Molecular radiotherapy: how much dose is the patient really getting?

Vere Smyth[1] Christophe Bobin[2], Jaroslav Šolc[3], Lena Johansson[1], Marco d'Arienzo[4], Maurice Cox[1]

[1]National Physical Laboratory, Teddington (NPL), UK.

[2]Commissariat à l'énergie atomique et aux énergies alternatives, (CEA), France

[3]Cesky Metrologicky Institut Brno (CMI), Czech Republic

[4]Agenzia Nazionale per le nuove tecnologie, l'energia e lo sviluppo economico sostenibile (ENEA), Italy

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What is molecular radiotherapy?

- Use of internally administered radiopharmaceuticals to target tumours or other tissues
- Also called "nuclear medicine therapy", "targeted radiotherapy"
- Most common is ^{131}I iodide to treat thyroid conditions
- Newer agents include Peptide Receptor Radionuclide Therapy (PRRT) using ^{90}Y and ^{177}Lu and alpha emiters (eg ^{233}Ra)

What is the problem?

- Administered “dose” only based on activity
- No account taken of individual uptake and retention
- A study showed that the same administered activity gave an absorbed dose to the tumour of 1Gy in one patient and 200Gy in another
- This has severe radiation protection implications
- The treatment outcome is uncertain.

Is it possible to measure the absorbed dose?

- Yes but it is difficult
- The process requires accurate quantitative imaging using SPECT or PET, modelling of the patient biokinetics, and calculation of the resulting dose.
- In-house methods are being developed in a number of clinical research centres
- There is a need for standard procedures in order to encourage take-up by non-research clinics

MetroMRT (Metrology for molecular radiotherapy)

- Collaborative project part-funded by the EC through the European Metrology Research Programme
- 6 national metrology laboratories
- 17 clinical research centres
- 8 different countries
- It started on 1 June 2012 and will run for 3 years
- The overall aim of the project is to develop methods of calibrating and verifying clinical dosimetry in MRT.

First consider the measurement chain used in external beam radiotherapy:

1. Dosemeter calibration against primary standard
2. Dose rate measurement under reference conditions in the user's beam (Gy/MU)
3. Calculation of 3D dose distribution in the patient (per MU) using a TPS that has been commissioned and validated using "best practice medical physics"
4. Dose to the ICRU reference point within 5% of the prescribed dose

Analysis of the links in the MRT dosimetry chain

1. Measurement of the administered activity;
2. Definition and delineation of the volumes of interest (target tissue; normal tissue);
3. Quantitative imaging (QI) procedure (tracer activity, full therapy activity, surrogate RP) to determine activity in the volume of interest relative to the administered activity;
4. Time sequence of activity measurements to determine biokinetics;
5. Integration procedure to obtain total disintegrations within defined volumes of interest;
6. Absorbed dose calculation procedure (Gy/MBq).

The "measurements"

1. Activity: measured in a calibrated well-chamber (less residual)
2. Quantitative imaging: a measurement of activity within a defined volume that can be calibrated
3. Calculation of dose from cumulative activity: can be validated against calibrated measurements of absorbed dose – possibly a primary standard of absorbed dose from unsealed radionuclides?

