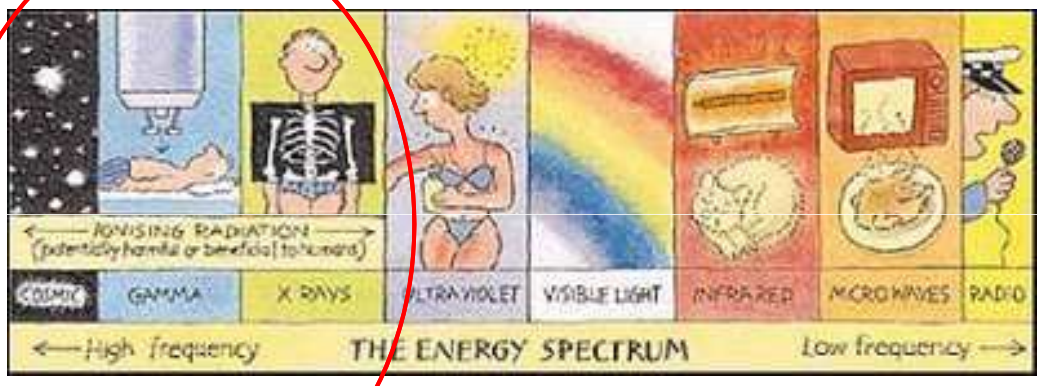
Ionising Radiation for Health

Lena Johansson
TC-IR chairperson

Ionising Radiation

Ionising Radiation – what is it?

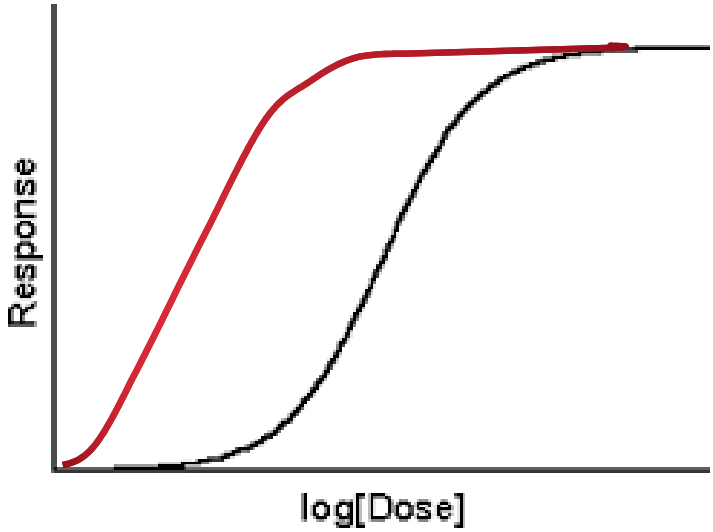


& particulate radiation, consisting of atomic or subatomic particles (electrons, protons, alpha particles etc.) which carry energy in the form of kinetic energy

Ionising Radiation

How to treat cancers with IR

- Dose response curve



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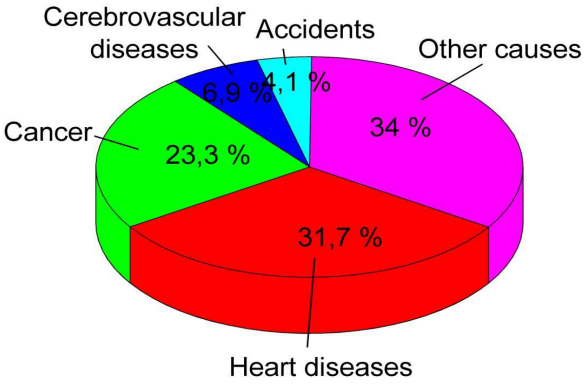
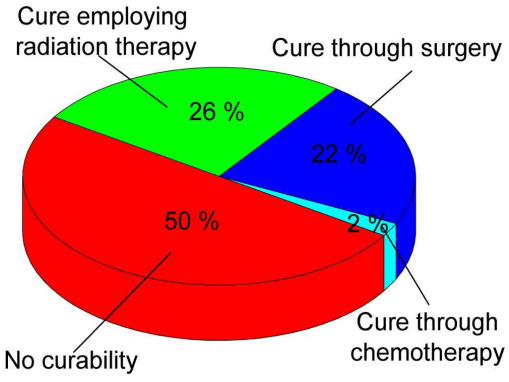
Rationale

Death causes



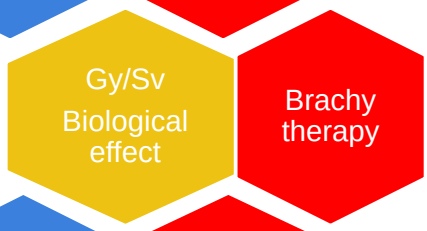
Curability of cancer



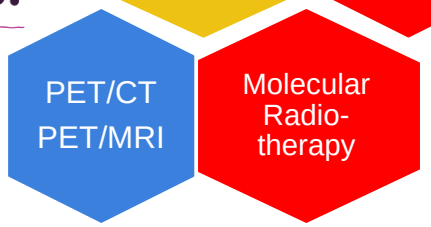
Ionising Radiation

Use of Ionising Radiation in direct Health Applications

Hadron Therapy
Photons/Electrons
IMRT
MRI guided therapies



Treating cancer isn't rocket science. Oh, hang on. Yes it is.



