PROSTATE BRACHYTHERAPY
UK & Ireland Conference 2019

Friday 22nd March 2019

Royal Armouries Museum, Leeds, West Yorkshire, LS10 1LT

Abstracts

Abstract number 1

LDR versus HDR brachytherapy boost in prostate cancer patients - a retrospective analysis

Rodda S, Slevin F, Murray L, Bottomley D, Bownes P, Henry A
Leeds Cancer Centre, Leeds Teaching Hospitals NHS Trust

Aims & Introduction: To report biochemical Progression Free Survival (bPFS) and toxicity in men with non-metastatic prostate cancer treated with LDR or HDR brachytherapy boost (BT) combined with external beam radiotherapy (EBRT).

Materials/Methods: 287 men consecutively treated with combination of BT boost and EBRT from 1996-2012 from a single centre were evaluated retrospectively. Data was extracted from electronic records. 116 had LDR (I-125) BT to a dose of 110Gy in combination with EBRT 45Gy in 20 Fractions (LDR-EB) treated from 1996-2007. 171 had HDR BT (17Gy in 2 fractions or 15Gy in 1 fraction) in combination with EBRT 35.75Gy in 13 or 37.5Gy in 15 fractions respectively (HDR-EB) treated from 2007-2012. Duration of androgen deprivation was at clinician discretion. bPFS was defined by PSA nadir +2 and toxicity scored using RTOG.

Results: Median follow-up was 74.1 and 57.0 months for LDR-EB and HDR-EB groups respectively. The LDR-EB group were slightly younger than HDR-EB group (63 versus 65 years: p=0.02) and had greater proportion of high risk disease (p=0.02). At 5 years there was a significant improvement in bPFS in LDR-EB compared to HDR-EB groups (90.5% vs. 77.6%, p=0.003). On multivariate analysis, Gleason grade ≥8 versus 6 (HR: 5.47) and treatment group LDR-EB versus HDR-EB (HR: 2.33) both predicted bPFS. 5-year cumulative incidence of G3 and above GU and GI toxicity was higher in LDR – EB (8% and 5%) compared to HDR-EB groups (4% and 1%) but was not statistically significant.

Conclusion: Risk of biochemical failure was more than double in men treated with HDR-EB compared to LDR-EB .There was higher grade 3+ GU and GI toxicity in the LDR-EB group although this did not reach statistical significance. LDR-EB may provide more effective PSA control at 5 years. Given its retrospective design and lack of randomisation, these results should be regarded as hypothesis-generating.

Abstract number 2

Pre-operative membranous urethral length predicts early return of continence in patients undergoing salvage robotic assisted radical prostatectomy

Yazdouni S*, Faure Walker N**, Mehan N**, Popert R**, Sahai A* **, Cathcart P**

* King's College London Medical School, London
** Guy's and St Thomas' NHS Foundation Trust, London

Introduction: Post-prostatectomy incontinence (PPI) rates are significantly greater in men undergoing salvage robot assisted radical prostatectomy (RARP) than for primary RARP. Longer membranous urethral length (MUL) is associated with a quicker return to continence. This study aims to evaluate the recovery of urinary continence after salvage RARP (sRARP) and the effect of pre-operative MUL.

Methods: Men who underwent sRARP following external beam radiotherapy (EBRT) or brachytherapy were retrospectively reviewed. Baseline patient and clinical characteristics were evaluated. MUL was defined as the distance between the proximal bulb of the penis and the apex of the prostate. Continence was defined as the use of no pad or safety pad. SPSS was used for statistical analysis.

Results: 37 men underwent post-radiotherapy salvage RARP by 2 surgeons between 2007 and 2018: 12 (32%) had received prior brachytherapy and 25 (67%) received EBRT. Mean age was 66 years (49-66 years). Mean pre-salvage treatment PSA was 15.41 ug/L (2.7–72.0 ug/L). Mean time from initial radiation to sRARP was 7.25 years (1.4-14.8 years). Mean MUL was 12.9 mm (5.5–26 mm). Of these, 26/37 (70.3%), 17/33 (51.5%) and 20/27 (74.1%) were continent at 3, 6 and 12 months. Using receiver operator characteristic (ROC) analysis a pre-operative MUL of >13.75 mm was significantly associated with early recovery of urinary continence at 6 months (p=0.037, log rank Mantel-Cox test).

Conclusion: Pre-operative MUL > 13.75 mm predicts early acquisition of urinary continence in patients who undergo sRARP and serves as an important tool in pre-operative counselling of patients undergoing sRARP.

