Results: A total of 32 patients were retrospectively analyzed. The median follow up of survivors was 181 months from first diagnosis and 33 month from second RT. At the time of analysis 4 patients had died. The median time between first and second RT was 9.9 years (range 1.8 - 20.3). Fifteen years after first diagnosis 86% of the patients were still alive. Four women died, 3 on cancer. After second RT only one acute G2 toxicity of the skin was reported (desquamation). Late toxicity was scored using the LENT-SOMA Score Criteria. Lymphedema (G1) of the ipsilateral arm was observed in 3.1%, 3.1% reported on intermittent pain in the breast and dermatitis. The occurrence of radiation ulcer was significantly related to the presence of ulcerating tumor before the start of the reRT-HT (P=0.004, HR = 4.4).

Conclusion: The combination of re-irradiation and hyperthermia is well tolerated and results in high response rates despite extensive disease and resistance to previous treatments. ReRT-HT is a worthwhile palliative treatment option for this patient group who suffer from extensive locoregional tumor growth and have a very poor prognosis.

Proffered Papers: Clinical 2: Adverse effects in radiotherapy

OC-0055
Pseudo-progression after stereotactic radiotherapy of brain metastases is serious radiation toxicity
R. Wiggenraad1, M. Mast1, J.H. Franssen2, A. Verbeek-de Kantèr1, H. Struijkman1
1Radiotherapy Centre West, Radiotherapy, The Hague, The Netherlands
2Haga Hospital, Radiotherapy, The Hague, The Netherlands

Purpose or Objective: Stereotactic radiotherapy (SRT) of brain metastases results in regression of most treated metastases, but subsequent lesion growth may occur and is caused by either tumor progression or pseudo-progression, which is probably a radiation effect on surrounding normal brain tissue. It is unknown if active treatment is indicated in symptomatic patients, or if it is better to wait for spontaneous recovery. The purpose of this study is to describe the clinical course of brain metastasis patients developing pseudo-progression after SRT to improve clinical decision-making.

Material and Methods: Follow-up MRI scans of all patients who received SRT of brain metastases from 2009 through 2012 were reviewed for post SRT lesion growth. Depending on the volume of the metastasis, the patients had received one fraction of 21Gy, 18Gy, or 15Gy, or three fractions of 8Gy or 8.5Gy. The GTV-PTV margin was 2mm. Pseudo-progression was considered to be the cause of this lesion growth if a histological diagnosis of necrosis had become available, if the lesion had shown subsequent regression or if two neuro-radiologists agreed upon this diagnosis based on a review of the follow-up perfusion MRI scans. The clinical course of the patients with these pseudo-progressive lesions was retrospectively studied.

Results: In a total of 237 treated patients we identified 37 patients with 50 pseudo-progressive lesions. The median follow-up of all patients still alive was 40.7 months. The main clinical symptoms that were attributed to this lesion growth were neurologic deficits, headache and seizures in 19 (51%), 3 (8%) and 4 (11%) patients respectively (unknown in one). Ten patients (27%) had no symptoms attributed to the lesion growth and remained asymptomatic afterwards. Of the 19 patients with neurologic deficits one improved after spontaneous regression of the lesion, one improved after surgery and 17 did not improve. Two out of the four patients with seizures improved with ant-epileptic drugs (AED’s), one improved after surgery and one did not improve. Only one of the three patients with headache improved with steroids. Spontaneous regression of an initially pseudo-progressive lesion was observed in 18 patients. Twelve of these 18 patients had symptomatic pseudo-progression, but only one of these 12 patients experienced neurologic improvement without treatment. In 6 patients their deaths were related to the pseudo-progressive lesion.

Conclusion: Patients with an asymptomatic pseudo-progressive lesion frequently remain asymptomatic. Patients with a symptomatic pseudo-progressive lesion only rarely recover spontaneously. Active treatment, such as surgery, should be considered for these patients. Therefore,
symptomatic pseudo-progression after SRT of brain metastases needs to be considered as a serious radiation induced toxicity. Reduction of the high dose volume of normal brain tissue may prevent this toxicity.

OC-0056
FLAME: Influence of dose escalation to 95Gy for prostate cancer on urethra-related toxicity and QOL
1UMC Utrecht, Radiation Oncology, Utrecht, The Netherlands
2The Netherlands Cancer Institute, Radiation Oncology, Amsterdam, The Netherlands
3University Hospital Leuven, Radiation Oncology, Leuven, Belgium
4University Medical Center Radboud, Radiation Oncology, Nijmegen, The Netherlands
5UMC Utrecht, Julius Center for methodology, Utrecht, The Netherlands

Purpose or Objective: Following EBRT for prostate cancer, patients can develop aggravation of urinary symptoms mostly due to a dose-escalated EBRT. With dose-escalated EBRT it is suggested that genitourinary toxicity increases with increasing dose. In the experimental arm of the FLAME-trial (284 patients) a dose of 77Gy to the entire prostate gland in 35 fractions was administered, with an integrated boost up to 95Gy to the macroscopic lesions. No dose constraints for the urethra were used during the trial. The objective of this study is to evaluate urethral dose parameters, urethra-related toxicity and prostate-specific QoL scores for patients treated with and without dose-escalated EBRT.

