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Current Awareness Bulletin

April 2017

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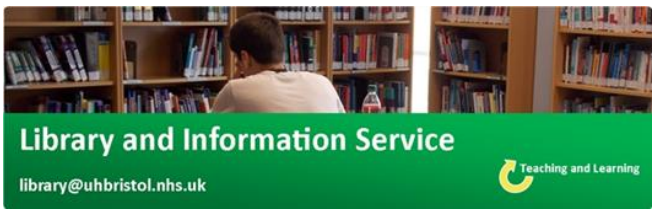

Lunchtime Drop-in Sessions

All sessions last one hour

April	**(12.00)**
Tues 18th	**Interpreting Statistics**
Thurs 27th	**Literature Searching**
May	**(13.00)**
Mon 8th	**Critical Appraisal**
Mon 15th	**Literature Searching**
Fri 26th	**Interpreting Statistics**
Wed 31st	**Critical Appraisal**

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Current Journals: Tables of Contents

Click on journal title (+ Ctrl) for hyperlink

Journal	Month	Volume	Issue
Radiotherapy and Oncology	April 2017	123	1
International Journal of Radiation Oncology Biology and Physics	May 2017	98	1
Clinical Oncology	May 2017	29	5

If you require full articles please email: library@uhbristol.nhs.uk

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Latest Evidence

NICE National Institute for Health and Care Excellence

A systematic review of methodologies, endpoints, and outcome measures in randomized trials of radiation therapy-induced nausea and vomiting

Source: PubMed - 31 March 2017 - Publisher: Supportive Care In Cancer : Official Journal Of The Multinational Association Of Supportive Care In Cancer

Cost of New Technologies in Prostate Cancer Treatment: Systematic Review of Costs and Cost Effectiveness of Robotic-assisted Laparoscopic Prostatectomy, Intensity-modulated Radiotherapy, and Proton Beam Therapy

Source: PubMed - 30 March 2017 - Publisher: European Urology

...assisted radical prostatectomy (RARP), intensity-modulated radiotherapy (IMRT), and proton beam therapy may be offset by better...s perspective compared with three-dimensional conformal radiotherapy, but also more cost effective when defined by an incremental...

The benefit of adjuvant radiotherapy after breast conserving surgery in older patients with low risk breast cancer- a meta-analysis of randomized trials

Source: PubMed - 23 March 2017 - Publisher: Radiation Oncology

Prognositc significance of SUVmax on pretreatment 18 F-FDG PET/CT in early-stage non-small cell lung cancer treated with stereotactic body radiotherapy: A meta-analysis

Source: PubMed - 07 March 2017 - Publisher: Journal Of Medical Imaging And Radiation Oncology

...standardized uptake value (SUVmax) for early stage non-small cell lung cancer (NSCLC) patients receiving stereotactic body radiotherapy (SBRT) is not well defined. The purpose of this meta-analysis is to evaluate the efficacy of SUVmax on pretreatment...

Interventions for the management of radiotherapy-induced xerostomia and hyposalivation: A systematic review and meta-analysis

Source: PubMed - 01 March 2017 - Publisher: Oral Oncology

...common and permanent adverse effect of radiotherapy to the head and neck. Randomised trials...effectiveness of available interventions for radiotherapy-induced xerostomia and hyposalivation...active controls for the treatment of radiotherapy-induced xerostomia. The results...

Cochrane Library

Abdel-Rahman O, Elsayed Z. External beam radiotherapy for unresectable hepatocellular carcinoma. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD011314. DOI: 10.1002/14651858.CD011314.pub2.

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011314.pub2/full

Lawrie TA, Green JT, Beresford M, Burden S, Lal S, Davidson SE, Henson CC, Andreyev HJN. **Interventions to reduce acute and late adverse gastrointestinal effects of pelvic radiotherapy (Protocol)**. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD012529. DOI: 10.1002/14651858.CD012529.

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012529/full

van de Wetering FT, Verleye L, Andreyev HJN, Maher J, Vlayen J, Pieters BR, van Tienhoven G, Scholten RJPM. **Non-surgical interventions for late rectal problems (proctopathy) of radiotherapy in people who have received radiotherapy to the pelvis**. Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD003455. DOI: 10.1002/14651858.CD003455.pub2.

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003455.pub2/full

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Overview of gastrointestinal toxicity of radiation therapy

Authors: Brian G Czito, MD; Jeffrey J Meyer, MD; Christopher G Willett, MD; Section Editor: Reed E Drews, MD; Deputy Editor: Shilpa Grover, MD, MPH, AGAF

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: Mar 2017. | **This topic last updated:** Feb 10, 2016.

INTRODUCTION — Gastrointestinal toxicity can occur following irradiation of thoracic, abdominal, or pelvic malignancies if gastrointestinal structures are located within the radiation therapy (RT) field. These toxicities can limit the maximum tolerated dose of RT and chemotherapy and thus may limit the efficacy of treatment.

This topic will review the adverse effects of RT on the gastrointestinal tract. A more detailed discussion of the indications for RT for specific cancer sites and stages can be found in topic reviews for each cancer site. (See "Radiation therapy techniques in cancer treatment".)

TIMING OF TOXICITY — RT can be associated with side effects that can occur at any time during treatment or even years later. For purposes of this topic review, we will adopt the following definitions of these toxicities:

- Acute toxicities refer to those with onset during or shortly after the course of treatment.
- Late toxicities are those occurring after three months after completion of RT. These often reflect the spectrum of radiation tissue changes that can be lasting and irreversible.

https://www.uptodate.com/contents/overview-of-gastrointestinal-toxicity-of-radiation-therapy?source=search_result&search=radiotherapy&selectedTitle=5~150

Guidelines

Royal College of Radiologists

Radiotherapy dose fractionation, second edition [PDF]

Source: Royal College of Radiologists - RCR - 09 March 2017

Recommending evidence-based radiotherapy treatment regimens and acceptable treatment options ranked according to the level of evidence available.

https://www.rcr.ac.uk/system/files/publication/field_publication_files/bfco163_dose_fractionation_2nd_ed_march2017.pdf

Interventional oncology: guidance for service delivery, second edition [PDF]

Source: Royal College of Radiologists - RCR - 03 April 2017
Outlining best practice in interventional oncology, looking at current models of practice, clarifying areas of responsibility and the importance of the interventional radiology procedures being part of the multidisciplinary care pathway of patients.
https://www.rcr.ac.uk/system/files/publication/field_publication_files/rcr172_io_guidance.pdf

Institute of Physics and Engineering in Medicine

The Design of Radiotherapy Treatment Room Facilities
Expected: Summer 2017
Update of Report 75
Practical Application of the European Directive on Artificial Optical Radiation in the Medical Sector
Expected: 2017
Physics Aspects of Quality Control in Radiotherapy (update of Report 81)
Expected: 2017
Medical and Dental Guidance Notes
Expected Summer 2018 after new Ionising Radiations Regulations come into force in early 2018.
Update of 2002 Edition

https://www.ipem.ac.uk/Publications/IPEMReportSeries/ForthcomingPublications.aspx

The Society of Radiographers

The Role of the Radiographer in Computed Tomography Imaging
Responsible officer: Lynda Johnson; **Date published:** 10 April, 2017**; ISBN:** 978-1-909820-155
http://www.sor.org/learning/document-library/role-radiographer-computed-tomography-imaging

Consultant Radiographer - Guidance for the Support of New and Established Roles
Responsible officer: Rachel Harris; **Date published:** 28 March, 2017; **ISBN:** 978-1-909802-14-8
http://www.sor.org/learning/document-library/consultant-radiographer-guidance-support-new-and-established-roles

Have you paused and checked? Radiotherapy
Responsible officer: Maria Murray; **Date published:** 7 March, 2017
http://www.sor.org/learning/document-library/have-you-paused-and-checked-radiotherapy

Current Awareness Database Articles

Below is a selection of articles recently added to the healthcare databases, grouped in the categories:

- CHHiP Trial Outcomes
- Late Effects of Radiotherapy – Bowel Toxicities

If you would like any of the articles in full text, or if you would like a more focused search on your own topic, please contact us: library@bristol.nhs.uk

CHHiP Trial Outcomes

1. Effect of dose to the penile bulb on erectile potency (EP) in prostate image-guided radiotherapy (IGRT)

Author(s): Murray J.; Dean J.; Dearnaley D.; Gulliford S.; Mossop H.; Hall E.

Source: Clinical Oncology; Mar 2017; vol. 29 (no. 3)

Publication Type(s): Journal: Conference Abstract

Abstract: Aims: Erectile dysfunction remains a common toxicity of prostate radiotherapy despite technological advancements [1]. Penile bulb (PB) dose has been proposed as a predictor of EP post-radiotherapy, however, PB dosevolume effects are not well established. We aim to determine the doseresponse characteristics of the PB in men treated within a randomised trial assessing prostate IGRT using patient- and physician-reported outcomes. Methods: 230 men treated with IGRT within the CHHiP IGRT sub-study (CRUK/06/16) had complete dosimetric and toxicity data. Patients were excluded if reported impotence at baseline or no 2 year EP data were available. EP was assessed at regular intervals using physician-based scores and at one time point (>3 years after radiotherapy) with the IIEF-5 questionnaire. Planning computed tomography scans and reference dose distributions were imported into analysis software (VODCA, MSS GmbH, Hagendorn, CH) and the PB was retrospectively contoured by one clinician using published guidelines [2,3]. PB dose-volume parameters were analysed and atlases of complication incidence created and evaluated against severe erectily dysfunction (IIEF-5) and impotence (RMH physician). Dose-volume constraints were derived using receiver operating characteristic (ROC) analysis (Youden index) and assessed against the no information rate. Results: 175 patients were eligible for analysis, 49% and 40% of patients had impotence at 2 years treated with standard or reduced clinical target volumeeplanning target volume (CTV-PTV) margins, respectively. PB mean dose was greater in patients with impotence (median: 23 Gy versus 15 Gy; P=0.01) or severe ED (median: 27 Gy versus 14 Gy; P =0.001). Statistically significant dose-volume constraints for EP were derived for 20, 30, 40, 45, 50, 60 and 65 Gy and mean dose. PB mean dose constraints derived using physician and patient scores were 20 Gy (AUC: 0.61, P =0.01) and 23 Gy (AUC: 0.68, P =0.001), respectively. Conclusion: There is a dose-volume effect between PB and EP characterised using both patient- and physician-reported data. Therefore, reducing the PB dose may lead to a significant increase in potency preservation rates after radiotherapy. A mean PB dose of <20 Gy should be achieved where possible when planning prostate radiotherapy.