Abstract number 3

Outcomes from intermediate risk, Gleason 7, localised prostate cancer treated with low-dose rate brachytherapy

Maher R, Gatfield E, Lees K, Beesley S

Kent Oncology Centre, Maidstone Hospital, Kent

Introduction: Low-dose rate (LDR) brachytherapy is a treatment option for men with low and intermediate risk, localised prostate cancer. This audit assessed the outcomes for patients with intermediate risk disease comparing initial Gleason pattern 3+4=7 and 4+3=7 disease, treated with iodine-125 brachytherapy, at a single UK centre.

Methods: Retrospective analysis of 294 patients who received LDR brachytherapy at Maidstone Hospital, between 2008 and 2016 inclusive. 262 patients had initial Gleason pattern 3+4=7 and 32 patients had 4+3=7 disease. Primary end-points included overall survival (OS), progression-free survival (PFS) and biochemical PFS.

Results: Median follow up was 47.6 months (4.9-117.1 months). Mean presenting PSA was 7.6ng/ml (2.4-19.8ng/ml). 5 year OS was 94.7% (95% CI 92.1-97.3%). No patients died due to their prostate cancer. 17 patients developed radiologically or biopsy confirmed local (12) or metastatic (5) recurrence, with a crude failure rate of 5.78% (17/294). 5 year PFS was 93.6% overall (95% CI 90.8-96.4), Gleason pattern 3+4=7 disease 94.0% (95% CI 91.1-96.9) and 4+3=7 disease 90.0% (95% CI 79.6-100.4). Fisher's exact test (Gleason 7) = 1, $p>0.05$. There were an additional eight patients with biochemical failure. 5 year biochemical PFS was 90.6% overall (95% CI 87.3-93.9), Gleason pattern 3+4=7 disease 91.4% (95% CI 88.0-94.8) and 4+3=7 disease 83.9% (95% CI 71.2-96.6). Fisher's exact test (Gleason 7) = 0.7453, $p>0.05$.

Conclusion: LDR brachytherapy is an extremely good treatment option for patients with localised, intermediate risk prostate cancer. The small relative numbers of Gleason 4+3=7 disease in this study is acknowledged, however these results have shown that, despite a suggestion of a trend to a worse 5 year biochemical PFS, there is no statistical difference in overall survival between the two groups. We feel that LDR brachytherapy can be considered an appropriate treatment option for both low and high intermediate risk disease, in selected cases.

Abstract number 4

Salvage High Dose Brachytherapy at the Bristol Cancer Institute - Experience and Challenges

Masson S, Closier P, Humphrey P, Bamisaye F, Brown A, Bahl A

Bristol Haematology and Oncology Centre, Bristol

Introduction: High dose rate salvage brachytherapy (HDRSB) is a minimally invasive treatment for locally recurrent prostate cancer following external beam radiotherapy (EBRT), particularly where prostatectomy is not appropriate in light of surgical morbidity (major complications in up to 35%[1]). Alternative management is ultimately palliative; however identifying those patients most likely to benefit from salvage procedures remains challenging. We describe our experience and highlight these issues from the first 5 HDRSB patients treated in Bristol.

Methods: All patients had biopsy proven recurrent prostatic adenocarcinoma following Prostate Specific Antigen (PSA) relapse after prior EBRT. All underwent staging using various modalities (Computed tomography, Technetium bone scan, Choline Positron Emission Tomography, whole body Magnetic Resonance Imaging).

Brachytherapy catheters were placed under spinal anaesthesia using a transperineal template approach and transrectal ultrasound guidance, taking care to avoid the rectal interface. 19Gy was delivered to the whole prostate with no focal boost. Following treatment, PSA and toxicity data were recorded using standardised questionnaires.

Results: There were no immediate complications from HDRSB. 1/5 (20%) required re-catheterisation on day 2. 5/5 (100%) experienced increased urinary frequency and urgency, 2/5 (40%) had residual grade 1 urinary toxicity at 1 year, and 2/5 (40%) reported late GI toxicity (at 2 years and 1 year respectively). 2/5 (40%) reported sexual dysfunction following HDR brachytherapy.

Reduction in PSA was observed in 4/5 patients (80%); during follow up 2/5 (40%) have developed metastatic disease, 1/5 (20%) is awaiting restaging for PSA relapse, 1/5 (20%) is receiving ADT for PSA relapse, and 1/5 (20%) has a stable low PSA.

Conclusion: HDRSB is technically feasible, with acceptable toxicity. A substantial proportion of patients have subsequently relapsed, which in part relates to difficulties with accurate staging in this group. Further work will include standardisation of staging, the use of rectal spacers and focal tumour HDRSB.

Reference

1. Tisseverasinghe S, Crook J. The role of salvage brachytherapy for local relapse after external beam radiotherapy for prostate cancer. Transl Androl Urol. 2018 Jun; 7(3): 414–435.

