

# Radiotherapy

## Current Awareness Bulletin

### January 2017




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 Teaching and Learning

# Lunchtime Drop-in Sessions

*All sessions last one hour*

## **January (13.00)**

Tues 10th	<b>Literature Searching</b>
Wed 18th	<b>Critical Appraisal</b>
Thurs 26th	<b>Statistics</b>

## **February (12.00)**

Fri 3 <sup>rd</sup>	<b>Literature Searching</b>
Mon 6 <sup>th</sup>	<b>Critical Appraisal</b>
Tue 14 <sup>th</sup>	<b>Statistics</b>
Wed 22 <sup>nd</sup>	<b>Literature Searching</b>

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## Current Journals: Tables of Contents

Click on journal title (+ Ctrl) for hyperlink

Journal	Month	Volume	Issue
<a href="http://www.thegreenjournal.com/issue/S0167-8140(16)X0015-1">Radiotherapy and Oncology</a> <a href="http://www.thegreenjournal.com/issue/S0167-8140(16)X0015-1">http://www.thegreenjournal.com/issue/S0167-8140(16)X0015-1</a>	December 2016	121	3
<a href="http://www.redjournal.org/current">International Journal of Radiation Biology and Physics</a> <a href="http://www.redjournal.org/current">http://www.redjournal.org/current</a>	January 2017	97	1
<a href="http://www.clinicaloncologyonline.net/">Clinical Oncology</a> <a href="http://www.clinicaloncologyonline.net/">http://www.clinicaloncologyonline.net/</a>	February 2017	29	2

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## Latest Evidence

**NICE** National Institute for  
Health and Care Excellence

Nothing to add



Nothing to add

**UpToDate**<sup>®</sup>

*OpenAthens login required. Register here: <https://openathens.nice.org.uk/>*

Nothing to add

**NHS 'Behind the Headlines'**

Nothing to add

## Current Awareness Database Articles

Below is a selection of articles recently added to the healthcare databases, grouped in the categories: Clarity – prostate verification; Radiotherapy – immobilisation; Protons. 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](mailto:library@bristol.nhs.uk)

### Clarity - prostate verification

1. Determining intrafractional prostate motion using four dimensional ultrasound system.
2. Changes in penile bulb dose when using the Clarity transperineal ultrasound probe: A planning study.
3. First evaluation of the feasibility of MLC tracking using ultrasound motion estimation.
4. The impact of CBCT-imaging and verification time on prostate motion using 4D TPUS Clarity system
5. 3D-Transabdominal Ultrasound and ConeBeam-CT: Comparison of prostate positioning
6. Monitoring of intra-fraction prostate motion with a new 4D ultrasound device
7. A new image quality protocol for ultrasound image-guided radiotherapy at University Hospital Galway

#### 1. Determining intrafractional prostate motion using four dimensional ultrasound system.

**Author(s):** Baker, Mariwan; Behrens, Claus F

**Source:** BMC cancer; 2016; vol. 16 ; p. 484

**Publication Type(s):** Journal Article

Available in full text at [BMC Cancer](#) - from ProQuest

Available in full text at [BMC Cancer](#) - from National Library of Medicine

Available in full text at [BMC Cancer](#) - from BioMed Central

**Abstract:** In prostate radiotherapy, it is essential that the prostate position is within the planned volume during the treatment delivery. The aim of this study is to investigate whether intrafractional motion of the prostate is of clinical consequence, using a novel 4D autoscan ultrasound probe. Ten prostate patients were ultrasound (US) scanned at the time of CT imaging and once a week during their course of radiotherapy treatment in an ethics-approved study, using the transperineal Clarity autoscan system (Clarity®, Elekta Inc., Stockholm, Sweden). At each US scanning session (fraction) the prostate was monitored for 2 to 2.5 min, a typical beam-on time to deliver a RapidArc® radiotherapy fraction. The patients were instructed to remain motionless in supine position throughout the US scans. They were also requested to comply with a bladder-filling protocol. In total, 51 monitoring curves were acquired. Data of the prostate motion in three orthogonal directions were analyzed. Finally, the BMI value was calculated to investigate correlation between BMI and the extent of prostate displacement. The patients were cooperative, despite extra time for applying the TPUS scan. The mean ( $\pm$ 1SD) of the maximal intrafractional displacements were [mm]; I(+)/S: ( $0.2 \pm 0.9$ ); L(+)/R: ( $-0.2 \pm 0.8$ ); and A(+)/P: ( $-0.2 \pm 1.1$ ), respectively. The largest displacement was 2.8 mm in the posterior direction. The percentage of fractions with displacements larger than 2.0 mm was 4 %, 2 %, and 10 % in the IS, LR, and AP directions, respectively. The mean of the maximal intrafractional Euclidean distance (3D vector) was  $0.9 \pm 0.6$  mm. For 12 % of the fractions the maximal 3D vector displacements were larger than 2.0 mm. At only two fractions (4 %) displacements larger than 3.0 mm were observed. There was no correlation between BMI and the extent of the prostate displacement. The prostate intrafractional displacement is of no clinically consequence for treatment times in the order of 2 - 2.5 min, which is typical for a RapidArc radiotherapy fraction. However, prostate motion should be considered for longer treatment times eg if applying conventional or IMRT radiotherapy.

#### 2. Changes in penile bulb dose when using the Clarity transperineal ultrasound probe: A planning study.

**Author(s):** Mantel, Frederick; Richter, Anne; Groh, Christian; Lawrenz, Ingulf; Weick, Stefan; Polat, Bülent; Guckenberger, Matthias; Flentje, Michael

**Source:** Practical radiation oncology; 2016; vol. 6 (no. 6); p. e337

**Publication Type(s):** Journal Article

**Abstract:** The Clarity system allows monitoring of intrafraction target organ movements in external beam radiation therapy of prostate cancer by using transperineal ultrasound. The probe positioning at the perineum

could lead to a compression and shift of the penile bulb (PB) toward the high-dose region. Dose to the PB has been reported to be associated with the risk of posttreatment erectile dysfunction. This planning study reports on PB translations and changes in volume and dose when applying the transperineal ultrasound probe. For 10 patients treated with external beam radiation therapy for prostate cancer between 2013 and 2014, a planning computed tomography scan with and without the ultrasound probe in place was acquired. The planning target volume and organs at risk including the PB were contoured in the computed tomography scan with and without the probe. Radiation therapy plans for both scenarios were calculated. In a second step, for planning with the probe in position, an additional objective for improved sparing of the PB was introduced. The median PB volume was 5.5 mL (range, 3.8-7.1 mL) without the probe and 3.5 mL (range, 2.0-5.8 mL) with the probe. The median shift of the PB was 1 mm in the posterior (range, 3 mm posterior-2 mm anterior) and 6 mm in the superior direction (range, 0-14 mm superior), with no relevant shift of the prostate. The median mean dose in 95% of the PB was 34.1 Gy (range, 6.0-50.4 Gy), 48.3 Gy (range, 7.2-56.8 Gy), and 39.4 Gy (range, 5.6-51.3 Gy) for plans without probe, with probe, and with probe and additional planning objective, respectively. Dose to the PB increased when using the transperineal probe. After introducing an additional plan-optimization objective for PB sparing, dose-volume parameters were below Quantitative Analyses of Normal Tissue Effects in the Clinic thresholds for all but one patient.

### **3. First evaluation of the feasibility of MLC tracking using ultrasound motion estimation.**

**Author(s):** Fast, Martin F; O'Shea, Tuathan P; Nill, Simeon; Oelfke, Uwe; Harris, Emma J

**Source:** Medical physics; Aug 2016; vol. 43 (no. 8); p. 4628

**Publication Type(s):** Journal Article

**Abstract:** To quantify the performance of the Clarity ultrasound (US) imaging system (Elekta AB, Stockholm, Sweden) for real-time dynamic multileaf collimator (MLC) tracking. The Clarity calibration and quality assurance phantom was mounted on a motion platform moving with a periodic sine wave trajectory. The detected position of a 30 mm hypoechoic sphere within the phantom was continuously reported via Clarity's real-time streaming interface to an in-house tracking and delivery software and subsequently used to adapt the MLC aperture. A portal imager measured MV treatment field/MLC apertures and motion platform positions throughout each experiment to independently quantify system latency and geometric error. Based on the measured range of latency values, a prostate stereotactic body radiation therapy (SBRT) delivery was performed with three realistic motion trajectories. The dosimetric impact of system latency on MLC tracking was directly measured using a 3D dosimeter mounted on the motion platform. For 2D US imaging, the overall system latency, including all delay times from the imaging and delivery chain, ranged from 392 to 424 ms depending on the lateral sector size. For 3D US imaging, the latency ranged from 566 to 1031 ms depending on the elevational sweep. The latency-corrected geometric root-mean squared error was below 0.75 mm (2D US) and below 1.75 mm (3D US). For the prostate SBRT delivery, the impact of a range of system latencies (400-1000 ms) on the MLC tracking performance was minimal in terms of gamma failure rate. Real-time MLC tracking based on a noninvasive US input is technologically feasible. Current system latencies are higher than those for x-ray imaging systems, but US can provide full volumetric image data and the impact of system latency was measured to be small for a prostate SBRT case when using a US-like motion input.

### **4. The impact of CBCT-imaging and verification time on prostate motion using 4D TPUS Clarity system**

**Author(s):** Pang P.P.E.; Boo H.S.A.; Loh M.Q.J.; Chan W.S.J.; Aryani S.N.; Tuan K.L.J.; Knight K.; Baird M.

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

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Purpose or Objective: Accuracy of radiotherapy to the prostate is often challenged by geometrical uncertainties due to inherent organ motion attributed to daily variations of the bladder and rectal volumes and contents. This study aims to simulate the use of 4D Clarity ultrasound image guidance without CBCT imaging to analyse the magnitude and trend of prostate motion during treatment (74Gy given in 37 fractions). The impact of CBCT imaging and verification time on prostate motion will be analysed. Material and Methods: 175 intra-fraction monitoring sessions from 5 patients who underwent radical prostate volumetric modulated arc therapy (VMAT) monitored using 4D transperineal ultrasound scan (TPUS) resulted in a total of 1461.2min of data (184,085 positioning points) being analysed. All patients were instructed to comply with a full bladder protocol (i.e. 300-450ml in 30-45min) without specific rectal preparation protocol. Mean prostate motion was calculated and analysed in relation to time in the subsequent fractions. Overall treatment time was defined from acquisition of CBCT to treatment beam off time and imaging time was defined from time of CBCT acquisition to first beam on. Imaging time was subtracted from the overall treatment time for analysis of prostate motion without CBCT for verification. The remaining duration was representative of treatment time using 4D Clarity ultrasound image

guidance alone. The impact of CBCT imaging and verification time on prostate motion was analysed. Results: Mean (median) imaging and overall treatment time was 4.6min (4.4 min) and 8.4min (8.3 min) respectively. Mean (median) prostate motion during overall treatment time was 0.7mm (0.6mm) Inf, 1.0mm (0.9mm) Post and 0.1mm (0.2mm) Lt respectively. Mean prostate motion without CBCT was 0.6mm (0.5mm) Inf, 0.9mm (0.8mm) Post and 0.1mm (0.1mm) Lt. Figure 1 demonstrates the observed prostate displacement over time in a single session from one of the patients. In general, the mean (median) maximum prostate drift during actual treatment alone tends to trend towards the following directions at 3.6mm (3.4mm) Inf, 7.4mm (5.2mm) Ant and 2.7mm (2.8mm) Lt. Magnitude of the median maximum prostate displacement increased relatively by 38.4%, 16.7% and 46.6% in the Inf, Ant and Lt directions respectively with added imaging time. Conclusion: Prolonged overall treatment time due to CBCT imaging and verification time increases the intra-fraction prostate motion. We propose the use of 4D Clarity TPUS in place of TPUS with CBCT to reduce imaging time before radiotherapy to reduced total verification time leading to reduced prostate movement. Consequently, the magnitude of intra-fraction prostate motion could be reduced from reduced image acquisition and reconstruction time. This reduces the total in room time per patient and maximises patient through-put and treatment efficiency which is important in a busy radiotherapy centre.

### 5. 3D-Transabdominal Ultrasound and ConeBeam-CT: Comparison of prostate positioning

**Author(s):** Boschetti A.; Bartoncini S.; Fiandra C.; Cavallin C.; Arcadipane F.; Trino E.; Levis M.; Ragona R.; Ricardi U.; Guarneri A.

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

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Purpose or Objective: External beam radiotherapy (EBRT) is a mainstay therapeutic option for prostate cancer and hypofractionated schedules were proposed as a suitable approach. Image guidance procedures are strongly needed to provide adequate accuracy precision, minimize geometric uncertainties and further diminishing unintended normal tissue irradiation. The Elekta Clarity™ platform allows the acquisition of three-dimensional ultrasound scans (3DUS) of the pelvic regions to perform image-guided radiotherapy. In our department, 3DUS is the reference IGRT modality and is used into daily clinical practice for prostate cancer radiotherapy (since from 2009) with optimal clinical results in terms of biochemical control and a good toxicity profile on 160 patients. Moreover 3DUS is a non invasive method with avoidance of extra radiation. In this study 3DUS was compared to grey-based positioning in kilovoltage Cone-Beam Computed Tomography (CBCT) during radiotherapy sessions. Material and Methods: 10 patients affected with organconfined prostate cancer were included. All patients should have a reliable ultrasound visualization of the prostate gland within the Clarity Platform. All patients received 61.1 Gy/26 fractions to the prostate gland and seminal vesicles and 70.2 Gy/26 fractions to the only prostate gland. The prostate positioning was controlled by 3DUS and CBCT. Patients were aligned to skin marks before all of the 260 treatment sessions. Control of the remaining inter-fractional setup error by 3DUS was successfully employed 147 times. During the remainder of fractions, insufficient bladder filling and patient movement were the most frequent obstacles to 3DUS. In total, 210 3DUS scans were compared to CBCT. Results: The average differences in the anterior-posterior (AP), superior-inferior (SI) and lateral (LL) directions from CBCT were 0.25±/0.53 cm, -0.08±/0.52 cm, -0.16±/0.57 cm for 3DUS. Student's t-test was used to test the difference between this US modality against CBCT and the distribution of the differences is reported in Figure 1. Conclusion: Based on the obtained results, significative differences with CBCT were found in all directions. However the average value of the differences is always less than 3 mm in all directions. Differences greater than 1 cm were observed in the AP direction (5%) showing that CBCT imaging modality is not safely interchangeable with 3DUS.

### 6. Monitoring of intra-fraction prostate motion with a new 4D ultrasound device

**Author(s):** Fargier-Voiron M.; Rit S.; Sarrut D.; Pommier P.; Biston M.C.

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

**Publication Date:** Apr 2016

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Purpose or Objective: The emergence of hypofractionated protocols in prostate cancer treatment requires a better accuracy in dose delivery because of an increased risk of toxicity to the safe tissues. The aim of this study was to evaluate intrafraction motions of the target volumes for prostate cancer patients imaged with a new transperineal ultrasound (TP-US) device. Material and Methods: The accuracy of the tracking of the TP-US (Clarity, Elekta, Stockholm, Sweden) probe was first investigated by comparing the measured positions of a target volume in a phantom with the Clarity device and the simultaneous use of a transmitter based positioning



device (RayPilot, Micropos Medical, Sweden). Then intra-fraction motions measured with the TP-US were analyzed for 13 prostate patients (426 sessions) and 14 post-prostatectomy patients (438 sessions). The fraction of time that the target volume was displaced by more than 3 and 5 mm was calculated for tracking times ranging between 60-420s, for each session and each patient. The mean displacements were also calculated for each direction. Percentages of sessions for which thresholds of 3 mm and 5 mm were exceeded during 15 s and 30 s in each direction were determined. Results: Differences between TP-US and transmitter based devices were below 1.5 mm for all directions. The observed motions were patients and sessions dependent and increased with the treatment time. During the first minute, 3D displacements above 3 mm were seen 5% and 1.9% of the time, for prostate and post-prostatectomy patients, respectively while they reached 38% and 10.8% of the time after 7 min of treatment. Maximum 3D displacements above 5 mm were observed after 7 min 11.6% and 1.6% of the time for prostate and post-prostatectomy patients, respectively. Mean displacements in AP, SI and LR directions were  $-0.9\pm 0.8$ mm,  $0.9\pm 0.8$ mm and  $-0.3\pm 0.5$ mm for prostate patients and  $-0.9\pm 0.5$ mm,  $0.2\pm 0.4$ mm and  $0.1\pm 0.4$ mm for postprostatectomy patients. The maximum percentage of sessions for which the prostate and post-prostatectomy volumes exceeded the 3 mm tracking limits for at least 15 s was observed in the AP direction (Table 1). Conversely, minimum displacements were observed in the lateral direction for prostate patients (4.5%), and in the SI direction for postprostatectomy patients (0.7%). Table 1: Conclusion: Results for prostate patients are in agreement with the previously published data [1]. 4D TP-US modality is a promising alternative to irradiating and/or invasive IGRT modalities for intrafraction prostate motion management. In contrast, smaller displacements were observed for postprostatectomy patients than those reported in the literature [2]. Further investigations are in progress to determine the causes of these discrepancies.

