Purpose/Objective(s): To investigate a novel method of generating synthetic CT data (syn-CT) from high spectral and spatial resolution (HiSS) MRI for radiotherapy treatment planning.

Materials/Methods: A phantom was constructed from a fresh beef shank containing muscle, fat, bone marrow, and cortical bone. The shank was embedded in a 1% agarose gel for spatial reproducibility from MRI to CT. A HiSS pulse sequence was used on a 1.5T Siemens Aera scanner to image the phantom with the following parameters: 1x1x4 mm³ voxels, echo train length = 89.9 ms, flip angle = 50°, 11.1 Hz spectral resolution, and number of echoes = 32. Data was processed offline [JMRI, 24, 1311(2006)] and images generated with pixel value proportional to water and fat peak height normalized by the spectral noise. The phantom was subsequently imaged with CT (1 x 1 x 3 mm³ voxels) to use as a reference or “gold standard.” A region-of-interest (ROI) was drawn for each tissue type (muscle, fat, bone marrow, and cortical bone) to determine whether these tissues have unique NMR characteristics. Water peak versus fat peak height values were plotted on a pixel-by-pixel basis and the resulting plot was used to establish thresholds for labeling different tissues. The syn-CT image data was then generated based on a look-up table (LUT) of the mean HU in the various tissues. A body contour was generated by thresholding and pixels outside of this contour were set to -1000 Hounsfield Units (HU), corresponding to air. The syn-CT data was then rigidly registered to the real CT data. A subtraction image was generated to visualize the differences in images. Both synthetic and real CT images were converted to physical density using a LUT and radiological path length Units (HU), corresponding to air. The syn-CT data was then rigidly registered to the real CT data. A subtraction image was generated to visualize the differences in images. Both synthetic and real CT images were converted to physical density using a LUT and radiological path length was calculated for rays emanating from a central point every 45°. Absolute differences in path length were calculated for each ray and the percent errors were reported.

Results: The syn-CT image was qualitatively very similar to the real CT image with the largest differences at tissue interfaces. The overall mean radiological path length (g/cm²) averaged over all angles was 6.7 for the synthetic CT and 6.8 for the real CT image. The mean percent error of the synthetic CT using the real CT as a gold standard was 2.3% ± 4.5 S.E.

Conclusion: We have shown that a novel classification algorithm based on HiSS imaging is able to produce images with contrast similar to CT. Based on the calculations of radiological path length coupled with modern algorithms we expect that the dose calculated on a HiSS syn-CT image may be as accurate as that calculated using real CT. Further studies along with optimization of the pulse sequence are planned to address this important question.

Abstract 142: Table 1

<table>
<thead>
<tr>
<th>Angle</th>
<th>Real CT Mean Path length (g/cm²)</th>
<th>Synthetic CT Mean Path length (g/cm²)</th>
<th>% Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>0°</td>
<td>6.5</td>
<td>7.3</td>
<td>-12.3</td>
</tr>
<tr>
<td>45°</td>
<td>7.3</td>
<td>6.5</td>
<td>12.3</td>
</tr>
<tr>
<td>90°</td>
<td>10.7</td>
<td>10.4</td>
<td>2.8</td>
</tr>
<tr>
<td>135°</td>
<td>7.4</td>
<td>7.3</td>
<td>1.4</td>
</tr>
<tr>
<td>180°</td>
<td>5.8</td>
<td>5.3</td>
<td>8.6</td>
</tr>
<tr>
<td>225°</td>
<td>4.2</td>
<td>4.2</td>
<td>0</td>
</tr>
<tr>
<td>270°</td>
<td>5.6</td>
<td>5.3</td>
<td>5.4</td>
</tr>
<tr>
<td>315°</td>
<td>7.3</td>
<td>7.5</td>
<td>2.7</td>
</tr>
</tbody>
</table>


Investigation of a Novel Synthetic Computed Tomography Algorithm Based on NMR Spectral Characteristics of Tissues A.M. Diak, S.M. Shea, M. Medved, G.S. Karczmar, R. Patel, S. Gros, W. Small, Jr., and J.C. Roecke, Loyola University Medical Center, Maywood, IL, University of Chicago, Chicago, IL, Stritch School of Medicine, Loyola University Chicago, Maywood, IL.

Subgroup Analysis of Functional Associations Between In Vitro Radiation Response of Fibroblasts and Late Toxicity After Breast Radiation Therapy C. Herskind, O. Nuta, N. Somaiah, S. Boyle, M.L.K. Chua, L. Gothard, K. Rothkamm, and J. Yarnold, Department of Radiation Oncology, Universitätsmedizin Mannheim, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany, Public Health England, Centre for Radiation, Chemical and Environmental Hazards, Chilton, United Kingdom, Division of Radiotherapy and Imaging, the Institute of Cancer Research, London, United Kingdom, National Cancer Centre Singapore, Singapore, Singapore, Department of Radiotherapy and Radiation Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.

Purpose/Objective(s): Late toxicity after tumor radiotherapy (RT) is considered to be determined by variations in multiple, low-penetrance genes each associated with moderate hazard ratios. Here we test the hypothesis that functional assays can distinguish subgroups of patients characterized by different mechanisms associated with patients’ risk of late reaction after radiotherapy.