Abstract number 5

The Design and Development of Patient-based Anthropomorphic Prostate Training Devices for Novice Oncologists for Trans rectal Ultrasound (TRUS) Guided Prostate Imaging

Doyle AJ*, King DM**, Sullivan FJ†‡, Cody D*, Browne JE*§

* School of Physics & Optometric Sciences , Medical Ultrasound Physics and Technology Group, Centre for Industrial and Engineering Optics, FOCAS, Technological University Dublin, Ireland
** Blackrock Clinic, Dublin, Ireland
† Hermitage Medical Clinic, Dublin, Ireland
‡ Prostate Cancer Institute, National University of Ireland, Galway, Ireland
§ Department of Radiology, Mayo Clinic, Rochester, MN, USA

Introduction: Although ultrasound forms a critical component of prostate cancer treatment, ultrasound training is not required as part of oncology training programs, nor does any objective competency measure exist to independently assess clinical performance. The purpose of this study was to develop a range of training devices which simulate both the anthropomorphic and sonographic characteristics of the different presentations of prostate cancer.

Methods: The development of the training devices was an iterative process that included feedback from clinical experts to ensure that the devices were clinically relevant. The design of the clinical features involved selection of patient cases and then rapid-prototyping the different anatomical features. Novel tissue mimicking materials were developed that had the sonographic appearance of the prostate and overlying tissues, as well as having the relevant mechanical compliance to give the training devices required haptic feedback. Prototype devices were designed and evaluated by clinical experts to ensure the devices were fit-for-purpose.

Results: Training devices based on patient cases, the cases were selected as each provided an opportunity for specific technical and clinical competencies to be evaluated and refined through the workshop; as they varied in terms of difficulty and complexity. Each patient case had known patient outcomes based on the optimum treatment and so provided the gold standard against which each trainee could be evaluated. An objective performance metric was developed based on clinical competency and a leader-board of performance was established on a collaborative learning website to provide an aspect of gamification to the training.

Conclusion: Patient-based anthropomorphic prostate training devices were developed and the 3D prototyped clinical features in these devices provided a more clinically relevant representation of the procedure, providing a more efficacious training opportunity for novice oncologists.

The incorporation of these training devices with accompanying training programme will provide an opportunity for the novice to develop technical and clinical competencies.

Abstract number 6

Robotic Prostate Biopsy and LDR/HDR Brachytherapy under MRI Guidance: Update from the EU-funded CoBra Project

Wilby S*, Polak W*, Hodgson D*, Nagar YS*, Palmer AL*, Labib A**, Jones D**, Firouzy S**, Merzouki R†

* Portsmouth Hospitals NHS Trust
** University of Portsmouth
† University of Lille, France

Introduction: We present a progress report on the five year CoBra (Cooperative Brachytherapy) project. CoBra aims to develop an innovative technology for robotic biopsy and brachytherapy under MRI guidance. The main deliverable will be a robotic arm for both biopsy and brachytherapy treatment (LDR and HDR), utilising a small number of perineal puncture needles, with high precision and accuracy. Funded by the EU Interreg 2 Seas body, this project involves multiple institutions, led by the University of Lille.

Methods: The project was divided into work packages assigned to collaborating institutions selected for each task. The packages have a set of milestones and progress is reviewed bi-weekly via web conference and every three months at a steering meeting.

Results: A detailed specification document was submitted by Portsmouth Hospital. The University of Portsmouth (UoP) have mapped prostate cancer incidence per year within the UK's 2 seas region as a function of distance to nearest treatment centre and are now focussing on trajectory planning for needles. Two steerable needle concepts are being considered by TuDelft. DEMCON, focussing on the biopsy module, have reviewed actuation principles for the needle positioning system in an MR environment and will progress with a pneumatic technique. They have also reviewed prostate cancer detection rates versus biopsy needle characteristics. Centre Oscar Lambert presented a proof of concept for a deep learning approach to generating pseudo CT datasets from MR images. The University of Lille have developed a workflow for the robot under MR guidance, including a patient positioning system and a controller shielded from magnetic field fringes. Additionally 3D simulation software is in development. Portsmouth hospital is collaborating with the UoP on the development of a physical phantom for quality assurance.

Conclusion: This exciting collaboration is progressing well, generating new knowledge of benefit to brachytherapy and biopsy, with broader applications in medical field.

