Abstract #01

A Novel miRNA-Based Predictive Model for Biochemical Failure Following Post-Prostatectomy Salvage Radiation Therapy

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Purpose: To develop a microRNA (miRNA)-based predictive model for prostate cancer patients of 1) time to biochemical recurrence after radical prostatectomy and 2) biochemical recurrence after salvage radiation therapy following documented biochemical disease progression post-radical prostatectomy.

Methods: Forty-three patients who had undergone salvage radiation therapy following biochemical failure after radical prostatectomy with greater than 4 years of follow-up data were identified. Formalin-fixed, paraffin-embedded tissue blocks were collected for all patients and total RNA was isolated from 1 mm cores enriched for tumor (>70%). Eight hundred miRNAs were analyzed simultaneously using the nCounter human miRNA v2 assay (NanoString Technologies; Seattle, WA). Univariate and multivariate Cox proportion hazards regression models as well as receiver operating characteristics were used to identify statistically significant miRNAs that were predictive of biochemical recurrence.

Results: Eighty-eight miRNAs were identified to be significantly (p<0.05) associated with biochemical failure post-prostatectomy by multivariate analysis and clustered into two groups that correlated with early (≤36 months) versus late recurrence (>36 months). Nine miRNAs were identified to be significantly (p<0.05) associated by multivariate analysis with biochemical failure after salvage radiation therapy. A new predictive model for biochemical recurrence after salvage radiation therapy was developed; this model consisted of miR-4516 and miR-601 together with, Gleason score, and lymph node status. The area under the ROC curve (AUC) was improved to 0.83 compared to that of 0.66 for Gleason score and lymph node status alone.

Conclusions: miRNA signatures can distinguish patients who fail soon after radical prostatectomy versus late failures, giving insight into which patients may need adjuvant therapy. Notably, two novel miRNAs (miR-4516 and miR-601) were identified that significantly improve prediction of biochemical failure post-salvage radiation therapy compared to clinicohistopathological factors, supporting the use of miRNAs within clinically used predictive models. Both findings warrant further validation studies.

Abstract #02

Study Protocol: Proton Plus Carbon Ion Radiotherapy versus Proton Radiotherapy Alone in Patients with Unresected Glioblastoma Multiforme: A Randomized Phase III Trial

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Background: Maximum resection followed by adjuvant radiotherapy (RT) is the mainstay treatment strategy for glioblastoma multiforme (GBM). The standard RT regimen is 60 Gy in 30 fractions using photon. Despite the effectiveness of adjuvant RT, the prognosis remains dismal for GBM patients, and the median survival time is ~15 months. Particle beam radiation therapy offers a number of advantages over photon radiotherapy in the treatment of brain malignancies. Proton radiotherapy, due to its inverted dose profile and the high local dose deposition within the Bragg peak, precise dose application and sparing of normal tissue is possible. However, the RBE of proton is comparable to photon. Carbon ion radiotherapy (CIRT) offers a similar but sharper dose distribution as compared to proton. In addition, CIRT offers an increased RBE over photon and proton which is considered to be 2–5 based on basic research results. Therefore, CIRT may offer both physical and biological advantages over proton and photon RT.

Preliminary results from two Japanese studies that evaluated the use of CIRT in the treatment of Grade 2 glioma and GBM indicated that (1)
CIRT used alone to a total dose of 55.2 Gy (in 24 fractions) is safe and efficacious in the treatment of WHO II glioma, and (2) CIRT used as a boost up to 24.8 Gy in 8 fractions to photon RT is efficacious in the treatment of GBM. 

Methods/Design: In the current randomized study, patients diagnosed with GBM who undergo a noncomplete resection will be treated with proton radiation therapy after surgery. Patients will be randomized to receive either standard dose of proton therapy, i.e., 60 Gy in 30 fractions (Control Arm) or the same dose with a CIRT boost to the macroscopic tumor to 10-15 Gy in 1 fraction (90% isodose line to cover GTV+0.5 cm excluding critical functional parts of the brain such as brain stem and optic nerve) based on tumor volume (Experimental Arm). Primary endpoint is overall survival, and secondary endpoints induce PFS, adverse-effects, and safety.

Discussion: This will be the first randomized trial that investigates the effect of CIRT used with a standard dose of proton therapy in GBM as a boost. We hypothesize that CIRT can significantly improve the overall survival.

References:

Abstract #03
Merkel Cell Carcinoma: Outcomes of Treatment with Adjuvant Radiation

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Purpose: Merkel cell carcinoma (MCC) is a rare, rapidly growing, invasive neuroendocrine tumor whose uniquely aggressive nature distinguishes it from other cutaneous malignancies. Though its mortality rate exceeds that of melanoma, there is no optimal universal standard in PROCEED Patients

Prior radiation treatment on Sipuleucel-T Product Parameters

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Purpose/Objectives: Sipuleucel-T (sip-T) is an autologous cellular immunotherapy indicated for asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer. Approval of sip-T was based primarily on the randomized, controlled, phase 3 study (IMPACT) that demonstrated a 22% reduction in the risk of death. In view of the belief that radiation treatment (tx) could suppress bone marrow function and therefore immune function, IMPACT excluded patients (pts) who received radiation ≥28 days prior to registration. PROCEED is an ongoing phase 4 registry enrolling pts tx with commercial sip-T in the real-world setting. Palliative radiation (PR) tx for bone pain prior to sip-T is not restricted in PROCEED, so the effects of prior radiation on sip-T manufacturing parameters can be evaluated.

Materials/Methods: Patients treated with sip-T ≤6 mo were eligible. Baseline patient demographics and disease characteristics were collected. Sip-T product parameters that were assessed included: total nucleated cell (TNC) count, antigen presenting cell (APC) count (large CD54+ cells), and APC activation (upregulation of CD54; a measure of product potency). Results: Data were available for 1244 pts enrolled by May 2013, who completed tx; of those, 112 (9.0%) pts received PR to bone metastases prior to sip-T and 517 (41.6%) pts had no prior radiation of any kind (NRT). To ensure that groups (grp) were homogeneous and to limit the
comparison of NRT pts with those who had PR only for bone metastases, pts with radical prostatectomy were isolated from each grp for further study, resulting in 44 pts in the PR grp and 159 pts in the NRT grp. Median cumulative APC counts were similar between grp, however TNC counts (PR: 9.89 vs. NRT: 12.09 x 10^9; P=0.002) and APC activation (PR: 34.2 vs. NRT: 38.5; P=0.048) were lower in the PR grp. However, the percentage of pts receiving all three infusions in each group was comparable (PR: 93.2 % vs NRT: 95.0 %; P=0.71).

**Conclusions:** In the real-world setting, there is no evidence that prior radiation inhibits successful production of sip-T. Although TNC counts and APC activation were lower, APC counts were comparable in radiation treated pts. Effects on in vivo post treatment immune measures are being collected prospectively in a companion trial called PRIME.

**Abstract #05**

**Outcomes of Combined Modality Treatment of Lower Extremity Soft Tissue Sarcoma: A 15-Year Retrospective Review**

Eric Miller, Nicole Andonian, Xiaokui Mo, Karl Haglund, John Grecula, Douglas Martin, David Liebner, James Chen, John Howard, Thomas Scharschmidt, Joel Mayerson, Raphael Pollock, Meng Xu-Welliver

Ohio State University, Columbus, OH, USA

**Purpose:** Limb preservation therapy of extremity soft tissue sarcoma (STS) requires a multidisciplinary approach. The purpose of this study is to evaluate outcomes of patients treated for lower extremity STS at our institution.

**Methodology:** The medical records of 95 consecutive patients with localized lower extremity STS treated definitively in the department of radiation oncology at Ohio State between 1998 and 2013 were reviewed. Analysis was performed using the Kaplan-Meier method and subsets were compared using a log rank test.

**Results:** Fifty-three men and 42 women were included with a median age of 57 years (range 21–86 years). The most common histologies included undifferentiated pleomorphic sarcoma (18 %), myxofibrosarcoma (13 %), and leiomyosarcoma (11 %). The majority of patients were stage III (60 %), had tumors in the proximal lower extremity (upper border of iliac crest to below the knee, 86 %), were deep in location (79 %), and were high grade (71 %). All patients underwent resection with limb-sparing surgery and received radiation therapy (RT) as part of their treatment. Surgical margins were positive in 15 % of patients with 27 % of those patients undergoing re-resection. Seventy-seven percent of patients had radiation delivered post-operatively with a median total dose of 60 Gy (range 50.4–71.9 Gy). The median total pre-operative dose was 50 Gy (range 50–60 Gy). Twenty-eight percent of patients were treated with intra-operative radiotherapy (IORT) (36 % of patients who received pre-operative RT and 26 % of post-operative RT patients, respectively) with a median dose of 10 Gy (range 10–15 Gy). Chemotherapy was delivered in 38 % of patients. At a median follow-up of 52 months (range 5–150 months), the 5-year and 10-year overall survival (OS), disease-free survival (DFS), and amputation-free survival (AFS) rates were 68 and 49 %, 54 and 48 %, and 91 and 91 %, respectively. Forty-four percent of patients ultimately failed with 79 % failing distantly, 10 % failing locally, and 11 % failing both locally and distantly. The use of IORT did not influence OS (p=0.25), DFS (p=0.11), or AFS (p=0.74). Radiotherapy timing did not impact OS (p=0.64), DFS (p=0.60), or AFS (p=0.98). In patients with high grade histology, there was an OS benefit with the addition of chemotherapy (p=0.013). Six percent of patients ultimately underwent amputation due to local failure or wound healing complications with a median time-to-amputation of 29 months (range 9–56 months).

**Conclusions:** RT combined with surgical resection provides good local control with a high likelihood of long-term limb preservation. Based on our data, the benefits of RT are achieved regardless of treatment timing or the use of IORT. Chemotherapy did benefit patients with high grade histology. Our data suggest that despite good control of local disease, patients with STS are most likely to fail distantly.

**RESIDENT ORAL PRESENTATIONS**

**Saturday, May 16, 2015 (4:30–5:30 pm)**

**Abstract #06**

**Impact of perineural invasion on long-term outcomes in locally advanced rectal cancer treated with neoadjuvant chemoradiotherapy: Results from a single institution and review of the literature**

Priyanka Chablani, Phuong Nguyen, Charles Robinson, Jeff Pan, Steve Walston, Amab Chakravarti, Evan Wuthrick, Terence Williams

The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA

**Purpose:** The use of adjuvant chemotherapy in patients with locally advanced rectal cancer (LARC) treated with neoadjuvant chemoradiotherapy (nCRT) is controversial. Recent studies have examined clinicopathologic variables associated with adverse clinical outcomes, including perineural invasion, in an effort to risk-stratify patients and guide the use of adjuvant therapy. We examined the association of perineural invasion (PNI) with outcomes in patients with LARC treated with nCRT to determine whether PNI is an independent variable that could be used as a prognostic biomarker to guide the use of adjuvant therapies.

**Methods:** We performed a retrospective study of 110 patients treated with nCRT and surgery for LARC at our institution from 2004–2011. Eighty-seven patients remained in our final analysis. We evaluated the association of PNI with outcomes, including distant metastasis-free survival (DMFS), disease-free survival (DFS), and overall survival (OS), using log-rank and Cox proportional hazard modeling. We reviewed the literature to find other studies on patients with LARC treated with nCRT reporting on the association of PNI with DMFS, DFS, and OS.