Antibodies - Alpha particles, beta particles, Auger electrons

Ionising Radiation

Units

Absorbed dose is the fundamental dosimetric quantity used in all applications of ionizing radiation, including in radiation oncology for prescribing, recording and report treatments of tumours, in radiological imaging for optimization of the dose image quality in radiation protection for defining protection quantities

Absorbed dose was introduced by ICRU in 1953 after almost 20 years of investigations aimed at finding a quantity which would relate quantitatively well with observed (biological) effects and could be used in radiation medicine.

While absorbed dose was introduced with success in cancer therapy with photons, it is well known that the predictive power of absorbed dose is limited. This is due to the fact that biological effects depend among others also on temporal aspects (dose rate) and on spatial relationships of radiation induced ionization events ("radiation quality").

Gy Sv Biological effectiveness

Ionising Radiation

Units

Dose Quantities

Absorbed dose

energy "deposited" in a kilogram of a substance by the radiation

Equivalent dose

absorbed dose weighted for harmful effects of different radiations
(radiation weighting factor w_R)

Effective dose

equivalent dose weighted for susceptibility to harm of different tissues
(tissue weighting factor w_T)

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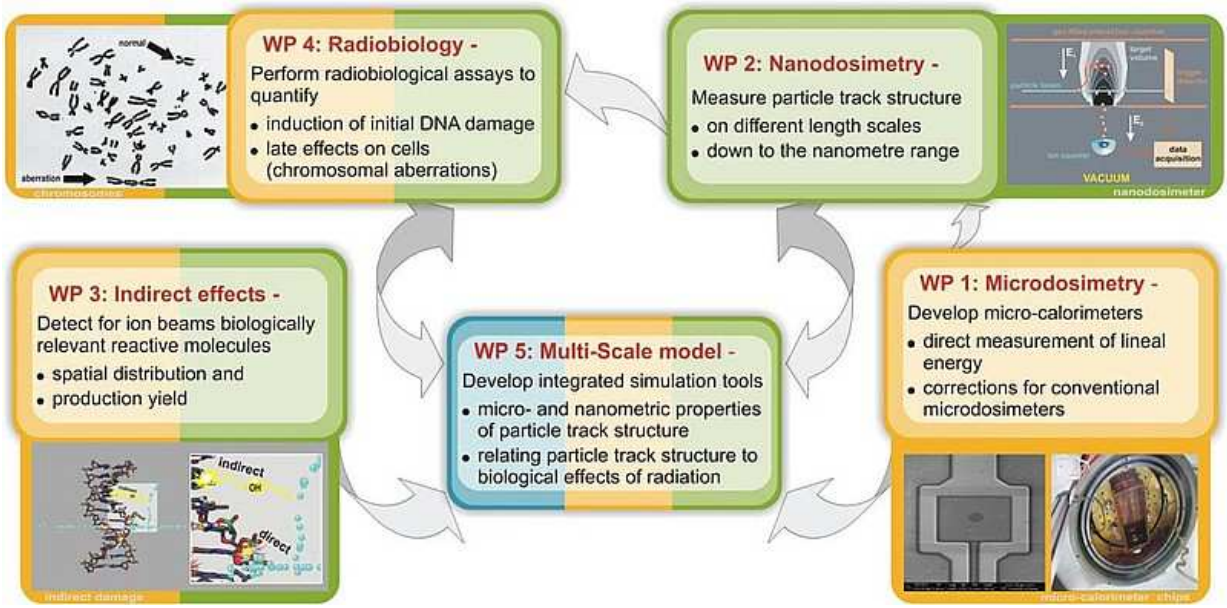
BioQuaRT

