1  CT-Guidance Allows Interstitial Implantation in an Outpatient Setting for Cervical Cancer Patients

M. Bernstein, R. Yaparpalvi, H. Kuo, S. Kalnicki, K. Mehta, Montefiore Medical Center, Bronx, NY

Purpose/Objectives: Cervical cancer patients with disease extending laterally into parametrial tissue often require interstitial trans-perineal implantation under general anesthesia and a hospital stay for brachytherapy treatments. A major disadvantage of intraoperative implantation is the lack of 3D image guidance during needle placement. Here, we describe real-time CT-guidance to allow interstitial implantation of catheters with the Utrecht Fletcher Applicator® (Nucletron™) in an ambulatory setting.

Materials/Methods: Following a mild oral analgesic and an anxiolytic, patients are placed on the CT simulator couch in the treatment position. The Utrecht tandem and ovoid (T&O) is inserted and a CT scan of the pelvis performed to confirm appropriate geometry. Delineating the extent of disease and organs at risk on the CT scan allows determination of the optimal number, distribution, and depth of insertion of each interstitial catheter. A CT is repeated after insertion of each catheter and adjustments are made in real time. Once all interstitial catheters are implanted, a final CT is performed for 3D optimization brachytherapy planning. Without movement or manipulation, the patients are then treated with HDR brachytherapy on the CT simulator couch. Following therapy, the Utrecht T&O applicator and interstitial needles are removed and patients are discharged home.

Results: A total of 77 treatments were performed in 18 patients. Ten out of eighteen patients (56%) required 2 or fewer needles placed to adequately dose the extent of disease. Persistent vaginal bleeding after removal of the applicator was observed in 4 patients necessitating an inpatient stay for close observation with 2 patients requiring blood transfusions. Only one did not continue with the interstitial implantations and was treated with standard T&O implant followed by an external beam parametrial boost. All other patients tolerated the treatments well with no complications documented.

Conclusions: Real-time CT-guided administration of interstitial catheters using the Utrecht applicator allows for proper positioning into parametrial disease. These implants are tolerated well and can be performed safely in an outpatient setting, obviating the need for placing interstitial needles in the operating room without 3-D image guidance.

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2  4DMRI Provides More Accurate Renal Motion Estimation in IMRT in Young Children

A. S. Pai Panandiker, A. Winchell, R. Loeffler, R. Song, M. Rolen, C. Hillenbrand, St. Jude Children’s Research Hospital, Memphis, TN

Purpose/Objectives: Highly conformal radiotherapy requires precise temporospatial definition of target and normal tissue. This is a preliminary report of a prospective Phase II study estimating a near-class solution for target volume and abdominal organ motion in very young children (age < 5 years).

Materials/Methods: From September 2011 through July 2012, 6 children have been enrolled to an ongoing study
designed to estimate local control and pattern of failure when treated with IMRT for high-risk abdominal neuroblastoma. Currently, 4 subjects (male=2; female=2; median age=3) have undergone imaging to define physiologic motion of the target volume and kidneys. To estimate renal motion, each patient received a 4DCT and 4DMRI in treatment position. The 4DCT consisted of axial slices (0.53x0.53x 3.0mm\(^3\)) covering the abdomen. The images were binned into 8 positions according to a respiratory trace from a pressure-sensitive Anzai belt. The 4DMRI consisted of 200 images acquired consecutively in a single coronal and sagittal position (duration 1:30 min per data set). A trueFISP sequence (image acquisition time of 546ms, TE 2.1ms, resolution 1.2-1.6 x1.2-1.6 x 7mm\(^3\)) was applied. Coronoral images were used to determine superior/inferior (SI) and medial/lateral (ML) physiologic motion, and sagittal image data sets for SI and anterior/posterior (AP) physiologic motion. The 4DMRI physiologic motion was measured by tracking the motion of user defined points along the kidney boundary in a custom graphical user interface written in Matlab. The smallest motion estimate was set to the voxel size.

**Results:** The 4DCT estimated left and right SI mean kidney motion as 3.75±1.5mm and 5.25±1.5mm compared to the 4DMRI estimates of 2.8±0.32mm and 3.13±0.77mm, respectively. Both the 4DCT and 4DMRI measured the same mean ML motion for the left and right kidney (1.85±0.5mm and 1.4±0.16 mm, respectively). For the left and right AP motion, 4DCT measured a mean motion of 1.6±0.57mm and 1.85±0.5mm, while 1.4±0.16mm was measured in both kidneys by 4DMRI. The largest renal motion extends in the SI direction; 4DMRI measured 34% and 68% less movement in left and right kidneys than 4DCT.

**Conclusions:** 4DMRI provides superior kidney tissue contrast when compared to 4DCT. 4DMRI provides two-fold higher resolution in the SI direction by enabling better organ edge detection and anatomic tracking. 4DMRI estimates an overall reduction in avoidance structure volume (PRV) by detecting less motion than 4DCT. Internal target volume margins can be reduced by as much as 50%; ionizing radiation doses to infants can be avoided when using MRI as a more accurate technique for renal motion tracking. 4DMRI provides the necessary resolution to aid in highly conformal treatment planning for IMRT and proton therapy.

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### Knowledge-based Organ-at-Risk Sparing Models in IMRT Planning

**Q. Wu\(^1\), L. Yuan\(^1\), T. Li\(^1\), F. Ying\(^1\), Y. Ge\(^2\), \(^1\)Duke University Medical Center, Durham, NC, \(^2\)Wake Forest University, Winston-Salem, NC**

**Purpose/Objectives:** This project focuses on the modeling and distribution of human expert knowledge in designing high quality IMRT plans, for adaptive and regular radiation therapy planning.

**Materials/Methods:** A major source of expert’s clinical knowledge is embedded in the prior treatment plans that have been developed by expert physicians and planners and proven to be effective and optimal for that patient. This project proposes a novel approach to learning from existing databases of high-quality plans and developing models to predict optimal dose coverage that are specific to an individual patient. Further, the knowledge models are trained to quantify the dose sparing trade-offs among different Organs-at-risk (OARs) and between OAR dose sparing and target dose coverage. IMRT plans of 88 prostate, 106 HN, and 21 spine SBRT plans were used to build the knowledge models for each site. The final models were tested by additional 24 prostate and 48 HN plans. The model for spine SBRT was tested by the leave-one-out method.

**Results:** For HN and prostate planning, the significant patient anatomical features that affect OAR sparing are: the distance between OAR and PTV, the portion of OAR volume within an OAR specific distance range, the overlap volume...
between OAR and PTV, and the portion of OAR volume outside the primary treatment field. For spine SBRT planning, the most significant patient anatomical feature that affects cord sparing is the tightness of the geometric enclosure of PTV surrounding the cord and the homogeneity of PTV dose coverage. The most significant OAR dose sparing trade-off is between bladder and rectum in prostate plans and between the left and the right parotids in HN plans. Trade-off is most apparent when the parotid on one side has very large overlap with the PTV. In most of these plans (83%), the planner chooses to loosen the dose constraint for that parotid in exchange for lower contra-lateral parotid median dose. The interaction between OAR dose sparing and PTV dose coverage is most significant in spine SBRT plans. The dosimetric parameters predicted for the test patient cases using the knowledge models were in agreement with those from the clinical plans in more than 75% of the cases, for all 3 sites.

Conclusions: The knowledge models are capable of predicting OAR dose sparing based on expert experiences and their prior plans. The dosimetric trade-off between multiple OARs and between PTV and OAR in IMRT planning is also included in the model. Such prediction helps to automate the re-planning for adaptive therapy and to reduce the trial-and-error process for regular IMRT planning.


4 Hepatic Function Model Based Upon HIDA SPECT and Dose for Physiological Adaptive RT

H. Wang, M. Feng, K. Frey, J. Balter, R. Ten Haken, T. Lawrence, Y. Cao, University of Michigan, Ann Arbor, MI

Purpose/Objectives: High dose radiation therapy (RT) for hepatic cancer treatment is limited by development of radiation-induced liver disease. We hypothesized that hepatic function measured by 99mTc-labeled iminodiacetic acid (HIDA) SPECT prior to and during RT, combined with radiation doses, could predict post-RT hepatic function, and thereby could support physiological adaptive RT.

Materials/Methods: Fourteen patients who had unresectable intrahepatic cancers and were treated with 3D conformal RT, IMRT or SBRT (median dose 52 Gy) underwent dynamic HIDA SPECT scanning prior to RT, after delivery of 50%-60% planned doses, and one month after the completion of RT. Indocyanine green (ICG) tests (a measure of overall liver function) were performed +/-1 day of each SPECT scan. The 27 dynamic HIDA SPECT volumes were acquired over 60-min after the administration of 5-15mCi 99mTc-labeled HIDA on a SPECT/CT scanner. The 3D volumetric hepatic extract fraction (HEF) images of the liver were quantified by deconvolution of the liver-voxel radioactivity curves from the vascular input function measured from a volume of interest in the spleen. After co-registration of CT/SPECT with treatment planning CT, planned 2 Gy-equivalent dose distributions were overlaid on the HEF images. The HEF dose-response functions during and post RT were generated for regions corresponding to planned iso-dose intervals of 4 Gy. To validate HEF, the mean HEFs in the whole liver were correlated with the ICG clearance rate. Two predictive models, one priori and another adaptive, based upon the HEF measured prior to or during RT and planned doses, were developed for prediction of hepatic function post RT by multivariate linear regression.

Results: The mean HEFs were significantly correlated with ICG clearance rates (r=0.83, p<0.001), regardless of the time of measurements. Dose-dependent reductions in the regional HEFs one month post RT were observed in 13 patients. In the priori model, the regional HEF post RT was predicted by the planned local total dose and the HEF assessed prior to RT (R²=0.35, p<0.00001); in which, as a group average, every Gy reduced the HEF by approximately 0.24%. In the adaptive model, the regional HEF post RT was predicted by the HEF re-assessed at the mid-course of RT and the planned remaining dose (R²=0.54, p<0.00001), indicating an improvement in the model prediction by the mid-course
HEF that measures individual patient and regional sensitivity to radiation. **Conclusions:** Predictive models relating planned doses with either hepatic function measured prior to RT, or that assessed at the mid-course of RT, could aid in physiological adaptive RT for intrahepatic cancer treatment and management of risks for liver injury. Supported by RO1CA132834.

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### 5. In Vivo Verification as a Tool to Tailor Daily IGRT and Flag Adaptive Radiotherapy

G. Olivera¹, W. Lu¹, D. Parnell¹, X. Mo¹, M. Chen¹, C. Mantz², E. Fernandez³, D. Dosoretz², S. E. Finkelstein⁴, D. Galmarini⁵, et al., ¹21st Century Oncology, Madison, WI, ²21st Century Oncology, Fort Myers, FL, ³21st Century Oncology, Fort Lauderdale, FL, ⁴21st Century Oncology, Scottsdale, AZ

**Purpose/Objectives:** Use the information generated during the in-vivo verification process to define IGRT strategies and flag possible needs for adaptive therapy. Report information during treatment to infer the impact of machine behavior, patient setup and anatomical changes. Create a system and metrics to flag possible issues and trending. Create procedures to assist in identifying the clinical impact and troubleshoot possible problems. Generate suggestions for daily IGRT based on the in-vivo verification findings and possible adaptive re-planning.

**Materials/Methods:** An automatic system for in-vivo verification that retrieves and processes machine and patient information during treatment from the TomoTherapy archive was developed. In vivo dosimetry consists of using the exit detector data and comparing a reference fraction with respect to daily treatment deliveries using the Gamma metric. A set of metrics including trending and flagging at the patient and fraction level was created. By analyzing the report using metrics and flags, a reviewer can very easily identify machine, setup, and/or anatomical issues. A set of tools including daily adaptive dose recalculation complemented the results and aided troubleshooting issues and estimating the clinical impact and infer-possible needs for adaptation.

**Results:** More than 42,000 fractions were analyzed from 14 helical TomoTherapy machines at different clinics. The data was collected in a period of approximately a year. The level of in vivo flags was independent of patient load. Machine output is a variable that needs to be considered on the in vivo dosimetry gamma value. The number of in vivo flags reduces considerably as a function of the length of time the system is used by tailoring IGRT procedures to specific anatomical sites and specific patients based on the information provided by the system. The level of combined yellow and red gamma flags ranks between 10 percent for prostate and up to 40 to 50 percent for head and neck. The number of in-vivo verification flags depends on the length of the daily setup CT length. For certain anatomical sites, long CTs may not reduce the number of in-vivo verification flags, however, in vivo dosimetry still indicate the possible problem locations.

**Conclusions:** Exit dosimetry Gamma flags seem to be an adequate surrogate to flag possible issues regarding deposited dose. Even though flags do not always represent actual delivery errors or deviations, unless a system like this is used, many errors may go undetected. With such information the IGRT approach can be tailored for each patient’s needs and adaptive needs can be evaluated.

Image Guided Concomitant Boost Radiotherapy Technique Leads to Safe Dose Escalation and Improves Local Tumor Control

D. Katsochi, C. Paraskeuopoulou, DTCA Hygeia, Athens, Greece

**Purpose/Objectives:** One of the main objectives in patients with advanced unresectable head and neck, lung, cervical and brain carcinoma is to improve local control of tumor disease. The introduction of image guided radiotherapy offers the opportunity to safely apply a supplementary dose to the macroscopic disease. This accelerated radiotherapy course, known as concomitant boost, has the advantage of increasing the total dose delivered and tumor response without increasing the number of fractions.

**Materials/Methods:** From May 2009 to May 2012, 85 patients were treated with concomitant boost technique. The distribution of primary tumors was 47 patients with lung cancer, 28 patients with head and neck cancer, 7 patients with brain tumors and 3 patients with cervical cancer. 76 patients received chemotherapy during radiation therapy. Patients were treated using the conformal or VMAT technique. Planning target volume (PTV) was treated daily with 1.8 Gy for 5 to 6 weeks to a total dose of 45-54 Gy, while the dose to the Gross Tumor Volume (GTV) was boosted up to 55-65 Gy depending on the anatomic region. Organs at risk were irradiated to safe limits. In 74% of the patients we readapted the treatment plan due to local tumor regression using image guidance data (CBCT).

**Results:** All patients completed the treatment plan with no major toxicity. Follow up was scheduled at the end of the treatment, three and nine months after. All patients achieved local tumor control, 52 patients with complete tumor response, 27 patients with partial response and 6 with stable disease.

**Conclusions:** Concomitant boost in combination Image Guided Radiotherapy is a feasible, safe and effective treatment for patients with unresectable carcinomas. Results are encouraging and promising regarding locoregional disease control.

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CT Heterogeneity as a Prognostic Marker in Primary Esophageal Cancer Following Neoadjuvant Chemotherapy

C. S. P. Yip\(^1\), F. Davnall\(^1\), R. Kozarski\(^2\), D. Landau\(^{1,3}\), R. Mason\(^1\), J. Lagergren\(^1\), G. Cook\(^4\), V. Goh\(^{1,3}\), Guy’s & St Thomas’ NHS Foundation Trust, London, United Kingdom, \(^2\)University of Hertfordshire, Hatfield, United Kingdom, \(^3\)Division of Imaging Sciences and Biomedical Engineering, King’s College London, London, United Kingdom, \(^4\)Division of Imaging Sciences and Biomedical Engineering, King’s College London, London, United Kingdom

**Purpose/Objectives:** Outcome following curative surgery remains poor in early stage esophageal cancer, thus neoadjuvant chemotherapy is advocated to improve local and distant control. At present, there is no established imaging or histological biomarker that identifies responders or good prognosis patients who would benefit from surgery. We hypothesized that CT texture analysis which assesses intratumoral heterogeneity may prognosticate in patients treated with neoadjuvant chemotherapy for primary esophageal cancer.

**Materials/Methods:** 31 patients (median age 63 years, range 49-77; 19 males; 22 adenocarcinoma, 9 SCC; 1 stage I, 12 stage II, 17 stage III, 1 stage IV) who received neoadjuvant chemotherapy for esophageal cancer in our center between 2007-2010 were identified retrospectively from our institutional database. All patients received platinum and fluorouracil-based chemotherapy (ECF, ECX or PF) followed by surgery. 11 patients received adjuvant treatment. CT
texture analysis of the primary tumor was performed using proprietary software (TexRAD, University of Sussex) on staging and post-chemotherapy scans. Texture parameters (mean-grey level intensity (M), entropy, uniformity, kurtosis, skewness and standard deviation of histogram (SD)) were derived for 4 filter values to highlight structures of different spatial width: 1.0 (fine texture), 1.5-2.0 (medium) and 2.5 (coarse). Overall survival was estimated using Kaplan-Meier method and comparison between dichotomized texture parameters was performed with log-rank test. A subgroup of 26 patients were grouped as responders and non-responders based on pathological Mandard score (score 1-3 vs. 4-5 respectively). The association between treatment response and texture parameters was done using Mann-Whitney U (MWU) and Fisher exact test. A p value ≤0.01 was considered significant.

Results: Median follow-up was 24.7 months (range 9.6-56.9). Baseline texture parameters: lower entropy (filter 2.5: median OS 34.1mo vs. 9.3mo, p=0.01), lower SD (filter 2.5: MOS 34.1mo vs. 8.1mo, p<0.001) and higher uniformity (filter 2.5: MOS 34.1mo vs. 9.3mo, p=0.01); and post-treatment parameters: lower M (filter 1.0: MOS 36.1mo vs. 10.5mo, p<0.001) and negative skewness (filter 2.0: MOS 34.1mo vs. 4.3mo, p<0.001) were significant positive prognostic factors. There were 11 responders: 5 complete, 6 partial; and 15 non-responders. Baseline SD (filter 1.5, p=0.006) and post-treatment SD (filter 1.0, p=0.009) as continuous variables had significant associations with pathological tumor response.

Conclusions: CT texture analysis has the potential to be a prognostic biomarker following neoadjuvant therapy in esophageal cancer.


8 Pretreatment SUVmax as a Marker for Progression-Free Survival in Stage I NSCLC Treated With SBRT

Z. D. Horne, D. A. Clump, S. Shah, J. A. Vargo, S. A. Burton, N. A. Christie, M. J. Schuchert, R. J. Landreneau, J. D. Luketich, D. E. Heron, University of Pittsburgh Medical Center, Pittsburgh, PA

Purpose/Objectives: This study aims to assess pretreatment SUV<sub>max</sub> as a prognosticator for primary stage 1 NSCLC treated with stereotactic body radiation therapy.

Materials/Methods: This study includes 95 medically inoperable patients identified between October 2005 and May 2011 (median age 77 years) with primary, biopsy-confirmed peripheral stage 1A/1B NSCLC. No tumor was located within 2cm of the proximal bronchial tree and no patient had been previously treated for lung cancer. All patients had pre-SBRT FDG-PET/CT scans with documented pretreatment SUV<sub>max</sub>. Treatment fractionation consisted of 60Gy in 3 fractions with a median treatment time of six days (range 3-21 days). Local, regional, and distant failures specified from the last day of treatment were evaluated independently according to the terms of RTOG 1021. Tumor control, overall- and progression-free survivals were estimated by the Kaplan-Meier method. Cox proportional hazards regression was performed to determine whether SUV<sub>max</sub> age, KPS, gender, tumor size/T stage, or smoking history influenced outcomes. SUV<sub>max</sub> was evaluated as both a continuous and as a dichotomous variable using a cutoff of <5 and ≥5.

Results: With a median follow-up of 15 months, median OS and PFS were 25.3 and 40.3 months, respectively. In the univariate analysis, pretreatment SUV<sub>max</sub> with a cutoff value of 5 predicted for OS and PFS (p=0.024, each) but did not achieve significance for LC (p=0.256). On Cox univariate regression analysis, SUV as a dichotomous variable predicted
for both OS and PFS (p=0.027 and p=0.030, respectively). Defined as a continuous variable, SUV\text{max} continued to predict for OS and PFS (p=0.003, each), but also predicted LC (p=0.045) and trended toward significance for DC (p=0.064). Tumor stage, histology, KPS, and age were significant for OS on univariate analysis and were included in multivariate analyses. On ANOVA test, tumor T-stage and histology were both significantly correlated to SUV\text{max} (p=0.013 and p<0.001, respectively). Tumor stage remained a significant predictor of OS on multivariate analysis (p=0.05), though SUV\text{max} did not predict for OS as a dichotomous or continuous variable (p=0.209 and p=0.223, respectively). It did, however, predict for PFS as a continuous variable (p=0.009) and neared significance as a dichotomous variable (p=0.053). SUV\text{max} also trended toward significance for local control as a continuous variable (p=0.076).

**Conclusions:** SUV\text{max} appears to be a statistically and clinically significant independent prognostic marker for progression-free survival in patients with Stage 1 NSCLC treated with SBRT. Prospective studies to more accurately define the role of tumor FDG uptake in the prognosis of NSCLC are warranted.


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**Correlation of Quantitative Diffusion-Weighted and Dynamic Contrast-Enhanced MRI Parameters With NCCN Risk Group, Gleason Score and Maximum Tumor Diameter in Prostate Cancer**

M. Kamrava\textsuperscript{1}, M. Chung\textsuperscript{1}, S. Mesko\textsuperscript{1}, J. Wang\textsuperscript{1}, S. Raman\textsuperscript{2}, D. Margolis\textsuperscript{2}, L. Marks\textsuperscript{3}, P. Kupelian\textsuperscript{1}, \textsuperscript{1}UCLA Radiation Oncology, Los Angeles, CA, \textsuperscript{2}UCLA Radiology, Los Angeles, CA, \textsuperscript{3}UCLA Urology, Los Angeles, CA

**Purpose/Objectives:** To determine if there is a correlation between quantitative parameters from diffusion-weighted (DWI) and dynamic contrast-enhanced (DCE) MRI with NCCN risk group, Gleason score (GS), and maximum tumor diameter (MTD) in prostate cancer.

**Materials/Methods:** In this IRB approved retrospective study we reviewed 3T multiparametric MRI reports on patients with biopsy-proven prostate cancer performed during evaluation for radiation treatment or as part of an active surveillance protocol. DCE pharmacokinetic modeling parameters evaluated included: $K_{\text{trans}}$ (forward volume transfer constant, minute\textsuperscript{-1}), $K_{\text{ep}}$ (reverse reflux rate constant between extracellular space and plasma, minute\textsuperscript{-1}), and iAUGC (initial area under the gadolinium concentration curve in the first 30 seconds after injection, mmol/L sec). The average values of regions of interest on the apparent diffusion coefficient (ADC) maps of diffusion weighted imaging (b values of 0, 100, 400, and 800 s\textsuperscript{2}/mm) were also recorded. The relationship between MRI metrics and NCCN risk group, GS, and MTD were examined using one-way analysis of variance (ANOVA). Statistical significance was defined as p < 0.05.

**Results:** 52 patients were included in the study. 37%, 44%, and 19% had low (L), intermediate (I), or high (H) risk disease per NCCN risk groups. One-way ANOVA analysis revealed iAUGC scores were significantly different when stratified by L/I/H risk groups (mean±SD 8.9±5.0, 9.8±5.1, 13.8±4.1) (p=0.05), GS (9.1±4.8, 9.8±5.2, 13.8±4.1) (p=0.05), and MTD ≤ 2 cm vs > 2 cm (9.6±4.8, 14.5±5.0) (p=0.02). $K_{\text{trans}}$ and $K_{\text{ep}}$ were not significantly different when stratified by risk grouping or GS. $K_{\text{trans}}$ was significantly different when stratified by MTD ≤ 2 cm vs > 2 cm (0.5±0.3, 0.9±0.6) (p=0.01) but $K_{\text{ep}}$ was not. ADC significantly correlated with L/I/H risk groups (1071±220, 1040±225, 851±66) (p=0.02) and GS (1063±229, 1046±217, 851±66) (p=0.02) but not MTD ≤ 2 cm vs > 2 cm.

**Conclusions:** iAUGC values significantly correlate with NCCN risk group, GS, and MTD. $K_{\text{trans}}$ also significantly correlates with MTD but ADC values did not. Further investigation is warranted to determine whether these MRI metrics are complementary or independent prognostic factors in prostate cancer.
A Phase 2 Multi-institutional Study to Evaluate Gemcitabine and Fractionated Stereotactic Radiotherapy for Unresectable, Locally Advanced Pancreatic Adenocarcinoma

A. T. Wild¹, D. T. Chang², K. A. Goodman³, D. A. Laheru¹, L. Zheng¹, S. P. Raman¹, L. A. Columbo², C. L. Wolfgang¹, A. C. Koong², J. M. Herman¹, ¹Johns Hopkins University School of Medicine, Baltimore, MD, ²Stanford University, Stanford, CA, ³Memorial Sloan-Kettering Cancer Center, New York, NY

Purpose/Objectives: Phase I/II studies with single-fraction (25 Gy) stereotactic body radiotherapy (SBRT) for pancreatic ductal adenocarcinoma (PDA) have shown local progression free survival (LPFS) rates of >90%, but are limited by late GI toxicity and minimal tumor response. We performed a phase II multi-center trial of gemcitabine (GEM) and fractionated SBRT to determine if a high rate of LPFS with reduced toxicity could be achieved.

Materials/Methods: After multidisciplinary review, 32 pts with locally advanced PDA received GEM in sequence with SBRT (6.6 Gy in 5 consecutive daily fractions, 33 Gy total). LPFS, metastasis free survival (MFS), and overall survival (OS) were measured from date of tissue diagnosis. Objective tumor response (OTR) was assessed by RECIST/PERCIST. EORTC QLQ-C30/PAN26 questionnaires were used to measure QOL.

Results: Median follow-up was 12 months (range, 2-23). Mean age was 69.9 yrs (SD, 9.8) and 62% were male. Patients received a mean of 2.2 (SD, 1.0) GEM doses prior to SBRT and 8.3 (SD, 5.6) doses total. All patients completed SBRT. Median OS was 15.9 months (95% CI, 12.7-18.8). Stratification by CA19-9 > or < 90 at diagnosis yielded a hazard ratio of 6.2 for > 90 (p=0.021). Median LPFS has not been reached and median MFS was 10.2 mos (95% CI, 2.9-17.5). LPFS rate at 1 year was 87%. OTR on CT was seen in 41%, while 41% had stable disease and 18% progressed. Tumor metabolic activity decreased in 17/18 patients with pre/post-SBRT PET available. Mean peak SUV was 4.0 pre-SBRT versus 2.4 post-SBRT (p=0.002). Median CA19-9 was reduced from 124.7 prior to SBRT to 43.9 afterwards. Acute toxicity included: grade 2 anorexia (37%), fatigue (28%), nausea (22%), abdominal pain (19%), weight loss (9%), diarrhea (3%); grade 3 nausea (9%); and grade 4 nausea (6%). Late grade ≥3 GI toxicity was seen in 9%. Mean QOL score 4 weeks post-SBRT was similar to baseline (p=0.38). At 6 months there was a trend towards improved QOL (p=0.07).

Conclusions: Fractionated SBRT with GEM achieves high rates of LPFS and tumor response. Minimal grade ≥3 acute and late toxicity was observed. SBRT is more likely to benefit patients with CA 19-9 <90. A combination of SBRT with more aggressive chemotherapy may further improve outcomes.

Purpose/Objectives: While concurrent chemoradiotherapy has increasingly been accepted as a standard approach for locally advanced head and neck cancer, management of the post-treatment neck is controversial, particularly for patients with residual lymphadenopathy on computed tomography (CT) in the setting of negative post-treatment positron emission tomography (PET). The purpose of this study was to analyze outcomes among this subset of patients based on whether or not they subsequently underwent neck dissection.

Materials/Methods: Retrospective review of patients treated by definitive cisplatin-based chemoradiotherapy for stage III/IV squamous cell carcinoma of the head and neck between January 2007 and December 2011 identified 49 patients with residual lymphadenopathy but negative PET based on standardized uptake value (SUV) of less than 3. All patients had previously been treated to a median dose of 70 Gy (range, 60 to 74 Gy). The median duration from completion of chemoradiotherapy to post-treatment PET was 10 weeks (range, 4 to 20 weeks). The median size of residual lymphadenopathy was 1.5 cm (range, 1.0 to 6.5 cm).