Abstract number 7

Acute urinary toxicity following HDR brachytherapy for prostate cancer: comparing outcomes with CT only treatment planning versus CT and MRI

Farrow E*, Simpson E**, Davies T†, Woolcot T†, Robinson AJ†, Nikapota A†

* Brighton and Sussex Medical School, United Kingdom
** Brighton and Sussex University Hospitals NHS Trust, United Kingdom
† Sussex Cancer Centre, Royal Sussex County Hospital, United Kingdom

Introduction: HDR brachytherapy treatment planning can be real-time using USS or CT/MRI based. With CT only, planning limitations include overestimation of the prostate and difficulty identifying the bladder neck/trigone[1,2]. This can lead to excess dosage to normal tissues, causing adverse effects, such as acute urinary toxicity (AUT)[3]. MRI is better at visualising soft tissue structures, due to this, incorporation of MRI into prostate brachytherapy may improve dose distribution, thus reducing likelihood of AUT[4]. This study will compare AUT of patients undergoing high dose (HDR) brachytherapy using CT only for contouring and those planned using CT with MRI image fusion.

Methods: Retrospective study of patients treated with HDR brachytherapy at Royal Sussex County Hospital. On a 2-patient brachytherapy list there was capacity to do MRI on 1 patient. International Prostate Symptom Score (IPSS) data was recorded at baseline (pre-treatment) and 3 months post-treatment. AUT was defined as an increase of 10 points in IPSS score at 3 months. Urinary symptom resolution was defined as an IPSS score within 5 points of baseline at 3 months.

Results: 103 patients (median age 70 Â± 22) were recruited. AUT occurred in 14 of 78 (17.95%) undergoing CT and 2 of 25 (8%) undergoing CT and MRI (p=0.232). Urinary symptoms resolution occurred in 13 of 78 patients (16.66%) undergoing CT and 6 of 25 (24%) undergoing CT and MRI (p=0.411).

Conclusion: This study suggests patients planned with both MRI and CT for prostate brachytherapy had reduced acute urinary toxicity. This is probably due to improved target volume definition enabled with MRI fusion, leading to reduced dose to bladder neck/trigone. Further data is needed to validate these findings.

References

1. Henderson DR, Murray JR, Gulliford SL, Tree AC, Harrington KJ, Van As NJ. An Investigation of Dosimetric Correlates of Acute Toxicity in Prostate Stereotactic Body Radiotherapy: Dose to Urinary Trigone is Associated with Acute Urinary Toxicity. Clin Oncol 2018; 30(9):539-547
2. Hathout L, Folkert MR, Kollmeier MA, Yamada Y, Cohen GN, Zelefsky MJ. Dose to the bladder neck is the most important predictor for acute and late toxicity after low-dose-rate prostate brachytherapy: implications for establishing new dose constraints for treatment planning. Int J Radiat Oncol Biol Phys 2014; 90(2):312-9
3. Al-Qaisieh B, Ash D, Bottomley DM, Carey BM. Impact of prostate volume evaluation by different observers on CT-based post-implant dosimetry. Radiother Oncol 2002; 62(3):267-73
4. Tanderup et al. Semin Radiat Oncol 2014; 24:312-9

Abstract number 8

Patient satisfaction and patient reported outcomes (PROMS) following HDR brachytherapy for prostate cancer at the Sussex Cancer Centre

Nikapota AD, Cowtan F, Johns A, Appleyard S, Robinson AJ

Sussex Cancer Centre, Royal Sussex County Hospital, United Kingdom

Introduction: The prostate brachytherapy service at the Sussex Cancer Centre commenced in March 2014. To date 180 patients (pts) have received treatment, mostly as a boost in combination with external beam radiotherapy. Since commencing treatment as part of our quality assurance, service evaluation and to detect and respond to pts symptoms/poor QOL we have been prospectively collecting PROMS on all patients at 6 weeks, and annually from completion of radiation.

Methods: Here we present the data on the first 109 patients treated with a minimum of 24 months follow up. PROMs was assessed using a customised outcome form collecting validated symptom and QOL PROM items.

Results: Patient characteristics: median age 65 (range 51-79), 95% of pts had NCCN high risk disease. With a median follow up 41 months (range 25 – 60 months) biochemical/clinical relapse free survival is 97%. PROMS data is available for 100 pts. Overall satisfaction with treatment received – 93% (93/100) of patients satisfied/extremely satisfied. Ability to enjoy life: 81% good/v good; 18% fair. Ability to perform usual activities: 84% good/very good.

Conclusion: The use of PROMS should be routine in clinical practice to evaluate patient distress and symptomatology, but is still predominantly only collected in the clinical research setting. In our population we have demonstrated that the routine collection of PROMS is feasible with a high response rate to the questionnaire. We have demonstrated a high level of patient satisfaction and functional ability in an unselected group of patients treated with prostate brachytherapy. Early biochemical outcomes are excellent in this high risk population and consistent with published data.