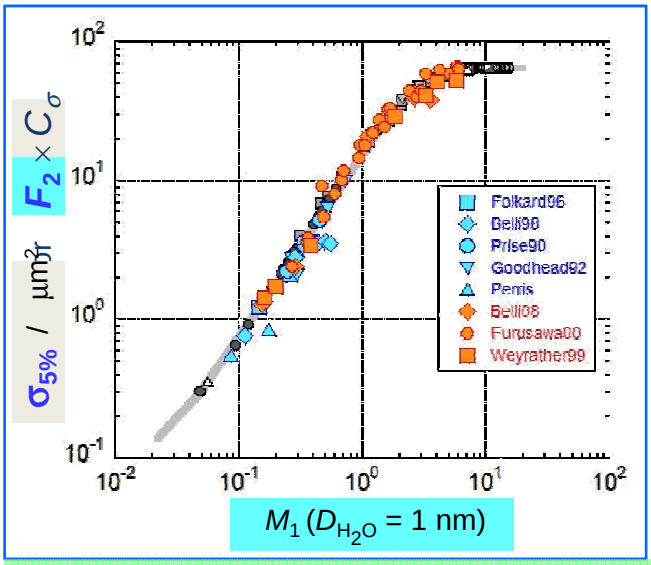


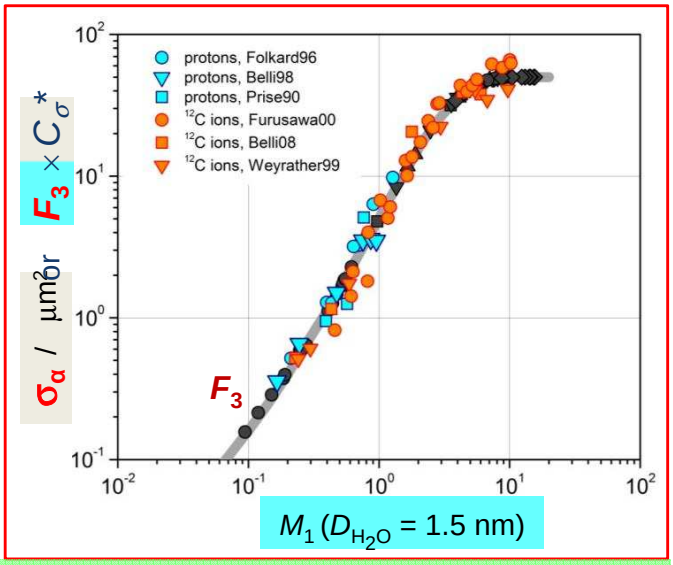
develop measurement and simulation techniques for determining the physical properties of ionising particle track structure on different length scales, and to investigate at the cellular level how these track structure characteristics correlate with the biological effects of radiation.

Inactivation Cross Section of V79 cells by Protons and Carbon ions

Inactivation cross sections calculated from slope of the survival curves at 5% survival

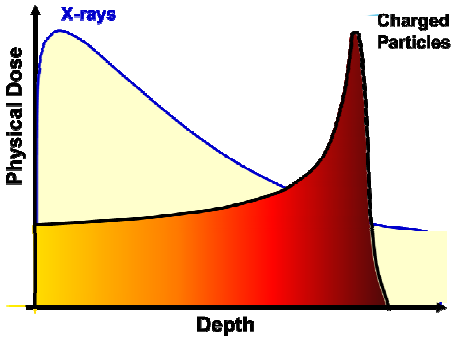
Inactivation cross sections calculated from the initial slope of the survival curves





These findings support the conclusion that for low doses the radiobiological effectiveness is related to the incidence of complex DNA double strand breaks, while for high doses the cell lethality depends on the frequency of double strand break induction.

Biological Effectiveness



What are the key parameters ?
Parameterization of
- Relative Biological Effectiveness (RBE)
- Biological Effective Dose (BED)
- ….

Impact on:
Biological Vs Physical dose optimization

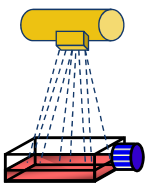
Personalized radiotherapy

Implementation of functional imaging

Long term risks

Evaluation of clinical trials

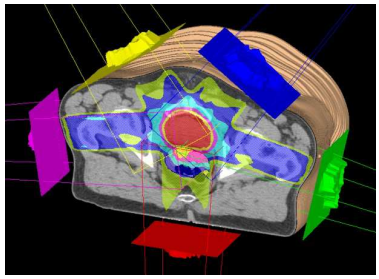
Conventional Radiation Biology Experiment



?

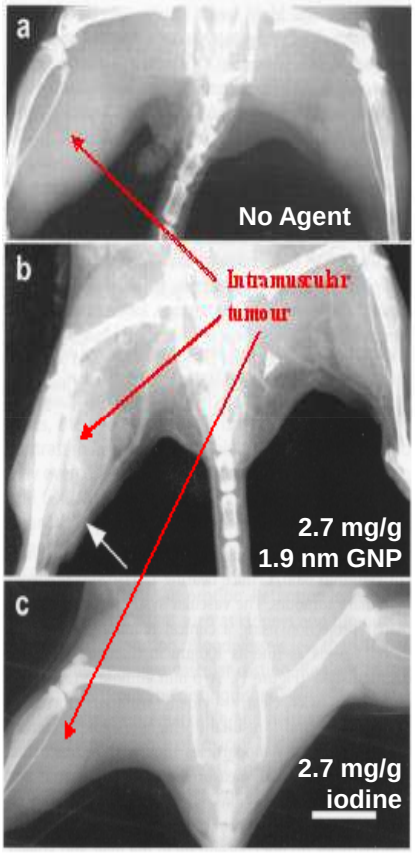
Single unidirectional uniform irradiation

Current patient exposures (e.g. IMRT)



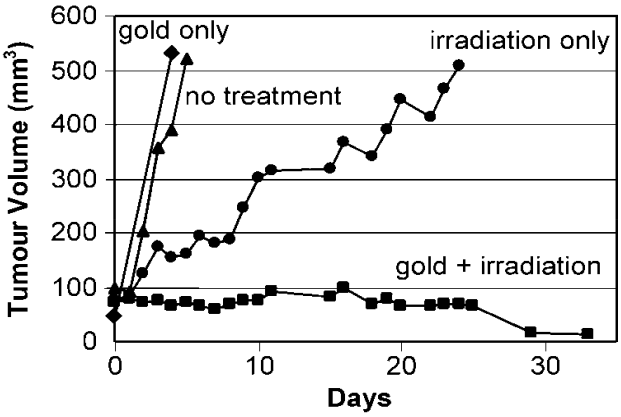
Irradiation from multiple directions using highly attenuated beams at different times