Results: Among the 49 patients with residual lymphadenopathy but with negative PET, twenty-five subsequently underwent neck dissection, with only 1 patient (4%) having evidence of pathological disease. The remaining 24 patients were observed with none developing evidence of local-regional progression. With a median follow-up duration of 30 months (range, 6 to 62 months), the 3-year estimates of overall survival (89% versus 92%, p=0.57), progression-free survival (91% versus 90%, p=0.42), and local-regional control (95% versus 100%, p=0.68), did not significantly differ between patients treated by neck dissection or observation.

Conclusions: Omission of neck dissection appears to be a reasonable option for patients with residual lymphadenopathy but negative PET after concurrent chemoradiotherapy for locally advanced head and neck cancer. Although PET appears to be associated with a low false-negative rate in the post-chemoradiotherapy setting, prospective data is needed to confirm these findings.


12 Diffusion Abnormality Index: A New Imaging Biomarker for Early Assessment of Tumor Response to Therapy

R. Farjam, C. I. Tsien, F. Y. Feng, J. A. Hayman, T. S. Lawrence, Y. Cao, University of Michigan, Ann Arbor, MI

Purpose/Objectives: Diffusion heterogeneity in a brain tumor presents a challenge to use a diffusion change as an indicator for therapy response. Hence, we developed a diffusion abnormality index (DAI) for early prediction of brain tumor response to radiotherapy.

Materials/Methods: For each patient, a normal tissue ADC histogram (HNT, ADC) is obtained in a normal brain volume of 3-4cc and normalized to have a peak intensity equal to 1. A tumor ADC histogram is generated in the tumor volume defined on post-Gd T1 weighted images. The tumor ADC histogram usually spreads beyond the normal tissue ADC histogram, and the latter divides the first into three categories: low (high cellularity), normal, and high (edema and necrosis) diffusion. Thus, an abnormal diffusion probability function (ADPF) of the tumor is defined by 1-HNT, ADC and band-pass filtered to reduce noise influence at the two tails. Considering that an increase in the low-ADCs of the high tumor cellularity region could predominantly determine response compared to a change in the high ADCs, a weighting factor (α) is used to weight the low ADCs related to the high ADCs in the ADPF. Finally, a DAI of a tumor is defined as an integral of the ADPF-weighted ADC histogram of the tumor.

The DAI was evaluated for predicting post-RT radiographic response in 20 patients who had brain metastases and were treated by whole brain radiotherapy (WBRT). Of a total of 45 lesions, 16 were responsive, 18 stable and 11 progressive. The group differences in the changes of the DAIs from pre-RT to 2 weeks (2W) after start of RT were tested...
The performance of DAI for predicting non-responsive lesions was evaluated by Receiver Operating Characteristic (ROC) analysis and compared with the changes in gross tumor volumes (GTVs) observed within the same time interval.

**Results:** The percentage decrease in DAI from pre-RT to 2W was significantly greater in responsive tumors than in stable and progressive ones (p < 0.0009). The ROC analysis revealed that a change in the DAI (AUC = 0.90) from pre-RT to 2W was a significantly better predictor than a change in the GTV (AUC = 0.68) for post-RT response (p < 0.01), suggesting that physiological change occurs before the volumetric change.

**Conclusions:** The diffusion abnormality index, accounting for both low and high diffusion caused by high cellularity and edema, respectively, could be a better diffusion-imaging biomarker for early assessment of tumor response to therapy.

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**POSTER PRESENTATIONS**

100 Deglutition-Induced Real-Time Directional Displacements in Head-and-Neck Cancer Patients - Dynamic Volume Shuttle Imaging Analysis

V. Shankar¹, C. Haritha¹, V. B. Patel², J. D. Prajapathi¹, P. K. Mathews¹, G. J. Sunith³, P. Shinde¹, L. N. Chaudhari¹, M. Meshram¹, J. Joseph¹, et al., ¹M.S.Patel Cancer Center, Karamsad, Gujarat, India, ²Dept of Radiodiagnosis, Shree Krishna Hospital, Karamsad, Gujarat, India, ³GE Healthcare, Mumbai, India

**Purpose/Objectives:** 4D respiration-correlated imaging using external metric system is ideal way to capture range of motion for moving targets. However momentary breath hold during swallowing leads to sorting errors & deters this modality from being used to track motion displacements in head and neck region. Dynamic helical Volume shuttle (DHVS), a special tool used for 4-D CT Angiography & joint motion studies, is a modality which possibly fills this gap. Present study aims to assess the actual deglutition induced displacement in patients with head and neck cancer using DHVS imaging and thus determine asymmetric Internal/PRV margin component needed for target volumes /OAR in Head & neck (HNC) IMRT treatments.

**Materials/Methods:** 20 patients of head and neck cancer following immobilization were setup in treatment position on GE - Optima 128 slice multidetector CT scanner and DHVS images acquired. DHVS is a continuous bidirectional scan which offers 120 mm of z-coverage with a 40 mm detector width at 120KV, 220mA & 0.9sec pitch with ASiR 50%. The resulting image at the central location of scan range has an average temporal sampling of 1.5 seconds. Dynamic Pitch Cone Beam Reconstruction (DPCB), RetroRecon, offers reconstruction for dynamic helical pitch during accelerated and decelerated acquisitions minimizing “overscanning” or “overranging”. Image data for single patient were acquired during *Voluntary swallowing act* at two alternating table positions with the table shuttling back and forth between two positions. Retrorerecon for 15 passes @ 1.25mm slice thickness resulted in at least 3000 images which were reformatted & cine looped to quantify the range of motion happening in head and neck region during swallowing. A total of 60,000 VHS & retrorerecon images acquired were studied to quantify the range of motion.

**Results:** The deglutition frequency and mean duration were found to vary among patients. Deglutition-induced maximal GTV displacements ranged from 3mm to 18 mm with mean and standard deviation of 3.5 +/- 2, 2.50 +/- 1.51, 1.75 +/- 4.0, and 9.60 +/- 7.7 mm in the A, P, I, and S directions, respectively. The calculated IMs were dependent on
deglutition frequency, ranging from 3.2 - 4.2 mm for the lowest deglutition frequency patient to 3.6-6.4 mm for the highest. A statistically significant difference was detected between IMs calculated for P and S directions (p = 0.001). For OAR, the Spinal cord displacement ranged from 2.8mm+/−1.2mm, 2.2mm+/− 1.4mm in A,P direction.

**Conclusions:** This is the first study reported in literature using DHVS for deglutition displacements quantification. Asymmetric IM’s & PRV margins, derived from directional displacement, using DVS imaging should be employed to account for tumor motion in HNC IMRT treatments.


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101 Renal Remodeling in the First 24 Months After Abdominal Radiotherapy

L. K. Tran, K. E. Maturen, M. U. Feng, E. Wizauer, K. Watcharotone, J. H. Ellis, *University of Michigan, Ann Arbor, MI*

**Purpose/Objectives:** To analyze renal changes after therapeutic abdominal radiation including volume and length, time to effect, and serum creatinine (sCr).

**Materials/Methods:** IRB approval was obtained for HIPAA-compliant retrospective review of clinical and imaging data for patients receiving abdominal radiation from 2001 to 2010. This pilot study included 10 patients with 1) two kidneys, 2) a treatment plan exposing at least one kidney but not directed at either kidney, 3) survival > 1 year post-radiation, and 4) at least three follow-up CT scans available. Their diagnoses included abdominal sarcoma, adrenocortical carcinoma, and carcinoid tumor. Kidney volume and length were measured on a dedicated 3D workstation for pre-radiation therapy CT scans (Time 0), as well as at 0-3, 3-6, 6-12, and 12-24 months post-radiation (Times 1-4 respectively). Serum Cr was correlated with each scan. Mixed models ANOVA was used to test renal volume and length, sCr, and time against multiple models to assess temporal effects; specific time points were analyzed using pairwise comparisons.

**Results:** Mean prescribed dose to extrarenal therapeutic targets was 53 Gy (SD ±10). Mean sCr increased from 0.9 mg/dL (SD ±0.23) pretreatment to 1.2 (SD ±0.37) at Time 4 (p<.01). Mean length and volume of exposed kidneys decreased in a continuous fashion, with total loss of 10% (p<.01) and 22.6% (p=.01) respectively at Time 4. While mean length of the unexposed kidneys was unchanged, their volume increased by 5%. However, this was not statistically significant.

**Conclusions:** Non-target radiation to the kidney as a bystander organ resulted in progressive atrophy of exposed kidneys, with volume changes greater than length changes. Despite slight compensatory hypertrophy in contralateral kidneys, we documented a modest decline in renal function. Radiologists should be aware of this phenomenon when interpreting follow-up imaging, even several years after radiation therapy.

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102 Evaluating Effects of Radiation Therapy Treatment on 4DCT-Calculated Lung Ventilation

K. Latifi, T. J. Dilling, S. E. Hoffe, C. W. Stevens, E. G. Moros, G. G. Zhang, *Moffitt Cancer Center, Tampa, FL*
Purpose/Objectives: Ventilation imaging using 4DCT would facilitate integration of lung functional information in radiation therapy (RT) treatment planning to spare normal functional lung volumes. This study uses the diffeomorphic morphons (DM) deformable image registration (DIR) method and the ΔV ventilation calculation algorithm to derive ventilation from 4DCT scans and evaluate the effects of radiation treatment on lung ventilation.

Materials/Methods: DM DIR of the normal end-expiration and end-inspiration phases of 4DCT images was used to correlate the voxels between the two phases. The ΔV method, which is a direct geometrical calculation of the volume change, was used to calculate the local lung expansion or contraction. 4DCT sets from before and after RT were used to derive ventilation for 10 previously treated SBRT lung patients. Doses ranged from 40-60 Gy delivered in 4-5 fractions. Time between end of treatment and the follow up scan ranged from 3-16 months. Dose and normalized ventilation were superimposed on the CT volume resulting in each voxel having a volume, normalized ventilation and a dose. A reduced lung mask was used in order to avoid any possible artifacts near the lung boundary due to sliding motion. Furthermore, the images were normalized based on the volume coverage in the accumulative ventilation-volume histogram for the lung to remove the effects of breathing differences from before and after RT. Dice similarity coefficient (DSC) index was used to calculate the similarity between the two ventilation volumes. Mean ventilation within the 20 Gy and 30 Gy regions was calculated before and after RT.

Results: Mean DSC index was 0.57 with a range 0.53 to 0.68. For lung tissue regions receiving more than 20 Gy, a decrease in ventilation was observed in nine of the 10 patients. For the nine cases ventilation within the 20 Gy isodose was reduced by 13.3 % (range 2.6 to 29.5 %). For regions receiving more than 30 Gy, nine of the ten patients had a decrease of ventilation by 18.1% (range 4.0 to 43.6 %). One patient had an increase of ventilation of 8.8% within the 20 Gy and 6.9% within the 30 Gy region.

Conclusions: Lung ventilation prior to and following radiotherapy can be measured using 4DCT and DIR techniques. Changes in ventilation were observed with a correlation between ventilation change and dose outside of the PTV. These data suggest that ventilation calculated from 4DCT may be a reliable tool for measuring/predicting the effects of dose on ventilation. Incorporating 4DCT calculated ventilation in treatment planning would aid in avoiding well ventilated regions and possibly preventing lung injury. More data points will enable us to make a stronger conclusion on the changes of ventilation for patients undergoing radiotherapy treatment.


103 Characterization of Patient-Induced Geometric Distortions in Clinical Brain MRI on a 3T MR Simulator

Y. Cao, H. Wang, J. M. Balter, University of Michigan, Ann Arbor, MI

Purpose/Objectives: To characterize subject-induced geometric distortions of clinical brain MRI on a 3T scanner for supporting MR-based radiation therapy (RT).

Materials/Methods: We analyzed 19 patients with brain tumors who received treatment planning MRI scans on a 3T simulator (Siemens, Skyra) for MR-CT based RT. The routine MRI series, including 3D volumetric T1 weighted images with 1x1x1 mm³ voxel size pre and post contrast, were acquired, and corrected on-line for gradient non-linearity related distortion. To evaluate susceptibility induced geometric distortion, gradient field maps were acquired twice during the same imaging session using two gradient echo sequences with ΔTE=3.3 ms to map B0 inhomogeneity and stability. The gradient field maps were unwrapped using the fsl library and then corrected for gradient non-linearity using vendor software. After co-registration with T1 weighted images, the field maps were converted to voxel displacement maps using the frequency sampling rate of the T1 weighted images. The maximum displacement and
error frequency were characterized. Iso-displacement surfaces were generated. The locations of the maximum displacements were identified.

**Results:** At the first field mapping, 95.3% of the brain voxels (range 86.7% to 96.8%) had <0.56 mm displacements, 4.9% (range 3.1% to 9.5%) had >0.56 mm but < 1.1 mm, and 0.37% (range 0.03% to 0.96%) had > 1.1 mm but < 1.67 mm. Only three patients had more than 0.1% voxels displaced > 1.67 mm. Only four patients had voxel maximum displacements > 2 mm. The maximum displacement observed in any patient was 2.6 mm. The largest displacements were noted near and around the sagittal sinus, and the second largest distortions were located in the inferior temporal lobes near the ear air canal. At the second field mapping, (56.4 min later than the first one), a minor systematic field shift, -0.18 mm, was observed, consistent with eddy currents decaying over time. However, the overall field distributions in the brains at the second mapping were similar in shape to the first ones as suggested by the standard deviations of the field maps changing by no more than 0.02 mm. The maximum observed displacement across all patients was 2.2 mm.

**Conclusions:** Subject-induced distortion in the brain is acceptably small at 3T on the magnet studied. The largest susceptibility-induced displacements occur in tissue in very close proximity to air. The very narrow distributions indicate that, with appropriate care, the relative distortion of the majority of brain tissue is less than 1 mm for this system. Future work will include methods to correct the displacement of voxels for the displacements estimated from the gradient field maps.

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**Purpose/Objectives:** With the increasing use of advanced techniques in radiation therapy, there is an increasing need for fast, useful radiologic correlation with surgical anatomy. Accordingly, our purpose is to develop deformable imaging capability for the Radiation Therapy Oncology Group (RTOG) consensus panel atlas of musculoskeletal anatomy (CAMAS) for planning 3D conformal and intensity-modulated external beam radiotherapy (IMRT) for soft tissue sarcoma (STS) of the extremities.

**Materials/Methods:** CAMAS structures contoured on CT and MRI images of lower extremities were examined and reviewed by sarcoma experts (radiation oncologists, surgeons, radiologists). A consensus meeting achieved agreement about radiologic correlation with anatomy. A proprietary deformable registration algorithm is employed to transform the CAMAS atlas to the patient specific planning volume thereby providing detailed anatomical segmentations within the patient space.

**Results:** Definitions of musculoskeletal anatomy to be employed as guidelines for pre-operative therapy of sarcoma were achieved. Detailed contouring guidelines of lower extremity anatomic compartments (uniquely characterized by critical structures) / joints (including knee) / normal tissue structures are delineated and transformed to the patient specific planning volume. Deformable proprietary image registration technology can allow for pretreatment contouring as well as post-treatment response evaluation integrating CAMAS into clinical use for both diagnostic and therapeutic
intent.

**Conclusions:** CAMAS helps facilitate a common system of communication and reporting to enhance standards of contouring, treatment, and follow-up response evaluation with deformable registration utilized to transform the atlas into the patient specific planning volume. This report further enhances definition of musculoskeletal anatomy / normal tissue structures for planning 3D conformal and IMRT of STS.

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- **S.E. Finkelstein:** O. Patent/License Fee/Copyright; Co-inventor of technology licensed to company.
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- **C.W. Stevens:** None.

### 105 Effects of Noise in 4D CT on Deformable Image Registration and Derived Ventilation Data

G. G. Zhang\textsuperscript{1}, K. Latifi\textsuperscript{1}, T. Huang\textsuperscript{2}, V. Feygelman\textsuperscript{1}, C. W. Stevens\textsuperscript{1}, T. J. Dilling\textsuperscript{1}, E. G. Moros\textsuperscript{1}, W. van Elmpt\textsuperscript{3}, A. Dekker\textsuperscript{3},
\textsuperscript{1}Moffitt Cancer Center, Tampa, FL, \textsuperscript{2}China Medical University, Taichung, Taiwan, \textsuperscript{3}Maastricht University Medical Centre, Maastricht, Netherlands

**Purpose/Objectives:** Proposals have been made to use 4D-CT and deformable image registration (DIR) to generate ventilation images. Quantum noise is common in CT images and is a persistent problem in accurate ventilation imaging using 4D-CT. This study focuses on the effects of noise in 4D-CT on DIR and the derived ventilation data.

**Materials/Methods:** A total of 6 sets of 4D-CT data with landmarks delineated in different phases, called point-validated pixel-based breathing thorax models (POPI), were used in this study. The DIR algorithms, including diffeomorphic morphons (DM), diffeomorphic demons (DD), optical flow (OF) and B-Spline, were used to register the end inspiration phase to the end expiration phase of the POPI models. The DIR deformation matrices (DIRDM) were used to map the landmarks from expiration phase to the inspiration phase for each POPI model and the mapped landmarks were compared to the delineated landmarks in the inspiration phase. Target registration errors (TRE) were calculated as the distance errors between the delineated and the mapped landmarks. Mathematically, the amplitude of the quantum noise is closely represented by Gaussian distribution. A computer program in C language was developed and applied to add noises of Gaussian distribution with different standard deviations (SD) in amplitude to the POPI models to simulate different levels of quantum noises. Ventilation calculation using 4D-CT data was performed using the ΔV algorithm which calculates the volume change geometrically based on the DIRDM. The ventilation images were compared between noise levels. Dice similarity coefficient (DSC) was used in the comparison.

**Results:** The root mean square (RMS) values of the landmark TRE over the 6 POPI models for the 4 DIR algorithms are stable when the noise level is low (below an SD of 150 Hounsfield Units (HU)) and increase with the added noise level when the level is high. The most accurate DIR is DD with a mean RMS of 1.5 ± 0.5 mm at 0 added noise and 1.8 ± 0.5 mm at noise SD = 200 HU. The DSC values between the ventilation images from the 4D-CT with added noise and the ones without decrease with the noise level even when the noise level is low. The most consistent DIR is DM with mean DSC = 0.89 ± 0.01 and 0.66 ± 0.02 for top 50% ventilation volumes between 0 added noise and SD = 30 and 200 HU respectively.

**Conclusions:** Although the landmark TRE shows stable versus noise level with low noise, the difference between ventilation images increase with noise level, indicating ventilation imaging from 4D-CT is sensitive to image noise. Therefore high quality 4D-CT is essential for accurate ventilation images.

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- **G.G. Zhang:** None.
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- **C.W. Stevens:** None.
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- **E.G. Moros:** None.
- **W. van Elmpt:** None.
- **A. Dekker:** None.
106  Cardiac and Respiratory Motion Assessment With Cine-MRI in Patients With Left-Sided Breast Cancer


Purpose/Objectives: The purpose of this study was to investigate the significance of cardiac and respiratory motion during whole breast radiation therapy (RT) in patients with left-sided breast cancer.

Materials/Methods: Five patients with left sided breast cancer underwent cardiac cine MRI during simulation for RT treatment planning; four were evaluable. Cine MRI was obtained during deep inspiration as well as during full expiration. For each patient, the left ventricular wall (LVW) was contoured on 5 different phases of the cardiac cycle from end-systole to end-diastole during both deep inspiration and full expiration, for a total of 10 different contours per patient and 40 contours total. RT was planned using tangent fields to a dose of 5040 cGy to the whole breast followed by a boost to the lumpectomy cavity. Dose volume analysis was performed to evaluate the variation in dose to the LVW during each phase of the cardiac cycle, during both deep inspiration and full expiration.

Results: After controlling for respiratory cycle, the variation in cardiac cycle was slightly more pronounced during expiration. Our results, however, did not demonstrate a significant absolute difference between the maximum percent volume and minimum percent volume of the left ventricular wall receiving 30Gy (mean volume difference: 2.5% during inspiration vs. 4.6% during expiration, p=0.08), 25Gy (mean difference: 3.1% during inspiration vs. 5.0% during expiration, p=0.11), or 10 Gy (mean difference: 5.0% during inspiration vs. 5.7% during expiration, p=0.72).

Overall, there was a significant difference in the V30 (1.5% vs. 9.7%, P=0.0002), V25 (3.1% vs. 10.0%, p=0.0001) and V10 (7.6% vs. 18.3%, p=0.0001) between inspiration vs. expiration, resulting in higher radiation doses to the LVW during expiration. However, there was one patient, who was an outlier. In this patient, there was no statistically significant difference in V30 (3.5% vs. 3.5%), V25 (4.1 vs. 4.3%) or V10 (6.4 vs. 7.6%).

Conclusions: Our results demonstrate that variation in cardiac cycle does not significantly contribute to the radiation dose delivered to the LVW during RT with tangent fields for left-sided breast cancers. Overall, deep inspiratory breath hold may benefit patients. However, the data acquired from one outlier patient suggest that deep inspiration may not benefit all patients. We will continue to enroll patients on this prospective study to evaluate the impact of cardiac and respiratory cycle on cardiac dose in these patients.


107  Improving Tumor-to-Tissue CNR of 4D-MRI Using Deformable Image Registration

J. Cai, Z. Chang, B. Czito, F. Yin, Duke University Medical Center, Durham, NC

Purpose/Objectives: 4D-MRI has the potential to image organ respiratory motion with improved soft-tissue contrast. We have previously developed a 4D-MRI technique using a fast 2D MR sequence: Fast Imaging Employing Steady-state Acquisition (FIESTA). While demonstrating improved soft-tissue contrast as compared to 4D-CT, it did not provide optimal tumor-to-tissue contrast-to-noise ratio (CNR) as a T2-w sequence given FIESTA is T2*/T1 weighted. The objective of this study is to investigate the feasibility of improving tumor-to-tissue CNR by combining T2-w MRI and deformable image registration (DIR).

Materials/Methods: Three patients with hepatic tumors were included in this IRB-approved study. All underwent 4D-
MRI imaging on a 1.5T scanner (Signa, GE, Milwaukee, WI). Parameters of the T2*/T1-w FIESTA sequence were: TR/TE, 3.2/1.0 ms; FA, 50°; SL, 5 mm; pixel: 1.9x1.9 mm. The reconstructed 4D-MRI has 6 phases, where phase 4 is end-exhalation. All patients were also imaged with T2-w fast recovery fast spin-echo (FRFSE) sequence at the end-of-exhalation phase with the following parameters: TR/TE, 2400/100.5ms; SL, 3 mm; pixel: 1.7x1.7mm. All MR images were imported into a commercial software (VelocityAI, Velocity, Atlanta, GA) for DIR, which was carried out in 3 steps: (1) T2-w FRFSE was co-registered to Phase 4 of 4D-MRI; (2) Phase 4 of 4D-MRI was registered to all other phases of 4D-MRI using DIR; and (3) T2-w FRFSE was deformed to all other phases of 4D-MRI using corresponding deformation vectors determined in Step 1 to generate pseudo T2-w 4D-MRI. Tumor-to-tissue CNR was determined for both original T2*/T1-w 4D-MRI and pseudo T2-w 4D-MRI as: (tumor intensity - liver intensity)/standard deviation of noise. Image quality of pseudo T2-w 4D-MRI was qualitatively evaluated. To validate our method, we performed a simulation study using a 4D digital human phantom, in which the 6-phase ‘4D-MRI’ images of the phantom were generated by mimicking tumor and organ signal intensities to those of FIESTA and FRFSE sequences. Pseudo T2-w ‘4D-MRI’ images of the phantom were generated via DIR method as described above and were compared to the true T2-w ‘4D-MRI’ of the phantom.

**Results:** In phantom study, pseudo T2-w ‘4D-MRI’ matched well with true T2-w ‘4D-MRI’, with only minimal differences between the two that were potentially due to residual errors in DIR. Pseudo T2-w 4D-MRI improved tumor-to-tissue CNR (32.2 ± 5.9) as compared to those of original T2*/T1-w 4D-MRI (16.1 ± 2.0), while both showed superior CNR over 4D-CT (1.4 ± 1.2). Pseudo T2-w 4D-MRI revealed similar motion patterns of organs and tumor as observed in T2*/T1-w 4D-MRI.

**Conclusions:** Improvement in tumor-to-tissue CNR of 4D-MRI by combining T2-w MRI and DIR is feasible. Further validation of the proposed method is required.

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**108 Anorectal Angle Is Associated With Bowel Toxicity One Month Following Radiation Therapy for Prostate Cancer**

M. Gossweiller\(^1\), A. Waggoner\(^2\), S. Ninneman\(^3\), R. Huang\(^1\), G. Hughes\(^1\), S. Wendt\(^3\), M. Brown\(^4\), B. Tinnel\(^1\), D. M. Macdonald\(^1\), \(^1\)Madigan Healthcare System, Tacoma, WA, \(^2\)Pacific Northwest University of the Health Sciences, Yakima, WA, \(^3\)The Geneva Foundation, Tacoma, WA, \(^4\)University of Washington School of Medicine, Seattle, WA

**Purpose/Objectives:** Bowel toxicity following radiation therapy (XRT) for prostate cancer can cause a significant decrease in patient quality of life. Some of this toxicity - such as rectal bleeding - seems to relate directly to damage to the rectal wall, while other elements of bowel toxicity - such as urgency, frequency, or fecal leakage - may be related to anal canal geometry and musculature. The anorectal angle (ARA) and the volume of the puborectalis muscle (VPRM) - which assists in maintaining the anorectal angle - are two image-based measurements which are known to be related to the maintenance of fecal continence. Here we explore whether a large pre-treatment ARA or a small VPRM are associated with increased bowel toxicity following XRT.

**Materials/Methods:** We studied 10 consecutive patients with low-to-intermediate risk prostate cancer treated on a prospective study with definitive intensity-modulated radiation therapy (IMRT). All patients completed the EPIC quality of life questionnaire at the end of treatment, and at 1 and 4 months post-treatment. We used the patients’ answers on the bowel section of these questionnaires to divide the patients into two groups: one with few side effects as reflected
by a score within 10% of the most favorable score possible, and the other with more side effects as reflected by a lower score. The patients’ VPRMs were measured by contouring on planning CT scans. The anorectal angle was measured on sagittal CT scan reconstructions as the angle between the line down the center of the long axis of the anal canal, and the line down the center of the long axis of the rectum immediately superior to the anal canal. Both the VPRM and the ARA measurements were then categorized as “small” or “large” using the mean as the dividing line. We used Fisher’s exact test to evaluate for a significant association between ARA and bowel toxicity and between VPRM and bowel toxicity.

**Results:** EPIC bowel toxicity scores varied from a low of 56.7 to a high of 100, with a mean of 83.8 and standard deviation of 14.76. VPRM varied from 6.45cc to 15.87cc (std. dev. 3.13), and was not associated with bowel toxicity ($p = 1.000$ at all time points). ARA varied between 93.5 and 121.8 deg (std. dev. 9.69), and was correlated with bowel toxicity one month following completion of therapy ($p = 0.048$), but not at the end of XRT ($p = 1.000$) or at 4 months post-treatment ($p = 0.524$).

**Conclusions:** These results are hypothesis-generating and based on a very small sample size. Further evaluation of the association of ARA with bowel toxicity following XRT for prostate cancer in a larger cohort is warranted. If there is an association between baseline ARA and bowel toxicity, measuring the ARA on a pre-treatment CT scan could allow more informed counseling of patients regarding the risks for bowel toxicity following XRT.


109  See Oral Abstract Presentation #11

110  See Oral Abstract Presentation #9

111  Benefit of MRI Scanning in the Pretreatment Assessment of Anal Canal Carcinoma

V. G. Swami, K. Joseph, D. Severin, K. Tankel, N. Usmani, T. Nijjar, University of Alberta, Edmonton, AB, Canada

**Purpose/Objectives:** Anal canal carcinoma is an uncommon curable malignancy. The AJCC staging manual does not recommend any specific diagnostic tests for staging. Most clinical practice guidelines, including those from the NCCN, suggest a DRE, anoscopy, chest imaging, and a CT or MRI of the abdomen and pelvis to stage the disease. It has still not been established whether MRI should be used routinely for local staging. We compared the benefit of MRI versus CT in the pre-treatment assessment and staging of anal canal carcinoma.