Materials/Methods: Early-passage fibroblast cultures were established with informed consent from selected breast cancer patients with minimal (RT-resistant, n = 15) or marked breast changes (RT-sensitive, n = 19) after breast conserving therapy and were irradiated with 6MV X-rays in vitro. Residual DNA double-strand breaks (DSBs) were scored by 53BP1 foci 24h after irradiation with 4 Gy. Molecular markers p53 and Ki-67 were detected by immunofluorescence microscopy and the plating efficiency (PE) was determined by the colony formation assay. The non-parametric Wilcoxon/Mann-Whitney test, Spearman’s rank correlation test, and a linear model, were used to test for statistical significance.

Results: RT-sensitive patients showed significantly increased residual 53BP1 foci (2.48 ± 0.22 vs 1.86 ± 0.11 per cell; P = 0.007) and an increased basal p53-positive fraction of cells without irradiation (7.1 ± 1.5 vs 2.5 ± 1.0 pct.; P = 0.02). In addition, the subgroup of RT-sensitive patients with severe reaction relative to known risk factors (n = 10) showed vigorous early upregulation of p53 2h after irradiation (P = 0.005) in contrast to RT-sensitive patients with more moderate reaction (n = 9) and RT-resistant patients. RT sensitivity showed no significant correlation with proliferation marker Ki-67. However, in the patient subgroup with low fibroblast proliferation activity (Ki-67 index), RT sensitivity correlated with proliferation marker Ki-67. These results establish an association between the radiation response of fibroblasts and late reaction of the breast after RT and provide novel evidence for the existence of patient subgroups. We suggest that functional assays can distinguish subgroups of patients characterized by different mechanisms associated with patients’ risk of late reaction after radiotherapy.

Conclusion: These results establish an association between the radiation response of fibroblasts and late reaction of the breast after RT and provide novel evidence for the existence of patient subgroups. We suggest that defects in the p53 stress response or DSB repair pathways may contribute to late reaction in RT-sensitive patients, possibly via increased misrepair and genomic instability. Functional studies may synergize with “omics” approaches and help unravel the mechanisms of normal-tissue reaction after RT.

Purpose/Objective(s): To determine the risk of radiation-induced optic neuropathy (RION), following high dose pencil beam scanning proton therapy (PBS PT) to skull base tumors.

Materials/Methods: Between 1999 and 2010, 157 patients with a mean age of 47.3 years (range 18 - 77), were treated with PBS PT for chordoma (N = 87), chondrosarcoma (N = 38), meningioma (N = 22), adenoid cystic carcinoma (N = 7), pituitary tumor (N = 2) and a giant cell tumor (N = 1). The median administered dose to the planning target volume (PTV) of the gross tumor volume (GTV) was 74 Gy RBE (range 54.0 - 77.4). In 40 patients (25.5%) the tumor involved the orbital cavity and/or the optic canal at the planning CT. Visual complications were scored according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 grading scale. The median follow-up was 75.3 months (range 28.1 - 195.5).

Results: RION developed in 13 (8.3%) patients at a median time of 13.4 months (range 4.8 - 51.5) following PBS PT. The 5-year actuarial freedom from RION following this treatment was 91.5 ± 2.3%. The majority of the affected patients (8/13) developed unilateral grade 4 RION, 2 patients presented with unilateral grade 3 toxicity and the rest had bilateral involvement (1 patient with bilateral grade 4 RION and 2 patients presented with grade 4 and grade 2 toxicities in either eye). Tumor involving the optic apparatus at the start of the proton therapy was statistically associated with RION (P = 0.01). The presence of visual deficits either at diagnosis (P = 0.72) or at the start of PBS PT (P = 0.82) was, however, not associated with this complication. The mean percentage of the optic nerve-volume receiving 60 Gy or more (V60 GyRBE) was significantly higher in the patients presenting with RION (4.21 ± 14.5% vs. 0.89 ± 3.7%; P = 0.03). However, RION was not more frequent in patients who received a mean dose per fraction of 1.9 GyRBE or more (≥1.9 GyRBE) to the optic nerves (P = 0.2) or to the chiasm (P = 0.69). Similarly, a maximum dose per fraction of ≥1.9 GyRBE to these structures was not related to higher rates of RION (P = 0.74 and P = 0.76, respectively). The mean percentage of the chiasm V60 GyRBE of patients with and without RION was 8.24 ± 27.6% and 1.19 ± 7.03%, respectively, which was statistically significant (P = 0.018). A higher mean of the maximum dose (Dmax) as well as of the mean dose (Dmean) delivered to the chiasm was not associated with developing RION (57.7 ± 3.5 GyRBE vs. 56.8 ± 5.1 GyRBE; P = 0.56 and 50.8 ± 7 GyRBE vs. 46.8 ± 11 GyRBE; P = 0.2, respectively).

Conclusion: This data suggests that high-dose PBS PT for skull base tumors is associated with a relatively low risk of RION. In this group of patients we found that optic apparatus metrics (V60 GyRBE) can be related to visual outcome and therefore should be carefully considered in treatment planning.