**Results:** Fourteen patients (16 %) were PNI-positive and 73 patients (84 %) were PNI-negative. Median follow-up was 27 months (range 0.9–84 months). The median DMFS was 13.5 months for PNI+ and median not reached (>40 months) for PNI- (p<0.0001). The median DFS was 13.5 months for PNI+ and 39.8 months for PNI- (p<0.0001). In a multivariate model including PNI, PT stage, pN stage, pathologic grade, lymphovascular invasion, distance from anal verge, radial margin status, type of surgery, and adjuvant chemotherapy use, PNI remained a significant independent predictor of OS, DFS, and DMFS (p<0.0001). In one study, PNI was significant for OS on multivariate analysis. In one study, PNI was significant for PNI+ and median not reached (>40 months) for PNI- (p<0.0001). The median OS was not significantly different between the two groups (55.4 months for PNI+ versus 83.6 months for PNI-; p=0.14), perhaps due to censoring of patients and limited follow-up. We found eight similar studies in which PNI was associated with long-term outcomes. The number of patients ranged from 88 to 581; the percent of patients with PNI ranged from 8.3 to 27.3 %; median follow-up ranged from 27 to 79 months. In six studies, PNI was significant for DFS on multivariate (MV) analysis. In one study, PNI was significant for DMFS on MV analysis. In four studies, PNI was significant for OS on MV analysis, however in two studies, PNI was not associated with OS on MV analysis.

**Conclusions:** For patients with LARC treated with nCRT, PNI found at the time of surgery is significantly associated with worse DFS, DMFS, and possibly OS. Prospective trials are needed to determine the benefit of adjuvant chemotherapy in patients with PNI and other high-risk features to optimize the use of this therapy.
Immunologic Implications for Combination Therapy Following Standard Radiation Approaches for Prostate Cancer

Francisco A. Myslicki1, Sharon A. Salenius2, Neal D. Shore1, Constantine A. Mantz2, Daniel E. Dosoretz2, Eduardo B. Fernandez3, Steven E. Finkelstein1

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Abstract: Historically, treatment approaches combining immunotherapy and targeted radiation therapy were precluded by the notion that radiotherapy could be immunosuppressive in certain settings. However, the interplay between radiation and immune reactivity is now known to be more complex than previously imagined. Recent research suggests that radiotherapy may actually have immunostimulatory effects, thus introducing the idea of a synergistic union between the two for the treatment of cancer.

Conclusion: In patients treated with external beam radiation therapy for high-risk prostate cancer is immune modulating.

Pencil-beam Scanning Proton Therapy for Anal Cancer: a Dosimetric Comparison with Intensity-modulated Radiotherapy

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Purpose: Concurrent chemoradiotherapy cures most patients with anal squamous cell carcinoma at the cost of significant treatment-related toxicities. Intensity-modulated radiotherapy (IMRT) reduces side effects compared to older techniques, but whether proton beam therapy (PBT) offers additional advantages is unclear. To our knowledge, this is the first quantitative analysis of PBT for anal cancer.

Abstract:

Pencil-beam scanning PBT is clinically feasible and can be robustly delivered for anal cancer patients. Compared with IMRT, PBT reduces low- to intermediate-dose radiation to important organs at risk in comparison to IMRT at higher doses. Mean small bowel V15 and V25 for PBT versus IMRT was 14 vs. 40 % (p = 0.008), respectively. Mean total pelvic bone marrow V10 and V20 for PBT versus IMRT were 72 vs. 89 % and 54 vs. 75 %, respectively (p = 0.008). Mean external genitalia V20 for PBT versus IMRT was 14 vs. 40 % (p = 0.008). Overall mean external genitalia dose was 7.4 Gy with PBT and 19.4 Gy with IMRT. Due to beam geometry, lumbosacral bone marrow V20-45 was higher with PBT than IMRT. Lumbosacral marrow V20 was 89 % with PBT and 86 % with IMRT (p = 0.04). PBT was delivered with ≤ 1.3 % interfraction deviation in the dose received by 98 % of the clinical target volumes. Mean absolute deviation in CTV D98% from the original plans for all patients over all scans was 0.24±0.28 %.

Conclusions: Pencil-beam scanning PBT is clinically feasible and can be robustly delivered for anal cancer patients. Compared with IMRT, PBT reduces low- to intermediate-dose radiation to important organs at risk in this population. While the clinical benefit of these differences remains to be shown, existing data suggest that limiting low dose to the small bowel and pelvic bone marrow may reduce treatment toxicity.

Repeat Stereotactic Radiosurgery is an Appropriate Approach for New/Recurrent Brain Metastases

Megan Kummerlowe, Colette Shen, Kristin Redmond, Michael Lim, Daniele Rigamonti, Lawrence Kleinberg

Johns Hopkins Hospital, Baltimore, MD, USA

Purpose: Stereotactic radiosurgery (SRS) is widely used in the treatment of brain metastases in place of whole brain radiotherapy (WBRT), with the goal of reducing treatment toxicity balanced against the increased risk of developing new metastasis. The goal of this study was to evaluate the

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Purpose: Stereotactic radiosurgery (SRS) is widely used in the treatment of brain metastases in place of whole brain radiotherapy (WBRT), with the goal of reducing treatment toxicity balanced against the increased risk of developing new metastasis. The goal of this study was to evaluate the
outcomes of a strategy using repeat courses of SRS in the management of recurrent/new brain metastases.

Methodology: We conducted a retrospective review of 66 patients treated with at least two courses of SRS without WBRT and followed for brain metastases between 2004 and 2013. Outcome metrics included survival, development of symptomatic rather than imaging-detected new brain metastases, neurologic symptoms at death or last follow up, and ultimate use of WBRT.

Results: Sixty-six patients with a median age of 57 years (range, 24–85 years) underwent a median of two courses of SRS (range, 2–6), with a median of two lesions treated both in the initial course (range, 1–9) and on re-treatment (range, 1–16). Histology included non-small cell lung cancer (35 %), melanoma (30 %), breast cancer (11 %), and other (24 %). The median interval between SRS treatments was 4.6 months (range, 1.2–30.2 months). Recurrent brain metastases were detected by scheduled follow up imaging (not in response to symptom development) in 86 % of cases. Median intracranial progression-free survival after repeat SRS was 3.9 months. Median overall survival (OS) from repeat SRS was 9.1 months and from initial diagnosis of brain metastasis was 17.5 months. On univariate analysis, ECOG performance status of 0–1 was associated with improved OS from initial brain metastasis diagnosis (19.8 vs 12.6 months, p=0.004, HR 0.20 [95 % CI=0.068–0.59]). In addition, control of extracranial disease was associated with improved OS from initial brain metastasis diagnosis (43.9 vs 14.5 months, p<0.001, HR 0.29 [95 % CI=0.16–0.54]). Twenty-eight percent of patients had symptomatic intracranial metastatic disease at the time of death or last follow up, and 24 % of all patients subsequently received WBRT (at a median of 4 months following last stereotactic radiation).

Conclusions: Repeat SRS is a reasonable option for patients with recurrent brain metastases. Our results suggest that survival outcomes are not adversely affected by omitting WBRT even when new/recurrent lesions are detected after initial radiosurgery alone. In addition, it is uncommon for new lesions to cause neurologic symptoms before detection with routine follow-up imaging, and a minority of patients had symptomatic intracranial disease at death or last follow up.

Abstract #10*

Pure and Mixed Early Stage Clear Cell Carcinoma With and Without Adjuvant Radiation Treatment: Outcomes and Patterns of Recurrence

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Purpose: Clear cell carcinoma (CCC) of the uterus is known to have aggressive behavior. Given its rarity, the role of adjuvant therapy for stage I-II disease is unclear. Additional uncertainty lies in understanding the behavior of pure CCC versus mixed with endometrioid adenocarcinoma (EA) or papillary serous (PS) carcinoma. Our study investigated outcomes and patterns of failure in these patients.

Methodology: From 1995–2012, our cancer registry identified 6402 patients with stage I-II endometrial cancer. Pathology reports with CCC were reviewed with a gynecologic pathology specialist. We found 64 cases of CCC, including 26 of pure CCC, 21 mixed with EA, and 17 mixed with PS. Adjuvant treatment was given 55 %, via either chemotherapy, external beam radiation therapy (EBRT) with or without vaginal brachytherapy (VB), or both.

Results: Median follow-up was 50 months. Median age was 65. Lynch syndrome was present in 9 %. Per FIGO 2009 staging, 75 % were stage I (38 IA, 7 IB) and the remainder stage II. Lymph node dissection was done in 73 % (majority para-aortic and pelvic) with median of 18 nodes.

Progression occurred in 19 %. Median time to progression was 20.7 months (2–40 months). By Kalpana-Meier estimate, 3 year vaginal recurrence free survival (RFS) was 94 %, pelvis RFS was 93 %, and distant metastasis (DM) FS, cancer specific survival and overall survival were 86 % each. There were no significant differences between histologies (pure versus mixed, or pure/EA vs mixed PS) in any survival measure, but a trend over time for worse locoregional recurrence with PS involvement. Of the 12 patients who progressed, 9 had some form of local progression but only 5 had isolated locoregional first site of recurrence. DM was documented for 10 patients. Sites included brain, pleural effusion, bone, ascites, omentum, inguinal nodes and supravacularar node. Eight of those who progressed were among the 35 adjuvantly treated. Of 19 patients who received VB, one (treated with EBRT and VB) progressed at the vaginal cuff 41 months later, followed by suspected spread to lung. Of 21 patients who received EBRT, 2 developed pelvic recurrences with simultaneous DM. Of 29 patients observed, 4 progressed. Two had DM alone and the other two had isolated vaginal recurrences. Salvage was attempted for both vaginal recurrences, but only one was successfully treated with EBRT and VB with no evidence of disease almost 10 years later. No other patients were successfully salvaged.

Conclusions: We did not find any significant differences in survival measures for pure versus mixed CCC, although comparison was limited by disease rarity. Recurrences were often fatal and a high proportion developed distant disease. Based on patterns of failure, more aggressive adjuvant therapy (including radiation) may be warranted despite early stage.

Abstract #11*

Incidence of Esophageal Strictures in Oropharyngeal Cancer Patients Treated with Intensity Modulated Radiation Therapy

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Background: Esophageal stricture is a known significant complication of radiation therapy in head and neck cancer patients. Prior reports identified increased stricture rates in laryngeal and hypopharyngeal primaries. In the modern era, there has been a concomitant rise of the incidence of oropharyngeal squamous cell carcinoma (OPSCC) and the use of intensity-modulated radiation therapy (IMRT). To the best of our knowledge, the rate of stricture in this specific population of patients has yet to be reported.

Methods: We conducted a retrospective review of patients treated at Ohio State University Wexner Medical Center with a diagnosis of OPSCC between 2010 and 2013. Both postoperative patients who received at least 6000 cGy (range 6000–6600 cGy, n=47) and definitively (range 6996–7020 cGy, n=183) treated patients were included. All patients were treated with IMRT. The esophagus was contoured uniformly, including the proximal 5 cm of the esophagus, starting at the inferior cricoid cartilage. Statistical analysis using the Kaplan-Meier and independent sample t-test using a univariate analysis and multivariate analysis of patient, tumor, and treatment factors including dosimetric parameters were performed. Modified barium swallow and endoscopic evaluation were used for diagnosing strictures.

Results: Two hundred thirty patients were eligible, with a median follow up of 24.7 months. Median age was 58. 83.9 % were male. Tumor site was base of tongue (49.1 %), tonsil (47.9 %), and other (3 %). Stage was IVA in 82.2 %, IVB 6.1 %, III 8.7 %, II 1.7 %, and I 1.3 %. At a median follow up of 24.7 months, 12 out of 230 (5.2 %) patients were found to have esophageal strictures. On univariate analysis a trend towards significance for formation of stricture was found for maximum esophageal dose (6074 cGy in stricture group vs. 5731 cGy in non-structure group; p=
Brachytherapy using Cesium-131 in the treatment of low or intermediate-risk prostate cancer

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Purpose: Cesium-131 sources designed for prostate seed implantation (PSI) have the potential for better dose homogeneity and a potentially higher biological effective dose. Give the short half-life of 9.7 days, more rapid resolution of acute toxicity might also be anticipated. Published clinical efficacy and toxicity outcomes for cesium-131 remain limited however.