Material and Methods: Between 2009 and 2015, 571 intermediate and high risk prostate cancer patients were enrolled in the FLAME trial, a phase 3, single blind, multicenter randomized controlled trial (NCT01168479). The control arm (287 patients) received a dose of 77Gy to the entire prostate gland in 35 fractions. The experimental arm (284 patients) received the same dose, but with an integrated boost up to 95Gy to the multi-parametric MRI-based intraprostatic lesion. For this study, the urethra was delineated retrospectively on T2 weighted MRI, using a circle shape with a diameter of 3 mm, to obtain dose parameters. These dose parameters, the Genitourinary Toxicity scores(CTCAE v3.0) and the urinary symptoms scale of the EORTC QLQ-PR25, were compared for both treatment arms. The physician in attendance scored toxicity at baseline, weekly during treatment, 4 weeks after treatment and every 6 months up to 10 years. QoL was filled out 1 week before the start of treatment and the next questionnaires were sent to the patient every 6 months up to 10 years. Mean differences between groups at 1 year of follow-up were calculated using an independent samples t-test (dosimetry and QoL), Chi-square test or Fisher's exact test (toxicity). Statistical significance was considered P<0.01.

Results: Results after analysis of 100 patients (50 patients in each treatment arm) with a median follow-up of 22 months show for the control arm an average Dmean (mean dose to the urethra) of 77.3 ± 0.5 Gy (range 75.9-78.0 Gy), with an average Dmax (maximum dose to the urethra) of 79.6 ± 0.8 Gy (range 78.0-81.3). In the experimental arm, average Dmean was 82.0 ± 2.8 Gy (range 77.4-89.0 Gy) and average Dmax was 89.7 ± 0.6 Gy (range 80.7-97.7 Gy). For both Dmean and Dmax the difference between treatment arms was significant (p<0.000). Grade 3 GU toxicity did not occur, grade 2 GU toxicity occurred in a subset of patients, although no significant difference was found between both treatment arms for the separate GU items (table 1). Urinary symptoms-related QoL was not significantly different across treatment arms.

<table>
<thead>
<tr>
<th>Time of follow-up</th>
<th>77Gy</th>
<th>95Gy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary frequency/urgency</td>
<td>15 (30%)</td>
<td>14 (29%)</td>
<td>0.83 (Chi-Square)</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>4 (8%)</td>
<td>2 (4%)</td>
<td>-</td>
</tr>
<tr>
<td>Bladder spasms</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>-</td>
</tr>
<tr>
<td>Incontinence, urinary</td>
<td>3 (6%)</td>
<td>2 (4%)</td>
<td>-</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>-</td>
</tr>
<tr>
<td>Dysuria</td>
<td>5 (10%)</td>
<td>5 (10%)</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 1. Incidence of GU toxicity at 1 year after radiation treatment.

Conclusion: Results showed a significant difference in urethral dose, but no significant differences in toxicity or quality of life when comparing both treatment arms of the FLAME trial.

OC-0057
Cardiotoxicity and cardiac substructure dosimetry in dose-escalated lung radiotherapy
S. Vivekanandan1, N. Counsell2, A. Khwanda1, S. Rosen2, E. Parsons2, Y. Nga1, L. Farrell2, L. Hughes2, M. Hawkins1, D. Landau2, J. Fenwick1
1University of Oxford, Oncology, Oxford, United Kingdom
2University College London Clinical Trials Unit, Clinical Trials Unit, London, United Kingdom

Purpose or Objective: Radiotherapy of lung cancer delivers quite high doses of radiation to the heart. We explored associations between overall survival (OS) and radiation dose to heart and its substructures and electrocardiographic (ECG) changes.

Material and Methods: We analysed data from 79 patients in IDEAL CRT, a phase I/II trial of isotoxic radiotherapy (RT) dose escalation trial, sponsored by University College London (C13530/A10424). Mean and maximum prescribed doses were 69 and 75.6Gy calculated as 2Gy fractionation equivalents (EQD2, α/β=10Gy). Whole heart, left ventricle (LV), right ventricle (RV), right atrium (RA), left atrium (LA) and AV node (AVN) were outlined on RT planning scans and differential dose volume histograms (DVHs) extracted, converting physical DVHs to EQD2s (α/β=3). Patient-to-patient DVH variability was represented using a small number of Varimax-rotated principal components (PCs) explaining 95% of total variance. ECGs were analysed at baseline, 6 and 12 months after treatment, and changes in heart rate (HR) recorded, with patients dichotomised according to presence or absence of 'any ECG rhythm change' (conduction abnormalities or ischaemia). OS was modelled using Cox regression from the start of treatment. Univariate analysis (UVA) and multivariate analysis (MVA) of clinical factors included ‘any rhythm ECG change’ at 6 and 12 months, change in HR at 6 or 12 months, planning target volume (PTV), and prescribed dose (PD). MVA of whole heart dosimetric factors included all 7 Heart PCs, PTV, and PD. MVA of heart substructures included heart substructure PCs with p<0.2 on UVA having similar dosimetric distributions to significant Heart PCs, PTV and PD.