



Leeds Cancer  
Centre



UNIVERSITY OF LEEDS



RO-PIP



Mount Vernon  
Cancer Centre



The Christie  
TOWARDS A FUTURE WITHOUT CANCER

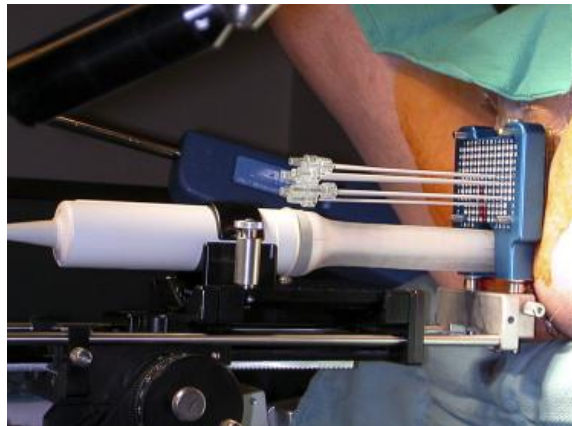
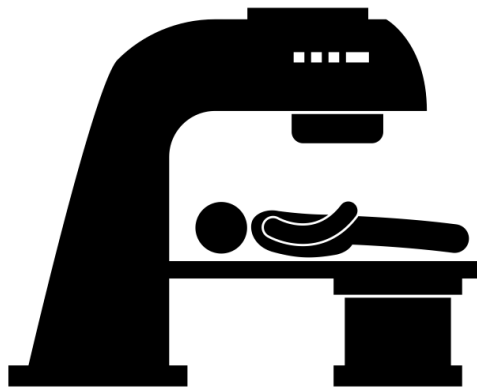
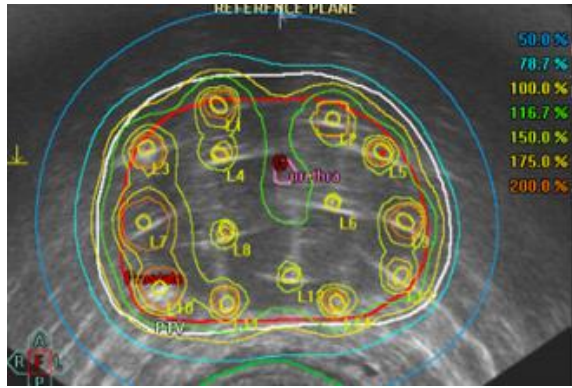
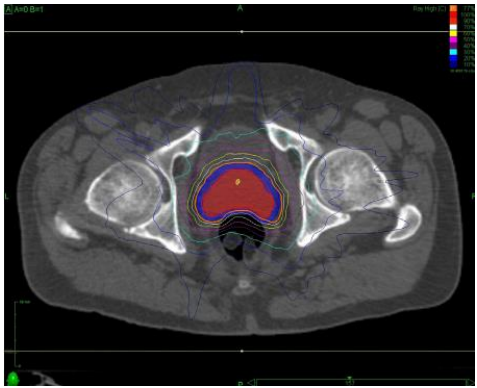
# Reirradiation Options for Previously Irradiated Prostate cancer (RO-PIP)

*Feasibility randomised clinical trial investigating toxicity outcomes following reirradiation with ultra-hypofractionated external beam radiotherapy vs. high dose rate brachytherapy*



# Salvage Reirradiation Options for Locally Recurrent Prostate Cancer: A Systematic Review

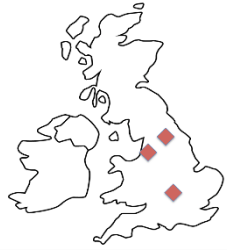
Frontiers in Oncology  
Published on 09 Sep 2021



- Salvage reirradiation of radiorecurrent prostate cancer using HDR-BT or hypofractionated EBRT/ SBRT provides similar biochemical control and acceptable late toxicity.
- Challenges exist in comparing BT and SBRT from inconsistencies in reporting with missing data/ small studies
- Only 1/3 studies included PROMs
- Prospective randomised trials needed