Au Nanoparticles for Diagnostic and Radiotherapy



Hainfeld et al *Gold nanoparticles: a new X-ray contrast agent*, Br J Radiol, 2006

Ideal contrast agent:
- Bio-compatible
- Natural Target specificity
- Easy functionalization chemistry
- High atomic number



J Hainfeld et al, *The use of gold nanoparticles to enhance radiotherapy in mice,* Phys Med Biol, 2004

Clinical use hampered by lack of models and mechanistic information on dose enhancement effects.
Macroscopic models based on mass attenuation are not adequate.
Need for radiobiological characterization assays

iMERA and EMRP JRPs

T2.J06 Brachytherapy Increasing cancer treatment efficacy using 3D brachytherapy Maria Pia Toni (ENEA)

T2.J07 EBCT External Beam Cancer Therapy Ulrike Ankerhold (PTB)

HLT06 MRI safety Metrology for next-generation safety standards and equipment in MRI Bernd Ittermann (PTB)

HLT09 MetrExtRT Metrology for radiotherapy using complex radiation fields Jean Marc Bordy (CEA)

HLT11 MetroMRT Metrology for molecular radiotherapy Vere Smyth (NPL)

External Beam Radiation Therapy

Ionising Radiation

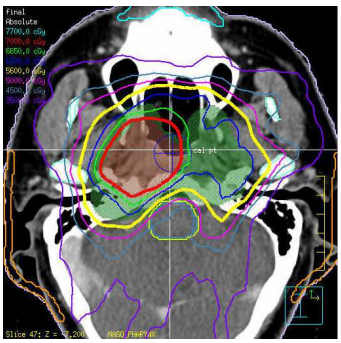
NEW RT MODALITIES

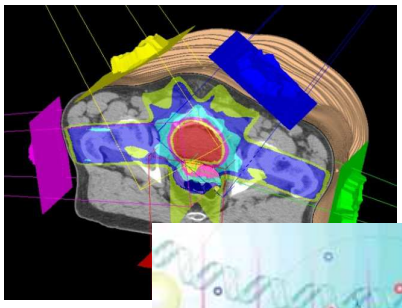
Fast development of new Radio-Therapy modalities.

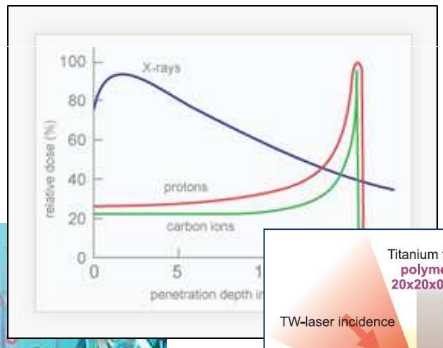
Very complex dose distributions can now be delivered employing a variety of approaches and radiation modalities.

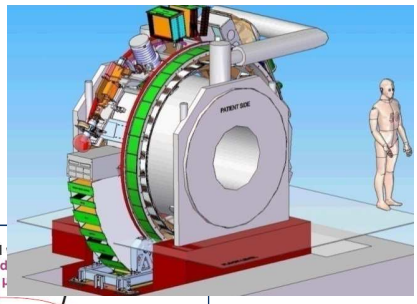
Complex spatio-temporal dose deliveries require dedicate tools and procedures

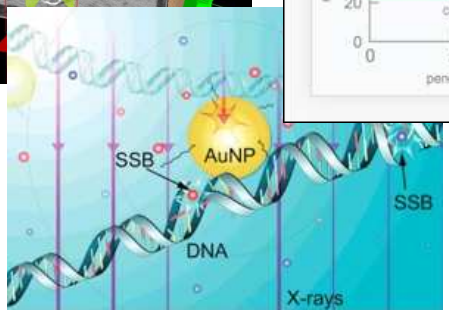
Dose is a very good biomarker but by itself it is not adequate to predict cellular and tissue response.

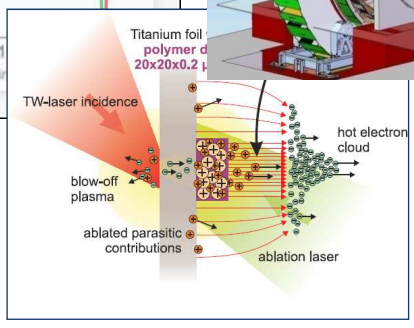






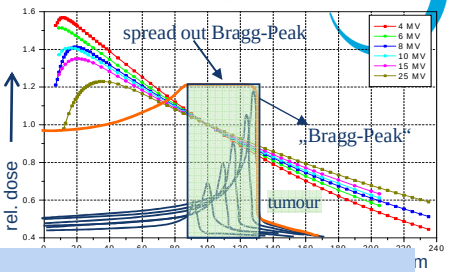






Hadron Therapy

- **Method:** A high degree of conformity between tumour shape and dose distribution can be obtained by superimposing several monoenergetic beams of different primary energies



By 2015, an additional nine proton and four carbon ion therapy centres will commence operation in Europe.
The number of treatments worldwide with these therapies has increased from about 3000 patients in 2005 to about 14000 patients in 2013.

proton and carbon ion beams and for the dissemination of D_w using ionisation chambers

Graphite calorimetry: Determination of the conversion of the measured quantity absorbed dose to graphite to the required quantity D_w as well as the determination of correction factors.

