UT-DRO
Annual Research Day

Friday, May 4, 2018

Chestnut Conference Centre
University of Toronto

Radiation Oncology
UNIVERSITY OF TORONTO

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Schedule

12:00 – 12:30	**Registration/Lunch**		
12:30 – 12:40	**Welcome Remarks – Dr. Fei-Fei Liu, Chair**		
12:40 – 1:25	**Keynote Speaker: Dr. Shelly Dev**		
1:25 – 1:55	**Oral Presentations – Section 1 (Moderator: Aisling Barry)**		
Time	#	Abstract Title	Presenter
1:25 – 1:32	1	Germline structural variation shapes the somatic architecture and risk of relapse in localized prostate cancer	Alexandre Rouette
1:32 - 1:39	2	Rapid release of circulating tumour DNA as a biomarker of treatment response in preclinical models of head and neck squamous cell carcinoma	Ariana Rostami
1:39 - 1:46	3	Plasma metabolomic profiles in hepatocellular carcinoma patients before and after stereotactic body radiotherapy	Sylvia Ng
1:46 – 1:53	4	Identifying novel metabolic targets in the reversal of radiation fibrosis	Pamela Psarianos
1:55 – 2:05	**Rapid Fire Presentations 1 (Posters #1-7) Moderator: Scott Bratman**		
2:05 – 2:20	**Break/Poster Viewing**		
2:20 – 2:50	**Oral Presentations – Section 2 (Moderator: Ali Hosni Ali Abdalaty)**		
Time	#	Abstract Title	Presenter
2:20 - 2:27	5	Comparison of local failure and radionecrosis according to dose prescription for small to medium sized brain metastasis treated with radiosurgery	Fabio Ynoe de Moraes
2:27 - 2:34	6	Outcomes following definitive single fraction stereotactic radiosurgery for larger brain metastases	Archya Dasgupta
2:34 - 2:41	7	Stereotactic body radiotherapy (SBRT) For spinal metastases at the extremes of the spine: Imaging-based outcomes for cervical and sacral metastases	Kang Liang Zeng
2:41 - 2:48	8	Using online cone-beam CT simulation for VMAT treatment of bony metastases	Roja Zakariaee

2:50 – 3:00	**Rapid Fire Presentations 2 (Posters #8-15) Moderator: Jennifer Croke**		
3:00 – 3:15	**Break/Poster Viewing**		
3:15 - 3:45	**Oral Presentations – Section 3 (Moderator: David Shultz)**		
Time	#	Abstract Title	Presenter
3:15 – 3:22	9	Machine learning prediction of early distant progression for oligometastatic and oligoprogressive colorectal cancer (CRC) patients treated with stereotactic body radiotherapy (SBRT)	Pencilla Lang
3:22 – 3:29	10	Clinical evaluation of a machine learning-based automated treatment planning method for prostate radiotherapy	Leigh Conroy
3:29 – 3:36	11	Screening MRI for radiation induced meningioma in childhood cancer survivors with prior cranial radiation	Jayson Co
3:36 – 3:43	12	A novel method of calibration for improving accuracy and sensitivity in dual energy computed tomography perfusion+C23G2D22:G23	Hedi Mohseni
3:45 – 3:55	**Rapid Fire Presentations 3 (Posters #16-22) Moderator: Kathy Han**		
3:55 – 4:10	**Break/Poster Viewing**		
4:10 - 4:40	**Oral Presentations – Section 4 (Moderator: Brian Liszewski)**		
Time	#	Abstract Title	Presenter
4:10 - 4:17	13	Quantifying upstage rate as a function of delay from diagnostic imaging for locally-advanced lung cancer patients	Mohammad Hasan
4:17 - 4:24	14	Free PSA ratio as a predictor of adverse outcomes after curative-intent external beam radiation therapy for prostate cancer: a novel application of an "old" biomarker	Rachel Glicksman
4:24 - 4:31	15	Change of radiotherapy practice pattern in lymphoma at a large academic center	Melody Qu
4:31 – 4:38	16	Improvement in patient-reported distress after chemo-radiation in cervical cancer patients	Jessica Conway
4:40 – 5:00	**Closing Remarks – Dr. Mike Milosevic**		

Poster list

Poster Location	#	Abstract Title	Presenter
001	P1	Exploring the use of virtual reality as a supplemental educational tool in traditional first day teaching for patients receiving external beam radiation therapy to the pelvis	Kalaina Johnson
002	P2	Validation of a viability assay for assessing radiation response and investigating drug/radiation combinations	Meghan Lambie
003	P3	Loss of RSPO3 as a potential mechanism of greater invasiveness in prostate cancer	Aruz Mesci
004	P4	Evaluating the kinetics and thermodynamics of Gafchromic (EBT3) films in the context of radiation dosimetry of megavoltage beams	Eric Da Silva
005	P5	Lymph node ratio as a predictor of distant metastases in major salivary gland carcinomas	Nhu-Tram Nguyen
006	P6	Prostate treatment in a MRI-Linac for patients with bilateral hip implants	Syed Ahmad
007	P7	Patient-reported acute fatigue in elderly breast cancer patients treated with and without regional nodal radiation	Shagun Misra
008	P8	Impact of immobilization on interfractional errors for upper extremity soft tissue sarcoma radiation therapy	Aran Kim
009	P9	Creation of a high-fidelity computer-based simulation to improve resident competency in radiotherapy treatment plan evaluation	Jenna Adleman
010	P10	Tumor-targeted dose escalation for localized prostate cancer using MR-guided HDR brachytherapy (HDR) or integrated VMAT (IB-VMAT) boost: Dosimetry and early toxicity analysis	Noelia Sanmamed
011	P11	Dose reconstruction for lung cancer patients with gross anatomical changes during radiotherapy	Jeff Winter
012	P12	Intrafraction tracking for spinal SBRT and motion assessment on an Elekta Linac	Daniel Markel
013	P13	Automatic contour propagation of organs-at-risk on serial MRIs and dosimetric implications in glioblastoma patients undergoing chemo-radiation	Sangjune Lee
014	P14	Dosimetric study on patient transfer between Varian Clinac iX and TrueBeam Linacs	Shima Yaghoobpour Tari