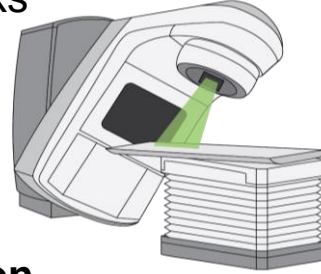
**Recruitment Locations:**

- Leeds
- Christie
- Mount Vernon



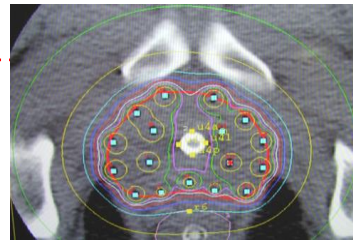
**External Beam Radiation Therapy (EBRT) (n=30)**

Dose: 36.25 Gy in 5 fractions  
 Timing: Alternating days over 2 weeks



**High Dose Rate Brachytherapy (HDR-BT) (n=30)**

Dose: 19 Gy single fraction or 27 Gy in 2 fractions  
 Timing: Up to 2 weeks between each implantation



**Randomisation**

**Radiotherapy (RT) Treatment**

**MAIN STUDY OUTCOMES**

**PRIMARY**

1. Feasibility of recruitment

**SECONDARY/ EXPLORATORY**

1. Toxicity - Incidence of clinician-reported (CTCAE) and patient-reported acute (0-3 months) and long-term toxicity (>3 months) and impact on QoL determined by EPIC-26, EORTC QLQ-C30 and IPSS.
2. Identify MRI biomarkers predictive of toxicity
3. Adequacy of image quality and repeatability of prostate functional imaging for detecting hypoxia

**TRANSLATIONAL ARM**

1. **Imaging Biomarkers/ Radiomics**  
MRI at baseline, 1 month and 1 year post-RT
2. **Hypoxic Signatures/ Proteomics**  
Pre-treatment prostate biopsy/ Blood+Urine

**Identifying suitable patients**

**Checklist:**

Imaging:  
 PET-CT  
 mpMRI



Biopsy



EORTC QLQ-C30, IPSS and EPIC-26 QoL questionnaires



Screening

Baseline

Treatment

Treatment Complete

Month 1,3,6

Month 12

Month 24

# Objectives


## PRIMARY OBJECTIVE

Feasibility and recruitment potential over 2 years

## SECONDARY OBJECTIVES

1. Toxicity/ Quality of Life
2. Predictive MRI biomarkers of Toxicity
3. Evaluate quality and repeatability of hypoxia MRI sequences
4. Effect of RT on hypoxia associated gene signature and proteomic/ immune markers

**BMJ Open** Reirradiation Options for Previously Irradiated Prostate cancer (RO-PIP): Feasibility study investigating toxicity outcomes following reirradiation with stereotactic body radiotherapy (SBRT) versus high-dose-rate brachytherapy (HDR-BT)

Jim Zhong <sup>1,2</sup> Sarah Brown <sup>3</sup> Maria Serra,<sup>4</sup> Pam Shuttleworth,<sup>5</sup> Peter Bownes,<sup>5</sup> Christopher Thompson,<sup>5</sup> Rachel Reed,<sup>6</sup> Kimberley Reeves,<sup>6</sup> Michael Dubec <sup>6,7</sup> Damien McHugh <sup>6,7</sup> Cynthia Eccles <sup>4,6</sup> Robert Chuter <sup>6,7</sup> Yat Man Tsang <sup>8</sup> N Jane Taylor <sup>9</sup> Catharine West <sup>6</sup> David Buckley <sup>10</sup> Andrew Scarsbrook <sup>1,2</sup> Ananya Choudhury <sup>4,6</sup> Peter Hoskin <sup>6,8</sup> Ann Henry <sup>1,5</sup>