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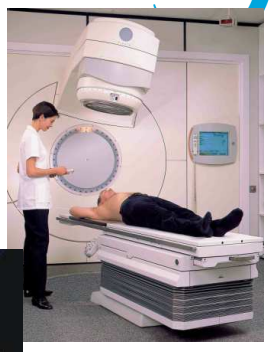
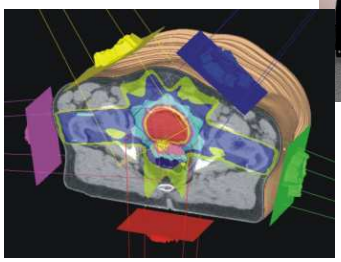
IMRT

- **Method:** Generation of a „tumour matched“ dose distribution in the patient by superimposing a large number of small, irregularly shaped photon radiation fields to achieve a high dose in the tumour volume and a strong reduced dose in the healthy tissue.





- **However:** Existing protocols for clinical dosimetry are applicable to field sizes of typically of 10 cm x 10 cm, i.e. reference conditions. They are not suitable for IMRT conditions.

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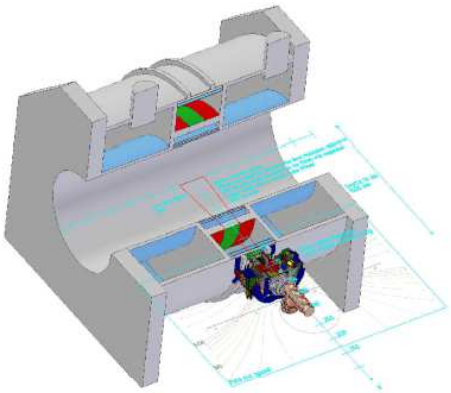
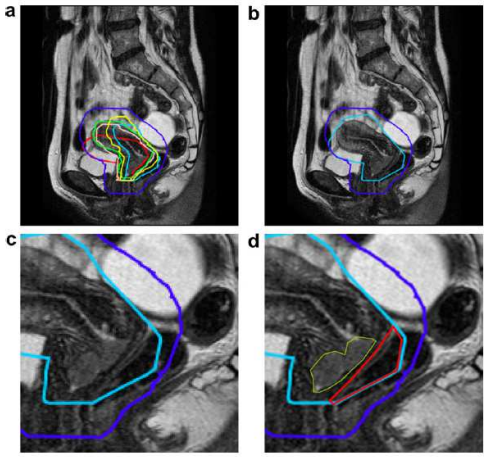
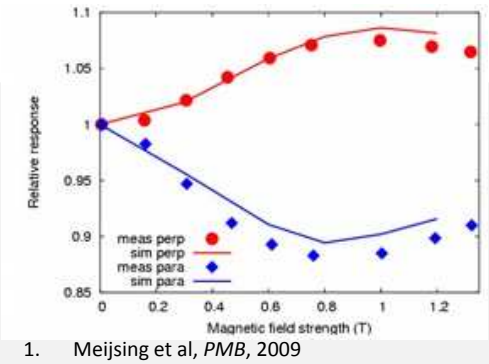
Dosimetry in MR guided RT





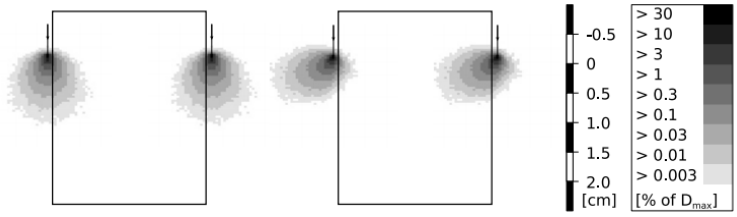


1. Meijsing et al, *PMB*, 2009
2. Reynolds et al, *Med. Phys.* 40 (4), 2013

- Image Guided Radiotherapy with high soft tissue contrast
- Combination of MRI and MV photon beams
- Dosimeters are highly affected by B_0-field
- <u>Need:</u>
  - Traceability is lacking
  - No dosimetry protocols available
  - Radiobiological effects unknown

