Development of a novel system for microdosimetry and cellular radiation response

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OVERVIEW

- **Goal**: Link cellular scale energy deposition to biological response.
- **Approach:** Develop a novel cells-on-radiochromic film (cells+RCF) platform for direct measurement of energy deposition alongside cellular and biochemical response.
- **This work:** provides an overview of the three-phase study, with results from Monte Carlo (MC) simulation and initial investigations of cellular response to radiation.

METHODS

Phase 1. Micron-scale radiation response of RCF

EBT3 irradiated with 6 MV photons (0-10 Gy)

- MC simulations evaluated micron-scale energy deposition.
  - Specific energy (z = ϵ/m) scored in the film active layer [1].
- Film response measured by optical density scanner, and micron-scale Raman Spectroscopy (RS) [1,2].

Phase 2. MC38 cells radiation response

MC38 murine colon cancer cells in a petri dish irradiated with 6 MV photons (0-10 Gy).

- MC simulations modelled energy deposition in cells.
- Radiation response characterized using:
  1. RS: radiation induced biochemical changes in cell nuclei.
  2. Flow cytometry: mitochondrial superoxide generation, cell membrane integrity and proliferation.

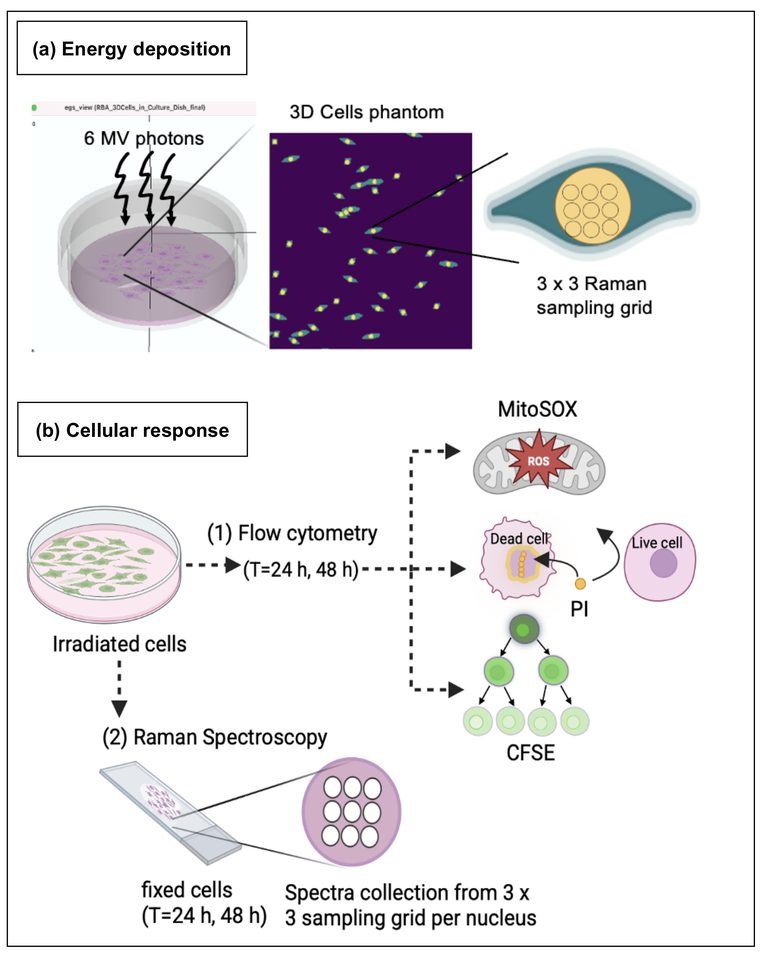


Fig. 1: (a) MC simulations of the experimental irradiations of the cells.
(b) Experimental workflow for measurement of cellular response at 24 and 48 hr timepoint post cells irradiations.

Phase 3. Cells+RCF Setup (Ongoing)

- Cells grown directly on RCF and co-irradiated (0-10 Gy).
- Simultaneous assessment of physical dose (RCF) and biological response (cells).

Feasibility test: The cells+RCF system is studied using MC simulations to evaluate correlations between energy deposition in cells and in RCF.

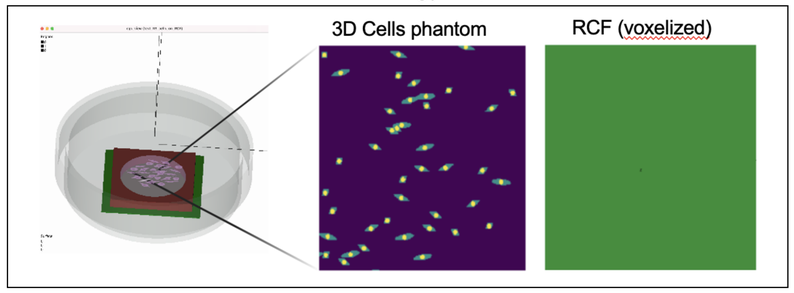


Fig. 2: MC simulations: Specific energy is scored in cells phantom (voxel size: 1 um^3) and the RCF beneath.