# Eligibility Criteria

## INCLUSION

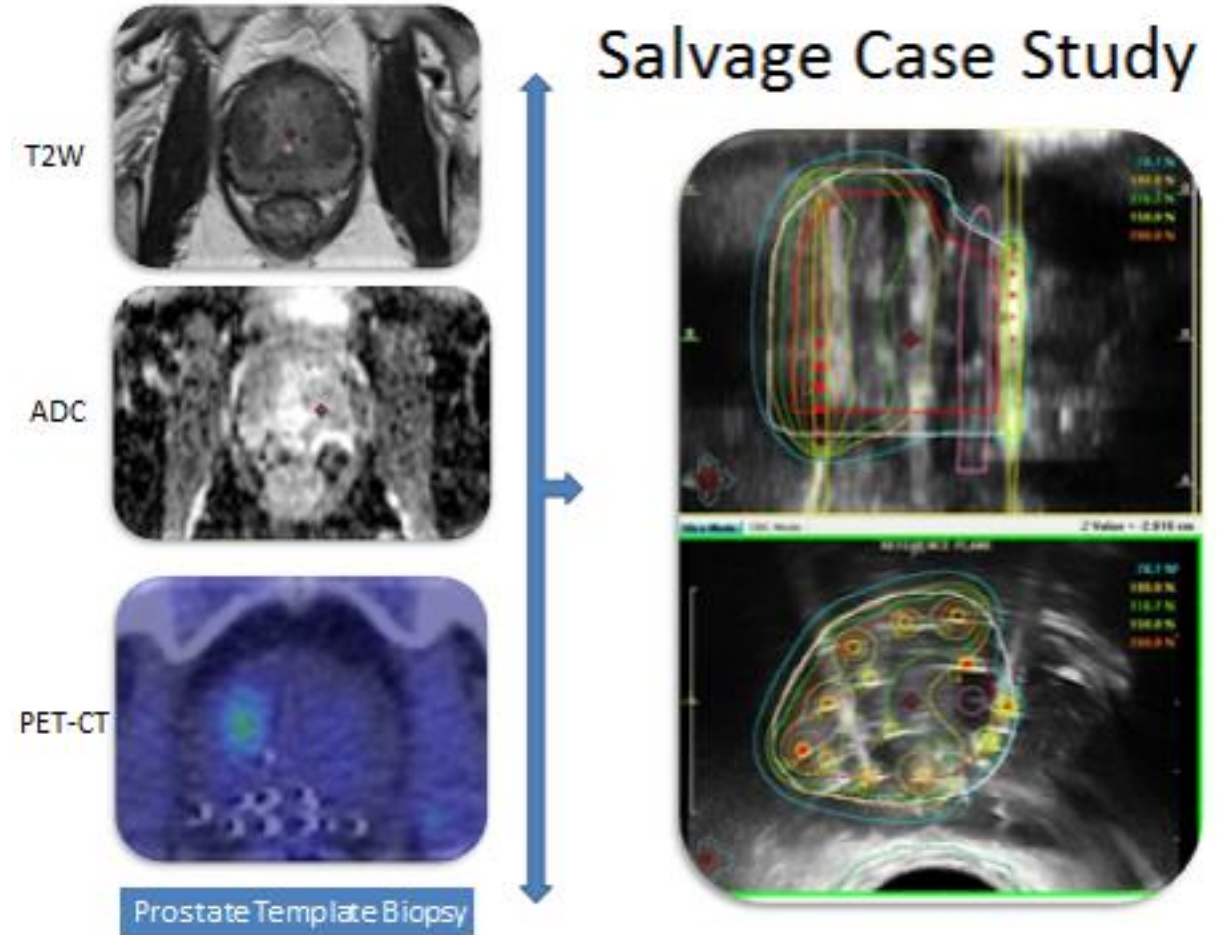
- Biopsy proven locally recurrent prostate cancer
- T1-3 N0 M0 Any Gleason/ISUP grade group adenocarcinoma prostate
- Recurrence at least 2 years after primary radiation treatment completed
- Greater than 10 year life expectancy
- Reasonable urinary function (IPSS < 20 and Qmax > 10 ml/second on flow tests)
- No metastatic disease (PET-CT - any of choline/ fluciclovine/ PSMA)
- No prior prostatectomy (TURP > 3 months before randomisation is acceptable)
- No history of inflammatory bowel disease

Androgen Deprivation Therapy may be initiated at the discretion of the treating oncologist



# HDR BT planning

- **GTV +3mm** constrained to the urethra and rectum is used to define the PTV for focal treatments.
- **GTV (prostate)+3mm** constrained to the rectum used to define PTV for whole gland treatments.
- **HDR-BT Dose and Fractionation** - 27 Gy in 2 fractions up to 2 weeks apart (19Gy single used at MVH)



