Hydrogel based models of muscle invasive bladder cancer for understanding radiotherapy response and resistance.

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Introduction

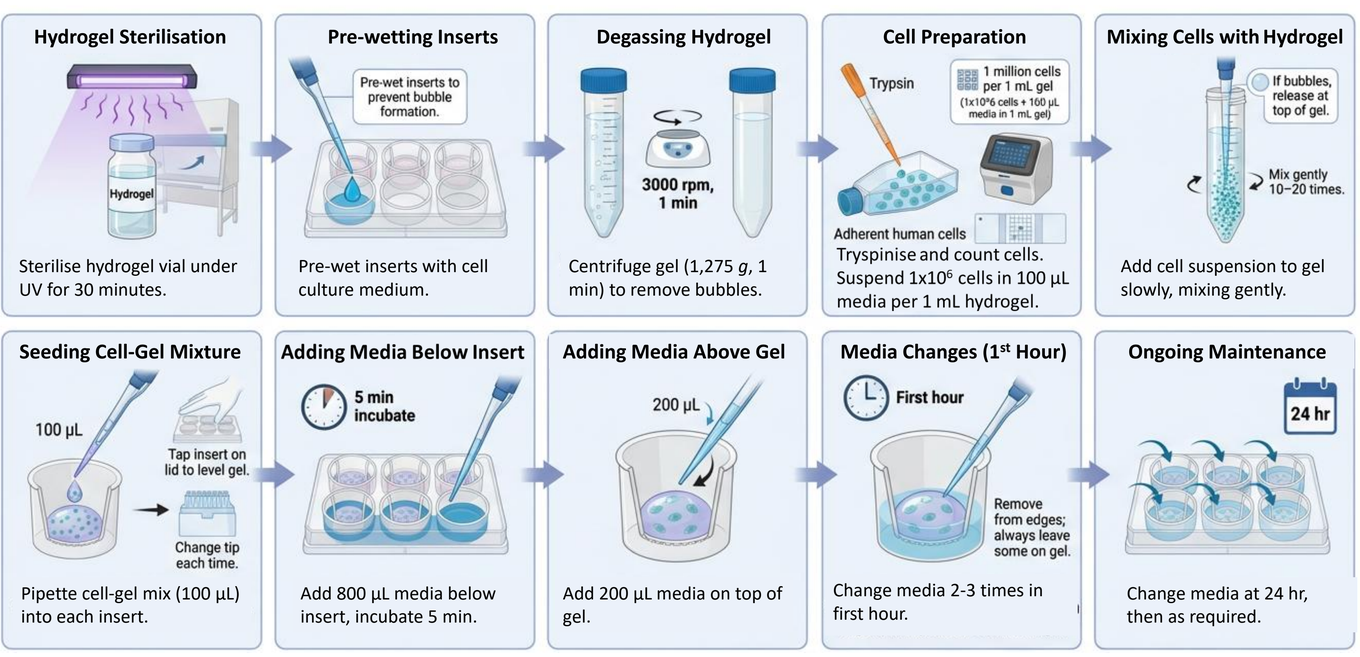
- Muscle-invasive bladder cancer (MIBC) has a five-year survival (~21%) and high rates of radioresistance [1].
- Extracellular matrix (ECM) remodelling and tumour fibrosis drives radioresistance [2].
- Self-assembling peptide hydrogel (SAPH) platforms spanning physiologically-relevant stiffness ranges can be used to mimic the TME stiffness.