## 7. A new image quality protocol for ultrasound image-guided radiotherapy at University Hospital Galway

**Author(s):** Owens I.; Kleefeld C.; O'Brien A.

**Source:** Physica Medica; Feb 2016; vol. 32 (no. 2); p. 420

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Introduction: The Clarity Ultrasound System located in the radiotherapy department at University Hospital Galway is used for localisation of the prostate in ultrasound image-guided radiotherapy. The system consists of an ultrasound transducer and an infrared camera which tracks it. Clarity system QA is focused on 3D spatial tracking, little attention is paid to image quality. Clarity manufacturers provide little support for image quality analysis, third party software (Matlab, QA4US) is required. System presets have a huge impact on image quality. No pre-set information is provided to the user. Methods: This study tested the performance of the Patient and QA presets during routine QA procedures in accordance with AAPM TG154. The study also aimed to find the optimum spatial and contrast resolutions based on user variable parameters, gain and dynamic range respectively. Resolution was measured using CIRS 40 and CIRS 047 ultrasound phantoms as well as QA4US software. In an order to streamline and provide added support for the image quality analysis measurements, fixed 50 mm image calipers were coded onto the images using Matlab software. Conclusion: Optimal image quality parameters for the Clarity system at University Hospital Galway were found and standard QA procedures were changed accordingly. New Matlab support has significantly sped up the analysis procedure.

### Search strategy

Medline, EMBASE

(clarity AND prostate).ti,ab [DT FROM 2016]

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## Radiotherapy - Immobilisation

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1. [A randomised comparison of three different immobilisation devices for thoracic and abdominal cancers.](#)
2. [Stereotactic ablative body radiotherapy for non-small-cell lung cancer: setup reproducibility with novel arms-down immobilization.](#)
3. [Feasibility study of a non-invasive eye fixation and monitoring device using a right-angle prism mirror for intensity-modulated radiotherapy for choroidal melanoma.](#)
4. [Comparison of set up accuracy among three common immobilisation systems for intensity modulated radiotherapy of nasopharyngeal carcinoma patients.](#)
5. [Do we really need customized immobilization devices for modern SBRT in lung cancer?](#)

6. Reproducibility of a non-invasive system for ocular immobilization in robotic stereotactic radiotherapy of ocular melanoma
7. Slant board immobilisation of head-and-neck radiotherapy patients who cannot tolerate a flat position
8. Impact of hydrogel spacer injections on interfraction prostate motion during prostate cancer radiotherapy.
9. A patient immobilization device for prone breast radiotherapy: Dosimetric effects and inclusion in the treatment planning system.
10. Improved setup and positioning accuracy using a three-point customized cushion/mask/bite-block immobilization system for stereotactic reirradiation of head and neck cancer.
11. Comparison of setup errors and comfort levels of two immobilisation systems for head and neck cancer
12. Reproducibility of prone immobilization in breast treatment-a retrospective study
13. Quality assurance for IMRiS phase II study of IMRT in sarcomas: A survey of limb immobilisation
14. Rectal immobilisation device in stereotactic prostate treatment: Intrafraction motion and dosimetry
15. Accurate and stable immobilisation with Lorca Marin masks for head and neck IMRT treatment
16. Immobilization and dosimetric performance of a MRI compatible frame for head and neck patients
17. Less is more: An evaluation of two immobilization devices for prostate cancer radiotherapy
18. Laying the foundation for palliative spine VMAT delivery: A single centre study of rotational error and immobilization
19. Initial experience with an active breathing coordinator device for breath hold radiotherapy treatment of breast

### **1. A randomised comparison of three different immobilisation devices for thoracic and abdominal cancers.**

**Author(s):** Hubie, Catherine; Shaw, Maddison; Bydder, Sean; Lane, Jonny; Waters, Gemma; McNabb, Megan; Kearvell, Rachel; Concannon, Alicia; Bharat, Chrianna; Appleyard, Rob

**Source:** Journal of medical radiation sciences; Dec 2016

**Publication Type(s):** Journal Article

**Abstract:** Patient immobilisation is critically important for both highly conformal conventionally fractionated radiotherapy and for stereotactic body radiotherapy. Different immobilisation devices are available to maintain patient position for radiotherapy but the most suitable one remains unknown. Forty-five patients were randomly allocated to one of three immobilisation devices; the Q fix arm shuttle, BodyFIX without wrap or BodyFIX with wrap. Patients were imaged before and after treatment to ascertain intra-fraction and inter-fraction motion. Bony anatomy was used for matching to determine the positional accuracy of each device. Treatments were timed using a standard method. Patient comfort and staff satisfaction questionnaires were also issued to determine comfort, ease of use and preferences for each device. The BodyFIX without wrap was the more accurate device; however, the differences between the devices were not statistically significant. The BodyFIX with wrap was found to take significantly longer to set up and set down compared to the arm shuttle and the BodyFIX without wrap (all  $P < 0.001$ ). Patients (37%) marginally preferred the BodyFIX with wrap. Most (81%) staff preferred the BodyFIX without wrap. Immobilisation using the BodyFIX without wrap was deemed to be suitable for clinical use. It was a clinically accurate device, the more efficient in terms of set up and set down time, the most preferred by staff and was accepted by patients.

### **2. Stereotactic ablative body radiotherapy for non-small-cell lung cancer: setup reproducibility with novel arms-down immobilization.**

**Author(s):** Moore, Karen; Paterson, Claire; Hicks, Jonathan; Harrow, Stephen; McJury, Mark

**Source:** The British journal of radiology; Dec 2016; vol. 89 (no. 1068); p. 20160227

**Publication Type(s):** Journal Article

**Abstract:** A clinical evaluation of the intrafraction and interfraction setup accuracy of a novel thermoplastic mould immobilization device and patient position in early-stage lung cancer being treated with stereotactic radiotherapy at the Beatson West of Scotland Cancer Centre, Glasgow, UK. 35 patients were immobilized in a novel, arms-down position, with a four-point Klarify™ (Klarify Medical Products, Ohio, US) clear thermoplastic mould fixed to a SinMed (CIVCO Medical solutions, Iowa, US) head and neck board. A knee support was also used for patient comfort and support. Pre- and post-treatment kilovoltage cone beam CT (CBCT) images were fused with the planning CT scan to determine intra- and interfraction motion. A total of 175 CBCT scans were analysed in the longitudinal, vertical and lateral directions. The mean intrafraction errors were  $0.05 \pm 0.77$  mm (lateral),  $0.44 \pm 1.2$  mm (superior-inferior) and  $-1.44 \pm 1.35$  mm (anteroposterior), respectively. Mean composite three-dimensional displacement vector was  $2.14 \pm 1.2$  mm. Interfraction errors were  $-0.66 \pm 2.35$  mm (lateral),  $-0.13 \pm 3.11$  mm (superior-inferior) and  $0.00 \pm 2.94$  mm (anteroposterior), with

three-dimensional vector  $4.08 \pm 2.73$  mm. Setup accuracy for lung image-guided stereotactic ablative radiotherapy using a unique immobilization device, where patients have arms by their sides, has been shown to be safe and favourably comparable to other published setup data where more complex and cumbersome devices were utilised. There was no arm toxicity reported and low arm doses. Advances in knowledge: We report on the accuracy of a novel patient immobilization device.

### **3. Feasibility study of a non-invasive eye fixation and monitoring device using a right-angle prism mirror for intensity-modulated radiotherapy for choroidal melanoma.**

**Author(s):** Inoue, Toshihiko; Masai, Norihisa; Shiomi, Hiroya; Oh, Ryoong-Jin; Uemoto, Kenji; Hashida, Noriyasu

**Source:** Journal of radiation research; Nov 2016

**Publication Type(s):** Journal Article

Available in full text at [Journal of Radiation Research](#) - from Highwire Press

**Abstract:** We aimed to describe the feasibility and efficacy of a novel non-invasive fixation and monitoring (F-M) device for the eyeballs (which uses a right-angle prism mirror as the optic axis guide) in three consecutive patients with choroidal melanoma who were treated with intensity-modulated radiotherapy (IMRT). The device consists of an immobilization shell, a right-angle prism mirror, a high magnification optical zoom video camera, a guide lamp, a digital voice recorder, a personal computer, and a National Television System Committee standard analog video cable. Using the right-angle prism mirror, the antero-posterior axis was determined coincident with the optic axis connecting the centers of the cornea and pupil. The axis was then connected to the guide light and video camera installed on the couch top on the distal side. Repositioning accuracy improved using this method. Furthermore, the positional error of the lens was markedly reduced from  $\pm 1.16$ ,  $\pm 1.68$  and  $\pm 1.11$  mm to  $\pm 0.23$ ,  $\pm 0.58$  and  $\pm 0.26$  mm in the horizontal direction, and from  $\pm 1.50$ ,  $\pm 1.03$  and  $\pm 0.48$  mm to  $\pm 0.29$ ,  $\pm 0.30$  and  $\pm 0.24$  mm in the vertical direction (Patient #1, #2 and #3, respectively). Accordingly, the F-M device method decreased the planning target volume size and improved the dose-volume histogram parameters of the organ-at-risk via IMRT inverse planning. Importantly, the treatment method was well tolerated.

### **4. Comparison of set up accuracy among three common immobilisation systems for intensity modulated radiotherapy of nasopharyngeal carcinoma patients.**

**Author(s):** Lin, Cheng-Guang; Xu, Sen-Kui; Yao, Wen-Yan; Wu, Yu-Qi; Fang, Jian-Lan; Wu, Vincent W C

**Source:** Journal of medical radiation sciences; Sep 2016

**Publication Type(s):** Journal Article

**Abstract:** In intensity modulated radiotherapy (IMRT) of nasopharyngeal carcinoma (NPC) patients, an effective immobilisation system is important to minimise set up deviation. This study evaluated the effectiveness of three immobilisation systems by assessing their set up deviations. Patients were randomly assigned to one of the three immobilisation systems: (1) supine on head rest and base plate (HB); (2) supine with alpha cradle supporting the head and shoulder (AC); (3) supine with vacuum bag supporting the head and shoulder (VB). CBCT was conducted weekly for each patient on the linear accelerator. Image registration was conducted at the nasopharynx (NP) and cervical regions. The translational displacements (latero-medial, antero-posterior and cranio-caudal), rotational displacements (pitch, yaw and roll) and 3D vectors obtained at the NP and cervical regions were recorded and compared among the three systems. The mean translational and rotational deviations were within 3 mm and  $2^\circ$ , respectively, and the range of 3D vector was 1.53-3.47 mm. At the NP region, the AC system demonstrated the smallest translational and rotational deviations and 3D vector. The differences were significant except for the latero-medial, yaw and roll directions. Similarly, at the cervical region, the AC system showed smaller translational and rotational deviations and 3D vector, with only the cranio-caudal and yaw deviations that did not reach statistical significance. Set up deviation was greater in the neck than the NP region. The set up accuracy of the AC system was better than the other two systems, and it is recommended for IMRT of NPC patients in our institution.

### **5. Do we really need customized immobilization devices for modern SBRT in lung cancer?**

**Author(s):** Faria S.; Amri I.A.; Gluszko J.; Patrocinio H.

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

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Purpose: To assess the intra-fraction tumour stability of lung cancer patients treated by cone beam

computed tomographyguided (CBCT) stereotactic body radiotherapy (SBRT) without any frame or immobilization devices. **Materials and Methods:** Localized lung cancer patients were treated with SBRT, positioned supine, with arms held above the head, a foam support under the knees and without any further immobilization. Internal target volume (ITV) was generated from 4D-CT simulation around which a 5 mm symmetric PTV margin was added. All patients (except one) received 48 Gy in 3 fractions. Treatments were planned on Eclipse software (Varian Medical Systems, Inc) using 7-9 static fields or two volumetric modulated arcs for delivery on Varian linacs. Kilovoltage free breathing CBCTs were taken both for initial patient positioning and also immediately after treatment. The pre- and posttreatment CBCTs were compared to confirm that the lung tumour remained inside the PTV and to assess the stability and the suitability of the PTV margin used. Comparisons were performed using a visual match by at least two experienced professionals in Varian's Offline Review software. The time interval between both CBCTs was extracted trying to have a measure of the treatment time. **Results:** There were 44 cases/treatments with pre- and posttreatment CBCTs reviewed. The mean time between the CBCTs (treatment time) was 16.5 +/- 6 minutes (range: 10 to 34 minutes). In all cases the tumour was appropriately kept inside the PTV in the post-treatment CBCT. The mean corrections between pre and post-treatment CBCTs were -0.7 +/- 1.6 mm (range -5.0 to 3.0 mm) vertically, -0.3 +/- 1.7 mm (range -4.8 to 3.0 mm) longitudinally, and -0.4 +/- 1.5 mm (range -4.0 to 2.0 mm) laterally. **Conclusions:** There was no tumour displaced outside the PTV even during relatively slow SBRT delivery in all our lung cancer patients treated with SBRT without any customized immobilization. For our cohort of patients, the PTV margin (5 mm) used was consistent with the measured residual intrafraction motion, also reported in other studies. This experience goes along with the growing trend in frameless, free-breathing SBRT for lung tumours.

#### **6. Reproducibility of a non-invasive system for ocular immobilization in robotic stereotactic radiotherapy of ocular melanoma**

**Author(s):** Iskanderani O.; Beliveau-Nadeau D.; Doucet R.; Coulombe G.; Deborah P.; Roberge D.

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

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Purpose: Amongst uncommon primary ocular tumours, choroidal melanoma represents the most common diagnosis. Our preferred treatment for juxtapapillary tumours has been stereotactic radiotherapy using the Cyberknife radiosurgery system. We aim to describe our immobilization system and quantify its reproducibility. **Methods and Materials:** Patients treated for choroidal melanoma were identified in our radiosurgery database. Patients were imaged at CT simulator with an in-house system which allows visual monitoring of the eye as the patient fixates a small target. All patients were re-imaged at least once prior to and/or during radiotherapy. The patients were treated on the Cyberknife system, 60 Gy in 10 daily fractions, using skull tracking in conjunction with our visual monitoring system. In order to quantify the reproducibility of the eye immobilization system CT scans were co-registered using rigid 6D skull registration. With the scans co-registered x, y and z displacement of the lens/optic nerve insertion were measured manually. From these displacements, a 3D vector was calculated. **Results:** Thirty-four patients were identified, having been treated from October 2010 to September 2015. Thirty-nine coregistrations were performed using 75 scans (2-3 scans per patient). The mean displacements of lens and optic nerve insertion were 0.1 mm and 0.0 mm - confirming that there was no systemic shift from planning to treatment. The median 3D displacements (absolute value) of lens and nerve insertion were 0.8 and 0.7 mm (SD 0.5 and 0.6 mm). Ninety-eight percent of 3D displacements were below 2 mm (maximum 2.4 mm). Following this analysis, we have not changed our GTV to PTV margin of 2-3 mm as it is also meant to account for uncertainties in planning MRI to CT registration, skull tracking as well as contouring variability. **Conclusions:** We have found our stereotactic eye immobilization system to be highly accurate (< 1 mm) and free of systematic error.

#### **7. Slant board immobilisation of head-and-neck radiotherapy patients who cannot tolerate a flat position**

**Author(s):** Qu S.; Singer L.; Chen J.; Shugard E.; Garsa A.A.; Yom S.S.

**Source:** Journal of Radiotherapy in Practice; Sep 2016; vol. 15 (no. 3); p. 303-308

**Publication Type(s):** Journal: Article

**Abstract:** Purpose Patients treated with intensity-modulated radiation therapy (IMRT) for head-and-neck cancer are often positioned supine on a carbon fibre board to which a thermoplastic mask is attached to immobilise the head and shoulders. For patients unable to tolerate a supine position, we developed a tilting board that accommodates a full-scale head-and-shoulder mask. **Materials and methods** Phantom measurements were obtained to confirm the dosimetric accuracy of our treatment planning system when using this board. A patient was simulated in the flat and tilted positions on the board. The two corresponding treatment plans were evaluated by comparing the target coverage and doses with organs at risk. The patient's intra-fraction motion

was quantified during his tilted treatments. Results Phantom measurements confirmed the accuracy of the dosimetric calculations. The tilted plan met dosimetric standards for clinical acceptability. The intra-fraction motion of the patient in the tilted position was  $>3$  mm in any direction. Conclusions The tilting board met clinical requirements for IMRT planning and delivery. Full-scale head-and-shoulder immobilisation was achieved in a more tolerable tilted position.

