Margin Reduction in Prostate Radiotherapy

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Presentation outline

• How prostate radiotherapy works.
• What are the problems?
• Current studies to reduce margins.
External Beam Prostate Radiotherapy

x 1

x 39!!!
Aims of Prostate Radiotherapy

CTV
= Prostate
+/- Seminal Vesicles

An adequate dose

An adequate dose for movement

No dose
(if possible)

PTV

OAR

No dose
What we would like to aim for.

- CTV = Prostate +/- Seminal Vesicles
- An adequate dose
- An adequate dose for movement
- No dose (if possible)
- OAR: No dose
- PTV

No dose
What we aim to treat/avoid
But what does the prostate really do?
But what does the prostate really do?
But what does the prostate really do?
Why does it do this?
The prostate moves with the rectum!
(and bladder)
Small Rectum
Larger rectum (with gas)
Large rectum
Lucky we have our margins!
Plus we have an ACE up our sleeves!
Hitting the target!

- Image taken every day before treatment!
Does the prostate stay that way?

Unfortunately, no.
A lot can happen in 7 minutes!

From this…

Pre-Treatment

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…to this!

Post-Treatment

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All well-known problems.

- Gas and faeces in the rectum responsible for deformation of shape of the target volume (Langen & Jones, 2001; Ghilezan et al, 2005).

- Prostate motion is correlated with rectal filling of either gas or faeces (Ghilezan et al, 2005; Mah et al, 2002; Padhani et al, 1999).

- Changes in rectal filling are the major cause of prostate motion (Padhani et al, 1999; Ghilezan et al, 2005).
Aims and Objectives of Research Program

• Aim
  – To reduce the CTV to PTV expansion margin for prostate radiotherapy.

• Objectives:
  – To investigate the impact of a diet intervention on rectal volume variation and prostate motion.
  – To investigate a method of applying an adaptive margin based on Image Guided Radiotherapy (IGRT).
  – To investigate the feasibility of implementing an adaptive margin based on IGRT.
# Structure of Research Program

<table>
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<th>Study Theme</th>
<th>Study Focus</th>
<th>Study</th>
<th>Degree</th>
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<tr>
<td>Diet</td>
<td>Diet diary recording</td>
<td>Study 1</td>
<td>MPhil</td>
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<td>Diet intervention early phase</td>
<td>Study 2</td>
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<td>Study 4</td>
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Study 1

A feasibility study and baseline data collection for patients receiving radical radiotherapy to the prostate.

Richard Oates, Michael LimJoon, Narelle McPhee, Michal Schneider & Tomas Kron.
Objectives

• **Primary Objective**
  – To assess the compliance of patients with prostate cancer to record their dietary intake in a diary over an 8 week course of radiation therapy.

• **Secondary Objective**
  – To collect baseline data of fibre and fluids in an ‘ordinary’ diet for 10 patients.
Results

• Demonstrated feasibility of recording diet diary with a median (range) number of days recorded during treatment of 100 % (90.4-100%).

• Baseline recording of fibre and water in patient’s diet, mean (±SD) 21.5g (±5.5g) and 2227.1g (±733.1g) respectively.

Study 2

Dietary intervention to maintain a consistent rectal volume for patients receiving radical radiotherapy to the prostate: A Randomised Study

Richard Oates, Michael LimJoon, Narelle McPhee, Daryl Jones, Michal Schneider & Tomas Kron.
Diet Intervention
Objectives

• **Primary Objective**
  – To estimate the reduction in rectal volume variation of a dietary intervention compared to standard treatment for patients receiving radical radiation therapy to the prostate.

• **Secondary Objectives**
  – To estimate the magnitude of the change; interfraction & intrafraction prostate motion; rectal volume and rectal filling
  – To pilot, validate and establish the best methods of using CBCT to measure organ motion inter- and intrafraction and rectal filling for patients in both arms of the study.
  – To investigate the quality of life (QoL) during the intervention.
  – To assess the safety of the intervention.
Hypothesis

- A diet intervention of an anti-flatulent diet supplemented with psyllium husk will reduce rectal volume variation compared to standard treatment.
Schema

Radical EBRT for Prostate Cancer (n=30)

Inclusion Criteria

Consent

Randomisation

Exclusions

Not Consent

Standard Therapy (n=15)

Diet Intervention (n=15)

Primary Endpoint: Rectal volume variability

Secondary Endpoints:
- Image Quality
- Rectal centroid
- Rectal diameter
- Rectal filling
- Rectal Dose
- Interfraction motion
- Intrafraction motion
- Target volume rotation
- Adverse events
- QoL
- Compliance
Results – Rectal Volume Variation

Not significant (p = 0.1334).