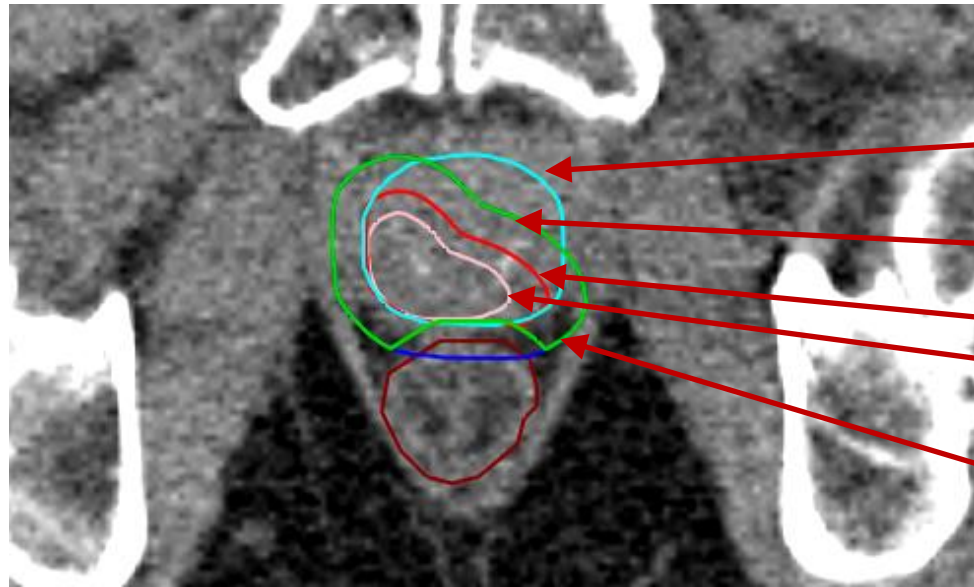
# EBRT Planning

- **GTV\_4000** either **whole gland** or **focal** using information from the diagnostic MRI, PET-CT and prostate biopsy.
- 3mm margin **constrained to the prostate capsule** defines **CTV for focal treatments**.
- The **PTV\_3625** is the **CTV + 3-5 mm** margin

	Optimal	Mandatory
PTV V36.25Gy	≥ 85-95%	none
PTV V34.4Gy	≥ 98%	none
Maximum dose within GTV	105-130%	130%
GTV V40Gy	≥ 95%	none

Organ	Limit type	Optimal	Mandatory
Rectum	V 23.4 Gy		< 1 cc
Bowel Loops	V18.1 Gy	< 5 cc	
Bowel Loops	V 30 Gy		< 1 cc
Bladder	V 27 Gy	< 10 cc	< 15 cc
Femoral Heads	V 14.5 Gy	< 5 %	

