Improvements in Cervix Brachytherapy Planning and Outcomes Between 2013 and 2022 at Coventry

Claire Fletcher, Dr Mark Hocking

Claire.fletcher@uhcw.nhs.uk

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• Summary of changes to brachy service at UHCW
• Analysis of changes to planned doses delivered to patients - 2013 and 2022
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Cervix Treatment Developments

**Brachytherapy**
- 2013: 3D planning using CT for OARs only, standard plans
- 2014: MRI/CT fusion, standard plans
- 2016: Conformal and Interstitial planning
- 2020: MR only planning where no needles

**External Beam**
- 2013: 45Gy/25# or 50.4Gy/28# 3D conformal planning
- 2018: 45Gy/25# VMAT planning
- 2018: +/- SIB of 55Gy or 57.5Gy to nodes
Cervix 3D Planning Aims

Planning aims based on RCR guidance 2009 / Embrace

2013

Adopted Embrace II trial aims and limits

2016
Patients Reviewed - Brachytherapy

• 191 patients treated between 2013-2022
• 2013 to 2015
  – 48 Patients planned using standard plans
• 2016 to 2022
  – 143 Patients planned conformally
  – 65 of these used interstitial needles
• All patients planned using:
  – Oncentra Masterplan Brachytherapy planning system
  – CT and/or MRI imaging to outline OARs
• All patients from 2015 planned using MRI to outline HRCTV
Target Coverage

- Increased achievement of HRCTV D90 dose limits and aims over time
  - Lower HRCTV coverage in 2016
    - First year of conformal planning
  - HRCTV dose limits are consistently met in > 65% of plans since 2017

- Larger tumours less likely to meet target aims but still showing improvement over time
HRCTV Dose Improvements

• Average HRCTV D90 has improved over time
  – For all patients Mean D90 is 89.3Gy ±12Gy
  – For standard plans Mean D90 is 83.5Gy ±15Gy
  – For conformal plans Mean D90 is 89.5Gy ±12Gy

• Similar to dose improvements seen in the literature during the switch to MRI image guided planning
  – Vienna [3] mean D90 of 81Gy ±16Gy was achieved during a learning period 1998-2000)and 90Gy ±15Gy was achieved during 2001-2003
  – Ribeiro [4] mean D90 of 84.8Gy ±8.36Gy
OAR Dose Improvements

- Increased achievement of D2cc dose limits to all OARs
  - D2cc <75Gy for the Rectum achieved by 100% of plans since 2016 and has always been >94%
  - Biggest improvement seen in 2016 once conformal planning started
    - Sigmoid improved from 40-60% of plans achieving D2cc<75Gy to >90%
    - Bladder improved from 80-90% of plans achieving D2cc<80Gy to >90%
OAR Dose: HRCTV Size

- Biggest difference for optimal dose aims, much more likely to be achieved for smaller HRCTVs
Comparison Between Standard and Conformal Plans

<table>
<thead>
<tr>
<th>% of Plans Meeting Target Aims and Limits</th>
<th>% of Plans Meeting OAR Aims and Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;85Gy to HRCTV D90</td>
<td>&lt;75Gy to rectum D2cc</td>
</tr>
<tr>
<td>&gt;90Gy to HRCTV D90</td>
<td>&lt;65Gy to rectum D2cc</td>
</tr>
<tr>
<td>&gt;65Gy to pt A</td>
<td>&lt;75Gy to sigmoid D2cc</td>
</tr>
<tr>
<td></td>
<td>&lt;70Gy to sigmoid D2cc</td>
</tr>
<tr>
<td></td>
<td>&lt;90Gy to bladder D2cc</td>
</tr>
<tr>
<td></td>
<td>&lt;80Gy to bladder D2cc</td>
</tr>
</tbody>
</table>

- Blue bars: conformal and interstitial
- Red bars: standard
Patient Follow-up

• Clinical notes reviewed for 113 patients treated between 2013-2019
• Majority of patients stage II, Squamous cell carcinoma for both standard and conformal plans
  – More later stage tumours in conformal planning cohort
Disease Free Survival