015	P15	Neurological death is common in patients with EGFR mutant non-small cell lung cancer	Matthew Ramotar
016	P16	Three-dimensional-guided perineal-based interstitial brachytherapy in primary vaginal cancer: A systematic review of local control and toxicities	Yonatan Weiss
017	P17	Re-irradiation of primary adult CNS tumors: Outcomes, toxicity and dosimetric factors	Aisha Alqaderi
018	P18	Whole genome characterization of cervical cancer	Jelena Lukovic
019	P19	Dixon-based magnetic resonance imaging for improved detection of brain metastases for radiosurgery planning	Jay Detsky
020	P20	Multi-institutional study of salvage irradiation with single-modality interstitial brachytherapy for the treatment of recurrent gynecological tumours in the pelvis	Hamid Raziee
021	P21	Global characterization of protein secretion rates in normoxia and hypoxia	Sandy Che-Eun Lee
022	P22	Utility of a decision aid for accelerated partial breast irradiation in older women with low risk breast cancer	Matthew Neve

Thank you to the Research Day Organizing Committee!

- Mike Milosevic, Chair
- Andrea Bezjak
- Peter Chung
- Ezra Hahn
- Anne Koch
- Marianne Koritzinsky
- Eric Leung
- Brian Liszewski
- Andrea McNiven
- Pablo Munoz
- Thomas Purdie
- Ananth Ravi

01 Germline structural variation shapes the somatic architecture and risk of relapse in localized prostate cancer

Alexandre Rouette, Yu-Jia Shiah, Jay Jayalath, Cindy Q. Yao, Kathleen E. Houlahan, Michael Fraser, Theodorus van der Kwast, Robert G. Bristow, Paul C. Boutros

Purpose

Broadly, the origins of cancer can be separated into three categories: environmental, hereditary and stochastic. Some germline variants are tightly associated with somatic phenotypes, like those in RB1, BRCA2 and TP53. However recently our group and others have described common germline variants that bias tumours towards specific evolutionary pathways. Surprisingly, though, there has been no systematic survey on the relationship between germline structural variation and somatic evolution in any tumour type. Indeed, germline DNA structural variants (SVs), including duplications, inversions, and deletions, are a significant source of genetic variability. To fill this gap, I focused on prostate cancer (PC): the most common non-skin malignancy in men. I leveraged genomic, pathologic and clinical outcome data to identify the role germline SVs play in influencing somatic and clinical phenotypes.

Methods

My discovery cohort comprised of 300 patients with intermediate-risk localized PC, whole-genome sequencing (WGS; tumour and blood) of their index lesion, and a minimum of 5-year clinical follow-up, collected through the Canadian Prostate Cancer Genome Network (CPC-GENE) program. First, for each patient we detected germline SVs (deletions, duplications, inversions) from abnormal paired-end mapping of reads on reference genome and refined using split reads and read-depth to obtain a high-confidence list of ~20,000 germline SVs. Then, we employed genome-wide association analysis to uncover novel associations between common (MAF >0.05) germline SVs, known somatic driver events and relapse.

Results

We identified specific germline deletions in non-coding regions that were associated with an increased frequency of BRCA1 somatic deletions and other SVs with TMPRSS2:ERG fusions. Furthermore, we identified >10 germline SVs univariately associated with biochemical recurrence – the relapse of PC after local therapy – with the majority being deletions in non-coding regions. The presence of >1 of any of these SVs in patients strongly increases risk of early recurrence and ultimately of metastasis. In most situations, they were associated with dysregulated mRNA abundance of nearby genes in cis, and enriched in chromatin marks of active transcription such as H3K27 acetylation, DNase hypersensitivity or predicted transcription factor binding sites. Together these risk SVs were assembled into multivariate signature able to predict early recurrence with >80% accuracy.

Conclusion

While large tumour sequencing studies have shed light on the somatic genomic aberrations in tumours, little is known about how the germline genome influences tumour evolution and clinical outcomes. We find that germline DNA structural variants play can guide the somatic evolution and ultimate clinical aggressivity of localized prostate cancer. They have the potential to serve as clinical biomarkers, identifiable with blood tests and present at birth, in order to reduce aggressive treatment for indolent cancers and identify aggressive disease for treatment intensification trials. Power-analyses suggest that hundreds of germline-somatic

interactions remain to be detected, and the extent to which germline, environmental and replication-associated effects influence cancer risk and mutational profiles remains a question of extensive discussion.

02 Rapid release of circulating tumour DNA as a biomarker of treatment response in preclinical models of head and neck squamous cell carcinoma

Ariana Rostami, Caberry Yu, Marco A. Di Grappa, Scott Bratman

Purpose

Standard treatment for locally advanced head and neck squamous cell carcinoma (HNSCC) includes high-dose radiotherapy (RT). Despite known molecular prognostic biomarkers in HNSCC, such as the presence of human papillomavirus (HPV) within tumour tissues, RT regimens remain one-size-fits-all without any patient-specific individualization. We hypothesize that rapid release of circulating tumour DNA (ctDNA) can act as a biomarker of treatment response in HNSCC by reflecting tumour cell death in response to RT.

Methods

Four HNSCC cell lines, two HPV- (Cal33, FaDu) and two HPV+ (HMS-001, 93-Vu147T) were evaluated for ctDNA release following single dose RT in vitro using quantitative polymerase chain reaction (qPCR) with primers amplifying the human long interspersed nuclear element 1 (hLINE1). RT-induced apoptosis was measured using a luminometric caspase 3/7 assay and RT-induced senescence was evaluated using a fluorometric senescence associated β-galactosidase assay (SA-β-Gal). The pan-caspase inhibitor, z-vad-fmk, was used to block RT-induced apoptosis. Subcutaneous cell-line xenografts were established in Nod-Scid-Gamma (NSG) mice, where plasma from serial blood draws was purified and quantified for ctDNA release using hLINE1 qPCR. Endpoint tumours were evaluated for mechanisms of cell death by histological staining.