2. Prostate Hypofractionated Radiotherapy Trial Results Need to be Interpreted with Caution due to Undertreatment of the Control Arm in the CHHiP Trial

Author(s): Sivanandan M.A.; Walker G.; Sundar S.

Source: Clinical Oncology; Dec 2016; vol. 28 (no. 12); p. 797

Publication Type(s): Journal: Letter

3. Response to: Sivanandan et al. Prostate Hypofractionated Radiotherapy Trial Results Need to be Interpreted with Caution due to Undertreatment of the Control Arm in the CHHiP Trial

Author(s): Dearnaley D.; Hall E.; Gulliford S.; Syndikus I.

Source: Clinical Oncology; Dec 2016; vol. 28 (no. 12); p. 798-799

Publication Type(s): Journal: Letter

4. Re: Hypofractionated Radiotherapy versus Conventionally Fractionated Radiotherapy for Patients with Intermediate-Risk Localised Prostate Cancer: 2-Year Patient-Reported Outcomes of the Randomised, Non-Inferiority, Phase 3 CHHiP Trial.

Author(s): Taneja, Samir S

Source: The Journal of urology; Nov 2016; vol. 196 (no. 5); p. 1445-1447

Publication Type(s): Journal Article

Available in full text at Journal of Urology - from Ovid

5. Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial

Author(s): Dearnaley D.; Mossop H.; Khoo V.; Parker C.; Gao A.; Cruickshank C.; Hassan S.; Pugh J.; Griffin C.; Hall E.; Bidmead M.; Naismith O.; Syndikus I.; Malik Z.; Mayles H.; Birtle A.; Bloomfield D.; Tremlett J.; Graham J.; Kirkbride P.; Logue J.; Money-Kyrle J.; South C.; O'Sullivan J.M.; Panades M.; Patterson H.; Scrase C.; Staffurth J.; Stockdale A.

Source: The Lancet Oncology; Aug 2016; vol. 17 (no. 8); p. 1047-1060

Publication Type(s): Journal: Article

Available in full text at Lancet Oncology - from ProQuest

Abstract: Background Prostate cancer might have high radiation-fraction sensitivity that would give a therapeutic advantage to hypofractionated treatment. We present a pre-planned analysis of the efficacy and side-effects of a randomised trial comparing conventional and hypofractionated radiotherapy after 5 years follow-up. Methods CHHiP is a randomised, phase 3, non-inferiority trial that recruited men with localised prostate cancer (pT1b-T3aN0M0). Patients were randomly assigned (1:1:1) to conventional (74 Gy delivered in 37 fractions over 7.4 weeks) or one of two hypofractionated schedules (60 Gy in 20 fractions over 4 weeks or 57 Gy in 19 fractions over 3.8 weeks) all delivered with intensity-modulated techniques. Most patients were given radiotherapy with 3-6 months of neoadjuvant and concurrent androgen suppression. Randomisation was by computer-generated random permuted blocks, stratified by National Comprehensive Cancer Network (NCCN) risk group and radiotherapy treatment centre, and treatment allocation was not masked. The primary endpoint was time to biochemical or clinical failure; the critical hazard ratio (HR) for non-inferiority was 1.208. Analysis was by intention to treat. Long-term follow-up continues. The CHHiP trial is registered as an International Standard Randomised Controlled Trial, number ISRCTN97182923. Findings Between Oct 18, 2002, and June 17, 2011, 3216 men were enrolled from 71 centres and randomly assigned (74 Gy group, 1065 patients; 60 Gy group, 1074 patients; 57 Gy group, 1077 patients). Median follow-up was 62.4 months (IQR 53.9-77.0). The proportion of patients who were biochemical or clinical failure free at 5 years was 88.3% (95% CI 86.0-90.2) in the 74 Gy group, 90.6% (88.5-92.3) in the 60 Gy group, and 85.9% (83.4-88.0) in the 57 Gy group. 60 Gy was non-inferior to 74 Gy (HR 0.84 [90% CI 0.68-1.03], pNI=0.0018) but non-inferiority could not be claimed for 57 Gy compared with 74 Gy (HR 1.20 [0.99-1.46], pNI=0.48). Long-term side-effects were similar in the hypofractionated groups compared with the conventional group. There were no significant differences in either the proportion or cumulative incidence of side-effects 5 years after treatment using three clinician-reported as well as patient-reported outcome measures. The estimated cumulative 5 year incidence of Radiation Therapy Oncology Group (RTOG) grade 2 or worse bowel and bladder adverse events was 13.7% (111 events) and 9.1% (66 events) in the 74 Gy group, 11.9% (105 events) and 11.7% (88 events) in the 60 Gy group, 11.3% (95 events) and 6.6% (57 events) in the 57 Gy group, respectively. No treatment-related deaths were reported. Interpretation Hypofractionated radiotherapy using 60 Gy in 20 fractions is non-inferior to conventional fractionation using 74 Gy in 37 fractions and is recommended as a new standard of care for external-beam radiotherapy of localised prostate cancer. Funding Cancer Research UK, Department of Health, and the National Institute for Health Research Cancer Research Network.

6. Extreme hypofractionation: Indications and results

Author(s): Widmark A.; Beckman L.; Thellenberg-Karlsson C.; Franzen L.; Gunnlaugsson A.; Nilsson P.; Hoyer M.; Lagerlund M.

Source: Radiotherapy and Oncology; Apr 2016; vol. 119

Publication Type(s): Journal: Conference Abstract

Abstract: The alpha-beta ratio for prostate cancer (PCa) is postulated to be low; 7, PSA 10-20). No hormones were used. Patients were randomized to either conventionally fractionated RT (39 fr; 2.0 Gy/fr) over 7 weeks, or to a schedule with extreme hypofractionation (7 fr; 6.1 Gy/ fr) in 2.5 weeks (always including two weekends). The two treatment arms are designed to be equieffective for late normal tissue complications assuming alpha/beta=3 Gy. Primary endpoint will be mature within 2 years, and toxicity data will be reported by late this year.

7. Effect of dose and image guided radiotherapy (IGRT) on erectile potency (EP) in prostate radiotherapy

Author(s): Murray J.; Dearnaley D.; Dean J.; Gulliford S.; Mossop H.; Hall E.

Source: Radiotherapy and Oncology; Apr 2016; vol. 119

Publication Type(s): Journal: Conference Abstract

Abstract: Purpose or Objective: IGRT enables accurate target volume localisation, potentially permitting reduced treatment margins, which may decrease normal tissue toxicity. Erectile dysfunction is a common toxicity of prostate RT and the penile bulb (PB) is suggested as a surrogate for undetermined structures critical for erectile function. However, PB dose-volume effects are not well established. We aim to determine dose-response characteristics of the PB in prostate cancer patients treated using IGRT with standard and reduced margins. Material and Methods: Men with previously untreated localised prostate cancer were randomised within the multicentre CHHiP (Conventional or Hypofractionated High dose Intensity Modulated Radiotherapy for Prostate Cancer) IGRT sub-study (CRUK/06/16). Men were randomised to receive 2Gy or 3Gy per fraction, delivered either with or without daily online image-guidance, with standard or reduced CTV-PTV margins. Short course hormone therapy (HT) was allowed and details were recorded. EP was assessed at baseline, pre-RT and at 6 monthly intervals to 2 years, then annually to 5 years post-RT. EP was physician graded as normal erection (G0), decreased (G1), absent (G2) and unknown. Analysis included the subset of men treated with IGRT within the sub-study with an EP assessment at 2 years. Planning CT scans and reference dose distributions were imported into analysis software (Vodca, MSS GmbH). The PB was retrospectively contoured using established anatomical boundaries (1) and published guidelines (2,3) by one clinician. In-house software was used to convert the hypofractionated plans into equivalent dose in 2Gy per fraction using the Withers formula (alpha/beta = 3Gy). PB dosevolume (DVH) parameters were evaluated against EP at 2 years using atlases of complication incidence (ACI) (Matlab, Mathworks, Natick, MA) for G2 EP. Dose-volume constraints were derived using ROC analysis (Youden index) and assessed against the no information rate. Results: Between June 2010 and June 2011, 293 men entered the study. Complete dose-EP data sets were available for 129 men treated with IGRT. 14/129 men had G2 EP at baseline and were excluded. At 2 years, 27/52 (52%) men treated with standard margins (IGRTS) and 25/63 (40%) men treated with reduced margins (IGRTR) had G2 EP. HT characteristics between the two groups were similar. The PB volume was 7.1(+/-2.8)cm3 in IGRTS group and 6.5(+/-2.5)cm3 in IGRTR group. The reduced margins resulted in a reduction in dose to the PB and statistically significant dose-volume constraints for G2 EP were derived for 45, 50, 55, 60 and 65Gy (Table 1). The ACI is presented in Figure 1 and demonstrates a dosevolume response. (Table Presented) Conclusion: There is evidence to suggest a dose volume effect between the PB and EP. Discriminatory PB dosevolume constraints were found to predict G2 EP. Further analysis is in progress to include patient reported outcomes related to EP.

8. Modelled effects of hypofractionation on radiotherapy demand in England

Author(s): Mee T.; Kirkby N.F.; Kirkby K.J.; Jena R.

Source: Radiotherapy and Oncology; Apr 2016; vol. 119

Publication Type(s): Journal: Conference Abstract

Abstract: Purpose or Objective: Current clinical trials and studies are identifying hypofractionation as a viable treatment option when compared with current fractionation regimens. Our work estimates the reduction in the number of fractions prescribed and the potential effect on the overall demand for radiotherapy across the whole of England. With the evidence based estimates of demand for radiotherapy currently outstripping the supply capacity in England, this potential reduction in fraction demand needs to be calculated to assess the potential effects for radiotherapy service and infrastructure planning. Material and Methods: The Malthus Program, a tool for modelling radiotherapy demand, was used to calculate the potential effect of three hypofractionation studies/trials for the population of England. Well-published and potential clinical indications for hypofractionation have been modelled for prostate cancer, non-small cell lung cancer (NSCLC) and breast

cancer. The hypofractionation indications for radiotherapy were mapped into the original Malthus clinical decision trees and simulations completed to study the effects of hypofractionation on demand. Results: If the CHHiP prostate trial achieves universal uptake throughout England then it has the potential to reduced radiotherapy demand by 3,500 fractions per million population (#pmp). SBRT for medically inoperable (or refusal of surgery) for stage 1 and stage 2 NSCLC has the potential to reduce the demand by a further 700 #pmp. The FAST-Forward trial, using 5# instead of 15# for T1-3 N0-1 M0 breast cancer has the potential to reduce demand by 4,600 #pmp. A potential reduction in modelled demand of 8,800 #pmp arises from these three studies alone. Across the total population of England, this translates to approximately 479,600 fractions per year. Conclusion: The current clinical indications and trials for hypofractionation have the potential to reduce the evidencebased estimates of demand of radiotherapy sufficiently to be achievable with a modest increase of the current levels of equipment in England. While the presented calculations are for England as a whole, the Malthus program offers the facility to calculate the changes in modelled demand at a regional level within England, enabling a more precise calculation for treatment centres and their local catchment.

