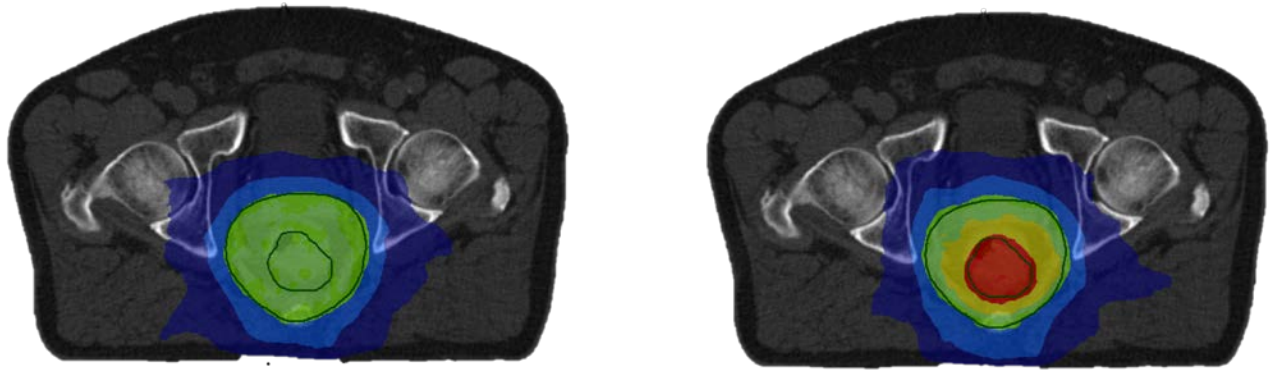
Proposed study:

APHRODITE - A Phase II trial of Higher RadiOtherapy Dose In The Eradication of early rectal cancer

Dr Ane L Appelt (Radiotherapy Lead), Dr Simon Gollins (Clinical Lead), Professor Maria Hawkins, Professor Walter M. Gregory, Ms Lucy McParland, Ms Alexandra Smith, Dr Alexandra Gilbert, Mr Simon Bach, Dr Nick West, Dr Carole Burnett, Ms Monica Jefford, Ms Gill Evans. **Professor David Sebag-Montefiore (Senior Trial Mentor)**



Pitch Your Study

- *Aim:*
  Can dose escalation increase the cCR rate with acceptable toxicity in patients with early rectal cancer who are not suitable for radical surgery?

- *Design:*
  Phase II multicentre randomised trial

- *Patients:*
  Patients with early rectal cancer not suitable for radical surgery and for whom radiotherapy treatment is indicated
  - *T1-T3b (up to 5mm extra-mural spread), M0*
  - *N0 or N1 disease on MRI (positive lymph nodes confined to mesorectum)*
  - *Max tumour diameter 4cm*
  - *ECOG PS 0-2*
  - *Patient not thought to be suitable for radical TME resection of their tumour by treating team*

Pitch Your Study

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APHRODITE study design

Patients with early rectal cancer not suitable for radical surgery and for whom radiotherapy treatment is indicated

Biopsy proven adenocarcinoma rectum
T1-T3b (up to 5mm extra-mural spread)
No evidence of metastatic disease
N0 or N1 disease on MRI (positive lymph nodes confined to mesorectum)
Max tumour diameter 4cm
ECOG PS 0-2

Randomised 1:2

CRT 50.4Gy

CRT 62Gy

Primary end point:
Clinical complete response at 6 months

Then management according to treating team's discretion

Radiotherapy – mesorectal IMRT

- Control
  CTV 50.4y GTV 50.4 in 28F
- Experimental
  CTV 50.4Gy GTV 62.0Gy in 28 F

Concurrent chemotherapy

- Capecitabine or 5FU

Research question

- Does dose escalation increase CCR with acceptable toxicity

Primary end point

- Complete clinical response @6/12

Key secondary end points

- Acute toxicity
- PROMS (EORTC QLQ-C30 and CR29, EQ-5D and LARS) baseline, 3, 6, 9 and 12/12
- Organ preservation rate