Results

HNSCC cell lines exhibited variable magnitude and timing of ctDNA release and apoptosis. Maximal ctDNA release occurred between 72 and 144 hours post-RT. The release of ctDNA over time was not correlated with HPV status nor with the amount of apoptosis occurring following RT. To further interrogate the contribution of apoptosis to ctDNA release, we treated cells with a pan-caspase inhibitor and evaluated ctDNA release and caspase activity following RT. Although caspase inhibition resulted in a near complete reduction in RT-induced caspase activity (84.0% ± 8.1%), a comparatively minor reduction in ctDNA release (28.9% ± 8.9%) was observed. To evaluate the impact of senescence to RT-induced ctDNA release, we measured SA-β-Gal activity post-RT. The degree of senescence following RT was inversely associated with ctDNA release. Within cell line xenografts grown in NSG mice, maximal ctDNA release into mouse plasma occurred 96 hours following RT. Staining patterns of endpoint tumours for caspase-3, TUNEL, p21, and Ki67 is currently under analysis.

Conclusion

Our results demonstrate a robust and sensitive method for longitudinal evaluation of ctDNA release and cell death following RT both in vitro and in vivo. Timing of ctDNA release demonstrate peaks around 72-96 hours post-RT, highlighting the potential for ctDNA to depict early response to treatment. On-going studies aimed at further investigating ctDNA release in association with mechanisms of cell death in vivo will help further elucidate the potential for ctDNA as a biomarker of therapeutic response.

03 Plasma metabolomic profiles in hepatocellular carcinoma patients before and after stereotactic body radiotherapy

Sylvia S. W. Ng, Gun Ho Jang, Irwin J. Kurland, Yunping Qiu, Chandan Guha, Laura A. Dawson

Purpose

Grade 1 and 2 toxicities such as fatigue and nausea are common following SBRT for hepatocellular carcinoma (HCC). Less commonly, grade 3 or higher hepatic (e.g., non-classic radiation-induced liver toxicity seen in 30% of patients) and non-hepatic (e.g., luminal gastrointestinal) toxicities develop following HCC SBRT, and are often associated with irreversible injury, and high morbidity and mortality. There is a need to identify biomarkers that can detect radiation-induced liver/luminal gastrointestinal injury early for appropriate medical intervention or radiation dose reduction, and predict tumor response, allowing tailoring of SBRT to improve the therapeutic ratio for individual patients, ideally prior to completion of SBRT. The objectives of this study are two-fold: a) to identify the profile of changes in metabolite levels in the plasma of HCC patients at baseline and following the first or second fraction of SBRT, and b) to correlate such changes with clinical liver/luminal gastrointestinal toxicities and radiologic tumor response.

Methods

HCC patients were treated with SBRT to a total dose of 30-54 Gy in 6 fractions on a previously published clinical trial (Bujold et al., *J Clin Oncol*, 2013). Plasma samples were collected from 50 HCC patients at baseline and after completion of the first or second fraction (within 5 days from the first fraction) of SBRT on an IRB approved companion protocol. Targeted metabolomic profiling was performed using the Biocrates p180 kit and liquid chromatography/tandem mass spectrometry, while untargeted metabolomic profiling was conducted using gas chromatography/mass spectrometry. GC/MS metabolite annotation was performed with comparing the mass spectrum and retention time to commercially available libraries such as Fiehn, GOLM and NIST. Paired t-test and spearman correlation were used for statistical analyses.

Results

Four hundred and eighty-three metabolites were detected, of which 293 were annotated. Significant differences were seen following SBRT from baseline in 34 annotated metabolites (p-values <0.05) and 39 non-annotated spectral signatures (p-values <0.05). Methyl linoleate, cysteine, tryptophan and tyrosine were amongst the metabolites that demonstrated the highest fold increases, while succinic acid, campesterol and complex lipids with low degree of unsaturation in their fatty acid chains were amongst those that showed the highest fold decreases following one or two fractions of SBRT compared to baseline.

Conclusion

This study demonstrated significant fold changes in groups of plasma metabolites following one or two SBRT fractions for HCC. Some of the identified plasma metabolites were shown to be associated with liver injury in previous preclinical studies. Correlation analyses are underway to determine if these metabolites are associated with clinical radiation-induced liver/luminal gastrointestinal toxicities and tumor response.

04 Identifying novel metabolic targets in the reversal of radiation fibrosis

Pamela Psarianos, Xiao Zhao, Daniel De Carvalho, Kenneth Yip, Fei-Fei Liu

Purpose

As many as 50% of all cancer patients undergo radiation therapy during their cancer lifetime; however, radiation toxicity to surrounding normal tissue remains a significant problem. Radiation fibrosis (RF) is a major long-term consequence of radiation damage, affecting up to 70% of patients undergoing radiotherapy. This inflammatory scarring condition is histologically characterized by excessive collagen and extracellular matrix (ECM) accumulation, severely decreasing patients' quality of life. Our laboratory has demonstrated that a shift from fatty acid oxidation (FAO) to glycolysis is a predominant and sustained alteration in RF, and that transplantation of adipose-derived stromal cells (ADSCs) can restore metabolic homeostasis while reducing fibrosis severity. It has recently been shown that epigenetic alterations might in part underlie the pathogenesis of fibrosis; hence, we hypothesized that epigenetic regulation of metabolism may be central to the development and treatment of RF.

Methods

While there is a vast landscape of epigenetic differences between normal and fibrotic tissue, our rationale was that only a subset of these alterations are likely to drive the switch between normal and RF phenotypes. Therefore, we profiled radiated control versus radiated, ADSC-treated tissue to gain insight to alterations specifically associated with RF reversal. Genome-wide methylation profiling was performed using reduced representation bisulfite sequencing, and the HOMER motif discovery algorithm was then used to identify differentially methylated regions associated with RF reversal. A TGFB1-activated primary human fibroblast model was utilized in vitro to examine the pharmacological inhibition of a novel target identified through methylation profiling. Western blotting and quantitative polymerase chain reaction (qPCR) were used to assess the efficacy of this pharmacological agent in modulating the expression of fibrotic markers.

Results

ADSCs induced hypermethylation at the promoter of FOXO1 ($p=0.01$), a transcription factor involved in metabolic regulation. qPCR demonstrated that FOXO1 regulated FAO homeostasis and pro-fibrotic pathways in vitro. Furthermore, western blotting revealed that pharmacological inhibition of FOXO1 decreased the expression fibrotic markers such as fibronectin, collagen, and PAI-1. Finally, to elucidate a mechanism of action of FOXO1, we have recently identified a novel interaction between FOXO1 and the prostaglandin E2 pathway in the process of ECM regulation.