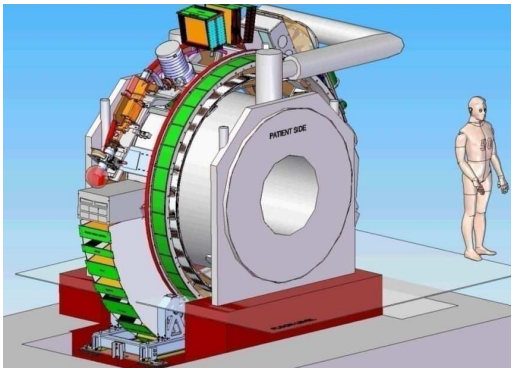
Dutch Metrology Institute

MRI-LINACS



Magnetic Field Alters Dose Distribution

Meijsing, PMB 2009



Magnetic Field Alters Electron Path in Detectors

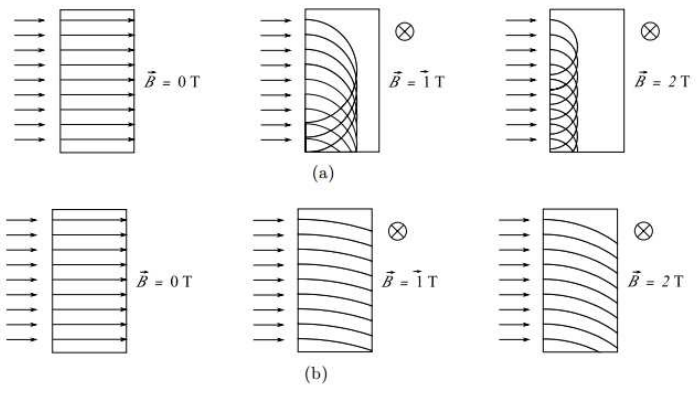
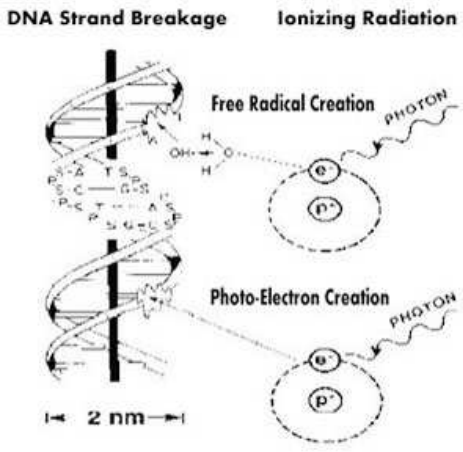


Figure 8. Schematic of the electron tracks depending on their own energy and the external magnetic field. Configuration I: (a) 1 MeV, schematic of the electron tracks at 0 1 and 2 T, (b) 6 MeV, schematic of the electron tracks at 0 1 and 2 T.



Magnetic Field is likely to increase ionization clustering and affect radical recombination

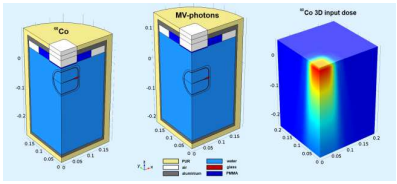
HLT06: Metrology for next-generation safety standards and equipment in MRI
WP5 Emerging technologies: MRI-accelerator combination (VSL, PTB)

Task 5.1 (VSL, PTB)**:** Realisation of a **water calorimeter** as primary dosimetry standard for MRI accelerator combinations

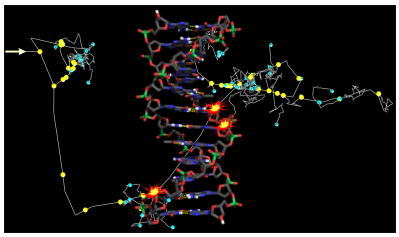
Task 5.2 (VSL)**:** Establishment of a **traceability chain for dosimetry** in MRI-accelerator combinations

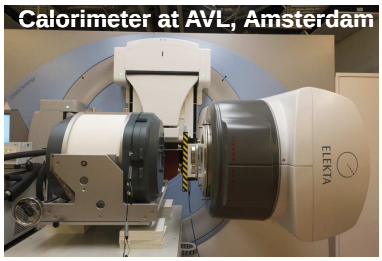
Task 5.3 (PTB)**:** Influence of a magnetic field on radiation transport and **relative biological effectiveness** of photon beam irradiation

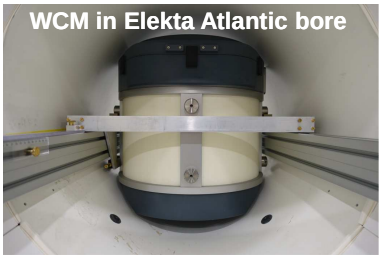
calorimeter heat transport model



nano-scale DNA radiation damage







Main achievements MetroExtRT

MetrExtRT

EURAMET

Medium energy photons: new primary standards in terms of absorbed dose to water based on different principles have been established, a comparison has been organized

The diamond detector studied within the REG “Tor Vergata” is now included in a new dosemeter made commercially available by PTW

The 3D gel dosemeter studied within the REG “Univ. d’auvergne” associated with a remote treatment of the data measured by MRI has been validated and allow checking the limit of exposure for the Organ at Risk in the vicinity of the tumor.

For high energy photons: the concept of dose area product to overcome the lack of primary standard for point quantity has been validated. Primary and secondary standards have been tested.

Many improvement about the standard for high energy proton/hadron therapy and scanned beams have been made

A Pilot study of the external quality control for Intensity Modulated RadioTherapy has been made

New phantom for the quality control of the treatment have been produced.