Late Effects of Radiotherapy – Bowel toxicities

1. Rectal/urinary toxicity after hypofractionated vs conventional radiotherapy in low/intermediate risk localized prostate cancer: Systematic review and meta analysis

Author(s): Di Franco R.; Ametrano G.; Rossetti S.; Romano F.J.; D'Aniello C.; Cavaliere C.; Iovane G.; Piscitelli R.; Facchini G.; Borzillo V.; Ravo V.; Falivene S.; Cammarota F.; Muto P.; Berretta M.

Source: Oncotarget; 2017; vol. 8 (no. 10); p. 17383-17395

Publication Type(s): Journal: Review

Abstract: Purpose: The aim of this review was to compare radiation toxicity in Localized Prostate Cancer (LPC) patients who underwent conventional fractionation (CV), hypofractionated (HYPO) or extreme hypofractionated (eHYPO) radiotherapy. We analyzed the impact of technological innovation on the management of prostate cancer, attempting to make a meta-analysis of randomized trials. Methods: PubMed database has been explored for studies concerning acute and late urinary/gastrointestinal toxicity in low/intermediate risk LPC patients after receiving radiotherapy. Studies were then gathered into 5 groups: detected acute and chronic toxicity data from phase II non randomized trials were analyzed and Odds Ratio (OR) was calculated by comparing the number of patients with G0-1 toxicity and those with toxicity > G2 in the studied groups. A meta-analysis of prospective randomized trials was also carried out. Results: The initial search yielded 575 results, but only 32 manuscripts met all eligibility requirements: in terms of radiation-induced side effects, such as gastrointestinal and genitourinary acute and late toxicity, hypofractionated 3DCRT seemed to be more advantageous than 3DCRT with conventional fractionation as well as IMRT with conventional fractionation compared to 3DCRT with conventional fractionation; furthermore, IMRT hypofractionated technique appeared more advantageous than IMRT with conventional fractionation in late toxicities. Randomized trials meta-analysis disclosed an advantage in terms of acute gastrointestinal and late genitourinary toxicity for Hypofractionated schemes. Conclusions: Although our analysis pointed out a more favorable toxicity profile in terms of gastrointestinal acute side effects of conventional radiotherapy schemes compared to hypofractionated ones, prospective randomized trials are needed to better understand the real incidence of rectal and urinary toxicity in patients receiving radiotherapy for localized prostate cancer.

2. Concurrent chemoradiotherapy vs. radiotherapy alone in locally advanced cervix cancer: A systematic review and meta-analysis

Author(s): Datta N.R.; Stutz E.; Liu M.; Rogers S.; Bodis S.; Klingbiel D.; Siebenhuner A.; Singh S.

Source: Gynecologic Oncology; Dec 2017

Publication Type(s): Journal: Article In Press

Abstract: The efficacy of concurrent chemoradiotherapy (CTRT) in locally advanced cervix cancer (LACC, stages IIB-IVA) is contentious. This is due to the variable extent of therapeutic benefit reported in different randomized clinical trials and meta-analyses that usually include all stages of cervix cancer. A systematic review and meta-analysis was therefore conducted to evaluate the efficacy of concurrent CTRT over radiotherapy (RT) alone, predominantly in LACC for the key endpoints; complete response (CR), long-term loco-regional control (LRC), overall survival (OS), grade III/IV acute and late toxicities. Six databases namely -

PubMed, EMBASE, SCOPUS, Web of Science, Google Scholar and Cochrane library were explored and supplemented by hand-searching. Only prospective randomized trials conducted in LACC between concurrent CTRT and RT alone with no surgical interventions were included. Fourteen English language articles from 1788 citations were shortlisted for the final analysis. Of the 2445 patients evaluated (CTRT: n = 1217; RT: n = 1228), 95.7% had LACC and 96% had a squamous cell histology. Eight studies used cisplatin alone, 4 had cisplatin-based combination chemotherapy (CT) while 2 used mitomycin-C, either alone or in combination. CTRT improved the CR (+. 10.2%, p = 0.027), LRC (+. 8.4%, p. <. 0.001) and OS (+. 7.5%, p. <. 0.001) over RT alone. However a 10.4% higher incidence of grade III/IV acute toxicities (p. <. 0.001) was also evident with CTRT. Late toxicities in both groups were equivalent. Subgroup analysis and meta-regression did not reveal any significant advantage in outcomes between the 3 CTRT regimens. Thus, although concurrent CTRT provides conclusive therapeutic benefit over RT alone in LACC, the choice of CT agents should be based on their cost-effectiveness and the anticipated expenses for the management of any associated acute toxicities. This assumes importance particularly in resource-constrained low-middle-income countries with the highest burden of LACC, where majority of the patients meet the treatment costs as out-of-pocket expenses. Copyright © 2017.

3. Acute and late toxicity in high-risk prostate cancer patients treated with androgen suppression and hypofractionated pelvic radiation therapy

Author(s): Faria S.; Cury F.; Duclos M.; Souhami L.; Ruo R.

Source: Practical Radiation Oncology; Oct 2017

Publication Type(s): Journal: Article In Press

Abstract: Purpose: To report acute and late toxicity rates in patients with high-risk prostate cancer treated with androgen deprivation therapy (ADT) and moderate hypofractionated radiation therapy (HypoRT) to the prostate and nodal areas. Methods and materials: Patients with localized, high-risk prostate cancer were treated with a HypoRT regimen of 60 Gy in 20 fractions (4 weeks) to the prostate volume while the nodal areas received 44 Gy in the same 20 fractions delivered with intensity modulated RT with a simultaneous integrated boost technique. ADT started 2 to 3 months before HypoRT and was given to all patients. Acute and late toxicity were prospectively assessed and graded according to the Common Terminology Criteria for Adverse Events, version 3. Results: A total of 105 patients treated between September 2010 and November 2013 were reviewed. Median follow-up was 41 months, with 97% of patients followed for more than 26 months. Median ADT duration was 18 months. Acute grade 2 or higher gastrointestinal (GI) or genitourinary (GU) toxicity was seen in 18 (17%) and 19 (17%) patients, respectively, with only 1 and 3 patients experiencing either a GI or GU acute grade 3 toxicity. The worst grade 2 or higher late GI and GU toxicity were seen in 7 (7%) and 8 (8%) patients, respectively. There was no grade 4 or 5 toxicity. At the last follow-up, the rate of grade 2 GI and GU toxicity was 5% and 3%, respectively, with no residual grade >3 toxicity. The 48-month actuarial progression free survival is 82%. Conclusions: ADT with moderate HypoRT delivered with IMRT and an integrated simultaneous boost to the prostate (60 Gy) and pelvic nodes (44 Gy) in 20 fractions is feasible and well tolerated. This approach shortens treatment duration and is convenient for patients and the health system, and its results support a randomized trial. Copyright © 2017.

4. Long-term Toxicity and Health-related Quality of Life after Single-fraction High Dose Rate Brachytherapy Boost and Hypofractionated External Beam Radiotherapy for Intermediate-risk Prostate Cancer

Author(s): Shahid N.; Loblaw A.; Chung H.T.; Cheung P.; Szumacher E.; Danjoux C.; Morton G.; Sankreacha R.; Zhang L.; Deabreu A.; Mamedov A.

Source: Clinical Oncology; Aug 2017

Publication Type(s): Journal: Article In Press

Abstract: Aims: To report health-related quality of life (HRQOL) and toxicity in prostate cancer patients treated with single-fraction high dose rate (HDR) brachytherapy boost and external beam radiotherapy (EBRT). Materials and methods: Patients with intermediate-risk prostate cancer were accrued to a phase II clinical trial of 15 Gy HDR boost and EBRT to a dose of 37.5 Gy in 15 fractions. HRQOL (Expanded Prostate Cancer Index Composite [EPIC]), urinary symptoms (International Prostate Symptom Score [IPSS]), erectile function (International Index of Erectile Function [IIEF]) and toxicity (Common Terminology Criteria for Adverse Events [CTCAE], version 3.0) were monitored prospectively. Univariate and multivariate logistic regression analysis was used to investigate associations between HRQOL/toxicity and baseline covariates. Results: The median follow-up time was 5.2 years. The change in the median EPIC scores from baseline to year 5 in the urinary domain was from 91 to 85 (P = 0.0028), in the bowel domain was from 98 to 96 (P = 0.03), in the sexual domain was from 63 to 35 (P 3 occurred in 29, 59 and 4% of patients, respectively. The rates of late

gastrointestinal toxicity grade 1, 2 and >3 were documented as 45, 19 and 0%, respectively. On multivariate logistic regression analysis, patients with larger prostates were more likely to develop a urinary late toxicity grade >2 (P = 0.01). The dose to 10% of the urethra was the only factor associated with a decline in the EPIC urinary domain score (P = 0.012). Prostate volume >43 ml was associated with higher late genitourinary toxicity grade >2. Conclusions: Single 15 Gy HDR brachytherapy with EBRT has a low rate of late genitourinary and gastrointestinal toxicities. Late urinary morbidity may be minimised by limiting the dose to the urethra, particularly for patients with larger prostates.

5. Acute and Late Adverse Events Associated With Radical Radiation Therapy Prostate Cancer Treatment: A Systematic Review of Clinician and Patient Toxicity Reporting in Randomized Controlled Trials

Author(s): Holch P.; Henry A.M.; Gilbert A.; Shearsmith L.; Ingleson E.; Albutt A.; Velikova G.; Franks K.; Davidson S.; Routledge J.