Methodology: From September 2006 through September 2008, 78 patients were treated with PSI monotherapy using Cesium-131 seeds at the University of Wisconsin. All patients had low or intermediate-risk prostate cancer by the D’Amico classification system. A pre-plan technique or intra-operative planning with stranded sources in the periphery and loose sources centrally was used to prescribe 115 Gy to the periphery of the prostate gland. Patients were then followed clinically at 1 month and monitored at 3–6 month intervals with clinical assessment and PSA testing. The International Prostate Symptom Score (IPSS) was used during follow-up time of 44 months, two patients experienced PSA failure, respectively. Fifty-three percent of patients required the use of an alpha-blocker for greater than 1 year after treatment. Forty-two percent of patients reported worsening of erectile function after treatment, the most common being erectile dysfunction requiring the use of a PDE5 inhibitor. Acute Grade 3 toxicity developed in 5 patients, including diarrhea (3), cystitis requiring IV antibiotics (1), and a thrombosed hemorrhoid requiring a procedure (1). One late grade 3 rectal toxicity was observed: persistent diarrhea for >90 days after PSI. Three patients underwent minor cautery for rectal bleeding and one patient with a significant smoking history was diagnosed with a transitional cell carcinoma of the bladder 34 months after undergoing PSI.

Conclusions: In patients with OPSCC treated with IMRT, the rate of esophageal stricture was 5.2%. A trend to a higher rate of esophageal stricture occurrence was seen in patients receiving six fractions per week and a higher maximum esophageal dose. This esophagus should be contoured in all patients and care should be taken to minimize the maximum radiation dose, in particular patients receiving concurrent chemotherapy.

Abstract #13*

Leptomeningeal Carcinomatosis: Institutional Outcomes in the setting of Non-Small Cell Carcinoma Primary

Jeffrey Brower1, Sandeep Saha1, Stephen Rosenberg1, Pranshu Mohindra2, H. Ian Robins1

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Purpose: Limited outcome data are currently available to direct treatment recommendations for the management of leptomeningeal carcinomatosis (LMC). Improvements in diagnostic imaging along with advances in local and systemic therapies have likely resulted in the increasing incidence of LMC diagnoses. Lung cancer is a common cause of central nervous system metastases including LMC. Here we report on the outcomes of patients with non-small cell lung cancer (NSCLC) with documented radiological LMC.

Results: Median age was 66 years (35–89). Median follow-up was 21 months (6–82 months). Mean tumor volume was 5.8 cc (0.18–23.8 cc); mean treatment volume was 8.6 cc (0.29–40.4 cc). Seventy-two percent of our patients had no prior surgical resection. Eighty percent were female. All treated tumors were either stable or decreased in size. No patients had surgical intervention for tumor progression. A single patient required surgical resection for severely symptomatic edema. Thirty-seven patients (30%) developed intracranial edema after SRS with 18 (13%) patients symptomatic. On logistical regression analysis, there was a correlation between post-SRS edema and tumor volume (p=0.01), treatment volume (p=0.003), and convexity tumors (p=0.004); the same factors were correlated with symptomatic edema. Other variables were not significant. ROC curve analysis of tumor volume found that a cut point of 3.2 cc was predictive of development of post-SRS edema with sensitivity of 73% and specificity of 51%. Tumor volume of 5 cc was predictive of development of post-SRS toxicity with sensitivity of 76% and specificity of 48%.

Conclusions: We found that tumors greater than 5 cc and convexity tumors are more likely to develop symptomatic edema after single fraction SRS. Patients with these tumor characteristics may benefit from alternative treatment modalities or reduced prescribed dose.

Abstract #14*

Predictors of Toxicity after Single Fraction Stereotactic Radiosurgery for Intracranial Meningiomas

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Background: Stereotactic radiosurgery (SRS) is an effective treatment option for meningiomas but a 10–15% rate of post-SRS edema and the
development of neurologic symptoms in 5–10 % of treated patients have been reported.

**Purpose:** Determine factors predictive of post-treatment toxicity after single fraction SRS to identify patients at risk of complications.

**Materials/Methods:** We identified 134 patients that had at least one post-SRS MRI available for review after SRS treatment for an intracranial meningioma. Both patients with and without prior surgical resection were included in this analysis totaling 122. Patients with meningiomatosis \( n=10 \) or concurrent intracranial malignancy \( n=2 \) were excluded. All patients had pre- and post-SRS MRIs. Follow up imaging was typically obtained 6 and 12 month post-SRS, then annually thereafter. All pre- and post-SRS MRIs were reviewed for analysis. Tumor size was assessed on T1 post-contrast images. Edema volume was assessed on fluid attenuated inversion recovery (FLAIR) or equivalent T2 sequence. All reported edema represents new edema after SRS.

All patients were treated with the Leksell Gamma Knife 4C (Elekta Instruments, Norcross, GA). Treatment planning was performed on MRI acquired the day of SRS using Gamma Plan (Elekta Instruments, Norcross, GA). Tumor volumes were delineated by the treating neurosurgeon and radiation oncologist. The median prescription was 14 Gy (10–19 Gy) to the 50 % isodose line (30–60 %). Tumor volume, treatment volume, age, gender, tumor location, conformity index, and marginal dose were evaluated for association with edema and symptomatic edema using chi-square and logistical regression.

**Results:** Median age was 66 years (35–89). Median follow-up was 21 months (6–82 months). Mean tumor volume was 5.8 cc (0.18–23.8 cc); mean treatment volume was 8.6 cc (0.29–40.4 cc). Seventy-two percent of our patients had no prior surgical resection. Eighty percent were female.

All treated tumors were either stable or decreased in size. No patients had surgical intervention for tumor progression. A single patient required surgical resection for severely symptomatic edema.

Thirty-seven patients (30 %) developed intracranial edema after SRS with 18 (13 %) patients symptomatic. On logistical regression analysis, there was a correlation between post-SRS edema and tumor volume \( p=0.004 \); the same factors were correlated with symptomatic edema. Other variables were not significant.

ROC curve analysis of tumor volume found that a cut point of 3.2 cc was predictive of development of post-SRS edema with sensitivity of 73 % and specificity of 51 %. Tumor volume of 5 cc was predictive of development of post-SRS toxicity with sensitivity of 76 % and specificity of 48 %.

**Conclusions:** We found that tumors greater than 5 cc and convexity tumors are more likely to develop symptomatic edema after single fraction SRS. Patients with these tumor characteristics may benefit from alternative treatment modalities or reduced prescribed dose.

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**Abstract #15**

**Bladder-preservation using radiotherapy with or without chemotherapy for muscle-invasive bladder cancer**

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**Purpose/Objective(s):** To report the outcomes of patients with muscle-invasive bladder cancer treated definitively with radiation therapy with or without concurrent chemotherapy. Materials/Methods: The clinical records were reviewed for all patients with biopsy-proven, muscle-invasive bladder cancer who received definitive radiation therapy (with or without chemotherapy), at our institution between January 2000 and December 2012. All patients had at least 3 months of oncologic follow up after treatment to be eligible. A total of 48 patients were eligible for assessment. Of these, 29 (60 %) patients were deemed to be medically inoperable, while the remaining 17 patients elected bladder-preservation therapy. Thirty-three (69 %) patients received concurrent chemotherapy; all but two of these patients received platinum-based regimens. The majority of patients received bladder and pelvic nodal radiation \( n=37 \) compared to bladder radiation alone \( n=11 \). Patients were staged according to AJCC 7th edition and were: 73 % stage II, 17 % stage III, and 10 % stage IV.

**Results:** The median follow-up was 17 months (interquartile range of 6–34.5 months). Median age was 80.2 years (overall range, 59–90); 39 (81 %) were male. The median dose to the bladder was 6480 cGy (range 5125–7250 cGy) and the median dose to the pelvic lymph nodes was 4500 cGy (range 3960–5000 cGy). There were 15 bladder, 4 pelvic, and 15 distant failures. All bladder failures were biopsy-proven. Of these, 8 were muscle-invasive disease versus 7 were only superficial or in situ failures. The 2-year local, pelvic, and distant control was 60, 88, and 66 %, respectively. Median overall survival was 33 months and 2-year overall survival was 60 %. Acute urinary and gastrointestinal (GI) toxicity (CTCAE grade 2 or greater) was seen in 30 and 19 % of patients, respectively. Late urinary and GI toxicity was 27 and 2 %, respectively.

**Conclusions:** The use of definitive radiation with or without chemotherapy for muscle-invasive bladder cancer is a reasonable option for patients who are medically inoperable or who desire bladder preservation.

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**Abstract #17**

**Long-term Follow Up Of Adaptive Multi-stage Stereotactic Radiosurgery For Treatment Of High Grade Arteriovenous Malformations**

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**Purpose:** To evaluate the safety and efficacy of multi-staged stereotactic radiosurgery (SRS) with treatment of the entire arteriovenous malformation (AVM) nidus to achieve complete obliteration of high-grade AVMs.

**Methodology:** Patients with high-grade Spetzler-Martin (S-M) III-V AVMs that were treated with at least two multi-stage SRS treatments from 1989 to 2013. Clinical outcomes of obliteration rate, major/minor adverse events (AE) and treatment data were collected. Patients with less than 12 months of follow up after second multi-stage SRS treatment were excluded.

**Results:** Forty-three patients met inclusion criteria \( n=27 \), S-M III; \( n=13 \), S-M IV; \( n=3 \), S-MV). Median follow up was 9.6 years after first SRS. Median number of staged SRS treatments was 2 and median interval between SRS treatment stages was 3.5 years. Median dose was 15 Gy per stage and cumulative median dose at last follow up or obliteration was 34 Gy. Twenty-three patients had prior embolization and two patients had incomplete resection before SRS.

Complete AVM obliteration rate was 40 %. Median volume reduction for non-obliterated AVMs was 64 %. A lower complete AVM obliteration rate was significantly associated with a higher S-M grade \( p=0.02 \). AVMs that underwent pre-SRS embolization had a trend towards a lower rate of obliteration \( p=0.06 \).
Thirty-one post-SRS AEs were observed: persistent headache (n=5), new/persistent seizures (n=13), post-SRS intracranial hemorrhage (n=8), neurologic deficits/TIA (n=4) and radiation necrosis (n=1). The post-SRS AE rate was 7.3 % per year after initial SRS. The major AE rate and post-SRS hemorrhage rate were 2.1 and 1.9 % per year, respectively.

**Conclusions:** Treatment of high-grade AVMs with multi-stage SRS to the entire nidus demonstrates AVM obliteration in a meaningful proportion of patients with acceptable AE rates. Lower obliteration rates were associated with higher S-M grade and pre-SRS embolization. This approach should be considered with caution as partial obliteration does not protect from hemorrhage.

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**Abstract #18**

Development and Implementation of a Weekly Nutrition Clinic for Head and Neck Cancer Patients

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**Purpose:** Locally advanced Head and Neck Cancer is often treated with concurrent chemotherapy and radiation therapy. We have previously published a retrospective analysis of 193 Head and Neck Cancer patients treated through our Multi-disciplinary clinic that revealed a 38 % hospitalization rate despite an 83 % PEG tube placement rate. The main reason for the admission was dehydration/malnutrition, leading to the conclusion that patients were not educated enough about their PEG tubes and need for tube feeding and that, our infrastructure for support was insufficient. Therefore a weekly nutrition clinic was implemented to address these issues.

**Methods:** The nutrition clinic consists of an initial 60 min post-PEG tube placement instruction with weekly visits by the Registered Dietitian. A nutrition panel and patient weights are monitored weekly in addition to evaluation of tolerance to tube feeding and compliance with the recommended tube feeding regimen. Patients were prospectively monitored and data on hospitalization rate due to dehydration and malnutrition, treatment interruption, and PEG tube complications were prospectively collected.

**Results:** At 1 year since the initiation of the clinic, 25 patients were enrolled, 18 of whom received concurrent chemo-radiation. Of these, 14 had a PEG tube placed, 12 prophylactically and 2 reactively. At this time, no long term data is available but short term evaluation show a decrease in hospitalization due to dehydration and malnutrition from 38 % in our published retrospective cohort to 17 % in this prospective cohort. Hospital stays were significantly shorter for the patients in the nutrition clinic cohort (median 4 days) compared with patients from the retrospective study (median hospital stay 7 days). The median length of stay for those hospitalized for dehydration or malnutrition versus other reasons was 3 versus 16.5 days respectively. One patient, who was status post kidney transplant and blind from diabetic retinopathy, died from apparent complications from hypoglycemia.