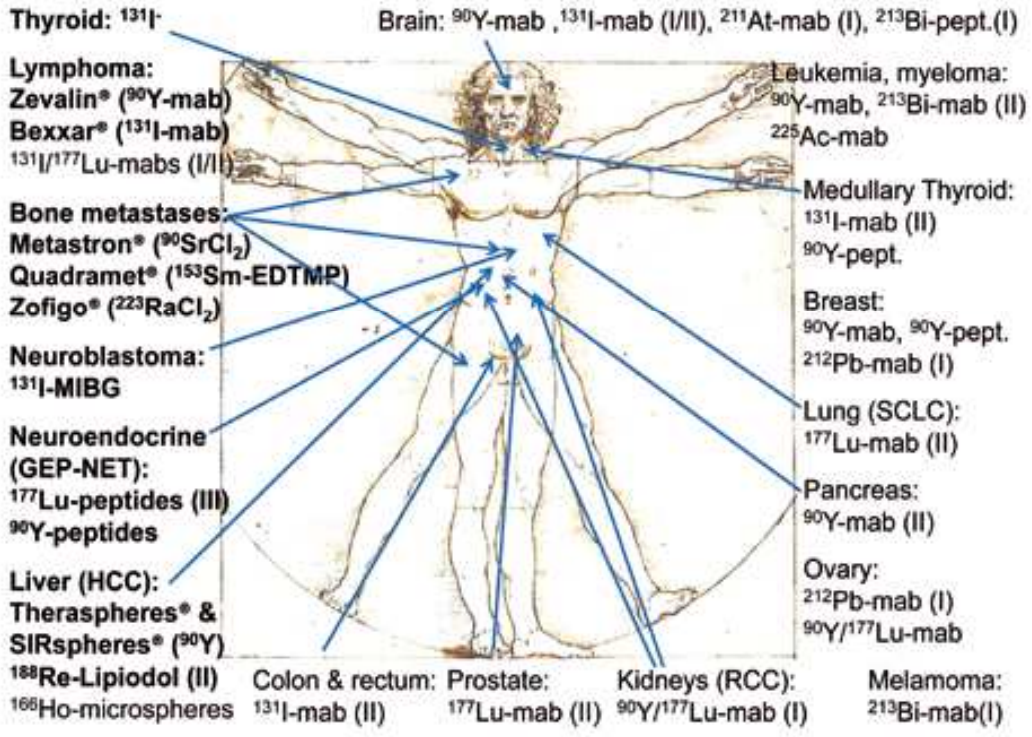
A traceability chain for new electronic brachytherapy units have been established.

Implementation of the results of the JRP in the international protocol has started.

The results of the JRP will be presented to the end users during a special workshop organized during the next French medical physicist conference in Lilles (France) .

LNE-LNHB CMI ENEA MKEH NPL National Physical Laboratory PTB SMU Slovak Institute of Metrology STUK DTU VSL

Therapeutic Radiopharmaceuticals



Same Activity = Same Dose?

- Mean absorbed doses from fixed or weight-based administrations
- 993)
- 02)
- 2)
- g)
- Y-90 DOTATOC for NETs (Bodei et al - *EJNM 2004)*
  - Kidneys 6 - 46 Gy
  - Marrow 0.2 – 1.9 Gy

There is a clear need for image guided individual dose planning of MRT and New EU Directive to be implemented by 2018

Metrology for Molecular Radiotheraphy - MetroMRT

1. Measurement of the administered activity;

Developed a transfer protocol for clinics to accurately measure Y-90 SIR spheres (SIRTeX). Improved nuclear data.

2. Quantitative imaging (QI) procedure

Provided a protocol for harmonisation of calibration and validation of quantification using SPECT/CT for Lu-177 therapies.

Determined uncertainties and improved accuracy in QI.

3. Calculation of absorbed dose within the volume of interest

Developed a model for calculating uncertainties related to biokinetics from a time sequence of activity measurements.

Etc.

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Metrology for Molecular Radiotheraphy - MetroMRT

During two days at NPL all major players in Europe in the field of Molecular Radiotherapy (MRT) participated in a workshop for "clinical implementation of dosimetry for MRT". Overall it was more than 80 participants ranging from all major camera manufacturers, software developers, clinicians, clinical trials organisations, radiopharmaceutical companies, decision makers (EU directives), world leading medical physicist, international organisations (ICRU and IAEA) and the European nuclear medicine association.

The general feedback from the participants was that the breadth of knowledge and expertise made this event truly unique and promised for a real shift in the possibility to implement individualised dosimetry for MRT clinically.

Ionising Radiation

Health in 2015 – where do we go from here?

From the SRA: “Innovations in healthcare that will deliver real-time and non/minimally invasive measurements, personalised healthcare, and modern therapies, require metrological research and development in clinical applications to guarantee quality and assurance, reliability and comparability of measurements.“

PRTs for example:

- **MR guided radiotherapy** VSL
- **Molecular radiotherapy** NPL
- **Metrology for comparability of different imaging modalities** PTB
- **Small beams radiotherapy** LNE-LNHB
- **Hadron therapy** NPL
- **Biological effectiveness** PTB

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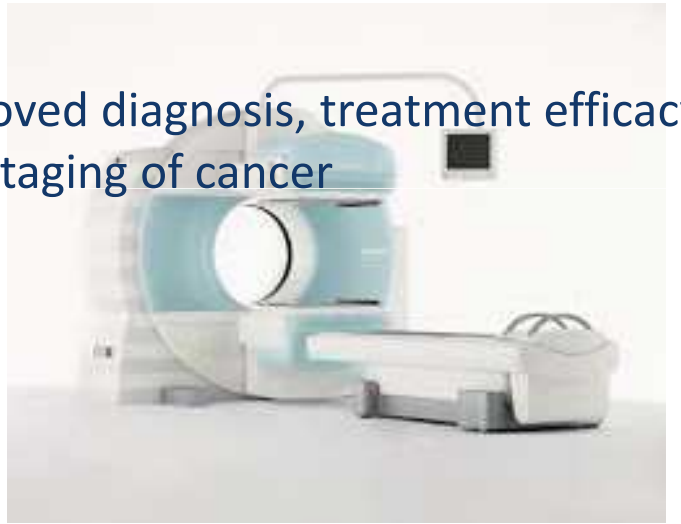
Still to be address is science related to Quantitative Imaging