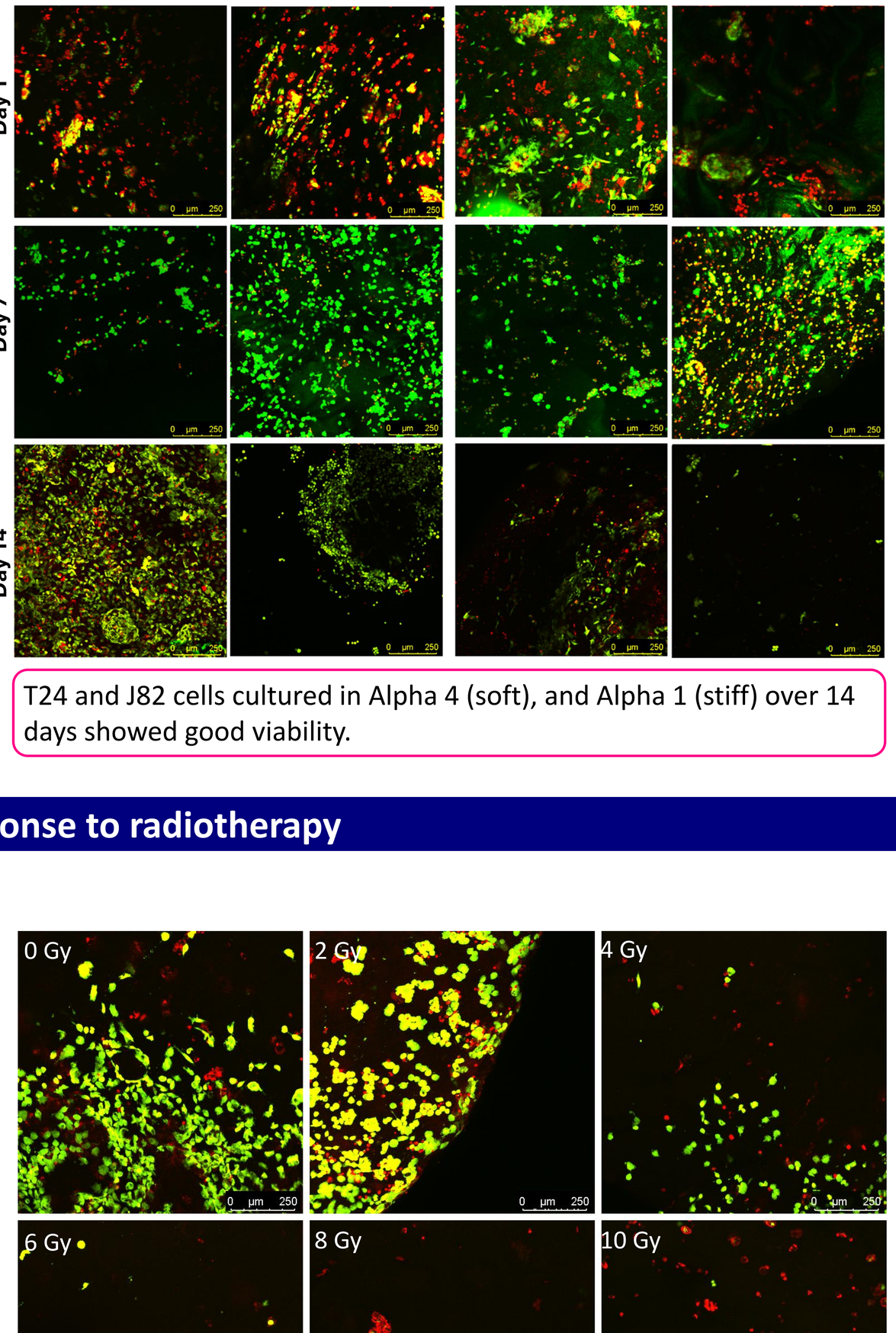
Generating 3D cell culture models

PeptiGel™ SAPH were used due to their favourable features:

✓ Synthetic and highly tuneable
✓ Biocompatible
✓ Nanofibrous architecture mimics tumour environment

Alpha 4 (0.7-1.3 kPa) and Alpha 1 (3-5 kPa) were used to mimic different stages of cancer progression.