**Materials/Methods:** This prospective cohort study included 31 consecutive patients from 2007 to 2011 with a histopathologically confirmed anal canal carcinoma who underwent curative-intent treatment at the Cross Cancer Institute. Patients underwent contrast-enhanced CT of the chest, abdomen and pelvis and pelvic MRI following clinical examination as part of the staging work-up. All the images were evaluated prospectively to record tumor size, extent and the TNM stage.

**Results:** MRI visualized the primary anal canal lesion in all cases (31 of 31), while CT only visualized 39% (12 of 31) of lesions. Compared to CT, MRI altered T staging in 84% (26 of 31) of cases. MRI upstaged 81% (25 of 31) of cases and
downstaged 3% (1 of 31) of cases. Compared to clinical examination, MRI altered T staging in 52% (16 of 31) of cases. MRI upstaged 35% (11 of 31) of cases and downstaged 16% (5 of 31) of cases. Pathologic lymph nodes were detected by MRI in 52% (16 of 31) of cases, CT in 19% (6 of 31) of cases, and clinical examination in 26% (8 of 31) of cases. Compared to N Staging by CT, MRI upstaged 32% (10 of 31) of cases and did not downstage. Compared to clinical examination N staging, MRI upstaged 32% (10 of 31) of cases and did not downstage. MRI was able to assess the depth of bowel wall invasion in all cases and detected positive wall invasion in 81% (25 of 31) of cases. CT was only able to assess the depth of wall invasion in 29% (9 of 31) of cases and detected positive wall invasion in only 6% (2 of 31) of cases. While CT did not detect involvement of the anal sphincter muscles, MRI detected involvement of the internal anal sphincter in 61% (19 of 31) of cases and the external anal sphincter in 48% (15 of 31) of cases. CT did not upstage any cases to T4, while MRI upstaged 6 cases to T4 by detecting vaginal invasion.

**Conclusions:** MRI was more sensitive than CT in detecting primary anal canal lesions. MRI was superior to CT in detecting lymph node involvement and bowel wall invasion of the tumor. There was considerable upstaging of both T and N staging using MRI versus CT scans. Also, MRI provides consistency in T and N stage assessment compared to clinical evaluation where subjective variation exists. We support routine use of MRI for initial local staging of anal canal cancers.


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112 **Correlation Between Nasopharyngeal Carcinoma Tumor Volume and the 2002 International Union Against Cancer Tumor Classification System**

Z. Wu¹, M. Gu¹, Y. Su¹, R. Zeng², S. Huang¹, ¹Department of Radiation Oncology, Cancer Center, Sun Yat-sen University, Guangzhou, China, ²Department of Tumor, the First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China

**Purpose/Objectives:** The correlation between primary tumor volume and nasopharyngeal carcinoma (NPC) UICC 2002 T classification, N classification and distant metastasis after radiation therapy was discussed to provide further evidence for the inclusion of tumor volume into the TNM classification staging system.

**Materials/Methods:** Between February 2001 and December 2008, 666 patients with NPC treated with intensity-modulated radiation therapy (IMRT) were analyzed retrospectively. Primary gross tumor volume was calculated from treatment planning computed tomography scans. The Kruskal-Wallis and Mann-Whitney tests were used for comparison of continuous variables and the chi-square test was used for categorical variables. A logistic regression model was used for multivariate analysis.

**Results:** Median primary tumor volume of the 666 patients was 20.35 ml (range, 0.44–192.63 ml), and it gradually increased with T classification. Statistically significant differences in tumor volume were observed between patients with different T classifications \((p < 0.001)\). The cervical lymph node metastasis rate was 64.7% (430/666); the differences in primary tumor volume between patients with or without lymph node metastasis were statistically significant \((p < 0.001)\). Post treatment distant metastasis occurred in 100 NPC patients, and the distant metastasis rate was 15.0% (100/666). Univariate and multivariate analyses showed that N classification \((p < 0.001)\) and tumor volume \((p = 0.007)\) were the main factors influencing distant metastasis.

**Conclusions:** Tumor volume was correlated with T classification, cervical lymph node metastasis and distant metastasis after radiation therapy in nasopharyngeal carcinoma, suggesting that tumor volume should be included into the TNM staging system.
High Sensitivity and Specificity of PET/CT and Laparoscopic Diagnostic Lymph Node Excision for Lymph Node Metastases in Cervical Cancer Patients

H. Hansen¹, A. Loft², A. K. Berthelsen²,¹, S. Lassen¹, C. Høgdall³, S. A. Engelholm¹, ¹Department of Radiation Oncology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, ²Department of Clinical Physiology, Nuclear Medicine & PET, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, ³Department of Gynecology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

Purpose/Objectives: In cancer of the uterine cervix, lymph node (LN) metastases are associated with poor prognosis. The purpose of this study was to evaluate the efficacy of PET/CT to guide and verify laparoscopic diagnostic lymph node excision in cervical cancer patients.

Materials/Methods: A single institution retrospective analysis of procedure efficacy and survival in cervical cancer patients with PET/CT positive LN as well as identifying possible sources of error. Patient inclusion criteria: Histopathological diagnosis of cervical cancer, LN metastases at PET/CT prior to staging, laparoscopic diagnostic lymph node excision, control PET/CT after surgery. Missed Lesion (ML) was a lesion seen on the staging PET/CT with no sign of tumor tissue at histological analysis and a subsequent planning PET/CT revealing the same lesion as before laparoscopy. False Positive Lesion (FPL) was a lesion seen on the staging PET/CT with no sign of tumor tissue at histological analysis and verified by the planning PET/CT. Kaplan-Meier plots and log-rank tests were performed. Histopathology of removed LN number of FPL over time was registered.

Results: Sixty-five patients were included. Laparoscopy confirmed metastatic spread to LN in 39 patients. In 4 of 26 patients with negative laparoscopic results, post-operative PET/CT showed ML. Of these, three patients were re-operated of which two had LN metastases confirmed, and one continued having no evidence of metastatic disease. Of the total 23 patients with twice verified negative LN pathology, one patient died of metastatic breast cancer. Of the 42 patients with metastatic disease, 15 died. For the entire staging procedure sensitivity and specificity were calculated to 0.98 and 1.00 respectively. Positive and negative predictive values were 1.00 and 0.96. Of the 23 patients with FPL, histopathology of removed LN showed nonspecific changes of reactive origin in 65% (C.I. 43-84%), fibrosis in 17% (5-39%), calcifications in 13% (3-34%), histiocytosis in 35% (16-57%), follicular hyperplasia in 9% (1-28%) and necrosis in 4% (0-21%) (some showed more than one type). Completely normal architecture was observed in 17% (5-39%) of the patients. No change in frequency of FPL was observed over time.

Conclusions: PET/CT as control of laparoscopic diagnostic lymph node excision provides high sensitivity and specificity as well as high positive and negative predictive values, for lymph node staging in cervical cancer patients. However, a high number of FPL was observed at PET/CT, mainly due to inflammation. Although no change in frequency over time was observed, a blinded revision of the original PET/CT scans is currently in progress.

114  Quantifying Tumor Aggressiveness Using Diffusion-Weighted MRI for Prostate Cancer

M. Sanders¹, K. Nandalur², N. Tyagi², D. Schulze², D. Yan², D. Krauss², ¹William Beaumont Hospital, Royal Oak, MI, ²Beaumont Hospital, Royal Oak, MI

Purpose/Objectives: To quantify tumor aggressiveness based on apparent diffusion coefficient (ADC) in prostate cancer for therapy assessment.

Materials/Methods: 42 patients (median age: 68 yrs, median serum prostatic specific antigen (PSA):6.9) with biopsy-proven prostate cancer underwent diffusion weighted images of the prostate using an optimized single-shot echo planar imaging sequence at 3T with an endorectal coil. Quantitative apparent diffusion coefficient (ADC) maps were generated via a mono-exponential fit using three b-values (50, 400 and 800s/mm²). Anatomical images include high resolution axial, sagittal and coronal T2-weighted images. T2, DWI and ADC maps were imported into our clinical treatment planning system and rigidly registered using manual registration. Tumor foci in peripheral zone (pz), central gland (cg) and seminal vesicles (sv) were delineated on ADC maps at the sites of visible tumor on T2, DW images and ADC maps using T2-weighted images as a reference. Statistical parameters and tumor volumes extracted from tumor foci were used as a measure of tumor aggressiveness. Multivariate linear regression models were estimated to test for associations between mean ADC and age, tumor volume (TV), histology grade Gleason score (GS) and PSA. The multivariate regression model was also used to generate predictions for mean ADC.

Results: A total of 63 MR lesions (42 in pz, 18 in cg and 3 in sv) were identified. Both GS (ρ = -0.57, p<0.0001) and TV (ρ =0.47, p=0.0014) were significantly correlated with the mean ADC for the tumors in entire prostate gland. For tumors located in PZ, the correlation was even stronger for GS (ρ = -0.63, p<0.0001) and TV (ρ = 0.5, p<0.0001). When age, GS, PSA and TV were all included as predictors in a multivariate regression model for pz tumors, only GS (p=0.002) had a statistically significant effect but not PSA (p=0.532), age (p=0.297) or TV (p=0.558). The model is able to explain a fairly significant amount of the variation in the mean ADC (adjusted R-squared =0.337). The correlation between the predicted and observed values of mean tumor ADC is 0.638 (p< 0.001).Central gland tumors did not show statistically significant association with any of the clinical parameters.

Conclusions: Increased tumor cellularity in high GS tumors results in a negative correlation between mean tumor ADC and GS. Quantifying tumor aggressiveness based on ADC values has a potential to further improve the clinical risk models that are currently based on only GS and PSA.


115  Absolute Lymphocyte Count: A Novel Prognostic Factor for Merkel Cell Carcinoma

M. E. Johnson, A. Turaka, F. Zhu, T. Galloway, J. Farma, C. Perlis, Fox Chase Cancer Center, Philadelphia, PA

Purpose/Objectives: The incidence of Merkel Cell Carcinoma (MCC) is increased in immunocompromised patients. We report the prognostic impact of a simple, easy to test laboratory value, absolute lymphocyte count (ALC), as a surrogate of immune status for patients treated for MCC at Fox Chase Cancer Center (FCCC) from 1992 to 2010.

Materials/Methods: 124 patients treated for MCC at FCCC were identified. The population for this study is composed of the 64 patients who had a complete blood count with differential recorded in the month prior to definitive surgery, chemotherapy, or radiation. Clinical and outcome characteristics were obtained from chart review. An ALC of 1.5 k/mm³ was defined as the cut point based on review of outcomes and is our laboratory’s lower limit of normal.
Statistical analysis was performed utilizing log rank test and a Cox proportional hazards model. Endpoints of overall survival (OS) and disease free survival (DFS) from the time of diagnosis were calculated.

**Results:** Of the 64 patients, 40 were men and 61 were Caucasian. AJCC stage at presentation was: I (41%), II (14%), III (39%), and IV (6%). The most common primary site of disease was head and neck (41%), lower extremity (27%), and upper extremity (23%). Chemotherapy was given to 35% of patients and 75% received radiotherapy. For the cohort, 23 patients had an ALC <1.5 k/mm$^3$. They were more likely men (p=<0.01), more likely received chemotherapy (p=0.03), and had a higher AJCC stage (p=0.03) than the ALC ≥1.5 k/mm$^3$ group. Otherwise, there was no significant difference between the groups with regard to primary location, surgery type, radiotherapy, smoking history, alcohol use, race, or family history. The median OS for patients with an ALC <1.5 k/mm$^3$ was 25.2 months vs. 96.8 months for those with an ALC ≥1.5 k/mm$^3$ (p=0.0033). DFS at 60 months for those patients with an ALC <1.5 k/mm$^3$ was 24.0% vs. 66.5% for those patients with ALC ≥1.5 k/mm$^3$ (p=0.016). ALC remained a statistically significant predictor for OS when controlled for stage (HR 0.4, p=0.02), chemotherapy (HR 0.38, p=0.03), and gender (HR=0.38, p=0.04).

**Conclusions:** ALC is a simple, easy to evaluate laboratory value that independently impacts prognosis for patients diagnosed with MCC when utilizing a cut point of < 1.5 k/mm$^3$. This test, already commonly obtained during the workup of patients with MCC, provides additional prognostic information to clinicians and patients with MCC.

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**Ferumoxytol as a Lymph Node Contrast Agent in Patients With Metastatic Prostate Carcinoma**

S. M. Bravo, C. Myers, T. Bravo, C. Elenberger, R. Posniak, M. Dattoli, *Sand Lake Imaging, Orlando, FL*

**Purpose/Objectives:** To correlate the radiologic findings of MR imaging performed after Feraheme administration with biopsy lymph node specimens.

**Materials/Methods:** 41 patients with biochemical recurrence of prostate carcinoma (rising PSA) after definitive treatment underwent IV infusion of Feraheme at 6 mg/kg. No complications were encountered. All patients underwent MR imaging with T2* and T2 MEDIC sequencing 24 hours after infusion. Images were independently reviewed by two board certified diagnostic radiologists. Consensus interpretation was rendered. The patients subsequently underwent image-guided lymph node biopsy of abnormal lymph nodes. Radiology-pathology correlation was performed.

**Results:** 34 of the patients demonstrated failure of suppression of pelvic lymph nodes on MR imaging. 4 patients demonstrated failure of suppression of retroperitoneal lymph nodes. 1 patient demonstrated failure of suppression of mediastinal lymph nodes, and 1 patient demonstrated failure of suppression of a left supracavicular lymph node. 73 lymph nodes demonstrating abnormal T2* signal were sampled. 67 lymph nodes demonstrated metastatic prostate carcinoma. 2 lymph nodes demonstrated lymphoma. 5 lymph nodes were normal.

**Conclusions:** With T2* sequences, lack of suppression of signal in lymph nodes after the infusion of ferumoxytol may indicate evidence for lymphatic dissemination of metastatic disease in prostate cancer patients. The findings also suggest a lower limit to the resolution of focal lymph node metastases of 3-4 mm. 3T MR after Feraheme administration has the potential to identify neoplastic nodes down to a resolution of 3-4 mm, thereby markedly improving the detection of metastatic lymph node disease. This carries significant therapeutic implication when simulating rescue radiation therapy in high risk prostate cancer patients.

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Perfusion Imaging in Differentiating Tumor Recurrence From Pseudoprogression in Newly Diagnosed High Grade Gliomas Treated With Bevacizumab

M. Tam, A. Wilner, E. Raz, A. Narayana, G. Fatterpekar, New York University School of Medicine, New York, NY

Purpose/Objectives: A clinical trial of bevacizumab, temozolomide, and radiation therapy for newly diagnosed high grade gliomas (HGG) was recently conducted at our institution and showed excellent survival and progression-free outcomes. Anti-angiogenic therapy is known to affect the underlying vascular structure. The purpose of this study is to evaluate whether perfusion is an effective method in differentiating recurrence from pseudoprogression in HGG treated with bevacizumab, temozolomide, and radiation therapy.

Materials/Methods: Ten patients with HGG who had DSC MR imaging findings of progressive contrast enhancement and/or progressive FLAIR abnormality were included in this study. Perfusion MR imaging datasets were analyzed for relative mean and max values cerebral blood volume (rCBV), peak signal (rPS), and percent signal recovery (rPSR). Separate imaging analysis was performed in enhancement regions and FLAIR regions. Additional parameters of minimum apparent diffusion coefficient (minADC) and FLAIR volume changes from the first postoperative image were also evaluated.

Results: Four of these patients had biopsy-proven recurrences. The remaining six patients were considered to have pseudoprogression after an additional 8 months of follow-up imaging. Time from diagnosis to recurrence and pseudoprogression occurred at a median of 10.5 months and 8.9 months, respectively. Enhancement peak rCBV was significantly higher (p = 0.005) in patients with recurrent HGG (mean, 4.33, range, 1.41-6.76) than in patients with pseudoprogression (mean, 1.25, range, 0.56-1.55). Additionally, recurrent tumor had a significantly higher enhancement max rPS (p = 0.004). Enhancement volume, FLAIR volume, and minADC were not significantly different between the two groups.

Conclusions: Perfusion imaging is an effective method for differentiating between tumor recurrence and pseudoprogression in HGG treated with bevacizumab. Anti-angiogenic therapy may affect peak rCBV and rPS thresholds in distinguishing tumor from pseudoprogression.

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Radiographic Changes After Lung Stereotactic Ablative Radiotherapy (SABR) -- Can We Distinguish Fibrosis From Recurrence? A Systematic Review of the Literature

K. Huang¹, M. Dahele², S. Senan², M. Guckenburger³, G. Rodrigues¹, A. Ward⁴, R. G. Boldt⁴, D. A. Palma¹, ¹London Health Sciences Centre, LONDON, ON, Canada, ²VU University Medical Center, Amsterdam, Netherlands, ³University Hospital Wuerzburg, Wuerzburg, Germany, ⁴Western University, LONDON, ON, Canada

Purpose/Objectives: Stereotactic ablative radiotherapy (SABR) has emerged as a treatment option for stage I non-small cell lung cancer (NSCLC). Changes in lung density on computed tomography (CT) are common after treatment and can confound the early detection of recurrence, which is of paramount importance in patients who are candidates for salvage therapies. We performed a systematic review of the literature in order to describe findings on CT and positron-emission tomography (PET) following SABR, identify imaging characteristics that may predict recurrence, and propose a follow-up imaging algorithm based on current evidence.
Materials/Methods: A systematic literature search was conducted using MEDLINE, EMBASE and conference abstracts for studies providing detailed radiologic descriptions of anatomic and metabolic lung changes after SABR. Our search returned 824 studies; 26 studies (23 papers and 2 abstracts) met our inclusion criteria. Data were abstracted and presented according to PRISMA guidelines.

Results: Post-SABR lung changes follow characteristic acute and late patterns. Acute changes predominantly appear as consolidation (~45% of patients) or ground glass opacities (~16%). Late changes often demonstrate a modified conventional pattern of fibrosis (~62% of patients), and can evolve beyond two year after treatment. An enlarging CT opacity after SABR has been significantly correlated to recurrent disease. Fluorodeoxyglucose PET maximum standardized uptake values (SUVmax) may transiently rise immediately post-SABR and persist for over 12 months without recurrence. However, SUVmax ≥ 5 carries a high predictive value of recurrence. Although the published evidence is limited, a suggested imaging follow-up algorithm is presented.

Conclusions: CT density changes are common post-SABR. The available evidence suggests that recurrent disease should be suspected if an enlarging opacity is seen on CT with SUVmax ≥ 5 on PET. Further studies are needed to validate the predictive values of such metrics, and more advanced analysis of CT changes for early detection of potentially curable local recurrence.


119 Molecular Imaging FDG-PET/CT Response to Neoadjuvant Oxaliplatin and Chemoradiation in Rectal Cancer as Prognostic Factor in Surveillance

D. De La Mata, M. Gomez Espi, J. Carreras, E. Alvarez, F. Calvo, H.G.U. Gregorio Marañón, MADRID, Spain

Purpose/Objectives: To analyze post-neoadjuvant molecular events assessed by FDG-PET/CT imaging as prognostic factor in surveillance and to correlate pathological pattern of response.

Materials/Methods: 41 patients (p) with T3-4 induced with FOLFOX (2) and fluoropirimidin based neoadjuvant chemoradiation were staged and restaged with FDG-PET/CT (36p). Pathological response was assessed by Rödel’s tumor regression grade (TRG) classification. Parameters PET/CT analyzed: absolute difference SUVmax (>6) (difSUVmax), RI 66% (Response Index, relative), SUVmax diagnosis and restaging (SUV1max, SUV2max), volume diagnosis and restaging (vol1, vol2).

Results: Neoadjuvant treatment significantly decreased the mean SUVmax at initial staging: 8.77±3.6 vs 2.64±1.85 (p<0.001) and the mean volume of tumor from 51.33±70.2cc. vs 7.35±10.01cc. (p<0.001). All FDG-PET/CT parameters were significantly predictor factors of favorable pathologic response, TRG3-4 and pT0 (p<0.001, table 1), the best was SUV2max< 2. Mean time follow-up was 56.48 months (SD ±20.67), 5y-DFS was 84.6% and 5y-OS was 80.2%. The absolute difference SUVmax>6 (difSUVmax) was a significant prognostic factor in the univariate and multivariate analyses, either DFS than OS. Also initial tumor volume was an adverse prognostic factor in OS (p<0.05). Patients achieving intense molecular imaging response (difSUVmax>6) had superior 5y-DFS (100% vs 73.3, p<0.05) than patients with difSUVmax<6. Similar features were observed for 5y-OS in “good responders” patients (difSUVmax>6) versus “non-responders”, 94.4% vs. 68.4% (p<0.05, fig.1).

Conclusions: Postneoadjuvant molecular response is assessable using metabolic imaging (FDG-PET/CT). Results suggest that all parameters assessing “good response” to chemoradiation (difSUVmax>6, RI 66%, SUV2max < 2 ) were accurate predictors of pathologic response. The initial tumor volume and difSUVmax>6 were significant prognostic OS factors. Patients with good response (difSUVmax>6) do achieve better 5y-DFS and 5y-OS.
MicroDose Digital Mammography: Lowest Dose Innovation in Breast Cancer Screening. Technology Review and Implications to a Screening Population.

R. Tu1,2, N. Hai1, S. Rothenberg1, R. Charafeddine3,4, T. Williams4, 1The George Washington University, Washington, DC, 2Progressive Radiology, Falls Church, VA, 3Progressive Radiology, Washington, DC, 4United Medical Center, Washington, DC

Purpose/Objectives: We review the new technique of photon counting digital mammography, the latest innovation in digital mammography since its introduction to general practice. The unique photon counting technology, collimator design and novel detector design provides the 50micrometer resolution at up to half the radiation dose. In screening breast cancer programs in otherwise normal patients the lowest radiation dose reduces the cumulative radiation exposure in patients while providing the greatest resolution.

Materials/Methods: We completed a review of studies comparing various manufactures of digital mammography and analog film screen mammography equipment compared to photon counting mammography. We review the photon counting detector technology which is a novel and unique design compared to more common digital mammographic systems. Using a mathematical model we estimate cumulative x ray exposure in patients in a routine screening program initiated at age 40, compared to standard routine screening programs initiated age 40 and age 50 (per recent recommendations of the US Preventive Services Task Force recommendations (USPSTF).

Results: The photon counting digital mammographic technology provides the greatest resolution at the lowest radiation dose. This provides the lowest cumulative radiation exposure in patients in screening programs initiated at age 40 compared to standard digital mammographic systems.

Conclusions: The photon counting digital mammographic system provides valuable radiation dose savings at the highest resolution available. Such dose savings is superior to standard digital mammography programs initiated at age 50 per the USPSTF arguing that perhaps MicroDose digital mammography would be safer if instituted in screening programs beginning in the age 40 plus group. Such low dose solutions may be superior to higher dose tomosynthesis approach to screening. In patients with a history of breast cancer frequent diagnostic mammogram follow up at 6 month interval examinations with a lower radiation dose technique in an already at risk group for radiation induced breast cancer is a safer option.

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carcinoma (NSCLC) treated with stereotactic body radiation therapy (SBRT).

**Materials/Methods:** This study included 15 patients with histologically confirmed stage I NSCLC who underwent pretreatment MRI and $^{18}$F-FDG PET/CT and were treated with SBRT in our hospital between January 2010 and December 2010. The median age was 80 years old (range, 70 to 86 years). Eleven patients were male and 4 were female. T stages were distributed as follows: T1a in 4, T1b in 6, and T2a in 5 patients. According to the classification with recursive partitioning analysis (RPA) proposed by Matsuo et al. (Int J Radiat Oncol Biol Phys 2011), 7 patients were classified into class I, which includes female or T1a patients, and 8 patients were into class II, including male and T1b-T2a patients. The RPA class I was proved to have better prognosis than class II. The SBRT dose and fractions were 48Gy/4fr for T1a-T1b, 56Gy/4fr for T2a, and 60Gy/8fr for the tumors close to the mediastinum regardless of their size. Apparent diffusion coefficient (ADC) value and maximum standardized uptake value (SUVmax) were measured at the target lesion. The ADC value, SUVmax, and RPA class were evaluated for the correlation with Local progression (LP), disease progression (DP), and overall survival (OS). The Kaplan-Meier method, the log-rank test, and the Cox proportional hazards model were used to evaluate these factors.

**Results:** With a median follow-up period of 19.3 months, OS at 12 and 24 months were 93% and 52%, respectively. Cumulative incidence rates of LP and DP were 8% and 33% at 12 months, and 18% and 63% at 24 months, respectively. The median pretreatment ADC was $1.04 \times 10^{-3}$ mm$^2$/s (range 0.83-1.29); that of the SUVmax was 9.9 (range 1.6-30). When dividing the patients into two groups by an ADC value of $1.04 \times 10^{-3}$ mm$^2$/s, a significant difference was observed in DP ($p=0.023$), while no significant difference was observed in LP and OS. The group with lower ADC value had poor prognosis, and RPA class distribution was well balanced between the two groups. On the contrast, there was no significant difference in the groups divided by SUVmax of 9.9 in LP, DP and OS. In the multivariate analysis, ADC remained a borderline significant factor for DP ($p=0.063$).

**Conclusions:** Our preliminary data suggest pretreatment DWI with low ADC value may be a poor prognostic factor in NSCLC patients after SBRT.

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### Withdrawn

#### 122 Selection of Patients Benefited From PET CT Whole Body Protocol

*S. Andres, S. De Luca, C. Carrera, M. F. Grana, J. Codas Thompson, J. Codas Thompson, E. P. Eyheremendy, Hospital Aleman, Buenos Aires, Argentina*

**Purpose/Objectives:** To demonstrate the utility of a whole body PET CT examination protocol including brain and extremities to define the actual spread of certain diseases and therefore select those patients who would benefit with it.

**Materials/Methods:** We retrospectively evaluated PET-CT examinations performed in our institution in a hybrid computer-SIEMENS Biograph 16(Siemens, Erlangen, Germany), from January 2009 to May 2012 in which a whole body scan had been made. We first selected those with prevalent pathologies and pathological findings in the extremities and central nervous system. Then we analyzed 49 patients who were included within these entities. In many cases unexpected locations of the diseases were diagnosed, which would have been misdiagnosed without a whole body scan.
scan.

Results: The 49 patients studied had a confirmed histological or laboratory diagnosis of the underlying pathology. Of the total, 27 were patients with melanoma, 10 with sarcoma, 2 with T-lymphoma, 1 with fever of unknown origin, 1 with Merkel-Cell carcinoma, 3 with metastatic disease in the central nervous system and 4 with Multiple Myeloma. 9 patients (32.1%) revealed unusual locations of their underlying disease, resulting in a change in the staging and/or management. The greatest utility was recorded in patients with melanoma, accounting 55.5% of the positive findings.

Conclusions: We suggest the use of PET-CT whole body protocol in patients with melanoma, Merkel-Cell tumor, Multiple Myeloma, sarcoma, fever of unknown origin and T-lymphoma. In these cases whole body protocol allows a complete staging and therefore an appropriate therapeutic management.


124 Imaging and Pathological Findings of Solid Pseudopapillary Tumors of the Pancreas: A Report of 53 Cases

X. Chengqian, X. Zhao, Cancer Institute and Hospital, Chinese Academy of Medical Sciences, Beijing, China

Purpose/Objectives: The study aims to examine the imaging findings of Solid pseudopapillary tumors (SPTs) of the pancreas, in order to provide experiences for the management of this rare entity.

Materials/Methods: We retrospectively reviewed a series of 53 cases with pathologically proved solid pseudopapillary tumors (SPTs) of the pancreas and summarized the imaging signs and pathological results of these patients.

