Experimental validation of Monte Carlo-generated beta absorbed doses for 3D voxelwise dosimetry

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BACKGROUND

There is a growing interest in performing dosimetry post targeted radiopharmaceutical therapy to optimize the absorbed dose to achieve a clinically meaningful therapy response. The most accurate dosimetry approaches utilize dose point kernels that are based upon Monte Carlo-estimates of energy deposition of beta particles in tissue. The fundamental weakness of this approach is that, to date, Monte Carlo-based absorbed dose calculations have never been empirically validated due to the short range of therapeutic beta emitters in tissue. Given the potential for substantial downstream clinical use of these Monte Carlo- based absorbed dose calculations, experimental validation is mission critical. Here we present a simple experimental method to directly measure beta absorbed doses of ^{90}Y and ^{177}Lu in tissue equivalent materials using radiochromic EBT3 films.

The idea of patient-specific dosimetry is illustrated by the following graphics:

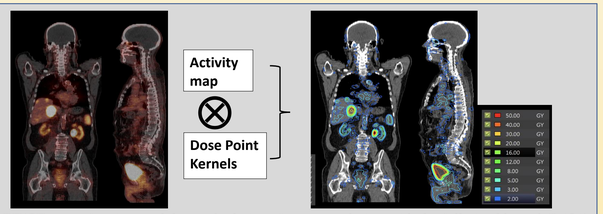

Fig 1. PET/CT scan of patient and dose calculations from convolution with the full-sized kernel (I-131).

OBJECTIVE - The aim is to validate the Monte Carlo-generated beta absorbed doses for radiopharmaceutical patient-specific dosimetry.

METHODS

Tissue-equivalent plastics (polyethylene (0.95 g/cm^3), cortical bone (1.90 g/cm^3), lung (0.30 g/cm^3)) and EBT3 films were utilized. The geometry and size of the tissue equivalent plastic blocks was chosen based on the range (energy) of beta particles in tissues of the radionuclides used. Aqueous line sources were constructed using ^{90}Y and ^{177}Lu radionuclides for beta exposures in the films. EBT3 film dosimeter was chosen for absorbed dose measurement because of its near soft-tissue equivalent density, minimal energy, and absorbed dose rate dependence.

Physical setup

- **Tissue Equivalent Plastics**: All were rectangular solids of dimension 5 × 5 cm^2 with a thickness of 2 cm.
- **Line source**: 13 cm long capillary tube with 0.42 mm inner diameter and 0.21 mm wall thickness. Activity densities in the line sources were (0.34 ± 0.015) MBq/cm and (0.35 ± 0.014) MBq/cm for ^{90}Y and ^{177}Lu exposures.

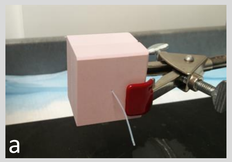

Fig 2a. Experimental setup

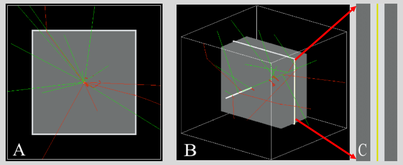

Fig 2(A-C). GATE Monte Carlo simulation setup

Monte Carlo simulations setup

All experimental geometries were precisely simulated within the GATE (GEANT4 Application for Tomographic Emission) Monte Carlo toolkit, which has previously been used to produce dose point kernels for ^{90}Y and ^{177}Lu [2].

Film Preparation, Calibration, Exposure, and Read-Out

- **Film preparation**: Calibration and experimental films were prepared, size ~3.8x3.8 cm^2 and sandwiched between tissue equivalent blocks. Experimental films were laser-cut to provide a 0.8 mm diameter hole to accommodate orthogonal line-sources of radioactivity.
- **Film calibration:** 6 MV bremsstrahlung x-rays from a calibrated linear accelerator (Siemens Oncor), in accordance with literature recommendations [1]. Film exposure densities were calibrated to absorbed dose (Figure 3).
- **Film exposures**: Exposed for different durations (10 minutes – 38 hours) to assure that we had films with exposures in the linear dose range of the film (0.1 – 10) Gy at different radii.
- **Film Digitization protocol:** Epson 12000XL, scan one at a time, 508 dpi (0.05 mm pixel), RGB format, 48-bit, TIFF image, reflective mode, no color corrections
- **Absorbed dose calculations**: Dual channel method using the red and green channel were used.

RESULTS

Film calibration: Three parameter rational function was found to best fit the calibration data, $X(D) = \frac{b + D}{a + Dc}$ where, X(D) is the scanner response, D is the absorbed dose and a, b, c are constants.