Conclusion

In summary, ADSC transplantation promoted the recovery of RF, providing insight to metabolic and epigenetic alterations that are specific to RF reversal. This information informed the discovery of FOXO1, a novel metabolic target for the treatment of RF. In vitro experimentation has confirmed the significance of FOXO1 in metabolism and ECM regulation, and has established a potential mechanism through which FOXO1 may regulate RF. To conclude, the discovery of targets such as FOXO1, and validation of their significance will have important implications for a deeper understanding of RF pathogenesis, providing insight to novel therapeutic strategies for the treatment of this condition.

05 Comparison of local failure and radionecrosis according to dose prescription for small to medium sized brain metastasis treated with radiosurgery

Fabio Y Moraes, Jeff Winter, Eshetu Atenafu, Archya Dasgupta, Catherine Coolens, Barbara-Ann Millar, Normand Laperriere, Derek S. Tsang, Mark Bernstein, Paul Kongkham, Gelareh Zadeh, Tatiana Conrad, Alejandro Berlin, David Shultz

Purpose

To examine the impact of gamma knife radiosurgery (SRS) marginal prescription dose (PD) (15 Gy vs. 16-20 Gy vs. > 20Gy) on local failure (LF) and radionecrosis (RN) for small- to medium-sized (≤ 2 cm) brain metastasis (BM) in a large single-institution series.

Methods

We identified patients from a prospective registry of BM patients treated with SRS between 2006 and 2017. At our institution, we commonly treat lesions adjacent to eloquent structures with a lower PD to reduce the likelihood of toxicity. We used defined criteria to differentiate LF from RN, including pathology, when available. Cumulative incidences of LF and RN were calculated using Fine and Gray's competing event analysis, with death as a competing event. Patient, tumor, and treatment factors were assessed for their impact on LF and RN.

Results

We reviewed 462 patients with 1609 BM ≤2 cm (Table 1- patients characteristics). Median overall survival and radiographic follow-up was 19.7 months (95%CI 17.4 to 23.3 months) and 13.4 months (IQR 7.9-22.4 months), respectively. 1065 lesions (66%) were treated with PD >20 Gy, 80 lesions (5%) with 16-20 Gy and 464 lesions (29%) with <15 Gy. Cumulative LF rates at 2 years were 15.2% (95%CI 6.2-24.3%) for 15 Gy, 11.9% (95%CI 0-29.5%) for 16-20 Gy, and 6.4% (95%CI 2.2-10.6%) for >20Gy ($p<0.0001$). Cumulative RN rates at 2 years were 5.5% (95%IC 0-11.6%) for 15 Gy, 6.2% (95%CI 0-17.9%) for 16-20 Gy and 6.4% (95%CI 2.4-10.3%) for >20Gy ($p=0.2381$). Tumor size ≤ 1 cm was associated with a significantly lower rate of LF (HR 0.318 (95%CI 0.216-0.468; $p<0.0001$) and RN (HR 0.194 (95%CI 0.120-0.314; $p<0.0001$) compared to BM > 1 cm. Cumulative LF and RN rates at 2 years for lesions ≤ 1 cm was 4.7% (95%CI 0.08-8%), and 2.6% (95%CI 0-5.4%), respectively. Cumulative LF and RN rates at 2 years for lesions were > 1 cm was 15.3% (95%CI 8%-22%) and 11.8% (5.1-18.5%), respectively. For lesions > 1 cm, LF occurred in 9.5% vs. 5% of tumors treated with 15 Gy and >20 Gy, respectively ($p=0.0003$). There was a significantly increased risk of RN for lesions >1 cm treated with >20 Gy vs. 15 Gy (6.10% versus 3.23%; $p=0.0011$).

Conclusion

Our results suggest that for BM >1 cm treated with SRS, 15 Gy provides inferior local control compared to> 20 Gy, but is associated with a lower rate of RN. For lesions ≤ 1 cm, LF and RN incidences are both < 5%.

06 Outcomes following definitive single fraction stereotactic radiosurgery for larger brain metastases

Archya Dasgupta, Fabio Y Moraes, Jeff Winter, Catherine Coolens, Barbara-Ann Millar, Normand Laperriere, Derek S. Tsang, Mark Bernstein, Paul Kongkham, Gelareh Zadeh, Tatiana Conrad, Alejandro Berlin, David B Shultz

Purpose

Limited data is available addressing the effectiveness of single fraction stereotactic radiosurgery (SRS) as a definitive treatment, without surgical resection, for larger brain metastases (LBM; largest diameter >2cm). We report the outcomes of patients treated for LBM with SRS at a single institution.

Methods

We queried a prospectively maintained registry of 2059 BM treated with SRS between 2006 and 2017 to identify 280 LBMs. We analyzed demographics and treatment details descriptively. For survival analyses, we used the Kaplan-Meier method, with survival calculated from the date of LBM treatment (per lesion analyses). We performed univariate analyses using log-rank tests, and multivariate analyses with Cox regression models.

Results

We identified 255 patients with a median 1 LBM (range 1-3). Median largest diameter was 2.52 cm (range 2.01-4.64 cm); 56 LBM were >3 but <4 cm and 9 were >4 cm. Eighty-one percent of patients had an ECOG <2 and 75% of lesions had peritumoral edema. Prior to SRS for LBM(s), 15% underwent resection of other BM, 13% received SRS for smaller lesions, and 62% of patients received systemic therapy. Mean prescribed dose was 17 Gy (range 10-24 Gy) and target minimum dose 15.1 Gy (range 5.7-21.2 Gy). During SRS for LBM, 27% had concomitant lesions (<2 cm) treated with SRS and 53% had measurable extracranial disease. Median overall survival was 10 months (range 1-98 months). At a median follow up of 7 months (range 1-95 months), 63 lesions (22%) had failed locally (LF), with 24 of 63 (8% of all lesions) exhibiting synchronous intracranial distant failure. Local control (LC) for LBM was 88%, 76%, and 55% at 6-months, 1-year and 2-years, respectively. The median time to LF was 7 months (range 1 to 61 months). No disease (site of primary, size/ volume of LBM, concomitant disease, prior radiation) or treatment (prescribed dose, minimum/ maximum target dose, conformity indices) related factors tested were significantly associated with LF on univariate analysis. Radionecrosis (RN) developed in 39 lesions, with 1-year and 2-year rates of 18%, and 28%, respectively. Prescription dose, use of steroids during SRS, and V12 Gy were not associated with the rate of RN.