- Survival rates slightly higher for conformal planning
  - Censored for patients lost to follow-up
  - Curves not statistically significantly different (p=0.819)

- 3 year disease free survival
  - 80% for conformal plans (95% CI 67-88%)
  - 78% for standard plans (95% CI 62-87%)

- 5 year disease free survival
  - 78% for conformal plans (95% CI 65-86%)
  - 75% for standard plans (95% CI 59-85%)
  - cf 68% reported by EmbraceI [1]
  - cf crude disease free survival rate 55.3% reported by Ribiero [4]
Tumour Stage

- No statistically significant difference between conformal and standard plans for either set of stages
HRCTV Dose

- <85Gy shows statistically significantly lower survival ($p=0.02$)
FIGO Stage

- Survival benefits due to dose more pronounced for stage III and IV, $p=0.02$
Toxicity

• Higher grade 3/4 toxicity reported for standard plans
  - Grading according to CTCAE v 5

• Average OAR doses higher for standard plans
Actuarial Cumulative Incidence of Grade 3/4 Toxicity

- Overall toxicity (bladder, bowel, vaginal, rectal)
  - Standard planning had higher rates of toxicity
  - Difference not statistically significant (at 0.05 level)

- 5 year cumulative incidence of Grade 3/4 toxicity:
  - 10% (95% CI 5-21%) for conformal planning
  - 20% (95% CI 11-35%) for standard planning

- Values from the literature
  - Embrace I [1]: 5 year act.l cumulative incidence, Gr3-4 overall events 18.4%
Actuarial 5 year Grade 3/4 Toxicity

• 5 year Bladder toxicity
  – 3% for standard plans (95% CI 0-17%)
  – 3% for conformal plans (95% CI 1-13%)

• 5 year Bowel toxicity
  – 4% for standard plans (95% CI 1-16%)
  – 0% for conformal plans

• Values from the literature
  – Embrace [1]: 5 yr act. cumulative incidence, Gr3-4 6.8% genitourinary, 8.5% gastrointestinal
  – Pötter 2011 [2]: 5 year actuarial rate Gr3-4 3% bladder events, 0% bowel events
  – Ribeiro 2016 [4]: Gr3-4 6% bladder morbidity, 2% sigmoid morbidity
Actuarial 5 year Grade 3/4 Toxicity

• 5 year Vaginal toxicity
  – 9% for standard plans (95% CI 4-23%)
  – 9% for conformal plans (95% CI 4-19%)

• 5 year Rectal toxicity
  – 9% for standard plans (95% CI 3-21%)
  – 2% for conformal plans (95% CI 0-12%)

• Values from the literature
  – EmbraceI [1]: 5 year act.i cumulative incidence, Gr3-4 events 5.7% Vaginal
  – Pötter 2011 [2]: 5 year act.i rate Gr3-4 3% vaginal events, 4% rectal events
  – Ribeiro 2016 [4]: Gr3-4 5% vaginal morbidity, 5% rectal morbidity
Vaginal Toxicity – Correlation to Dose

- Statistically significant correlation between dose to ICRU rectovaginal point and grade 3/4 vaginal toxicity (p<0.05)
- Values in the literature:
  - [5] doses of >65Gy are associated with a higher risk of >=G2 vaginal stenosis
Toxicity – Compared to Dose Limits Achieved

• All grades of Toxicity

• Higher incidence of toxicity reported where OAR dose limits were not met
  – Note: only small numbers didn’t reach dose limits – eg 1 out of 2 patients who didn’t achieve D2cc 65Gy to rectum had rectal toxicity

• Where OAR dose aims were met, less toxicity reported for all OARs studied
Conclusions

• Significant improvement since 2013, through new tech and planning
• Increasing % of plans achieving target / optimal doses to the HRCTV
• Conformal planning has enabled the OAR doses to meet hard limits
• Annual reviews audit the treatment and create improvement strategies
• 5yr disease free survival rate similar for standard and conformal plans
• Bigger increases to HRCTV dose since 2021 so not included in follow up
  – Repeat follow up analysis for this cohort
• Toxicity better for conformal plans
• Use of needles may further improve OAR toxicity, especially for small tumours
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References


