**Pushing the Dose to the Spinal Cord in Spine SBRT - Cord and Thecal Sac Dosimetric Correlation with Toxicity**

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**Purpose/Objectives:** Spine SBRT is widely performed and the reported risk of myelopathy is very low. Currently, guidelines vary on the maximum tolerable dose levels and designation of spinal cord vs thecal sac as the dose limiting structure. The current single institution study examines dose metrics to both structures and correlations with toxicity for patients treated with IMRT/VMAT.

**Materials/Methods:** The radiation plans and DVH parameters were exported for 46 patients treated with SBRT for spinal metastases between April 2008 and December 2010 at the Mayo Clinic Rochester. Diagnostic MRI and where applicable, CT myelograms, from each patient were fused with the CT planning set and used to contour the spinal cord and the thecal sac. High resolution PRV structures were created in 1 mm increments for the cord (1-7 mm) and the thecal sac (1-2 mm), to examine dose gradients. Using an alpha/beta of 2 Gy, the biologically equivalent 2 Gy dose maximum (Max(2)[EQ2Gy]) and high dose sub-volumes (Dxcc(2)[EQ2Gy]) were calculated for x = 0.1 cc to 1.0 cc in 0.1 cc increments from the dose volume histograms (DVHs). Toxicities for pain, nausea, myelitis, fatigue, fracture and radionecrosis were assessed (CTCAE v4.0). ROC analysis was used to define thresholds for constructing 2x2 contingency tables indicating toxicity using fisher exact test for significance (p < 0.01). Differences in mean values for groups with/without toxicity were assessed using t-tests for significance (p < 0.05).

**Results:** Median values of Max(2)[EQ2Gy] for the spinal cord and thecal sac were 38.5 (range 7.9-67.9 Gy) and 67.7 Gy (range 15.5-155.8 Gy) respectively. There were no cases of myelopathy (median follow-up 14 months). Median values for high dose sub volumes, Dxcc(2)[EQ2Gy], were 2 times higher than the doses for 5% predicted grade 3 cord toxicity recommended by Sahgal et al. (IJORBP: 2013; 85). Five patients had pain (4 with grade 1, 1 with grade 2). Four patients had nausea (3 with grade 1, 1 with grade 2). Cord D0.1cc(2)[EQ2Gy] ≥ 23.8 Gy was significant (p = 0.007) as an indicator for pain ≥1. Thecal sac D2.0cc(2)[EQ2Gy] ≥ 29.3 Gy was significant (p = 0.008) as an indicator for nausea ≥1. Distribution of Max(2)[EQ2Gy] values for the thecal sac corresponded most closely to spinal cord + 3.5 mm margin. Median survival was 14 months (range 1-64 months).

**Conclusion:** Current guidelines may overestimate the risk of myelopathy from spine SBRT. The current study’s population included patients who were both radiation naïve and retreated after conventional palliative radiotherapy. The actual risk of myelopathy may be much lower than predicted. For patients with limited survival, it may be appropriate to allow higher doses to cord if it would be expected to result in better QOL/functional outcomes/pain relief for the duration of their life.

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**First Clinical Implementation of Electromagnetic Transponder-Guided MLC Tracking**

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**Purpose/Objective(s):** MLC tracking presents a paradigm shift in radiotherapy allowing the widespread application of real-time adaptation during treatment delivery and promising a new level of dose conformity. The first prostate cancer patient has been treated with electromagnetic transponder-guided MLC tracking, as part of a 30 patient clinical trial to demonstrate feasibility (NCT02033343). The purpose of this work is to
present the development of novel clinical processes to ensure safe delivery of this pioneering technique and lessons learned from initial patients.

**Materials/Methods:** The MLC tracking system consists of an electromagnetic transponder tracking signal and in-house MLC tracking software combined with VMAT delivery. Planned analysis includes fractions successfully adapted, geometric accuracy and dosimetric accuracy of delivered versus planned dose accumulation. Failure Mode and Effects Analysis (FMEA) was applied to evaluate the safety of the MLC tracking system prior to the first treatment. The commissioning tests performed were; phantom measurements with 4D programmable motion platform utilizing previously measured prostate trajectories, system latency, coordinate system transfer and detection of anomalous conditions. Further patient specific quality assurance tests and novel clinical processes were developed by process mapping and FMEA to ensure safe patient treatment delivery.