**Conclusions:** In this small prospective cohort of patients, early analysis of patients undergoing concurrent chemotherapy and radiation therapy for Head and Neck Cancer and enrolled in a pilot nutrition clinic program has shown shorter hospital stays and lower hospitalization rate for dehydration and malnutrition. More studies are need on how to prospectively manage patients undergoing treatment for head and neck cancer.

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**Abstract #19**

Is oncoplastic breast surgery changing patterns of delivery of adjuvant radiation treatments in a potentially risky way?

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**Background:** Most recurrences after Breast Conservative Surgery (BCS) are around the index lesion. That’s the rational for need of a radiotherapy (RT) boost to the tumor bed, as demonstrated on data of multiple randomized trials. Oncoplastic breast surgery (OBS) is an effort to improve cosmesis, which remolds breast tissue, making the tumor bed localization unreliable by images.

We wanted to know if adjuvant RT practice has changed as a consequence of OBS.

**Methods:** A search in PubMed and Ovid MEDLINE databases was carried out. Keywords: “Therapeutic Mammaplasty”, “OBS” from 2010 to 2014. Articles without specification about use of boost were excluded. Use of boost and tumor bed marking in OBS were analyzed and compared to the results of the 2014 survey from 271 radiation oncologists: “Radiation practice patterns among USA radiation oncologist (RO) for postmastectomy breast reconstruction and oncoplastic breast reduction (RT.OBS)”.

**Results:** We found 6 studies, totaling 1180 patients. Four studies didn’t reported clip-marking. Three of these four studies, didn’t give a boost to any of the OBS patients, and the other one, gave a boost only to the OBS patients with +/-close margins. The two studies that reported clips, gave a boost to the patients. The overall analysis showed that 71 % of the patients didn’t receive a boost treatment.

In the RT.OBS survey, 271 radiation oncologist from the USA completed the survey showing that 65.4 % of them didn’t give a boost to all the patients systematically, 8.3 % indicated never utilization of boost and 38.7 % only gave a boost to patients with clips marking the tumor bed. Only 33.1 % of respondents indicated that they routinely collaborate with surgeons for clip placement at the time of breast reduction or complex tissue rearrangement.

**Conclusions:** OBS seems to be changing the standard patterns of care of BCS which include adjuvant radiation treatment with a boost. For the PubMed and Medline articles, patients without clips and clear margins; 71 % of the 1180, didn’t received boost. These results correspond with the survey RT.OBS, which showed that 61.3 % of radiation oncologist didn’t boost patients receiving OBS with clips.

OBS is changing patterns of delivery of adjuvant RT, without long-term outcomes supporting its safety. While OBS is perceived by the surgeons as a technique to improve cosmesis, it appears to negatively impact radiotherapy techniques proven to achieve adequate local control.
Abstract #20

Stereotactic radiosurgery in the initial treatment of small brain metastases: local control and prognostic factors of diffuse distant brain failure

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Purpose: In patients with small brain metastases (1.00 cc), it is important to identify prognostic factors associated with diffuse distant brain failure (DDBF) and neurological death (ND) in order to treat them appropriately with either stereotactic radiosurgery (SRS) and/or whole brain radiotherapy (WBRT). Avoidance of diffuse intracranial disease versus the neurotoxicity concerns of WBRT is frequently a clinical challenge that is often weighed in each case. We investigated the use of initial SRS (iSRS) in the management for patients with small brain lesions for local-control (LC) and the detection of patients at higher risk for DDBF and ND.

Methodology: A retrospective review from 2004 to 2014 identified 191 patients with 342 small brain metastases (1.00 cc) treated with iSRS. These patients had a median of 1 (range 1–8) brain metastases treated with iSRS. Kaplan-Meier estimates were calculated from date of iSRS for overall survival (OS), DDBF (defined as 4 or more new brain metastases at sequential imaging or intracranial leptomeningeal disease), any distant brain failure, and local failure. Cox proportional hazards modeling was conducted to establish prognostic factors (p<0.05) from the time of iSRS.

Results: With a median follow-up of 5.7 months from iSRS, median survival was 7.1 months (range 0.16–110.3) with 6- and 12-month OS of 56.7 and 34.2 %, respectively. Multivariate analysis showed reduced OS with lower KPS (HR 0.95, p<0.01) and melanoma (HR 1.97, p<0.01). Presence of systemic progression (HR 0.65, p=0.06) and extracranial metastases (HR 1.67, p=0.06) had borderline significance in OS. Cause of death was attributed as neurological death (ND) in 14.1 %, systemic failure 59.2 %, or unknown 11.0 %, with the remaining 15.7 % alive at analysis. Univariate analysis revealed ND was associated with melanoma histology (p<0.01) and 4 or more brain metastases treated at iSRS (p=0.05). DDBF occurred in 40 patients (20.9 %) with 36 (18.8 %) undergoing WBRT. The 6- and 12-month estimates for diffuse distant brain control were 83.2 and 74.1 %, respectively. On univariate analysis, extracranial metastases (p=0.03), 4 or more brain metastases at iSRS (p=0.02) and melanoma (p<0.01) were significantly associated with DDBF. Eighty-six (45.0 %) of the patients developed additional intracranial disease with 6- and 12-months intracranial progression-free estimates of 61.8 and 40.2 %, respectively. LC at 6- and 12-months was 94.3 and 88.2 %, respectively. Treatment volumes ~0.50 cc were associated with increased local-failure (p=0.01).

Conclusions: Upfront SRS provides excellent LC for small brain metastases. A subset of patients still have a higher risk of developing diffuse intracranial brain failure following SRS. Patients with multiple small brain metastases, extracranial metastatic disease, or melanoma may require increased surveillance and/or use of WBRT to prevent diffuse distant brain failure and neurological death.

Abstract #21

Is there prognostic value for risk stratification by NCCN guidelines version 1.2015 for localized prostate cancer treated with stereotactic body radiation therapy?

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Purpose: To update our experience using stereotactic body radiation therapy (SBRT) for the primary treatment of prostate cancer, risk stratified by the newly updated National Comprehensive Cancer Network (NCCN) guidelines, Version 1.2015, reporting efficacy in a community hospital setting.

Methods: From 2007 to 2012, 150 localized prostate cancer patients were treated with SBRT using Cyberknife. NCCN guidelines Version 1.2015 were analyzed which included very low (21 %), low (23 %), intermediate (35 %), high (18 %), and very high (3 %) risk groups. Additional pretreatment and treatment factors analyzed included race (African American, Caucasian, and other), pre-treatment PSA (<10 ng/mL, 10–20 ng/mL, >20 ng/mL) age at diagnosis (<60 years, >60 years), Gleason score (5–6), (7, ≥8), T-stage, use of androgen deprivation therapy (any use vs. no use) and dose (low 35Gy or 36.25Gy, high 37.5Gy). All treatments were delivered in five fractions. Kaplan-Meier estimates for freedom from biochemical failure (FFBF) were used to describe the patients overall, with log rank comparison.

Results: Five year FFBF for all men was 91.14 % with a median follow up time of 43.5 months. Five year FFBF was 100, 100, 86.9, 92.3, and 50 % for very low, low, intermediate, high, and very high risk patients respectively (p<0.0001). A significant improvement in FFBF was noted for high dose (100 %) vs. low dose (69.7 %) (p=0.0055), while a decrement was noted for Gleason score ≥5 (50 %) compared to 7 (84.7 %), and 5/6 (94.4 %). T-stage, use of androgen deprivation therapy, age at diagnosis, pre-treatment PSA and race did not affect FFBF rates. If very high risk patients are excluded from analysis, NCCN risk groups (very low, low, intermediate and high risk) and Gleason score were no longer significant for FFBF while dose remained significant.

Conclusions: Our updated SBRT experience for the primary treatment of localized prostate cancer demonstrates continued efficacy which compares favorably to the results reported for IMRT in the literature. The risk stratification used in the new NCCN guidelines version 1.2015 promotes stage migration with only the very highest risk group with significant decrement in survival. Exclusion of the very high risk group produces a more homogeneous group with excellent FFBF whether very low, low, intermediate or high risk.

Abstract #23

The effect of higher BEDs for optimal local control of lung metastases treated with CyberKnife SBRT

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Introduction: Stereotactic body radiation therapy (SBRT) is the standard non-surgical treatment modality for early-stage non-small cell lung
cancer. Limited retrospective data exists however with SBRT for non-surgical treatment of metastatic lung disease. We report our institutional experience with lung metastases from all primary sites excluding primary lung cancer with special emphasis on treatment factors particularly dose.

**Methodology:** From January 2008 to April 2014, 51 patients (median age of 64) with 67 metastatic lung lesions received CyberKnife high-dose SBRT (45–60 Gy in 3–5 fractions). All patients had at least 2 months follow up and CT of the Chest or PET/CT to assess local control. The 67 metastases arose from various primaries including; colorectal (n=24), renal (n=12), breast (n=8), head and neck (n=6), melanoma (n=6), uro-genital (n=6), GI (n=2), liver (n=2), and pancreas (n=1). Biologically effective dose (BED) calculations were performed for each tumor utilizing an alpha/beta ratio of 10 Gy. Variables assessed for outcome included age at SBRT, primary site, stage at initial diagnosis, time from initial diagnosis to SBRT, CTV size, number of lung metastases, BED, tracking method, central vs. peripheral presentation and dose calculation method. Toxicity assessment utilized RTOG Late Radiation Morbidity Scoring Schema. Kaplan Meier survival and local control curves were generated with GraphPad Prism and comparison of curves utilized log rank testing.

**Results:** Median age of the entire cohort was 64 years (range of 31 to 87). Actuarial overall survival (OS) and disease free survival (DFS) rates at 2 years for all patients were 59.6 and 52.3 % and at 3 years 44.9 and 28.8 % respectively. The median OS was 28.7 months and the median DFS was 26.1 months. Actuarial local control (LC) at both 2 and 3 years was 82.2 % respectively, with 11 treated lesions failing locally. Tumors receiving BED above 100 Gy10 (n=59) had higher rates of local control at 2 and 3 years than tumors receiving 100 Gy10 or less (n=8, 2 year LC rate of 86.7 vs 44.4 %, with no change at 3 years p=0.0017). No other factors analyzed were significant for local control in univariate analysis.

**Conclusions:** Due to limited published literature for SBRT of lung metastases, very little is known regarding dose response for local control. Our data suggests local control is improved with SBRT doses above BED above 100 Gy10 (82.2 % respectively, with 11 treated lesions failing locally. Tumors receiving BED above 100 Gy10 (n=59) had higher rates of local control at 2 and 3 years than tumors receiving 100 Gy10 or less (n=8, 2 year LC rate of 86.7 vs 44.4 %, with no change at 3 years p=0.0017). No other factors analyzed were significant for local control in univariate analysis.

No cases of grade ≥3 toxicity were observed.

**Abstract #25**

The nature of medical malpractice claims in radiation oncology from 1985–2012

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**Purpose:** We aim to determine the nature of radiation oncology malpractice claims closed during the last 28 years.

**Methodology:** We retrospectively analyzed malpractice claims filed against radiation oncologists from 1985 to 2012 collected by a nationwide liability insurance trade association. We analyzed the nature of claims and indemnity payments, including associated presenting diagnoses, procedures, alleged medical errors, and injury severity. Dollar amounts were adjusted for inflation (2012 index year).

**Results:** There were 1517 closed claims involving RO, 342 (23 %) of which were paid resulting in $95 million in indemnity payments. Average and median indemnity payments were $276,792 and $122,500, respectively. The most common alleged errors included: ‘errors in diagnosis’ (32 % of closed claims, 33 % of which were paid; 51 % ($49 million) of total indemnity); ‘no medical misadventure’ (27 % of closed claims, 3 % of which were paid; 1 % of total indemnity); and, ‘improper performance’ (20 % of closed claims, 25 % of which were paid; 22 % ($21 million) of total indemnity).