Source: International Journal of Radiation Oncology Biology Physics; Mar 2017; vol. 97 (no. 3); p. 495-510

Publication Type(s): Journal: Review

Abstract: Purpose This review aimed to determine the clinician and patient reported outcome (PRO) instruments currently usedin randomized controlled trials (RCTs) of radical radiation therapy for nonmetastatic prostate cancer to report acute and late adverse events (AEs), review the quality of methodology and PRO reporting, and report the prevalence of acute and late AEs. Methods and Materials The MEDLINE, EMBASE, and Cochrane databases were searched between April and August 2014 according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement. Identified reports were reviewed according to the PRO Consolidated Standards of Reporting Trials (CONSORT) guidelines and the Cochrane Risk of Bias tool. In all, 1149 records were screened, and 21 articles were included in the final review. Results We determined the acute and late AEs for 9040 patients enrolled in 15 different RCTs. Only clinician reported instruments were used to report acute AEs <3 months (eg, Radiation Therapy Oncology Group [RTOG] and Common Terminology Criteria for Adverse Events [CTCAE]). For late clinician reporting, the Late Effects on Normal Tissues-Subjective, Objective, Management and Analytic scale and RTOG were used and were often augmented with additional items to provide comprehensive coverage of sexual functioning and anorectal symptoms. Some late AEs were reported (48% articles) using PROs (eg, ULCA-PCI [University of California, Los Angeles Prostate Cancer Index], FACT-G and P [Functional Assessment of Cancer Therapy General & Prostate Module], EORTC QLQC-30 + PR25 [European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire & Prostate Module]); however, a definitive "preferred" instrument was not evident. Discussion Our findings are at odds with recent movements toward including patient voices in reporting of AEs and patient engagement in clinical research. We recommend including PRO to evaluate radical radiation therapy before, during, and after the treatment to fully capture patient experiences, and we support the development of predictive models for late effects based on the severity of early toxicity. Conclusion Patient reporting of acute and late AEs is underrepresented in radiation therapy trials. We recommend working toward a consistent approach to PRO assessment of radiation therapy-related AEs.

6. Prediction of rehabilitation needs after treatment of cervical cancer: what do late adverse effects tell us?

Author(s): Mikkelsen T.B.; Dieperink K.B.; Sorensen B.

Source: Supportive Care in Cancer; Mar 2017; vol. 25 (no. 3); p. 823-831

Publication Date: Mar 2017

Publication Type(s): Journal: Article

Abstract: Purpose: Women treated for cervical cancer with radiotherapy and chemotherapy have reported serious bowel, vaginal, and sexual late effects. The purpose of this study was to describe late adverse effects, health-related quality of life, and self-efficacy in a representative Danish cervical cancer population in order to describe rehabilitation needs. Methods: Women, mean age 55 years, treated for cervical cancer from January 2010 to July 2013, who were alive and without known relapse/metastases were included in this cross-sectional study. EORTC QLQ C30 and CX24 and self-efficacy questionnaires were sent to all participants. Results: The participation rate was 85/107 (79%). Participants below 45 years had significantly more menopausal symptoms and lower body image scores compared to elderly women. The frequency of participants with menopausal symptoms decreased with time since diagnosis. Symptom experience was significantly higher in participants with locally advanced disease than in those with local disease. Self-efficacy was significantly lower in

participants with locally advanced disease. The incidence of lymphedema was significantly higher among participants who were obese. Multiple analyses showed impaired quality of life, e.g., a lower body image and self-efficacy score, correlated with increasing BMI. Women who had surgery had greater risk of lymphedema, and women who received chemotherapy during treatment had a lower quality of life. All but one received radiotherapy. Conclusion: This study found that young, obese survivors with locally advanced cervical cancer and survivors who received chemotherapy may have a serious risk of developing late adverse effects; thus, rehabilitation should target these needs.

7. A review of uncertainties in radiotherapy dose reconstruction and their impacts on dose-response relationships.

Author(s): Vũ Bezin, Jérémi; Allodji, Rodrigue S; Mège, Jean-Pierre; Beldjoudi, Guillaume; Saunier, Fleur; Chavaudra, Jean; Deutsch, Eric; de Vathaire, Florent; Bernier, Valérie; Carrie, Christian; Lefkopoulos, Dimitri; Diallo, Ibrahima

Source: Journal of radiological protection : official journal of the Society for Radiological Protection; Mar 2017; vol. 37 (no. 1); p. R1

Publication Type(s): Journal Article

Abstract: Proper understanding of the risk of radiation-induced late effects for patients receiving external photon beam radiotherapy requires the determination of reliable dose-response relationships. Although significant efforts have been devoted to improving dose estimates for the study of late effects, the most often questioned explanatory variable is still the dose. In this work, based on a literature review, we provide an in-depth description of the radiotherapy dose reconstruction process for the study of late effects. In particular, we focus on the identification of the main sources of dose uncertainty involved in this process and summarise their impacts on the dose-response relationship for radiotherapy late effects. We provide a number of recommendations for making progress in estimating the uncertainties in current studies of radiotherapy late effects and reducing these uncertainties in future studies.

8. Intensity-modulated radiation therapy with stereotactic body radiation therapy boost for unfavorable prostate cancer: A report on 3-year toxicity

Author(s): Paydar I.; Cyr R.A.; Yung T.M.; Bullock E.G.; Lei S.; Satinsky A.; William Harter K.; Suy S.; Dritschilo A.; Collins S.P.; Pepin A.; King J.; Lynch J.H.; Kole T.P.

Source: Frontiers in Oncology; Feb 2017; vol. 7

Publication Type(s): Journal: Article

Abstract: Background: Recent data suggest that intensity-modulated radiation therapy (IMRT) plus brachytherapy boost for unfavorable prostate cancer provides improved biochemical relapse-free survival over IMRT alone. Stereotactic body radiation therapy (SBRT) may be a less invasive alternative to brachytherapy boost. Here, we report the 3-year gastrointestinal (GI) and genitourinary (GU) toxicities of IMRT plus SBRT boost. Materials and methods: Between March 2008 and September 2012, patients with prostate cancer were treated with robotic SBRT (19.5 Gy in three fractions) followed by fiducial-guided IMRT (45-50.4 Gy) on an institutional protocol. Toxicity was prospectively graded using the common terminology criteria for adverse events version 4.0 (CTCAEv.4) at the start of and at 1- to 6-month intervals after therapy. Rectal telangiectasias were graded using the Vienna Rectoscopy Score (VRS). Results: At a median follow-up of 4.2 years (2.4-7.5), 108 patients (4 low-, 45 intermediate-, and 59 high-risk) with a median age of 74 years (55-92) were treated with SBRT plus IMRT, with 8% on anticoagulation and an additional 48% on antiplatelet therapy at the start of therapy. The cumulative incidence of late >grade 2 GI toxicity was 12%. Of these, 7% were due to late rectal bleeding, with six patients requiring up to two coagulation procedures. One patient with rectal telangiectasias was treated with hyperbaric oxygen (grade 3 toxicity). No rectal fistulas or stenoses were observed. Ten patients had multiple non-confluent telangiectasias (VRS grade 2), and three patients had multiple confluent telangiectasias (VRS grade 3). The cumulative incidence of late grade 3 GU toxicity was 6%. Most late toxicities were due to hematuria requiring bladder fulguration. There were no late > grade 4 GU toxicities. Conclusion: Rates of clinically significant GI and GU toxicities are modest following IMRT plus SBRT boost. Future studies should compare cancer control, quality of life, and toxicity with other treatment modalities for patients with high-risk prostate cancer.

9. Identifying radiation-induced survivorship syndromes affecting bowel health in a cohort of gynecological cancer survivors

Author(s): Steineck G.; Skokic V.; Sjoberg F.; Bull C.; Alevronta E.; Bergmark K.; Wilderang U.; Dunberger

G.; Oh J.H.; Deasy J.O.; Jornsten R.

Source: PLoS ONE; Feb 2017; vol. 12 (no. 2)

Publication Type(s): Journal: Article

Available in full text at PLoS ONE - from EBSCOhost

Available in full text at PLoS ONE - from National Library of Medicine

Available in full text at PLoS One - from ProQuest

Abstract: Background: During radiotherapy unwanted radiation to normal tissue surrounding the tumor triggers survivorship diseases; we lack a nosology for radiation-induced survivorship diseases that decrease bowel health and we do not know which symptoms are related to which diseases. Methods: Gynecological-cancer survivors were followed-up two to 15 years after having undergone radiotherapy; they reported in a postal questionnaire the frequency of 28 different symptoms related to bowel health. Population-based controls gave the same information. With a modified factor analysis, we determined the optimal number of factors, factor loadings for each symptom, factor-specific factor-loading cutoffs and factor scores. Results: Altogether data from 623 survivors and 344 population-based controls were analyzed. Six factors best explain the correlation structure of the symptoms; for five of these a statistically significant difference (P< 0.001, Mann-Whitney U test) was found between survivors and controls concerning factor score quantiles. Taken together these five factors explain 42 percent of the variance of the symptoms. We interpreted these five factors as radiation-induced syndromes that may reflect distinct survivorship diseases. We obtained the following frequencies, defined as survivors having a factor loading above the 95 percent percentile of the controls, urgency syndrome (190 of 623, 30 percent), leakage syndrome (164 of 623, 26 percent), excessive gas discharge (93 of 623, 15 percent), excessive mucus discharge (102 of 623, 16 percent) and blood discharge (63 of 623, 10 percent). Conclusion: Late effects of radiotherapy include five syndromes affecting bowel health; studying them and identifying the underlying survivorship diseases, instead of the approximately 30 long-term symptoms they produce, will simplify the search for prevention, alleviation and elimination.

10. Rectal toxicity after extremely hypofractionated radiotherapy using a non-isocentric robotic radiosurgery system for early stage prostate cancer

Author(s): Shikama N.; Kumazaki Y.; Miyazawa K.; Tsukamoto N.; Nihei K.; Hashimoto S.

Source: World Journal of Oncology; 2016; vol. 7 (no. 5); p. 98-103

Publication Type(s): Journal: Article

Abstract: Background: The aim of the study was to evaluate toxicity after extremely hypofractionated radiotherapy (EHF-RT) using a non-isocentric robotic radiosurgery system for early stage prostate cancer. Methods: Eligibility criteria of this feasibility study were 50 - 84 years old, and low-risk to intermediate-risk disease. The prescribed dose to the iso-dose line of 95% of planning target volume was 35 Gy in five fractions over 2 weeks. The primary endpoint was the incidence of > grade 2 acute toxicity which indicated symptoms requiring medications. Results: We enrolled 20 patients from December 2012 to August 2014, and the median follow-up time was 30 months (range: 18 - 36). Sixteen patients had a short overall treatment time (OTT) of EHF-RT (9 - 10 days), and four patients had a long OTT (11 - 12 days) because of national holidays and patient's preference. The incidences of > grade 2 acute toxicity in all sites, that in the rectum, and that in the genitourinary system, were 30%, 20%, and 10%, respectively. No patient developed severe acute toxicity (> grade 3). Among 16 patients with a short OTT of EHF-RT, four patients developed grade 2 acute rectal toxicity. Rectum-V28 Gy (rectal volume receiving = 28 Gy) of 3.8 mL or higher had a tendency to increase grade 2 acute rectal toxicity (P = 0.058). One patient developed grade 3 late rectal toxicity and no patient developed severe late genitourinary toxicity. Conclusion: The incidences of > grade 2 acute toxicity in all sites and that in the rectum after EHF-RT of 35 Gy in five fractions were 30% and 20%, respectively. High rectum-V28 Gy was associated with grade 2 acute rectal toxicity after EHF-RT for early prostate cancer.