#### **8. Impact of hydrogel spacer injections on interfraction prostate motion during prostate cancer radiotherapy.**

**Author(s):** Picardi, Cristina; Rouzaud, Michel; Kountouri, Melpomeni; Lestrade, Laetitia; Vallée, Jean Paul; Caparrotti, Francesca; Dubouloz, Angèle; Miralbell, Raymond; Zilli, Thomas

**Source:** Acta oncologica (Stockholm, Sweden); Jul 2016; vol. 55 (no. 7); p. 834-838

**Publication Type(s):** Journal Article

**Abstract:**Background The dosimetric advantage of prostate-rectum spacers to displace the anterior rectal wall outside of the high-dose radiation regions has been clearly established in prostate cancer radiotherapy (RT). The aim of this study was to assess the impact of hydrogel spacer (HS) in the interfraction prostate motion in patients undergoing RT for prostate cancer. Material and methods Twenty prostate cancer patients implanted with three fiducial markers (FM) with ( $n = 10$ ) or without ( $n = 10$ ) HS were analyzed. Displacements between the prostate isocenter based on the FM's position and the bony anatomy were quantified in the left-right (LR), anterior-posterior (AP), superior-inferior (SI) axes by offline analyses of 122 cone beam computed tomography scans. Group systematic (M), systematic ( $\Sigma$ ) and random ( $\sigma$ ) setup errors were determined. Results In patients with or without HS, the overall mean interfraction prostate displacements were 0.4 versus -0.4 mm ( $p = 0.0001$ ), 0.6 versus 0.6 mm ( $p = 0.85$ ), and -0.6 mm versus -0.3 mm ( $p = 0.48$ ) for the LR, AP, and SI axes, respectively. Prostate displacements  $>5$  mm in the AP and SI directions were similar for both groups. No differences in M,  $\Sigma$  and  $\sigma$  setup errors were observed in the three axes between HS + or HS- patients. Conclusions HS implantation does not significantly influence the interfraction prostate motion in patients treated with RT for prostate cancer. The major expected benefit of HS is a reduction of the high-dose levels to the rectal wall without influence in prostate immobilization.

#### **9. A patient immobilization device for prone breast radiotherapy: Dosimetric effects and inclusion in the treatment planning system.**

**Author(s):** De Puyssseleyr, A; De Neve, W; De Wagter, C

**Source:** Physica medica : PM : an international journal devoted to the applications of physics to medicine and biology : official journal of the Italian Association of Biomedical Physics (AIFB); Jun 2016; vol. 32 (no. 6); p. 758-766

**Publication Type(s):** Journal Article

**Abstract:**To assess the dosimetric impact of a patient positioning device for prone breast radiotherapy and assess the accuracy of a treatment planning system (TPS) in predicting this impact. Beam attenuation and build-up dose perturbations, quantified by ionization chamber and radiochromic film dosimetry, were evaluated for 3 components of the patient positioning device: the carbon fiber baseplate, the support cushions and the support wedge for the contralateral breast. Dose calculations were performed using the XVMC dose engine implemented in the Monaco TPS. All components were included during planning CT acquisition. Beam attenuation amounted to 7.57% (6MV) and 5.33% (15MV) for beams obliquely intersecting the couch-top-baseplate combination. Beams traversing large sections of the support wedge were attenuated by 12.28% (6MV) and 9.37% (15MV). For the support cushion foam, beam attenuation remained limited to 0.11% (6MV) and 0.08% (15MV) per centimeter thickness. A substantial loss of dose build-up was detected when irradiating through any of the investigated components. TPS dose calculations accurately predicted beam attenuation by the baseplate and support wedge. A manual density overwrite was needed to model attenuation by the support cushion foam. TPS dose calculations in build-up regions differed considerably from measurements for both open beams and beams traversing the device components. Irradiating through the components of the positioning device resulted in a considerable degradation of skin sparing. Inclusion of the device components in the treatment planning CT allowed to accurately model the most important attenuation effect, but failed to accurately predict build-up doses.

#### **10. Improved setup and positioning accuracy using a three-point customized cushion/mask/bite-block immobilization system for stereotactic reirradiation of head and neck cancer.**

**Author(s):** Wang, He; Wang, Congjun; Tung, Samuel; Dimmitt, Andrew Wilson; Wong, Pei Fong; Edson,

Mark A; Garden, Adam S; Rosenthal, David I; Fuller, Clifton D; Gunn, Gary B; Takiar, Vinita; Wang, Xin A; Luo, Dershan; Yang, James N; Wong, Jennifer; Phan, Jack

**Source:** Journal of applied clinical medical physics; May 2016; vol. 17 (no. 3); p. 6038

**Publication Type(s):** Journal Article

**Abstract:**The purpose of this study was to investigate the setup and positioning uncertainty of a custom cushion/mask/bite-block (CMB) immobilization system and determine PTV margin for image-guided head and neck stereotactic ablative radiotherapy (HN-SABR). We analyzed 105 treatment sessions among 21 patients treated with HN-SABR for recurrent head and neck cancers using a custom CMB immobilization system. Initial patient setup was performed using the ExacTrac infrared (IR) tracking system and initial setup errors were based on comparison of ExacTrac IR tracking system to corrected online ExacTrac X-rays images registered to treatment plans. Residual setup errors were determined using repeat verification X-ray. The online ExacTrac corrections were compared to cone-beam CT (CBCT) before treatment to assess agreement. Intrafractional positioning errors were determined using prebeam X-rays. The systematic and random errors were analyzed. The initial translational setup errors were  $-0.8 \pm 1.3$  mm,  $-0.8 \pm 1.6$  mm, and  $0.3 \pm 1.9$  mm in AP, CC, and LR directions, respectively, with a three-dimensional (3D) vector of  $2.7 \pm 1.4$  mm. The initial rotational errors were up to  $2.4^\circ$  if 6D couch is not available. CBCT agreed with ExacTrac X-ray images to within 2 mm and  $2.5^\circ$ . The intrafractional uncertainties were  $0.1 \pm 0.6$  mm,  $0.1 \pm 0.6$  mm, and  $0.2 \pm 0.5$  mm in AP, CC, and LR directions, respectively, and  $0.0^\circ \pm 0.5^\circ$ ,  $0.0^\circ \pm 0.6^\circ$ , and  $-0.1^\circ \pm 0.4^\circ$  in yaw, roll, and pitch direction, respectively. The translational vector was  $0.9 \pm 0.6$  mm. The calculated PTV margins mPTV(90,95) were within 1.6 mm when using image guidance for online setup correction. The use of image guidance for online setup correction, in combination with our customized CMB device, highly restricted target motion during treatments and provided robust immobilization to ensure minimum dose of 95% to target volume with 2.0 mm PTV margin for HN-SABR.

### 11. Comparison of setup errors and comfort levels of two immobilisation systems for head and neck cancer

**Author(s):** Damodara Kumaran P.; John S.; Isiah R.; Das S.

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

**Publication Type(s):** Journal: Conference Abstract

**Abstract:**Purpose or Objective: This is a Prospective observational study. This study aims to quantify and compare the systematic and random error in two types of immobilization devices namely five point ray cast and BrainLAB immobilization system. This study also looks at the effect of weight loss on the setup error and patients comfort grade in both the immobilization devices. All patients of Head and Neck malignancy planned with Intensity Modulated Radiotherapy [IMRT] were assigned either a five point ray cast or BrainLAB ray immobilization as fixation device. Material and Methods: Patient diagnosed to have head and neck malignancy were assigned to either of the group and prospectively analysed the displacement errors. In both the groups, systematic and random errors were analysed. The CTV-PTV margin was calculated using Van Herks formula and compared. The upper neck and lower bony neck points were also analysed in terms of systematic error, random error and CTV-PTV margin. All the patients were serially monitored with weekly weight and its impact was analysed on the setup errors and margins. Patients' comfort level was analysed at the completion of treatment in both the immobilization devices. Results: The five point ray cast and BrainLAB immobilization was found to be similar in terms of systematic errors and random errors, except in the anterior-posterior [AP] and medial-lateral axis [ML]. BrainLAB showed significant less margin in ML axis [3.61 Vs 3.14 mm,  $p=0.0005$ ] and in AP axis [3.33 Vs 2.66 mm,  $p=0.0001$ ] The total margin required was similar in both the groups. The margin requirement in the upper neck fields was marginally better in the BrianLAB system than the five point ray cast. Weight loss of more than 3kg required more margins, but was not statistically significant. Comfort levels were same in both the groups. Conclusion: The total CTV-PTV margin requirement for five point ray cast and BrainLAB immobilization is less than 5mm in all three directions. In patients requiring only upper neck irradiation BrainLAB system is recommended. Overall Five point ray cast and BrainLAB immobilization was comparable in terms of setup errors, margins and comfort levels.

### 12. Reproducibility of prone immobilization in breast treatment-a retrospective study

**Author(s):** Rodrigues N.; Francisco A.; Vieira S.; Stroom J.; Ribeiro D.; Greco C.; Coelho M.

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

**Publication Type(s):** Journal: Conference Abstract

**Abstract:**Purpose or Objective: Many studies have been conducted regarding the dosimetric advantages of

prone positioning systems for breast radiotherapy treatments, especially for pendulous breasts. However, there is a shortage of publications considering the reproducibility of such systems. This study performs a retrospective patient set-up analysis of a prone positioning system. An estimation of the required safety margin was also calculated in an attempt to predict if patients undergoing breast irradiation in prone position could be safely treated without an online correction protocol. **Material and Methods:** A group of 21 patients with localized breast cancer were treated in prone position (New Horizon™ Prone Breastboard, CIVCO Medical Solutions) with a fractionation scheme of 3.2 Gy x 15 to the boost and simultaneously 2.7 Gy x 15 to the whole breast. An online correction protocol based on CBCT imaging was applied and the initial set-up deviations (i.e. the first registration data for each fraction) were used in this study. The overall mean population error ( $\mu$ ) for each translational direction was calculated, as well as the population systematic (SIGMA) and random (sigma) components. These outcomes were subsequently compared to the results derived from an equally numbered group of patients treated in supine position (C-QUAL™ Breastboard, CIVCO Medical Solutions) with the same fractionation scheme. In both treatment positioning systems CBCT matching criteria was prioritized according to: 1 - Breast contour; 2 - Boost position; 3 - Chest wall. The mean number of repositioning for each population was also considered. Geometrical margins were calculated according to the following margin recipe: (Equation presented) **Results:** Results regarding the evaluated overall mean population error ( $\mu$ ), population systematic (SIGMA) and random (sigma) components and estimated safety margin (Mgeo), for both immobilization techniques, are displayed in Table 1. A 5 mm safety margin is used in our institute and an online protocol is followed. However if an off-line protocol would be applied (50% reduction of systematic errors) the resulting Mgeo, for the prone positioning, would be of 7,6 mm (SI), 8,2 mm (ML) and 5,6 mm (AP) and the applied margin would be insufficient. Regarding workload, patients in prone position are, on average, repositioned 4 times during the 15 fractions against 1 repositioning for patients in supine position, which we consider to be acceptable when considering the dosimetric gains for PTV coverage and OAR. **Conclusion:** Comparing with supine, prone positioning is more unstable and suffers from larger set-up errors, due to both systematic and random components. Additionally, without an online imaging protocol it requires larger safety margins. However, given the dosimetric advantages of prone immobilization, we conclude that this type of positioning can be safely used as long as an adequate margin is applied and especially if an online imaging protocol is followed.

### **13. Quality assurance for IMRiS phase II study of IMRT in sarcomas: A survey of limb immobilisation**

**Author(s):** Simoes R.; Miles E.; Le Grange F.; Seddon B.; Bhat R.

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

**Publication Date:** Apr 2016

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Purpose or Objective: Soft tissue sarcomas are rare malignancies, commonly arising in limbs, with an annual incidence of 3,298 cases in the UK in 2010. Their rarity leads to a lack of published data and experience in limb immobilisation for radiotherapy planning. The IMRiS trial is a phase II study of intensity modulated radiotherapy (IMRT) in primary bone and soft tissue sarcoma, due to open in late 2015. As part of a pre-trial quality assurance (PT QA) programme, we report on the current UK practice of limb soft tissue sarcoma (LSTS) immobilization and the significance for multi-centre trial recruitment. **Material and Methods:** A facility questionnaire (FQ) was circulated to 29 IMRiS centres to investigate variation in immobilisation devices (ID), planning techniques, and imaging protocols. A workshop was held to address limb sarcoma immobilisation and patient set up. Robustness of patient setup at each centre was evaluated based on setup audits, frequency of imaging and the number of patients (pts) treated per centre per annum. **Results:** 27 questionnaires were returned. Less than 1/3 of the responders routinely treat their pts with IMRT (8/27). The remaining 2/3 have little or no experience with IMRT for LSTS. Vacuum bags are currently the most popular ID (9/27), followed by thermoplastic shells (7/27), limb boards (5/27), other devices (3/27) of which 2 used in-house developed and customisable devices, and 1 used common positioning pads. 2 centres combined the use of vacuum bag and shell. 9 centres had audited their setup. However, only 4 had calculated their setup margins on the basis of systematic and random error. The majority of centres follow the recommendations to perform imaging on days 1 to 5 and then weekly. 6 centres perform daily imaging (all 6 treat LSTS with IMRT). Of 6 centres with a high level of setup robustness, 3 are IMRT centres. On average centres treat 24 pts annually (range 3- 53). Currently over half the centres treat less than the calculated average number of pts. **Conclusion:** The results from the FQ and workshop demonstrate variations in treatment modality, ID and imaging frequency across the UK. 70% of IMRiS participating centres will be implementing or further developing IMRT in order to treat LSTS in the study. This will require a change in treatment modality (from 3DCRT to IMRT) in 9 centres. Comprehensive PT QA is required to ensure quality in a trial to be run at centres with such different levels of experience. Robustness of patient setup is important to decrease variability arising from different ID. The PT QA program



will encourage centres to assess robustness of setup through audit and calculation of centre specific margins. The majority of centres will need to review treatment verification as daily imaging is mandated for the trial. We anticipate that centres with less robust setup systems may need more support to safely implement IMRiS, and in response to this a discussion group will be created to allow centres to share their experience.

#### **14. Rectal immobilisation device in stereotactic prostate treatment: Intrafraction motion and dosimetry**

**Author(s):** De Leon J.; Keats S.; Jameson M.; Rai R.; Arumugam S.; Ngo D.; Sidhom M.; Holloway L.; Rivest-Henault D.; Wilton L.; Martin J.

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

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Purpose or Objective: PROMETHEUS (UTN: U1111-1167-2997) is a multicentre clinical trial investigating the feasibility of stereotactic radiotherapy (SBRT) as a boost technique for prostate cancer. The objective of this sub-study is to evaluate intrafraction motion, using cine MRI, and the dosimetric impact when using a rectal immobilisation device (RID). Material and Methods: The initial 10 patients recruited underwent planning CT and MRI, with and without a RID. Cine MRI images were captured using an interleaved T2 HASTE sequence in sagittal and axial planes with a temporal resolution of 5.4 seconds acquired over 4 minutes, the average time for a single SBRT VMAT fraction. Points of interest (POI) were outlined by a single investigator and a validated tracking algorithm measured displacement of these points over the 4 minutes in the anterior - posterior, superior - inferior and left - right directions (Figure 1). Planning CT and MRI scans were fused and contoured by a single investigator. They were planned using a VMAT technique to 19Gy in 2 fractions by a single investigator. The planning priority set for the non - RID plan was to match the coverage achieved in the RID plan. Dose Volume Histogram results of both plans were analysed. Results: There was an overall trend for increasing POI displacement in all directions as time progressed when no RID was in situ. POI remained comparatively stable with the RID. In the sagittal plane, the RID resulted in statistically significant improvement in the range of anterior - posterior displacement over the entire 4 minutes of the inferior anterior and posterior rectal wall (both  $p < 0.001$ ), mid anterior and posterior rectal wall (both  $p = 0.007$ ), anterior prostate ( $p = 0.019$ ), prostate apex ( $p = 0.003$ ) and prostate base ( $p = 0.011$ ). The RID also resulted in improvement in range of superior - inferior displacement of the inferior posterior rectal wall ( $p = 0.002$ ), mid anterior rectal wall ( $p = 0.043$ ) and posterior rectal wall ( $p = 0.023$ ). In the axial plane, the RID resulted in statistically significant improvement in the range of anterior - posterior displacement of the anterior rectal wall ( $p = 0.008$ ) and posterior prostate ( $p = 0.011$ ). For all these points, the RID approximately halved the range of displacements, with some points moving over 2mm when no RID was in situ. Dosimetrically, the use of a RID significantly reduced rectal V16 (0.27cc vs 1.71cc;  $p < 0.001$ ), V14 (1.12cc vs 2.32cc;  $p = 0.02$ ) and Dmax (15.72Gy vs 18.90Gy;  $p < 0.001$ ), as well as percentage of posterior rectal wall receiving 8.5Gy (7.38% vs 12.20%;  $p = 0.003$ ). There was no statistically significant difference between bladder or urethral Dmax, CTV D98 or conformity index between both plans. Conclusion: The rectal immobilisation device used in stereotactic prostate radiotherapy leads to reduced intrafraction motion of the prostate and rectum, with increasing improvement with time. It also results in significant improvement in rectal wall dosimetry.