The largest proportions of closed claims attributable to single diagnosis were for invasive breast cancer (5 %) and invasive lung cancer (4 %). ‘Errors in diagnosis’ resulting in death represents the largest proportion of total indemnity attributed to an alleged error (17 %, $16 million). Analysis of RO claims by injury severity show ‘emotional injury only’ and ‘insignificant injury’ representing a small proportion of claims (2 % of closed claims and <1 % of total indemnity, for both). Temporary injury accounts for 27 % of closed claims and 14 % of total indemnity. Minor/significant permanent injury (26 % of closed claims, 23 % of total indemnity) and major permanent injury (9 % of closed claims, 17 % of total indemnity) represent a large proportion of closed claims. Grave injury (6 % of closed claims, 19 % of...
total indemnity) and death (28% of closed claims, 27% of total indemnity) represent a large proportion of total indemnity. The proportion of claims resulting in payment for death was 19% (vs. 39% for grave injury), as compared to 10% and 8% for emotional or insignificant injuries, respectively. ‘No medical misadventure’ was the primary alleged error for less severe injuries (emotional, insignificant, and temporary injury). ‘Error in diagnosis’ was the most common alleged error for permanent injury, grave injury and death. Invasive malignancies of the female breast were the top presenting diagnoses for emotional, insignificant, major temporary, and all permanent injuries. Vertebral column fractures and invasive lung cancer were the most common diagnoses in grave injury. The most common diagnoses in death included invasive lung cancer and neoplasms of the back, flank or trunk with an unspecified point of origin.

Conclusions: These insights into the nature of liability claims against radiation oncologists can help to guide efforts in improving quality of care, improving patient safety and controlling costs.

Abstract #26

**Dosimetric Comparison of Intensity Modulated Radiation Therapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) for Stereotactic Body Radiation Therapy (SBRT) in Early Stage Lung Cancer**

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**Purpose:** Radiation alone for medically inoperable early stage lung cancer using conventional techniques has historically resulted in high rates of local failure. The advent of dose escalation and stereotactic body radiotherapy (SBRT) has reduced the rates of local failure. Techniques used to treat with SBRT continue to evolve. Recently volumetric modulated arc therapy (VMAT) has become a prevalent modality of treatment as opposed to intensity modulated radiation therapy (IMRT) with the premise of superior target coverage and avoidance of critical structures. This study was performed to evaluate the dosimetric differences using VMAT in patients previously treated with IMRT for SBRT in early stage lung cancer.

**Methodology:** We evaluated 10 consecutive medically inoperable lung cancer patients at the start of the SBRT program who were treated with IMRT from November 2010 to October 2011. These patients were treated using 6 MV energy. The 10 cases were then re-planned with VMAT performed with arc therapy using 6 MV energy. Target coverage, conformity, dose to organs at risk (OARs), and monitor units per plan were recorded. Conformality was defined as the volume receiving the prescribed dose divided by the volume of the planning treatment volume (PTV). The PTV was derived from the gross tumor volume (GTV) with a 5 mm expansion in all directions.

**Results:** Five patients were T1N0 and five patients were T2N0 with all tumors less than 5 cm. The mean age of patients was 72.6 (57–83). Six patients with peripheral tumors (2 cm from proximal bronchial tree) received 48 Gy in four fractions and four patients with central tumors received 50 Gy in five fractions. The average GTV was 14.92 cm3 (0.83–40.87) and average PTV was 43.57 cm3 (14.06–118.08). The IMRT plans had a mean of 7.1 angles (6–9) and 3242 monitor units (MUs) (2662–3534) per plan. The VMAT plans had a mean of 2.7 arcs (2–3) and 2585 MUs (1520–3053) per plan. VMAT had slightly more target coverage than IMRT with average increase in D95 of 2.53% (1.24–5.73) and D99 of 3.73% (0.88–8.77). The conformity was better for VMAT versus IMRT by an average of 28.63% (12.07–56). For OARs, VMAT produced lower doses to all critical structures. The largest reductions were in the maximum doses to the spinal cord with an average reduction of 26.2%, the esophagus with an average reduction of 20.8%, and the lung with an average reduction in the V20 of 15.83%. VMAT also produced lower doses away from the target with PTv+2 cm dose 12.39% less on average versus IMRT (1.36–25).

**Conclusion:** These findings suggest that using VMAT for SBRT in early stage lung cancer is superior to IMRT in terms of dose coverage, conformity, and in reduction of maximal dose to organs at risk.

Abstract #27

**Prognostic index for patients receiving CyberKnife-delivered stereotactic radiosurgery (SRS) for second brain metastatic event**

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**Objective:** While there exist multiple diagnosis-specific survival prediction tools for patients presenting with initial brain metastasis, survival data for patients experiencing a second brain metastatic event is lacking. The purpose of the present study is to develop a survival prediction index for patients receiving CyberKnife stereotactic radiosurgery (SRS) for second brain metastatic event (SBME) following initial treatment with whole brain irradiation (WBI), surgical resection, or previous SRS.

**Methods:** All patients treated for brain metastasis at Philadelphia CyberKnife between January 2006 and October 2013 were reviewed. Of the 148 patients in this review, 57 were excluded for first brain metastasis treatment or SRS boost and three were excluded for lack of follow-up, resulting in a study group of 88 patients. Patient demographics, first brain metastasis treatment history, and CyberKnife treatment statistics were compiled along with follow-up/survival data. Cox proportional-hazards multivariable modeling was used to identify significant factors impacting survival from the time of CyberKnife SRS for SBME. Predictors included primary disease, first brain metastasis treatment type, age, gender, number of brain metastases at SBME, Karnofsky performance score (KPS), and presence of extracranial metastasis.

**Results:** The median survival for all patients was 7.31 months. Primary cancers included lung (n=50), breast (n=16), colorectal (n=8), melanoma (n=6), renal cell (n=3), gynecologic (n=3), mesothelioma (n=1), and sarcoma (n=1). Median patient age was 59.3 years at time of SBME treatment with 35% male (n=31) and 65% female (n=57). Median dose was 20 Gy (13.5 Gy–30 Gy) delivered in 1 fraction (1–5 fractions). Log-rank comparison of Kaplan-Meier survival curves revealed significant differences in outcome by Karnofsky performance status (p=0.006) and first brain metastasis treatment type (p=0.008). There was increased median survival for patients who had not previously received WBI (14.7 months). Median survival was further increased in patients who had not received previous WBI and demonstrated KPS scores of 70–100 (19.5 months). Patients who received WBI prior to SBME treatment experienced a pronounced decrement in median survival (5.7 months), yet patients in this group who demonstrated strong KPS scores (80–100) experienced significantly increased survival (15.5 months).

**Conclusions:** These findings indicate that outcomes are most favorable for patients who have not received previous WBI or who have maintained strong performance status despite previous WBI. Primary cancer type, number of brain metastases, and presence of extracranial metastasis were not found to be significant predictors of survival from SBME despite their impact on survival from first brain metastasis reported in previous studies.
Due to a lack of national data on SBME treatment with SRS, further research is necessary to support these findings and develop a reliable survival estimation tool for patients receiving SRS for a second brain metastatic event.

Abstract #28

Radiation oncology externship selection: Fourth-year medical student motivations and associated implications

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Purpose: Clerkships for fourth-year medical students (MS4s) are an opportunity to gain experience in radiation oncology and evaluate residency programs. Despite this traditional rationale, MS4s may be completing additional clerkships primarily to audition for residency or to obtain letters of recommendation. Previous studies have shown that as MS4s complete more clerkships, their confidence with their decision to pursue radiation oncology as a career or to function as a radiation oncology resident does not increase. A survey was conducted to understand the basis upon which MS4s choose institutions for their clerkships.

Methods: After obtaining IRB approval, an anonymous, internet-based survey was emailed to all MS4s who applied to a single institution after the National Residency Matching Program rank list deadline during the 2013–14 academic year. The survey included questions regarding the number of clerkships students completed (1–5), setting of the radiation oncology facility (university medical center, academic medical center not affiliated with a medical school, community practice, or other), duration (1–4 weeks or other), and the primary reason for choosing each clerkship site (home institution, unique educational/research/technological opportunities, specific faculty members, historical prominence, to obtain letters of recommendation, to evaluate the residency program, to impress the faculty, or to explore an interesting location).

Results: The survey response rate was 39.6 % (78/197). Respondents were 77 % MD students, 19 % MD/PhD, 1 % DO, and 3 % other. Respondents reported information on 189 clerkship experiences. Of the respondents, 14, 29, 38, 14, and 4 % completed one, two, three, four, and five clerkships, respectively. MS4s chose their first clerkship site primarily because it was their home institution (81 %). Only 9 % of MS4s reported choosing their second clerkship primarily because it was their home institution. For the second clerkship, the MS4s’ most commonly cited motivation was “to impress the faculty to obtain a residency” position (26 %) followed by “to evaluate the residency program” (19 %), “to obtain letters of recommendation” (13 %), and to explore a particular location (13 %). Students who completed third and fourth clerkships also commonly reported motivation “to impress the faculty to obtain a residency” (third=44 %, fourth=50 %) and “to evaluate the residency program” (third=23 %, fourth=20 %). Selecting sites for unique educational, research, or technological opportunities was the motivation for 3, 12, 9, and 10 % of students on their first, second, third, and fourth clerkships, respectively.

Conclusions: A large proportion of MS4s complete clinical clerkships with a focus on their upcoming residency applications. Faculty who advise students considering a career in radiation oncology may want to encourage students to consider the educational value of clerkship sites in addition to potential impact on their residency application. Consideration also could be given to pursuit of clerkships in other oncologic disciplines to learn how radiation oncology integrates into optimal multi-disciplinary cancer care.

Abstract #29*

The Efficacy of Radiotherapy for Dupuytren’s Contracture and Morbus Ledderhose

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Purpose: Radiation Therapy (RT) has been shown to improve symptoms and decrease progression of Dupuytren’s Contracture (DC) and Morbus Ledderhose (ML). In the USA it is a successful treatment which is underutilized. We examined the experience and outcomes of patients treated at our facility.

Methods: 31 pts (14 males, 17 females) have been treated. All were mailed an informed consent and questionnaire to complete and return. Seventeen pts (55 %) responded, of which 40 sites were treated including 28 hands (70 %) and 12 ft (30 %). Utilizing the revised Tubiana’s Staging System, 18 had stage N, 5 had stage 1 and 2 had stage 2. RT was delivered with 6–12 MeV electron therapy with customized blocking and bolus. Treatment was 3Gy per fxn x 7 fxns in 5 days to a total dose of 21Gy. One hundred percent of the patients received the planned dose. Median post tx evaluation time was 28 months and the mean was 35 months (range 8–67 months).

Results: No pts had progression of flexion deformity or contraction after RT. There was a decrease or stabilization of DC or ML symptoms in 14 pts (82 %) with a treatment failure rate (progression of symptoms) of 18 %. Twelve percent of patients returned 5 months and 21 months after initial treatment for a second treatment. None of the patients had any additional txt for their DC or ML after RT. Acute toxicities of skin tenderness, redness, peeling, blistering or mild pain were experienced by 8 pts (50 %) with 88 % reporting mild symptoms and 1 reporting moderate symptoms. Chronic side effects of tightness of skin, dryness or thickening, swelling, worsened hand strength, decreased sensation were experienced by 5 pts (31 %). There was reduction of pretreatment symptoms (poor hand grip, reduced hand strength, decreased sensation) in 3 pts. Pretreatment pain was reported by 6 pts with DC and 5 pts with ML. One hundred percent, had reduction or complete disappearance of pain after RT. One pt had disappearance of nodules. Seven pts (58 %) had decreased size of nodules, 2 pts (17 %) had stable nodules. Two patients (17 %) had progression. 5 (56 %) reported improvement of cords, 2 (22 %) had stabilization, and 2 pts (22 %) had progression. 50 % of pts reported improvement in flexion deformity, the other 50 % reported stabilization.

