

**PhD Thesis Title:** Computational cell dosimetry for cancer radiotherapy and diagnostic radiology

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**Graduation date:** June 2018

**Available online:** <https://doi.org/10.22215/etd/2018-12914>

**Abstract:**

Computational radiation dosimetry, using *e.g.*, Monte Carlo (MC) techniques, is used to calculate the amount of energy per unit mass deposited in tissue (the absorbed dose) resulting from radiotherapy and diagnostic radiology procedures. Motivated by the radiobiological importance of subcellular structures such as the nucleus, this work seeks to develop a better understanding of energy deposition on the cellular level.

Multicellular models of healthy and cancerous human soft tissues are developed based on typical values of cell compartment sizes, elemental compositions and number densities found in the literature. MC simulations are used to investigate how energy deposition within the nucleus and cytoplasm depends on incident photon energy, dose level, cell morphology, cell arrangement method, elemental composition, and the microscopic details of the environment surrounding the target of interest. MC simulations are carried out for monoenergetic kilovoltage incident photon energies ranging from 20 to 370 keV. 120 kVp x-ray, Cobalt-60 and 6 MV medical linac photon spectra are also considered. Given the considerable computational resources required for simulations involving microscopic details, cavity theory is explored as a method for relating macroscopic (bulk tissue) and microscopic (cellular) dose descriptors without the need for MC simulations.

For low doses and small target sizes, the stochastic nature of radiation transport and energy deposition can lead to considerable variation in energy deposition across a target population; this variation is referred to as the microdosimetric spread. The microdosimetric spread is investigated in the context of experimental radiation response studies using micron-sized sampling volumes. These results are relevant for guiding measurement and data analysis techniques for Raman spectroscopy studies. Additionally, motivated by the lack of detail included in traditional breast dosimetry computational models, multiscale models of compressed breasts, combining macroscopic and microscopic features, are developed. A 30 kVp mammography spectrum is considered.

The sensitivity of results with respect to microscopic tissue structure model parameters emphasizes the importance of accurate knowledge of cellular properties. For incident photon energies < 50 keV, there are considerable differences between macroscopic and microscopic

dose descriptors. Results highlight the importance of microdosimetric considerations when scoring energy deposition in subcellular targets.

**References to author publications that relate specifically to the dissertation:**

1. **PAK Oliver** and RM Thomson, "Investigating energy deposition in glandular tissues for mammography using multiscale Monte Carlo simulations," *Med. Phys.* **46** (3), 1426-1436 (2019). DOI: <https://doi.org/10.1002/mp.13372>
2. **PAK Oliver** and RM Thomson, "Microdosimetric considerations for radiation response studies using Raman spectroscopy," *Med. Phys.* **45** (10), 4734-4743 (2018). DOI: <https://doi.org/10.1002/mp.13145>
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4. **PAK Oliver** and RM Thomson, "Cavity theory applications for kilovoltage cellular dosimetry," *Phys. Med. Biol.* **62** (11), 4440-4459 (2017). DOI: <https://doi.org/10.1088/1361-6560/aa6a42>
5. **PAK Oliver** and RM Thomson, "A Monte Carlo study of macroscopic and microscopic dose descriptors for kilovoltage cellular dosimetry," *Phys. Med. Biol.* **62** (4), 1417-1437 (2017). DOI: <https://doi.org/10.1088/1361-6560/aa5136>