Results: 53 patients with mean age of 32.7 years (range 13 to 68 years) were analyzed, and the male to female ratio was 1:9.6. From image observation, most of the tumors were cystic-solid mass with a percentage of 83.0%. Others were solid (15.1%) or cystic (1.9%) masses. Calcification and hemorrhage were noted in 28.3% and 24.5% cases respectively. Computed tomography scans showed a cystic-solid, solid or cystic mass with heterogeneous density in 44 patients, showing heterogeneous or homogeneous enhancement. A gradual delayed strengthening was noted in portal phase. Magnetic Resonance Imaging showed hypointensity or isointensity on T1-weighted images and a high or very high signal on T2-weighted and T2WI/FS images in all 20 cases. 18 patients underwent enhancement scan. The solid portion of 16 cases intensified slightly in arterial phase, with gradually increase in portal phase and delay phase. 1 case showed heterogeneous peripheral strengthening. No obvious enhancement was noted in one case. Hemorrhage was observed in 9 cases. All 53 patients underwent surgical treatment. 77.3% cases were benign and 15.1% were malignant or low malignant. Cytologic atypia were noted in 7.5% cases. 2 cases had lymph node metastasis. The immunohistochemical analysis demonstrated the highest positive rate (82.9%) of progesterone receptor (PR).

Conclusions: SPT of the pancreas is a rare pancreatic tumor that occurs mainly in young women, with imaging findings which in accordance with the pathology. The preoperative diagnostic rate may be increased by a combination of computed tomography, MRI and clinical features. SPT is of low malignancy and complete surgical resection is the primary curative strategy. Long-term follow up is advisable with high 5-year survival rate. The study demonstrated highest positive rate of progesterone receptor (PR), suggesting that progesterone might have played a role in the genesis of SPT.

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125 CT Findings, Clinicopathologic Features, and Treatment Modalities of Anorectal Melanoma: A Report of 10 Cases

X. Chengqian, X. Zhao, Cancer Institute and Hospital, Chinese Academy of Medical Sciences, Beijing, China

Purpose/Objectives: To retrospectively evaluate CT findings and clinicopathologic features in patients with pathologically proved anorectal melanoma, and to discuss the diagnosis and treatment modalities of this entity.

Materials/Methods: Clinicopathologic features, diagnosis, treatment modalities and survival of 10 patients (four men and six women; age range, 41-75years; mean age, 61years) with anorectal melanoma in CIAMS from 2006 to 2011, were analyzed. CT scans were evaluated by two radiologists for the involved site, size, morphology, infiltration, lymphadenopathy and metastasis.

Results: The most common presentation was rectal bleeding (n=8), followed by tenesmus(n=5) and Dyschezia (n=3). Distant metastasis was noted in 2 patients. The approximate mean length of the tumors was 3.1cm (range, 1.9~7.7cm) and the diameter was 2.5cm (range,1~7cm). All of the tumors appeared as polypoid or fungating intraluminal neoplasm. Perirectal infiltration could extended to the presacral space (n=2). 3 patients had lymphadenopathy, involving the perirectal, presacral and iliac vessel lymph node stations. There was no evidence of obstruction in any patients. 6 underwent abdominoperineal resection, 2 underwent local excision, 1 underwent sigmoid colostomy and 1 underwent adjuvant immunotherapy and chemotherapy. Most of the tumors invaded the dentate line confirmed by postoperative pathology (n=6). All 9 cases stained for HMB-45 and S-100. 8 stained for Melan A. 7 died with the median survival time of 24 months (range 8-70months). 1 is undergoing palliative therapy, approaching her end and 2 are under stable condition 21months and 31months after surgery.

Conclusions: On CT scans, anorectal melanoma appeared as intraluminal fungating masses, expanding the lumen without causing obstruction, with perirectal infiltration and lymphadenopathy. The preoperative staging has an important role in influencing treatment decisions and abdominoperineal resection may be considered as the first choice for the anorectal melanoma patients without distant metastasis.

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126 See Oral Abstract Presentation #3

127 See Oral Abstract Presentation #10

128 See Oral Abstract Presentation #6

129 See Oral Abstract Presentation #1
132 Dosimetric Impact of Intra-Fraction Prostate Motion Using a New Contour Shifting Method

M. K. Khan$^2$, S. Shin$^1$, A. Magnelli$^1$, P. Xia$^1$, $^1$Cleveland Clinic, Cleveland, OH, $^2$Emory University School of Medicine, Atlanta, GA

**Purpose/Objectives:** To use a newly developed in-house organ contour shifting algorithm to evaluate optimal planning treatment (PTV) margins using daily real-time intra-fraction organ tracking for prostate cancer patients undergoing intensity modulated radiotherapy (IMRT).

**Materials/Methods:** The dose matrices, planning CT images, and physician defined organ contours were exported from the treatment planning system into a new MATLAB algorithm. The new algorithm shifts the prostate organ contours according to real-time intra-fraction prostate tracking data (Calypso® Medical, Seattle, WA). The average prostate motion over each 30 second increment is used to shift the prostate contours within a static dose cloud to generate a composite dose volume histogram (cDVH) for an entire treatment plan (typically 38-39 fractions, each lasting about 10 minutes). The adequacy of the standard PTV margins (6 mm around the prostate and 4 mm posterior to the prostate) was compared against a smaller PTV margin (uniform 2 mm around the prostate). The dose to 90% (D90), 95% (D95), and 99% (D99) of the prostate were compared among the two different treatment margin schemes.

**Results:** Ten patients underwent IMRT (7600-7800 cGy in 38-39 fractions). Most (8) were either intermediate or high risk with six of these patients receiving androgen deprivation therapy. Each patient underwent daily Calypso alignment and prostate tracking during IMRT. The average prostate motion in the Superior-Inferior, Anterior-Posterior, and Right-Left directions were: 0.69 ± 0.8 mm, 0.38 ± 0.8 mm, and 0.11 ± 0.6 mm, respectively. The average magnitude vector was 1.55 ± 0.7 mm. For 6/4 and 2-mm PTV margins, adequate treatment was achieved in 10 out of 10 patients. The percent differences between the 6/4 and 2-mm plans for D90, D95, and D99 were negligible - less than 1.5% in all cases.

**Conclusions:** Our preliminary analysis is consistent with other reports that suggest that 2 mm PTV margins may be adequate with the use of intra-fraction real-time prostate tracking with little impact on the radiation doses delivered. Future work should address the biochemical outcome as well as the reduction in toxicity to surrounding normal organs when reduced PTV margins are employed.

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133 Use of Implanted Gold Fiducial Markers With MV-CBCT Image-Guided IMRT for Pancreatic Tumors

M. Packard, A. Kirichenko, O. Gayou, B. Weiss, S. Thakkar, E. D. Werts, Allegheny General Hospital, Pittsburgh, PA
Purpose/Objectives: Visualization of soft tissue targets such as pancreatic tumors by mega-voltage cone beam CT (MV-CBCT) is frequently difficult and daily localization is often based on more easily seen adjacent bony anatomy. Fiducial markers implanted into pancreatic tumors serve as surrogates for daily tumor position and may more accurately represent absolute tumor position. The purpose of this study using MV-CBCT image-guided IMRT was to compare differences in daily shifts based on alignment to implanted fiducial markers vs. alignment to adjacent bony anatomy.

Materials/Methods: Gold fiducial markers were placed into the primary pancreatic tumor under endoscopic ultrasound guidance in 12 patients. Patients subsequently received image-guided intensity modulated radiation therapy (IG-IMRT) at Allegheny General Hospital (Pittsburgh, PA). The markers were visible on both planning CT and daily MV-CBCT. MV-CBCT was performed prior to each fraction and shifts were calculated based on alignment to the fiducial markers. We retrospectively reviewed the archived MV-CBCT datasets and calculated shifts in lateral, longitudinal and vertical axes relative to the initial imaging plan based on alignment to adjacent bony anatomy for each fraction. These were compared to shifts based on alignment to fiducial markers.

Results: 243 fractions were analyzed. Neither complications secondary to fiducial marker placement nor instances of fiducial migration were observed. The mean absolute difference in shifts between those based on fiducial markers and those from alignment to bony anatomy was 3 mm (range 0-13 mm), 6 mm (range 0-21 mm), and 3 mm (range 0-12 mm), in the lateral, longitudinal and vertical directions respectively. The mean 3-dimensional vector shift difference between markers vs. bony anatomy alignment was 8.6 mm. Sixty-four (26.3%) fractions had a shift difference of at least 1 cm in at least one axis and 96 (39.5%) had a 3-dimensional vector shift of at least 1 cm.

Conclusions: These data suggest that fiducial markers used in conjunction with MV-CBCT improve accuracy of daily target delineation compared to localization using adjacent bony anatomy. The magnitude of the shift differences we report are consistent with those in other reports using gold markers implanted into pancreatic tumors in conjunction with portal imaging and to data using implanted electromagnetic transponders. The reasons for movement of pancreatic tumors relative to adjacent bony anatomy are unknown but may include daily variations in gastric distension or biliary drainage. Our series suggests that gold fiducial markers placed in pancreatic tumors under EUS-guidance are well-tolerated, easily visible on MV-CBCT and remain stably positioned in the tumor throughout the course of radiotherapy.


Clinically Significant Difference in Prostate Localization Using Daily Cone Beam CT (CBCT) and Electromagnetic Transponders

M. K. Khan, S. Das, T. Ogunleye, A. B. Jani, P. Rossi, J. Shelton, T. Liu, Emory University School of Medicine, Atlanta, GA

Purpose/Objectives: To directly compare daily kilovolt (kv) CBCT (using Synergy) and 4D image guidance using electromagnetic transponders (Calypso) for prostate localization, and to evaluate the impact of intra-fraction prostate motion post localization.

Materials/Methods: On an IRB-approved study, from a sample of 6 patients treated using Calypso at our institution, six had undergone daily CBCT imaging followed immediately by Calypso transponder beacon localization and intra-fraction prostate motion tracking. Differences in magnitude of greater than 3, 4, and 5 mm in isocenter shifts based on kvCBCT (using soft tissue and bony registration performed using commercial multi-modality registration software (Velocity Medical Solutions) were compared with the isocenter shifts recorded by the Calypso 4D localization and tracking system. Post localization, intra-fraction prostate excursions of greater than 3, 4, and 5 mm lasting greater than 30
Results: A total of 179 daily kvCBCT images and 238 Calypso sessions were analyzed. The percentage of fractions with a median magnitude difference of greater than 3, 4, and 5 mm in daily prostate localization using soft tissue kvCBCT and Calypso was 49.4+/−31.1% (range: 13.5-95.6), 43.2+/−32.1% (range:10.8-91.3), and 37.5+/−34.5% (range: 5-86.9), respectively. Similarly, the percent difference between bony kvCBCT and Calypso prostate localization was 54.7+/−24.9(21.6-91.3), 45.8+/−30.7 (10.8-91.3), 39+/−33.6 (5.4-86.9). After initial prostate localization, the percentage of time that intra-fraction prostate motion exceeded greater than 3 , 4, and 5 mm lasting greater than 30 seconds was 25.8 +/−18.5 (4.8-48.7), 5.39 +/−6.74 (0-17.9), and 1.267+/−2.1 (0-5.1), respectively.

Conclusions: A clinically significant difference (> 5 mm in magnitude) exists in prostate localization when comparing CBCT and Calypso and should be further evaluated in a prospective manner as the complementary information provided by the two localization approaches may have patient outcome implications. After initial setup, intra-fraction prostate motion was small in magnitude and can be addressed by using adequate treatment margins during a course of radiotherapy.


135 Dosimetric and Clinical Analysis of Retreatment of Vertebral Body Metastases Using Intensity Modulated Radiation Therapy

V. Chowdhry1, M. A. Cummings1, S. S. Hahn1, A. K. Chowdhry2, K. Stellingwerf3, A. Shapiro1, 1SUNY Upstate Medical University, Syracuse, NY, 2University of Rochester School of Medicine and Dentistry, Rochester, NY

Purpose/Objectives: The availability of intensity modulated radiation therapy (IMRT) and image guided radiotherapy (IGRT) has allowed precise delivery of radiotherapy dose to a tumor volume while sparing critical structures. Bony metastases to vertebral bodies pose a therapeutic challenge in the re-treatment setting as the spinal cord is often a limiting structure. The purpose of our study is to review re-treatment of vertebral body metastases using more sophisticated planning techniques in terms of toxicity and efficacy.

Materials/Methods: Ten patients who were re-treated to the vertebral bodies from 2009-2012 were retrospectively identified using an institutional tumor registry. The primary tumor histologies include non-small lung cancer (5), breast cancer (2), head and neck (1), small cell lung cancer (1), and prostate cancer (1). All patients were re-treated using TomoTherapy (7 patients) or conventional IMRT (3 patients). Nine patients had direct GTV overlap and one patient was treated to an adjacent vertebral body but had contribution of cord dose from the previous treatment. For all patients, a GTV involving the vertebral body was countered with avoidance of the spinal cord, cauda equina, and bilateral kidneys if applicable. Dose was sculpted to treat the volume of interest while creating a donut of low dose to protect the spinal cord.

Results: The median interval to re-treatment was 241 days. The median overall survival following radiotherapy was 49 days (range, 0-257 days). The mean GTV retreatment volume was 156 cm3. The median volume of GTV overlap was 76 cm3, (range, 0-386 cm3). The median vertebral body overlap was 2 vertebral bodies (range, 0-3). Initial radiation therapy was completed to a median dose of 3000 cGy in 10 fractions (range, 2500-4000). Retreatment was completed to a median dose of 2500 cGy in 5 fractions, (range 800 cGy in 1 fraction to 3000 cGy in 10 fractions). The median sum dose to the spinal cord was 4400 cGy (range, 3300-5500). The median volume of spinal cord or cauda equina getting greater than 5000 cGy was 0 cm3 (range, 0-1.3 cm3). The median % GTV receiving 95% of the prescription dose was 96% (range, 82-98%). Seven patients (70%) were noted to have improvement in pain symptoms following treatment, 95% CI
(35%-93%). Of the four patients who reported neurologic symptoms, all showed improvement.

**Conclusions:** The use of IMRT allows patients to be retreated to metastatic disease in the vertebral bodies while protecting the spinal cord. There appears to be a therapeutic benefit based on physician reported outcomes, although limited follow-up makes more definitive conclusions difficult.

**Author Disclosure Block:** V. Chowdhry: None. M.A. Cummings: None. S.S. Hahn: None. A.K. Chowdhry: None. K. Stellingwerf: None. A. Shapiro: None.

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**136 Verification of Respiratory Position Reproducibility With a Respiration Self-Monitoring Device: Results for 12 Patients With Lung Tumors**

S. Kawashiro, T. Nomiya, Y. Hagiwara, I. Ota, M. Ichikawa, Y. Kuroda, M. Murakami, K. Nemoto, *Department of Radiation Oncology, Yamagata University, Yamagata, Japan*

**Purpose/Objectives:** Respiratory movement of the tumors occurs during radiation therapy for patients with lung tumors. There are some techniques for decreasing intrafractional target motion derived from a patient’s respiratory movement. A respiration self-monitoring device called Abches (APEX Medical, Inc., Tokyo, Japan) was developed for the purpose of decreasing respiratory target motion. Abches has two arms: one senses respiratory motion of the chest and the other senses that of the abdomen. When Abches is set on a patient, the indicator moves in accordance with the patient’s respiration. Patients can adjust their respiration by looking at the indicator and can theoretically hold their breath at the same respiratory position every time. Abches is expected to be useful, but its accuracy has not been sufficiently determined. The aim of this study was to confirm its accuracy by obtaining radiation therapy planning computed tomography (RTP-CT) images with the use of Abches.

**Materials/Methods:** A total of 12 patients with primary or metastatic lung tumors underwent RTP-CT scans. First, they were asked to practice breath-holding at the same respiratory position with the use of Abches for 5 to 10 minutes prior to RTP-CT. Next, RTP-CT images were obtained while the patients were holding their breath at the same position as that in the practice session, which was indicated on Abches. This procedure was repeated 5 times continuously for each patient to obtain images to measure the movements of tumors. The 5 RTP-CT images for each patient were transferred to a radiation therapy planning system, Xio (Elekta) or Eclipse (Varian). The tumors of each image were contoured as gross tumor volumes (GTVs). Each edge of the tumors was recorded in every direction, i.e., anterior/posterior, left/right, and superior/inferior. The distance between the actual and the average of each edge was measured. As the indicator of the tumor shifts, the standard deviations (S.D.) of all measured data were calculated and analyzed.

**Results:** All values of 1.96 x S.D., which statistically include 95% of all data, were included within 3 mm in each direction. In other words, tumor shifts were included in a 3 mm margin with the use of Abches. This result can be applied to the determination of internal target volume (ITV) margins under respiration control with Abches.

**Conclusions:** Abches is useful for decreasing target motion with reproducible accuracy and for reducing ITV margins in radiation therapy for patients with lung tumors.

137 Advanced Radiation Techniques: Stereotactic Body Radiation Therapy (SBRT) In Early Stage Inoperable Lung Cancer Disease

S. Kosmidis, D. Katsochi, DTCA Hygeia, Athens, Greece

**Purpose/Objectives:** To present stereotactic body radiation therapy as a highly conformal treatment, in compare to conventional radiation therapy, that allows dose escalation and reduced treatment volumes, as a noninvasive alternative to operation in early lung cancer disease. Preliminary data of Clinical experience in Radiation Oncology Department of DTCA HYGEIA.

**Materials/Methods:** Between May 2009 and June 2012, 15 patients with pulmonary tumors, medically inoperable, were treated with SBRT using daily image guidance (cone beam CT) for patient positioning and target localization. Computed tomography (CT scan) and PET computed tomography (FDG/PET) were used for target delineation and planning. Median prescription dose was 36 Gy in 3 fractions in 9 pts or 30Gy in 5 fractions for 3 pts with poor pulmonary function.

**Results:** All patients completed treatment. Median follow up was 13 months (range 3-20). All patients achieved tumor local control, 12pts with complete tumor regression and 3pts with minimal residual tumor in which remains stable at follow up. None patient presented blood toxicity or pulmonary toxicity (pneumonitis) except for two patients who were treated with corticosteroids.

**Conclusions:** Image guided SBRT in selected patients is a feasible, safe, and effective treatment for medically inoperable early stage lung cancer.

**Author Disclosure Block:** S. Kosmidis: None. D. Katsochi: None.

138 Optimizing Options for Re-irradiation With Deformable Image Registration of Prior Plans

N. Saeed, K. Latifi, S. E. Hoffer, A. Cruz, D. W. Opp, E. G. Moros, G. G. Zhang, M. M. Budzevich, R. Shridhar, T. J. Dilling, Moffitt Cancer Center, Tampa, FL, Brown University, Providence, RI, University of South Florida, Tampa, FL

**Purpose/Objectives:** Patients who present for radiation treatment with a history of prior radiation pose a difficult challenge if there is overlap between the treatment fields. In the era of conformal therapy, new options offer re-treatment to small volumes of previously irradiated tissue.

**Materials/Methods:** Five patients who were considered for re-treatment were selected for this retrospective study. All previous treatment data were transferred to the Mirada system for deformable image registration (DIR) to the current treatment planning CT. The cases previously irradiated at our institution included: a patient treated preoperatively for esophageal cancer who now had an adrenal metastasis in a postoperative abdomen, a patient treated for gastroesophageal junction cancer with a liver metastasis in the upper abdomen, a patient treated postoperatively for pancreatic cancer who had subsequently developed an adjacent symptomatic abdominal recurrence, and a patient with metastatic breast cancer with prior radiation to the lumbosacral spine who now developed an iliac wing site of painful disease. The fifth patient had received definitive conformal radiation to his prostate elsewhere but now had developed an anal cancer. Initially, the physicians asked the dosimetry staff to meet constraints based on clinical estimates of normal tissue tolerances. Once the initial plan was approved by the patient’s treating physician, it was then fused to the prior plan in Mirada and a composite dose was then generated.

**Results:** In all five cases, the DIR enabled a composite plan to be performed that changed the current treatment plan. In the case of the patient with the adrenal metastasis, the composite plan showed that the dose to bowel in the vicinity of
the new treatment site would be prohibitively high precluding re-irradiation. The patient with the liver metastasis was able to receive a course of 50 Gy in 5 fractions with SBRT; the beam angles chosen were directly impacted by the patient’s prior upper abdominal IMRT radiation field. The patient with the anal cancer had to have their external beam dose significantly decreased; he received an endorectal brachytherapy boost. The patients with the metastatic pancreatic and breast cancers had their treatment fields modified after the composite dose plan was reviewed.

**Conclusions:** DIR enhances re-irradiation treatment planning by incorporating prior radiation dose. Composite dose distributions may affect final re-irradiation dose and beam arrangement. With DIR capabilities more widely available, the composite dose method is useful in optimizing options and may become a new standard of care for this increasing clinical problem.


139 SBRT Using Residual Lipiodol as Surrogate Fiducial for Image Guidance in the Treatment of Recurrent or Residual Hepatocellular Carcinoma

S. Sioshansi, L. Ding, T. J. FitzGerald, UMass Memorial Medical Center, Worcester, MA

**Purpose/Objectives:** One of the clear advantages of stereotactic body radiation (SBRT) is that it is a noninvasive procedure. However, many of the recently published and current trials of SBRT for hepatocellular carcinoma (HCC) require fiducial placement for image guidance. SBRT after transarterial chemoembolization (TACE) is an active area of investigation. One of the unique advantages of this sequence of therapies is that many patients have residual lipiodol, a lipid contrast emulsion used for TACE, within the tumor that is readily visible on non-enhanced CT scans. We report the feasibility of using the residual lipiodol within or adjacent to viable HCC as a surrogate fiducial.

**Materials/Methods:** Patients previously treated with TACE with residual lipiodol were referred for SBRT. Diagnostic 4-phase CT scans were evaluated and if the area of lipiodol deposition was clearly visualized in the vicinity of the enhancing tumor, fiducial placement was deferred. Patients were simulated with 4D-CT with free breathing. Target volume was contoured on the average scan of the 4D-CT based on fused diagnostic CT. The lipiodol was contoured on the maximum intensity projection (MIP), as well as on phase 0%, 30%, and 50% to determine extent of motion with respiration. The target volume was expanded accordingly to account for respiratory motion. Patients were treated to a total dose of 50-54 Gy in 3-5 fractions. Volumetric modulated arc therapy (VMAT) treatment planning technique was used. Prior to each treatment, kilovoltage orthogonal films and cone beam CT (CBCT) scans were obtained and fused with the planning CT. Patient alignment shifts were made to align the areas of lipiodol within the vicinity of the target.

**Results:** Lipiodol was not visible on the AP and lateral KV images, however it was visualized on the CBCT. Regardless of location and degree of lipiodol staining, windowing adjustments and color blending techniques were used to consistently identify the lipiodol on the CBCT and match to the contour of the lipiodol from the MIP. Shifts were generally decided within 3 minutes of completing the CBCT. Lipiodol to liver Hounsfield unit ratio was calculated for all cases and ranged from 4.5-8.5. The higher the ratio, the more readily visible the lipiodol is on CBCT. Other factors that impacts the degree of visibility of lipiodol is the size of the lipiodol deposit and the extent of motion which results in blurring on non-gated CBCT.

**Conclusions:** Using residual lipiodol as a surrogate fiducial for image guidance with CBCT is feasible, efficient, and non-invasive. The lipiodol to liver Hounsfield unit ratio correlate with ease of visualization on CBCT. Size of lipiodol deposit and extent of motion on 4D-CT are other factors that impact ability to see the lipiodol on CBCT.
Early Detection of Tumor Response Using 4D DCE-CT and DCE-MRI in Patients Treated With Radiosurgery for Brain Metastases

C. Chung, B. Driscoll, A. Gorjizadeh, W. Foltz, S. Lee, C. Menard, C. Coolens, Princess Margaret/University of Toronto, Toronto, ON, Canada

Purpose/Objectives: Early change in tumor perfusion following radiosurgery (RS) is a potential biomarker of response. But measurement of tumor perfusion using dynamic contrast enhanced (DCE) MRI has limitations in accuracy and precision, and DCE-CT is a standard for tracer-kinetic validation. A recent 4D temporal dynamic segmentation (TDS) method, which enables voxel-based, parametric analysis based on patient-specific dynamic behavior of contrast flow, might improve DCE-MRI analysis but its performance must be tested against DCE-CT. (IJROBP 84(3):S108) This study reports our preliminary experience with tumor perfusion measurement following RS for brain metastases using DCE-CT supported by 4D-TDS compared to a standard DCE-MRI approach.

Materials/Methods: Patients with brain metastases treated with RS as part of a REB-approved clinical trial underwent 4D DCE-CT (Toshiba, Aquilion ONE) and DCE-MRI (IMRIS 3T Verio) scans at baseline then 7 and 21 days post-RS. Tumor regions of interest (ROIs) were obtained from the planning scans and registered to the DCE-CT and MR images by skull-to-skull registration in Amira (Visage Imaging). Individual vascular input functions were selected in the internal carotid artery for DCE-CT and sagittal sinus for DCE-MRI. DCE-MRI data was analyzed using a ROI within a single slice at the tumor midline, and compared against voxel-based whole tumor TDS algorithm for DCE-CT using in-house software for tracer-kinetic analysis. Modified Tofts and semi-quantitative kinetic parameters ($K_{trans}$, AUC) were assessed within each tumor at all time points.

Results: In 3 patients, 7 tumors were evaluated with DCE-CT and 6 with DCE-MR. Of these tumors, 4 responded clinically and radiologically at 6 months. DCE-CT: With the 4D TDS approach, 2 of 7 tumors revealed a $K_{trans}$ reduction of 45±13% (p<0.05) at day 7 post-RS and all 4 responding tumors had a reduction in $K_{trans}$ of 50±12 % by day 20 (p<0.04). None of the non-responding tumors showed a $K_{trans}$ response (p>0.14). AUC reduction was 68±22% by day 20 (p<0.01) in all 4 responding tumors and 32% in one non-responding tumor (p<0.03). DCE-MRI: MRI results correlated with DCE-CT in 5 of 6 tumors for $K_{trans}$ (R² = 0.85 +/- 0.10) and AUC (R² = 0.93 +/- 0.04) at day 20, but 1 of 6 tumors showed a 54% reduction in $K_{trans}$ on DCE-MRI without DCE-CT or clinical response.

Conclusions: Early $K_{trans}$ reduction at 20 days following RS may be a promising response biomarker using 4D TDS DCE-CT. In comparison, DCE-CT measurements of AUC reduction were observed in both responding and non-responding tumors. DCE-MRI correlated with DCE-CT in all but 1 case for which the DCE-CT correctly predicted clinical response. It is anticipated that concordance between DCE-MRI and DCE-CT will improve with incorporation of 4D-TDS into the MRI assessment.

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Advancing Image Guided Visualization of Cellular-based Vaccines, In Vivo, During Combined Radiation/Immunotherapy Protocols

F. A. Myslicki¹, C. A. Mantz², S. E. Finkelstein¹, ¹21st Century Oncology Translational Research Consortium (TRC), Scottsdale, AZ, ²21st Century Oncology Translational Research Consortium (TRC), Fort Myers, FL

Purpose/Objective(s): To describe a technique that allows for in vivo visualization of IC administered as part of treatment combining radiation and immunotherapy.

Materials/Methods: ICs are labeled with 1mCi Indium Oxine or HMPAO in a class 100 environment. After washing, the radioactivity of the cells is measured. A gamma probe (US Surgical Navigator) with the window pre-set to optimize detection of Indium energy peaks is used for localization. The probe is held over target areas to non-invasively obtain baseline measurements of: the center of the tumor mass, tumor periphery, draining lymph nodes, and background tissue. Labeled ICs are administered via intratumoral injection under image guidance. Immediate post injection non-invasive measurements are obtained for the same sites. The patient is then imaged using a gamma camera (Siemens e-cam) at 20 minutes post injection and immediately prior to surgery. The camera has 20% windows at 171 kev and 245 kev Indium energy peaks. Images of the injection site, regional lymph node stations, and the area between the injection site and regional basins are acquired in at least two projections. Any sites identified with the gamma camera are marked using an indelible pen to assist further localization at the time of surgery. An intraoperative gamma probe is used to determine activity at the original target areas, as well as the tumor resection bed. The number of radioactive counts per 10 seconds within site is recorded.

Results: In vivo visualization of cell-based vaccine components has been accomplished safely during dual radiation/immunotherapy protocols. Time dependent changes in ratios of radioactivity for various sites, including tumor periphery to background, and lymph node to background, can be utilized as indicators of IC migration. Following correction for decay, the ratio of counts of cases performed at different times can be compared and correlated with the level of specific immune response.