Conclusion

Single fraction radiosurgery for LBM is associated with relatively poor rates of local control and relatively high rates of RN. Use of hypofractionated radiosurgery to deliver higher biologically effective doses more safely may expand the therapeutic index and result in improved outcomes.

07 Stereotactic body radiotherapy (SBRT) for spinal metastases at the extremes of the spine: Imaging-based outcomes for cervical and sacral metastases

K. Liang Zeng, Hany Soliman, Sten Myrehaug, Chia-Lin Tseng, Eshetu G. Atenafu, Mikki Campbell, Salman Faruqi, Young K. Lee, Mark Ruschin, Leodante da Costa, Victor Yang, Julian Spears, Chris Heyn, Pejman Jabehdar Maralani, Cari Whyne, Albert Yee, Arjun Sahgal

Purpose

Most of the data following spine stereotactic body radiotherapy (SBRT) are specific to thoracic and lumbar metastases. The unique anatomy and biomechanical features of the cervical spine and sacrum may impact treatment outcomes following SBRT. The purpose of this study was to report our imaging-based outcomes following SBRT specific to cervical and sacral metastases.

Methods

From our institutional prospectively maintained spine SBRT database, we retrospectively reviewed only cervical and sacral metastases. All patients were followed at 2 to 3-month intervals with a clinical visit and full spine MRI. Outcomes of interest were imaging-based local control (LC), overall survival (OS), vertebral compression fracture (VCF) and other serious adverse effects.

Results

A total of 52 patients and 93 spinal segments were identified consisting of 56 treated segments within the cervical spine and 37 within the sacrum. The median follow-up was 14.4 months and 19.5 months, respectively, and the median total dose and number of fractions was 24 Gy in 2, respectively, in both cohorts. Cumulative LC rates at 1- and 2-years were lower for the sacral cohort (86.5% and 78.7%) compared to the cervical spine cohort (94.5% and 92.7%). Lack of posterior spinal element involvement was predictive of LC in the cervical spine cohort (no local failures, $p<0.0001$) cohort, and absence of epidural disease (HR 0.275, 95% CI 0.076-0.989, $p=0.048$) predicted LC in the sacral cohort. Median OS was 16.3 months and 28.5 months in the cervical spine and sacrum cohorts, respectively. In the cervical spine group, presence vs. absence of liver and/or lung metastases was prognostic with a median survival of 10.8 months vs. not reached even after 48 months ($p=0.0494$), respectively. In the sacral cohort, patients with oligometastatic disease (HR 0.139, 95% CI 0.031-0.616, $p=0.0094$) and breast primary (HR 0.136, 95% CI 0.026-0.697, $p=0.0168$) had longer OS. Two cases of VCF in the sacrum, one brachial plexopathy and one lumbar-sacral plexopathy were observed.

Conclusion

Although high rates of LC were observed following SBRT to the cervical spine and sacrum, strategies specific to the sacrum may require further investigation to optimize results. Serious sequelae after SBRT to cervical spine and sacrum were rare.

08 Using online cone-beam CT simulation for VMAT treatment of bony metastases

Roja Zakariaee, Daria Comsa, Douglas Moseley

Purpose

Palliative volumetric modulated arc therapy (VMAT) for spinal metastases can be done using “Same-day Sim&Treat” method, where CT-simulation, treatment planning, preliminary QA, and treatment delivery, are performed all in the same day. The possibility and speed of this process might be affected by the availability of CT scanner, especially in smaller centres. Cone beam CT (CBCT) technology available on linacs offers an alternative for planning these treatments. However, because of the smaller field of view (FOV) of CBCT images, compared to CT, the entire width of some patients with larger separation may not be captured in a single CBCT. This is of particular importance for VMAT treatments where any truncation of the patient volume will result in overestimation of the delivered dose. This study looks into the feasibility of using CBCT images to plan VMAT LS-Spine treatments and develops methods to compensate for larger separation using two laterally shifted CBCT’s to achieve a larger FOV.

Methods

An anthropomorphic pelvic phantom was used to acquire one central and two pairs of CBCTs with lateral couch shifts of +/-5 and +/-10 cm. The left/right CBCTs for each pair were stitched in MATLAB to create one large-FOV panoramic CBCT image (pCBCT). The quality of the stitched images was compared to the central CBCT and CT images, in terms of artifacts and noise levels at different homogeneous locations inside the phantom. The dosimetric qualities of LS-spine VMAT plans created in Pinnacle® using CT images and transferred onto the pCBCT images were evaluated, for the pCBCT images. Also, the dosimetric properties of seven LS-Spine VMAT patient plans transferred onto their non-truncated daily IGRT CBCTs were evaluated. The CBCT stitching method was also applied to a set of patient data with truncated left/right CBCTs and the dosimetry of the LS-Spine VMAT plan was evaluated on the pCBCT image.

Results

Minor artifacts were observed in the lateral and pCBCTs, worsen with larger lateral shifts. The noise levels of the CT image, central CBCT, and two pCBCTs in the evaluated regions were on average 1.1%, 1.5%, 1.4% and 1.3%, respectively. PTV D90 values for the VMAT plan transferred onto the pCBCTs with small and large shifts were, respectively, 0.09% and 0.2% smaller than the original plan. The PTV D90 and max-dose values for the VMAT plans calculated on non-truncated daily CBCTs for the seven patients were on average within 0.6% and 1.9% of the original values, respectively, and for the patient plan with a stitched pCBCT were within 0.4% and 1.1%, respectively.

Conclusion

This study shows that planning palliative VMAT LS-Spine treatments on CBCT images is feasible and provides accurate dosimetric calculations. Target volume delineation for LS-Spine treatments on CBCT images as compared to CT images is yet to be verified.