11. Extreme hypofractionated image guided radiotherapy phase I-II trials experience and brachytherapy quality of life comparison in prostate cancer patients

Author(s): Ferrer Gonzalez F.; Laplana M.; Boladeras A.; Garcia E.; Ventura M.; Gutierrez C.; Rojas F.; Bavestrello P.; Martinez E.; Pera J.; Guedea F.; Pont A.; Garin O.; De Blas R.; Zardoya E.; Picon C.; Castells M.; Suarez J.F.

Source: European Urology, Supplements; Dec 2016; vol. 15 (no. 13)

Publication Type(s): Journal: Conference Abstract

Abstract:INTRODUCTION & OBJECTIVES: Extreme hypofractionated image guided radiotherapy or hypofractionated Stereotactic Body Radiation Therapy (SBRT) in prostate cancer is a novel precise strategy to reduce total treatment time and increase effective doses to the prostatic tumor taking into account prostate cancer and organs at risk radiosenstivity. 1) To evaluate the feasibility and toxicity of two regimens of hypofractionated Stereotactic Body Radiation Therapy (SBRT). 2) To obtain patients self-reported Quality Of Life (QOL) measures in two cohorts of SBRT and to compare with a LDR (Low Dose Rate)-brachytherapy for intermediate risk prostate cancer and HDR (High Dose Rate)- brachytherapy boost after 60Gy of external radiation EBRT for high risk patients. MATERIAL & METHODS: Two prospective phase I-II studies were approved by our institutional review and ethics board. Inclusion criteria were: Trial1) T1-2N0M0, Gleason Score 6-7, PSA< 20 ng/mL, and IPSS 0-7. Trial 2) T3aN0M0 Gleason score 8 or less (N+risk<25%) and IPSS <13. Hormonal-therapy was prescribed according to risk classification. Image Guided RT with Cone Beam CT was mandatory. Dose SBRT was delivered at a prescribed Planning Target Volume (PTV) 35 Gy in five fractions in 5 alternative days or 9 Gy after 60 Gy 2 Gy per fraction in 30 days, using with RapidArc IMAT, with 6 MV FFF photons. CTCAE v4.0 morbidity scores were used to assess toxicities. Health-related quality of life questionnaire, such as EPIC, was administered centrally by telephone interview before treatment and during follow-up (at 3, 6 and 12 months). Comparison of QLQ values by confidence intervals was done between Trial 1 patients and a cohort of 280 LDR-brachytherapy patients and external radiation combined plus HDR-brachytherapy 9 Gy boost in 88 patients vs Trial 2 patients. This work was supported by a grant from the Fundacion Mutua-Madrilena (AP87652011). RESULTS: Thirty-one patients have been recruited. Mean age was 70.6 years. Nineteen patients were included in trial 1 and 12 in trial 2. According to D'Amico risk classification for trial 1), 3/19 patients were low-risk and 16/19 were intermediate risk, for trial 2) 12 patients were high risk. All patients completed the treatment as programmed with good tolerance. No toxicity greater than grade 2 was observed. Acute GU and rectal toxicities were seen in 20/31 (64.5%) and 17/31 (54.8%) patients respectively. Both GU and rectal late toxicities G 2 were: 2/31 (6.4%) and 1/31 (3.2%). EPIC urinary values were significantly better at 3 and 6 moths for SBRT (5x7) vs LDR-brachytherapy and EPIC hormonal was higher at 3, 6 and 12 months in LDR-brachytherapy group, whereas in 9 Gy boost patients EPIC hormonal was lower at baseline and 3 months in SBRT group. Values on both bowel and sexual did not showed differences. CONCLUSIONS: Early findings indicate that both SBRT regimes with IMAT and FFF beams for lowintermediate- risk prostate cancer and high risk are feasible and well tolerated in selected patients. Although EPIC hormonal QLQ measures are worse than brachytherapy cohorts, EPIC values related to radiation treatment are not different. Long-term follow-up is needed for assessment of late toxicity and outcomes.

12. Stereotactic body radiotherapy as a monotherapy for localized prostate cancer: Late toxicity and quality of life

Author(s): Beltramo G.; Bossi Zanetti I.; Bergantin A.; Martinotti A.S.; Redaelli I.; Bonfanti P.; Invernizzi M.; Bresolin A.; Bianchi L.C.

Source: European Urology, Supplements; Dec 2016; vol. 15 (no. 13)

Publication Type(s): Journal: Conference Abstract

Abstract:INTRODUCTION & OBJECTIVES: Over the past decade, radiation techniques have evolved to allow administration of higher dose of radiation. Treatment, however, often impact the quality of life due to sideeffects and treatment -related toxicities. We report prospectively collected toxicity data from a cohort of localized prostate cancer patients treated with Cyberknife (CK) Stereotactic Body Radiation Therapy (SBRT). MATERIAL & METHODS: Between July 2007 to April 2011 a retrospective analysis was carried out on 83 consecutive patients with a median age of 74 years (range 60 - 85), mean prostate volume of 67,7 cc (range 37,03 -163,16), and clinically localized prostate cancer treated with Cyberknife stereotactic radiosurgery. The majority of patients 39 (47%) were low risk, 27 pts (33%) were intermediate risk and 17 pts (20%) were high risk using the NCCN criteria. Pre-treatment PSAs ranged from 1.75 to 51 ng.ml (median 7.6 ng.ml). 49% of patients had moderate to severe lower urinary tract symptom prior to treatment (baseline AUA > 8). The course of radiotherapy consisted of 3800 cGy over four fraction given daily to the GTV, which was defined as the prostate (plus seminal vesicles in High risk patients). Realtime intrafractional motion tracking was used. RTOG toxicity grades were assigned for Genitourinary (GU) and Gastrointestinal (GI). RESULTS: In total, 11 patients died during follow up for unrelated causes. Data to assess GI and GU Toxicity were available for 63 patients with a median follow up of 79 months (range 61 -106). Acute urinary symptoms (frequency, disurya, urgency, hesitancy and nicturia) were common with 58% of patients experiencing grade I-II RTOG acute urinary toxicity. No patients experienced RTOG grade 3 acute urinary toxicity in 4 patients (6%) we recorded RTOG grade 3 late urinary toxicity, in two of them urethral dilatation was required for bulbar urethral stricture. In one patient a grade four bladder fistula was observed. No RTOG grade 3 acute and late rectal toxicity was observed. the

median time from CK radiotherapy completion to the occurrence of late grade 3-4 GU toxicity was 29 months (range 18-45). CONCLUSIONS: Significant long term toxicities are minimal when Cyberknfe stereotactic Hypofractionated radiotherapy is performed as monotherapy, this probably reflect the ability for current technology to minimize adverse effects of therapy. Continued accrual and follow up will be necessary to confirm long-term results.

13. Image guided radiotherapy with fiducial markers and intensity modulated radiotherapy in prostate cancer. Long terms outcomes

Author(s): Salas C.; Gutierrez L.; Garduno S.; Macias M.J.; De Ingunza L.; Villanego I.; Gonzalez E.; Diaz L.; Diaz V.; Jaen J.

Source: European Urology, Supplements; Dec 2016; vol. 15 (no. 13)

Publication Type(s): Journal: Conference Abstract

Abstract:INTRODUCTION & OBJECTIVES: The use of gold seeds as radiopaque fiducials (MF) intraprostatic indirectly to locate and visualize the prostate treatment with Radiation Therapy (RT) dose escalation, it's called Image Guided Radiation Therapy (IGRT). Combined with Intensity Modulated Radiation Therapy (IMRT), we increased technical precision and high dose to the target volume with dose limiting to the rectum and bladder (Organ at Risk-OAR). To report long-term tumor control and late Gastrointestinal (GI) and Genitourinary (GU) toxicity rates in low, intermediate and high risk Prostate Cancer (PC) patients, treated with IGRT with fiducial markers and IMRT. MATERIAL & METHODS: Between January 2012 and April 2015, 104 men with PC (T1c-T3a), prostatespecific antigen [PSA] 5-20 ng/dL, or Gleason score [GS] 6 and 7, received normofractionated external radiation therapy and IGRT. 30% received short Androgen Deprivation (AD) and 70% without AD. The dose was 76 Gy at least 98% the planning target volume in 38 (2 Gy) daily fractions, using IMRT with 6 Mv. Daily image guidance of the prostate was performed with two Electronic Portal Imaging Device (EPID) (antero-posterior and lateral) by automatic matching of the four fiducial markers, in ONCOR. Planning target volume was defined as prostate +/- seminals vesicles with 7-mm. margin in all directions, except 5-mm. in rectal margin. Constraints: rectum V70<10%, V50<50%; bladder V70<35%, V65<50%. Biochemical failure was defined according to Phoenix criteria (nadir + 2ng/dL). In general, follow-up was every 6 months during first 3 years and annually thereafter. GI and GU toxicity were prospectively assessed and scored according to the Radiation Therapy Oncology Group (RTOG). RESULTS: Median follow-up was 43 months (range 36-48). Median age was 69 years (range 52-79); 12% had a Gleason score (GS) of 7 and 88% GS of 6. Median initial PSA was 7.8 ng/dL (range 3.6 -19 ng/mL), 79% had low , 15% intermediate and 6% high risk. One patient developed biochemical failure; one patient developed bone metastases, 3 patients died from other causes. Four-year actuarial biochemical recurrence-free, cancer-specific, and overall survival rates were 98%, 98%, and 95%, respectively. The worst grade 2-3 GU or GI late toxicity was 3% and 1%, respectively. At the last followup, grade 2-3 late GI and GU toxicity rates were 1 % for both groups. No grade 4 or 5 late toxicity occurred. CONCLUSIONS: IGRT with intraprostatic fiducial markers and IMRT for PSA< 20 ng/ml prostate cancer, is associated with excellent long-term biochemical control with very low late GU and GI toxicity.

14. Hypofractionated versus conventionally fractionated radiotherapy for localized prostate cancer: Systematic review and meta-analysis of the randomized trials in the dose-escalation era

Author(s): Morgan S.; Holmes O.; Malone S.