# Rectum sparing focal SBRT



Prostate

PTV

CTV

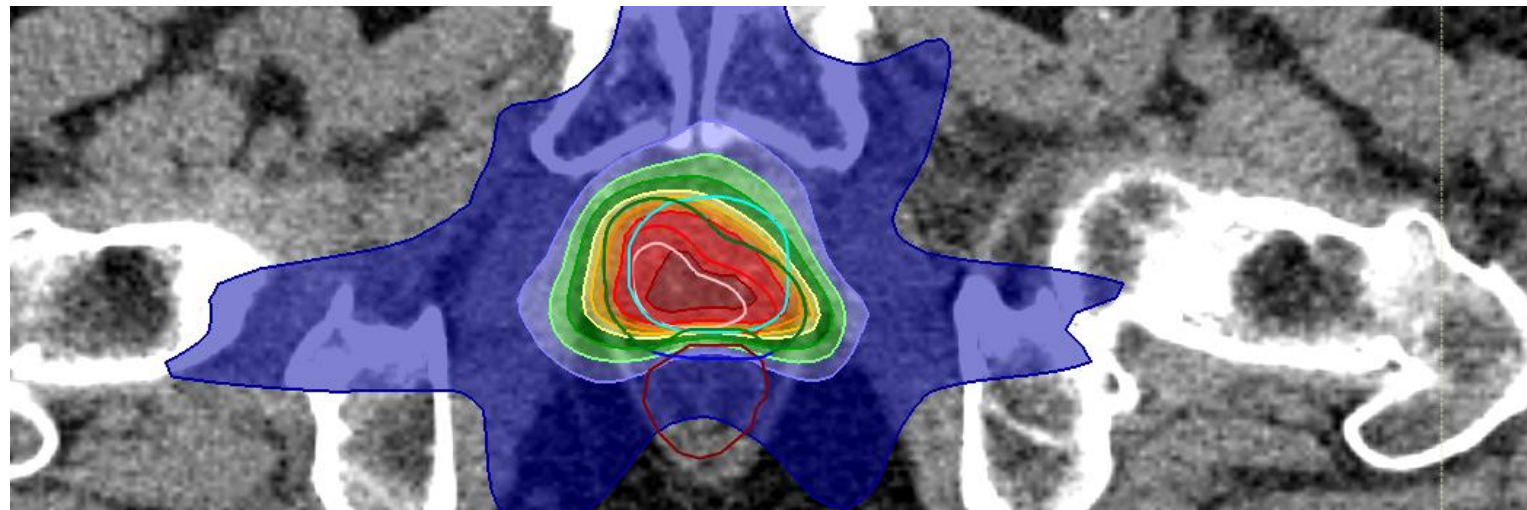
GTV

PTV\_Plan

CTV + 5mm

GTV + 3mm Clipped at Prostate

Clipped 3mm from rectum



% of 40.00

150

120

105

95

90

85

80

70

60

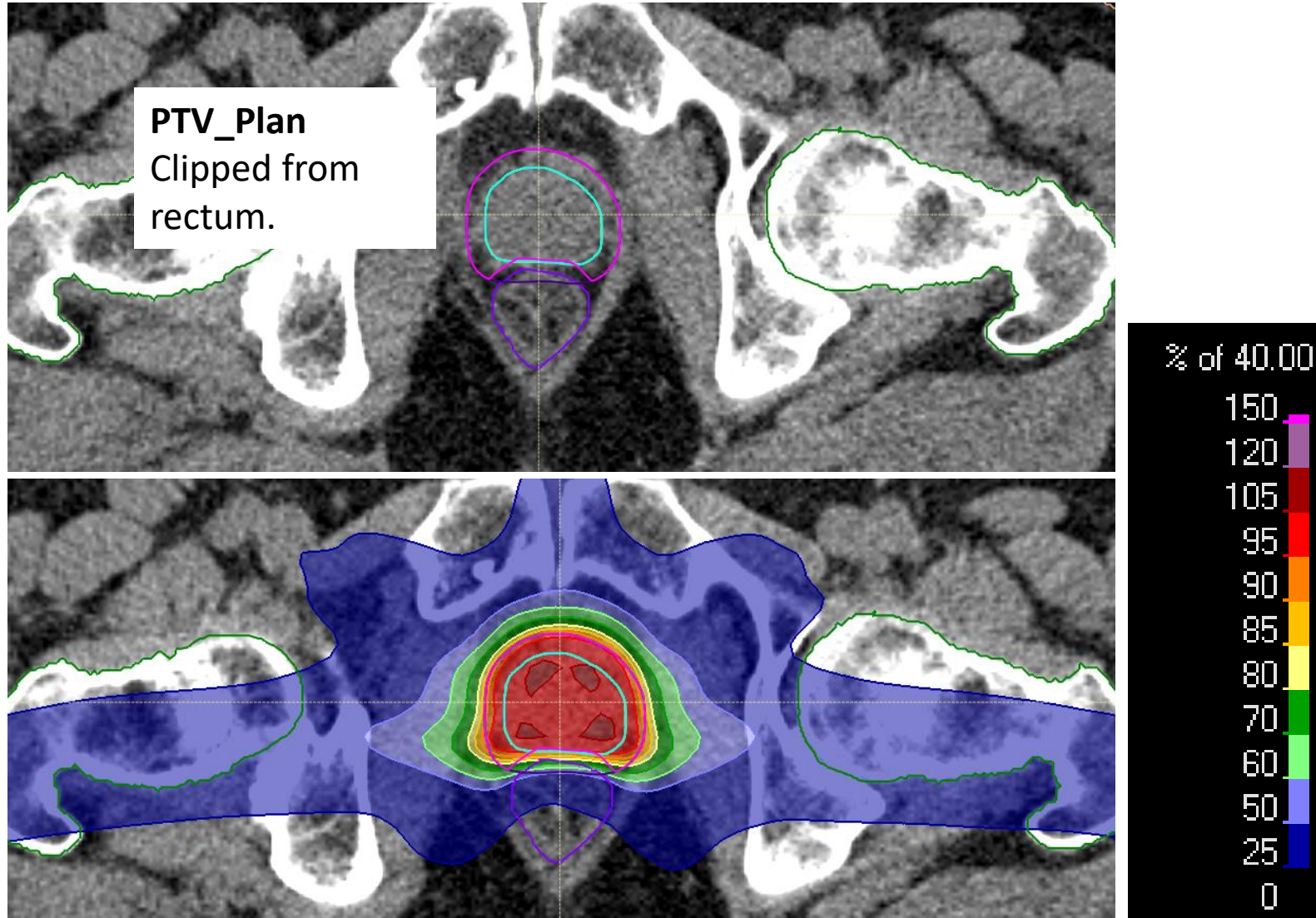
50

25

0

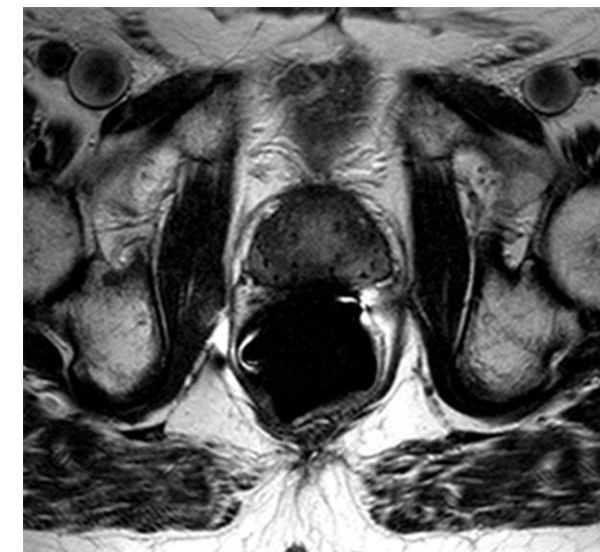