09 Machine learning prediction of early distant progression for oligometastatic and oligoprogressive colorectal cancer (CRC) patients treated with stereotactic body radiotherapy (SBRT)

Pencilla Lang, Mohammad Kayvanrad, Robert Thompson, Patrick Cheung, Efstathios D. Gennatas, Gilmer Valdes, Hans T Chung

Purpose

Recent studies show SBRT for oligo-metastases (OM) and oligo-progression (OP) confers good outcomes and low morbidity, but clinicians face significant challenges selecting patients who will benefit from SBRT, due to complex interactions of patient, tumour and treatment factors. This study examines the ability of machine learning (ML) based classifiers to identify patients who develop early distant progression (DP, ≤ 90 days since treatment completion) in CRC patients receiving SBRT.

Methods

All CRC patients treated with SBRT to any site at a single institution for OM/OP in 2009 - 2016 were retrospectively reviewed. Clinical characteristics included age, gender, pre-SBRT CEA, RAS status, ECOG performance, treatment indication (OM/OP), SBRT location, disease free interval since last treatment (DFI), number of prior lines of systemic of therapy, prior use of ablative local therapy, PTV volume and mean PTV BED. Univariable and multivariable logistic regression was used to identify predictors of DP. Classification methods included: logistic regression (LR) gradient boosting (GBM), adaptive boosting (ADA), and random forest (RF). Data was divided into training (75%) and testing (25%) cohorts with monte carlo cross-validation with 10 trials. Classifier performance was assessed by receiver operating characteristic curves. Area under the curve (AUC) values were compared using a paired t-test with Bonferroni adjustment.

Results

147 patients with 226 treated lesions were included; 203 treated for OM and 23 OP. 31 (15.2%) of the treated lesions were followed by DP within 90 days. No patients died or were lost to follow-up prior to the 90 days. In univariable analysis, age, CEA, treatment indication, DFI, number of systemic therapy lines and mean PTV BED were significantly associated with early DP ($p < 0.05$). In multivariable analysis treatment indication, DFI, number of systemic therapy lines, and mean PTV BED and were significant predictors of DP ($p < 0.05$). The AUC for each classifier was: LR (0.590), GBM (0.744), ADA (0.767), and RF (0.821). All ML classifiers were significantly better at identifying patients with DP compared to the logistic regression model ($p < 0.05$). There was no statistically significant difference in performance between the various ML classifiers. The top ranked variables by the RF classifier were DFI, PTV mean dose, number of systemic therapy lines, CEA and age. These are consistent with predictors found on univariable and multivariable analysis.

Conclusion

Treatment indication, DFI, number of systemic therapy lines, and mean PTV BED are associated with DP. ML classifiers were significantly better at identifying patients with DP compared to the logistic regression model. The ability to predict patients at risk of DP would assist clinicians in identifying patients who may benefit minimally from SBRT for OM/OP disease.

10 Clinical evaluation of a machine learning-based automated treatment planning method for prostate radiotherapy

Leigh Conroy, Alejandro Berlin, Michael C. Tjong, Tim Craig, Peter Chung, Chris McIntosh, and Thomas G. Purdie

Purpose

To evaluate the clinical applicability of an in-house developed automated planning method for radical prostate volumetric modulated arc therapy (VMAT) planning through direct blinded comparison of the automated plans to clinical plans..

Methods

Our machine learning-based automated planning method requires only the planning image dataset and contours for the target and organs-at-risk (OARs) as inputs. After training, the algorithm estimates the dose-per-voxel for a novel input patient based on the image features and OAR information from the most similar patients in the training database. In the final dose-mimicking step, a complete clinical plan, incorporating machine parameters and beam geometry effects, is produced. 116 consecutive clinically-approved radical prostate VMAT radiotherapy plans were used for algorithm training and testing. Two plans were left out due to incomplete contours. The automated planning framework was trained on 94 of the plans, and 20 independent plans were used for testing and clinical evaluation. Clinical and automatically-generated plans were evaluated by three independent blinded expert reviewers (two genitourinary radiation oncologists and one medical physicist). Reviewers evaluated six plan quality criterion as acceptable or unacceptable: target coverage, OAR sparing, high dose conformity, dose gradient at rectum, lateral dose symmetry, and overall approval. Reviewers were also asked to compare the two blinded plans head-to-head and chose a preferred plan.

Results

Automated plans were successfully generated for all 20 patients; 3 patients were removed from analysis due to metallic hip implants. In blinded review, both automated and clinical plans were considered clinically acceptable in 49/51 (96%) of the 17 cases across three reviewers. The overall majority score for each of the six scoring criteria was predominantly equivalent between the automated and clinical plans. When the evaluations differed, automated plans had higher approval rates than clinical plans for target coverage (100% vs. 90%) and OAR sparing (95% vs. 86%), and lower approval rates for high dose conformity (84% vs. 88%), dose gradient at the rectum (88% vs. 92%), and lateral dose symmetry (82% vs. 94%). In the head-to-head comparison, averaged across all three reviewers, automated plans were preferred for 12 patients, the plans were deemed equivalent (no preference) for 3 patients, and the clinical plans were preferred for 2 patients.

Conclusion

Our machine learning-based automated planning framework has potential to be integrated into the clinic to improve efficiency and consistency in prostate VMAT radiotherapy planning. Incorporation of this approach into our clinical practice, including prospective evaluation, is ongoing.

11 Screening MRI for radiation induced meningioma in childhood cancer survivors with prior cranial radiation

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Purpose

Radiation induced meningioma is a known late effect of cranial radiotherapy. Cranial MRI screening among the high risk population may detect these meningiomas early but currently its value is not well defined. This study describes the outcome of MRI screening among survivors of childhood leukemia who were treated with cranial RT (CRT).

Methods

The study cohort at risk for RIM was composed of childhood leukemia survivors who received CRT and attended the pediatric aftercare clinic in our cancer centre from January 2005 to February 2017. The screened group was composed of those who had screening cranial MRI from January 1, 2013 to February 2017. Outcomes of this group were compared with those at risk attending clinic from January 1, 2005 to December 31, 2012 before the implementation of routine screening who underwent cranial MRI only for symptomatic presentations.

