the seminal vesicles and their mobility relative to the prostate corpus.

Materials and Methods: Based on clinical staging and pretreatment MRI scans 3 groups of 30 patients with T2a-3bN0M0 prostate carcinoma were formed. The first group consists of patients with no seminal vesicles invasion . The second group had minimal invasion, ≤ 5 mm measured from the prostate corpus on the MRI scans. The third group had (>5 mm) extensive invasion (figure 1).

Online fiducial markers registrations were performed in all patients on the first 8 cone beam CT scans to establish the prostate corpus translational and rotational errors. To measure the translational and rotational errors of the seminal vesicles, registrations were performed using a 3D shaped region of interest of the seminal vesicles and a grey value algorithm. Due to poor CBCT quality 106 out of 720 CBCT's were excluded.

The mean and SD residual seminal vesicles displacement was calculated for all three groups in LR, CC, AP direction and LR, CC, AP rotation. A spearman rho correlation test was performed to determine the relation between the invasion and the displacement of the seminal vesicles. The displacement of the seminal vesicles was compared between the groups for all directions using a Mann-Whitney test.

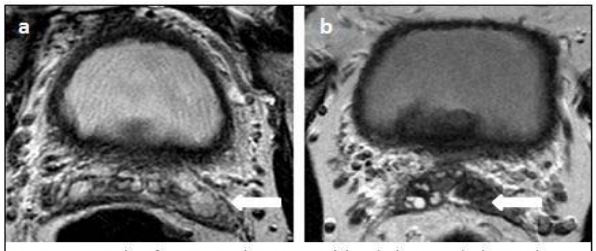

Figure1: Examples of a patient with no invasion (a) and a large residual seminal vesicles motion (LR 0.20, CC 0.34, AP 0.29 cm LRrot 7.0) and a patient with extensive invasion (b) and a small residual seminal vesicles motion (LR 0.05, CC 0.08, AP 0.12 cm LRrot 4.7).

Results: We found a significant reduction in random seminal vesicle displacement with increasing tumor invasion in the LR (ρ-0.263, p=0,012), CC (ρ-0.297,p=0,04), AP (ρ-0.333, p=0,001) direction and for the LR rotation (ρ-0,260, p=0,013). The SDs of the residual seminal vesicles displacement were significantly different between the group with minimal invasion and the group with extensive invasion in the CC and AP direction and for the LR rotation, see table 1. Between the group with no invasion and the group with extensive invasion, a significant difference in residual seminal vesicles displacement was found in the LR, CC and AP direction and for the LR rotation. No significant differences were found between the no invasion group and the minimal invasion group.

Direction	*Mann-Whitney analysis P-value*		
	No vs. Minimal invasion	No vs. Extensive invasion	Minimal vs. Extensive invasion
LR	0.525	***0.015***	0.053
CC	0.451	***0.004***	***0.001***
AP	0.564	***0.002***	***0.007***
LR rotation	0.836	***0.011***	***0.014***
CC rotation	0.988	0.701	0.433
AP rotation	0.274	0.894	0.117

Table 1 Results of the comparison of the seminal vesicles displacement between Groups with increasing seminal vesicle tumor invasion

Conclusions: Although increasing tumor invasion in the seminal vesicles reduces the mobility of the seminal vesicles, the mobility of the seminal vesicles still remains considerable, even in case of extensive invasion. Therefore strategies, such as adaptive radiotherapy, are needed for adequate seminal vesicle coverage despite their reduced mobility.

OC-0079

CTV-to-PTV margin for treatment setup errors: paediatric vs adult

M. Nazmy[1], E. O'Shea[1], E. McCrickard[1], C. O'Sullivan[1]
[1]St Luke's Radiation Oncology Network, Radiation oncology, Dublin, Ireland Republic of

Purpose/Objective: Most radiotherapy protocols give some flexibility for the Planning Target Volume (PTV) margin to each individual centre based on the immobilization devices and the Image Guided Radiotherapy (IGRT) protocol. Generally, radiation oncology centres have site specific guidelines for PTV margins and are not age specific. Factors affecting the PTV margin like breathing may differ according to the patient age. Applying the same PTV margin for an adult and a 3 year old child may not be correct. The aim of this work is to evaluate the required PTV margin in paediatric and adult patients treated in one centre with similar immobilisation and IGRT Protocol.