#### **15. Accurate and stable immobilisation with Lorca Marin masks for head and neck IMRT treatment**

**Author(s):** Ilundain A.; Prieto I.; Marquez E.; Esteban D.; Vasquez W.; Perez A.

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

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Purpose or Objective: The aim of this work is to analyze the setup accuracy and stability resulting from the use of the Lorca Marin thermoplastic masks during the complete course in head and neck cancer treatment with intensity modulated techniques. Material and Methods: 50 consecutive head and neck cancer treatments with intensity modulated radiotherapy (IMRT) were analyzed. Lorca Marin customized masks named Nature were used to immobilize head and neck. These 2-oxepanone polymer thermoplastic masks are 3-points immobilization with frontal and mental reinforcement and 3.2 mm thickness. 3-standard references were marked on the surface of the mask and on the middle chest of the patient for accurate positioning every day. Cone-beam computed tomography scan to verify online the position was performed during 5 consecutive days and after, weekly cone-beam until the end of the treatment. After weekly matching process using automated soft-tissue registration, translational movements along the three axes (x, y, z) were collected and the average for each treatment and each axis was calculated. Displacement's mean of the 50 averages and the standard deviations were analyzed. Results: The resulting displacement average after analyzing 50 treatments was less than 1 mm along the three axes:  $x = (0.62 \pm 0.51)$  mm,  $y = (0.83 \pm 0.63)$  mm,  $z = (0.65 \pm 0.59)$  mm. These setup displacements have remained under than 3 mm in 100% of treatments. These results achieve the International



Commission on Radiation Units and Measurements (ICRU) recommendations regarding the setup margin to compensate the immobilization and positioning errors. Conclusion: The type of patient immobilization devices and their contribution in the setup errors must be taken into account for IMRT. Additionally, the use of different imageguidance systems can significantly alter the size of the required margins. Lorca Marin thermoplastics masks show enough accuracy and stability during complete course of treatment with intensity modulated techniques in head and neck cancer patients.

#### **16. Immobilization and dosimetric performance of a MRI compatible frame for head and neck patients**

**Author(s):** Perez-Rozos A.; Jerez Sainz I.; Lobato Munoz M.; Toledo M.; Medina Carmona J.

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

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Purpose or Objective: Use of CT/RMI image registration for Head&Neck cancers is challenging because of the difficult to maintain the same position in simulation CT and in MRI system. A number of immobilization devices used in radiotherapy are not appropriate for use in MRI because of compatibility problems with the materials or with the acquisition coils. A novel head and neck board, fully compatible with Head and neck MRI coils (ExaFrame, Anatge(R)), has been presented and in this work we analyse setup accuracy of both conventional and MRI compatible board. Material and Methods: Attenuation measurements were done using a diode array (MapCheck2, SunNuclear) inside water equivalent phantom and 6MV photons (TPR<sub>20,10</sub>=0.685, Elekta Synergy) for orthogonal beams. Attenuation is evaluated in the area of mask fixation and in body area of frame. Five consecutive patients with head and neck tumors were assigned to simulation with MRI compatible frame using head and shoulder mask with four fixation points. Immobilization and reproducibility is improved using a customized silicone mold between patient's nose bridge and mask. Reproducibility Every treatment day CBCT images were acquired for treatment isocenter, and shifts in patient position were automatically measured using simulation CT as reference (xvi, Elekta). Displacements in antero-posterior (Vert), cranio-caudal (Long) and medio-lateral (Lat) directions, and rotations about major axis were calculated and compared with conventional carbon fiber immobilization. A total of 150 CBCT images were acquired for CompMRI frame. A group of 30 patients with conventional board was used as control (900 CBCT images). Distribution of displacements, rotation and 3D displacements were compared between both groups. Results: Attenuation measurement is shown in the image, and is lower than 4% for orthogonal incidence. No artifacts on MRI image were observed. Reproducibility between MRI and CT simulation was better than 1 mm in all cases studied, based in direct versus automatic registration. The mean and standard deviation of shifts for the CompMRI board versus conventional board are shown in table 1. An analysis of variance differences using a Fisher test gives statistically significant differences between variances of two groups ( $p < 0.01$ ). The distributions of the absolute displacements were similar in both groups. Conclusion: Our data show that the C-MRI board have low attenuation and a better immobilization and reproducibility than the conventional board. Position reproducibility from MRI simulation and CT simulation was excellent. Combination of MRI compatible board with silicone fixation provided robust immobilization and can be safely used for MRI-CT registration procedures eliminating the use of deformable and complex software algorithms. These data could be used for a potential reduction of margins for the PTV.

#### **17. Less is more: An evaluation of two immobilization devices for prostate cancer radiotherapy**

**Author(s):** Cumal A.; Liszewski B.; Holden L.; D'Alimonte L.

**Source:** Journal of Medical Imaging and Radiation Sciences; Mar 2016; vol. 47 (no. 1)

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Purpose/Aim: The rising expense associated with the implementation of more precise novel technologies in radiation medicine has led to a particularly heightened attention to maximizing value and decreasing costs in cancer care. In light of this focus on efficiency, the value of replacing a standard immobilization device with a potentially equally effective yet more cost efficient solution merits strong consideration for investigation. The utilization of an inexpensive footstrap in the place of the standard Vacloc™ immobilization in patients diagnosed with prostate cancer receiving external radiation will be discussed and evaluated in the context of cost effectiveness. Method/Process: Forty-six prostate cancer patients were accrued to participate in this investigation. Recruited patients were randomized to either the footstrap or the Vacloc™ immobilization and were treated with external beam radiotherapy according to the normal standard of care as defined by their prostate cancer risk category. Cone beam CT image guidance was performed daily prior to treatment and post-treatment scans were performed weekly. To compare intrafractional motion, the magnitude of shifts in the left-right (X), superior-inferior (Y) and anteriorposterior (Z) directions were recorded for each scan and subsequently analyzed. Results/Benefits/Challenges: Evaluating intrafraction

motion, preliminary comparisons from conebeam CT appear to demonstrate no significant difference in magnitude of shifts in any direction (X:  $p=0.66$ , Y:  $p=0.26$ , Z:  $p=0.41$ ) between the use of the Vacloc™ or the footstrap immobilization devices during radiation treatment. Conclusion/Impact/Outcomes: Our preliminary analysis indicates that the Vacloc™ and footstrap devices are comparable for immobilization in the delivery of prostate cancer radiation therapy and merits consideration of practice change to the more cost effective alternative.

### **18. Laying the foundation for palliative spine VMAT delivery: A single centre study of rotational error and immobilization**

**Author(s):** Rozanec N.; Chan E.; Abbas A.; Bhatti M.; Moseley D.

**Source:** Journal of Medical Imaging and Radiation Sciences; Mar 2016; vol. 47 (no. 1)

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Purpose/Aim: At the Stronach Regional Cancer Centre, delivery of palliative radiotherapy to the spine using VMAT is under development. Implementation of VMAT would significantly decrease treatment time, improve dose distributions and decrease toxicity to organs at risk. There has been much discussion regarding immobilization of these patients during treatment, and whether utilization of a thin mattress and knee wedge is appropriate to maximize patient comfort. The purpose of this study was to examine the rotational error in patients receiving radiotherapy to the spine who were immobilized with a thin mattress and knee wedge to ensure rotational errors consistently fall within current institutional guidelines, which would be utilized during implementation of VMAT for this patient population. Method/Process: 9 patients who underwent palliative spine radiotherapy with immobilized using a thin mattress and knee wedge were randomly selected. All daily cone-beam CT (CBCT) scans from all fractions of each treatment course ( $n=11$ ) were analyzed and the mean rotational errors and mean absolute rotational errors for roll, pitch and yaw were recorded. Rotational errors and absolute rotational error for roll, pitch and yaw were also calculated for each course of treatment. The standard deviation for mean rotational error was calculated to identify the magnitude and direction of potential systematic error present. Results/Benefits/Challenges: Absolute mean rotational errors for pitch, roll and yaw were equal to  $1.50^{\circ} \pm 1.59^{\circ}$ ,  $1.00^{\circ} \pm 1.23^{\circ}$  and  $1.00^{\circ} \pm 1.17^{\circ}$  respectively. Mean rotational error for pitch was  $0.81^{\circ} \pm 2.04^{\circ}$ ,  $-0.17^{\circ} \pm 1.58^{\circ}$  for roll and  $-0.10^{\circ} \pm 1.55^{\circ}$  for yaw. Systematic error for pitch was calculated to be  $4.81^{\circ}$ . Mean absolute rotational error for pitch ranged from  $0.4^{\circ}$  to  $3.57^{\circ}$  while roll mean absolute rotational error ranged from  $0.16^{\circ}$  to  $1.84^{\circ}$ , and yaw mean absolute rotational error ranged from  $0.2^{\circ}$  to  $2.83^{\circ}$ . Mean rotational errors in all directions fell well within the institutional tolerance of  $5^{\circ}$ . Conclusion/Impact/Outcomes: Immobilization of patients using a thin mattress and knee wedge produced minimal rotational errors for pitch, roll and yaw. A small systematic error was detected for pitch, but still falls within the  $5^{\circ}$  institutional tolerance for rotational error. The range of rotational errors observed also fell within the institutional tolerance of  $5^{\circ}$ . Therefore, it was concluded that achieving rotational stability is feasible utilizing simple immobilization devices which also promote comfort for palliative patients receiving radiotherapy to the spine.

### **19. Initial experience with an active breathing coordinator device for breath hold radiotherapy treatment of breast**

**Author(s):** Martignano A.; Menegotti L.; Valentini A.; Vanoni V.; Magri E.

**Source:** Physica Medica; Feb 2016; vol. 32

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Introduction: In this work first data on radiation therapy treatments with the Active Breathing Coordinator (ABC, Elekta) device are analyzed. Materials and Methods: The ABC device was used to immobilize the breathing motion in a mid-inhale position with a computer controlled valve. The patients were trained before the simulation CT to establish the patients specific volume threshold and breath hold time. A free breathing CT was also acquired. Two tangential beams treatment plans were created for each patient: one in breath hold and the other in free breathing. The planned dose was 50 Gy in 25 fractions. A software was written to analyze ABC software logs. Differences in ipsilateral lung volume, left ventricle distance from the PTV (for left breast treatments), reproducibility of inhale volume and patient positioning were evaluated. Patient setup reproducibility was verified by comparing EPID images acquired randomly during the treatment with DRR generated by the TPS. Results: Five patients have been evaluated thus far. The inhale breath hold volume threshold has an average value of  $1.34 \pm 0.42$  L and the breath hold duration has an average value of  $20.8 \pm 1.8$  s. The average volume increase of the ipsilateral lung using ABC compared to the free breathing situation is  $67.6 \pm 22.3\%$ . The mean minimum distance increment of the left ventricle to the PTV compared to the free breathing situation is of  $1.3 \pm 0.9$  cm. The mean number of breath holds per fraction is  $8.5 \pm 2.0$  and the

mean inhale volume is 1.7 +/- 0.5 L. The inter-fraction coefficient of variation (CV) of the inhale volume among the patients is 3.6 +/- 0.7%, while the mean intra-fraction CV is 3.5 +/- 1.2%. The mean random setup error during the treatment is below 2 mm. Conclusions: The ABC device is used to reduce respiratory motion in breast cancer patients. The device has demonstrated very good intra- and interfraction reproducibility of inhale volume and patient setup thus far.

### Search strategy

Medline, EMBASE	(immobilis* AND radiotherapy).ti,ab [DT FROM 2016] OR
Medline, EMBASE	(immobiliz* AND radiotherapy).ti,ab [DT FROM 2016]

### Protons

1. Emerging Technologies and Techniques in Radiation Therapy
2. Human papillomavirus status and the relative biological effectiveness of proton radiotherapy in head and neck cancer cells.
3. Long-term follow-up after proton beam therapy for pediatric tumors: A Japanese national survey.
4. Prioritized efficiency optimization for intensity modulated proton therapy.
5. Proton therapy - Present and future.
6. Volumetric response of intracranial meningioma after photon or particle irradiation.
7. Automated Monte Carlo Simulation of Proton Therapy Treatment Plans.
8. Benefit of particle therapy in re-irradiation of head and neck patients. Results of a multicentric in silico ROCOCO trial.
9. Late effects of craniospinal irradiation for standard risk medulloblastoma in paediatric patients: A comparison of treatment techniques
10. Evaluation of focal liver reaction after proton beam therapy for hepatocellular carcinoma examined using GD-EOB-DTPA enhanced hepatic magnetic resonance imaging
11. PRONTOX - proton therapy to reduce acute normal tissue toxicity in locally advanced non-small-cell lung carcinomas (NSCLC): study protocol for a randomised controlled trial.
12. Pencil beam scanning proton therapy vs rotational arc radiation therapy: A treatment planning comparison for postoperative oropharyngeal cancer.
13. Multi-institutional Prospective Study of Reirradiation with Proton Beam Radiotherapy for Locoregionally Recurrent Non-Small Cell Lung Cancer.
14. Intensity-modulated proton therapy, volumetric-modulated arc therapy, and 3D conformal radiotherapy in anaplastic astrocytoma and glioblastoma : A dosimetric comparison.
15. Dosimetric advantages of proton therapy over conventional radiotherapy with photons in young patients and adults with low-grade glioma.
16. An experimental demonstration of a new type of proton computed tomography using a novel silicon tracking detector.
17. Proton radiotherapy for gynecologic neoplasms.
18. 5 year outcomes after proton therapy for treatment of high-risk neuroblastoma (HR-NBL)
19. A prospective assessment of health-related quality of life (HRQOL) outcomes in patients with rhabdomyosarcoma treated with proton radiotherapy
20. A comparison of PedsQL HRQoL outcomes in medulloblastoma patients treated with modern photon (XRT) or proton radiotherapy (PT)
21. Quality-of-life after childhood rhabdomyosarcoma treated with pencil beam scanning proton therapy
22. Lifetime attributable risk of radiation-induced secondary cancer from proton beam therapy compared with that of intensity-modulated X-ray therapy in randomly sampled pediatric cancer patients.
23. A treatment planning study of proton arc therapy for para-aortic lymph node tumors: dosimetric evaluation of conventional proton therapy, proton arc therapy, and intensity modulated radiotherapy.
24. Safety and Local Control of Radiation Therapy for Chordoma of the Spine and Sacrum: A Systematic Review.
25. Proton therapy in paediatric oncology: an Irish perspective.
26. Effective particle energies for stopping power calculation in radiotherapy treatment planning with protons

and helium, carbon, and oxygen ions.

27. Clinical and instrumental characterization of patients with radiation necrosis after proton/carbon ion therapy: A cohort preliminary analysis

28. Proton therapy re-irradiation in large-volume recurrent glioblastoma

29. Can we spare the pancreas and other abdominal organs at risk? A comparison of conformal radiotherapy, helical tomotherapy and proton beam therapy in pediatric irradiation

30. Clinical outcomes and toxicities of proton radiotherapy for gastrointestinal neoplasms: a systematic review.

31. Clinical Outcomes of Proton Radiotherapy for Uveal Melanoma.

32. Clinical Outcomes and Toxicity of Proton Radiotherapy for Breast Cancer.

33. A systematic review of the cost and cost-effectiveness studies of proton radiotherapy.

### 1. Emerging Technologies and Techniques in Radiation Therapy

**Author(s):** Magnuson W.J.; Mahal A.; Yu J.B.

**Source:** Seminars in Radiation Oncology; Jan 2017; vol. 27 (no. 1); p. 34-42

**Publication Type(s):** Journal: Review

**Abstract:** The past decade has brought an improved ability to precisely target and deliver radiation as well as other focal prostate-directed therapy. Stereotactic body radiotherapy (SBRT), proton beam radiation, high-dose-rate (HDR) brachytherapy, as well as nonradiotherapy treatments such as cryoablation and high-intensity focused ultrasound are several therapeutic modalities that have been investigated for the treatment of prostate cancer in an attempt to reduce toxicity while improving cancer control. However, high-risk prostate cancer requires a comprehensive treatment of the prostate as well as areas at risk for cancer spread. Therefore, most new radiation treatment (SBRT, HDR, and proton beam radiation) modalities have been largely investigated in combination with regional radiation therapy. Though the evidence is evolving, the use of SBRT, HDR, and proton beam radiation is promising. Nonradiation focal therapy has been proposed mainly for partial gland treatment in men with low-risk disease, and its use in high-risk prostate cancer patients remains experimental.

### 2. Human papillomavirus status and the relative biological effectiveness of proton radiotherapy in head and neck cancer cells.