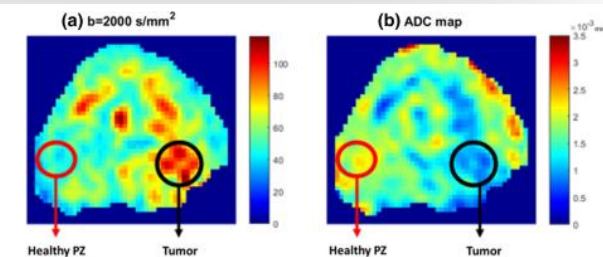
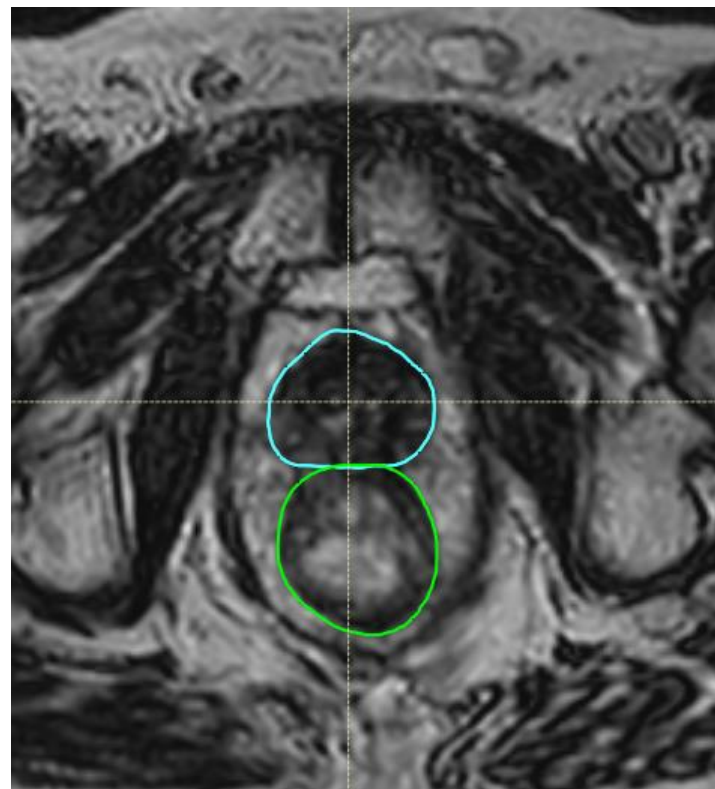


# Rectum Sparing whole gland SBRT



# Translational Imaging

- *Scanner(s)*
  - Diagnostic MRI and MRL
- *Sequences*
  - Standard: T1, T2, DWI/ ADC, DCE
  - Hypoxia: BOLD, IVIM
- *Time points*
  - Baseline
  - 1 month post-RT
  - 1 year post-RT