Conclusions: RT remains an underutilized, successful treatment method for DC and ML. Our experience demonstrates success in prevention of disease progression or reduction of symptoms.
Our experience demonstrates RT is very effective in stopping progression of flexion deformity and eliminating or decreasing the symptom of pain.


Abstract #30

Impact of an Empty Bladder on IMRT Treatment Planning for Cervical Cancer

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Purpose: To determine whether giving patients instructions to have an empty bladder at the time of intensity modulated radiotherapy (IMRT) for intact cervical cancer has a greater reproducibility with at least an equal sparing of healthy tissue, particularly small bowel, when compared to instructing patients to arrive for treatment with a comfortably full bladder, or not giving any instructions at all.

Methods: IRB-approved retrospective review of patients with intact locally advanced cervical cancer treated with IMRT at UCSD from May 2010 to May 2013. Each patient underwent 2 planning CT scans, one with a comfortably full bladder followed by one with an empty bladder. All patients had daily cone-beam CT (CBCT) scans for image guidance, on which bladder contours were drawn to calculate interfraction variation in bladder volume. To compare radiation dose to normal tissue with empty versus full bladder instructions, plans were created on both simulation CT scans using an automated knowledge-based planning (KBP) modeling program, a technique that has been previously used in other disease sites, and is validated in gynecologic cancer as part of this study. Dose to small bowel was evaluated using average bowel V45, per dose constraints defined in QUANTEC. Statistical analysis was performed using student’s t-test and linear regression.

Results: Twenty-nine patients were included in this study, of which 20 patients were given empty bladder instructions, 3 patients were given full bladder instructions, and 6 patients were given no instructions. The mean bladder volume at time of treatment planning as contoured on simulation CT scans was 79 cc for empty bladder plans (range 22–257 cc) and 226 cc for full bladder plans (range 55–656 cc). The mean bladder volume on empty bladder CBCTs was 67±22 cc, compared to 154±38 cc for full bladder, and 89±39 cc for no bladder instructions (p<0.0001). Compared to bladder volume on planning CT, mean percentage range of bladder volume was 130, 135, and 331 %, respectively. In the KBP-created plans, the average bowel V45 for the empty bladder plans was 190 cc, while the average for the full bladder plans was 134 cc (p<0.05). Nineteen patients had a lower bowel V45 in the KBP full bladder plan as compared to the corresponding empty bladder plan.

Conclusions: Patients given empty bladder instructions have higher bladder volume reproducibility throughout radiation treatments when compared to: 1) patients given full bladder instructions in prior studies and 2) patients given no instructions at all in this study. However, treating on an empty bladder results in a predicted DVH with a larger volume of bowel.

Abstract #31*

Locally Advanced Non-Small Cell Lung Cancer: Do Elderly Patients Reap the Benefits of Combined Modality Therapy?

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Purpose: To review our institution’s experience among patients with locally advanced non-small cell lung (LA-NSCLC) cancer treated with chemotherapy and radiation, and to determine the prognostic significance of age.

Methodology: An IRB-approved, retrospective study of patients treated from 2006–2014 for LA-NSCLC with radiation and chemotherapy was performed. Patients were included if they underwent either sequential or concurrent chemoradiotherapy. Medical records were reviewed to obtain clinical, radiographic, and pathologic data. Patients were stratified by age <70 and ≥70 years old. Kaplan-Meier survival analysis was performed to compare the overall survival (OS) and progression free survival (PFS) of the two patient groups. A two-tailed t-test was used to determine a difference in radiation pneumonitis rates between the two groups.

Results: One hundred and twenty-three patients were identified. The median age was 61 (range 40–90); 53 patients (43.1 %) were men. Ninety-seven patients were <70, whereas 26 patients were ≥70 years old. Five patients were included with stage IIB, 79 with IIIA, and 39 with IIB disease. The median radiotherapy dose was 6660 cGy (3780–7600 cGy). Chemotherapy regimens consisted of cisplatin/etoposide (n=54), carboplatin/paclitaxel (n=35), carboplatin/pemetrexed (n=30), gemcitabine (n=3), and erlotinib (n=1). For patients <70 years old, twenty-five (26 %) received sequential treatment, 34 (35 %) received neoadjuvant chemotherapy followed by concurrent chemoradiation, and 38 (39 %) received concurrent chemoradiotherapy alone. For patients ≥70, nine (35 %) received sequential treatment, 7 (27 %) received neoadjuvant chemotherapy followed by concurrent chemoradiation, and 10 (38 %) received concurrent chemoradiotherapy alone. In patients <70 years old, 40.2 % had adenocarcinoma, 44.3 % squamous cell carcinoma (SCC), 3.1 % large cell carcinoma, and 12.4 % with undifferentiated NSCLC. In patients ≥70 years old, 42.3 % had adenocarcinoma and 57.7 % had SCC. A higher percentage of elderly patients were men (73.1 versus 35.1 %) and received carboplatin/paclitaxel based chemotherapy (57.8 versus 20.6 %). Median follow-up was 15.4 months. There was no difference in outcomes based on age. The median PFS for patients <70 and ≥70 years old was 13.3 and 13.7 months, respectively (p=0.75). The median OS for patients <70 and ≥70 years old was 20 and 16.4 months, respectively (p=0.026). The rate of symptomatic pneumonitis was significantly higher in the elderly group, 42.3 versus 22.7 % in the younger cohort (p=0.03). For the entire population, there was no difference in pneumonitis based on chemotherapy regimens. The mean total lung V5, V20, and mean lung dose (MLD) did not differ significantly based on age. The V5, V20, and MLD were 41.5, 27.4, and 16.3 % for patients <70 and 41.0, 25.0, and 15.5 % for patients ≥70 years old.

Conclusions: Despite a higher rate of treatment-related pneumonitis, chemoradiotherapy is an effective treatment in elderly patients with LANSCLC, with outcomes similar to younger patients. Appropriately
An Ultra-Compact, Variable Energy, Continuous Wave, Fixed-Field Alternating Gradient Accelerator (FFAG) for Charged Particle Radiation Therapy

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Introduction: FFAG (Fixed-Field Alternating-Gradient) accelerators are a class of accelerators that merge the best features of cyclotrons and synchrotrons in that they deliver continuous beam in combination with low loss operation and variable energy. The FFAG blends the fixed fields of cyclotrons and the strong focusing of synchrotrons. Modern non-scaling FFAG designs incorporate several potentially useful features including isochronous orbits. This allows use of a fixed Radio-Frequency (RF) system along with continuous beam for maximum flexibility in real-time imaging and pencil-beam scanning. Constant tune would allow high intensities and efficient extraction with low losses. Straight sections might allow for flexibility in injection and variable energy extraction. These FFAG design features appear very well matched to the requirements of a next-generation ion beam therapy system and appear potentially very economical as well.

No FFAGs have been designed or built specifically for radiation therapy. We have been evaluating the potential of a new design for an ultra compact, variable-energy, non-scaling, isochronous FFAG for ion therapy.

Materials & Methods: We compared the capabilities of FFAG accelerator designs to the requirements for future ion beam therapy systems identified in a workshop hosted by the U. S. National Cancer Institute and Department of Energy. These requirements included the ability to deliver multiple light ion types (protons, deuterons, helium, carbon, possibly up to neon), short deposition times with image-guidance and real-time measurements of patient parameters, rapid beam scanning and energy modulation, with energies up to 430 MeV/nucleon, and with all components optimized for effective and safe operation.

Results: Analysis shows that an isochronous, non-scaling, (i.e., continuous wave or continuous beam) FFAG could have great potential as a highly compact and economically viable alternative to synchrotrons, cyclotrons, linear accelerators and cyclinacs for next-generation ion beam radiation therapy. The fixed fields and fixed RF simplify operations compared to synchrotrons which must ramp fields in coordination with swept RF. The injector could be a lower-energy FFAG which in principle can serve as a standalone accelerator for certain treatments (e.g., ocular melanoma) or could be used to accelerate protons to ~300 MeV for proton Computed Tomography (pCT).

Conclusions: We have designed a 90–430 MeV/nucleon FFAG in a racetrack layout that supports two opposing long straight sections for rapid acceleration and efficient injection and extraction, in a highly compact (~4 × 6 m) footprint with a total weight of ~20 t. This FFAG can accelerate ions with a charge to mass ratio of 1:2 (e.g., H2, He, B, Li, C) and appears ideal for radiation therapy. The long synchrotron-like straight sections permit rapid variable energy extraction on the timescale of microseconds eliminating the need for a substantive beam degrader. This system is under international development and details will be presented here.

Abstract #33*

Circadian variation in radiation induced mucositis in head and neck malignancies - Retrospective analysis

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Purpose and Objective: Concurrent chemoradiation has been the mainstay of treatment in head and neck malignancies for the past three decades. Normal tissue toxicity particularly mucositis has been a limiting factor. The purpose of our study is to investigate and analyse the role of circadian variation in the development of radiation induced mucositis, retrospectively. We wish to ascertain whether morning RT was beneficial in decreasing the severity of mucositis and reducing the number of treatment interruptions due to toxicity.

Material and Methods: We analysed the data of 142 patients of histologically proven squamous cell carcinoma of the head and neck sites (stage II to IVA), who underwent radical RT to a dose of 60–66 Gy in 30–33 fractions, out of which 73 patients underwent RT between 8 am to 11 am and 69 patients between 5 pm to 8 pm. The subsites analysed were oral cavity, oropharynx and nasopharynx. All the patients were treated with Cobalt 60, lateral parallel pair (60–66 Gy/33 #) and low anterior neck (50 Gy/25 #). The highest grade of mucositis by RTOG criteria and other relevant variables were noted. All the statistical analysis was done using SPSS version 16.0 software.

Results: Of the analysed 142 patients, 42.47 vs 60.9 % developed RTOG Grade 3 or 4 mucositis [severe] after morning vs evening RT, respectively (p=0.028) and the median time to development of severe mucositis was prolonged in the morning group (6 vs 5 weeks). Morning RT was also associated with significantly lesser no of patients for whom treatment had to be interrupted due to severe mucositis 17.8 vs 42.0 % (p=0.002). 62.7 % of the patients who smoked (n=67) during RT, developed severe mucositis compared to 41.3 % who didn’t smoke (p=0.011). Of the 76 patients, who received concurrent chemotherapy, 68.4 % developed severe mucositis, whereas only 31.8 % of patients who didn’t receive developed severe mucositis (p=0.0001).

Conclusions: Our analysis has shown a statistically significant decrease in the development of severe mucositis when RT is delivered in the morning hours when compared to afternoon. Treatment interruptions were significantly lower in the morning group. Smoking and concurrent chemoradiation are risk factors for development of severe mucositis. Limiting normal tissue toxicity is critical and the radiobiological potential of circadian rhythm in that aspect need to be studied in detail.

References:
- BJARNSON et al., Int. J. Radiation Oncology Biol 2009; 73
Abstract #38*

Currently accepted standard.

Conclusions:

Change in tumor volume was unknown in 4 (8 %) patients. Patients showed significant growth of their CSM at last follow-up, and the increase in tumor volume and 14 (26 %) patients with stable lesions. Eleven (21 %) patients had tumor recurrence prior to FCRT. After a median follow-up of 89 (45.0) cm³ before FCRT. FCRT was delivered in 30 (17–56) fractions at 1.8 (1.8–5.0) Gy/fraction at an isodose line of 90 % (70–100 %). The total radiation dose delivered to the patients’ CSM was 54.0 (50.4–50.8) Gy. Radiotherapy was delivered stereotactically in 45 (85 %) patients, by conventional external beam in seven (13 %) patients, and via an unknown mechanism in one (2 %) patient. Approximately half of the patients (n=27, 51 %) received previous treatment of their CSM prior to FCRT; 27 (51 %) patients had a history of surgical resection and 4 (8 %) patients received previous radiation. Of the 27 patients who received FCRT as a secondary treatment modality, 21 (78 %) patients had tumor recurrence prior to FCRT. After a median follow-up of 89 (1–276) months, 10 (19 %) patients experienced clinical improvement, 26 (49 %) patients remained clinically stable, and 13 (25 %) patients had worsening of their presenting symptoms. Clinical outcome at last follow-up was unknown in 4 (8 %) patients. Radiation-induced cranial neuropathy was observed in 10 (19 %) patients. Long-term tumor control was achieved in 38 (72 %) patients, with 24 (45 %) patients displaying shrinkage in tumor volume and 14 (26 %) patients with stable lesions. Eleven (21 %) patients showed significant growth of their CSM at last follow-up, and the change in tumor volume was unknown in 4 (8 %) patients.