Conclusions: The ability to characterize cellular migration holds great potential for advancing future combinational treatment approaches; this technique to track and analyze immune cell movement into tissues may augment our knowledge of treatments such as Sipuleucel-T.

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Superiority of a Real-Time Planning Technique Over Image Guided Radiation Therapy for the Treatment of Primary Prostate Cancers

S. Merrick, J. Wong, M. Karim, J. Gao, M. Li, R. Figueroa, S. Riley, Morristown Medical Center, Morristown, NJ

Purpose/Objectives: Image-Guided Radiation Therapy (IGRT) increases the precision and accuracy of external beam radiation therapy and provides a safer delivery of higher, more curative levels of radiation dose. However, when significant changes to internal anatomy occur, IGRT alone will not be able to compensate for the dose degradation that may occur from using the original IMRT plan. A real-time planning (RTP) or adaptive planning technique would enable the continued use of tight margins with the assurance of full target coverage and efficient normal tissue sparing. In its current stage, the adaptive planning technique requires a physician to manually redraw the involved structures before each treatment. These day-to-day contouring variations could potentially be significant and thus overestimate the
superiority of the newly created adaptive IMRT plan.

**Materials/Methods:** A total of 60 CT scans were used during the course of IMRT treatment of 6 prostate cancer patients. An in-room diagnostic CT-on-Rails was used for the purposes of performing daily IGRT in conjunction with an adaptive IMRT planning technique. While the data was analyzed for the standard purposes of IGRT, a brand new optimized IMRT plan was created based on a new set of structures drawn by the on-call physician. This resulting plan was then compared to the initial IMRT plan or “recalculated plan” which was copied onto the new data set and recalculated with the daily IGRT implemented shifts.

**Results:** The RTP plan consistently showed at least equal effectiveness in target coverage and normal-tissue sparing as the initial IMRT recalculated plan. In 25% of the cases, greater rectal sparing was seen in the RTP plan with the largest single case reducing V50 by 40% and V60 by 50%. The most frequent anomalies seen in this study, however, were target coverage of the prostate and PTV. While the RTP plan maintained minimum prescription dose coverage of 97% to the prostate, the recalculated IMRT plan’s minimum dose routinely fell below 95%, and in 20% of the cases, it dropped below 90%. In terms of PTV minimum coverage, the recalculated IMRT plan showed consistent dose degradation with 90% of the cases falling below 90% of the prescribed dose.

**Conclusions:** Daily changes of the internal anatomy warrant the need for RTP. To our knowledge, we are one of the first to implement this technique in our daily clinical practice on a consistent basis. RTP possesses the ability to treat other cancer sites besides the prostate and its full potential maybe realized once better and faster auto-segmentation programs are available to minimize manual contouring variability.

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**Hybrid Intensity Modulated Radiotherapy -- Stereotactic Radiosurgery for Treatment of Pituitary Macroadenomas**

**A. Vincent, J. Galle, A. Martino, S. Russo, R. Ove,** University of South Alabama Mitchell Cancer Institute, Mobile, AL

**Purpose/Objectives:** Pituitary adenomas are generally treated with a combination of surgery and radiotherapy. Microadenomas are often candidates for stereotactic radiosurgery, while macroadenomas are treated with fractionated radiotherapy, due to intolerance of the optic apparatus to hypofractionated irradiation. Cases in which the chiasm is compressed by the tumor and difficult to visualize are particularly challenging. We report on a novel use of fractionated radiosurgery to improve the efficacy of therapy while retaining the safety of conventional radiotherapy, for bulky macroadenomas abutting the optic chiasm.

**Materials/Methods:** Records of patients receiving CKRS for pituitary tumors at our institution were reviewed. 4 of these had disease precluding radiosurgery as the sole modality, and were treated with a combination of IMRT (Tomotherapy, 41.4 Gy in 23 fractions) plus 5 CK boost fractions. CKRS treatment was optimized in an inhomogeneous fashion to constrain dose to the optic apparatus at 1.8 Gy per fraction, while boosting inferior portions of the target. Boost doses of 20-25 Gy at 70-80% isodose could be delivered to 50-77% of the total target volume, while deliberately sparing the superior portions. Review of dose-volume histograms and isodose curves demonstrate that entire target volume as defined on MRI receives an minimum absolute dose of 8 Gy over 5 fractions, equivalent to standard fractionated radiotherapy. Review of isodose curves reflecting the CKRS portion of a treatment, illustrate planned under-coverage superiorly, and sparing of the adjacent brainstem and chiasm avoidance structure posteriorly and superiorly, respectively.

**Results:** The biological equivalent dose (BED) to the boost volume ranged from 112.9 to 132.9 Gy, compared to the BED
of standard fractionated radiotherapy (81 Gy). There were no associated adverse side effects. All patients had stable or improved MRI findings, and all secreting adenomas were noted to have improved outcomes at follow-up.

**Conclusions:** This IMRT-CKRS hybrid technique is an attractive approach that allows escalation of dose, with optic apparatus safety equivalent to that of fractionated radiotherapy. The treatment is well tolerated. Increase in delivered BED offers potential improvement in response with selectively sparing of radiosensitive structures. This approach may also be useful for treatment of other perisellar tumors.

**Author Disclosure Block:** A. Vincent: None. J. Galle: None. A. Martino: None. S. Russo: None. R. Ove: None.

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**144  Comparison of the Effectiveness of Radiofrequency Ablation With Stereotactic Body Radiation Therapy in Inoperable Stage I Non-Small Cell Lung Cancer: A Systemic Review and Meta-analysis**

N. Bi, K. Shedden, X. Zheng, F. Kong, University of Michigan, Ann Arbor, MI

**Purpose/Objectives:** SBRT is the standard care for medically inoperable patients with stage I NSCLC, for a significant survival improvement and good tolerance. RFA is also a promising minimally invasive and convenient non-surgical treatment option for small, peripheral tumors. However, it has only been evaluated in studies involving small numbers of patients and has not been directly compared with SBRT in randomized controlled trials. We performed a meta-analysis on the reported series of inoperable early stage NSCLCs treated with SBRT or RFA to compare clinical outcomes of these two techniques.

**Materials/Methods:** Literature search was performed using MEDLINE, Embase and Cochrane Library from January 2001 to July 2012. The eligibility criteria included: (1) stage I NSCLC diagnosis, (2) medical inoperability, and (3) adequate clinic information. Studies about RFA followed by immediate resection or radiotherapy, or SBRT with BED <100 Gy, fraction dose <8 Gy were excluded. Meta-analyses were performed to obtain estimates for pooled overall survival (OS), local tumor control rates (LCR), and the adverse events. Standard errors of LCR and OS were estimated and corrected by the number of patients and median follow-up time.

**Results:** A total of 44 one-arm original studies were identified: 31 studies on SBRT (2767 patients) and 13 studies on RFA (328 patients). LCR (95% confidence interval) at 1, 2, 3 and 5 years for RFA was 77% (70 - 85%), 48% (37 - 58%), 55% (47 - 62%), and 42% (30 - 54%) respectively, which was significantly lower than that for SBRT: 97% (96 - 98%), 92% (91 - 94%), 88% (86 - 90%), and 86% (85 - 88%), P<0.001. These differences were still significant even after correcting for each study’s proportions of stage IA and age (P<0.001 at 1 year, 2 years and 3 years; P=0.04 at 5 years). OS at 1-, 2-, 3- and 5-year for RFA was 85% (80 - 89%), 67% (61 - 74%), 53% (45 - 61%) and 32% (22 - 43%) respectively, compared to 85% (84 - 87%), 68% (66 - 71%), 56% (53 - 59%), and 40% (36 - 45%) for SBRT therapy (P>0.05). In view of acute toxicity, the most frequent complication of RFA is pneumothorax, which occurs in 32% (16 - 45%) patients, required chest tube insertion in 12% (7 - 39%) of patients. The most frequent grade 3 or greater toxicity for SBRT is radiation pneumonitis (RP), occurring in 2.2% of patients (95%CI: 0.6-3.9%). The second frequent toxicity is rib fracture, occurring in 2.1% of patients (95%CI: 1.2-2.9%).

**Conclusions:** LCR for SBRT is significantly higher than that for RFA, though OS is not different between two groups. Both SBRT and RFA are well tolerated. Therefore, at present patients should be offered RFA only if they are not candidates for SBRT. However, caution is warranted due to the relatively limited number of RFA studies.

**Author Disclosure Block:** N. Bi: None. K. Shedden: None. X. Zheng: None. F. Kong: None.
Selective Targeting of Brain Tumors With Nanoparticle-induced Radiosensitization and Contrast Enhancement


Purpose/Objectives: Successful treatment of brain tumors such as glioblastoma multiforme (GBM) is limited in large part by the cumulative dose of Radiation Therapy (RT) that can be safely given and the blood-brain barrier (BBB), which limits the delivery of systemic anticancer agents into tumor tissue. Consequently, overall prognosis remains grim. We report pilot studies in cell culture experiments and in an animal model of GBM in which RT is complemented by PEGylated-gold nanoparticles (GNPs). We characterize several versatile ways in which GNPs can be incorporated as adjuvants into brain tumor imaging and radiotherapy paradigms, serving as a potential “theranostic” agent.

Materials/Methods: We first investigated the ability for GNPs to act as radiosensitizers and vascular dose-painting agents that can enhance DNA damage to both GBM cells and vascular endothelial cells. Next, we assessed whether this GNP radiosensitization translated into improved survival in mice with orthotopic GBM. Finally, we utilized RT-induced disruption of the BBB in intracranial tumors as a noninvasive strategy to enhance the passive accumulation of GNPs across the BBB into orthotopic GBM xenografts. We also explored MRI contrast-enhancing capabilities of mixed-particle micelle (MPMs) in a novel nanoformulation which incorporates both gold and iron oxide.

Results: GNPs markedly increased cellular DNA damage inflicted by ionizing radiation in human GBM-derived cell lines and resulted in significantly reduced clonogenic survival (with dose-enhancement ratio of ~1.3). Combined GNP and RT also resulted in markedly increased DNA damage to brain blood vessels and brain-derived endothelial cells. Finally, the combination of GNP and RT increased survival of mice with orthotopic GBM tumors. Prior radiation treatment of mice with brain tumors resulted in increased extravasation and in-tumor deposition of GNP, suggesting that RT-induced BBB disruption can be leveraged to improve the tumor-tissue targeting of GNP and further optimize the radiosensitization of brain tumors by GNP. MRI of mice with brain tumors injected with MPMs showed hypointensity indicating significant and persistent MPM accumulation in the tumor.

Conclusions: These exciting results together suggest that GNPs in various formulations may be integrated into both imaging and RT treatment of brain tumors, with potential benefits from increased tumor cell radiosensitization and preferential targeting of tumor-associated vasculature, as well as enhanced contrast imaging properties of mixed-particle nanoformulations.


Investigation of VMAT Algorithms and Dosimetry

A. Taqaddas, Student at The Open University, UK, Milton Keynes, United Kingdom

Purpose/Objectives: Planning and dosimetry of different VMAT algorithms (SmartArc, Ergo++, Autobeam) is compared with IMRT for Head and Neck Cancer patients. Modeling was performed to rule out the causes of discrepancies between planned and delivered dose.

Materials/Methods: Five HNC patients previously treated with IMRT were re-planned with SmartArc (SA), Ergo++ and Autobeam. Plans were compared with each other and against IMRT and evaluated using DVHs for PTVs and OARs, delivery time, monitor units (MU) and dosimetric accuracy. Modeling of control point (CP) spacing, Leaf-end Separation
and MLC/Aperture shape was performed to rule out causes of discrepancies between planned and delivered doses. Additionally estimated arc delivery times, overall plan generation times and effect of CP spacing and number of arcs on plan generation times were recorded.

**Results:** Single arc SmartArc plans (SA4d) were generally better than IMRT and double arc plans (SA2Arcs) in terms of homogeneity and target coverage. Double arc plans seemed to have a positive role in achieving improved Conformity Index (CI) and better sparing of some Organs at Risk (OARs) compared to Step and Shoot IMRT (ss-IMRT) and SA4d. Overall Ergo++ plans achieved best CI for both PTVs. Dosimetric validation of all VMAT plans without modeling was found to be lower than ss-IMRT. Total MUs required for delivery were on average 19%, 30%, 10.6% and 6.5% lower than ss-IMRT for SA4d, SA2d (Single arc with 20 Gantry Spacing), SA2Arcs and Autobeam plans respectively. Autobeam was most efficient in terms of actual treatment delivery times whereas Ergo++ plans took longest to deliver.

**Conclusions:** Overall SA single arc plans on average achieved best target coverage and homogeneity for both PTVs. SA2Arc plans showed improved CI and some OARs sparing. Very good dosimetric results were achieved with modeling. Ergo++ plans achieved best CI. Autobeam resulted in fastest treatment delivery times.

**Author Disclosure Block:** A. Taqaddas: J. Funding Other; RMH provided financial support in terms of paying the University fee for the project module. N. Royalty; No royalty for this research; however, this research was mentioned in my physics VMAT book and I get royalty for my book.

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147 Radiation Exposure Incurred by Healthcare Providers During Radioactive Seed Localization for Surgical Resection of Nonpalpable Breast Cancers

J. Giesbrandt, M. McDonough, Mayo Clinic Florida, Jacksonville, FL

**Purpose/Objectives:** With the widespread implementation of mammographic screening, more breast cancers are being detected before they reach a size which can be detected clinically. Radioguided localization was first described in 1998 by Luini et al as an alternative to wire localization for resection of nonpalpable breast lesions. A few years later, a modified technique involving the use of radio-opaque titanium seeds containing radioactive Iodine-125 was reported. Radioactive seed localization (RSL) has largely replaced wire localization at our institution, as it is associated with fewer complications and has a much lower incidence of positive margins following surgical resection.

**Materials/Methods:** The Instadose dosimeter contains a USB port that allows accumulated radiation exposure to be recorded and reset in a matter of minutes from any computer with internet access. Two separate monitoring devices are used in this study- one worn at the wrist by the radiologist placing the seed and one worn at the wrist by the assisting technologist. Following each seed placement, data from both devices are entered into the system and then recalibrated in preparation for the next procedure. Each technologist and radiologist are also wearing personal ring detectors which will be collected and analyzed at the end of a 6 month time period. This project will not only allow us to determine the amount of radiation incurred during a single procedure, but also allow an estimate of the cumulative dose that could be expected of a full time breast radiologist or technologist.

**Results:** Preliminary data indicate that the level of radiation exposure incurred by both the radiologist and assisting technologist to be negligible, with only two technologists incurring a 1 month cumulative dose greater than the detectable level of our monitoring equipment (1 mrem/0.01 mSv). We will continue to monitor each radioactive seed placement for a total of 6 months, with an estimated study population of 100. This should allow for enough statistical power to confidently exclude any significant radiation exposure to radiologists and technologists involved with placement of radioactive seeds for nonpalpable breast lesions.
Conclusions: The titanium seed inserted during RSL contains 0.3 mCi of radioactive iodine-125. A series of 300 RSL procedures approximated the radiation exposure to the residual breast tissue to be 2 cGy, equivalent to a single two-view mammogram. However data looking at the cumulative exposure to medical staff involved with RSL has not been collected to confirm these beliefs. This study aims to confirm that there is not significant radiation exposure to radiologists or assisting mammography technologists involved in radioactive seed placement.

Author Disclosure Block: J. Giesbrant: None. M. McDonough: None.

148 Phase/Amplitude-matched Digital Tomosynthesis (DTS) Imaging for Moving Target Localization

L. Ren, Y. Zhang, F. Yin, Duke University, Durham, NC

Purpose/Objectives: To develop phase/amplitude-matched DTS imaging techniques for localization of moving targets prior to or during radiation therapy delivery.

Materials/Methods: Phase-matched reference DTS (Ref-DTS-4DCT-Phase) is reconstructed from digitally reconstructed radiographs (DRRs) of 4D-CT that have the same phases in the breathing cycle as the on-board OBI projections acquired for on-board DTS reconstruction. Amplitude-matched reference DTS (Ref-DTS-4DCT-Amp) is reconstructed from DRRs of 4D-CT that correspond to the same amplitudes in the breathing cycle as the OBI projections. Target positioning errors are determined by registering reference DTS with on-board DTS (OBI-DTS).

The 4D Digital Extended Cardiac Torso (XCAT) Phantom was used to simulate patient 4DCT, average intensity projection CT (AIP), free-breathing CT (FBCT) and on-board OBI projections using breathing patterns fed into the software. Target positioning errors were simulated by shifting the CT images along three axes by a known amount. An ROI surrounding the tumor was used for registration. The simulated shifts were compared with the registered shifts to evaluate the registration error. The following four scenarios were tested: 1). OBI DTS scan duration (t) = 5/6 breathing cycle (T), breathing amplitude in OBI scan (A_OBI) = amplitude in CT scan (A_CT); 2). t = 5/6T, A_OBI = 1.5 x A_CT; 3). t = T, A_OBI = A_CT; 4). t = T, A_OBI = 1.5 x A_CT. Note that T is 5sec in our simulation, which corresponds to a 30º scan angle.

Results: In scenario 1, the average vector registration errors for registering Ref-DTS-FBCT, Ref-DTS-AIP and Ref-DTS-4DCT-Phase with OBI-DTS are 6.62mm, 2.55mm, and 1.47mm, respectively. In scenario 2, the corresponding errors are 7.26mm, 2.57mm, and 1.58mm, respectively. In scenario 3, the average vector registration errors for registering Ref-DTS-FBCT, Ref-DTS-AIP, Ref-DTS-4DCT-Phase and Ref-DTS-4DCT-Amp with OBI-DTS are 5.62mm, 1.56mm, 1.22mm, and 1.20mm, respectively. In scenario 4, the corresponding errors are 4.46mm, 1.60mm, 1.56mm, and 1.00mm, respectively. In summary, Ref-DTS-FBCT has the worst registration accuracy among all the methods. Ref-DTS-4DCT-phase is more accurate than Ref-DTS-AIP for registering moving target position. Preliminary results indicated that the localization accuracy could be further improved with Ref-DTS-4DCT-Amp when breathing amplitude changes dramatically from CT scan to on-board DTS scan.

Conclusions: Both Ref-DTS-4DCT-Amp and Ref-DTS-4DCT-Phase are potentially very useful for moving target localization when used appropriately for different patient scenarios. Imaging dose can be significantly reduced using these methods compared to 3D or 4D CBCT.

Author Disclosure Block: L. Ren: None. Y. Zhang: E. Research Grant; Varian Medical System. F. Yin: None.
Organ Sparing Using MRI/CT Fusion for Localized Prostate Cancer

J. M. Baisden, H. P. Martin, 21st Century Oncology, Princeton, WV

**Purpose/Objectives:** The purpose of this study was to quantify the decrease in dose to the normal organs seen when adding MRI images for planning prostate cancer treatment. This was evaluated in the community clinic setting.

**Materials/Methods:** Planning CT images were gathered and individual treatment plans were performed for localized prostate cancer patients. MRI images were gathered at the community hospital. T2-weighted axial images were fused for planning purposes, and a second plan was generated using the fused images. Patients were treated with IMRT with daily CT image guidance using helical tomotherapy to a total dose of 81 Gy in 45 fractions at 1.8 Gy/fraction.

**Results:** Rectal doses were decreased significantly for the patients as treated with fused-MRI planning, compared to plans generated with CT data only. Discrepancies in prostate volume and associated PTVs were variable, highlighting the advantage of MRI over CT in delineating prostate anatomy. There was a 29.3% decrease in prostate volume with MRI compared to CT. Regarding rectal dose, the V80, V75, V70, V60, V50, and V40 were decreased by 82.6, 74, 65.9, 54.7, 43.7, and 31.4 percent, respectively. Similar improvements were seen in dose to the bladder and penile bulb. Patients tolerated the treatments with no Grade 3 or higher acute toxicities.

**Conclusions:** Fusion of MRI for planning purposes results in significant sparing of normal organs for prostate cancer IGRT/IMRT in the community setting. Further dose escalation is being pursued.

**Author Disclosure Block:** J.M. Baisden: None. H.P. Martin: None.
pneumothorax, with a substantial number of patients requiring chest tube placement.

**Conclusions:** Percutaneous CT-guided placement of fiducial markers for small pulmonary malignancies in high risk patients can be technically challenging, with a high incidence of complications. Understanding appropriate fiducial marker positioning, as well as overcoming technical challenges that arise during the procedure, increase the likelihood of clinically successful fiducial marker placement.

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**151 Implantable MRI Tissue Markers: Design and Phantom Studies**

K. S. Martirosyan\(^1\), S. J. Frank\(^2\), J. Stafford\(^2\), \(^1\)University of Texas at Brownsville, Brownsville, TX, \(^2\)M.D. Anderson Cancer Center, Houston, TX

**Purpose/Objectives:** The positive identification of implantable radioactive seeds under MRI has been actively investigated. The major problem is to accurately evaluate the titanium seed distribution by MRI due to artifacts that generated by titanium high frequency shielding. The development of a positive contrast MRI tissue marker to aid in seed detection and localization is a major technological advance for prostate brachytherapy, with the potential to significantly change the field by improving the quality of every implant performed. The goal of this study is to demonstrate optimal MRI tissue marker design and testing under brachytherapy phantom. The developed markers will provide a powerful tool for accurate delivery of radiation and improved assessment of the quality of prostate brachytherapy.

**Materials/Methods:** The MRI tissue marker consists of a sealed biocompatible polymer capsule containing a containing a cobalt chloride solution chelated with N-acetyl-cysteine (Co-NAC). To ensure ease of use and compatibility with current brachytherapy technology (implant needles and templates) the dimensions of the marker selected to be equivalent to those of the spacing devices typically placed between radioactive seeds. In this way the tissue marker can be easily integrated into implantable brachytherapy systems and simply placed between seeds in an implant needle.

**Results:** We designed the MRI marker to be 5.5 mm long, with an outer capsule diameter of 0.8 mm (inner diameter 0.6 mm); the Co-NAC contrast agent solution is contained within this capsule. The selection of the optimal capsule material, encapsulation methodology, and device sealing strategies has been critical to device development and design. An implantable grade of polyether ether ketone (PEEK) was selected because of its regulatory status as a key component of numerous FDA-approved implantable medical devices and its physical properties. We demonstrated based on brachytherapy phantom study that the MRI tissue markers placed next to the distal ends of radioactive seeds indicate the precise location of seeds with respect to the surrounding anatomy when imaged with MRI.

**Conclusions:** The MRI marker was clearly distinguishable from the needle track used to implant it in the prostate phantom. The MRI marker’s visibility under MRI was not altered after processing through a standard gamma irradiation sterilization technique.

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Comparison of Gold Seeds, Tight Embolization Coils, and Loose Embolization Coils Used as Fiducial Markers for Dynamic Tracking Using CyberKnife


Purpose/Objectives: To compare the ability of the CyberKnife (Accuray, Inc., Sunnyvale, CA) to track cylindrical gold seeds and variably packed platinum embolization coils used as fiducial markers.

Materials/Methods: Three gelatin-based phantoms of equal size (11 cm x 20 cm x 11 cm) were constructed. Three gold seed fiducial markers (Alpha-Omega Services, Bellflower, CA) measuring 0.8 mm in diameter x 5 mm long were implanted in a phantom using a 10 cm, 19 gauge needle from a vanSonnenberg biopsy set (Cook Inc., Bloomington, IN). In a second phantom, three 2 mm x 3 mm platinum Tornado Embolization Microcoils (Cook Inc., Bloomington, IN) were implanted with a 15 cm, 22 gauge needle. The coils were deployed such that they were packed or wound as tightly as possible. In the third phantom, three coils were also deployed; however, they were deliberately inserted sub-optimally (stretched or loosely coiled). All markers were deployed under fluoroscopy using a Siemens Artis Zee (Siemens Medical Solutions, Erlangen, Germany). The fiducial arrangements in the phantoms were identified in the CyberKnife treatment planning system, after which the phantoms were placed on the treatment table. Individual fiducial locations were extracted by the CyberKnife imaging system for a variety of table positions by translating and rotating the table by known measures in one degree of freedom while keeping all other positions fixed at the origin. Measurements were taken at 0, 5, and 10 mm of left/right, posterior/anterior, and inferior/superior translation as well as 0, 0.5, 1.0, and 1.5 degrees head-down/head-up and roll left-roll right, respectively.

Results: Relative tracking accuracy was determined by comparing the variance of the inter-fiducial distances calculated after each of the 25 translations and rotations. There were no statistically significant differences between the tracking accuracies of each phantom.

Conclusions: Neither the type of marker used nor the degree of packing of the embolization coils affected the ability of the CyberKnife to accurately track. This implies that embolization coils can confidently be used as fiducials using a smaller delivery system. This study is limited by the small number of coil configurations used.

External Beam Radiotherapy Is Associated With Increased Variability in Retinal Venous Oxygenation

B. S. Chera1, D. S. Higginson2, A. Saghôl3, M. V. Lawrence1, S. Moyer3, M. Stefanescu1, B. Qaqish4, A. Zanation5, L. B. Marks1, S. Gaarg3, 1Department of Radiation Oncology, University of North Carolina - Chapel Hill, Chapel Hill, NC, 2Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, 3Department of Ophthalmology, University of North Carolina - Chapel Hill, Chapel Hill, NC, 4Department of Biostatistics, University of North Carolina - Chapel Hill, Chapel Hill, NC, 5Department of Otolaryngology, University of North Carolina - Chapel Hill, Chapel Hill, NC

Purpose/Objectives: To evaluate in vivo changes in retinal oxygen saturation (SO2) via retinal oximetry after incidental radiation to the eyes.

Materials/Methods: We performed in vivo measurements of arteriole and venule SO2 (SaO2 and SvO2) in patients (n=9, 18 retinas) who received incidental radiation to their retinas (≥ 45 Gy to ≥ 25% of one retina) and healthy subjects (n=20, 40 retinas). Retinal oximetry, a non-invasive imaging modality, was used to measure SaO2 and SvO2. The repeatability of SO2 measurements and the variability in SaO2 and SvO2 between the irradiated patient cohorts and the unirradiated volunteers were evaluated. Variability was analyzed using a random effects model using vessel type (arterioles vs. venules), vessel caliber, and cohort (irradiated patients vs. unirradiated subjects) as co-variates.

Results: Retinal oximetry measurements were highly reproducible in both irradiated patients and unirradiated subjects with standard deviations of repeated measurements of the same vessels of 1.7 - 2.5%. The variability of SvO2 and SaO2 measurements of different vessels in the same patient was significantly larger in the irradiated cohort than the unirradiated cohort (standard deviation 62% higher: 8.2% vs 5.1% in venules, 4.5% vs 2.8% in arterioles, p<0.001).

Conclusions: Variation in repeated SO2 measurements using retinal oximetry was minimal. SaO2 and SvO2 varied significantly between irradiated patients and non-irradiated subjects suggesting alteration in retinal oxygenation after radiation therapy.


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FDG Pulmonary Uptake Changes During and Postradiotherapy Compared to Pretreatment in Predicting Radiation-induced Lung Toxicity in Non-Small Cell Lung Cancer

L. Li1,2, W. Wang1, P. Stanton1, N. Bi1, S. Kong1, 1University of Michigan, Ann Arbor, MI, 2Fudan University Shanghai Cancer Center, Shanghai, China

Purpose/Objectives: The primary aim of our study was to investigate the relationship between clinical RILT and pulmonary 18FDG uptake changes during and post-radiotherapy compared to pre-radiotherapy baseline.

Materials/Methods: We studied a prospectively recruited cohort of 56 non-small cell lung cancer patients treated with chemo/radiotherapy. All the patients had 18FDG PET performed before and during radiotherapy, and 38 patients had post-RT PET images. Pulmonary changes in 18FDG uptake between pre during and post radiation on PET images were
assessed using Hick’s visual grading scale (0-3) by a physician blinded to clinical RILT results: Grade 0~ no abnormality identified in normal tissues within the radiation treatment volume; Grade 1~ increased activity in the pleural reflections and soft tissues within the radiation treatment volume but no parenchymal lung changes; Grade 2~ increased parenchymal lung uptake in the radiation treatment volume of equal or lower intensity than normal soft tissues in the mediastinum or chest wall located outside the radiation field; Grade 3~ increased parenchymal lung uptake in the radiation treatment volume of greater intensity than normal soft tissues in the mediastinum or chest wall. Common Terminology Criteria for Adverse Events version 3.0 was used to score RILT and event was defined as grade 2 or higher.