**Results:** Application of FMEA QA framework produced measurement of system latency as 230±20ms, coordinate system and scaling was correct, all anomalous situations were detected and initiated a beam hold. The planning process for MLC tracking patients contained manual steps to set the MLC carriage position and to position the jaws away from leaf ends by a ‘tracking margin’ to allow MLC movement inside fixed jaw positions. We implemented checklists to ensure the additional processes were completed. All treatment fractions were successfully adapted and DVH’s produced to compare dose with and without tracking. The average treatment time for the dual-arc VMAT delivery was 114±2s. With MLC tracking there is no need for a pre-treatment couch shift or intra-treatment couch corrections of observed motion, thus improving patient flow further.

**Conclusions:** Clinical process and QA practices for the safe clinical implementation of electromagnetic transponder-guided MLC tracking for real-time adaptation in prostate cancer VMAT have been developed and implemented. The first electromagnetic transponder-guided MLC tracking patient has been treated as part of a 30-patient clinical trial to assess feasibility of the technique.


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**Presentation Number:** 48

**Site-Specific Range Uncertainties Due to by Dose Calculation Algorithms for Proton Therapy**

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**Purpose:** To investigate the impact of complex patient geometries on the capability of analytical dose calculation algorithms to accurately predict the range of proton fields and to verify currently used range uncertainty margins in proton therapy.

**Materials/Methods:** We compared dose distributions predicted by an analytical pencil-beam algorithm with Monte Carlo simulations (TOPAS). A total of 508 individual passively scattered treatment fields were analyzed for 7 disease sites (liver, prostate, breast, medulloblastoma spine and whole brain, lung and head & neck). Comparisons were performed voxel-by-voxel on two-dimensional distal dose surfaces calculated by the pencil-beam and Monte Carlo (MC) algorithm to obtain the ARDs (average range differences) and RMSDs (root mean square deviation) for each field for the distal position of the 90% dose level (R90) and the 50% dose level (R50). The ADD (average dose degradation) of the distal falloff region, the distance between the distal position of the 80% and 20% dose levels (R80-R20), was also analyzed. All ranges were calculated in water-equivalent distances.

**Results:** We found the RMSD for R90 to be clinically most significant when analyzing range differences. Differences in the R90 between the dose distributions from MC and the planning system in small regions distal to the target volume can be larger than currently applied range margins in proton therapy. We deduced
site-specific estimations, considering total range uncertainties and uncertainties from dose calculation alone. The results for all site are given in the table, showing the site-dependence of range uncertainties. Our results demonstrate that a reduction of currently used uncertainty margins is feasible for liver, prostate and whole brain fields even without introducing MC dose calculations. We recommend range margins of 2.8\% + 1.2mm for liver and prostate treatments and 3.1\% + 1.2mm for whole brain treatments, respectively. On the other hand, current margins seem to be insufficient for some breast, lung and head & neck patients, at least if used generically. A generic margin of 6.3\% + 1.2mm would be needed for breast, lung and head & neck treatments if no case specific adjustments are applied.

**Conclusion:** The currently used generic range uncertainty margins in proton therapy should be re-defined to be site-specific. Complex geometries may require a patient field specific adjustment. We recommend routine verifications of treatment plans using Monte Carlo simulations for patients with highly heterogeneous geometries.