Results

192 childhood leukemia survivors were included in this study, 86 in the screening group, 106 unscreened. Median time from RT to first screening MRI was 25 years (range 11-40 years). Screening MRI detected meningioma in 15 (17%) screened survivors. In the unscreened group, 17 (16%) had neurologic symptoms leading to an MRI, 9 of whom (8.5%) were diagnosed with meningioma. The cumulative incidence of meningioma 25 years after CRT were 6% and 3.4% in the screened and unscreened groups respectively (p= 0.09). There were no significant differences in age of detection, tumour size, multifocality, extent of resection, number of atypical and anaplastic histology, or use of adjuvant radiotherapy between screened and unscreened groups. There were 3 patients who had neurologic residual deficits in the unscreened group versus none in among screened patients, but this did not reach statistical significance (p= 0.25).

Conclusion

Screening MRI was able to detect meningioma before becoming clinically apparent, however we could not demonstrate a significant improvement in the chance of total resection or a significant decrease in morbidity. A larger sample could clarify potential reduction in neurologic sequelae associated with screening.

12 A novel method of calibration for improving accuracy and sensitivity in dual energy computed tomography perfusion+C23G2D22:G23

Hedi Mohseni, Catherine Coolens

Purpose

To combine dual energy computed tomography's (DECT) material differentiation, iodine parameterization, and CT perfusion to develop a Dual Energy Perfusion CT technique to overcome the current limitations of CT perfusion and improve the accuracy of imaging-derived pharmacokinetic parameters. Computed tomography perfusion assesses temporal changes in attenuation in tissues following the administration of an iodinated contrast agent. Iodine signal enhancement in tissues, expressed with respect to relative electron density (ρe), is relatively small due to the inherent low sensitivity of single energy CT in differentiating between iodine and other materials. DECT has the ability to better differentiate between materials with similar ρe values, but different effective atomic numbers (Zeff) by acquiring data in high and low energies and decomposing the X-ray attenuation information into ρe and Zeff. Furthermore, parameterizing the response of the DECT specifically to iodine through stoichiometric calibration can improve the sensitivity of the DECT to iodine, thus improving detectability.

Methods

Dual energy scans of phantoms containing clinically relevant concentrations of the iodinated contrast agent were acquired with a 64-row dual source CT scanner (Siemens Somatom Definition Flash). Values of ρe and Zeff were calculated in each voxel by modeling the X-ray spectra using SpekCalc software. Response of the DECT scanner to iodine was parameterized using stoichiometric calibration, taking into account both the CT numbers and chemical composition of known contrast materials. The calibrated response was used to create a map of Zeff for iodine concentrations.

Results

The preliminary results indicated that the combination of Zeff and stoichiometric calibration resulted in a 55% reduction in average error in estimation of iodine across the clinically relevant range of concentrations in phantoms, compared to ρe. Stoichiometric calibration improved the average error in Zeff-based estimation of iodine concentrations by 10% when compared to the uncalibrated Zeff.

Conclusion

Using DECT and CT number calibration with respect to Zeff, as opposed to ρe, together with stoichiometric parameterization of the DECT leads to improved accuracy in estimating iodine concentrations. These results will be applied to DECT perfusion to redefine contrast perfusion enhancement curves with respect to Zeff. Furthermore, these results will be validated in a head and neck cancer clinical trial to assess their efficacy in improving quantitative analysis of perfusion parametric maps.

13 Quantifying upstage rate as a function of delay from diagnostic imaging for locally-advanced lung cancer patients

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Purpose

Diagnosis and characterization of non-small cell lung cancer is done with diagnostic F18-FDG PET imaging as it is superior in sensitivity and specificity compared to conventional helical CT scans. Due to the aggressive nature of NSCLC, upstaging of disease is a concern for patients scheduled to undergo radical radiotherapy. We have reviewed our institution's experience with treatment planning PET-CT scans and quantified the upstage rates.

Methods

As part of a REB-approved study, PET-CT images acquired for treatment planning purposes. They were compared with PET-CT scans used for initial staging by two independent assessors. Patients' age at diagnosis, sex, tumor histology, stage & date at diagnostic PET-CT, stage & date at treatment PET-CT and survival/follow-up were collected prospectively. AJCC 7th edition TNM Staging System was applied. Reported stages were compared and differences were reconciled by a third independent party. Descriptive statistics were calculated and the estimates of the upstage rates were obtained using the Kaplan-Meier product-limit method.

Results

Between October 2009 and February 2012, 28 patients were accrued to the study. The mean age was 64 years (range: 41-81). Eight were female and 19 were male. The majority of patients had Stage IIIA disease (15), with others having Stage IIIB (11), Stage IIA (1) and Stage IIB (1) disease.

Predominant tumor histology was adenocarcinoma (71%). Median time between diagnostic and planning PET-CT scans was 21 days (range: 2-73). Overall upstaging occurred in 25% of patients. The TNM upstage breakdown was as follows: T-stage 7%, N-stage 14% and M-stage 11%. The 3 patients were found to have metastatic disease were switched to treatment with palliative intent. New nodal stations were found in 32% of patients, thereby necessitating a change in the treatment volumes. With the Kaplan-Meier product limit method the rate of overall upstaging increased with delay between staging and treatment planning PET-CT scans: 13% at 20 days (95% CI: 4%-95%), 33% at 40 days (95% CI: 14%-86%), and 56% at 60 days (95% CI: 29%-71%).

Conclusion

The use of a treatment planning PET-CT demonstrated upstaging which altered patients' treatment plans. Lengthened interval period between diagnostic PET and planning PET scans showed an increase in upstaging. Our data is consistent with two published studies which showed similar upstaging rates.

14 Free PSA ratio as a predictor of adverse outcomes after curative-intent external beam radiation therapy for prostate cancer: a novel application of an "old" biomarker

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Purpose

Most serum PSA circulates in complex with protease inhibitors, but 5%-45% does it as enzymatically inactive free PSA (fPSA). PSA produced from prostate cancer (PC) cells appears to escape proteolytic processing, resulting in a greater fraction of complexed PSA (e.g. lower fPSA). Based on this, fPSA ratio is commonly used as an adjunct marker to improve the accuracy of PSA for screening. Within the PSA range 4-10 ng/mL, a fPSA ratio higher than 0.15 correlates with lower risk of harbouring PC. Nonetheless, post treatment fPSA is rarely quantified, and its prognostic value after radical external beam radiotherapy (EBRT) remains unexplored.