RESULTS & DISCUSSION

RCF: Dose deposition and radiation response

- **MC simulations**: ($\sigma_2/\bar{z}$) ↓ with ↑ dose and is dependent on size of sensitive volume [1].
- **RS**: 1445 and 2060 cm-1 identified as radiation sensitive peaks. A linear dose response obtained using mean intensity of 1445 cm-1 peak [1,2].

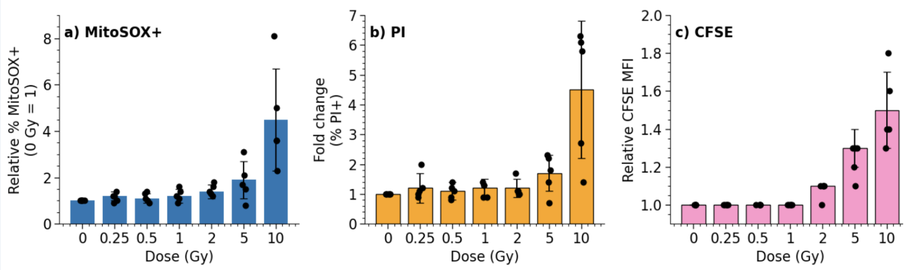
MC38 Cells: Dose deposition and radiation response

Energy deposition:

- MC simulations show decreased variability in cellular energy deposition ($\sigma_2/\bar{z}$) with ↑ dose.
- Sampling partial nuclear volume (RS-SV) may exaggerate variability in observed cellular response compared with full nucleus.

Radiation response:

- **Flow cytometry**: higher response at 5 and 10 Gy.



- **RS**: DNA/RNA peaks (e.g. 782 cm^{-1}) show significant ↓ in intensity, proteins peaks (e.g. 1001 cm^{-1}) show ↑ in intensity with ↑ in dose.

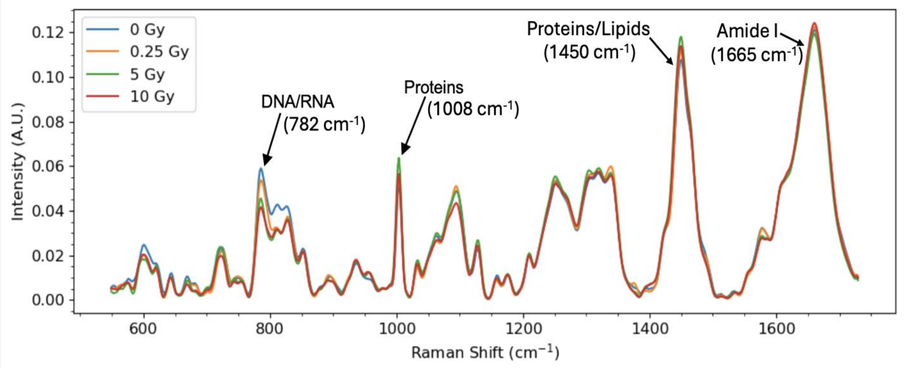
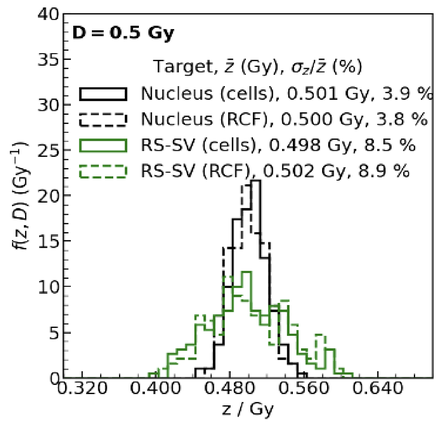


Fig. 3: Dose dependent responses of MC38 cells at 48 h post irradiation.

Feasibility test: Cells+RCF



- MC simulations of cells+RCF show agreement between mean specific energy deposited in nuclei and in the RCF, with differences <2% across all doses.

Fig. 4: Comparison of $\bar{z}$ between cells and RCF geometries: % difference <2.5% in all cases

CONCLUSIONS

- Established micron-scale RS analysis of RCF radiation response and demonstrated a linear dose-response [1,2].
- Characterised MC38 cells using RS and identified radiation sensitive spectral features.
- MC simulations suggests high variability in energy deposition at low doses.
- MC simulations of the integrated cells+RCF system shows promise for microdosimetric characterization of cellular response.

Future works: RS measurements from the integrated system and use of machine learning to quantitatively correlate energy deposition to radiation response in cells.

REFERENCES

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