Source: European Urology, Supplements; Dec 2016; vol. 15 (no. 13)

Publication Type(s): Journal: Conference Abstract

Abstract:INTRODUCTION & OBJECTIVES: Prostate cancer is associated with a low alpha-beta ratio. This provides a rationale for hypofractionated radiotherapy (that is, delivery of >2 Gy per fraction) as a means of potentially improving the therapeutic ratio. We undertook a systematic review of the Randomized Controlled Trials (RCTs) evaluating hypofractionated external beam Radiotherapy (RT) in the primary treatment of localized prostate cancer. MATERIAL & METHODS: Relevant RCTs were identified by searches of MEDLINE and the conference proceedings of ASCO, ASTRO, ECCO, and ESTRO. RCTs were eligible for inclusion in this systematic review if they compared radical-intent moderately hypofractionated RT (2.4-3.5 Gy per fraction) with conventionally fractionated RT (1.8-2.0 Gy per fraction) in patients with localized prostate cancer of any risk group. Trials conducted prior to the dose-escalation era (that is, prescribed dose in the conventional arm 2 GU toxicity (OR 1.03, 95% CI 0.91-1.16, p=0.64) but there was a significantly greater incidence of acute grade >2 GI toxicity with hypofractionated RT (OR 1.47, 95% CI 1.16-1.87, p=0.001). There were no differences in late grade >2 GU toxicity (OR 1.10, 95% CI 0.95-1.27, p=0.19) or late grade >2 GI toxicity (OR 1.03, 95% CI 0.77-1.39, p=0.83). CONCLUSIONS: With a minimum median follow-up of 5.0

years across the trials reporting efficacy outcomes, there was no difference in bPFS or OS between moderately hypofractionated and conventionally fractionated RT. While an excess of acute grade >2 GI toxicity was identified with hypofractionated RT, significant differences in late grade >2 GU or GI toxicity were not seen across the groups. Taken together, these results support the adoption of moderately hypofractionated RT as a new standard definitive treatment in localized prostate cancer. Longer-term follow-up of these trials is nonetheless awaited to exclude late-appearing differences in toxicity or efficacy.

15. Modelling late stool frequency and rectal pain after radical radiotherapy in prostate cancer patients: Results from a large pooled population

Author(s): Cicchetti A.; Rancati T.; Palorini F.; Valdagni R.; Ebert M.; Kennedy A.; Joseph D.J.; Fiorino C.; Denham J.W.; Vavassori V.; Fellin G.; Avuzzi B.; Stucchi C.

Source: Physica Medica; Dec 2016; vol. 32 (no. 12); p. 1690-1697

Publication Type(s): Journal: Article

Abstract: Aim To investigate late gastrointestinal toxicity in a large pooled population of prostate cancer patients treated with radical radiotherapy. Normal tissue complication probability models were developed for late stool frequency and late rectal pain. Methods and materials Population included 1336 patients, 3-year minimum follow-up, treated with 66-80 Gy. Toxicity was scored with LENT-SOMA-scale. Two toxicity endpoints were considered: grade 2 rectal pain and mean grade (average score during follow-up) in stool frequency >1. DVHs of anorectum were reduced to equivalent uniform dose (EUD). The best-value of the volume parameter n was determined through numerical optimization. Association between EUD/clinical factors and the endpoints was investigated by logistic analyses. Likelihood, Brier-score and calibration were used to evaluate models. External calibration was also carried out. Results 4% of patients (45/1122) reported mean stool frequency grade >1; grade 2 rectal pain was present in the TROG 03.04 RADAR population only (21/677, 3.1%): for this endpoint, the analysis was limited to this population. Analysis of DVHs highlighted the importance of mid-range doses (30-50 Gy) for both endpoints. EUDs calculated with n = 1 (OR = 1.04) and n = 0.35 (OR = 1.06) were the most suitable dosimetric descriptors for stool frequency and rectal pain respectively. The final models included EUD and cardiovascular diseases (OR = 1.78) for stool frequency and EUD and presence of acute gastrointestinal toxicity (OR = 4.2) for rectal pain. Conclusion Best predictors of stool frequency and rectal pain are consistent with findings previously reported for late faecal incontinence, indicating an important role in optimization of mid-range dose region to minimize these symptoms highly impacting the quality-of-life of long surviving patients.

16. Individual patient data meta-analysis shows a significant association between the ATM rs1801516 SNP and toxicity after radiotherapy in 5456 breast and prostate cancer patients

Author(s): Andreassen C.N.; Overgaard M.; Overgaard J.; Alsner J.; Rosenstein B.S.; Kerns S.L.; Ostrer H.; De Ruysscher D.; Cesaretti J.A.; Barnett G.C.; Dunning A.M.; Burnet N.G.; Elliott R.; Coles C.; Dorling L.; West C.M.L.; Hall E.; Fachal L.; Vega A.; Gomez-Caamano A.; Talbot C.J.; Symonds R.P.; De Ruyck K.; Thierens H.; Ost P.; Chang-Claude J.; Seibold P.; Popanda O.; Dearnaley D.; Yarnold J.R.; Sydes M.R.; Azria D.; Koch C.A.; Parliament M.; Blackshaw M.; Sia M.; Fuentes-Raspall M.J.; Ramon y Cajal T.; Barnadas A.; Vesprini D.; Gutierrez-Enriquez S.; Molla M.; Diez O.; Bentzen S.M.

Source: Radiotherapy and Oncology; Dec 2016; vol. 121 (no. 3); p. 431-439

Publication Type(s): Journal: Article

Abstract: Purpose Several small studies have indicated that the ATM rs1801516 SNP is associated with risk of normal tissue toxicity after radiotherapy. However, the findings have not been consistent. In order to test this SNP in a well-powered study, an individual patient data meta-analysis was carried out by the International Radiogenomics Consortium. Materials and methods The analysis included 5456 patients from 17 different cohorts. 2759 patients were given radiotherapy for breast cancer and 2697 for prostate cancer. Eight toxicity scores (overall toxicity, acute toxicity, late toxicity, acute skin toxicity, acute rectal toxicity, telangiectasia, fibrosis and late rectal toxicity) were analyzed. Adjustments were made for treatment and patient related factors with potential impact on the risk of toxicity. Results For all endpoints except late rectal toxicity, a significantly increased risk of toxicity was found for carriers of the minor (Asn) allele with odds ratios of approximately 1.5 for acute toxicity and 1.2 for late toxicity. The results were consistent with a co-dominant pattern of inheritance. Conclusion This study convincingly showed a significant association between the ATM rs1801516 Asn allele and increased risk of radiation-induced normal tissue toxicity.

17. The long-term and late effects of the diagnosis and treatment of colorectal cancer

Author(s): Carlile A.

Source: European Journal of Surgical Oncology; Nov 2016; vol. 42 (no. 11)

Publication Type(s): Journal: Conference Abstract

Abstract: Background: Colorectal cancer is the 3rd most common cancer in the UK. Through early detection and improved treatments more people than ever are surviving this disease. Surgery, chemotherapy and radiotherapy are the cornerstones of management but these invasive treatments can cause a number of long-term and late effects. Using qualitative methods this study aimed to; explore people's experiences with long-term and late effects of colorectal cancer, how these effects impacted on their lives and how participants managed them. Method: Semi-structured qualitative interviews were conducted with 15 participants who had completed curative treatment. Interviews were transcribed and analysed using the Framework approach to identify themes and categorise text data. Results: Many long-term and late effects of colorectal cancer were explored including bowel dysfunction, sexual dysfunction, pain, metastatic disease and cognitive dysfunction. These effects caused distress for many and were linked to depression and social limitation. Previously unidentified long-term effects included decreased libido and joint pain which respondents attributed to chemotherapy. Anxiety and depression were found predominantly to be late effects. Management of long-term and late effects was varied with healthcare services often ineffective. Conclusion: Insight gained into long-term and late effects and their treatment, indicated that many participants suffered as a result of their after- effects and had unmet health needs. It adds a qualitative insight into an area where quantitative research has already been conducted. Improvements in cancer follow-up could offer opportunities to effectively identify manage and monitor these effects. Further interventional studies are required to develop effective care pathways to achieve optimal care.

18. Prostate external beam radiotherapy combined with high-dose-rate brachytherapy: Dose-volume parameters from deformably-registered plans correlate with late gastrointestinal complications

Author(s): Moulton C.R.; House M.J.; Ebert M.A.; Lye V.; Tang C.I.; Krawiec M.; Joseph D.J.; Denham J.W.

Source: Radiation Oncology; Oct 2016; vol. 11 (no. 1)

Publication Date: Oct 2016

Publication Type(s): Journal: Article

Available in full text at Radiation Oncology - from National Library of Medicine

Available in full text at Radiation Oncology - from BioMed Central

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Abstract: Background: Derivation of dose-volume correlated with toxicity for multi-modal treatments can be difficult due to the perceived need for voxel-by-voxel dose accumulation. With data available for a single-institution cohort with long follow-up, an investigation was undertaken into rectal dose-volume effects for gastrointestinal toxicities after deformably-registering each phase of a combined external beam radiotherapy (EBRT)/high-dose-rate (HDR) brachytherapy prostate treatment. Methods: One hundred and eighteen patients received EBRT in 23 fractions of 2 Gy and HDR (TG43 algorithm) in 3 fractions of 6.5 Gy. Results for the Late Effects of Normal Tissues - Subjective, Objective, Management and Analytic toxicity assessments were available with a median follow-up of 72 months. The HDR CT was deformably-registered to the EBRT CT. Doses were corrected for dose fractionation. Rectum dose-volume histogram (DVH) parameters were calculated in two ways. (1) Distribution-adding: parameters were calculated after the EBRT dose distribution was 3D-summed with the registered HDR dose distribution. (2) Parameter-adding: the EBRT DVH parameters were added to HDR DVH parameters. Logistic regressions and Mann-Whitney U-tests were used to correlate parameters with late peak toxicity (dichotomised at grade 1 or 2). Results: The 48-80, 40-63 and 49-55 Gy dose regions from distribution-adding were significantly correlated with rectal bleeding, urgency/tenesmus and stool frequency respectively. Additionally, urgency/tenesmus and anorectal pain were associated with the 25-26 Gy and 44-48 Gy dose regions from distribution-adding respectively. Parameter-adding also indicated the low-mid dose region was significantly correlated with stool frequency and proctitis. Conclusions: This study confirms significant dose-histogram effects for gastrointestinal toxicities after including deformable registration to combine phases of EBRT/HDR prostate cancer treatment. The findings from distribution-adding were in most cases consistent with those from parameter-adding. The mid-high dose range and near maximum doses were important for rectal bleeding. The distribution-adding mid-high dose range was also important for stool frequency and urgency/tenesmus. We encourage additional studies in a variety of institutions using a variety of dose accumulation methods with appropriate inter-fraction motion management. Trial registration: NCT NCT00193856. Retrospectively registered 12 September 2005.

19. Long-term toxicities after treatment of childhood cancer

Author(s): Quidde J.