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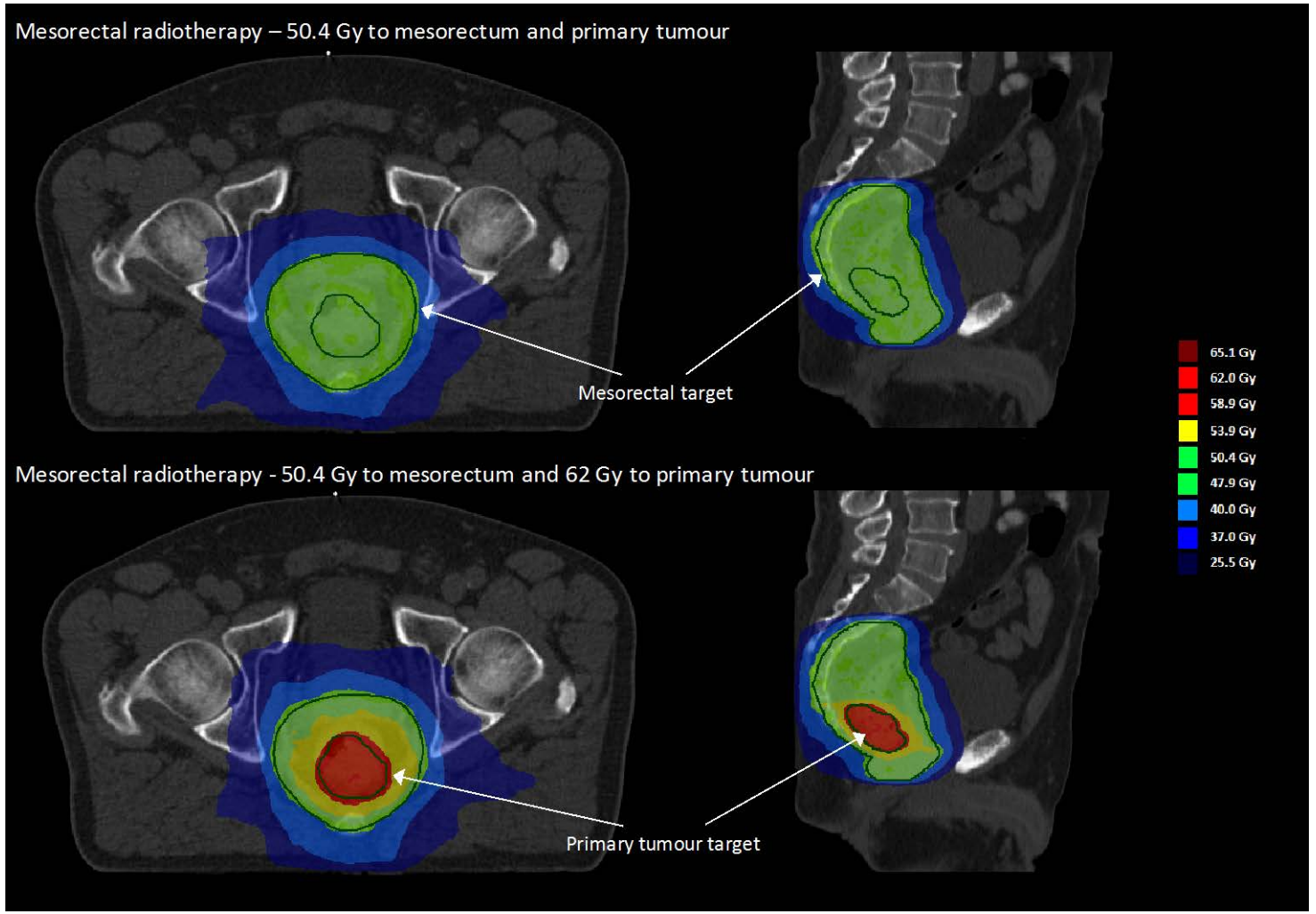

Daily CBCT image guidance

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What will this study will teach us?

- *Effect of dose escalation on clinical complete response*
- *Use of chemoradiotherapy as alternative to surgery in elderly and frail patients with early cancer*
- *Contribute to radiosensitivity translational research*
- *Data for later studies in non-frail patients*

- *Number pts needed:*
  104 patients
  - Assume 20% absolute difference in cCR at 6 months post-treatment
  - cCR rate of 35% in the standard CRT, 55% cCR in dose escalation arm.
  - 80% power, 1-sided type 1 error rate of 20
  - 5% loss to follow-up
  - 1:2 allocation ratio
  - The design is robust to variation in the standard arm cCR rate; i.e. a 20% difference from a standard cCR rate of 25% will still be detectable with the proposed sample size.

- *Small UK study (~8 centres, recruitement over 2 years)*

- *Contact information*
  Ane Appelt (a.l.appelt@leeds.ac.uk)
  Simon Gollins (simon.gollins@wales.nhs.uk)

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