<table>
<thead>
<tr>
<th>Site</th>
<th># of fields</th>
<th>ARD$_{R90}$ [%] Mean ± std. dev. [Min., Max]</th>
<th>ARD$_{R50}$ [%] Mean ± std. dev. [Min., Max]</th>
<th>RMSD$_{R90}$ [%] Mean ± std. dev. [Min., Max]</th>
<th>RMSD$_{R50}$ [%] Mean ± std. dev. [Min., Max]</th>
<th>ADD [%] Mean ± std. dev. [Min., Max]</th>
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</thead>
<tbody>
<tr>
<td>Head &amp; Neck</td>
<td>248</td>
<td>-1.5 ± 1.5 [-14.8, 0.9]</td>
<td>-0.5 ± 0.6 [-3.4, 1.1]</td>
<td>3.2 ± 1.9 [0.6, 19.9]</td>
<td>1.8 ± 0.8 [0.1, 4.7]</td>
<td>0.05 ± 1.2 [-4.8, 3.1]</td>
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<tr>
<td>Lung</td>
<td>30</td>
<td>-2.0 ± 1.8 [-5.8, -0.1]</td>
<td>-0.6 ± 1.0 [-2.2, 1.8]</td>
<td>4.0 ± 1.3 [1.8, 7.0]</td>
<td>2.1 ± 0.5 [1.2, 6.3]</td>
<td>1.2 ± 1.8 [-1.6, 6.3]</td>
</tr>
<tr>
<td>Spine</td>
<td>69</td>
<td>-2.3 ± 1.9 [-7.1, -0.4]</td>
<td>-1.3 ± 0.8 [-3.7, -0.5]</td>
<td>3.4 ± 2.4 [1.3, 9.6]</td>
<td>2.1 ± 0.9 [1.1, 4.6]</td>
<td>-0.9 ± 1.7 [-5.1, 1.3]</td>
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<tr>
<td>Whole Brain</td>
<td>49</td>
<td>-0.6 ± 0.4 [-1.5, -0.1]</td>
<td>-0.6 ± 0.2 [-1.2, 0.1]</td>
<td>1.7 ± 0.2 [1.5, 2.1]</td>
<td>1.4 ± 0.2 [1.2, 1.9]</td>
<td>0.2 ± 0.3 [-0.3, 0.7]</td>
</tr>
<tr>
<td>Breast</td>
<td>48</td>
<td>-1.2 ± 0.9 [-3.5, 0.8]</td>
<td>-0.7 ± 0.8 [-3.8, 0.4]</td>
<td>2.6 ± 1.0 [1.1, 6.0]</td>
<td>1.8 ± 0.9 [0.8, 7.3]</td>
<td>0.2 ± 0.8 [-1.1, 3.4]</td>
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<tr>
<td>Prostate</td>
<td>42</td>
<td>-0.2 ± 0.3 [-0.8, 0.4]</td>
<td>-0.2 ± 0.3 [-0.9, 0.3]</td>
<td>0.9 ± 0.3 [0.6, 1.5]</td>
<td>0.6 ± 0.2 [0.3, 1.0]</td>
<td>0.4 ± 0.1 [0.2, 0.7]</td>
</tr>
<tr>
<td>Liver</td>
<td>22</td>
<td>-0.3 ± 0.4 [-1.2, 0.5]</td>
<td>-0.3 ± 0.4 [-1.2, 0.4]</td>
<td>1.0 ± 0.4 [0.4, 2.0]</td>
<td>0.7 ± 0.3 [0.4, 1.2]</td>
<td>0.4 ± 0.3 [-0.1, 1.1]</td>
</tr>
</tbody>
</table>

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**Presentation Number:** 46

**Dosimetric Evaluation of a Limited-angle Intrafraction Verification (LIVE) System**

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**Purpose/Objective:** Recently we developed a LIVE system for fast intrafraction target verification during arc treatment delivery or in-between static beams. Compared with CBCT, LIVE has the advantages of high efficiency, high-quality volumetric images and low imaging dose. Our preliminary results demonstrated that LIVE was able to localize the target volume accurately using only 15°-30° scan angle. Another important application of LIVE is to use the volumetric images from LIVE for dose calculation for adaptive radiotherapy (ART). We hypothesize that LIVE images are accurate for dose evaluation as they represent actual target location during treatment. The purpose of this study is to evaluate the accuracy of LIVE images for dose evaluation.

**Materials/Methods:** The LIVE system acquires limited-angle kV projections simultaneously during arc
treatment delivery or in-between static beams as the gantry moves from one beam to the next. Orthogonal limited-angle MV projections are also acquired from the exit fluence of arc treatment or in-between static beams. MV projections are linearly converted to kV projections. Patient prior planning CT at one phase is used as the prior image, and the on-board image is considered as a deformation of the prior image. The deformation field is solved using the data fidelity constraint, a breathing motion model extracted from the planning 4D-CT and a free-form deformation model. To evaluate LIVE, 4D Digital Extended Cardiac Torso (XCAT) phantom was used to simulate a lung cancer patient with 3cm-diameter tumor in the planning CT. Four patient scenarios were simulated in the on-board image: 1). tumor shrinkage to 2.5 cm; 2). tumor growth to 4 cm; 3). tumor motion baseline drift of 8 mm along a single axis; 4). tumor motion baseline drift of 5 mm along all three axes. 30° kV-MV projections were used for LIVE reconstruction. A dynamic conformal arc plan was made to deliver 12 Gy*4 to the PTV at the end expiration phase in a gated treatment. The plan was mapped to the on-board ground-truth and LIVE images to evaluate the actual dose delivered to PTV.