Conclusions: FCRT offers effective long-term tumor control and a favorable clinical outcome. However, tumor progression may occur after several years of stability, suggesting the need for a longer follow-up than the currently accepted standard.

Abstract #38*

Preliminary Report of proton therapy for first four patients with lung cancer using active scanning beam

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Purpose: To assess the safety and efficacy of proton therapy for patients with lung cancer using IONTRIS active beam scanning technique

Methods and materials: Between July and September in 2014, four patients with lung cancer were treated in our center. All participants provided written informed consent before treatment. Breath control techniques (gating or ABC-active breath control) and 4-dimensional simulation CT were used to minimize the impact of tumor motion caused by respiration. Gating window was determined to reach residual motion of less than 6 mm based on the amplitude of individual respiration. The internal tumor volume (ITV) was obtained by combining the gross tumor volumes (GTV) at different respiratory phases within the gating window. PET-CT scan without tracer injection was performed to verify the position accuracy within 10 min after the completion of each plan’s first treatment.

Results: Four patients (5 lesions) received proton radiotherapy, 3 with primary stage I non-small cell lung cancer (NSCLC), and 1 with both hilar metastasis from sigmoid colon cancer. For motion control, three of them used gating system and 1 used ABC. Tumor sizes were from 1.9 to 4.2 cm. Prescription doses to CTVs were 60 or 63 Gy (equaled BED10 89–96 GyE) in 10 or 15 fractions for patients with primary NSCLC, which were delivered once a day, 5 days a week. The patient with both sides of hilar metastasis was given a total dose of 48 GyE in 15 fractions. Each side was treated once daily and at least 6 h interval was required between 2 deliveries. Ten scans of verification PET-CT were conducted after irradiation, and all of them showed acceptable patient positions by raw eyes of both physicians’ and physicists’. All patients’ last follow-ups were 12 weeks after proton therapy. Two of them achieved PR (partial response), and another 2 were SD (stable disease) per RECIST v1.0. Among the three patients who had both pre- and post-treatment diagnostic PET-CT scans, all of them achieved partial metabolic response (PMR) and one of them was SD per RECIST. Acute CTCAE v4.0 Grade 1 skin toxicities related to proton therapy were observed in 2 patients. One Grade 1 leukocytosis was observed, which only transiently appeared at the follow-up 4-week after treatment. No Grade 2 or higher acute toxicities were observed.

Conclusions: Preliminary results from this study indicated the safety and efficacy of proton-beam radiotherapy in terms of acute toxicity (using beam scanning technique by IONTRIS facility combined with breath control techniques) for patients with inoperable lung cancer. Due to the extremely limited number of cases, further researches with more patients enrolled are warranted.

Abstract #39*

Concurrent Radiotherapy with Cetuximab or Platinum-based Chemotherapy for Locally Advanced Cutaneous Squamous Cell Carcinoma of the Head and Neck

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Objective: There is growing interest in combining radiotherapy (RT) with concurrent cetuximab (Cx) or platinum-based chemotherapy (Pt) to improve outcomes in patients with high-risk cutaneous squamous cell carcinoma of the head and neck (cSCCHN). Data on this approach is scarce and largely retrospective. The objective of this study is to review outcomes for patients with locally advanced and/or unresectable cSCCHN treated at our institution with RT and concurrent Cx or Pt.

Methods: From Jan 2007 to Jan 2014, we identified 23 patients treated at our institution fitting the above criteria. All patients were being treated for recurrent cSCCHN. Treatment-related toxicity was scored using CTCAE version 4.0.

Results: Mean follow-up was 24 months (range 3–87). Median age was 71 in the Cx group and 59 in the Pt group (p=0.04). Aside from age, there were no significant differences between the two treatment groups. Most of the patients (91 %) were male, 9 % were immunosuppressed, 22 % presented with cranial nerve palsy. The majority (87 %) of patients had stage III/IV disease. Treatment for all patients consisted of concurrent RT with either Cx (35 %) or Pt (65 %) for either definitive (48 %) or adjuvant (52 %) purposes. The patients who underwent surgery had the following tumor characteristics: 92 % node positive, 58 % poorly differentiated, 33 % perineural invasion, 33 % close or positive resection margins. Median RT dose was 60 Gy (range 50–70). Incidences of RT and systemic therapy delay or modification were 30 % in the Cx group and 48 % in the Pt group. There were no treatment-related grade 4 or 5 toxicities. Incidence of grade 2–3 acneiform rash was significantly higher in the Cx group (63 % Cx vs. 0 % Pt, p=0.03).

At time of analysis, local recurrence or progression was observed in 63 and 47 % of patients in the Cx and Pt groups, respectively (p=0.67); distant
Purpose/Objective(s): Wisconsin at La Crosse, College of Science and Health, Medical shifts than those of patients with a small rectal planning.

Conclusions: Concurrent RT with either Cx or Pt appears to offer N. Although study size is limited, our findings suggest that choice and overall survival in the Cx vs. Pt group: 50 vs. 30 % (p =0.32), respectively. Median survival for Cx group was 35.0 vs. 18.1 months for Pt group (HR 1.93, 95 % CI 0.50–7.48, p =0.32).

Abstract #41
Evaluation of hyperthermia and radiotherapy for the treatment of patients with locally advanced pelvic tumors: Preliminary findings

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The prognosis for patients diagnosed with unresectable, locally advanced pelvic tumors is grim. These tumors are notoriously difficult to treat due to their refractory behavior with current available treatments. As such, novel treatment approaches are needed. Research has demonstrated that combined hyperthermia and radiation therapy can increase overall survival rates in patients with advanced pelvic tumors. This presentation details our hospitals early experience in evaluating patients (n =10) undergoing this combined approach. Patients enrolled in the protocol received hyperthermia one to two times per week after radiation therapy (170–200 cGy/fraction; 4–5 fraction/week). Hyperthermia treatments were administered using the BSD-2000 Hyperthermia System (BSD Medical Corp. Salt Lake City, Utah, USA). Commonly reported adverse events among patients included pain, cramping, or discomfort in the region of hyperthermia. In most instances, pain could be mitigated by simple adjustments to the heating focus. Two patients receiving palliative therapy (n = 4) had noted disease regression, reduced disease related pain, and an increase in performance status following therapy. In four patients receiving curative treatment (n = 6) a complete clinical response was observed. Overall, patients tolerated hyperthermia quite well, however several issues served to complicate/delay therapy delivery. Issues of note included elevated pulse and blood pressure rates in some patients, machine malfunction, and hyperthermia accessory availability. In sum, the results of the initial evaluation of this study are encouraging and provide motivation for continual inquiry into the utilization of hyperthermia as an adjuvant standard of care in patients with pelvic tumors.

Abstract #42
Effect of Planning Rectal Volume on Daily Shifts from IMRT Prostate Cancer Treatment Plan

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Purpose/Objective(s): To determine whether patients being treated with IMRT (Rapid Arc) for localized prostate cancer with a large rectal planning volume will require larger couch vertical and longitudinal daily shifts than those of patients with a small rectal planning.

Materials/Methods: We retrospectively analyzed 60 patients who completed a course of IMRT (Rapid Arc) for localized prostate cancer and divided them into two equal subgroups based on rectal planning volume. One subgroup was considered to have large rectal volumes (>90 cc), and the other was considered to have small rectal volumes (<50 cc). Patient’s daily shifts were measured from the CBCT image for each fraction. The mean daily shift over the course of radiation treatment was calculated in absolute value. Results were determined using Pearson correlation and Z score calculations to assess any correlations.

Results: Calculated on a 95 % confidence interval (CI), the mean treatment shifts for the small planned rectal volume subgroup were evaluated. Findings concluded that the mean shift should, for a given small rectal volume, fall between 0.544 and 0.709 cm. A Pearson product moment correlation coefficient, determined to be –0.006, indicated no linear relationship was present between the small planned rectal volumes and the corresponding mean treatment shifts. Large planned rectal volumes, also calculated on a 95 % CI, concluded that the mean shifts lie between 0.594 and 0.857 cm. This interval indicates a larger span in potential mean shift, however this is only supported by a Pearson coefficient of 0.1005. Thus indicating a weak correlation, albeit stronger in magnitude than that of the small planned rectal volume subgroup.

Conclusions: Without further investigation, and research into the 3-Dimensional directionality of the calculated shifts, it would be hard to claim a strong connection exists between the planned rectal volumes with our observed treatment shifts. Graphical representations of the data are promising for future research, specifically regarding linear relationships among large planned rectal volumes and corresponding treatment shifts.

Abstract #45
Large Prostate Volumes Treated With Autonomous Continuous Image Guidance Stereotactic Body Radiation Therapy For Prostate Cancer

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Background: Although stereotactic body radiotherapy (SBRT) using either the robotic CyberKnife System or linac-based systems has demonstrated promise for organ-confined prostate cancer, trials of linac-based SBRT have typically excluded patients with large prostate glands (e.g., volumes greater than 60 cc) while robotic SBRT trials have allowed much larger prostates. Here we present data from a retrospective study on toxicity and short-term efficacy for patients with prostates 100 cc or larger.

Patients: Twenty-five men with organ-confined disease and prostate volumes ranging from 100 to 192.6 cc were studied. Forty-four had low-risk, 6 had intermediate, and 5 had high-risk disease. Most received 36.25 Gy delivered in 5, 7.25-Gy fractions using the CyberKnife system; 3 received 35 Gy in 5, 7-Gy fractions. Androgen-deprivation therapy was administered pre-treatment in 1 high-risk patient and in 1 low-risk patient for prostate downsizing. L-glutamine (15 g, BID) was recommended and used by all patients. Flomax was routinely recommended and dose was doubled when nocturia greater than x2 occurred. Ibuprofen was utilized for dysuria and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow. PSA, genitourinary (GU) and gastrointestinal (GI) symptoms were assessed prior to and at the end of treatment, and decreased flow.

Results: At a median PSA follow-up of 12 months, biochemical failure was noted in two men, both with high-risk disease at treatment; neither had confirmed local recurrence. PSA decreased with time since treatment, to a median of 1.0 ng/ml in the 10 patients tested at 2 years. GU symptoms, measured using the IPSS scaled, were highly variable at baseline.
All men experienced a worsening of the IPSS score, followed by a decline to near baseline in most, but not all, men. Acute GU symptoms were more severe than noted in patients with smaller prostate volumes. At the last treatment 9/25 men reported some bowel symptoms, mostly urgency and diarrhea; one man experienced ulcerative colitis, weight loss, and diarrhea for about 2 weeks starting 1 week after treatment, resolved by 4 weeks. **Conclusions:** In early follow-up robotic SBRT has yielded promising disease control with tolerable GU and GI toxicity for men with prostates greater than 100 cc. Acute side effects tended to be more severe than in our patients with smaller prostates; based on this finding we recommend treating patients with low-grade, low volume disease with 35 Gy instead of 36.25. It is possible that steep dose fall-off and frequent image-guided correction of beam aim with the CyberKnife System allows high doses to be more safely delivered to men with large prostate glands.

**Abstract #46**

**Radiation Therapy for Aneurysmal Bone Cysts**

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**Purpose:** Aneurysmal bone cyst (ABC) is a rare, benign tumor that usually affects children under the age of 20. The mainstay treatment for ABC is surgery. This study aims to evaluate the long-term effectiveness of radiation therapy (RT) as an adjuvant or alternative treatment for patients with ABC.