# Translational Imaging Objectives

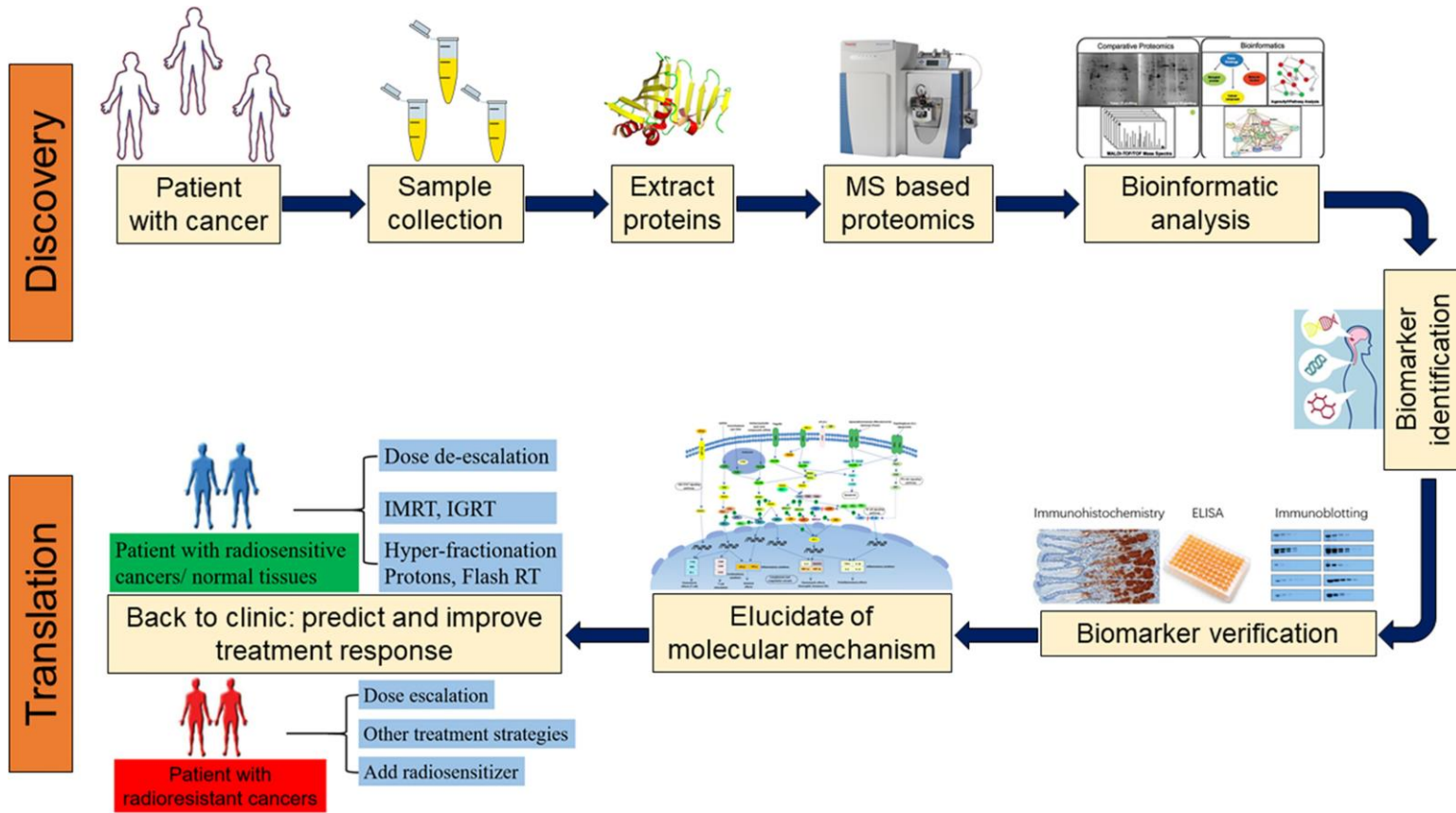
1. To identify MRI biomarkers that may be predictive of hypoxia
2. To evaluate image quality and reproducibility of prostate functional imaging for detecting hypoxia
3. To identify MRI biomarkers that may be predictive of GU and GI toxicity