Results: On during-RT PET images, 48 (85.7%), 6 (10.7%), 2 (3.6%) and 0 (0%) patients had grade 0, 1, 2 and 3 changes, respectively. At 3 months after completion of RT, 45% patients had visible changes: 11 (28.9%) grade 1, 2 (5.3%) grade 2, and 4 (10.5%) grade 3 on the post-RT PET images. Overall, 10 patients (17.9%) developed RILT and the median time to RILT after radiotherapy was 4.2 months (range: 2-10). Among patients developed clinical RILT, 5 patients (50.0%) had grade 0, 5 (50.0%) grade 1-2, 0 (0%) had grade 3 FDG uptake on the during-RT PET images. In 8 patients with increased FDG uptake during-RT, 5 (62.5 %) developed RILT, and 2 of them had grade 3 and above. Among 8 RILT patients with post-RT PET images available for assessment, 7 (89%) had grade 1-3 changes on FDG uptake. There was a significant correlation between the incidence of RILT and FDG uptake changes on during-RT (\(P=0.002\)) and post-RT (\(p<0.001\)) PET images.

Conclusions: FDG uptake is commonly increased at 3 months after RT, but infrequently increased on the during-RT PET. Increase in FDG update in lung either during- or post-RT is associated with increased risk of RILT. Increased uptake during-RT may identify patients at highest risk for RILT. Visual assessment of PET may identify patients at high risk for toxicity and guide individualized radiation plan to decrease RILT.

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158 Withdrawn

159 A Pilot 11C-Choline PET-CT Imaging Study in Patients With Locally Advanced Esophageal Cancer


Purpose/Objectives: As concomitant chemoradiation followed by esophagectomy has become standard treatment for locally advanced esophageal cancer, there has been increasing emphasis on identifying a reliable imaging modality to assess treatment response. Given the high false negative and false positive findings with 18F-FDG-PET in the post-treatment setting, many have sought to pursue other radiopharmaceuticals that could potentially better delineate sites of malignancy. Choline, a component of the key cell membrane building block phosphatidylcholine, has emerged as a potential useful radiotracer target for PET/CT imaging in evaluating treatment-response after neoadjuvant chemoradiation.

Materials/Methods: Eight eligible patients were selected to undergo baseline and post-treatment 11-C Choline PET/CT imaging. Treatment-related changes seen on 11-C Choline PET were then compared to pathologic, radiographic and/or clinical follow-up data.

Results: On review of our small series, the observed pCR rate was 25%. Six of the eight patients had 11C Choline PET imaging that correlated with their overall clinical outcomes, as defined by pathology and/or follow-up imaging. Two of eight patients had resolution of their primary lesion following treatment, as visualized on 11-C Choline PET. Neither
patient went on to surgery, but both had confirmed negative post-treatment EGD pathology and corresponding negative conventional imaging. Two patients exhibited partial responses to therapy, as seen on 11-C Choline PET, which was confirmed on surgical pathology. A single patient was found to have unchanged disease burden on post-treatment 11-C imaging with subsequent conventional follow up concordant with stable disease. On review of the eight patients, there was a greater difference in pre- and post-treatment primary lesion SUV observed in patients who reached a CR on 11-C imaging (SUV 7.8) as compared to those who reached PR/SD on 11-C imaging (SUV 2.5).

Conclusions: To our knowledge, this is the only prospective pilot study investigating the use of 11-Choline PET/CT for response assessment in locally advanced esophageal cancer treated with neoadjuvant chemoradiation. Although no correlation between SUVmax and pathologic response could be established with such a small cohort, the overall findings support development of a larger trial to investigate the sensitivity, specificity, and positive and negative predictive values of 11C Choline PET/CT for neoadjuvant treatment assessment in esophageal cancer.


160 Inter-method Comparison and Optimization of [18F] FDG PET Metabolic Response Assessment in Non-Small Cell Lung Cancer

F. Kong2, J. Wang1,2, K. Wong2, M. Piert2, K. Frey2, 1Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, 2University of Michigan, Ann Arbor, MI

Purpose/Objectives: Based on 18F-fluorodeoxyglucose PET/CT in patients with NSCLC, this study aimed to: 1) compare qualitative and semi-quantitative assessment of categorical metabolic response; 2) evaluate the prognostic value of categorical metabolic response; 3) investigate the relationship between numerical post-treatment change of metabolic activity and overall survival (OS) and explore an optimal cutoff to distinguish better responders.

Materials/Methods: This is a secondary analysis of prospective studies. Enrolled patients with NSCLC underwent PET/CT imaging within 2 weeks prior to and following radiation treatment (RT). Metabolic therapeutic response was assessed using following methods; 1) visual assessment and 2) semi-quantitative assessment based on FDG uptake reduction using mediastinum blood pool (MBP) normalized maximum SUV (NSUV-A). Kappa coefficient was rendered to evaluate the agreement between various categorical variables. Survival analysis and Cox proportional hazard regression model were adopted to analyze the effect of various response criteria on overall survival (OS).

Results: Forty-four patients (36M: 8F, median age 70 ± 10) were eligible for present analysis. The median follow-up time was 25.2 months and the minimum follow-up interval for surviving patients was 13.5 months. The median interval between end of RT and post-RT PET/CT scan was 93 days. A poor agreement was observed between visual and semi-quantitative responses (Kappa coefficient = 0.393). Categorical responses were significantly correlated with OS independent of employed response assessment criteria (p < 0.001) and those with complete metabolic response (CMR) obtained the longest OS. As a continuous variable, reduction percentage of NSUV-A also showed pronounced association with OS (hazard ratio, HR=0.128, p < 0.001). Sixty percent of NSUV-A reduction was identified as the most discriminative cutoff to distinguish patients with even better OS from traditional PMR population (p < 0.001).

Conclusions: For NSCLC patients acquiring radical chemoradiotherapy, there was great discrepancy between visual and semi-quantitative assessment in metabolic response, most often in the CMR identification. Currently used categorical responses demonstrated significant association with OS and CMR group reached best outcome. The relationship between metabolic change and prognosis was gradual rather than having a fixed cutoff point. Sixty percent of SUV
reduction may be the optimal cutoff for the prediction of survival for the semi-quantitative evaluation of metabolic response.


161 Repeated Monitoring of Tumor Oxygen While Breathing Carbogen to Determine the Therapeutic Potential of Hyperoxic Therapy

H. M. Swartz, B. B. Williams, L. A. Jarvis, B. I. Zaki, D. J. Gladstone, The Geisel School of Medicine at Dartmouth, Hanover, NH

Purpose/Objectives: The level of oxygen in a tumor is one of the most important factors that affect the response to therapy. Patients vary in their baseline tumor PO$_2$ and the level of tumor oxygen changes with disease progression and with therapy in a complex and unpredictable manner. It therefore is not surprising that attempts to use hyperoxygenation to enhance therapy have had suboptimal results. Direct measurements are needed to follow it repeatedly. For this to be implementable, it needs to be able to be done under clinically applicable conditions. Then with such information available it should be feasible to enhance and individualize therapy by delivering single or multimode therapy at the times of most favorable oxygen levels in the tumor.

Materials/Methods: We have developed an approach, based on electron paramagnetic resonance (EPR) that now makes it feasible to make such measurements in the clinical setting under conditions compatible with clinical routines. These in vivo measurements are made using low frequency (1.2 GHz) EPR spectroscopy and surface loop resonators, which enable measurements to be made in vivo at superficial sites, providing direct, non-invasive (after placing the ink in the tissues), repeatable measurements of tissue PO$_2$. Ongoing EPR oximetry studies in human subjects include oximetry in tumors during courses of radiation and chemotherapy, where hypoxia can limit efficacy and measurement of subcutaneous PO$_2$ in the feet of healthy volunteers to develop procedures that could be used in the treatment of peripheral vascular disease. In each case, we aim to provide quantitative measurements which will aid physicians in the characterization of disease status and the effects of therapeutic measures, so that treatments can be applied with optimal effectiveness by taking into account the oxygen-dependent aspects of the therapy. The overall goal is to enhance clinical outcomes.

Results: Tumor oximetry measurements have been performed in tumor tissues of 12 patients during courses of radiation and chemotherapy. Tumor types include melanoma, basal cell, soft tissue sarcoma, and lymphoma, and measurement sites have ranged from the feet to the scalp. Very recent results and analyses indicate that using a simple clinically applicable approach with breathing carbogen, tumors can be characterized in regard to whether or not they respond to this hyperoxic treatment which does raise the PO$_2$ in the vascular system. Some tumors did not respond at all and some had only minimal changes while others had robust changes in tumor PO$_2$.

Conclusions: These results indicate that it should be feasible to more adequately determine the effectiveness of hyperoxic treatments and, therefore, both individualize therapy and develop more robust strategies for optimizing hyperoxic therapies.

162 Accuracy of 3 Month Posttherapy FDG PET/CT in Resected Oral Cavity Cancer Patients Who Received Adjuvant Radiation

M. Marquardt, C. M. Anderson, S. Steen, A. Hoover, L. Karnell, G. Funk, Y. Menda, M. Graham, J. Buatti, University of Iowa, Iowa City, IA

**Purpose/Objectives:** F-18 Fluorodeoxyglucose (FDG) PET/CT plays an increasingly important role in treatment response monitoring for head and neck squamous cancer patients, however investigation is lacking on the accuracy of this imaging modality when applied to patients treated with definitive surgery and adjuvant (chemo)radiotherapy. This work describes the 3 month post-therapy PET/CT accuracy in resected oral cavity patients.

**Materials/Methods:** A retrospective review examined oral cavity patients receiving a definitive surgical resection, adjuvant (chemo)radiotherapy, and 3 month post-therapy PET/CT at the University of Iowa Hospitals and Clinics between 2005 and 2012. Scans were considered positive or negative based on reports from the medical record. PET/CTs were ultimately found to be true or false based on clinical follow-up within one year of the scan.

**Results:** Forty oral cavity cancer patients with a median follow-up of 41 months met inclusion criteria. Seven (17.5%) received concurrent chemoradiotherapy adjuvantly; the remainder received radiation therapy alone. Seventeen patients (42.5%) had a positive PET/CT scan. Eleven (27.5%) patients had PET/CTs that were read as positive in the head and neck. Ultimately, there were 5 true positive locoregional recurrences (12.5% of cohort), one of which also had distant metastasis. In 6 patients with a negative head and neck (15% of entire cohort), PET/CT discovered metastatic disease (5 patients) or second primary (1 patient). Thus, PET/CT revealed 11 true recurrences (27.5%), 5 of whom were potentially curable (12.5% of cohort). For locoregional recurrence, PET/CT sensitivity, specificity, positive predictive value, and negative predictive values were 56%, 81%, 45%, and 86%, respectively. For distant recurrence, the respective values were 100%, 91.4%, 62.5%, and 100%.

**Conclusions:** A PET/CT 3 months after adjuvant (chemo)radiation in oral cavity patients reveals recurrence in 27.5% and potentially curable disease in 12.5%. False negatives and false positives remain problematic.

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163 The Value of Positron Emission Mammography (PEM) in Management of Breast Cancer

T. Khanna, H. El-Arousy, N. Thakur, R. Khanna, G. Arora, Radiological Institute of The Villages, The Villages, FL

**Purpose/Objectives:** To determine the value of few key parameters measured from 3D-PEM breast images in breast cancer management.

**Materials/Methods:** One hundred nine, pathology proven, female breast cancer patients with mean age of 66 ± 11 (ranging from 28 to 83) years underwent PEM imaging for surgical planning at our institute. Ten mCi of 18-flourodeoxyglucose (FDG) was administered intravenously. One hour post-injection, multiple tomographic sections of the right and left breast were obtained in medio-lateral, oblique and cranio-caudal (cc) positions. Retrospectively, lesion depth (using cc image), lesion size, lesion shape (ovoid, circular, irregular ovoid, irregular circular, ring-like, linear) and maximum standard uptake value (SUV_{max}) of FDG in lesion and normal fatty breast area was evaluated. The ratio of SUV_{max} of lesion to normal fatty breast area was computed. Whole body PET/CT FDG images were used for staging the breast cancer.
**Results:** Out of 109 patients 53.0% had left sided lesion and 47.0% were right sided. Seventy six percent of the patients had a single lesion and the remaining 24.0% had multiple lesions. The most common shape was found to be circular for 42.4% of the patients, 23.6% irregular circular, 21.2% irregular ovoid, 8.3% ovoid, 3.0% linear and 1.5% ring like. Less than 2.0% had a lesion depth of ≤ 0.7 cm. Remaining 98% had lesions at depths ranging from 0.9 cm to 10.8 cm with mean depth of 3.8 ± 1.9 cm. All patients with lesions ≥ 0.7 cm were candidates for treatment with single lumen balloon catheter using Xoft E-brachytherapy system for accelerated partial breast irradiation (APBI). Patients with lesion depths ≤ 0.7 cm were candidates for multi-lumen balloon catheter. The average value for maximum PEM SUV ($SUV_{max}$) in the lesion was 1.49 ± 1.09 (ranging from 0.46 to 7.48) and in normal fatty breast tissue was 0.25 ± 0.13 (ranging from 0.07 to 0.90). The mean ratio of $SUV_{max}$ of lesion to normal tissue was 6.35 ± 4.04 (ranging from 0.88 to 24.1). The number of metastatic lesions was determined from PET/CT images. Preliminary findings suggest a correlation of this ratio with staging of the breast cancer determined from whole body PET/CT scan of these patients.

**Conclusions:** PEM imaging may provide valuable parameters such as accurate lesion depth measurement which in turn helps decipher the selection of single vs multi-lumen catheter for APBI. In addition to this the ratio of $SUV_{max}$ may help predicting the stage and hence, prognosis and management of breast cancer.

**Author Disclosure Block:** T. Khanna: None. H. El-Arousy: None. N. Thakur: None. R. Khanna: None. G. Arora: None.

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**164 Detection of Axillary Lymph Node Metastases and Extra-Axillary Metastases With FDG PET/CT in Breast Cancer Patients Scheduled for Neoadjuvant Chemotherapy**

G. M. Jacobson, G. Marano, H. Hazard, J. Abraham, West Virginia University, Morgantown, WV

**Purpose/Objectives:** The purpose of this study is to assess the incidence of axillary and extra-axillary metastases identified by FDG PET/CT in patients scheduled for neoadjuvant chemotherapy, and how often this information could change post-operative radiation planning.

**Materials/Methods:** We performed a retrospective analysis of 38 patients with breast cancer scheduled for neoadjuvant chemotherapy between January 2011 and July 2012. 10 patients were clinical stage II, 26 clinical stage III, 2 clinical stage IV. All patients had a FDG PET/CT within 1 month of diagnosis. 28/32 patients had pathologic confirmation of ipsilateral axillary lymph nodes. We identified the incidence of positive axillary lymph nodes and extra axillary metastases, correlated this with stage, and identified how often this could change radiation planning.

**Results:** Axillary lymph nodes were positive in 32/38 patients (84.2%); 5/10 (50%) stage II, 25/26 (96.2%) stage III, 2/2 (100%) stage IV. 28/32 (87.5%) of patients with PET positive axillary lymph nodes had pathologic confirmation. 16/38 patients had extra-axillary metastases. These were identified in 14/26 stage III patients (53.8%) and 2/2 stage IV patients (100%). Sites of extra-axillary PET positive metastases were: subpectoral 11/38 (28.9%), internal mammary chain (IMC) 6/38 (15.8%), supraclavicular 2/38 (5.3%), subclavian 1/38 (2.6%), mediastinal lymph node 1/38 (2.6%), and pulmonary nodule 1/38 (2.6%). One patient with positive IMC nodes did not have positive axillary nodes. In all other cases (15/16) patients with extra-axillary metastases had axillary metastases. Metastases to subpectoral, IMC, supraclavicular, and subclavian lymph nodes could potentially require modification of post-operative radiation therapy fields. (Total 20/38, 52.6%)

**Conclusions:** FDG PET/CT detected positive axillary lymph nodes in 84.2% of breast cancer patients scheduled for neoadjuvant chemotherapy; in 50% of Stage II patients, 96.2% of stage III patients and 100% of Stage IV patients. Extra-axillary metastases were identified in 42.1% of patients, 53.8% of stage III patients and 100 % of stage IV patients. In 52.6 % of patients, non-axillary regional metastases were identified that could potentially change radiation treatment plans. In clinical stage III and limited stage IV disease, FDG/PET CT could contribute to modified radiation treatment
A Method to Determine the Optimal Number of Bins in 4D PET


Purpose/Objectives: The standard uptake value (SUV), gross tumor volume, and thus the stage of cancer in the thoracic region, are affected by respiratory or cardiac motion. The state of current technology allows tracking of spatial changes using different kinds of respiratory motion management systems in combination with list-mode acquisition. Intuitively, it may seem that the more bins over the respiration period, the more accurate the data. On the contrary, increasing the number of bins (gates) lowers the counting statistics in each bin consequently requiring longer scan times. Moreover, the more bins the longer the processing time; for example, a 10-bin reconstruction can be twice as long as a 6-bin reconstruction. Therefore, the choice of number of bins is important for both accuracy and efficiency. In this study we present a technique to determine the optimal number of bins.

Materials/Methods: Three sinusoidal motion patterns in 3D space were accomplished with peak-to-peak amplitudes of 1.0, 2.0 and 2.4 cm using a custom motion platform. The respiratory period was set to 4.8 s. In order to investigate target size dependency a Jaszczak Phantom™ containing six hollow spheres (0.95 - 3.18 cm inner diameters) was used. The background and the six spheres were filled with 18F-FDG solution to achieve two source-to-background ratios (SBR): 3:1 and 17:1. After the acquisition of 4D PET scans, the data were re-binned into 2, 4, 6, 8, 10, 11, 12 and 13 phased series based on the motion file from the Real-Time Position Management System (RPM, Varian Medical Systems, Inc.). Images were retrospectively reconstructed using the iterative algorithm. The corresponding 4D CT phase was used for attenuation correction for each PET phase. The targets were segmented based on a threshold of 45% of the maximum SUV. The displacement of the center of mass (DCM) between exhalation and inhalation (DEI) was plotted as a function of the number of bins in the reconstruction.

Results: The DEI was calculated for each simulated motion and SBR. The DEI increased with the number of gates until it reached a plateau corresponding to the actual value of DCM. For a 1.0 cm motion the DEI reached a plateau at 4 bins, for the 2.0 cm amplitude at 6 bins, and for 2.4 cm amplitude at 8 bins. The behavior of DEI remained the same for different SBR values and different target sizes.

Conclusions: The optimal number of bins is a function of the motion amplitude and the scanner resolution. This phantom study shows that the DEI consistently reaches plateau as the number of bins increases. Since increasing the number of bins in the plateau region does not add information about motion, our technique can be used to determine the optimal number of bins. We will apply this technique to human data.

166 Predicting Outcomes in Locally-Advanced Rectal Cancer Using Pretreatment FDG-PET Imaging


**Purpose/Objectives:** FDG-PET/CT imaging has been shown to have clinical utility in the management of rectal cancers. The purpose of this study was to investigate multiple FDG-PET/CT parameters to predict for outcome after neoadjuvant chemoradiation (CRT) in patients (pts) with locally advanced rectal adenocarcinoma.

**Materials/Methods:** We retrospectively evaluated pts with locally advanced (T2-4, N0-2, M0) rectal adenocarcinoma treated with neoadjuvant CRT who received FDG-PET/CT scans for radiation therapy planning. We evaluated the impact of SUVmax and metabolic tumor volume (MTV, determined by using PET Edge MimVista), as well as dual-time point PET parameters of retention index (RI, difference in SUVmax between the two PET scans) and RI/time. Endpoints of pathologic complete response (pCR), tumor grade, margin status and pathologic downstaging were assessed using t-tests, ANOVA or non-parametric analysis when appropriate. Progression-free survival (PFS) and overall survival (OS) were assessed with Kaplan Meier estimates.

**Results:** Of the 28 consecutive pts with FDG-PET/CT planning scans identified, 25 pts underwent surgical resection. All patients received a 5-FU based concurrent chemotherapy regimen with RT (median RT dose: 50.4 Gy). Median follow-up was 21 months. The median MTV was 45 cc. Compared to pts with a MTV>45 cc, pts with a MTV<45 cc had T4 tumors vs. 0% of pts with MTV<45, p=0.17). MTV did not correlate with the other endpoints (pCR, tumor grade, margin status, pathologic downstaging). SUVmax did not correlate with any of the identified endpoints. Of the patients with dual-time point PET/CT scans (N=19), RI and RI/time did not correlate with any of the identified endpoints.

**Conclusions:** Pretreatment MTV correlates with PFS and OS in patients with locally advanced rectal cancer treated with neoadjuvant chemoradiation. For pts with large MTVs, more aggressive treatment approaches should be considered. Dual-time point FDG-PET imaging does not appear to add clinical value in this patient population.


167 Understanding the Role of 18Flurodeoxyglucose PET in Predicting Improved Survival in Locally Advanced Pancreatic Cancer

A. S. Dholakia, J. P. Leal, A. T. Wild, A. Hacker-Prietz, M. Chaudhry, L. Diaz, R. L. Wahl, D. Laheru, C. L. Wolfgang, J. M. Herman, Johns Hopkins University School of Medicine, Baltimore, MD

**Purpose/Objectives:** Prior studies have demonstrated the prognostic value of pre- and post-treatment positron emission tomography (PET) parameters in other disease sites including lung and breast cancer. However, the role of PET in pancreatic cancer is still being established. This study aims to analyze the prognostic utility of PET for locally advanced pancreas cancer patients undergoing fractionated stereotactic body radiation therapy (SBRT).

**Materials/Methods:** This study includes patients treated on a phase II multi-center trial. After multidisciplinary review, 50 patients with locally advanced pancreatic ductal adenocarcinoma received gemcitabine (GEM) in sequence with SBRT (6.6 Gy in 5 consecutive daily fractions, 33 Gy total). All patients received a baseline PET-CT. Patients received a follow-up PET at the 3 months after SBRT. At the time of this abstract, 16 of these patients had scans available for analysis. Another 22 patients (N=38 total) have evaluable PET-CT scans that will be reviewed and presented at the meeting. Peak standardized uptake value (SUVpeak) on pre- and post-treatment PET-CT was calculated using an in-
High-SUVpeak and low-SUVpeak subgroups based on group median SUVpeak were generated. Patients were also divided into groups of short (< 16 months) or long (≥ 16 months) overall survival groups. SUVpeak groups were correlated with predictive value for survival groups.

Results: Of the 16 patients with pre- and post-treatment PET-CT scans analyzed, median overall survival (OS) was 17.3 months (95% CI 13.8-20.3). Median OS of long survival group was 22.3 months (95% CI 14.3-30.2) vs. 9.1 months (95% CI 2.3-16.0) for short survival group. Age and proportion of patients with Ca 19-9 > 90 U/mL were not statistically different between groups. Post-radiation SUVpeak groups showed greater predictive ability for survival groups than pre-radiation SUVpeak groups. Using the group median post-radiation SUVpeak of 2.44 as a cut-off, 6/9 low SUVpeak group patients were in the long survival group compared to only 2 patients with low SUVpeak who were not in this group. In our series, low post-radiation SUVpeak had a sensitivity of 75%, specificity of 78%, positive predictive value of 82% and negative predictive value of 78% to predict for an improved survival group.

Conclusions: Our results demonstrate the first report of utilizing SUVpeak criteria in pancreatic cancer treated with fractionated SBRT to predict for improved survival. Reliable clinical predictors for improved survival following radiation may identify patients who would be more likely to benefit from more aggressive chemotherapy following SBRT.

A Pilot Study of F18 EF5 PET/CT Imaging in Patients With Carcinoma of the Cervix

L. L. Lin, D. Pryma, C. Koch, S. Evans, University of Pennsylvania, Philadelphia, PA

Purpose/Objectives: The aim of this study was to assess pretreatment tumor hypoxia using Positron Emission Tomography/Computed Tomography (PET/CT) imaging of the hypoxia tracer 18F-EF5 in patients receiving definitive chemoradiotherapy for carcinoma of the cervix.

Materials/Methods: Eight patients with biopsy proven locally advanced cervical cancer referred for definitive radiotherapy at the University of Pennsylvania were included in this prospective study. Stage distribution was: IB2(3), IIB(2), IIIA(3); two had positive pelvic lymph nodes and 3 had positive para-aortic lymph nodes on pretreatment 18F-FDG PET/CT. All patients underwent pretreatment 18F-EF5 PET/CT imaging as well as clinical 18F-Fluorodeoxyglucose (FDG) PET/CT imaging. Static 18F-EF5 images were acquired 180 minutes after injection. 18F EF5 uptake was determined semi-quantitatively by calculating the tumor to muscle ratio (T/M).

Results: All patients completed their intended course of therapy. Median follow-up for all patients was 17 months (range 4.2-28 months). Four patients developed distant metastases; one patient developed local relapse 14 months post treatment, one patient had persistent FDG uptake on a 3 month post-treatment FDG-PET/CT and had confirmed pathologically persistent disease. The median tumor to muscle ratio was 1.35 (range 0.88-1.79). A T/M threshold of 1.35 was used as a cutoff threshold. 2/6 patients with T/M ratios above 1.35 had persistent disease/local relapse vs 0/2 patients with T/M ratios below 1.35. 4/6 patients with T/M ratios above 1.35 developed metastatic disease vs 1/2 patients with T/M ratios below 1.35 who developed metastatic disease.

Conclusions: PET imaging with 18F EF5 is feasible for patients with uterine cervical cancer. This is a small pilot study, and the utility of 18F EF5 and its predictive value need to be further investigated for this population.

Preliminary Evaluation of Dedicated PET/MRI in Gastrointestinal Malignancy: Qualitative and Quantitative Comparison to PET/CT

S. Partovi, S. Thomas, B. J. Traughber, R. Ellis, P. Faulhaber, University Hospitals Case Medical Center, Case Western Reserve University, Cleveland, OH

Purpose/Objectives: MRI and PET/CT are powerful imaging modalities that are frequently used for image guided radiation therapy planning. New dedicated PET/MRI systems leverage the superior soft-tissue contrast of MRI and functional data with the sensitivity and molecular information of PET. As a prerequisite for multimodality multiparametric treatment planning, we sought to compare both the qualitative and quantitative performance of PET/MRI to the gold-standard PET/CT in patients with gastrointestinal malignancies.

Materials/Methods: This prospective study was approved by the IRB. Ten patients (6 males, 4 females, mean age 63.7 ± 10.6 mean age) with gastrointestinal cancer (2 esophageal, 1 pancreatic, 4 colon, 2 rectal, and 1 anal) were referred for clinically indicated FDG PET/CT (Philips Gemini TF PET/CT, Philips Healthcare, Andover, MA). Immediately following PET/CT patients were scanned on a dedicated PET/MRI system without additional radiotracer administration (Philips
Ingenuity TF PET/MR, Philips Healthcare, Andover, MA). The number and anatomical location of lesions were identified independently on both examinations. The maximum and mean standard uptake values (SUVs) and the longest and shortest diameter according to RECIST (Response Evaluation Criteria In Solid Tumors) were determined in both modalities for each lesion. Pearson R correlation coefficients were determined for the primary tumor volume as well as secondary abdominal lesions between the CTAC and MRAC SUV values.

**Results:** All lesions were detected by both PET/CT and PET/MRI (gastrointestinal primary lesions n=7; other abdominal lesions n=5 with 3 liver metastases, 2 lymph nodes in iliac chains and portocaval; lung lesion n=1). Mean longest/shortest diameters were as follows: gastrointestinal primary lesions 3.8/2.4 cm for PET/MRI vs. 4.0/2.7 cm for PET/CT (p=0.79/p=0.64, no significant difference); in secondary abdominal lesions 2.3/1.7 cm for PET/MRI vs. 2.6/1.8 cm for PET/CT (p=0.98/p=0.77, no significant difference); the lung lesion 1.8/1.5 for PET/MRI vs. 1.5/1.4 cm for PET/CT. The SUVmax and SUVmean correlations between MRAC and CTAC for gastrointestinal primary lesions (R=0.95 and R=0.91) and secondary abdominal lesions (R=0.98 and R=0.87) were very high.