Rand A = Standard Therapy
mean 15.8cc (95% CI: 10.9 - 20.7)
Rand B = Diet Intervention
mean 11.8cc (95% CI: 9.1 - 14.5).

Figure 1. Boxplot of patient rectal volume standard deviations per randomisation. Bar represents the median, box represents the inter-quartile range, whiskers represent the range.
Results – Rectal Filling

• A significant relationship was found with the rectal filling at the centre level of the prostate and treatment arm. The diet intervention arm were more likely to have an empty rectum, absent of gas and faeces. No relationship was demonstrated between diet intervention and moving gas.

Study 3

Adaptive radiotherapy margins for prostate cancer: a modelling study.

Background

- Most treatment fractions result in a small, intrafraction motion of the prostate.

Background

- Prostate motion is correlated to rectal filling and time.

Source: Ghilezan et al, 2005.
Objectives

• To investigate a method for predicting prostate motion by measuring the diameter of the rectum on cone beam CT (CBCT).

• Compare dose to the organs at risk (rectum and bladder) using an adaptive PTV margin protocol and standard technique.

• To estimate the absolute dose escalation possible with adaptive margin image-guided radiotherapy (IGRT) in prostate cancer radiotherapy.
Figure 2. Scatterplot of maximum rectal diameter versus intrafraction displacement for 194 fractions in ten patients
Results

- 53% (104/196) of fractions had a true maximum rectal diameter of 3.5cm or less and the prostate moved 4mm or less in 98% (102/104) of the fractions.

- Estimated that the volume of rectum receiving 25Gy, 50Gy, 60Gy and 70Gy would reduce by around 4, 4, 8 and 16% respectively if the margin can be reduced to a 6mm uniform margin from standard margins.

- The volume of bladder receiving those dose points would reduce by approximately 40%.

- Estimate an average dose escalation of 4.2 Gy would be possible for this patient group.
Study 4


Richard Oates, Amy Brown, Alex Tan, Suki Gill, Farshad Foroudi, Michael LimJoon, Mathias Bressel, Michal Schneider & Tomas Kron.
Objectives

• **Primary Objectives**
  – To find the ideal maximum rectal diameter to utilise in a prospective study of adaptive prostate radiotherapy.

• **Secondary Objectives**
  – Identify predictors of prostate motion during a treatment fraction.
  – Compare the average normal tissue complication probability (NTCP) for rectum per patient for standard vs adaptive margin.
  – Assess treatment fraction duration of prostate cancer radiotherapy on XVI treatment machines with pre-treatment CBCT.
  – Assess the image quality of CBCTs acquired during the study.
Hypothesis

• Patients who present with an empty rectum (e.g. maximum rectal diameter ≤3.5cm) will be likely to have a smaller intrafraction prostate motion compared to patients who present with a full rectum.
Patients who have received radical prostate radiotherapy. N=55

Inclusion Criteria

Exclusion Criteria

Primary Endpoints
Maximum rectal diameter to correctly predict 90 percent of prostate displacements of 4mm or less.

Secondary Endpoints
Predictors of prostate motion.
NTCP dose for standard versus adaptive margin.
Treatment fraction in minutes.
CBCT image quality.
Progress

• Rectum contoured, gas volume and diameter measurements completed on 2126 pre-treatment CBCTs

• Intrafraction motion data collated for all fractions.

• Currently under analysis.

• Presentation at CSM 2014 – Melbourne.
Significance

• Diet and adaptive protocols should complement each other.

• Reduction of prostate margins will allow dose escalation

• 1.8% reduction in the risk of biochemical failure for every 1Gy increase in treatment dose (Viani et al, 2009).

• Reduction in side effects and improved quality of life.

• Large population who benefit.

• Use technologies and techniques widely available.
Thank You!

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