A DATA-DRIVEN APPROACH TO OPTIMISE PARAMETERS OF A COMPUTATIONAL DIGITAL TWIN MODEL IN RESPONSE TO SBRT ON MR-LINAC

Valentin Septiers[1,2] , Joséphine Colineaux[1] , Carlos Sosa-Marrero[1] , Jennifer Le Guévelou[1] , Kaoutar Elouahabi[1] , Léo Le Bozec[1] , Renaud de Crevoisier[1] , Hervé Saint-Jalmes[1] , Anaïs Barateau[1] , Maria A. Zuluaga[2] , and Oscar Acosta[1]

1. Univ Rennes, CLCC Eugène Marquis, Inserm, LTSI - UMR 1099, F-35000 Rennes, France
2. EURECOM, Data Science Department, F-06410 Biot, France

OBJECTIVES

- **OPTIMISING** RADIOBIOLOGICAL PARAMETERS OF A **COMPUTATIONAL DIGITAL TWIN MODEL** IN RESPONSE TO **SBRT**
- **IDENTIFYING PATIENT-SPECIFIC TUMOUR EVOLUTION** DURING SBRT TREATMENT ON **MR-LINAC**

OUR CONTRIBUTIONS

- **OPTIMISED RADIOBIOLOGICAL PARAMETERS** BASED ON **PATIENT-SPECIFIC** TUMOUR EVOLUTION DURING **SBRT** ON **MR-LINAC**
- **RELEVANCE** OF A COMPUTATIONAL DIGITAL TWIN MODEL TO **MIMIC PATIENT TUMOR EVOLUTION** DURING TREATMENT

BACKGROUND

→ **RT treatments** prescribed to the **majority of patients (~ 60%)**

Up to 20% recurrence for **high risk group** → Crucial to **personalise RT**

→ **Stereotactic Body Radiotherapy (SBRT)** to reduce toxicity and recurrence risk, alongside the use of **new precision systems** : **MR-Linac**

→ **Impact of SBRT unknown** on **individual patients** with **MR-Linac**

→ **Computational digital twin models** able to simulate different RT treatments on infinite digital tissues

→ **Several radiobiological parameters to adapt specifically to patients, some being unobservable**

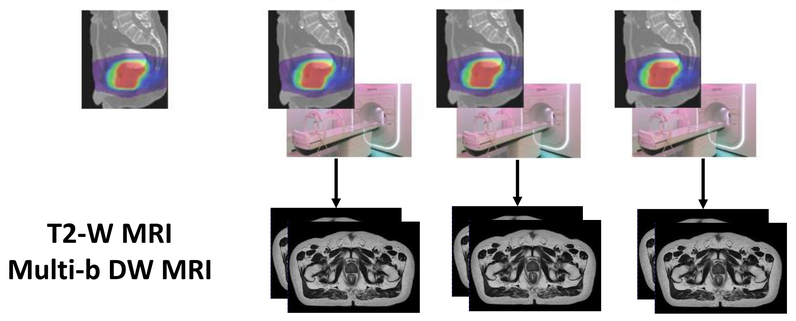
PATIENT DATA FROM MR-LINAC

3 PATIENTS

Prostate frontline 5*8 Gy

Planning — SBRT treatment (2 days interval)

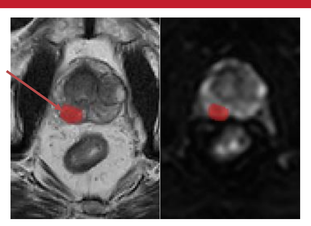
40 Gy = 8 Gy + 8 Gy + 8 Gy + … **N = 5**



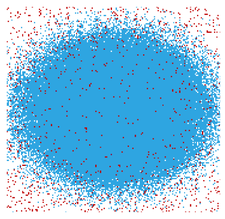
T2-W MRI
Multi-b DW MRI

1) LONGITUDINAL qMRI ACQUISITIONS

DIGITAL TWINS CONSTRUCTION



2) BIOMARKERS EXTRACTION



Volume and **Sphericity** of the tumour (Pyradiomics)

Vessel density (from DW MRI)

3) DIGITAL TWINS INITIALISATION

IntraVoxel Incoherent Motion model (IVIM) applied to DW MRI

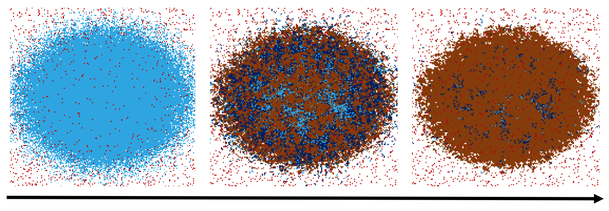
$$\frac{s(\boldsymbol{b})}{s0} = \boldsymbol{fBV}.e^{-\boldsymbol{b}.\boldsymbol{D}^*} + (1 - \mathbf{fBV}).\,\mathrm{e}^{-\mathbf{b}.\mathbf{ADC}}$$

Apparent Diffusion Coefficient → **Tumour density**

COMPUTATIONAL DIGITAL TWIN MODEL[1]

Radiobiological mechanisms included — Radiotherapy Simulator

- ANGIOGENESIS
- OXYGENATION
- TUMOUR AND HEALTHY CELLS DIVISION
- RESPONSE TO IRRADIATION



Simulation example

Healthy cells · Tumor cells · Damaged tumor cells · Pre-existing vessels · Neo-created vessels · Hypoxic necrotic cells · Mitotic catastrophe cells · Apoptotic cells