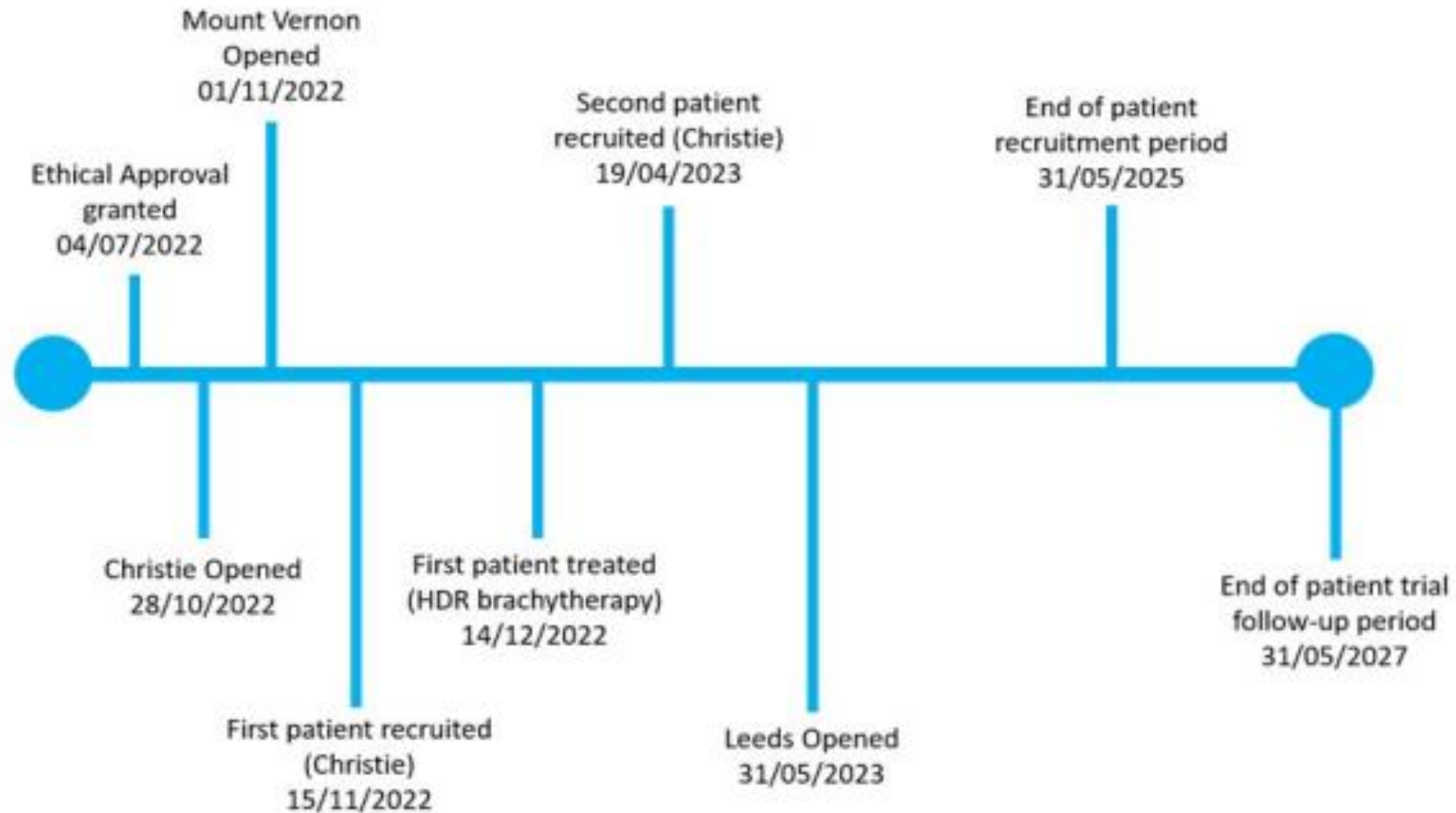




# (OPTIONAL) Translational Study Objectives

1. **Prostate tissue** – measure effect of radiotherapy on hypoxia gene signatures.
2. **Urine** - measure the inflammatory response via damage-associated molecular patterns.
3. **Blood** - measures changes in cytokine response and other proteomics analyses.





Recruitment to date: 10/60

4 Leeds

2 Christie

4 Mount Vernon

***Initial Patient feedback:***

- *SABR preferred as non-invasive*
- *one refused HDR BT when randomised*

***Centre feedback:***

- *Fewer eligible patients if follow up in primary care*
- *Travelling a challenge if out of area*



# Conclusions

- 10/60 patients recruited to date
- 1 further year of recruitment
- 2 year minimum follow-up all patients
- Challenges in randomisation between HDR-BT and EBRT around patient preference, comorbidities and local follow-up policies



Thank you for your attention!

Please direct enquiries to  
[jim.zhong@nhs.net](mailto:jim.zhong@nhs.net)

CRUK Leeds Clinical Trials Unit Fellow