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.

Results: We found a significant reduction in random seminal vesicle displacement with increasing tumor invasion in the LR (p=0.263, p=0.012), CC (p=0.297, p=0.04), AP (p=0.333, p=0.001) direction and for the LR rotation (p=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.

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.

<table>
<thead>
<tr>
<th>Direction</th>
<th>No vs. Normal invasion</th>
<th>No vs. Extensive invasion</th>
<th>Normal vs. Extensive invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td>LR</td>
<td>0.525</td>
<td>0.015</td>
<td>0.053</td>
</tr>
<tr>
<td>CC</td>
<td>0.451</td>
<td>0.004</td>
<td>0.004</td>
</tr>
<tr>
<td>AP</td>
<td>0.354</td>
<td>0.002</td>
<td>0.007</td>
</tr>
<tr>
<td>LR rotation</td>
<td>0.836</td>
<td>0.011</td>
<td>0.024</td>
</tr>
<tr>
<td>CC rotation</td>
<td>0.986</td>
<td>0.703</td>
<td>0.433</td>
</tr>
<tr>
<td>AP rotation</td>
<td>0.274</td>
<td>0.896</td>
<td>0.027</td>
</tr>
</tbody>
</table>

Table 1: Results of the comparison of the seminal vesicles displacement between groups with increasing seminal vesicle tumor invasion.

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 immobilisation technique between 2012 and 2014. PTV margin for setup error was calculated in the three orthogonal directions (x, y, and z) according to the Van Herk formula, _M_ = 2.5 _σ_ + 0.7 _θ_.

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
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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 linear 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 viscoil 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) demonstrating 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.


**Proffered Papers: Radiobiology 1: Prediction of response using genetics**

**OC-0081**

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

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**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 underlying SNPs were amplified into significant associations for the individual SNPs that can be entered into a predictive multiple SNP model that should finally be validated in an independent dataset.

**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 Andreasen 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**

<table>
<thead>
<tr>
<th>Author, year</th>
<th>N</th>
<th>XRC1 codon 399</th>
<th>XRC2 codon 244</th>
<th>TOP1 codon 161</th>
<th>ATM codon 1812</th>
<th>p-value for the entire model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andreasen, 2003</td>
<td>61</td>
<td>Arg</td>
<td>Thr</td>
<td>Pro</td>
<td>-</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Azria, 2008</td>
<td>57</td>
<td>Ctn</td>
<td>-</td>
<td>-</td>
<td>Arg</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alsbeih, 2010</td>
<td>60</td>
<td>Arg</td>
<td>Val</td>
<td>Leu</td>
<td>-</td>
<td>0.008</td>
</tr>
<tr>
<td>Zschenker, 2010</td>
<td>68</td>
<td>Ctn</td>
<td>-</td>
<td>-</td>
<td>Arg</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

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


**OC-0082**

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

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**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.