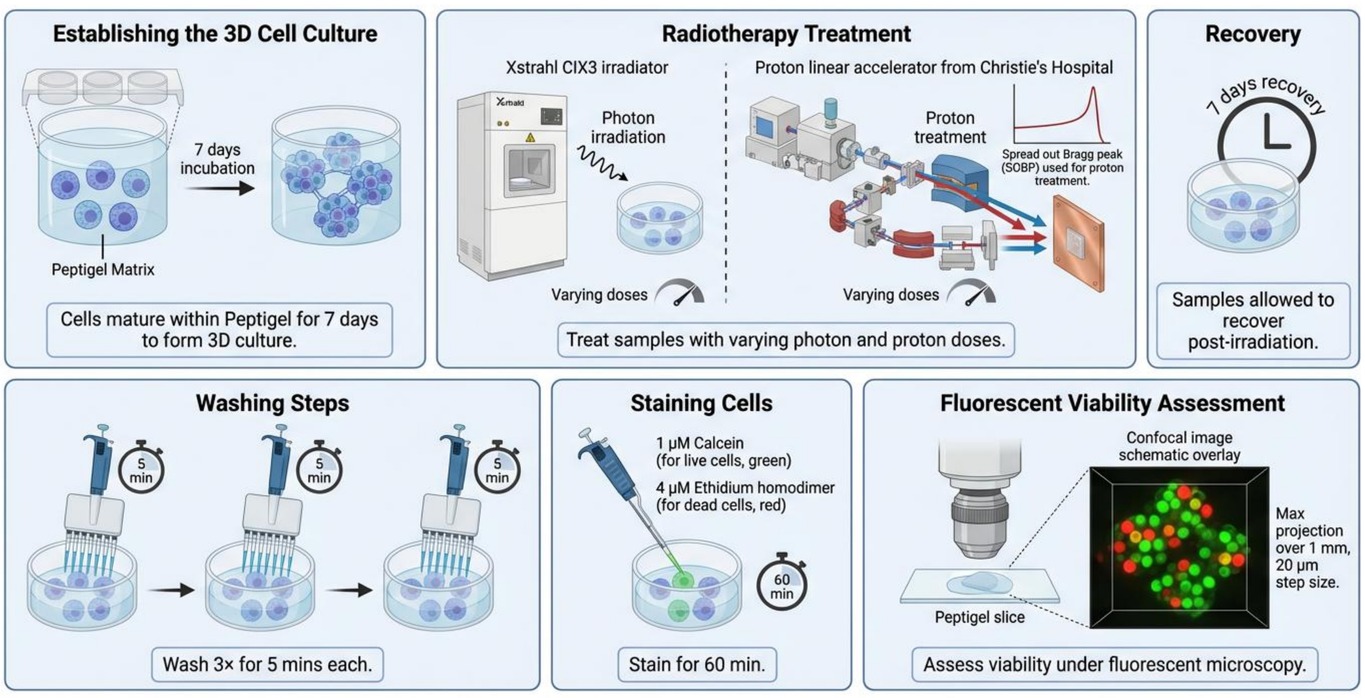


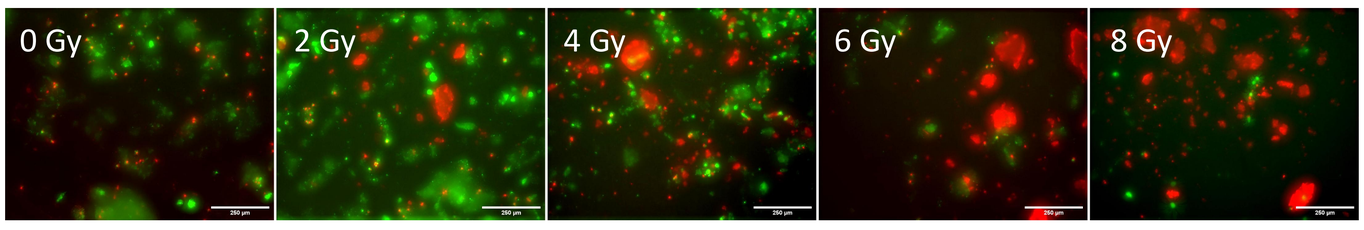


The 3D models were assessed using a Viability/Cytotoxicity stain. Z-stack images were taken on a spinning disk confocal microscope and displayed as maximum projections.

T24 and J82 cells cultured in Alpha 4 (soft), and Alpha 1 (stiff) over 14 days showed good viability.

3D models to understand response to radiotherapy





T24 cells cultured in Alpha 1 (stiff hydrogel), 14 days post **proton irradiation**, demonstrate increased cell death with increased doses of radiotherapy.

T24 cells cultured in Alpha 4 (soft), 14 days post **photon irradiation**, demonstrate increased cell death with increased doses of radiotherapy.

Discussion and Future work

- By integrating cell-matrix interactions and biomechanical cues, this 3D system enables the discovery of strategies that sensitise MIBC to radiotherapy and improve therapeutic outcomes.
- Future work includes conducting a transcriptomics screen across samples to explore resistance pathways that may be exploited in combination therapies.

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[1] Catto, *et al.* (2023). *BJU International* [2] Guerrero Quiles, *et al.* (2025) *Front Oncol.*