Source: Oncology Research and Treatment; Oct 2016; vol. 39 ; p. 247

Publication Type(s): Journal: Conference Abstract

Abstract: Multimodality and new treatment approaches offer an increasing number of patients the chance of cure and survival. The last decades have seen tremendous improvements in survival of children, adolescents and young adults diagnosed with cancer, with 5-year survival rates approaching 80%. Therefore, the population of cancer survivor is growing. Besides improved efficacy, multimodality treatment increases the risk for physiological, psychological and social long-term sequelae. Complication of cancer treatment may not become apparent until years later. Cancer therapies may have a lasting effect on any organ, e.g. heart, lungs, gastrointestinal tract, kidneys and bladder, skin, eyes, brain, bones and the endocrine and reproductive systems. Adolescents and young adults (AYAs) receiving their cancer treatment during childhood are at particular risk for long-term side effects. According to the Childhood Cancer Survivor study two of three AYAs have treatment related long-term toxicities including learning and memory difficulties, anxiety, depression, hearing loss, cardiac dysfunction, cataracts, obesity, thyroid problems, infertility or second cancer. In addition, an amount of psychosocial issues, like long-term educational, social, behavioural difficulties and facing barriers related to obtaining ongoing medical care, support, and surveillance for late effects are all common. Oeffinger et al compared the health status of 10,397 childhood cancer survivors treated from 1970 to 1987 with 3,034 of their siblings. 62% of the survivors had at least one chronic health condition, and 27% had a serious or life-threatening condition. The major long-term toxicity and cause of mortality after treatment of childhood cancer are cardiovascular diseases like cardiomyopathy, chronic heart failure and valvular problems. Compared to general population AYAs have a 5 to 15-fold increased risk of cardiovascular diseases. Individual risk is determined by treatment related factors (e.g. kind of chemotherapy, way and time of application, number of cycles, cumulative dose of chemotherapy, and combination with radiotherapy) and non-treatment related factors (nicotine abuse, diabetes mellitus, dyslipoproteinemia and hypertension. The talk about "Long-term toxicities after childhood cancer" will be focused on the AYAs at high risk for late effects include patients treated for bone tumors, brain tumors and Hodgkin lymphoma.

20. The Three-item ALERT-B Questionnaire Provides a Validated Screening Tool to Detect Chronic Gastrointestinal Symptoms after Pelvic Radiotherapy in Cancer Survivors

Author(s): Taylor S.; Byrne A.; Sivell S.; Nelson A.; Adams R.; Hanna L.; Staffurth J.; Turner J.; Green J.; Farnell D.

Source: Clinical Oncology; Oct 2016; vol. 28 (no. 10)

Publication Type(s): Journal: Article

Abstract: Aims Although pelvic radiotherapy is an effective treatment for various malignancies, around half of patients develop significant gastrointestinal problems. These symptoms often remain undetected, despite the existence of effective treatments. This study developed and refined a simple screening tool to detect common gastrointestinal symptoms in outpatient clinics. These symptoms have a significant effect on quality of life. This tool will increase detection rates and so enable access to specialist gastroenterologists, which will in turn lead to improved symptom control and quality of life after treatment. Materials and methods A literature review and expert consensus meeting identified four items for the ALERT-B (Assessment of Late Effects of RadioTherapy - Bowel) screening tool. ALERT-B was face tested for its usability and acceptability using cognitive interviews with 12 patients experiencing late gastrointestinal symptoms after pelvic radiotherapy. Thematic analysis and probe category were used to analyse interview transcripts. Interview data were presented to a group of experts to agree on the final content and format of the tool. ALERT-B was assessed for reliability and tested for validity against the Gastrointestinal Symptom Rating Scale in a clinical study (EAGLE). Results Overall, the tool was found to be acceptable in terms of wording, response format and completion time. Participant-reported experiences, including lifestyle modifications and the psychological effect of the symptoms, led to further modifications of the tool. The refined tool includes three questions covering rectal bleeding, incontinence, nocturnal bowel movements and impact on quality of life, including mood, relationships and socialising. ALERT-B was successfully validated against the Gastrointestinal Symptom Rating Scale in the EAGLE study with the tool shown broadly to be internally consistent (Cronbach's alpha = 0.61 and all item-subscale correlation [Spearman] coefficients are > 0.6). Conclusion The ALERT-B screening tool can be used in clinical practice to improve post-treatment supportive care by triggering the clinical assessment of patients suitable for referral to a gastroenterologist.

21. Acute and late toxicity in high-risk prostate cancer patients treated with androgen suppression and hypofractionated radiotherapy (HypoRT) to the prostate and pelvic nodes

Author(s): Faria S.; Cury F.; Duclos M.; Souhami L.; Petrucelli M.

Source: Radiotherapy and Oncology; Sep 2016; vol. 120

Publication Type(s): Journal: Conference Abstract

Abstract: Purpose: Moderate HypoRT is an acceptable option in the curative treatment of prostate cancer. Among different fractionation regimens, the dose of 60 Gy in 20 fractions was used in prospective randomized trials (PROFIT, CHiiP), mainly for low and intermediate-risk patients where the PTV is only the prostate(+/- seminal vesicle(SV) but not the pelvic nodes. We report here the acute and late toxicity in high-risk prostate cancer patients treated with androgen suppression and HypoRT to the prostate and pelvic nodes with doses of 60 Gy to prostate and 44 Gy to the pelvic nodes given in 20 fractions with a simultaneous integrated boost. Methods and Materials: Localized high-risk prostate cancer patients (T3, or PSA>20ng/ml, or GS >8) were treated with androgen suppression (6-24 months) started 2-3 months before HypoRT. Radiotherapy was delivered using IMRT with daily IGRT. Constraints for organs at risk were the same of RTOG-0126 corrected with the linear-quadratic model (alpha/beta=3Gy). A dose of 44 Gy (2.2 Gy/fraction) was delivered to the pelvic nodes and 60 Gy (3 Gy/fraction) to the prostate (+/-SV) with a concomitant boost in 20 fractions (4 weeks). Cone beam CT was used daily to guide the treatment accuracy. Acute and late toxicities were assessed prospectively and scored using the National Cancer Institute Common Terminology Criteria for Adverse Events, version3.0. Biochemical failure was determined using the Phoenix definition. Results: 105 patients treated between September/2010 and November/2013 were reviewed. Median age, median initial PSA and T stage were 72 years (52-84), PSA=14(1.8-108), T1c = 36 and T3= 22 patients. Median follow up is 35 months (12-61). Acute GI toxicity (%) was as follows: Grade 0 = 38, Grade 1 = 45, Grade 2 = 16 and Grade 3 = 1. Acute GU toxicity(%): Grade 0 = 32, Grade 1 = 50, Grade 2 = 14 and Grade 3 = 3. The worst late GI toxicity(%) was, as follows: Grade 0 = 74 Grade 1 = 19, Grade 2/3 = 7. The worst late GU toxicity(%) was: Grade 0 = 77, Grade 1 = 15, Grade 2/3 = 8. There was no Grade>3 toxicity. At the last follow-up the incidences of grade 2 late GU and GI toxicity were 5% and 3%, respectively (no residual grade >2 toxicity). At this limited follow-up, 13 patients developed biochemical failure at a median time of 27 months with 8 of them showing evidence of metastatic disease. Three patients died so far, and one from prostate cancer. Conclusion: Androgen suppression with moderate HypoRT IMRT and IGRT to the prostate (60Gy) and pelvic nodes (44Gy) delivered with simultaneous integrated boost in 4 weeks (20 fractions) is feasible and well tolerated. Further follow-up is needed to establish long-term PSA control rates and survival outcomes.

22. Intensity-modulated Radiotherapy and Anal Cancer: Clinical Outcome and Late Toxicity Assessment

Author(s): De Francesco I.; Thomas K.; Wedlake L.; Tait D.

Source: Clinical Oncology; Sep 2016; vol. 28 (no. 9); p. 604-610

Publication Type(s): Journal: Article

Abstract: Aims To assess the potential impact on long-term consequences of treatment (intensity-modulated radiotherapy with concomitant chemotherapy) in patients diagnosed with anal cancer. Materials and methods We identified 43 eligible patients treated with concomitant chemoradiotherapy (pelvic intensity-modulated radiotherapy) at the Royal Marsden Hospital between 2010 and 2013. We determined late genitalia and bowel side-effects using specific questionnaires [Pelvic Symptom Questionnaire, Vaizey Incontinence Questionnaire, Inflammatory Bowel Disease Questionnaire (IBDQ) and IBDQ-B]. Using descriptive statistics, we report clinical outcomes in all patients, by time, since the end of treatment (grouped as 1-1.5, 1.5-2.5 and 2.5-3.5 years). Results Twenty-seven of 43 (63%) patients were identified as available for questionnaire follow-up. Reasons for unavailability were death (n = 3), lost to palliative care service (n = 1), referred to surgery (n = 4), lost to follow-up (n = 8). In the 27 patients studied, bowel toxicity was assessed by IBDQ, IBDQ-B and the Vaizey Incontinence Questionnaire. The median value was 208 for IBDQ, 38 for IBDQ-B and 3.0 for the Vaizey Incontinence Questionnaire, as assessed at 1 year or more post-completion of treatment. Treatment was reported to affect quality of life/sexual function in two of the female patients (n = 21) and three male patients (n = 6). No insufficiency fractures have been reported. Bone marrow function remained stable over the time of the follow-up. Conclusions Although there are data supporting a reduction in acute effects using intensity-modulated radiotherapy in anal cancer, there is very little in the literature to establish the late toxicity profile. Our results indicate that there is an effect on bowel and sexual function, but it does not increase over the period observed. These data provide a benchmark against which to compare outcomes with future manipulation in treatment, and provide us with real information to give patients as to the expectation of their functional outcome after treatment. Copyright © 2016 The Royal College of Radiologists

23. Hypofraktionierte stereotaktische Radiotherapie SHARP ist eine gut tolerierte Behandlung beim Prostatakarzinom: Beurteilung der Toxizitat und LebensqualitatSHARP hypofractionated stereotactic radiotherapy is well tolerated in prostate cancer: Toxicity and quality of life assessment

Author(s): Rucinska M.; Kieszkowska-Grudny A.; Nawrocki S.