**Results:** Dose is presented as percentage of the prescription dose. PTV Min, Max and Mean doses are: scenario 1). 97%, 112%, 106% in the ground-truth, 98%, 114%, 108% in LIVE; scenario 2). 41%, 113%, 100% in the ground-truth, 41%, 115%, 102% in LIVE; scenario 3). 57%, 111%, 97% in the ground-truth, 58%, 114%, 99% in LIVE; scenario 4). 29%, 110%, 94% in the ground-truth, 30%, 113%, 96% in LIVE. The DVH and isodose lines in LIVE also match with those in the ground-truth images.

**Conclusion:** Simulation study indicated that LIVE provided accurate evaluation of the dose delivered to the target based on the actual target location during treatment. By improving the accuracy of ART, LIVE could potentially improve the tumor control and reduce toxicity for lung cancer treatments.

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**Presentation Number: 202**

**The Dawn Of A New Era: First Ever MR - IGRT Treatments - Initial Experiences And Future Implications**


**Purpose/Objective(s):** We report on the clinical implementation of the first magnetic-resonance imaging-guided radiation therapy (MR-IGRT) program, experiences with the initial patient treatments, and the implications for the future developmental and clinical work. The goal of this project was to develop and clinically implement an MR-IGRT program for the full spectrum of indications normally treated with conventional external beam RT (EBRT), which seamlessly integrates within the established EBRT clinical practice and provides the ability to treat normally seen cases with minimal alternations to the existing clinical workflows.

**Materials/Methods:** The MR-IGRT system consists of a split 0.35T MR scanner straddling three 60Co heads mounted on a ring gantry, each head equipped with independent doubly-focused multileaf collimators. The MR and RT systems share a common isocenter, enabling simultaneous and continuous MR imaging during RT delivery. Following commissioning of the system, five patients started treatment on an institutionally approved registry over the initial three-week period; one patient was not able to complete the treatment due to medical reasons and was excluded from the results. The first treatments included a patient with T4 colon cancer invading abdominal wall, a patient with an unresectable intraabdominal desmoid tumor, a patient with a metachronous 4th lung cancer over a 14 year interval, a patient with lung cancer painful iliac metastasis, and a patient with isolated, nodal breast cancer recurrence at the aortic arch with prior chest wall RT. These cases were selected due to desires for MR-IGRT and soft tissue visualization, to reduce treatment margins, and/or to have increased ability to control for any observed changes. All cases were evaluated for any additional findings on daily MR images, localization ability based on MR imaging, and the degree of tumor and surrounding anatomy motion.

**Results:** This work demonstrated that an MR-IGRT program can be integrated efficiently within the scope of
existing EBRT practices. Notable observations on the first treated patients included 1) additional bone metastasis that were occult on planning CT, 2) physicians reporting good ability to localize tumors daily on MR images, and 3) observations of normal anatomy movement that affected target motion in ways that possibly require further research (e.g., continuous MR imaging showed how pulsatile nature of the aortic arch affected position of the nodal disease).

**Conclusions:** The first ever MR-IGRT program has begun clinical treatments and, based on the initial observations reported here, this approach should lead to significant research and clinical developments in radiation therapy.

**Author Disclosure:**

**S. Mutic:** F. Honoraria; Varian Medical Systems, ViewRay, Inc. I. Travel Expenses; Varian Medical Systems, ViewRay, Inc. K. Advisory Board; ViewRay, Inc. M. Stock; Radalogica, LLC. O. Partnership; Treat Safely. P. Royalty; Modus Medical. Q. Patent/License Fee/Copyright; Varian Medical Systems. S. Leadership; Radalogica, LLC. 

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**C.G. Robinson:** None.

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**L. Santanam:** None.

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**J.M. Michalski:** None.

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**C.G. Robinson:** None.

**V. Rodriguez:** I. Travel Expenses; ViewRay, Inc.

**L. Santanam:** None.

**K. Tanderup:** I. Travel Expenses; ViewRay, Inc.

**J.M. Michalski:** None.

**J.R. Olsen:** G. Consultant; Dfine, Inc. I. Travel Expenses; Dfine, Inc.; RSNA (Resident and Fellow Committee).

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**K. Tanderup:** I. Travel Expenses; ViewRay, Inc.