**Conclusions:** This pilot study provides preliminary evidence that dedicated PET/MRI provides comparable qualitative and quantitative performance as evaluated by lesion detection and SUV measurements compared to PET/CT. Future work will evaluate the clinical impact of multiparametric MRI/PET on delineating target volumes for radiation therapy planning.


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**171 A Pilot 11C-Choline PET/CT Imaging Study Investigating the Ability to Detect Occult Metastatic Osseous Disease in Newly Diagnosed High-Risk Prostate Adenocarcinoma**


**Purpose/Objectives:** Prostate cancer is the second most common cause of cancer death among US men. One hindrance to the development of effective therapies is insensitive and inaccurate staging studies. A significant portion of patients may be treated with curative intent when micrometastatic disease is present, but not detectable on current studies. Molecular imaging approaches including PET/CT have been investigated to improve the detection of metastatic disease in patients with prostate cancer. Given the high number of false positive and false negative results with 18F-FDG PET, there has been an interest in developing novel tracers, including 11C-Choline for earlier identification and greater visualization of metastatic disease.

**Materials/Methods:** Nine eligible patients with high-risk histologically confirmed adenocarcinoma of the prostate underwent standard initial workup including a history and physical examination, transrectal ultrasound guided biopsy, and PSA evaluation. As normal standard of care, patients underwent a CT scan and bone scan as part of their initial workup. In addition, they underwent an experimental 11-C Choline PET/CT scan to evaluate extent of disease and predict for occult metastatic disease. Pre-treatment Bone Scan and 11-C Choline PET/CT interpretations were compared with follow up imaging, laboratory values, and overall clinical assessments, to determining the predictive value of pre-treatment 11-C imaging with overall outcomes.

**Results:** Of the nine patients who underwent 11-C Choline PET with their initial imaging workup, three had radiographic evidence of osseous metastatic disease on both conventional CT and Bone Scans. Two of those three patients had corresponding clinical findings, with all three patients exhibiting baseline PSA levels >50. Of the three patients deemed
metastatic by conventional methods, only two of three corresponding 11-C Choline PET images were in agreement with conventional imaging findings. The final patient had a negative 11-C Choline study with identification of a T10 sclerotic focus on conventional imaging that was unchanged in follow-up scans, even in the presence of post-treatment biochemical failure. A fourth patient was deemed to be without evidence of osseous metastatic disease by conventional methods, with a positive 11-C Choline PET scan on initial workup. In follow-up, the patient was found to have diffuse osseous metastatic disease.

**Conclusions:** In this limited prospective case series, our imaging results suggest an increased sensitivity of 11-C Choline PET/CT in identifying active lytic lesions and true bony disease. These observations encourage further inquiry into the role for 11C Choline PET in initial evaluation of high risk prostate patients.

**Author Disclosure Block:** D.N. Ayala-Peacock: None. N. Onyeuku: None. A.J. Thomas: None. P. Garg: None. A.W. Blackstock: None.

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**172 FDG Uptake on PET/CT Can Assess Response to Chemoradiotherapy in Patients With Anal Cancer**


**Purpose/Objectives:** Anal canal carcinoma is an uncommon curable malignancy. Recent literature suggests that PET/CT may be useful in the management of anal cancer, though its routine use has not been validated by clinical practice guidelines. The NCCN guidelines recommend primarily DRE, anoscopy and inguinal node palpation for monitoring response to treatment. Our objective was to investigate whether PET/CT is useful in assessing response to chemoradiotherapy.

**Materials/Methods:** This prospective cohort study included 23 consecutive patients from 2009 to 2011 with a histopathologically confirmed anal canal carcinoma at the Cross Cancer Institute. All patients underwent curative-intent treatment consisting of 6 weeks of radiotherapy with 2 courses of 5-Fluorouracil chemotherapy. Patients had PET/CT scans at pre-treatment workup and 3 months post-treatment. All PET/CT scans were evaluated prospectively to record FDG uptake for each lesion, measured as the Standardized Uptake Value (SUV).

**Results:** Pre-treatment PET/CT detected a primary anal canal lesion in 21 of 23 patients, with an average SUV of 12.7 ± 1.3. A primary lesion was not detected in 2 patients due to previous surgical excision. Of the 21 patients with a primary anal canal lesion on pre-treatment scan, 3 month post-treatment PET/CT demonstrated markedly decreased SUVs compared to pre-treatment scans in 20 cases, consistent with response of primary tumor to chemoradiotherapy. Average SUV at 3 month PET/CT for primary lesions was 3.0 ± 0.3, which was significantly lower (p<0.00001) than average SUV at pre-treatment scan with a percent decrease of 71.4% ± 5.3%. In 1 patient, there was minimal change in FDG uptake compared to initial PET/CT as a remnant tumor focus was still present, demonstrating poorer response to treatment. Pre-treatment PET/CT detected pathologic lymph nodes in 10 of 23 patients, with an average SUV of 7.0 ± 1.1. Three month post-treatment PET/CT showed markedly decreased lymph node FDG uptake measured by SUV on all 10 patients with enlarged lymph nodes on pre-treatment PET/CT, consistent with response of enlarged lymph nodes to treatment. Average SUV on PET/CT was 2.0 ± 0.5 at 3 months for lymph nodes that were previously enlarged at initial screening, which was significantly lower (p<0.0005) than the average SUV of these lymph nodes at pre-treatment scan.

**Conclusions:** Follow-up PET/CT at 3 months post-treatment shows significantly decreased FDG uptake of the primary anal canal lesion and pathologic lymph nodes compared to pre-treatment values. Our results show that metabolic FDG uptake on PET/CT can be used to assess response to chemoradiotherapy in patients with anal canal carcinoma.
173  4D PET/CT: Radiology Imaging to Radiation Therapy


Purpose/Objectives: To integrate clinical 3D and 4D PET/CT and radiation treatment planning.
Materials/Methods: In 2009 two 4D PET/CT protocols were standardized for use by Radiation Therapy based on a trial population of 116 4D PET/CT studies. Protocol A acquires the 3D and the 4D PET/CT in the same scan, extending the imaging time of the bed positions over the region of interest. This ROI is post processed separately after the scan is ended. Protocol B uses separate acquisitions for the 3D and the 4D PET/CT. Both scans result in two reconstructions, one for gated data, and one for standard data. Variables such as dose amount (10-15mCi FDG), acquisition times (3-15 minutes per bed), and reconstruction parameters (matrices, filters, bins to phase attenuation, subsets and iterations) have been tested. A committee composed of radiation oncologists, radiologists, physicists and PET technologists meets regularly to review data and technical issues.

Results: Over 140 RT patients have been scanned using these 4D PET/CT protocols as of August 1, 2012. Protocol A is best suited for patients who are able to keep their arms overhead for approximately 45 minutes. Many patients have difficulty holding still during this lengthy acquisition. Protocol B results in better patient compliance but requires an extra 25 minutes of scan time for the additional exam. Quantification by imaging physicists may identify reconstruction parameters which can optimize results, and should be carefully considered when structuring the final protocol. Using our standard 3D PET/CT matrices, iterations and subsets for initial reconstruction of the gated 4D PET/CT yielded good visual quality, lowering the FWHM (Gaussian) filter slightly to give a better edge of definition to the ROI by decreasing the smoothing effect on the images prior to binning. Our 3D PET/CT FDG dose is 10mCi, with uptake time of 90 minutes and 2-3 minutes scan time per bed; our 4D PET/CT FDG dose is 13-15mCi for best visualization of 8-10 bins, with uptake time of 60 minutes and 10 minutes per bed. We are currently studying tumor motion as relates to the optimal number of PET and CT bins for XRT use.

Conclusions: Our protocols have been successful but challenges remain. Physical characteristics of the patient, varying levels of technologist skill and knowledge of the mechanics of the hardware/software may affect the outcome of the 4D scan. New techniques are in progress that may decrease acquisition and reconstruction times, these will need to be implemented clinically in a manner similar to what has been described. A multidisciplinary team approach is necessary for a thorough understanding and execution of the process, from patient prep through scan acquisition and therapy planning to radiation treatment.


174  Voxelized Dose--FDG-PET Response in HDR Brachytherapy of Rectal Cancer

Purpose/Objectives: Dose-response studies in radiation therapy are typically using single response values for tumors across ensembles of tumors. Using the high dose rate (HDR) treatment plan dose grid and pre- and post-therapy FDG-PET images, we look for correlations between voxelized dose and FDG uptake response in individual tumors.

Materials/Methods: Five patients were treated for localized rectal cancer using 192Ir HDR brachytherapy in conjunction with surgery. FDG-PET images were acquired before HDR therapy and 6-8 weeks after treatment (prior to surgery). Treatment planning was done on a commercial workstation and the dose grid was calculated. The two PETs and the treatment dose grid were registered to each other. The difference in PET SUV values before and after HDR was plotted versus absorbed radiation dose for each voxel. The voxels were then separated into bins for every 400 cGy of absorbed dose and the bin average values plotted similarly.

Results: Four of the five patients showed a significant positive correlation ($R^2 = 0.18$, 0.70, 0.81, 0.82 and 0.89, respectively) between PET uptake difference in the targeted region and the absorbed dose for the binned voxels.

Conclusions: By considering larger ensembles of voxels, such as organ average absorbed dose or the dose bins considered here, valuable information may be obtained. The dose-response correlations as measured by FDG-PET difference potentially underlines the importance of FDG-PET as a measure of response, as well as the value of voxelized information.


175 Feasibility Study of 4D Perfusion CT for Hepatocellular Carcinoma Patients Treated With Radiation and Sorafenib

C. Coolens, B. Driscoll, L. Dawson, Princess Margaret Hospital, Toronto, ON, Canada

Purpose/Objectives: Quantitative functional imaging methods measuring vascular change have become an important component in optimizing the timing of anti-angiogenic therapies and radiation therapy. Dynamic contrast-enhanced (DCE) CT, with high resolution and clinical convenience, is a key potential method in this regard. Clinical Trials in Hepatocellular carcinoma (HCC) patients treated with Radiation and Sorafenib are ongoing. Recently, a novel Functional Analysis method for DCE (FADE) Imaging was developed based on 4D DCE data acquired with a 320-slice CT scanner. This technology provides advantages over conventional DCE CT methods, allowing simultaneous fast dynamic scanning of arterial input and tissues of interest. This work aims to assess the feasibility of 4D FADE CT in providing 3D perfusion parameter maps in a group of HCC patients and assess its sensitivity in evaluating changes in liver and tumor perfusion as a response to treatment.

Materials/Methods: Three patients with HCC, treated with stereotactic body radiation (SBRT) and Sorafenib, underwent 4D DCE CT on a 320-slice CT as part of a REB approved protocol that allowed perfusion imaging at 5 different times during and following treatment. Sorafenib was delivered for one week prior to SBRT, then during and for 4 weeks after at study dose, then escalation up to standard of care dose. SBRT dose of 54Gy in 6 fractions was given over 2 weeks. Deformable registration was used to reduce residual liver motion during DCE CT. 4D FADE was performed on primary liver GTV and normal liver. Metrics of interest were perfusion parameters Ktrans, Kep & Vb as calculated with a modified Tofts model; Time to Onset, Slope and Area under the curve (AUC). Histogram analysis and 3D visualization were performed to attempt to observe temporal changes over the course of treatment.

Results: 3D perfusion results were obtained for all scans. One patient interrupted treatment for non-medical reasons. In the GTV, a reduction Ktrans and AUC was seen over the course of treatment and as early as after 1 week of Sorafenib. A marked reduction in normal liver perfusion was also seen throughout the course of treatment both in
Ktrans and AUC values. This was observed for all dose levels between baseline and 3m follow-up (p=0.0021 for 50Gy). The perfusion reduction was strongly dependent on dose exposure (p=0.0012).

**Conclusions:** The proposed methodology has demonstrated its feasibility in creating 3D volumes of functional vasculature and perfused tissue in the liver. This is an important milestone towards achieving a volumetric, quantitative functional imaging method.

**Author Disclosure Block:** C. Coolens: None. B. Driscoll: None. L. Dawson: None.

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**176 A Translational Feline Model of Oral Squamous Cell Carcinoma for Evaluating Tumor Volume Delineation With PET/CT**

E. Randall, H. Yoshikawa, S. Kraft, S. LaRue, *Colorado State University, Fort Collins, CO*

**Purpose/Objectives:** Oral squamous cell carcinoma (SCC) is a locally invasive naturally occurring tumor in cats that responds poorly to radiation therapy. Most cats succumb to failure from local recurrence within 6 months. Feline SCC has comparable histological characteristics, higher pretreatment epidermal growth factor (EGFR) and microvascular density (MDV) values that are associated with a worsened prognosis, similar to human oral SCC. Unlike rodent models, spontaneous tumors in cats are heterogeneous and often hypoxic. The tumors are large enough to obtain adequate biopsy material, and the cats can be imaged and treated with the same modalities as cancer patients. Positron emission tomography-computed tomography (PET/CT) with $^{18}$F-fluoro-2-deoxy-D-glucose detects areas with higher glucose metabolism. The goal of the current study was to evaluate the role of $^{18}$F-FDG PET for feline radiation therapy patients with oral SCC, as a model of tumor delineation for human disease.

**Materials/Methods:** Twelve cats with oral SCC underwent pre-treatment $^{18}$F-FDG PET/CT with a Philips Gemini TF PET/CT Big Bore instrument. Two different gross tumor volumes (GTV), based solely on either contrast-enhanced CT or $^{18}$F-FDG PET were created and compared (GTV$_{CT}$ and GTV$_{PET}$, respectively). To evaluate the degree of overlap between these two GTVs, “mismatch fractions” were calculated.

**Results:** All tumors were FDG avid and conspicuous, with an average maximal standard uptake value of 9.88 +/- 5.33 SD. Lymphoidal metastases were normal on CT but intensely hypermetabolic on FDG-PET images. FDG-PET provided unique and therapeutically relevant supplemental information to CT for evaluating feline oral SCC. GTV$_{PET}$ was significantly smaller than GTV$_{CT}$ in the mandibular/maxillary SCC group (n=8, P=0.006) as well as in total (n=12, P=0.017), but not in the lingual/laryngeal group (n=4, P=0.71). Mismatch fraction analysis revealed that most of the lingual/laryngeal patients had a large area of $^{18}$F-FDG avid region outside of GTV$_{CT}$. Their soft tissue infiltrate was highly visible on PET images but only subtle on CT images. The mismatch fraction was significantly less in the mandibular/maxillary group (P=0.028) although some patients in the latter group also had a large $^{18}$F-FDG avid region outside the GTV$_{CT}$. $^{18}$F-FDG PET enabled detection of more potential primary tumor both in the lingual/laryngeal and mandibular/maxillary cases.

**Conclusions:** Feline oral SCC are naturally occurring tumors sharing many features of human oral SCC including morphology, biomarkers, tumor microenvironment and FDG-PET/CT characteristics. This model represents a valuable preclinical translational model that could be used to evaluate new methods for imaging and modulating tumor hypoxia and other malignant features.

**Author Disclosure Block:** E. Randall: None. H. Yoshikawa: None. S. Kraft: None. S. LaRue: None.
177  **Positron Emission Tomography Texture Analysis of Necrosis in Primary Adenocarcinomas of the Lung**  

J. A. Oliver¹,², M. Budzevich¹, G. Zhang¹,², E. G. Moros¹,², K. Latifi¹, C. Kuykendall¹, S. Hoffe¹, J. Montilla-Soler¹, E. Eikman¹, T. Dilling¹, ¹Moffitt Cancer Center, Tampa, FL, ²University of South Florida, Tampa, FL  

**Purpose/Objectives**: To determine if the spatial and statistical properties of Positron Emission Tomography (PET) image texture would differ between lung tumors with a necrotic core and non-necrotic tumors.  

**Materials/Methods**: We selected eight lung cancer patients with adenocarcinoma ages 48 to 81. Four of the patients had necrotic tumors and four had non-necrotic tumors. Mirada Medical software was used to view and select the tumor slices that would be analyzed. We used Mathematica 8.0 as programming framework to perform texture analysis on pre-selected slices. Prior to the texture analysis, the original pixel intensity data in medical format (DICOM) was converted to a two-dimensional array. These array values were then converted to Standardized Uptake Values (SUV). Regions of interest (ROIs) were selected and plotted. The square ROI encompassed the tumor region and a normal tissue margin for contrast. After the image data was in the proper format we applied algorithms to the two-dimensional SUV data (slice by slice) to extract run-length, SUV mean, SUV maximum, SUV minimum, intensity histograms, skewness, kurtosis, variance, standard deviation, co-occurrence matrices, energy, contrast, and local homogeneity. In addition, we computed the gradient of the image (SUV) data and extracted the texture features of the gradient image data.  

**Results**: Parameters of local homogeneity, skewness, kurtosis, SUV maximum, SUV minimum, and run length provided inconclusive results. We have observed that the SUV mean value versus slice number curves, particularly for the gradient processed images, are Gaussian shaped for non-necrotic tumors whereas for necrotic tumors are flatter and even bimodal.  

**Conclusions**: The SUV mean gradient versus slice number curves may provide sufficient information to distinguish between necrotic and non-necrotic tumors automatically. All other texture parameters were non-conclusive for the small number of cases considered here. We will continue to add more patients (tumors) to the database.  


178  **Remove Impurities in 18F-FDG PET Uptake Distributions for Use in Dose Painting in NSCLC Tumors**  

K. Wijesooriya¹, C. B. Griffin¹, T. Pan², A. Goode¹, P. Judy¹, P. W. Read¹, J. M. Larner¹, ¹University of Virginia, Charlottesville, VA, ²MDACC, Houston, TX  

**Purpose/Objectives**: Lung cancer is one of the most frequent lethal cancers, with a 5 year survival rate of 20%. However, higher radiation doses (120 Gy) yield a higher local control rate (90%). Molecular imaging studies reveal tumor heterogeneity which may explain therapeutic resistance. Hence the use of ¹⁸F FDG to dose paint lung tumors is a viable strategy. We hypothesize that a functional fit to SUV uptake distribution represents intrinsic heterogeneity of the tumor and this function could be used for dose painting. However, variations observed in SUV uptake may not be entirely due to intrinsic heterogeneity of tumor, but due to effects of PET position resolution (volume dependence) or tumor motion. The objective of this study is to derive a functional form of SUV uptake by eliminating resolution and motion effects.
Materials/Methods: We conducted a patient and a phantom study: I. Patient study: 25 peripheral NSCLC tumors with motion amplitudes less than 5mm, and tumor volumes of 5cc to 550cc. PET SUV uptake values for each tumor were fit with a Woods-Saxon model with 2 parameters: radius and skin depth. When ratio of radius to skin depth becomes small, this simplifies to a Gaussian. II. Phantom study: spheres of homogeneous 18F-FDG activity of motion amplitudes (0, 5, 10, 15, 20, 25, 30 mm) and volumes (internal diameter 10, 13, 17, 22, 28, 37 mm). Any variation observed in SUV uptake distribution with homogeneous activity spheres must be due to motion and volume effects. Therefore, we used this data to quantify uptake variations as a function of motion and volume.

Results: The patient study shows that for small tumors up to about 45cc, SUV uptakes can be described by a Gaussian distribution in all three dimensions, peaking at center and dropping as distance from center increases. For Intermediate tumor volumes (50 cc to 200 cc) SUV uptakes show a flat central region surrounded by a skin region over which activity drops. For large tumors, (> 200 cc) SUV uptakes are low in the center of the tumor and higher in the surrounding shell before dropping at the edge. Phantom study for stationary spheres shows that for volumes larger than 5 cc, uptake distribution is flat across much of the sphere, with only a thin skin. This flat uptake behavior does not change with motion up to amplitudes of 10 mm. We have also developed a matrix of correction factors to the flat behavior for motion amplitudes and tumor volumes beyond these limits.

Conclusions: Our data demonstrate true heterogeneity of NSCLC tumors can be modeled by SUV uptake which takes a Gaussian, Woods-Saxon or double-peaked functional form depending on tumor volume. The model we developed defines the “true” SUV distribution within tumor free of artifacts due to motion, and tumor volume and will therefore allow PET and potentially other metabolic studies to be optimally integrated into treatment plans.


Mapping Patterns of Nodal Metastases in Seminoma: Rethinking Radiotherapy Fields

J. J. Paly1, J. A. Efstathiou1, S. S. Hedgire1, P. W. M. Chung2, M. O’Malley2, A. Shah3, J. E. Bekelman3, M. Harisinghani4, A. L. Zietman1, C. Beard4, 1Massachusetts General Hospital, Boston, MA, 2Princess Margaret Hospital and University of Toronto, Toronto, ON, Canada, 3University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, 4Dana-Farber Cancer Institute/Brigham and Women’s Hospital, Boston, MA

Purpose/Objectives: Historically, radiation therapy for testicular seminoma has targeted the retroperitoneal and pelvic lymph nodes via standard anterior-posterior/posterior-anterior fields based upon skeletal anatomy. The purpose of our study was two-fold: to map the anatomic locations of radiographically positive lymph nodes in clinical stage (CS) IIA/B and recurrent CS I patients; and to determine the relationship of these nodal locations to vascular, as well as bony, anatomy and to the borders of conventional radiation fields in order to ascertain whether smaller radiation fields are feasible.

Materials/Methods: Ninety patients from four academic centers diagnosed between 1996 and 2011 with CS IIA/B or recurrent CS I seminoma after orchiectomy were included. Their staging scans (CT, MRI), prior to any adjuvant therapy, were reviewed by a single radiologist. 53% of patients had left-sided primaries, 46% right-sided, and 1% bilateral disease. The position of each node was recorded and then transferred to a standardized CT template scan based upon its relation to arterial vasculature. Para-aortic fields were overlaid on the template, extending from T10/T11 to L5/S1 and bounded laterally by the contralateral transverse processes and ipsilateral renal hilum. Extended fields included ipsilateral iliac lymph node chains. The location of involved nodes within these conventional fields was assessed.

Results: 145 nodes were identified as radiographically positive. 84% of all nodes were located in the PA region, 9% in
the common iliac nodal chain, and 7% in the pelvic region. 99% of nodes in this study were contained within a 2.5 cm lateral and posterior expansion excluding overlapping vertebral bodies, and a 2.1 cm anterior expansion of the arterial vasculature. No positive nodes were identified within the renal hilar region or superior to L1 for patients with left-sided seminomas. For right-sided seminomas, no positive nodes were superior to L2, though there was one renal hilar node. 4% of all nodes fell outside a modified treatment field which utilizes the aforementioned expansions and inferior border at the cranial rim of the acetabulum.

**Conclusions:** Nodal metastases from our contemporary cohort localized to a smaller area than is targeted using conventional fields. Notably, no positive nodes were identified superior to L1. Modified treatment fields based on vascular rather than bony anatomy may allow for a significant decrease in normal tissue irradiation and its associated toxicities. Validation of these results may inform guidelines for a redefined clinical target volume and allow for more targeted radiation delivery in the treatment of seminoma.


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180  See Oral Presentation #4

181  **Delineation and Visualization of Prostate Cancer in Multiparametric MRI**

R. Stoyanova, K. Sandler, A. Pollack, *University of Miami, Miami, FL*

**Purpose/Objectives:** The precise delineation of a tumor mass from its surrounding normal tissues would allow the delivery of a boost-dose of radiation for complete eradication of tumor cells. Dynamic Contrast-Enhanced MRI (DCE-MRI) and Diffusion Weighted Imaging (DWI) can significantly improve cancer detection by highlighting the areas with focal changes in diffusion and/or increased microvascularity. The objective is to develop a reliable platform for delineation of prostate cancer and translation of the functional imaging findings into standard RT planning.

**Materials/Methods:** We have developed an integrated platform in Interactive Data Language (IDL, Boulder, CO)/Java for handling large amounts of imaging data from acquisition to analysis, and visualization of tumor. An unsupervised pattern recognition technique identifies tumor regions, based on the characteristic for the tumor contrast temporal pattern: rapid uptake and continuous washout of the contrast. The DCE and low ADC maps are color-coded in red and green and the resultant overlap is depicted in yellow and overlaid with the T2 weighted MRI.

**Results:** We analyzed multiparametric MRI scans from 65 primarily planned and treated patients, acquired between November, 2008 and July, 2011. Patient age was mean ± SD: 66.3 ± 6.9 yr, median = 67 yr, range 46 – 81 years. Patients with Gleason score 6, 7, 8 and 9 represented 27%, 48%, 17% and 8% of the total. PSA measurements before treatment or at the time of consult were: 9.99 ± 12.08, median = 6.24, range 1.9 – 70 ng/mL. We identified tumor lesions in 54 (83%) of the analyzed patients. The tumor volumes were from 0.3 to 11.7 cc; mean ± stdev: 2.9 ± 2.7; median = 1.85 cc. The prostate volumes were: 40.1 ± 20.9 cc; median = 34.7; range: 14 to 111.17 cc. Tumors were detected in PZ, TZ or both in 34 (63%), 11 (20%) and 9 (17%) patients, respectively. The tumors in PZ were bilateral in 12 patients. We selected pixels in normal peripheral (PZ) and transition zone (TZ), and also within the tumor. We used Toft’s pharmacokinetic model to average DCE curves from these regions. There was no statistical difference between the perfusion and ADC values of tumors in PZ and TZ. All functional parameters for healthy appearing PZ were statistically different compared to the tumor based on Student’s T-test (p < 0.05). $K_{trans}$ and ADC were statistically different between TZ and
tumors.

**Conclusions:** Our analyses indicate that we can detect and visualize the area of tumor burden. The constructed 3D maps can be directly imported into DICOM-RT ready format to the RT planning system for targeting of the tumor areas specifically in order to improve tumor control and limit toxicity. Including ADC in addition to the DCE-MRI enhances the ability to differentiate malignant from benign tissue, especially in the transition zone of the prostate.

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**182 Computerized Tomography-based Simulation and 3-Dimensional Radiotherapy Planning Improves Heterotopic Ossification Outcomes**

W. F. Mourad¹,², R. A. Shourbaji¹, M. A. Khan³, S. Vijayakumar¹, S. Packianathan¹, ¹Department of Radiation Oncology, University of Mississippi Medical Center, Jackson, MS, ²Department of Radiation Oncology, Albert Einstein College of Medicine of Yeshiva University, Bronx, NY., Bronx, NY, ³Department of Radiology, University of Mississippi Medical Center, Jackson, MS

**Purpose/Objectives:** To report the impact of computerized tomography (CT) based simulation and treatment planning on heterotopic ossification (HO) outcomes among patients who underwent radiotherapy (RT) prophylaxis.

**Materials/Methods:** This is a single institution retrospective study of medical records and radiographs of 532 patients’ status post traumatic acetabular fractures (TAF). All patients underwent open-reduction internal-fixation (ORIF) of the TAF followed by RT ± Indomethacin for prophylaxis of HO. Postoperative RT was delivered within 72 hours in a single fraction of 700 cGy prescribed to mid-plane using 6-18 MV photons. Fields included the soft tissues around the proximal femur & acetabulum without bone shielding. The patients were classified into two groups based on their simulation and treatment modality: CT based simulation (Group A) vs. clinical (LINAC) based simulation and treatment after review of portal images (Group B). CT simulation was used as a surrogate measure to assess HO outcome.

**Results:** Between January 2004 and January 2009, 532 patients underwent follow up at well documented time intervals. After a median follow up of 8, 3, and 8 years for the whole cohort, group A, and group B respectively the incidence of HO in all patients was 21.6% (115/532). Multivariate regression analysis, after adjusting for all variables, revealed that the (6/90) patients in Group (A) had 6.6 % HO, whereas the (109/442) patients in Group (B) had 24.6% HO (p<0.001). In addition, Group (A) (2) patients had a 2.2% rate of developing Brooker grades (≥3) while Group (B) (48) patients had a 10.8% rate of Brooker grades (≥3) (P= 0.007). The odds of developing HO & Brooker grades 3 & 4 are 4.7 & 4.5 times higher, respectively, in patients who underwent LINAC-based treatment.

