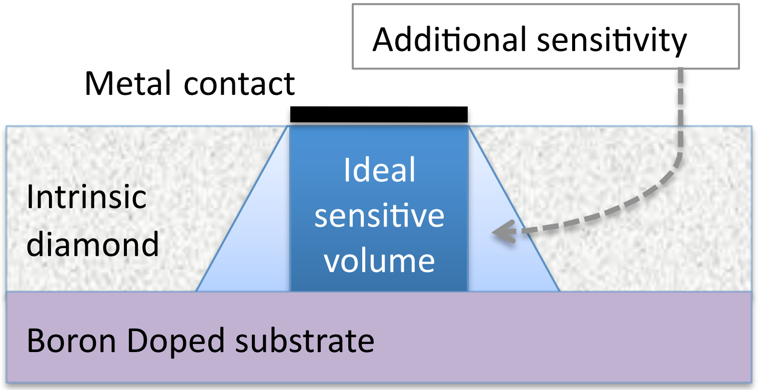


2 dimensional example

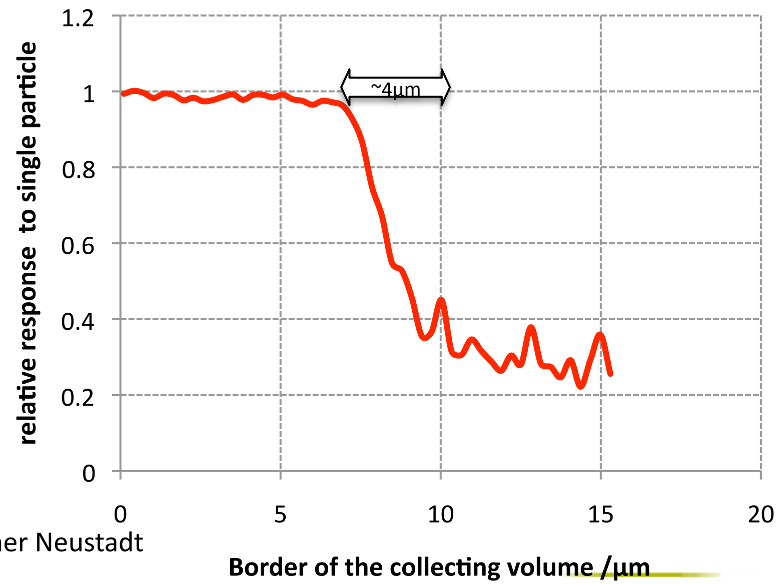


Tor Vergata University-MedAustron tests in diamond

Definition of collecting volume



4 MeV Carbon-ion micro-beam analysis of diamond detector



Studies for reduction of the detector cross section:
Higher relative distortion at low electrode diameter

Research activity between
Tor Vergata University, Rome; **Ruđer Bošković** Institute, Zagreb; **MedAustron**, Wiener Neustadt

ebg MedAustron

Open issues

In the selection of the preferred geometry

- What equivalent thickness to use in the range of 1µm to 10µm.
- How to deal with noise level which correspond to lineal energies of several keV/µm
- Diamond and tissue equivalence
- How many events to collect for a spectrum, 10^5?
- Values obtained that are different from both, LET and $\bar{y}_D$, and are "something in between".
- Wall effects…

In general

- Focus on "close" and "distant" feedbacks
- Are rare events well described by distribution?

Good intentions for the future

- To refer to a typical clinical absorbed dose:
  2 Gy for the radiation under test
  (as the daily dose of conventional radiotherapy)

- To refer to RBE indicating all relevant parameters (dose, type of effect…)

ebg MedAustron

Thank you