**Author(s):** Wang, Li; Wang, Xiaochun; Li, Yuting; Han, Shichao; Zhu, Jinming; Wang, Xiaofang; Molkentine, David P; Blanchard, Pierre; Yang, Yining; Zhang, Ruiping; Sahoo, Narayan; Gillin, Michael; Zhu, Xiaorong Ronald; Zhang, Xiaodong; Myers, Jeffrey N; Frank, Steven J

**Source:** Head & neck; Dec 2016

**Publication Type(s):** Journal Article

Available in full text at [Head and Neck](#) - from Ovid

**Abstract:** Human papillomavirus (HPV)-positive oropharyngeal carcinomas response better to X-ray therapy (XRT) than HPV-negative disease. Whether HPV status influences the sensitivity of head and neck cancer cells to proton therapy or the relative biological effectiveness (RBE) of protons versus XRT is unknown. Clonogenic survival was used to calculate the RBE; immunocytochemical analysis and neutral comet assay were used to evaluate unrepaired DNA double-strand breaks. HPV-positive cells were more sensitive to protons and the unrepaired double-strand breaks were more numerous in HPV-positive cells than in HPV-negative cells (p 1.06). Cell line type and radiation fraction size influenced the RBE. HPV-positive cells were more sensitive to protons than HPV-negative cells maybe through the effects of HPV on DNA damage and repair. The RBE for protons depends more on cell type and fraction size than on HPV status.

### 3. Long-term follow-up after proton beam therapy for pediatric tumors: A Japanese national survey.

**Author(s):** Mizumoto, Masashi; Murayama, Shigeyuki; Akimoto, Tetsuo; Demizu, Yusuke; Fukushima, Takashi; Ishida, Yuji; Oshiro, Yoshiko; Numajiri, Haruko; Fuji, Hiroshi; Okumura, Toshiyuki; Shirato, Hiroki; Hideyuki, Sakurai

**Source:** Cancer science; Dec 2016

**Publication Type(s):** Journal Article

**Abstract:** Proton beam therapy (PBT) is a potential new alternative to treatment with photon radiotherapy that may reduce the risk of late toxicity and secondary cancer, especially for pediatric tumors. The goal of this study was to evaluate the long-term benefits of PBT in cancer survivors. A retrospective observational study of pediatric patients who received PBT was performed at four institutions in Japan. Of 343 patients, 62 were followed up for 5 or more years. These patients included 40 males and 22 females, and had a median age of 10

years (range: 0-19 years) at the time of treatment. The irradiation dose ranged from 10.8 to 81.2 GyE (median: 50.4 GyE). The median follow-up period was 8.1 years (5.0-31.2 years). The 5-, 10- and 20-year rates for grade 2 or higher late toxicities were 18%, 35% and 45%, respectively, and those for grade 3 or higher late toxicities were 6%, 17% and 17% respectively. Univariate analysis showed that the irradiated site (head and neck, brain) was significantly associated with late toxicities. No malignant secondary tumors occurred within the irradiated field. The 10- and 20-year cumulative rates for all secondary tumors, malignant secondary tumors, and malignant nonhematologic secondary tumors were 8% and 16%, 5% and 13%, and 3% and 11%, respectively. Our data indicate that PBT has the potential to reduce the risk of late mortality and secondary malignancy. Longer follow-up is needed to confirm the benefits of PBT for pediatric tumors.

#### **4. Prioritized efficiency optimization for intensity modulated proton therapy.**

**Author(s):** Müller, Birgit S; Wilkens, Jan J

**Source:** Physics in medicine and biology; Dec 2016; vol. 61 (no. 23); p. 8249-8265

**Publication Type(s):** Journal Article

**Abstract:** A high dosimetric quality and short treatment time are major goals in radiotherapy planning. Intensity modulated proton therapy (IMPT) plans obtain dose distributions of great conformity but often result in long delivery times which are typically not incorporated into the optimization process. We present an algorithm to optimize delivery efficiency of IMPT plans while maintaining plan quality, and study the potential trade-offs of these interdependent objectives. The algorithm is based on prioritized optimization, a stepwise approach to implemented objectives. First the quality of the plan is optimized. The second step of the prioritized efficiency optimization (PrEfOpt) routine offers four alternatives for reducing delivery time: minimization of the total spot weight sum (A), maximization of the lowest spot intensity of each energy layer (B), elimination of low-weighted spots (C) or energy layers (D). The trade-off between dosimetric quality (step I) and treatment time (step II) is controlled during the optimization by option-dependent parameters. PrEfOpt was applied to a clinical patient case, and plans for different trade-offs were calculated. Delivery times were simulated for two virtual facilities with constant and variable proton current, i.e. independent and dependent on the optimized spot weight distributions. Delivery times decreased without major degradation of plan quality; absolute time reductions varied with the applied method and facility type. Minimizing the total spot weight sum (A) reduced times by 28% for a similar plan quality at a constant current (changes of minimum dose in the target <1%). For a variable proton current, eliminating low-weighted spots (C) led to remarkably faster delivery (16%). The implementation of an efficiency-optimization step into the optimization process can yield reduced delivery times with similar plan qualities. A potential clinical application of PrEfOpt is the generation of multiple plans with different trade-offs for a multicriteria optimization setting. Then, the planner can select the preferred compromise between treatment time and quality for each individual patient.

#### **5. Proton therapy - Present and future.**

**Author(s):** Mohan, Radhe; Grosshans, David

**Source:** Advanced drug delivery reviews; Dec 2016

**Publication Type(s):** Journal Article Review

**Abstract:** In principle, proton therapy offers a substantial clinical advantage over conventional photon therapy. This is because of the unique depth-dose characteristics of protons, which can be exploited to achieve significant reductions in normal tissue doses proximal and distal to the target volume. These may, in turn, allow escalation of tumor doses and greater sparing of normal tissues, thus potentially improving local control and survival while at the same time reducing toxicity and improving quality of life. Protons, accelerated to therapeutic energies ranging from 70 to 250 MeV, typically with a cyclotron or a synchrotron, are transported to the treatment room where they enter the treatment head mounted on a rotating gantry. The initial thin beams of protons are spread laterally and longitudinally and shaped appropriately to deliver treatments. Spreading and shaping can be achieved by electro-mechanical means to treat the patients with "passively-scattered proton therapy" (PSPT) or using magnetic scanning of thin "beamlets" of protons of a sequence of initial energies. The latter technique can be used to treat patients with optimized intensity modulated proton therapy (IMPT), the most powerful proton modality. Despite the high potential of proton therapy, the clinical evidence supporting the broad use of protons is mixed. It is generally acknowledged that proton therapy is safe, effective and recommended for many types of pediatric cancers, ocular melanomas, chordomas and chondrosarcomas. Although promising results have been and continue to be reported for many other types of cancers, they are based on small studies. Considering the high cost of establishing and operating proton therapy centers, questions have been raised about their cost effectiveness. General consensus is that there is a need to conduct randomized trials and/or collect outcomes data in multi-institutional registries to unequivocally demonstrate the advantage of protons. Treatment planning

and plan evaluation of PSPT and IMPT require special considerations compared to the processes used for photon treatment planning. The differences in techniques arise from the unique physical properties of protons but are also necessary because of the greater vulnerability of protons to uncertainties, especially from inter- and intra-fractional variations in anatomy. These factors must be considered in designing as well as evaluating treatment plans. In addition to anatomy variations, other sources of uncertainty in dose delivered to the patient include the approximations and assumptions of models used for computing dose distributions for planning of treatments. Furthermore, the relative biological effectiveness (RBE) of protons is simplistically assumed to have a constant value of 1.1. In reality, the RBE is variable and a complex function of the energy of protons, dose per fraction, tissue and cell type, end point, etc. These uncertainties, approximations and current technological limitations of proton therapy may limit the achievement of its true potential. Ongoing research is aimed at better understanding the consequences of the various uncertainties on proton therapy and reducing the uncertainties through image-guidance, adaptive radiotherapy, further study of biological properties of protons and the development of novel dose computation and optimization methods. However, residual uncertainties will remain in spite of the best efforts. To increase the resilience of dose distributions in the face of uncertainties and improve our confidence in dose distributions seen on treatment plans, robust optimization techniques are being developed and implemented. We assert that, with such research, proton therapy will be a commonly applied radiotherapy modality for most types of solid cancers in the near future.

### **6. Volumetric response of intracranial meningioma after photon or particle irradiation.**

**Author(s):** Mozes, Petra; Dittmar, Jan Oliver; Habermehl, Daniel; Tonndorf-Martini, Eric; Hideghety, Katalin; Dittmar, Anne; Debus, Jürgen; Combs, Stephanie E

**Source:** Acta oncologica (Stockholm, Sweden); Dec 2016 ; p. 1-7

**Publication Type(s):** Journal Article

**Abstract:** Meningiomas are usually slow growing, well circumscribed intracranial tumors. In symptom-free cases observation with close follow-up imaging could be performed. Symptomatic meningiomas could be surgically removed and/or treated with radiotherapy. The study aimed to evaluate the volumetric response of intracranial meningiomas at different time points after photon, proton, and a mixed photon and carbon ion boost irradiation. In Group A 38 patients received proton therapy (median dose: 56 GyE in 1.8-2 GyE daily fractions) or a mixed photon/carbon ion therapy (50 Gy in 2 Gy daily fractions with intensity modulated radiotherapy (IMRT) and 18 GyE in 3 GyE daily dose carbon ion boost). Thirty-nine patients (Group B) were treated by photon therapy with IMRT or fractionated stereotactic radiotherapy technique (median dose: 56 Gy in 1.8-2 Gy daily fractions). The delineation of the tumor volume was based on the initial, one- and two-year follow-up magnetic resonance imaging and these volumes were compared to evaluate the volumetric tumor response. Significant tumor volume shrinkage was detected at one- and at two-year follow-up both after irradiation by particles and by photons. No significant difference in tumor volume change was observed between photon, proton or combined photon plus carbon ion boost treated patients. WHO grade and gender appear to be determining factors for tumor volume shrinkage. Significant volumetric shrinkage of meningiomas could be observed independently of the applied radiation modality. Long-term follow-up is recommended to evaluate further dynamic of size reduction and its correlation with outcome data.

### **7. Automated Monte Carlo Simulation of Proton Therapy Treatment Plans.**

**Author(s):** Verburg, Joost Mathijs; Grassberger, Clemens; Dowdell, Stephen; Schuemann, Jan; Seco, Joao; Paganetti, Harald

**Source:** Technology in cancer research & treatment; Dec 2016; vol. 15 (no. 6); p. NP35

**Publication Type(s):** Journal Article

**Abstract:** Simulations of clinical proton radiotherapy treatment plans using general purpose Monte Carlo codes have been proven to be a valuable tool for basic research and clinical studies. They have been used to benchmark dose calculation methods, to study radiobiological effects, and to develop new technologies such as in vivo range verification methods. Advancements in the availability of computational power have made it feasible to perform such simulations on large sets of patient data, resulting in a need for automated and consistent simulations. A framework called MCAUTO was developed for this purpose. Both passive scattering and pencil beam scanning delivery are supported. The code handles the data exchange between the treatment planning system and the Monte Carlo system, which requires not only transfer of plan and imaging information but also translation of institutional procedures, such as output factor definitions. Simulations are performed on a high-performance computing infrastructure. The simulation methods were designed to use the full capabilities of Monte Carlo physics models, while also ensuring consistency in the approximations that are common to both pencil beam and Monte Carlo dose calculations. Although some methods need to be tailored to institutional

planning systems and procedures, the described procedures show a general road map that can be easily translated to other systems

### **8. Benefit of particle therapy in re-irradiation of head and neck patients. Results of a multicentric in silico ROCOCO trial.**

**Author(s):** Eekers, Daniëlle B P; Roelofs, Erik; Jelen, Urszula; Kirk, Maura; Granzier, Marlies; Ammazalorso, Filippo; Ahn, Peter H; Janssens, Geert O R J; Hoebbers, Frank J P; Friedmann, Tobias; Solberg, Timothy; Walsh, Sean; Troost, Esther G C; Kaanders, Johannes H A M; Lambin, Philippe

**Source:** Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology; Dec 2016; vol. 121 (no. 3); p. 387-394

**Publication Type(s):** Journal Article

**Abstract:**In this multicentric in silico trial we compared photon, proton, and carbon-ion radiotherapy plans for re-irradiation of patients with squamous cell carcinoma of the head and neck (HNSCC) regarding dose to tumour and doses to surrounding organs at risk (OARs). Twenty-five HNSCC patients with a second new or recurrent cancer after previous irradiation (70Gy) were included. Intensity-modulated proton therapy (IMPT) and ion therapy (IMIT) re-irradiation plans to a second subsequent dose of 70Gy were compared to photon therapy delivered with volumetric modulated arc therapy (VMAT). When comparing IMIT and IMPT to VMAT, the mean dose to all investigated 22 OARs was significantly reduced for IMIT and to 15 out of 22 OARs (68%) using IMPT. The maximum dose to 2% volume (D2) of the brainstem and spinal cord were significantly reduced using IMPT and IMIT compared to VMAT. The data are available on [www.cancerdata.org](http://www.cancerdata.org). In this ROCOCO in silico trial, a reduction in mean dose to OARs was achieved using particle therapy compared to photons in the re-irradiation of HNSCC. There was a dosimetric benefit favouring carbon-ions above proton therapy. These dose reductions may potentially translate into lower severe complication rates related to the re-irradiation.

### **9. Late effects of craniospinal irradiation for standard risk medulloblastoma in paediatric patients: A comparison of treatment techniques**

**Author(s):** Leman J.

**Source:** Radiography; Dec 2016; vol. 22

**Publication Type(s):** Journal: Review

**Abstract:**Background Survival rates for standard risk medulloblastoma are favourable, but craniospinal irradiation (CSI) necessary to eradicate microscopic spread causes life limiting late effects. Aims The aim of this paper is to compare CSI techniques in terms of toxicity and quality of life for survivors. Methods and materials A literature search was conducted using synonyms of 'medulloblastoma', 'craniospinal', 'radiotherapy' and 'side effects' to highlight 29 papers that would facilitate this discussion. Results and discussion Intensity modulated radiotherapy (IMRT), tomotherapy and protons all provide CSI which can reduce dose to normal tissue, however photon methods cannot eliminate exit dose as well as protons can. Research for each technique requires longer term follow up in order to prove that survival rates remain high whilst reducing late effects. Findings/conclusion Proton therapy is the superior method of CSI in term of late effects, but more research is needed to evidence this. Until proton therapy is available in the UK IMRT should be utilised.

### **10. Evaluation of focal liver reaction after proton beam therapy for hepatocellular carcinoma examined using GD-EOB-DTPA enhanced hepatic magnetic resonance imaging**

**Author(s):** Takamatsu S.; Yamamoto K.; Maeda Y.; Shibata S.; Sato Y.; Shimizu Y.; Tameshige Y.; Sasaki M.; Kawamura M.; Terashima K.; Asahi S.; Kondou T.; Kobayashi S.; Matsui O.; Gabata T.