Source: Strahlentherapie und Onkologie; Jul 2016; vol. 192 (no. 7); p. 449-457

Publication Type(s): Journal: Article

Abstract: Background: Quality of life (QoL) is one of the most significant issues in prostate cancer treatment decisions. This study aimed to investigate the toxicity of hypofractionated stereotactic radiotherapy (SBRT) and QoL after treatment in localized prostate cancer patients. Materials and methods: A prospective single-center clinical study was performed in low- and intermediate-risk prostate cancer patients. Patients received 33.5 Gy in 5 fractions (SHARP regimen). Acute and late toxicity was assessed according to RTOG/EORTC score. Patients filled out EORTC QLQ-C30 and prostate cancer-specific QLQ-PR25 questionnaires. Results: The analysis included 68 prostate cancer patients (55-83 years, median 73) with clinical stage T1c-T2cN0M0, median combined Gleason score of 6 (3-8), and median prostate-specific antigen (PSA) level of 10 ng/mL (4-20 ng/mL). Neoadjuvant androgen deprivation therapy was given to 52 patients (76.5 %), and stopped in 31 patients (45.5 %) after 6 months; in 21 patients (31 %) after 2-3 years. Average and median follow-up was 24 months (18-45). Median nadir PSA level was 0.03 ng/mL for all patients and 0.6 ng/mL for patients without hormone treatment. No patients had PSA failure. There were no acute grade IV toxicities. One patient (1.5 %) developed grade III and 24 patients (35.3 %) grade II acute bladder toxicity. No one developed grade III and 7 patients (10.3 %) grade II acute rectal toxicity. No grade III or IV late gastrointestinal or genitourinary toxicities were reported. Grade II late urinary symptoms were observed in 8 patients (11.8 %) and gastrointestinal symptoms in 3 patients (4.4 %). Global health status/QoL was good and improved during the observational period. Conclusion: SBRT for prostate cancer patients is a well-tolerated treatment in terms of toxicity and QoL, has no negative impact on functioning and everyday life, with the important benefit of a short treatment period. However, long-term follow-up data are needed.

24. Late rectal toxicity from image-guided intensity modulated radiotherapy for prostate cancer

Author(s): Maki S.; Itoh Y.; Kubota S.; Okada T.; Nakahara R.; Ito J.; Kawamura M.; Kamomae T.; Naganawa S.; Yoshino Y.; Gotoh M.; Ikeda M.

Source: Anticancer Research; Jun 2016; vol. 36 (no. 6); p. 2967-2973

Publication Type(s): Journal: Article

Abstract: Aim: Late rectal toxicity (LRT) was retrospectively evaluated in men with prostate cancer treated with image-guided intensity modulated radiotherapy (IGIMRT). Patients and Methods: Between May 2008 and December 2009, 47 men with prostate adenocarcinoma were treated with IG-IMRT using in-room computed tomography (CT). Results: The median time to grade 2 LRT was 12 months (range=1-24 months). Two of 3 men who developed grade 2 LRT had received treatment for diabetes, and the other was receiving anticoagulant/antiplatelet therapy (AC therapy). Their rectal wall V70 (the volume of rectal wall receiving 70 Gy) values were 12.6%, 13.0%, and 13.3%. Univariate analysis revealed that V70 of the rectal wall was the only significant risk factor for LRT (p=0.0073). Conclusion: No man with V70 12.0% experienced grade 2 LRT. Strict rectal wall V70 12% dose constraints should be considered when treating prostate cancer patients who are also receiving diabetic or AC therapy.

25. Meta-analysis of Genome Wide Association Studies Identifies Genetic Markers of Late Toxicity Following Radiotherapy for Prostate Cancer

Author(s): Kerns S.L.; Stock R.; Stone N.N.; Rosenstein B.S.; Dorling L.; Pharoah P.D.P.; Barnes D.R.; Michailidou K.; Tyrer J.P.; Fachal L.; Ahmed S.; Dunning A.M.; Barnett G.C.; Carracedo A.; Vega A.; Bentzen S.; Gomez-Caamano A.; Carballo A.M.; Peleteiro P.; Dearnaley D.P.; Gulliford S.L.; Hall E.; Sia M.; Sydes M.R.; Parliament M.; Ostrer H.; Burnet N.G.; West C.M.L.

Source: EBioMedicine; May 2016

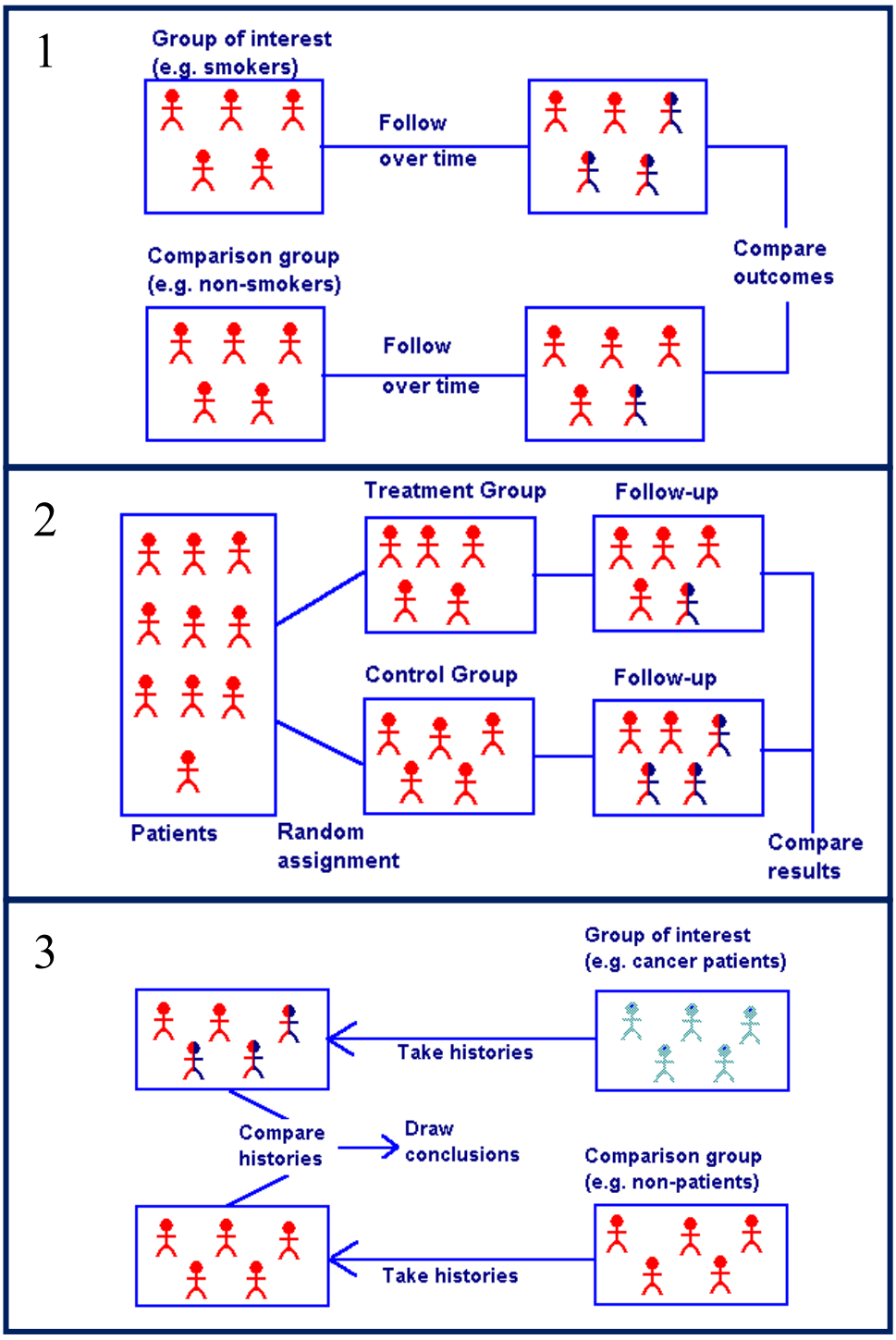
Publication Type(s): Journal: Article In Press

Abstract: Nearly 50% of cancer patients undergo radiotherapy. Late radiotherapy toxicity affects quality-of-life in long-term cancer survivors and risk of side-effects in a minority limits doses prescribed to the majority of patients. Development of a test predicting risk of toxicity could benefit many cancer patients. We aimed to meta-analyze individual level data from four genome-wide association studies from prostate cancer radiotherapy cohorts including 1564 men to identify genetic markers of toxicity. Prospectively assessed two-year toxicity

endpoints (urinary frequency, decreased urine stream, rectal bleeding, overall toxicity) and single nucleotide polymorphism (SNP) associations were tested using multivariable regression, adjusting for clinical and patient-related risk factors. A fixed-effects meta-analysis identified two SNPs: rs17599026 on 5q31.2 with urinary frequency (odds ratio [OR] 3.12, 95% confidence interval [CI] 2.08-4.69, p-value 4.16x10-8) and rs7720298 on 5p15.2 with decreased urine stream (OR 2.71, 95% CI 1.90-3.86, p-value=3.21x10-8). These SNPs lie within genes that are expressed in tissues adversely affected by pelvic radiotherapy including bladder, kidney, rectum and small intestine. The results show that heterogeneous radiotherapy cohorts can be combined to identify new moderate-penetrance genetic variants associated with radiotherapy toxicity. The work provides a basis for larger collaborative efforts to identify enough variants for a future test involving polygenic risk profiling.

Exercise: Research Designs

Match the diagrams to the corresponding research designs.



A: Randomised Controlled Trial
B: Cohort Study
C: Case-control Study

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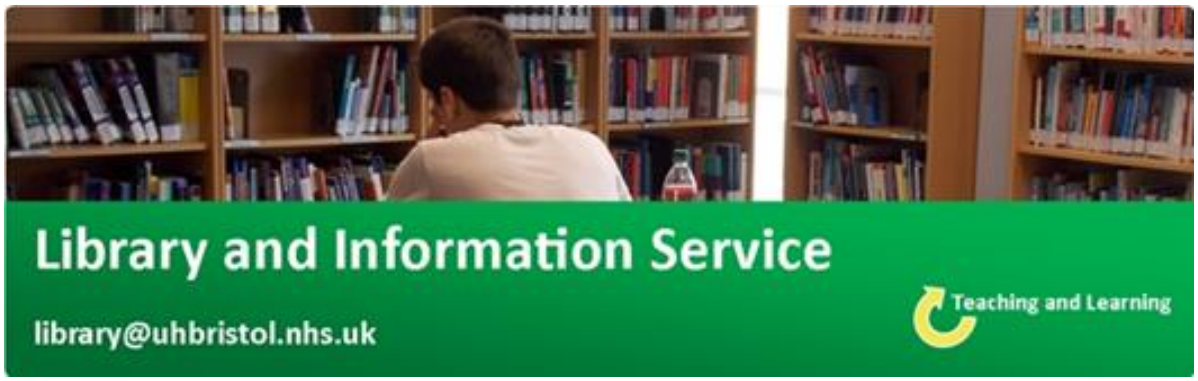

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