**Methodology:** The medical records of 12 patients who received RT at the our institution for ABC between 1964 and 2011 were reviewed, and patients were contacted, when possible, for follow-up. Follow-up duration ranged from 3 to 36 years (median, 20.5 years). Patient age at the time of RT ranged from 3 to 23 years (mean, 12.75 years), with 7 females and 5 males. Four patients were treated for recurrent ABCs. Three patients were treated with surgical interventions (intralosseal curettage, subtotal resection, or selective arterial embolization) prior to RT, and the rest received open biopsy only. The prescribed doses ranged from 20 to 60 Gy (mean, 30.15 Gy). Ten (83.3 %) patients received between 1.5 and 2.0 Gy per fraction.

**Results:** All 12 patients were doing well and free of any adverse reaction to RT as of the latest follow up, including 1 who passed away from cardiac problems 34 years since completing RT and 3 who were lost to follow up (at 16, 16, and 19 years) but were doing well at the last follow up.

**Conclusions:** RT continues to result in an excellent prognosis for patients with ABC who receive either RT alone or adjuvant RT after surgery.

**Abstract #47**

**Frameless Stereotactic Radiosurgery For Brain Metastaases Using Face Mask Immobilization**

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**Purpose:** To evaluate our experience of frameless stereotactic radiosurgery (SRS) using face mask immobilization in patients with brain metastases.

**Methods and Materials:** Fifteen patients with brain metastases (range, 1–3), were selected to undergo SRS. Dose of SRS was 1800–2500 cGy in 3–5 fractions. All patients underwent MRI brain prior to treatment. MRI of the brain was then fused to our CT simulation. Gross tumor volume was expanded by 3 mm to create the planning tumor volume. All patients were immobilized using aquaplast face mask. Follow-up magnetic resonance imaging (MRI) occurred on average between 1 and 2 months post SRS. Patients who had CNS metastases recurrences after SRS were treated with salvage whole brain radiation.

**Result:** From June 2012 till April 2015, 6 out 15 patients died. Two (13.3 %) developed local recurrences at the treated sites, 4 (26.6 %) developed new intracranial distant recurrences, and 9 (60 %) were recurrence free. The actuarial survival rates of local recurrence-free were 91 % for 12 months and 72 % for 24 months. The actuarial survival rates of distant recurrence-free were 56 % for 12 months and 42 % for 24 months. The actuarial overall survival rates were 70 % for 12 months and 55 % for 24 months. WBRT was administered on 3 (20 %) of the 15 patients.

**Conclusion:** Our results on the use of frameless SRS are favorable to the literature. This suggests the use of face mask immobilization would not lead to inferior outcomes in patients who require SRS for brain metastasis. This may obviate the need for the more invasive and cumbersome immobilization techniques. This would lead to increased convenience and comfort of the patient while ensuring similar efficacy and outcomes.

**Abstract #48**

**Clinical Validation of Unified SBRT Dose Tolerance Limits for Small Bowel**

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**Purpose:** Inconsistencies permeate the literature regarding dose tolerance limits for gastrointestinal tract involving the small bowel for stereotactic body radiation therapy (SBRT) treatments. The purpose of this study is to organize these diverse published limits into a unified framework of low-risk and high-risk SBRT dose tolerance limits for small bowel, and to validate these limits with clinical data.

**Methodology:** A literature review found 36 dose-volume constraints for small bowel in 1 to 5 fractions (J Appl Clin Med Phys. 2011;12:267–292). To arrange these into a unified format, they were first grouped by volume; then within each group the limits with relatively higher dose were designated as high-risk. Quantitative estimates of risk for each selected dose tolerance limit were obtained by dose–response modeling of clinical data. Dose volume histogram (DVH) data for 193 treatments in 1–5 fractions near small bowel was analyzed; 84 treatments from Barney 2013, JROBP Sep 1;87(1):73–80, were combined with 109 new cases from the CyberKnife at MD Anderson at Cooper University Hospital. The new cases were comprised of 68 % liver treatments, 15 % pancreas treatments, and 17 % other upper-abdomen treatments. All doses were converted to three-fraction equivalent dose using the linear quadratic (LQ) model with alpha/beta=3Gy prior to any analysis. Toxicity was scored using Common Terminology Criteria for Adverse Events, version 4.0. The published dataset included 7 grade 3 or higher complications, and no grade 3 or higher complications were encountered in the new dataset. The DVH Evaluator software (DiversiLabs LLC, Huntingdon Valley, Pa) was used to perform maximum likelihood parameter fitting of the probit dose response model to the clinical data.
SBRT is well tolerated and provides effective local control with minimal toxicity in well-selected patients with adrenal metastases.

Abstract #50*

Neoadjuvant Partial Breast Irradiation Utilizing a Novel Breast Specific Stereotactic Radiotherapy Device (GammaPod) Yields Substantial Dosimetric Improvements Over Adjuvant Approaches

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Purpose: Adjuvant external beam radiotherapy remains the most common method for delivery of partial breast irradiation (PBI). Unfortunately, recent reports have documented a significant increase in worsened cosmetic outcomes utilizing three-dimensional conformal radiotherapy PBI as compared to whole breast irradiation. Previous efforts have yielded promising outcomes and tolerance of single fraction, radiosurgical approaches to PBI (Horton et al. Int J Radiat Oncol Biol Phys 2015). A novel breast specific stereotactic radiotherapy (BSRT) device developed at our institution, the GammaPod, has demonstrated considerably enhanced dose distributions akin to brachytherapy approaches. We hypothesized that this device’s delivery technique would prove especially well-suited to the neoadjuvant setting.

Methodology: Previously treated breast cancer patients were enrolled on an IRB-approved protocol and underwent CT simulation in the prone position utilizing the GammaPod, unique breast immobilization device. Sixteen patients were eligible for neoadjuvant BSRT planning, while only twelve were eligible for postoperative planning based on physical limitations of the device. Two sets of treatment volumes were generated per the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-39 protocol for intensity modulated partial breast irradiation (IMRT PBI) and GammaPod planning utilizing the lumpectomy cavity for postoperative planning (Post_PTVeval_10mm) and gross tumor (simulated based on pathologic tumor size for each patient) for neoadjuvant planning (Pre_PTVeval_10mm). Stereotactic PTVs were also generated for GammaPod planning based on the immobilization device’s previously validated reproducibility of less than 3 mm (Post and Pre_PTVeval_3mm). For each plan, the volume of the ipsilateral breast, breast skin, chest wall, lung, and heart receiving each of several percentages of the prescribed dose (Vx%) were recorded. Paired-sample T-tests were used for statistical analysis.

Results: Both the PTVeval_10mm (38.3%) and PTVeval_3mm (46.0%) expansions showed significant reductions in volume in the neoadjuvant setting as compared to post-lumpectomy (p<0.001). Almost invariably, treatment in the preoperative setting yielded significant (p<0.05) decreases in dose to normal structures. The relative reductions in Vx% were, in general, more profound with GammaPod, as compared with IMRT PBI, as its dynamic dose-painting technique was better able to exploit the neoadjuvant treatment volume size and shape. Neoadjuvant GammaPod planning further reduces dose to non-coplanar static aperture ARCs and non-coplanar static fields. Treatments were delivered using a linear accelerator with a 6MV beam. Toxicity was measured using the Common Terminology Criteria for Adverse Events (CTCAE). Survival, local control, and disease control analyses were completed using the Kaplan-Meier estimates.

Conclusion: Neoadjuvant GammaPod planning further reduces dose to normal structures over and above the improvements realized with this treatment technique versus IMRT PBI. This approach deserves further investigation.
exploration in the form of a preoperative clinical trial, which will be initiated through our institution in the coming months.

Abstract #51*

Palliative Radiation Oncology in Developing Countries: a Focus on Ghana

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Background: Ghana, a West African country located along the Gulf of Guinea and the Atlantic Ocean, is one of the poorest countries in the world and is at the heart of a growing cancer epidemic. According to the Ministry of Health and Social Welfare and the World Health Organization, 80% of cancer patients in developing countries like Ghana present with late-stage incurable cancer in need of palliative care, and this number is expected to rise by 70% over the next two decades. Although Ghana has made strides toward implementing comprehensive cancer care in Accra, there remains a huge need for improved cancer care, particularly with regard to offering palliative radiotherapy. Palliative radiation care is an essential component of affordable and effective cancer care. We review the current need as a means to advocate awareness and contribute to our awareness of the need for improved quality of life cancer care in African countries.

Materials and Methods: We estimate the patterns of care for end-stage and symptomatic patients receiving palliative radiotherapy in Ghana. The International Atomic Energy Agency (IAEA) maintains an international database which comprises radiation centers in DCs, known as the Directory of Radiotherapy Centers (DIRAC). The DIRAC was analyzed and numbers of radiation centers, megavoltage machines, personnel, institutions and resources available are reported. Benchmarks including census, megavoltage machines/million population are compared to worldwide standards to estimate current need of radiation machines.

Results: Africa has an estimated population of one billion and has 1 megavoltage machine per 5 million people, 48% being cobalt machines, with no particle therapy. Ghana has 3 cancer centers (2 government-operated including Komfo-Anokye Teaching Hospital in Kumasi and the Korle-Bu Teaching Hospital in Accra with 3 cobalt machines, and 1 private facility, including the Swedish Ghana Medical Center in Accra with 1 linear accelerator). These facilities represent 1 radiation machine for every 6 million people. Ghana is neighboried by countries that have no radiotherapy facilities (Côte d’Ivoire, Burkina Faso, Togo, Benin and Sierra Leone), further increasing cancer burden in the region. In contrast, the US has 1 megavoltage machine for 105,000 people, 2% being cobalt teletherapy machines, with additional particle therapy facilities.

Conclusion/Discussion: There remains a huge unmet need for palliative radiotherapy in DCs, owing to the vast majority of cases presenting with end-of-life disease. The main goal of this review is to contribute to our awareness of the need for improved quality of life cancer care in African countries by describing the situation in Ghana. To that end, Radiating Hope describes the current state of cancer and cancer treatment in Africa, and particularly Ghana.

Abstract #52*

ACRO and Radiating Hope: A partnership for Now and the Future

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Founded by mountain-climbing radiation oncologists with a desire to help cancer patients around the world, Radiating Hope is a 100% volunteer-run, cancer-cure focused nonprofit 501(c) (3) organization with a mission to improve cancer care, specifically radiation oncology care, around the globe. Radiating Hope strives to deliver much needed radiation equipment to countries where oncologic care is limited with a focus on providing effective, safe, and sustainable use of the equipment through intensive in-person and remote training on a long-term basis. The American College of Radiation Oncology (ACRO) has forged a strong collaboration and partnership with Radiating Hope, providing structural, advertising, and financial support to help further Radiating Hope’s mission of improving availability and access to radiation oncology services in sub-Saharan Africa. Through its Global Radiation Oncology Workforce (GROW) Scholarship program, ACRO provides scholarships to residents and new practitioners to participate in Radiating Hope led trip abroad. In 2013, a Radiating Hope team including GROW scholars sponsored by ACRO embarked on a trip to Dakar, Senegal to place the first ever HDR machine in Senegal and to start a cervical brachytherapy program that Radiating Hope continues to support through remote training programs.

Most recently, ACRO provided 3 GROW scholarships for a planned Radiating Hope trip to Accra, Ghana to help start an HDR cervical brachytherapy program in late November 2014. While the trip was eventually cancelled (due to the Ebola crisis in West Africa at that time), the Radiating Hope Ghana project director visited the Korle-Bu teaching Hospital in Ghana with ACRO’s support to donate Radiation equipment and establish a partnership with Radiating Hope and the Institution. This partnership is focused on training, improvement of physics QA through equipment donation and remote training in their use, using information technology to improve radiation treatment planning and delivery, as well as establishing lasting partnership with US institutions and Korle-Bu for mentorship and training.

Radiating Hope’s relationship with ACRO serves as a model of how large specialty organizations can support smaller cause-specific non-profit organizations working in that specialty in a mutually beneficial, sustainable, long-term partnership.