**Source:** PLoS ONE; Dec 2016; vol. 11 (no. 12)

**Publication Type(s):** Journal: Article

Available in full text at [PLoS ONE](https://doi.org/10.1371/journal.pone.0166000) - from National Library of Medicine

Available in full text at [PLoS One](https://doi.org/10.1371/journal.pone.0166000) - from ProQuest

**Abstract:**Background: Proton beam therapy (PBT) achieves good local control for hepatocellular carcinoma (HCC), and toxicity tends to be lower than for photon radiotherapy. Focal liver parenchymal damage in radiotherapy is described as the focal liver reaction (FLR); the threshold doses (TDs) for FLR in the background liver have been analyzed in stereotactic ablative body radiotherapy and brachytherapy. To develop a safer approach for PBT, both TD and liver volume changes are considered clinically important in predicting the



extent of damage before treatment, and subsequently in reducing background liver damage. We investigated appearance time, TDs and volume changes regarding FLR after PBT for HCC. **Material and Methods:** Patients who were treated using PBT and were followed up using gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid-enhanced magnetic resonance imaging (Gd-EOBDTPA MRI) after PBT were enrolled. Sixty-eight lesions in 58 patients were eligible for analysis. MRI was acquired at the end of treatment, and at 1, 2, 3 and 6 months after PBT. We defined the FLR as a clearly depicted hypointense area on the hepatobiliary phase of Gd-EOBDTPA MRI, and we monitored TDs and volume changes in the FLR area and the residual liver outside of the FLR area. **Results:** FLR was depicted in all lesions at 3 months after PBT. In FLR expressed as the 2-Gy equivalent dose ( $\alpha/\beta = 3$  Gy), TDs did not differ significantly ( $27.0 \pm 6.4$  CGE [10 fractions [Fr] vs.  $30.5 \pm 7.3$  CGE [20 Fr]). There were also no correlations between the TDs and clinical factors, and no significant differences between Child-Pugh A and B scores. The volume of the FLR area decreased and the residual liver volume increased, particularly during the initial 3 months. **Conclusion** This study established the FLR dose for liver with HCC, which might be useful in the prediction of remnant liver volume for PBT. Copyright © 2016 Takamatsu et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

### **11. PRONTOX - proton therapy to reduce acute normal tissue toxicity in locally advanced non-small-cell lung carcinomas (NSCLC): study protocol for a randomised controlled trial.**

**Author(s):** Zschaecck, Sebastian; Simon, Monique; Löck, Steffen; Troost, Esther G C; Stützer, Kristin; Wohlfahrt, Patrick; Appold, Steffen; Makocki, Sebastian; Bütof, Rebecca; Richter, Christian; Baumann, Michael; Krause, Mechthild

**Source:** Trials; Nov 2016; vol. 17 (no. 1); p. 543

**Publication Type(s):** Journal Article

Available in full text at [Trials](#) - from BioMed Central

Available in full text at [Trials](#) - from National Library of Medicine

**Abstract:** Primary radiochemotherapy with photons is the standard treatment for locally advanced-stage non-small cell lung cancer (NSCLC) patients. Acute radiation-induced side effects such as oesophagitis and radiation pneumonitis limit patients' quality of life, and the latter can be potentially life-threatening. Due to its distinct physical characteristics, proton therapy enables better sparing of normal tissues, which is supposed to translate into a reduction of radiation-induced side effects. This is a single-centre, prospective, randomised controlled, phase II clinical trial to compare photon to proton radiotherapy up to 66 Gy (RBE) with concomitant standard chemotherapy in patients with locally advanced-stage NSCLC. Patients will be allocated in a 1:1 ratio to photon or proton therapy, and treatment will be delivered slightly accelerated with six fractions of 2 Gy (RBE) per week. The overall aim of the study is to show a decrease of early and intermediate radiation-induced toxicity using proton therapy. For the primary endpoint of the study we postulate a decrease of radiation-induced side effects (oesophagitis and pneumonitis grade II or higher) from 39 to 12%. Secondary endpoints are locoregional and distant failure, overall survival and late side effects. Registered at ClinicalTrials.gov with Identifier NCT02731001 on 1 April 2016.

### **12. Pencil beam scanning proton therapy vs rotational arc radiation therapy: A treatment planning comparison for postoperative oropharyngeal cancer.**

**Author(s):** Apinorasethkul, Ontida; Kirk, Maura; Teo, Kevin; Swisher-McClure, Samuel; Lukens, John N; Lin, Alexander

**Source:** Medical dosimetry : official journal of the American Association of Medical Dosimetrists; Nov 2016

**Publication Type(s):** Journal Article

**Abstract:** Patients diagnosed with head and neck cancer are traditionally treated with photon radiotherapy. Proton therapy is currently being used clinically and may potentially reduce treatment-related toxicities by minimizing the dose to normal organs in the treatment of postoperative oropharyngeal cancer. The finite range of protons has the potential to significantly reduce normal tissue toxicity compared to photon radiotherapy. Seven patients were planned with both proton and photon modalities. The planning goal for both modalities was achieving the prescribed dose to 95% of the planning target volume (PTV). Dose-volume histograms were compared in which all cases met the target coverage goals. Mean doses were significantly lower in the proton plans for the oral cavity (1771cGy photon vs 293cGy proton,  $p < 0.001$ ), contralateral parotid (1796cGy photon vs 1358 proton,  $p < 0.001$ ), and the contralateral submandibular gland (3608cGy photon vs 3251cGy proton,  $p = 0.03$ ). Average total integral dose was 9.1% lower in proton plans. The significant dosimetric sparing seen with



proton therapy may lead to reduced side effects such as pain, weight loss, taste changes, and dry mouth. Prospective comparisons of protons vs photons for disease control, toxicity, and patient-reported outcomes are therefore warranted and currently being pursued.

### **13. Multi-institutional Prospective Study of Reirradiation with Proton Beam Radiotherapy for Locoregionally Recurrent Non-Small Cell Lung Cancer.**

**Author(s):** Chao, Hann-Hsiang; Berman, Abigail T; Simone, Charles B; Ciunci, Christine; Gabriel, Peter; Lin, Haibo; Both, Stefan; Langer, Corey; Lelionis, Kristi; Rengan, Ramesh; Hahn, Stephen M; Prabhu, Kiran; Fagundes, Marcio; Hartsell, William; Mick, Rosemarie; Plastaras, John P

**Source:** Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer; Nov 2016

**Publication Type(s):** Journal Article

**Abstract:**The management of recurrent NSCLC in the setting of prior radiation therapy is challenging. Proton radiotherapy (PRT) is ideally suited to minimize toxicity to previously irradiated organs. We report the safety/feasibility of PRT for NSCLC reirradiation in a prospective multi-institutional study. Between October 2010 and December 2015, 57 patients with recurrent NSCLC in or near their prior radiation field were treated at three proton centers. Patients were classified by tumor volume, location, and clinical characteristics. Toxicities were scored using the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0. Survival outcomes were estimated by using Kaplan-Meier analysis. Fifty-two patients (93%) completed the reirradiation course. Their median age was 65 years (41-86). Patients with high tumor volume (clinical target volume-to-internal target volume ratio  $\geq 250$  cm<sup>3</sup>) were closed to enrollment owing to infeasibility in August 2012. Concurrent systemic therapy was delivered to 67% of patients. Fourteen patients (25%) had evidence of local (n = 9) or regional (n = 5) recurrence. Distant metastases after reirradiation developed in six patients (11%). The 1-year rates of overall and progression-free survival were 59% and 58%, respectively. In total, grade 3 or higher acute and/or late toxicity developed in 24 patients (42%), acute toxicity developed in 22 (39%), and late toxicity developed in seven (12%). Six grade 5 toxicities were observed. Increased overlap with the central airway region, mean esophagus and heart doses, and concurrent chemotherapy were associated with significantly higher rates of grade 3 or higher toxicity. Decreased overall survival was seen with increased mean esophagus dose (p = 0.007). In this prospective study, PRT for recurrent NSCLC is feasible but can be associated with significant toxicity. Providers should remain cautious in reirradiating NSCLC, paying close consideration to tumor volume, location, and relevant dosimetric parameters. Further research is needed for optimal patient selection to improve overall outcomes.

### **14. Intensity-modulated proton therapy, volumetric-modulated arc therapy, and 3D conformal radiotherapy in anaplastic astrocytoma and glioblastoma : A dosimetric comparison.**

**Author(s):** Adeberg, S; Harrabi, S B; Bougaff, N; Bernhardt, D; Rieber, J; Koerber, S A; Syed, M; Sprave, T; Mohr, A; Abdollahi, A; Haberer, T; Combs, S E; Herfarth, K; Debus, J; Rieken, S

**Source:** Strahlentherapie und Onkologie : Organ der Deutschen Rontgengesellschaft ... [et al]; Nov 2016; vol. 192 (no. 11); p. 770-779

**Publication Type(s):** Journal Article

**Abstract:**The prognosis for high-grade glioma (HGG) patients is poor; thus, treatment-related side effects need to be minimized to conserve quality of life and functionality. Advanced techniques such as proton radiation therapy (PRT) and volumetric-modulated arc therapy (VMAT) may potentially further reduce the frequency and severity of radiogenic impairment. We retrospectively assessed 12 HGG patients who had undergone postoperative intensity-modulated proton therapy (IMPT). VMAT and 3D conformal radiotherapy (3D-CRT) plans were generated and optimized for comparison after contouring crucial neuronal structures important for neurogenesis and neurocognitive function. Integral dose (ID), homogeneity index (HI), and inhomogeneity coefficient (IC) were calculated from dose statistics. Toxicity data were evaluated. Target volume coverage was comparable for all three modalities. Compared to 3D-CRT and VMAT, PRT showed statistically significant reductions (p < 0.05) in mean dose to whole brain (-20.2 %, -22.7 %); supratentorial (-14.2 %, -20.8 %) and infratentorial (-91.0 %, -77.0 %) regions; brainstem (-67.6 %, -28.1 %); pituitary gland (-52.9 %, -52.5 %); contralateral hippocampus (-98.9 %, -98.7 %); and contralateral subventricular zone (-62.7 %, -66.7 %, respectively). Fatigue (91.7 %), radiation dermatitis (75.0 %), focal alopecia (100.0 %), nausea (41.7 %), cephalgia (58.3 %), and transient cerebral edema (16.7 %) were the most common acute toxicities. Essential dose reduction while maintaining equal target volume coverage was observed using PRT, particularly in contralaterally located critical neuronal structures, areas of neurogenesis, and structures of neurocognitive functions. These findings were supported by preliminary clinical results confirming the safety and feasibility of

PRT in HGG.

**15. Dosimetric advantages of proton therapy over conventional radiotherapy with photons in young patients and adults with low-grade glioma.**

**Author(s):** Harrabi, S B; Bougaf, N; Mohr, A; Haberer, T; Herfarth, K; Combs, S E; Debus, J; Adeberg, S

**Source:** Strahlentherapie und Onkologie : Organ der Deutschen Röntgengesellschaft ... [et al]; Nov 2016; vol. 192 (no. 11); p. 759-769

**Publication Type(s):** Journal Article

**Abstract:**Low-grade glioma (LGG) is a very common brain tumor in pediatric patients typically associated with a very good prognosis. This prognosis makes it imperative that the risk of long-term treatment-related side effects be kept at an absolute minimum. Proton therapy (PRT) provides a radiation technique that has the potential to further reduce the genesis of radiogenic impairment. We retrospectively assessed 74 patients with LGG who underwent PRT. Conventional three-dimensional photon and PRT plans were generated after contouring structures of neurogenesis, crucial neuronal structures, and areas susceptible to secondary malignancies. Target volume coverage was evaluated using the homogeneity index (HI) and inhomogeneity coefficient (IC). Results were compared using the Wilcoxon-signed rank test, with  $p < 0.05$  being statistically significant. Target volume coverage was comparable for the photon and proton plans. Overall, we could show an essential reduction in maximal, mean, and integral doses in critical neurologic structures, areas of neurogenesis, and structures of neurocognitive function. The study indicated specifically how contralaterally located structures could be spared with PRT. PRT is a highly conformal radiation technique offering superior dosimetric advantages over conventional radiotherapy by allowing significant dose reduction for organs at risk (OAR) that are essential for neurologic function, neurocognition, and quality of life, thus demonstrating the potential of this technique for minimizing long-term sequelae.

**16. An experimental demonstration of a new type of proton computed tomography using a novel silicon tracking detector.**

**Author(s):** Taylor, J T; Poludniowski, G; Price, T; Waltham, C; Allport, P P; Casse, G L; Esposito, M; Evans, P M; Green, S; Manger, S; Manolopoulos, S; Nieto-Camero, J; Parker, D J; Symons, J; Allinson, N M

**Source:** Medical physics; Nov 2016; vol. 43 (no. 11); p. 6129

**Publication Type(s):** Journal Article

**Abstract:**Radiography and tomography using proton beams promise benefit to image guidance and treatment planning for proton therapy. A novel proton tracking detector is described and experimental demonstrations at a therapy facility are reported. A new type of proton CT reconstructing relative "scattering power" rather than "stopping power" is also demonstrated. Notably, this new type of imaging does not require the measurement of the residual energies of the protons. A large area, silicon microstrip tracker with high spatial and temporal resolution has been developed by the Proton Radiotherapy Verification and Dosimetry Applications consortium and commissioned using beams of protons at iThemba LABS, Medical Radiation Department, South Africa. The tracker comprises twelve planes of silicon developed using technology from high energy physics with each plane having an active area of  $\sim 10 \times 10$  cm segmented into 2048 microstrips. The tracker is organized into four separate units each containing three detectors at  $60^\circ$  to one another creating an x-u-v coordinate system. Pairs of tracking units are used to reconstruct vertices for protons entering and exiting a phantom containing tissue equivalent inserts. By measuring the position and direction of each proton before and after the phantom, the nonlinear path for each proton through an object can be reconstructed. Experimental results are reported for tracking the path of protons with initial energies of 125 and 191 MeV. A spherical phantom of 75 mm diameter was imaged by positioning it between the entrance and exit detectors of the tracker. Positions and directions of individual protons were used to create angular distributions and 2D fluence maps of the beam. These results were acquired for 36 equally spaced projections spanning  $180^\circ$ , allowing, for the first time, an experimental CT image based upon the relative scattering power of protons to be reconstructed. Successful tracking of protons through a thick target (phantom) has demonstrated that the tracker discussed in this paper can provide the precise directional information needed to perform proton radiography and tomography. When synchronized with a range telescope, this could enable the reconstruction of proton CT images of stopping power. Furthermore, by measuring the deflection of many protons through a phantom, it was demonstrated that it is possible to reconstruct a new kind of CT image (scattering power) based upon this tracking information alone.

### **17. Proton radiotherapy for gynecologic neoplasms.**

**Author(s):** Verma, Vivek; Simone, Charles B; Wahl, Andrew O; Beriwal, Sushil; Mehta, Minesh P

**Source:** Acta oncologica (Stockholm, Sweden); Nov 2016; vol. 55 (no. 11); p. 1257-1265

**Publication Type(s):** Journal Article

**Abstract:** Proton beam therapy (PBT) is increasingly being used globally to treat a variety of malignancies. This is the first review assessing PBT for gynecologic neoplasms. Dose distribution to organs-at-risk (OARs), particularly bone marrow (BM), is addressed. Clinical outcomes and toxicity data are detailed. Systematic searches of PubMed, EMBASE, abstracts from meetings of the American Society for Radiation Oncology, Particle Therapy Co-Operative Group, and American Society of Clinical Oncology were conducted for publications. There were no restrictions on publication dates. Sixteen original investigations were identified and analyzed for this review. The available evidence for PBT in treating gynecologic cancers is of both low quantity and quality. The most studied scenarios for PBT include treatment of para-aortic lymph nodes, re-irradiation, and as an alternative to brachytherapy, and these also represent indications with the greatest opportunity for demonstrating as yet unproven toxicity reductions. Dosimetric studies have shown significantly decreased dose to OARs, such as the rectum, bladder, bowel, kidneys, BM, and femoral heads. This dose reduction to OARs with PBT is more pronounced within the low-dose volumes than the higher dose volumes, which radiobiologically could be expected to lower second malignancy rates. Clinical data, though no level 1 evidence, show appropriate stage-specific tumor control and outcomes with PBT treatment, along with low toxicity rates. The existing data, albeit limited, warrant and can help guide larger scale and higher quality studies addressing whether PBT could provide clinically meaningful differences in toxicities and outcomes in women with gynecologic neoplasms.

### **18. 5 year outcomes after proton therapy for treatment of high-risk neuroblastoma (HR-NBL)**

**Author(s):** Hill-Kayser C.; Kurtz G.; Lustig R.; Tochner Z.; Balamuth N.; Womer R.; Maris J.; Mosse Y.; Fox E.; Balis F.; Grupp S.; Miller A.; Bagatell R.

**Source:** Pediatric Blood and Cancer; Nov 2016; vol. 63

**Publication Date:** Nov 2016

**Publication Type(s):** Journal: Conference Abstract

**Abstract:** Background/Objectives: Patients with HR-NBL require radiation to the primary tumour site. Proton radiotherapy (PRT) may promote organ sparing, but long-term outcomes have not been studied. Design/Methods: Sequential patients with HR-NBL received PRT at our institution: 2160 cGy(RBE) was delivered to the primary tumour bed (pre-surgical gross tumour volume, 1 cm expansion to clinical target volume, and 0.5 cm expansion to planning target volume). Residual disease was boosted to 3600 cGy(RBE). Persistent metastatic sites received 2160 cGy(RBE). 4D CT was utilized for planning. All procedures were IRB approved. Results: From 9/2010-9/2015, 45 patients with HR-NBL received PRT following multiagent chemotherapy, resection, and high-dose chemotherapy; 10 (22%) also received therapeutic MIBG. Median age was 46m at the time of PRT (10m - 12y); 24 (53%) were boys. Primary tumors were adrenal in 40 (89%); 11 (24%) received boost. Ten metastatic sites in 8 patients were radiated. Double scattered (DS) proton beams were used for 19 (41%) patients, in combination with x-rays for 2 (4%). The remaining 26 (58%) received pencil beam scanning (PBS) which became available in 1/2013. With median follow-up of 26m (6 - 58m) from PRT, 38 (84%) patients are alive, and 36 (80%) disease free. One (2%) experienced abdominal local recurrence; the remaining 8 (18%) experienced relapse at distant, non-radiated sites. No patient has experienced WHO G3/4 long-term toxicity. Intended constraints for organs at risk were achieved for all, including 80% of combined kidneys < 1800 cGy(RBE) and 70% of liver < 20 cGy(RBE). Posterior beams were used for both DS and PBS, although PBS plans required, on average, fewer iterations. Conclusion: We observe excellent outcomes in patients treated with PRT for HR-NBL over a 5 year period, with 84% of patients alive and 98% free of local recurrence. This safe treatment maximizes normal tissue preservation and is appropriate for this patient population.