improved diagnosis, treatment efficacy and staging of cancer



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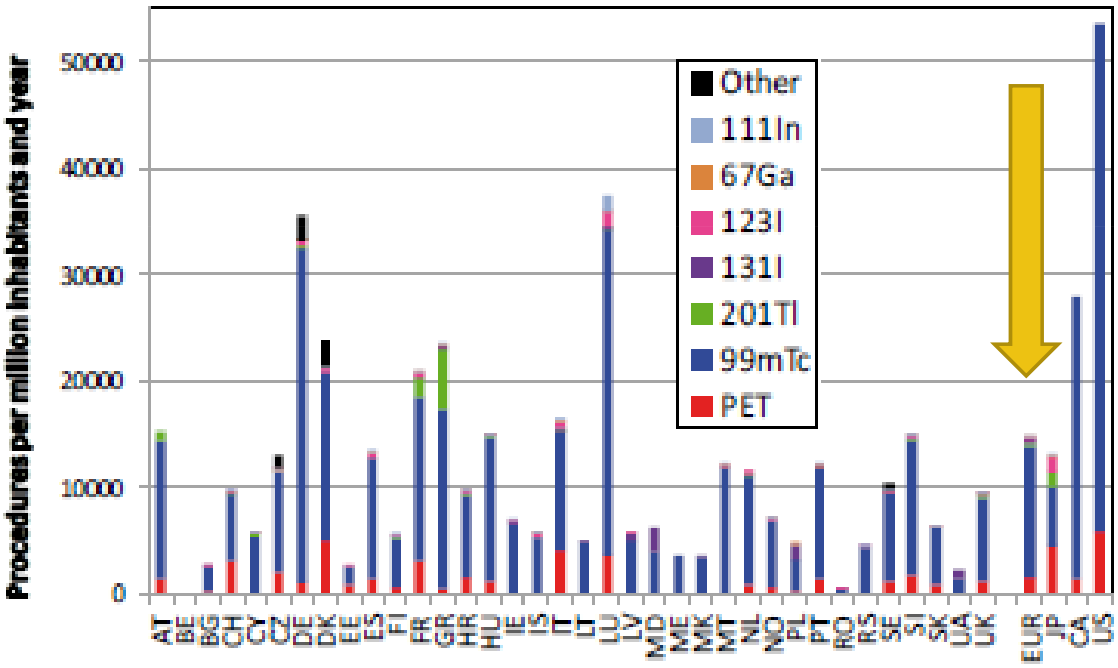
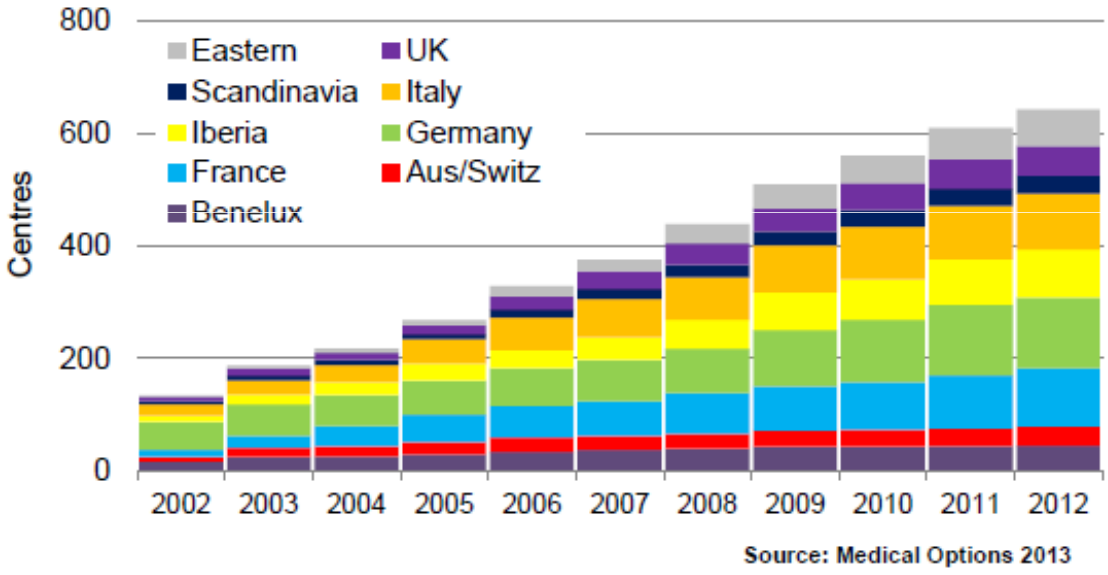
Number of nuclear medicine scans 2012



Growth in PET and PET/CT in Europe



“As cancer is one of the major causes of ill health in the European Union, associated with a considerable cost to society, it is essential to invest in Europe’s future health by taking long-term and sustainable actions to tackle cancer.”

Thank you !

Ionising Radiation