Materials and Methods: Thirty nine paediatric patients less than 7 years old (23 Brain/Head and Neck, 16 Abdomen) and 48 adult patients greater than 18 years of age (25 Brain, 23 Abdomen), were identified. All patients were imaged using 3D kV Cone Beam CT (CBCT) with minimum of 5 CBCTs. All patients were treated radically, planned in the supine position with similar immobilization technique between 2012 and 2014. PTV margin for setup error was calculated in the three orthogonal directions (x, y, and z) using the Van Herk formula, $M=2.5\Sigma + 0.7\sigma$.

Results: The required PTV margin for Brain in adult patients was 3mm, 2mm and 3mm, while it was 2mm, 2mm and 3mm in Brain/ Head and Neck in paediatric patients in the X Y Z directions respectively. Regarding the required PTV margin in the abdomen region, it was 6mm, 8mm and 6mm in adult patients and 6mm, 5mm and 5mm in paediatric patients again in the X Y Z directions respectively and the only clinically significant difference was in the Y direction in treating abdominal cases.

Conclusions: There is a clinically significant difference in the required PTV margin in the Y direction while treating the abdomen in paediatric patients. A small difference also exists in the Z direction while treating the abdominal region and the X direction while treating the Brain/Head and neck region. Each department should have separate guidelines for paediatric and adult patients regarding the PTV margin required for each treatment site.

OC-0080

Dynamic tumor tracking with the Vero4DRT system using a single fiducial marker for early stage lung cancer

C. Collen[1], K. Poels[1], T. De Vin[1], B. Engels[1], M. Boussaer[1], G. Storme[1], D. Verellen[1], M. De Ridder[1]
[1]Universitair Ziekenhuis Brussel, Radiotherapy, Brussels, Belgium

Purpose/Objective: Dynamic tumor tracking (DTT) requires a fiducial as surrogate for tumor position. Clinical results applying multiple spherical gold markers, placed around the tumor using a bronchoscope, were reported previously (1). We report on the use of a single fiducial marker placed inside the tumor percutaneously.

Materials and Methods: A prospective phase II trial was initiated using a gimbaled linac for stereotactic radiosurgery of early stage lung cancer (NCT 02224547). If tumor motion on 4DCT exceeded 8 mm, patients were eligible for DTT and a single fiducial marker (Visicoil, IBA, Louvain-la-neuve, Belgium) was implanted. Otherwise an internal target volume

(ITV) approach was applied. To evaluate the clinical benefit of DTT, the tumor motion amplitude on 4DCT was compared to the mean maximal peak-to-peak amplitude on fluoroscopy sequences acquired during DTT and the difference in PTV volume (DTT versus ITV) was calculated. Treatment-related toxicity was scored according to the Common Terminology Criteria for Adverse Events v.4.0.

Results: A total of 38 lesions were treated in 35 patients. The delivered dose schedules were as follows: 48Gy/4 fractions (n=32), 51Gy/3 fractions (n= 4), 60Gy/8 fractions (n=2). Mean superior-inferior (SI) motion exceeded 8 mm in 14 out of 38 lesions. DTT was used for 7 lesions. Reasons for omitting DTT were: pulmonary function or lesion location not allowing visicoil insertion and history of prior pneumothorax. Mean treatment time for a DTT session was 28.6 minutes (20-34.8 minutes). Mean SI motion on 4DCT in DTT lesions was 11.8 mm (8.6-16.9 mm). The mean maximal peak-to-peak amplitude observed during fluoroscopy was 20.4 mm (8.2-50.5 mm) demonstraing a significant variability in respiration induced tumor motion. DTT achieved a median reduction of 58% in PTV volume. With a median follow-up of 7 months (3-19 months), 1 local failure was observed in a centrally located lesion treated with an ITV approach. Only 1 patient experienced a grade 2 radiation pneumonitis and 2 patients presented with a COPD exacerbation in the weeks following radiation. No toxicity was observed in the patients treated with DTT.

Conclusions: DTT with the Vero4DRT system using a single fiducial marker proved to be clinically feasible and safe. DTT can be performed in an acceptable time frame, is able to account for respiratory variability and results in a substantial reduction in PTV volume.

(1) Matsuo Y, Ueki N, Takayama K, et al. Evaluation of dynamic tumour tracking radiotherapy with real-time monitoring for lung tumours using a gimbal mounted linac. Radiother Oncol 2014.

Proffered Papers: Radiobiology 1: Prediction of response using genetics

OC-0081

Prediction of normal tissue radiosensitivity from random numbers??? Be cautious out there!