### **19. A prospective assessment of health-related quality of life (HRQOL) outcomes in patients with rhabdomyosarcoma treated with proton radiotherapy**

**Author(s):** Vatner R.; Goldberg S.; Gaudet D.; Gallotto S.; Goebel C.; MacDonald S.; Tarbell N.; Yock T.; Friedmann A.; Kuhlthau K.

**Source:** Pediatric Blood and Cancer; Nov 2016; vol. 63

**Publication Type(s):** Journal: Conference Abstract

**Abstract:**Background/Objectives: HRQoL outcomes are not well described for children with rhabdomyosarcoma. We report the child-self-report (CSR) and parent-proxy-report (PPR) PedsQL HRQoL Core and Cancer module scores in a proton treated cohort. Design/Methods: Children with rhabdomyosarcoma enrolled on a prospective HRQoL protocol were assessed during proton therapy (baseline) and annually from 2005-present. Mean QoL scores were compared with published data from healthy controls using Student's t-test. Linear mixed effects models were generated to determine longitudinal trajectory of PedsQL scores, dichotomized by age (>///1 year followup). Baseline mean Total Core Scores (TCS) were lower compared to controls (CSR: 76.9 vs. 83.8, p=0.05; PPR: 71.2 vs. 82.7, pGrade 3 toxicity during treatment (p=0.001) and for IRS Group 1-2 patients who underwent surgery prior to radiotherapy (p=0.001). Conclusion: Children with rhabdomyosarcoma treated with proton therapy had lower QoL scores during treatment compared to healthy controls, but these scores increased after treatment and became indistinguishable from healthy controls. Younger age, surgical resection prior to radiotherapy, and severe toxicity during treatment had a negative effect on survivors' HRQoL.

## **20. A comparison of PedsQL HRQoL outcomes in medulloblastoma patients treated with modern photon (XRT) or proton radiotherapy (PT)**

**Author(s):** Yock T.; Goldberg S.; Gaudet D.E.; Gallotto S.L.; Weyman E.A.; MacDonald S.M.; Tarbell N.J.; Nartowicz J.A.; Stone J.F.; Saran F.; Wharram B.; Mandeville H.C.; Zacharoulis S.; Ebb D.H.; Kuhlthau K.A.

**Source:** Pediatric Blood and Cancer; Nov 2016; vol. 63

**Publication Type(s):** Journal: Conference Abstract

**Abstract:**Background/Objectives: Comparative HRQoL outcomes in proton and photon treated cohorts are lacking. Here we compare the child-self-report (CSR) and parent-proxy-report (PPR) Ped-sQLHRQOL Core scores in contemporary (2004-2014) proton-treated (PT) and photon-treated (XRT) cohorts. Design/Methods: In the proton cohort, medulloblastoma patients were enrolled on a prospective HRQoL protocol and assessed with PedsQL annually if NED; the latest available follow-up survey was used for analysis. In the photon cohort, medulloblastoma survivors were administered the PedsQL Core survey in a cross-sectional study design. Mean scores in both groups were compared using student's t-test. Then subgroups by age (<8 v. 8+), boost volume (TB v. WP), posterior fossa syndrome (PFS, yes/no), sex, and M-stage(M0v.M+) were compared between by modality. Results: There were 73 patients (69 CSR, 71 PPR) in the proton cohort and 52 (45 CSR, 35 PPR) in the photon cohort. Median PT follow-up was 4.0 (1.0-10.0) years and median XRT follow up was 5.9 (1.3-11.6) years. Proton PPR report Total-Core-Score(TCS) of 69.3 and XRT PPR report scores of 53.1 (p<0.001). Proton children report TCS of 76.0 and XRT children report scores of 63.3 (p<0.001). Proton children report TCS of 7.8 points lower than US healthy control children (p<0.001); whereas proton parents report 13.4 points lower than controls (p<0.001). Photon children report TCS 20.6 points lower than UK controls (p<0.001); whereas parents report 31.5 points lower than UK controls (p<0.001). PedsQL subscores (physical/ psychosocial) and affects of the clinical variables will be reported at the meeting. Conclusion: In this comparison of contemporarily treated proton and photon children with medulloblastoma, TCS QoL outcomes appear better in children treated with proton radiotherapy in both child and parent proxy reports. However, both cohorts score lower than the US healthy control population.

## **21. Quality-of-life after childhood rhabdomyosarcoma treated with pencil beam scanning proton therapy**

**Author(s):** Weber D.C.; Albertini F.; Kliebisch U.; Bojaxhiu B.; Bolsi A.; Walser M.; Lomax T.; Schneider R.; Leiser D.; Malyapa R.; Timmermann B.; Calaminus G.

**Source:** Pediatric Blood and Cancer; Nov 2016; vol. 63

**Publication Type(s):** Journal: Conference Abstract

**Abstract:**Background/Objectives: Radiotherapy can impair the Quality-of-Life (QoL) of children with cancer treated with this modality. Proton therapy (PT) could potentially mitigate this effect and consequentially the QoL of children with rhabdomyosarcoma (RMS) treated with Pencil Beam Scanning (PBS) PT was assessed at the Paul Scherrer Institute. Design/Methods: QoL data were prospectively collected between January 2005 to December 2014 in RMS patients (n=34) aged 5 - 16 (median, 7) years treated with PBS PT. The PedQoL questionnaire is an established, multidimensional instrument that covers 8 domains and is available as proxy-rating version for the parents (PedQoL proxy) and self-rating version for children older than 4 years (PedQoL self). Cross-sectional QoL data from an independent normative group with proxy assessments of healthy children between 5 and 16 years of age provided the comparison data. Results: All QoL scores of patients were significantly (p<0.01) lower when compared to the normative group (Fig.) at the start of PT (E1). Globally the mean QoL scores were 81.02+/-17.34 and 54.17+/-30.53 for the normative population and patients, respectively. Two years after PT (E2), mean scores of patients in all but 3 domains were however either equal or superior to

the normative population (Fig.). In two domains (i.e. self-esteem and social functioning family), the observed mean QoL E2 scores were higher in patients when compared to the normative population, although this difference was statistically not significant. The greatest increase of mean scores at (E1) and (E2) was observed for the subjective well-being (E1: 54.17+/-30.53 vs. E2: 83.33+/-19.50) and physical functioning (E1: 50.17+/-15.15 vs. E2: 66.33+/-7.93) domains. Conclusion: The QoL was excellent in a majority of children with RMS 2 years after the start of PBS PT. Mean QoL scores of patients were not significantly impaired in all domains when compared to the normative population.

## **22. Lifetime attributable risk of radiation-induced secondary cancer from proton beam therapy compared with that of intensity-modulated X-ray therapy in randomly sampled pediatric cancer patients.**

**Author(s):** Tamura, Masaya; Sakurai, Hideyuki; Mizumoto, Masashi; Kamizawa, Satoshi; Murayama, Shigeyuki; Yamashita, Haruo; Takao, Seishin; Suzuki, Ryusuke; Shirato, Hiroki; Ito, Yoichi M

**Source:** Journal of radiation research; Oct 2016

**Publication Type(s):** Journal Article

Available in full text at [Journal of Radiation Research](#) - from Highwire Press

**Abstract:** To investigate the amount that radiation-induced secondary cancer would be reduced by using proton beam therapy (PBT) in place of intensity-modulated X-ray therapy (IMXT) in pediatric patients, we analyzed lifetime attributable risk (LAR) as an in silico surrogate marker of the secondary cancer after these treatments. From 242 pediatric patients with cancers who were treated with PBT, 26 patients were selected by random sampling after stratification into four categories: (i) brain, head and neck, (ii) thoracic, (iii) abdominal, and (iv) whole craniospinal (WCNS) irradiation. IMXT was replanned using the same computed tomography and region of interest. Using the dose-volume histograms (DVHs) of PBT and IMXT, the LARs of Schneider et al were calculated for the same patient. All the published dose-response models were tested for the organs at risk. Calculation of the LARs of PBT and IMXT based on the DVHs was feasible for all patients. The means  $\pm$  standard deviations of the cumulative LAR difference between PBT and IMXT for the four categories were (i)  $1.02 \pm 0.52\%$  ( $n = 7$ ,  $P = 0.0021$ ), (ii)  $23.3 \pm 17.2\%$  ( $n = 8$ ,  $P = 0.0065$ ), (iii)  $16.6 \pm 19.9\%$  ( $n = 8$ ,  $P = 0.0497$ ) and (iv)  $50.0 \pm 21.1\%$  ( $n = 3$ ,  $P = 0.0274$ ), respectively (one tailed t-test). The numbers needed to treat (NNT) were (i) 98.0, (ii) 4.3, (iii) 6.0 and (iv) 2.0 for WCNS, respectively. In pediatric patients who had undergone PBT, the LAR of PBT was significantly lower than the LAR of IMXT estimated by in silico modeling. Although a validation study is required, it is suggested that the LAR would be useful as an in silico surrogate marker of secondary cancer induced by different radiotherapy techniques.

## **23. A treatment planning study of proton arc therapy for para-aortic lymph node tumors: dosimetric evaluation of conventional proton therapy, proton arc therapy, and intensity modulated radiotherapy.**

**Author(s):** Rah, Jeong-Eun; Kim, Gwe-Ya; Oh, Do Hoon; Kim, Tae Hyun; Kim, Jong Won; Kim, Dae Yong; Park, Sung Yong; Shin, Dongho

**Source:** Radiation oncology (London, England); Oct 2016; vol. 11 (no. 1); p. 140

**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

Available in full text at [Radiation Oncology](#) - from ProQuest

**Abstract:** The purpose of this study is to evaluate the dosimetric benefits of a proton arc technique for treating tumors of the para-aortic lymph nodes (PALN). In nine patients, a proton arc therapy (PAT) technique was compared with intensity modulated radiation therapy (IMRT) and proton beam therapy (PBT) techniques with respect to the planning target volume (PTV) and organs at risk (OAR). PTV coverage, conformity index (CI), homogeneity index (HI) and OAR doses were compared. Organ-specific radiation induced cancer risks were estimated by applying organ equivalent dose (OED) and normal tissue complication probability (NTCP). The PAT techniques showed better PTV coverage than IMRT and PBT plans. The CI obtained with PAT was  $1.19 \pm 0.02$ , which was significantly better than that for the IMRT techniques. The HI was lowest for the PAT plan and highest for IMRT. The dose to the OARs was always below the acceptable limits and comparable for all three techniques. OED results calculated based on a plateau dose-response model showed that the risk of secondary cancers in organs was much higher when IMRT or PBT were employed than when PAT was used. NTCPs of PAT to the stomach (0.29 %), small bowel (0.69 %) and liver (0.38 %) were substantially lower than those of IMRT and PBT. This study demonstrates that there is a potential role for PAT as a commercialized instrument in the future to proton therapy.

#### **24. Safety and Local Control of Radiation Therapy for Chordoma of the Spine and Sacrum: A Systematic Review.**

**Author(s):** Pennicooke, Brenton; Laufer, Ilya; Sahgal, Arjun; Varga, Peter P; Gokaslan, Ziya L; Bilsky, Mark H; Yamada, Yoshiya J

**Source:** Spine; Oct 2016; vol. 41

**Publication Type(s):** Journal Article

**Abstract:** Systematic literature review. To assess the toxicity, common radiation doses, and local control (LC) rates of radiation therapy for chordoma of the spine and sacrum and identify the difference in LC and toxicity between adjuvant, salvage, and primary therapy using radiation. Chordoma of the spine is typically a low-grade malignant tumor thought to be relatively radioresistant with a high rate of local recurrence and the potential for metastases. Improved results of modern radiation therapy in the treatment of chordoma support exploration of its role in the management of primary/de novo chordoma or recurrent chordoma. We conducted a systematic literature review using PubMed and Embase databases to assess information available regarding the toxicity, LC rates, and overall survival (OS) rates for adjuvant, salvage, and primary radiation therapy for spinal and sacral chordoma. A total of 40 articles were reviewed. Evidence quality was low or very low. The highest rates of LC and OS were with early adjuvant RT for primary/de novo disease. Salvage RT for recurrent disease has very small cohorts and thus strong conclusions were not able to be made. The use of pre- and/or post-operative photon image-guided radiotherapy (IGRT), proton or carbon ion therapy should be considered for patients undergoing surgery for the treatment of primary and recurrent chordomas in the mobile spine and sacrum, since these RT modalities may improve local control. Preoperative evaluation by the surgeon and radiation oncologist should be used to formulate a cohesive treatment plan. The use of photon IGRT or carbon ion therapy as the primary treatment of chordoma, when currently in its developmental stage, shows promise and requires clear delineation of toxicity profile and long-term local control. 2.

#### **25. Proton therapy in paediatric oncology: an Irish perspective.**

**Author(s):** Lee, K A; O'Sullivan, C; Daly, P; Pears, J; Owens, C; Timmermann, B; Ares, C; Combs, S E; Indelicato, D; Capra, M

**Source:** Irish journal of medical science; Oct 2016

**Publication Type(s):** Journal Article

**Abstract:** Proton therapy (PT) is a radiotherapy treatment modality that uses protons, rather than conventional photons. PT is often used in paediatric oncology due to its reported capability to reduce acute and late adverse treatment effects. As PT is unavailable in Ireland, patients are referred abroad for treatment. To: (1) produce a descriptive study of Irish children referred abroad for PT, and (2) discuss the case for PT in general. A retrospective review of all children referred for PT before October 2015 was performed. Information was gathered regarding demographics, diagnosis, referral timeline, adverse effects attributable to PT, current status and cost. A review of the relevant literature was performed. Seventeen children treated in Ireland have been referred abroad for PT. The largest number was in the 0-4 year old group. At initial diagnosis the median age was 4.8 years. The average cost per child was €37,312. Two patients suffered disease relapse. Four have encountered PT-related adverse effects. Despite the fact that >100,000 patients worldwide have been treated with PT, the level of published evidence to support superiority over conventional treatment remains low. It is debated that randomised control trials in this area would be inconsistent with the principle of clinical equipoise. In contrast, there is a call for level 1 evidence to justify drastic changes in patient care, particularly in light of recent reports of unexpected toxicities. In time, careful evaluation, follow-up and clinical trials will likely support the preferential use of PT in children.

#### **26. Effective particle energies for stopping power calculation in radiotherapy treatment planning with protons and helium, carbon, and oxygen ions.**

**Author(s):** Inaniwa, T; Kanematsu, N

**Source:** Physics in medicine and biology; Oct 2016; vol. 61 (no. 20); p. N542

**Publication Type(s):** Journal Article

**Abstract:** The stopping power ratio (SPR) of body tissues relative to water depends on the particle energy. For simplicity, however, most analytical dose planning systems do not account for SPR variation with particle energy along the beam's path, but rather assume a constant energy for SPR estimation. The range error due to this simplification could be indispensable depending on the particle species and the assumed energy. This error can be minimized by assuming a suitable energy referred to as an 'effective energy' in SPR estimation. To date,

however, the effective energy has never been investigated for realistic patient geometries. We investigated the effective energies for proton, helium-, carbon-, and oxygen-ion radiotherapy using volumetric models of the reference male and female phantoms provided by the International Commission on Radiological Protection (ICRP). The range errors were estimated by comparing the particle ranges calculated when particle energy variations were and were not considered. The effective energies per nucleon for protons and helium, carbon, and oxygen ions were 70 MeV, 70 MeV, 131 MeV, and 156 MeV, respectively. Using the determined effective energies, the range errors were reduced to  $\leq 0.3$  mm for respective particle species. For SPR estimation of multiple particle species, an effective energy of 100 MeV is recommended, with which the range error is  $\leq 0.5$  mm for all particle species.

### **27. Clinical and instrumental characterization of patients with radiation necrosis after proton/carbon ion therapy: A cohort preliminary analysis**

**Author(s):** Diamanti L.; Bini P.; Bernini S.; Sinforiani E.; Galimberti C.; Berzero G.; Iannalfi A.; Ciurlia E.; Vitolo V.; Viselner G.