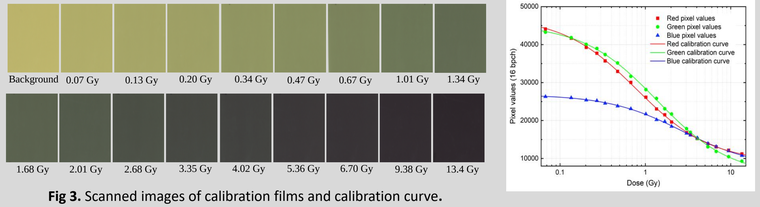

Fig 3. Scanned images of calibration films and calibration curve.

Experimental film exposures:

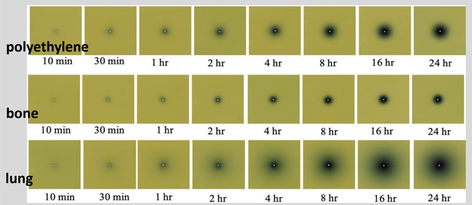

Fig 4a. Scanned images of ^{90}Y exposed films.

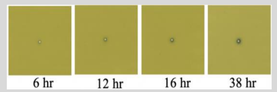

Fig 4b. Scanned images of ^{177}Lu exposed films in lung equivalent phantom.

Uncertainty estimates and results of gamma index test:

- Optical densities for red, green, and blue channels were 0.78%, 0.80%, and 0.94%
- Average uncertainty in activity measurement was 5.82%
- Curve fitting uncertainties were 2.20% and 3.61% for red and green channels and calculation of absorbed dose was 4.56%
- Overall, the combined uncertainty was 8.64%
- The average statistical uncertainties in Monte Carlo simulations were ~4.5%
- The mean local percentage difference in the dose distribution compared to Monte Carlo simulation was ~6.0%
- Overall, the percentage of points passing the preset tolerances of 10%/1 mm in absorbed dose, averaged over all tests was 93.5%.

Experiment vs Monte Carlo absorbed dose comparisons

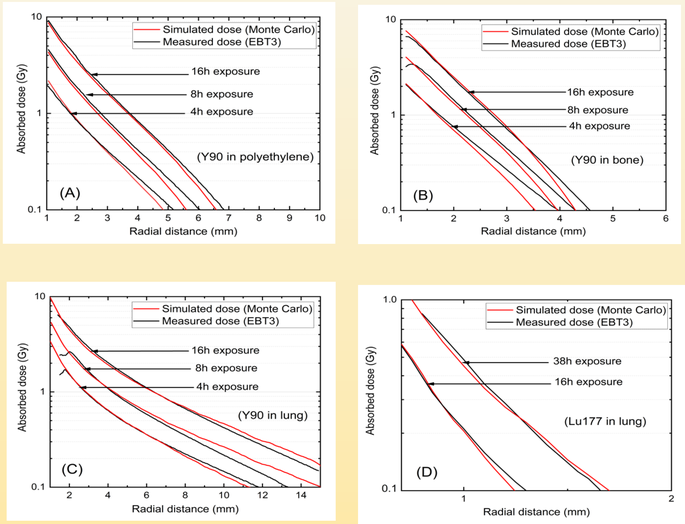

Fig 5. (A-C) Comparison of absorbed doses in the linear range of the film (0.1 -10)Gy using ^{90}Y as a source in different tissues and (D) using ^{177}Lu in lung phantom.

CONCLUSIONS

- Experimental absorbed dose distributions agreed remarkably well with Monte Carlo simulations for ^{90}Y and ^{177}Lu, suggesting that dosimetry based on beta dose point kernels derived from Monte Carlo simulations are sufficiently accurate for clinical use.
- EBT3 film has sufficient sensitivity and spatial resolution to be used as a tool for measuring beta decay absorbed dose distributions.
- Future work should expand these methods to other therapeutic radionuclides and measurement geometries.

REFERENCES

1. D. A. Low, J. M. Moran, J.F. Dempsey, L. Dong and M. Oldham, “Dosimetry tools and techniques for IMRT”, Med. Phys. 38(3):1313-38 (2011).
2. A. Tiwari, S. A. Graves, J. Sunderland, “The Impact of Tissue Type and Density on Dose Point Kernels for Patient-Specific Voxel-Wise Dosimetry: A Monte Carlo Investigation”, *Radiat Res.* 2020;193(6):531-542.
3. D.A. Low, W. B. Harms, S. Mutic, and J. A. Purdy, “A technique for the quantitative evaluation of dose distributions,” Med. Phys. 25, 656–661 (1998).