C. Andreassen[1]

[1]*Aarhus University Hospital, Department of Experimental Clinical Oncology, Aarhus C, Denmark*

Purpose/Objective: Background: During the last decade, several studies have established predictive models for normal tissue radiosensitivity based on multiple SNPs (1-8). Typically, these studies assessed a limited number of SNPs. For some of these SNPs, a 'risk allele' was defined and the studies then looked for an association between the total number of risk alleles and normal tissue complication risk. Even though many of these models have yielded highly significant results, the models have often been inconsistent with each other (table 1). This probably relates to the way these models were constructed. The process had three steps: 1) For each of the included SNPs, a risk allele (minority vs. majority allele) was defined based on the observation that it was (often non-significantly) associated with the outcome parameter of the study (radiosensitivity). 2) A model was established based on these risk alleles. 3) A statistical test was carried out to determine if the number of risk alleles was significantly associated with radiosensitivity (the same parameter as used for the selection of the risk alleles). By doing so, a circularity is introduced into the analysis that makes it likely that random fluctuations (for the individual SNPs) are amplified into significant associations (for the entire model).

Materials and Methods: In order to further explore this potential problem, we reanalyzed the dataset originally used to establish the multiple SNP model published by Andreassen et al. in 2003 (1). Instead of the actual SNP genotypes we randomly assigned 'genotypes' to the patients for 7 fictitious SNPs that had the same relative distribution as the SNPs in the original dataset. Subsequently, we selected risk alleles for these 'SNPs' and established a multiple SNP model exactly as in the original study. This procedure was repeated 10 times.

Results: In 8 out of 10 times a significant result was found for the model. This clearly demonstrates that the process of actively fitting the model to the dataset is indeed per se capable of producing nominally significant results for the entire model.

Conclusions: Great caution should be taken when a predictive model is established and tested within the same patient cohort. A significant finding for a multiple SNP model established in this way cannot be used to indirectly validate the underlying SNPs. Thus, we have to establish robust associations for the individual SNPs that can be entered into a predictive multiple SNP model that should finally be validated in an independent dataset.

Table 1: Alleles assigned as 'risk alleles' in four different multiple SNP models

Author, year	N =	XRCC1 codon 399 Arg/Gln	XRCC3 codon 241 Thr/Met	TGFB1 codon 10 Leu/Pro	ATM codon 1853 Asp/Asn	p-value for the entire model
Andreassen, 2003	41	Arg	Thr	Pro	-	<0.05
Azria, 2008	37	Gln	-	-	Asn	<0.001
Alsbeih, 2010	60	Arg	Met	Leu	-	0.006
Zschenker, 2010	69	Gln	-	-	Asp	0.0005

- = SNP not included in the model. Note that other SNPs were included in some of the models.

References: (1) Andreassen CN. R&O 2003;69:127-135. (2) Azria D. Clin Cancer Res 2008;14:6284-6288. (3) Alsbeih G. Radiat Res 2010;173:505-511. (4) Zschenker O. R&O 2010;97:26-32.(5) Terrazzino S. IJROBP 2012;83:504-511. (6) Tucker SL. IJROBP 2013;85:251-257. (7) Borghini A. Cancer Biother Radiopharm 2014 PMID: 25099761. (8) Reuther S. Strahlenther Onkol. 2014 PMID: 25156511

OC-0082

A machine learning method demonstrates that a large number of SNPs contribute to clinical radiosensitivity

J. Oh[1], S. Kerns[2], H. Ostrer[4], B. Rosenstein[3], J.O. Deasy[1]

[1]*Memorial Sloan Kettering Cancer Center, Department of Medical Physics, New York NY, USA*

[2]*University of Rochester Medical Center, Department of Radiation Oncology, Rochester NY, USA*

[3]*Mount Sinai School of Medicine, Department of Radiation Oncology, New York NY, USA*

[4]*Albert Einstein College of Medicine, Departments of Pathology and Genetics, New York, USA*

Purpose/Objective: Rectal bleeding is one of the common radiation-induced complications following radiotherapy in prostate cancer patients, which can greatly impair the quality of life for cancer survivors. The purpose of this study was to investigate whether single nucleotide polymorphisms (SNPs) are associated with susceptibility to late rectal bleeding in men treated with radiotherapy for prostate cancer using a genome-wide association study (GWAS) dataset.