**Source:** Neuro-Oncology; Oct 2016; vol. 18

**Publication Type(s):** Journal: Conference Abstract

**Abstract:**Background And Purpose: Radiation necrosis is a delayed radiation- induced complication, that can causes heterogeneous neurological deficit. However, patients can manifest poor symptoms, in view of a serious radiological situation. Furthermore, the clinical evaluation contemplates the use of brief and analytic-less tools (RTOG/EORTC criteria or CTCAE). Hence, other conditions, such as cognitive impairment, are underestimated. Across this vague scenario and the lack of longitudinal studies in literature, the decision about starting therapy become difficult. We aim to describe the characteristics of our cohort, in order to redefine the clinical spectrum of patients with radiation necrosis, and provide a punctual therapeutic approach. Methods: We retrospectively enrolled 15 patients (11 females and 4 males; age range, 28-73 years at the moment of radiotherapy), that developed radiation necrosis after proton/carbon ion therapy for skull base tumors: non typical meningioma (2), nasopharyngeal carcinoma (5), chordoma (6), chondrosarcoma (2). Patients were recruited in Pavia (C. Mondino Neurological National Institute and National Centre of Oncological Hadrontherapy), from March 2015 to March 2016. Brain MRI with gadolinium, neuropsychological tests, electroencephalogram (EEG) were performed in all patients. Results: The median prescribed dose was 64.4 Gy (range, 14-74 Gy) and the dose per fraction was 2 Gy. One patient underwent two carbon ion therapies, while three patients received prior conventional radiation treatment. The median time from the end of radiation therapy until the diagnosis of radiation necrosis was 18.1 months (range, 7-37), and the lesions were almost always in the temporal lobe (only one in the frontal lobe). Apparently, in 7 patients (almost 50%) radiation necrosis was an incidental finding during the radiological follow up, and the others manifested low grade clinical symptoms (median RTOG/EORTC grade, 1.8). In contrast, when tested, more than 70% of patients had cognitive impairment (memory was the most affected domain in most of them), and EEG evidenced abnormalities (epileptic or focal slow alterations corresponding to the lesion) in about 50% of patients. From the radiological point of view, brain MRI revealed multiple lesions in 5 patients, involving bilateral temporal lobe in 2 of them. The median LENT-SOMA grade for the radiologic part was 2.4. Eventually, 8 patients were put on steroids. Conclusions: The application of the common clinical scales for the evaluation of patients with radiation necrosis is poor. We suggest to screen patients for cognitive functions and electroencephalographic activity, because the abnormalities can be only revealed by instrumental assessment. Brain MRI supplies further clues for the structural definition of lesions. This approach allows to collect many elements that are pivotal in the therapeutic decision.

### **28. Proton therapy re-irradiation in large-volume recurrent glioblastoma**

**Author(s):** Amelio D.; Widesott L.; Vennarini S.; Fellin F.; Righetto R.; Lorentini S.; Farace P.; Schwarz M.; Amichetti M.; Maines F.

**Source:** Neuro-Oncology; Oct 2016; vol. 18

**Publication Type(s):** Journal: Conference Abstract

**Abstract:**Purpose: To report preliminary results of re-irradiation with proton therapy (PT) in large-volume recurrent glioblastoma (rGBM). Matherial/Methods: Between January and December 2015 ten patients (pts) with rGBM were re-irradiated with PT. All pts were previously treated with photon radiotherapy (60 Gy) with concomitant and adjuvant TMZ for 1-20 cycles (median, 7). Seven pts were re-irradiated at first relapse/progression. Four patients were re-irradiated after partial tumor resection. Median age and Karnofsky performance status at re-irradiation were 57 years (range, 41-68) and 80%, (range, 70-100), respectively. Median time between prior radiotherapy and PT was 9 months (range, 5-24). Target definition was based on CT,

MR, and 18F-DOPA PET imaging. GTV included any area of contrast enhancement after contrast medium administration plus any pathological PET uptake regions. CTV was generated by adding to GTV a 3-mm uniform margin manually corrected in proximity of anatomical barriers. CTV was expanded by 4 mm to create PTV. Median PTV volume was 90 cc (range, 46-231). All pts received 36 GyRBE in 18 fractions. Four pts also received concomitant temozolomide (75 mg/m<sup>2</sup>/die, 7 days/week). All pts were treated with active beam scanning PT using 2-3 fields with single field optimization technique. RESULTS: All pts completed the treatment without breaks. Registered acute side effects (according to Common Terminology Criteria for Adverse Events version 4.0 - CTCAE) include grade 1-2 skin erythema, alopecia, fatigue, conjunctivitis, concentration impairment, dysphasia, and headache. There were no grade 3 or higher toxicities. One patient developed grade 1 neutropenia. Five pts started PT under steroids (2-7 mg/daily); two of them reduced the dose during PT, while three kept the same steroids dose. None of remaining pts needed steroids therapy. Registered late side effects (according to CTCAE version 4.0) include grade 1-2 alopecia, fatigue, concentration impairment, and dysphasia. During follow-up two pts (20%) developed radionecrosis (diagnosed at imaging) with mild symptoms controlled with steroids. There were no grade 3 or higher toxicities. The median progression-free survival (PFS) was 6.4 months, while the 3-, 6- and 9-month PFS rates were 80%, 67% and 22%, respectively. Median overall survival (OS) after PT was not achieved, while the 6- and 12-month survival after PT rates were 100% and 60%, respectively. Conclusion: PT re-irradiation of large-volume rGBM showed to be feasible and safe even with concomitant chemotherapy administration. Despite the small number of patients and the retrospective nature of the study PFS and OS rates were promising and deserve further evaluation in a larger pts sample.

### **29. Can we spare the pancreas and other abdominal organs at risk? A comparison of conformal radiotherapy, helical tomotherapy and proton beam therapy in pediatric irradiation**

**Author(s):** Jouglar E.; Demoor-Goldschmidt C.; Mahe M.-A.; Supiot S.; Wagner A.; Lacornerie T.; Delpon G.; Champion L.; Meingan P.; Bernier V.

**Source:** PLoS ONE; Oct 2016; vol. 11 (no. 10)

**Publication Type(s):** Journal: Article

Available in full text at [PLoS ONE](#) - from National Library of Medicine

Available in full text at [PLoS One](#) - from ProQuest

**Abstract:** Objectives Late abdominal irradiation toxicity during childhood included renal damage, hepatic toxicity and secondary diabetes mellitus. We compared the potential of conformal radiotherapy (CRT), helical tomotherapy (HT) and proton beam therapy (PBT) to spare the abdominal organs at risk (pancreas, kidneys and liver- OAR) in children undergoing abdominal irradiation. Methods We selected children with abdominal tumors who received more than 10 Gy to the abdomen. Treatment plans were calculated in order to keep the dose to abdominal OAR as low as possible while maintaining the same planned target volume (PTV) coverage. Dosimetric values were compared using the Wilcoxon signed-rank test. Results The dose distribution of 20 clinical cases with a median age of 8 years (range 1+/-14) were calculated with different doses to the PTV: 5 medulloblastomas (36 Gy), 3 left-sided and 2 right-sided nephroblastomas (14.4 Gy to the tumor + 10.8 Gy boost to para-aortic lymphnodes), 1 left-sided and 4 right-sided or midline neuroblastomas (21 Gy) and 5 Hodgkin lymphomas (19.8 Gy to the para-aortic lymphnodes and spleen). HT significantly reduced the mean dose to the whole pancreas (WP), the pancreatic tail (PT) and to the ipsilateral kidney compared to CRT. PBT reduced the mean dose to the WP and PT compared to both CRT and HT especially in midline and right-sided tumors. PBT decreased the mean dose to the ipsilateral kidney but also to the contralateral kidney and the liver compared to CRT. Low dose to normal tissue was similar or increased with HT whereas integral dose and the volume of normal tissue receiving at least 5 and 10 Gy were reduced with PBT compared to CRT and HT. Conclusion In children undergoing abdominal irradiation therapy, proton beam therapy reduces the dose to abdominal OAR while sparing normal tissue by limiting low dose irradiation. Copyright © 2016 Jouglar et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

### **30. Clinical outcomes and toxicities of proton radiotherapy for gastrointestinal neoplasms: a systematic review.**

**Author(s):** Verma, Vivek; Lin, Steven H; Simone, Charles B; Mehta, Minesh P

**Source:** Journal of gastrointestinal oncology; Aug 2016; vol. 7 (no. 4); p. 644-664

**Publication Type(s):** Journal Article



**Abstract:** Proton beam radiotherapy (PBT) is frequently shown to be dosimetrically superior to photon radiotherapy (RT), though supporting data for clinical benefit are severely limited. Because of the potential for toxicity reduction in gastrointestinal (GI) malignancies, we systematically reviewed the literature on clinical outcomes (survival/toxicity) of PBT. A systematic search of PubMed, EMBASE, abstracts from meetings of the American Society for Radiation Oncology, Particle Therapy Co-Operative Group, and American Society of Clinical Oncology was conducted for publications from 2000-2015. Thirty-eight original investigations were analyzed. Although results of PBT are not directly comparable to historical data, outcomes roughly mirror previous data, generally with reduced toxicities for PBT in some neoplasms. For esophageal cancer, PBT is associated with reduced toxicities, postoperative complications, and hospital stay as compared to photon radiation, while achieving comparable local control (LC) and overall survival (OS). In pancreatic cancer, numerical survival for resected/unresected cases is also similar to existing photon data, whereas grade  $\geq 3$  nausea/emesis and post-operative complications are numerically lower than those reported with photon RT. The strongest data in support of PBT for HCC comes from phase II trials demonstrating very low toxicities, and a phase III trial of PBT versus transarterial chemoembolization demonstrating trends towards improved LC and progression-free survival (PFS) with PBT, along with fewer post-treatment hospitalizations. Survival and toxicity data for cholangiocarcinoma, liver metastases, and retroperitoneal sarcoma are also roughly equivalent to historical photon controls. There are two small reports for gastric cancer and three for anorectal cancer; these are not addressed further. Limited quality (and quantity) of data hamper direct comparisons and conclusions. However, the available data, despite the inherent caveats and limitations, suggest that PBT offers the potential to achieve significant reduction in treatment-related toxicities without compromising survival or LC for multiple GI malignancies. Several randomized comparative trials are underway that will provide more definitive answers.

### **31. Clinical Outcomes of Proton Radiotherapy for Uveal Melanoma.**

**Author(s):** Verma, V; Mehta, M P

**Source:** Clinical oncology (Royal College of Radiologists (Great Britain)); Aug 2016; vol. 28 (no. 8); p. e17

**Publication Date:** Aug 2016

**Publication Type(s):** Journal Article

**Abstract:** Although clinical experience with proton beam radiotherapy (PBT) for most tumours is limited, there is relatively longstanding experience for uveal melanomas. Because of potential to reduce ocular toxicities, PBT is an attractive option for these tumours. However, summative data remain scarce. We systematically reviewed clinical outcomes of uveal melanoma patients treated with PBT, to comprehensively assess outcomes such as tumour control, survival, enucleation rates, toxicity and visual acuity preservation. A systematic search of PubMed, EMBASE, abstracts from meetings of the American Societies for Radiation Oncology and Clinical Oncology, and the Particle Therapy Co-Operative Group was conducted from 2000 to 2015. Fourteen original investigations from 10 different institutions were analysed. Most tumours were choroidal and medium-/large-sized, and received 50-70 Cobalt Gray equivalent dose; more recent data reported lower doses. Five year local control rates exceed 90%, which persisted at 10 and 15 years. Five-year overall survival rates ranged from 70 to 85%, 5 year metastasis-free survival and disease-specific survival rates from 75 to 90%, with more recent series reporting higher values. With the removal of smaller studies, 5 year enucleation rates were consistently between 7 and 10%. Many patients (60-70%) showed a post-PBT visual acuity decrease, but still retained purposeful vision ( $>20/200$ ); more recent, higher-volume series reported superior numbers. Complication rates were quite variable but showed improvements on historical plaque brachytherapy data. Only one randomised trial directly compared particle therapy (helium) with plaque brachytherapy, showing the former to be superior; this is addressed separately. PBT is an excellent modality to treat uveal melanomas, with high survival outcomes and visual acuity preservation. Although there are low toxicity and enucleation rates, the recent development of supportive therapies for radiation toxicities can further decrease clinical adverse effects.

### **32. Clinical Outcomes and Toxicity of Proton Radiotherapy for Breast Cancer.**

**Author(s):** Verma, Vivek; Shah, Chirag; Mehta, Minesh P

**Source:** Clinical breast cancer; Jun 2016; vol. 16 (no. 3); p. 145-154

**Publication Type(s):** Journal Article Review

**Abstract:** Proton beam radiotherapy (PBT) represents a rapidly expanding modality for the treatment of several malignancies. We examined the current state of PBT for breast cancer to evaluate its role in the modern era of breast radiotherapy. Systematic searches were performed using PubMed, EMBASE, and abstracts from the American Society for Radiation Oncology, American Society of Clinical Oncology, and Particle Therapy Co-Operative Group of North America annual meetings, using the Preferred Reporting Items for Systematic

Reviews and Meta-Analyses guidelines. Nine original investigations were analyzed. Despite the dearth of overall data, skin toxicity after PBT might be equivalent or better than that of photons. Conventionally fractionated breast/chest wall PBT produces grade 1 dermatitis rates of approximately 25% and grade 2 dermatitis in 71% to 75%. This is comparable or improved over the published rates for photons. The incidence of esophagitis was decreased if the target coverage was compromised in the medial supraclavicular volume, a finding that echoes previous results with photon radiotherapy. The rates of esophagitis were also comparable to the previous data for photons. Using PBT-based accelerated partial breast irradiation, the rates of seroma/hematoma and fat necrosis were comparable to those reported in the existing data. Radiation pneumonitis and rib fractures remain rare. PBT offers excellent potential to minimize the risk of cardiac events, keeping the mean heart dose at  $\leq 1$  Gy. However, definitive clinical experiences remain sparse. The recently begun randomized trial of protons versus photons will further aid in providing robust conclusions.

### 33. A systematic review of the cost and cost-effectiveness studies of proton radiotherapy.

**Author(s):** Verma, Vivek; Mishra, Mark V; Mehta, Minesh P

**Source:** Cancer; May 2016; vol. 122 (no. 10); p. 1483-1501

**Publication Type(s):** Journal Article Review

**Abstract:** Economic analyses of new technologies, such as proton-beam radiotherapy (PBT), are a public health priority. To date, no systematic review of the cost-effectiveness of PBT has been performed. Systematic searches of PubMed, EMBASE, abstracts from American Society for Radiation Oncology and American Society of Clinical Oncology meetings, and the Cost-Effectiveness Analysis Registry were conducted (2000-2015) along with abstracts from the Particle Therapy Co-Operative Group of North America for both years of existence (2014-2015). Eighteen original investigations were analyzed. The cost-effectiveness for prostate cancer—the single most common diagnosis currently treated with PBT—was suboptimal. PBT was the most cost-effective option for several pediatric brain tumors. PBT costs for breast cancer were increased but were favorable for appropriately selected patients with left-sided cancers at high risk of cardiac toxicity and compared with brachytherapy for accelerated partial breast irradiation. For non-small cell lung cancer (NSCLC), the greatest cost-effectiveness benefits using PBT were observed for locoregionally advanced-but not early stage-tumors. PBT offered superior cost-effectiveness in selected head/neck cancer patients at higher risk of acute mucosal toxicities. Similar cost-effectiveness was observed for PBT, enucleation, and plaque brachytherapy in patients with uveal melanoma. With greatly limited amounts of data, PBT offers promising cost-effectiveness for pediatric brain tumors, well-selected breast cancers, locoregionally advanced NSCLC, and high-risk head/neck cancers. Heretofore, it has not been demonstrated that PBT is cost-effective for prostate cancer or early stage NSCLC. Careful patient selection is absolutely critical to assess cost-effectiveness. Together with increasing PBT availability, clinical trial evidence, and ongoing major technological improvements, cost-effectiveness data and conclusions from this analysis could change rapidly.

#### Search strategy

Medline, EMBASE

(proton\* AND radiotherapy).ti,ab  
[DT FROM 2016]

#### Next Month:

Cystitis for radiotherapy cystitis post brachytherapy

## Exercise: Relative Risk

The relative risk is the ratio of probability of an event (a specified outcome) occurring in one group (i.e. those exposed to a particular intervention) compared to those in another group (i.e. those not exposed – a control group).

The relative risk can be interpreted using the following chart. First, you must determine whether the event (the outcome measure) is adverse or beneficial.

Relative Risk	Adverse outcome (e.g. death)	Beneficial outcome (e.g. recovery of limb function)
<1	Intervention better than control	Intervention worse than control
1	Intervention no better or worse than control	Intervention no better or worse than control
>1	Intervention worse than control	Intervention better than control

Have a go at interpreting the relative risks for these three studies using the chart above. Is the intervention better or worse than the control?

	Intervention	Population	Outcome measure (think: adverse or beneficial?)	Relative Risk
<b>Study 1</b>	Drug X	Adults at risk of a heart attack	Heart attack	1.2
<b>Study 2</b>	Therapy programme Y	Smokers	Smoking cessation	0.8
<b>Study 3</b>	Probiotic Z	Children on antibiotics	Diarrhoea	0.3

Find out more about relative risk in one of our Statistics training sessions.

For more details, email [library@uhbristol.nhs.uk](mailto:library@uhbristol.nhs.uk).

Answers: Study 1: worse; Study 2: worse; Study 3: better



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