**Conclusions:** Our data show higher risk of HO amongst patients who underwent clinical simulation compared to the patients who underwent CT-based treatment planning. Using CT-based treatment planning allowed more accurate delineation of the tissues and better 3 dimensional RT delivery. Although CT-based RT is associated with slight additional costs and increase in radiation exposure, the efficacy of CT-based treatment planning reduces the risk of HO, consequently decreasing the need for additional surgical interventions and decreases the overall medical care cost.

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MR Susceptibility-Weighted Imaging (SWI) Complements Conventional Contrast Enhanced Imaging for Melanoma Gamma Knife Radiosurgery Planning

J. V. Kuo¹, J. Huang², M. E. Linskey¹, ¹University of California Irvine, Orange, CA, ²Hoag Memorial Hospital Presbyterian, Newport Beach, CA

Purpose/Objectives: Detection of brain metastases from melanoma benefits from the sensitivity of susceptibility weighted imaging (SWI) to deoxyhemoglobin and melanin-related paramagnetic tissue effects. In some cases, SWI can clarify lesions difficult to diagnose primarily on MPRAGE due to hemorrhage and disruption. Though its imperfect spatial fidelity makes SWI alone unsuitable for radiosurgery planning, its extreme sensitivity to blood products suggests its utility as a qualitative aid for screening pts at the time of radiosurgery planning for metastatic lesions.

Materials/Methods: 8 pts with melanoma metastatic to the brain undergoing Gamma Knife radiosurgery underwent target imaging on a 3T MRI scanner. Axial SWI and double-dose, contrast-enhanced MPRAGE 3D data sets were obtained with the stereotactic localizer and coordinate frame. Both data sets were imported into Gamma Plan Version 9 and co-registered. Lesions on both imaging data sets were analyzed primarily using the SWI to screen for lesions that could be confirmed on MPRAGE images. The radiosurgery plan was based solely on the MPRAGE sequences. The volumes and visibility of each MPRAGE lesion were compared to their SWI counterparts.

Results: 11 procedures in 8 pts treated between 11/2011 and 8/2012 form this report. For each procedure, the mean number of lesions visualized on MPRAGE was 6.9 (1-28) and on SWI was 4.7 (1-21). Of the 76 total lesions identified by MPRAGE, SWI visualized 52 (68%) but failed to visualize 24 (32%) of the lesions. The SWI-identified lesions were more visible in 32 of 76 (42%) lesions. For 25 lesions, the greater visibility on SWI compared to MPRAGE was due to their larger imaging footprint (mean 223% larger by volume) but 7 lesions were more visible even though smaller on SWI due to the eye-catching contrast between the lesion and the surrounding brain parenchyma.

Conclusions: SWI sequences will identify a significant proportion of lesions also seen on conventional radiosurgery planning scans. Moreover, many (42%) of lesions are more visible on SWI than on the conventional planning sequences largely due to the lesions’ larger imaging footprint but also their increased visibility on SWI. While SWI sequences alone are insufficient for radiosurgery planning, they can be a useful and complementary adjunct to conventional planning scans for pts with metastatic melanoma.

Author Disclosure Block: J.V. Kuo: None. J. Huang: None. M.E. Linskey: None.

Seminal Vesicle Target Delineation for Intermediate-Risk Prostate Cancer IMRT

M. E. Johnson, K. Ruth, M. K. Buuyounouski, E. M. Horwitz, Fox Chase Cancer Center, Philadelphia, PA

Purpose/Objectives: The radiation target defined for IMRT for intermediate risk prostate cancer (IRPC) includes both the prostate and seminal vesicles (SV). The amount of SV included has considerable variation. Common prescriptions are 80Gy to prostate and proximal seminal vesicles (PSV), with or without 56Gy to the distal seminal vesicles (DSV). PSV is defined as the most caudal 1cm of SV. We report the association between inclusion or exclusion of the SV and their relationship to toxicity and clinical outcomes for men treated at Fox Chase Cancer Center (FCCC) with IMRT from 2001 to 2008.

Materials/Methods: 448 patients treated for IRPC at FCCC were identified through query of our clinical database. 159 were treated to both PSV and DSV. Clinical and outcome characteristics were obtained from chart review. Statistical analysis was performed utilizing log rank test and a Cox proportional hazards model. Endpoints of freedom from
biochemical failure (FFBF), overall survival (OS), and toxicity from the time of consultation were investigated.

**Results:** The study cohort had a median age of 69 years, 83% were Caucasian. AJCC T stage at presentation was as follows: <T1b (1%), T1c (68%), T2a (16%), T2b (12%), and T2c (4%). All patients underwent both CT and MRI simulation and had daily image guidance.

For the cohort, 159 patients were treated to both PSV and DSV. They were more likely to have a Gleason score 7 (p<0.0001), and were more likely to have PSA <10 (p=0.0001). There was no significant difference between the groups in regard to T stage, smoking history, or race. Mean treated SV volume was 10.3 cm³ in the PSV+DSV group and 7.5 cm³ in the PSV group, with a mean volume difference of 2.8 cm³ (p<0.0001). Median volume difference was 2.55 cm³ (p<0.0001). Total treated target volume mean was 65.9 cm³ for the DSV group, and 63.6 cm³ for the PSV group (p=0.42). Median follow-up was 48.3 months.

There were no significant differences for acute or late GI or GU toxicity, grade 2 or higher. For the PSV and DSV groups, overall incidence of acute GI toxicity was 3.5% vs. 5% (p=0.457), GU toxicity was 20.6% vs. 27% (p=0.127) respectively. Incidence of late GI toxicity by 60 months was 6.1% vs. 5.3% (p=0.98), GU toxicity at 60 months was 11.7% vs. 11.3% (p=0.47) respectively. FFBF at 60 months was 85.9% for the PSV group vs. 85.3% for the DSV group (p=0.62).

**Conclusion:** Optimal target delineation of the SV for IMRT in IRPC has not been well defined. These data suggest that the addition of 56Gy to the DSV does not result in additional acute or late toxicity when compared to the prescription of 80Gy to prostate and PSV as long as all dose constraints are met. Additionally, this series shows no detriment to treating prostate and PSV alone. Both approaches are reasonable target delineation when using IMRT for the treatment of IRPC.

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185 A Comparison of Planning Target Volume Definition by the Patient-Specific Margins and the Generic Margins for Thoracic Esophageal Cancer

W. Wang, J. Li, Y. Zhang, J. Xing, H. Qi, Shandong Cancer Hospital, Jinan, China

**Purpose/Objectives:** To compare the centroid position and volumetric differences of planning target volume (PTV) definition by 3DCT and 4DCT, the addition of the patient-specific margins, or the generic margins for the thoracic primary esophageal cancer.

**Materials/Methods:** Forty-three patients with esophageal cancer underwent 3DCT and 4DCT simulation scans during free breathing. The motion of primary tumors located in the proximal (group A), mid-(group B), and distal(group C) thoracic esophagus were obtained from the 4DCT scans. PTV3D was defined on 3DCT using the tumor motion measured based on 4DCT; PTVconv was defined on 3DCT using a 1.0 cm margin to CTV; PTV4D was defined as the union of the target volume contoured on the 10 phases of 4DCT images.

**Results:** The median centroid shifts between PTV3D and PTV4D, PTVconv and PTV4D in the 3D directions were all less than 0.3 cm for the three groups. The median size ratio of PTV4D to PTV3D was 0.80,0.88,0.71 for group A, B and C, and for PTV4D to PTVconv was 0.67,0.73,0.76 respectively (χ²=3.18,-2.98,-3.06,P=0.001,0.003,0.002). The median dice similarity coefficient (DSC) were 0.87,0.90,0.81 between PTV4D and PTV3D, with 0.80,0.84,0.83 between the PTV4D and PTVconv(χ²=3.18,-2.98,-3.06,P=0.001,0.003,0.002). The difference between degree of inclusion of PTV4D in PTV3D and PTV4D in PTVconv was all less than 2%. Compared with PTVconv, PTV3D decreased 11.81% and 11.86% of irradiated normal tissue in group A and B respectively, but increased 2.93% for group C.

**Conclusions:** For proximal and mid- esophageal cancer, 3DCT-based PTV using asymmetrical margins provides a good
coverage of PTV4D, meanwhile for distal esophageal cancer, 3DCT-based PTV using conventional margins provides an ideal conformity with PTV4D.

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186 The Pattern of Lymphatic Metastasis and Influencing Factors of Thoracic Esophageal Squamous Cell Carcinoma

H. Ge, C. Liu, R. Qiu, Y. Lu, K. Ye, C. Yang, X. Liu, X. Zheng, C. Zhai, Cancer Hospital of Henan Province, Zhengzhou, China

Purpose/Objectives: To investigate the frequency, distribution, and feature of lymph node metastasis in thoracic esophageal squamous cell carcinoma, and to provide evidence for surgeon and radiation oncologists to treat this disease.

Materials/Methods: The clinical data of 2740 patients with thoracic esophageal carcinoma from 2007 to 2012 who had undergone esophagectomy and esophagogastric cervical anastomosis and plus lymph node dissection were analyzed. According to the guideline of the Japanese Society for Esophageal Diseases (JSED), lymphatic nodes were named and were divided into three groups. Potential influencing factors including age, gender, location, shape, differentiation grade, the length and the depth of invasion, vascular tumor embolus were stratified and analyzed with SPSS17.0 software.

Results: Totally 8958 of lymph node groups (with 27861 nodes) were dissected. The lymph node metastasis rate was 33.87%. Location, shape, differentiation grade, the length and the depth of invasion, vascular tumor embolus influenced the lymphatic metastasis (P<0.05), while age and gender had a little influence on the lymphatic metastasis (P>0.05). The tumor located in different places extended in both up-and-down directions and metastasized by leaping over. For the upper ESCC, the most common node metastasis was in the upper mediastinal (12.84%) and followed by the cervical (5.50%), the abdominal (3.67%), the middle mediastinal (0.46%) nodes, but none in the lower mediastinal nodes. For the middle ESCC, the highest incidence of node spread was in the middle mediastinal (18.49%) and similar rates in the abdominal (18.30%) and followed by the cervical (5.06%), the upper mediastinal (3.03%) nodes, but the least in lower mediastinal (0.67%) nodes. For the lower ESCC, more node metastasis occurred in abdominal (26.01%), and followed by the lower mediastinal (19.51%), the middle mediastinal (7.62%), the cervical (1.35%) and the upper mediastinal (0.86%) nodes. There were significant differences in cervical lymph nodes metastasis rate among the patients of different locations (χ²=12.371, P=0.002). There were significant differences in celiac lymph nodes metastasis rate among the patients of different locations (χ²=48.727, P<0.001).

Conclusions: The lower of location, the lower of grade and the longer of invasion, the easier to get independent lymph node metastasis. Lymphatic metastasis had no significant differences among the four stages (T1-T4). Skip metastasis was more easily to be found than the other patterns of lymph node metastasis in this investigation.

187  The Impact of Computed Tomography on Early Glottic Cancer Outcomes

W. F. Mourad1,2, R. A. Shourbaji1, D. Ishihara1, W. Lin1, K. S. Hu1, L. B. Harrison1, Beth Israel Medical Center, New York, NY, Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, NY

Purpose/Objectives: To evaluate the impact of computed tomography (CT) based simulation (CT sim) and planning on early glottic cancer outcomes and toxicity.

Materials/Methods: This is a single-institution retrospective study. Two hundred and fifty three patients with T1-2 glottic cancer underwent radiation therapy (RT) via 2 or 3 dimensional RT with Co60 or linear accelerator (LINAC) from January 1998 to 2010. Group A (203 patients, 80%) and B (50 patients, 20%) underwent 2-dimensional RT (2DRT) and 3 dimensional RT (3DRT), respectively. The median age was 65 years for the whole cohort), 67 years for group-A and 63 years for group-B. Males made up 87% of the population in both groups. T1 were 76 and 84% in groups A and B, respectively. The median dose and fraction size were 63Gy and 2.25Gy, respectively.

Results: With a median follow-up of 83, 93, and 30 months for the whole cohort, group A and B respectively, the loco-regional control (LRC) was 97.6%. According to the T classification, rates of LRC for T1 (195) and T2 (58 patients) were 99.5 and 91%, respectively. According to the RT modality, rates of LRC were 99.4 and 100% for T1 while they were 89.8 & 100% for T2 in groups A and B, respectively. Acute dysphagia grades ≤2 and 3 were 94 and 0.5 % for group A and 72 and 0% for group B, respectively. Long term toxicity was negligible in both groups. Kaplan-Meier Curve showed the 5-year cause-specific survival to be 100%. Chi square and multivariate analysis tests showed a significant relationship between CT simulation (3DRT) and LRC (P<0.0001).

Conclusions: CT-based simulation and planning provided better LRC and less acute side effects compared to 2 DRT.


188  Glioblastoma Multiforme: Use of Clinical Target Volumes as Possible Prognostic Factors to Progression-Free Survival

I. T. Carvalho1, H. F. Braga1, H. A. Carvalho1, J. V. Salvajoli1, A. B. B. Borges1, D. B. Freitas2, W. Nadalin1, E. Weltman1, University of Sao Paulo - School of Medicine, Sao Paulo, Brazil, Cancer Institute of the State of São Paulo (ICESP), Sao Paulo, Brazil

Purpose/Objectives: To evaluate the outcome of patients with Glioblastoma Multiforme (GBM) treated in a single institution, establish clinical prognostic factors for overall (OS) and progression-free survival (PFS), and evaluate the influence of irradiated volumes in the outcome.

Materials/Methods: A retrospective analysis was performed in 81 patients with newly diagnosed GBM treated at University of São Paulo. Data were gathered from those who initiated postoperative radiation therapy (RT) between January 2008 and October 2011. The analyzed variables were age, gender, KPS, type of excision, number of surgical interventions before RT, time to initiate RT after last surgical procedure, duration of the RT treatment, total dose, fractionation, use of concurrent chemotherapy and magnetic resonance imaging (MRI) pattern of failure. Besides radiological progression, raise on the corticosteroid dose or documentation of clinical deterioration were also considered as failures. Volumetric parameters of irradiation were included in the analysis, as the absolute CTVs and the Equivalent-Sphere Diameter (ESD) CTVs. OS was considered from diagnosis and PFS from the beginning of RT. Survival curves were estimated by Kaplan-Meier Method and the variables compared by log-rank test.
Results: There were 51 (63%) men, with a median age of 58.9 years (24 to 80 years) and 90.1% presented with Karnofsky performance status (KPS) of at least 60%. Most patients (52.1%) had a complete macroscopic resection and 71.6% received chemotherapy. All patients were treated with 3D conformal RT. Conventional fractionation (30 x 2 Gy) was delivered to 69 (85.1%) patients, and 12 (14.8%) were treated with hypofractionation (15 x 2.67 Gy); 58 patients (71.6%) received concurrent chemotherapy. There was a mean of 71 ± 46 days interval from surgery to the start of RT. With a median follow-up of 7.8 months, there were 45 deaths (55.5%) and 62 (76.5%) failures. Of these, MRI progression was detected in 43 patients, with 61 recurrence sites: 39 (90.6%) central progression of previous injury or cavity edges, 10 (23.2%) new non-contiguous lesions in-field, 4 (9.3%) marginal, and 8 (18.6%) distant. Median OS was 14.1 months and median PFS was 4.0 months. Age 60 and concurrent chemotherapy were significantly related to better OS and PFS (p < 0.05). PFS was also related to the absolute CTV of the boost (50 cc cutoff, p = 0.03) and to the ESD CTV of the boost (4.5 cm cutoff, p = 0.03).

Conclusions: Besides the well-known clinical prognostic factors for this population, the CTV of the boost showed to be practical and easy for prognostic evaluation.


189 Usefulness of Double Dose Contrast-enhanced Magnetic Resonance Imaging for Clear Delineation of Gross Tumor Volume in Stereotactic Radiotherapy Treatment Planning of Metastatic Brain Tumors: A Dose Comparison Study

K. S. Subedi, Gunma University, Maebashi, Japan

Purpose/Objectives: To compare the size and clearness of gross tumor volumes (GTV) of metastatic brain tumors on T1-weighted magnetic resonance (MR) images between a single dose contrast administration protocol and a double dose contrast administration protocol to determine the optimum dose of contrast-enhancement for clear delineation of GTV in stereotactic radiotherapy (SRT).

Materials/Methods: A total of 28 small metastatic brain tumors were evaluated in 13 patients by intra-individual comparison of GTV measurements using single dose and double dose contrast-enhanced thin-slice (1-mm) magnetic resonance imaging (MRI). All patients had confirmed histological types of primary tumors and had undergone hypofractionated SRT for metastatic brain tumors.

Results: The mean tumor diameter with single dose and double dose contrast-enhancement was 12.0 ± 1.1 mm and 13.2 ± 1.1 mm respectively (p < 0.001). The mean incremental ratio (MIR) obtained by comparing mean tumor diameters was 11.2 ± 0.02 %. The mean volume of GTV-1 (single dose contrast-enhancement) and GTV-2 (double dose contrast-enhancement) was 1.38 ± 0.41 ml and 1.59 ± 0.45 ml respectively (p < 0.01). The MIR by comparing mean tumor volumes was 32.3 ± 0.4 %. The MIR of GTV-1 with < 1ml volume and GTV-1 with > 1ml volume was 41.8 ± 0.05 % and 12.4 ± 0.03 % respectively (p < 0.001).

Conclusions: Double dose contrast-enhanced thin-slice MRI is more useful technique than single dose contrast-enhanced thin-slice MRI, especially for clear delineation of GTVs of small metastatic brain tumors in treatment planning of highly precise SRT.

K.S. Subedi: None.
190 Cranial Nerves Contouring Among Patients Treated With IMRT for Base of Skull, Nasopharyngeal, and Paranasal Sinus Cancer

W. F. Mourad1,2, K. S. Hu1, R. A. Shourbaji1, A. Khorsandi1, L. B. Harrison1, 1Department of Radiation Oncology, Beth Israel Medical Center, New York, NY, 2Department of Radiation Oncology, Albert Einstein College of Medicine of Yeshiva University, Bronx, NY

Purpose/Objectives: To develop a standardized methodology for cranial nerves IX-XII contouring among patients treated with intensity-modulated radiotherapy (IMRT) for head and neck cancer (HNC).

Materials/Methods: Using anatomic texts, radiologic data, and T1/2 magnetic resonance imaging (MRI), a standardized method for delineating the cranial nerves IX-XII on computed tomography (CT) was performed. A neuroradiologist assisted with identification of the cranial nerves IX-XII and adjacent structures (i.e., Midbrain, Pons, and Medulla Oblongata). These organs at risk were then contoured on 5 consecutive patients undergoing IMRT for locally advanced HNC (i.e., base of skull, nasopharyngeal and Paranasal-sinus cancer). Dose-volume histogram (DVH) curves were generated by applying the proposed cranial nerves contour to the initial treatment plan. Due to anatomical nature and proximity of cranial nerves IX, X and XI, they were contoured as one structure while cranial nerve XII was contoured individually.

Results: The median total dose to the planning target volume (PTV) was 70 (ranged from 66-70 Gy). The median cranial nerves (IX-XI) and (XII) volumes were 20 cm3 (15-25) and 18 cm3 (15-22) respectively. The median V50, V60, V66, and V70 of the cranial nerves (IX-XI) and (XII) volumes were (85, 77, 71, 65) and (88, 80, 74, 64) respectively. The maximal dose to the cranial nerves (IX-XI) and (XII) were 72 (66-77) and 71 Gy (64-78) respectively.

Conclusions: The proposed methodology provides a highly reproducible, defined and standardized way for delineating the cranial nerves IX-XII organ at risk on IMRT based CT planning. Our dosimetric analysis should serve as pilot data for prospective studies for patients undergoing IMRT for HNC to establish a limiting dose for these structures at risk.


191 Quantitative Assessment of Volumetric Changes Using Fan Beam and Cone Beam Computed Tomography During Head and Neck Image Guided Radiotherapy

M. E. Schutzer1, S. Song1, M. Fatyga2, D. A. Asher1, W. Sleeman1, N. Dogan1, 1Virginia Commonwealth University, Richmond, VA, 2Mayo Clinic, Scottsdale, AZ

Purpose/Objectives: Adaptive radiotherapy (ART) has been shown to improve dosimetric parameters of head and neck (HN) IMRT by accounting for anatomic changes seen on fan beam CT (FBCT). However, the utility of cone beam CT (CBCT) scans in ART has not been well studied. This study aims to investigate the potential role of CBCT in adaptive IMRT planning for HN tumors and to quantify changes in target and normal tissue volumes over the course of treatment.

Materials/Methods: Patients with biopsy proven HN tumors treated under an IRB approved imaging protocol were included in this study. IMRT planning was based on initial contrast enhanced FBCT using Pinnacle software. In addition, patients were re-imaged with weekly FBCTs and up to 5 CBCTs per week, taken at the time of treatment. Due to the limited field of view of the Varian CBCT imager, CBCT images consisted of dual orbit CBCT scans, one covering upper neck and the second covering lower neck, which were then fused. Target volumes and avoidance structures were
contoured manually, and volumetric parameters were measured using FBCT as the reference. Correlation between FBCT and CBCT volumes were calculated using Pearson’s Correlation Coefficient.

**Results:** To date, 5 of our anticipated 15 patients have completed therapy on this protocol, 4 of whom had oropharyngeal cancer and 1 of whom had cancer of the retromolar trigone. All 5 patients received chemotherapy. Compared to initial volumes, weekly FBCT showed an average volume decrease of 2.3%/fraction (±0.4%) for the primary tumor (PT), 1.9%/fraction (±0.5%) for the pathologically enlarged lymph nodes (LN), and 1.2%/fraction (±0.3%) for parotid glands (PG). The image quality of CBCT was not sufficient to accurately track changes in PT and LN volumes. The PG volumes did correlate well between FBCT and CBCT (r= 0.83), and CBCT demonstrated PG volume decrease of 1.6%/day (±0.7%)

**Conclusions:** CBCT can reliably assess changes in PG volume, and can therefore potentially contribute to the ART planning. PT and LN volumes could not be accurately measured on CBCT. In contrast to previously reported data, this study suggests that the tumor volume may decrease more rapidly for PT than for LN. While the role of CBCT in ART has not been defined, it can potentially provide information regarding the optimal timing of re-planning.

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**Dosimetric Implications of Treating 4D PET/CT-Defined Maximum Inhale Versus Exhale Target Volumes in Esophageal Cancer**

N. Figura\(^2\), K. Latifi\(^1\), T. J. Dilling\(^1\), C. C. Kuykendall\(^1\), E. A. Eikman\(^1\), E. G. Moros\(^1\), G. G. Zhang\(^1\), S. Leuthold\(^1\), C. Mehra\(^1\), S. E. Hoffe\(^1\), \(^1\)Moffitt Cancer Center, Tampa, FL, \(^2\)University of South Florida, Tampa, FL

**Purpose/Objectives:** The potential role of integrating 4D PET/CT based volumes into the treatment planning of esophageal cancer patients is not well defined. In our study, we evaluated whether there would be a potential dosimetric photon advantage of treating patients with maximum inhale vs. exhale technique.

**Materials/Methods:** Five esophageal cancer patients who had undergone 4D PET/CT for radiation treatment planning were selected for this retrospective review. Of these, four with adenocarcinoma of the distal esophagus were deemed suitable for inclusion; due to major artifacts in the 4D PET/CT one case was excluded. The data sets representing maximum inhalation and exhalation were exported from the AW workstation to the Mirada system. The inhale/exhale PET/CT phases were deformably registered to their respective planning CT phase. A data set representing the PET/CT volume of the tumor in maximum inhalation vs. maximum exhalation was created for each patient. We computed the volume of the PET GTV in each phase by using the auto-contour SUV 2.5 function and added a 3cm superior and inferior expansion and a 1cm radial expansion for the CTV. A 0.5cm expansion on the CTV created the PTV. The fused scans and structures were then exported into Pinnacle. Based on published dosimetric series using the set angles of 80, 110, 160, 210 and 240, we ran 6 MV IMRT plans with at least 94% PTV coverage to a dose of 5040cGy in 28 fractions on each data set using the position of the tumor in maximum inhale vs. exhale. The plans were then compared in terms of mean lung dose, total lung V5 and V20, heart mean dose and V30, and liver mean dose.

**Results:** Results showed that in three of the four plans, the GTV defined with the auto-contouring SUV 2.5 parameter was smaller on the exhale plan by 9%, 15% and 30%. Yet in all three of these cases, there was not uniform superiority of the exhale phase in all of the parameters studied. The total lung V5 was better on the exhale plans in the majority (3/4) of the cases. There was one patient with the best parameters on the inhale phase. The heart V30 showed a less than 5% difference between inhale and exhale in all cases. The heart mean dose, however, showed more variation with two cases exhibiting lower DVHs by 6.5-8.6% in the exhale phase. The liver mean was lowest in inhale phase for all cases.
Conclusion: This study suggests there may be variation in delineation of maximum inhalation vs. exhalation 4D PET/CT esophageal cancer volumes which may be exploited to maximize lung and cardiac sparing. Our data suggests that personalizing the patient’s treatment parameters by evaluating maximum inhalation vs. exhalation dosimetry is worthy of further study.


193  Diffusion-Weighted Whole-Body Imaging With Background Body Signal Suppression (DWIBS) -- Application in Planning for Cyberknife Therapy in Patients With Gliomas

R. Balaji, R. Devi, J. Stumpf, Apollo Cancer Hospitals, CHENNAI, India

Purpose/Objectives: To describe the use of DWIBS Diffusion-weighted whole-body imaging with background body signal suppression for CyberKnife therapy in patients with gliomas.

Materials/Methods: Eighteen patients with the gliomas underwent planning MRI with DWIBS imaging of the brain in addition to high resolution T1 contrast imaging.

Results: DWIBS produces PET like images and helps in better tumor delineation and increase confidence levels to outline tumor margins especially in infiltrative gliomas.

Conclusions: DWIBS can be adapted for planning protocols for CyberKnife therapy in patients with gliomas as an adjunct to routine high resolution T1 contrast imaging.

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194  Reflectance Confocal Microscopy in Patients Undergoing Radiation Therapy

C. A. Barker, Memorial Sloan-Kettering Cancer Center, New York, NY

Purpose/Objectives: Radiation therapy (RT) is frequently used in the management of cutaneous malignancies. Targeting of skin cancers with RT is often achieved by direct inspection. However, some parts of the tumor may be occult on physical examination. Moreover, some cutaneous malignancies are not easily discernible on direct inspection. Cancer imaging modalities frequently used in conjunction with RT (computed tomography, magnetic resonance imaging, positron emission tomography) do not image the skin adequately. In recent years, RCM has emerged as a novel skin imaging modality that allows clinicians to assess morphology of the skin, and identify pathologic conditions like cancer. The objective of this study was to search and analyze the literature reporting the use of RCM in patients undergoing RT.

Materials/Methods: The Web of Science online academic citation index was searched for the terms "reflectance confocal microscopy" and "radiation therapy" or "radiotherapy". Reference textbooks on the subject of reflectance confocal microscopy (Reflectance Confocal Microscopy of Cutaneous Tumors and Reflectance Confocal Microscopy for Skin Diseases) were also searched. Results of the literature search were analyzed.

Results: Eight-hundred and eleven studies on RCM were identified. Many dealt with applications of RCM in the treatment of skin disease. Two reports of using RCM after breast RT in six patients have been reported. In one case
report, the technique was used after treatment to detect cutaneous recurrence in the skin after breast RT. In a case series reporting on five patients, RCM was used to characterize the dermatologic response of the normal skin to RT (radiation dermatitis). No studies reported the use of reflectance confocal microscopy for targeting purposes, or treatment response of primary skin cancers.

**Conclusions:** RCM is a potentially useful tool in the evaluation of the skin cancer patients undergoing dermatologic RT. Further study is necessary to determine the value of RCM in skin cancer RT targeting and treatment response.

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