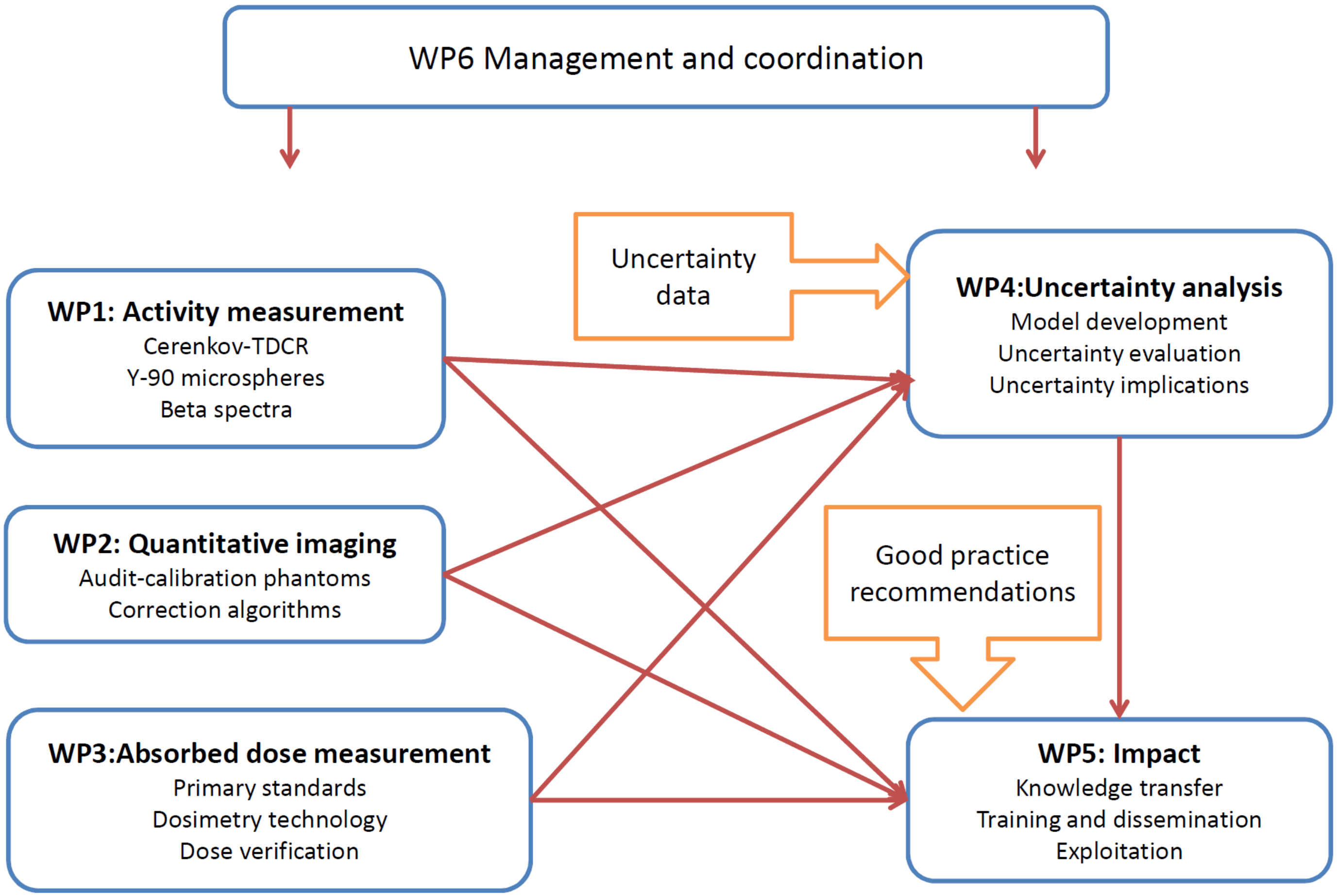
The bits in between

1. Volume delineation
2. Choice of time-sequence of QI measurements
3. Integration of QI measurements to give cumulative activity

What can we do about them?

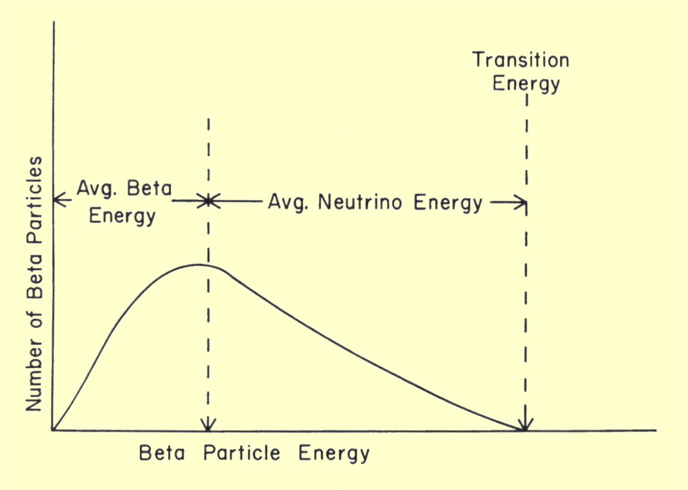
1. Develop best practice guidelines
2. Estimate the uncertainty within the constraints of best practice methods

MetroMRT workpackage structure



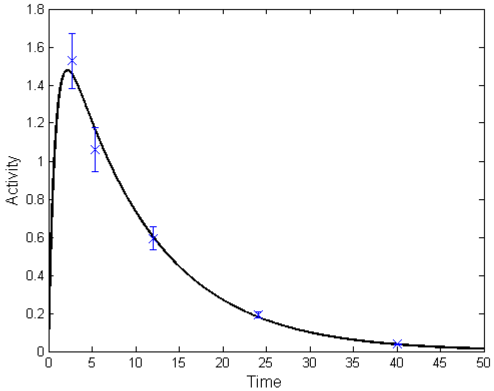
Workpackage 1: Activity measurement

- Development of the TDCR-Cerenkov technique for direct standardisation of radiopharmaceuticals
- Development of standardisation and transfer methods for 90Y microsphere samples
- Determination of beta spectra



Workpackage 2: Quantitative imaging

- Investigation of methods calibrating a QI measurement with traceability to an activity standard
- Use of “anthropomorphic” phantoms for verification of QI and evaluation of accuracy implications of different image reconstruction algorithms and correction factors
- Investigation of the accuracy of different approaches to integrating the activity-time curve



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Workpackage 3: absorbed dose evaluation

- Investigation of dose measurement methods
- Dosimeter calibration methods and investigation of the feasibility of a primary standard
- Depending on feasibility, develop of one or more prototype primary standards
- Assessment of the accuracy of methods of calculation of absorbed dose from cumulative activity

Workpackage 4: uncertainty analysis

- Errors and uncertainties in input data and other quantities
- Modelling and uncertainty evaluation
- Overall model and uncertainties for absorbed dose calculation
- Ramifications of modelling and uncertainty

Workpackage 5: Impact

- Website http://projects.npl.co.uk/metromrt/
- Look for sessions at IPEM, EANM, ESTRO, etc.
- Deliverables will include guidelines to be used in writing Good Practice Guides, protocols, etc.
- Calibration and auditing services will be developed from equipment and procedures developed.

What is the relevance for MELODI?

- Medical use of radiation is the greatest source of man-made exposure to humans
- It is also providing some of the best research databases
- Many scientific questions in common:
  - Measurement of biokinetics
  - Effects of dose-rate
  - Effects of inhomogeneity
  - Radiation quality effects

Thank you for your attention