4) COMPUTATIONAL SIMULATION OF THE TUMOUR DENSITY EVOLUTION DURING SBRT TREATMENT

PARAMETER OPTIMISATION

RESPONSE TO IRRADIATION	
Parameter	**Range**
α_{tumG1} (Gy^{-1})	0.024 - 0.356
α_{tumS} (Gy^{-1})	0.017 - 0.256
α_{tumG2} (Gy^{-1})	0.025 - 0.381
α_{tumM} (Gy^{-1})	0.028 - 0.425
α_{tumG0} (Gy^{-1})	0.105 - 0.195
T_{arrest} (h)	4.2 - 39

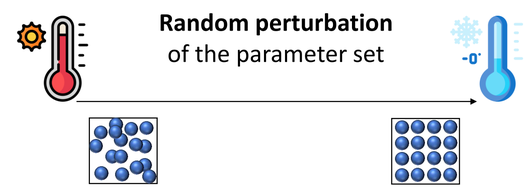
OXYGENATION	
Parameter	**Range**
pO_2^{nec} (mmHg)	0 - 1.3
D^{O2} (µm²/ms)	1.02 - 2.87
V^{O2}_{max} (mmHg/ms)	0.006 - 0.029
K^{O2}_{M} (mmHg)	0.119 - 7.67
p^{preEnd}_{O2} (mmHg)	8.4 - 93.6
p^{neoEnd}_{O2} (mmHg)	8.4 - 93.6

TUMOUR CELLS DIVISION	
Parameter	**Range**
T_{tum} (h)	85 - 1310
N	1 - 3

Cell Cycle: **G0** = G0 phase, **G1** = G1 phase, **S** = Synthesis, **G2** = G2 phase, **M** = Mitosis

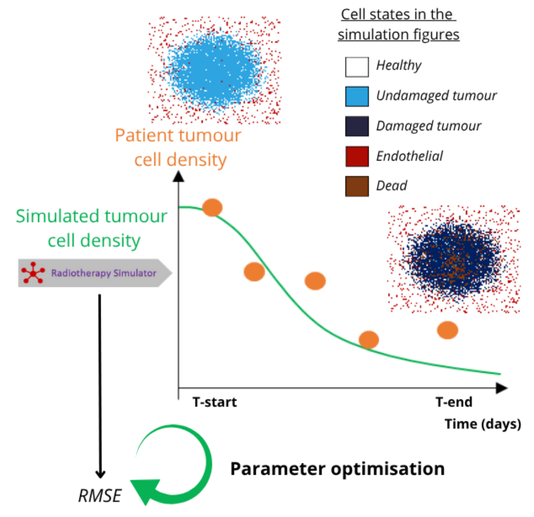
13 parameters to **adapt specifically** to each patient after sensitivity analysis

5) SIMULATED ANNEALING OPTIMISATION

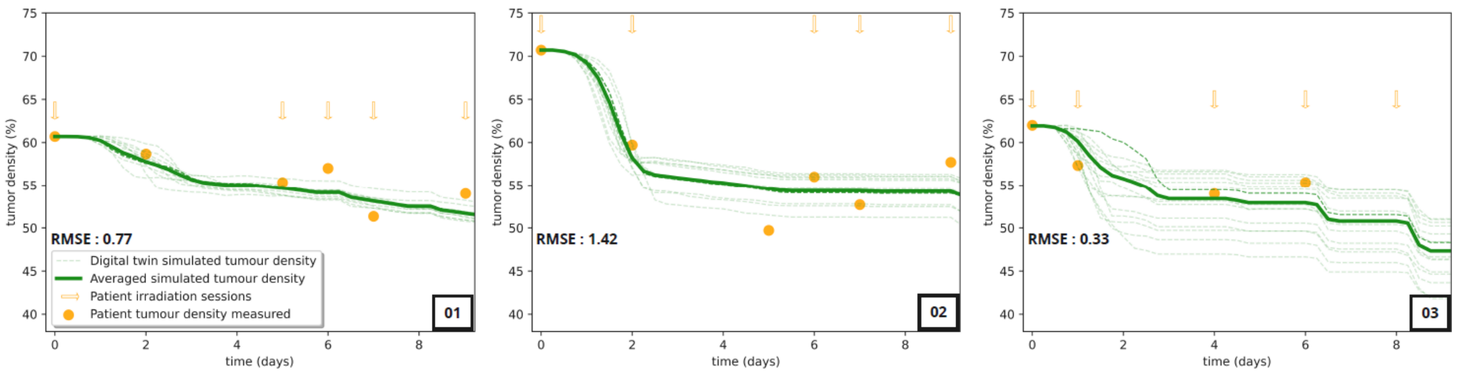


Unstable structure => Parameters are **changing** a lot

Stable structure => Parameters reaching an **ideal solution**



RESULTS



Parameters	Patient 01	Patient 02	Patient 03
Doubling time of tumour cells (h)	842	1217	594
Arrest duration in the cell cycle when irradiated (h)	10.4	38.4	31.4
α radiosensitivity parameter in G1 phase (Gy^{-1})	0.319	0.045	0.063
pO_2 of pre existing endothelial cells (mmHg)	86.93	54.21	82.97

Simulations in **accordance** with **patient tumour density** measured on MRI

Offers **insights into the radiobiology** of the tumour, even for **unobservable** parameters

With financial support from ITMO Cancer of Aviesan within the framework of the 2021-2030 Cancer Control Strategy, on funds administered by Inserm.

[1]***Towards a Reduced In Silico Model Predicting Biochemical Recurrence After Radiotherapy in Prostate Cancer***, *Sosa-Marrero et al. TBME, 2021*

FUTURE WORK

INCLUSION OF **NEW PATIENTS** IN THE STUDY

CLASSICAL LQ MODEL TO BE REDEFINED FOR **HIGH DOSES?**

3D-BASED DIGITAL TWINS (SUITABLE FOR OPTIMISATION PROCESS?)