Methods

Institutional databases were queried to identify intermediate- and high-risk PC patients treated between 1992 and 2012 with EBRT, who had at least one ascertainment of fPSA during follow-up. Patients were stratified according to a fPSA cut-off of 0.15. Multivariable Cox regression models were performed to determine the correlation of post-EBRT fPSA and clinical outcomes.

Results

A total of 355 patients were identified. Of these, 262 (73.8%) and 93 (26.2%) had a fPSA ratio<0.15 and ≥0.15, respectively. Mean age, pre-treatment total PSA, and clinical T-category were similar in both

groups (Table 1). However, patients with a fPSA ratio ≥0.15 had a higher biopsy Gleason score (GS), NCCN risk group, and were more often treated with combined EBRT and androgen deprivation therapy (ADT). Mean follow-up time was similar in both groups (109.5 months vs. 111.9 months, p=0.725). Biochemical recurrence (BCR) rate were similar in both groups (77.6% vs. 80.5%, p=0.58), as expected from the Institutional lab policy of ascertaining fPSA when total PSA is in the 4-10ng/mL range and therefore BCR most likely already established. However, the metastasis and castrate resistant prostate cancer (CRPC) rates were higher in the fPSA ≥0.15 group (41.3% vs. 21.5%, p<0.001, and 67.4% vs. 37.5%, p=0.002, respectively). Multivariable models demonstrated that along with higher GS, a fPSA fraction ≥0.15 conferred a statistically significantly higher hazard ratio (HR) for metastasis (HR 2.027, 95% CI 1.28-3.21, p=0.003), and CRPC (HR 3.066, 95% CI 1.565-6.004, p=0.01).

Conclusion

This study suggests that a fPSA ratio ≥0.15 in the setting of post curative-intent EBRT denotes a more aggressive disease, reflected in higher rates of metastasis and CRPC. Our findings suggest a reversal in the significance of fPSA ratio in the post treatment state, and a potential novel role for this widely available and low-cost biomarker.

15 Change of radiotherapy practice pattern in lymphoma at a large academic center

Melody Qu, Richard Tsang, David Hodgson, Alexander Sun, Normand Laperriere, Woodrow Wells, Mary Gospodarowicz

Purpose

To compare the practice pattern of radiotherapy (RT) in lymphoma between 2000 and 2015 at a large academic center with stable volumes and referral pattern. Decrease utilization of RT has been observed in population studies over the last 20 years, however, little has been reported in the change of practice pattern.

Methods

All patients who received RT in 2000 or 2015 for lymphoma at our centre were reviewed. In patients who received multiple courses of RT in the same year, the first course was indexed. Proportions of groups between the two calendar years were compared by Pearson chi-square/Fisher exact tests and adjusted for multiple comparisons when indicated. Wilcoxon rank-sum test were used to compare RT doses.

Results

Our center provided RT to 270 lymphoma patients (300 courses) in 2000 and 253 patients (282 courses) in 2015. Shift in lymphoma types that received RT was observed with a decrease in Hodgkin's lymphoma (HL, n=72 vs 44, 27% vs. 17%, p=0.075) and an increase in mantle cell lymphoma (MCL, n=5 vs 19, 2% vs. 8%, p=0.016) while other types remained stable: DLBCL 39% vs 32%; follicular lymphoma(FL) 13% vs 15%; MALT lymphoma 11% vs 12%, primary CNS lymphoma 2 vs 6%, others 7 vs 9% (comparing 2000 vs. 2015). RT use as a component in primary management has decreased (n=195 vs 140, 72% vs. 55%, p<0.001). Overall, significant change in the role of RT was observed from 2000 to 2015 (p<0.001) with decreased combine modality therapy received (CMT, n=126 vs. 70, 47% vs. 28%, p<0.001); while palliative RT increased (n=52 vs 103, 19% vs. 41%, p<0.001). Conditioning total body irradiation in the setting of stem cell transplant increased due to its use in MCL in 2015 (n=0 vs. 12, 0 vs. 5%, p=0.002). For adult HL patients, the absolute number of cases of CMT decreased from 48 to 23 in 2015. The prophylactic upper abdominal RT in stage I-II HL (n= 18, 34% in 2000) was not used in 2015 (p<0.001). The RT dose for CMT in HL and DLBCL had decreased from 2000 to 2015 (median 35Gy vs. 30Gy, p<0.001). For DLBCL, a trend of decrease in CMT (n=60 vs. 32, 58% vs. 39%, p=0.057) and an increase in palliation (n=22 vs. 33, 21% vs. 40%, p=0.028) were observed. No significant practice pattern change was seen in FL and MALT lymphoma.

Conclusion

Significant practice change of RT in lymphoma has been observed over 15-year period at a large academic institution. The shifting RT role toward palliative setting was observed.

16 Improvement in patient-reported distress after chemo-radiation in cervical cancer patients

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Purpose

Curative treatment of cervical cancer with definitive chemo-radiotherapy (CRT) can be associated with significant morbidity impacting quality of life and causing distress. Our objective was to evaluate the clinical utility of prospectively collected patient-reported distress over time in cervical cancer patients treated with definitive CRT using the Edmonton Symptom Assessment System (ESAS) questionnaire.

Methods

Between 2011 and 2016, consenting cervical cancer patients treated with definitive CRT who completed > 2 questionnaires at routine clinical visits, including baseline, were included. The ESAS is a validated 10-item patient-reported symptom screening tool. Items are scored 0-10 and summed to a total score with higher scores indicating higher distress. Mean total scores were calculated at all time points and compared to baseline using a paired t-test. For each patient, a slope was created using linear regression. A one-sample t-test was performed on the slopes to determine whether the degree of change differed from zero. The minimal clinically important difference (MCID) for total ESAS score was defined as a change of 3-points for improvement and 4-points for deterioration. A mixed model was used to evaluate the longitudinal change in the MCID from baseline.

Results

Of the 98 patients initially identified, 68 met inclusion criteria. Median (range) follow-up was 16 mos (2-57) and compliance at 12 mos was 57% (39/68). The median (range) age at diagnosis was 46 years (30-77) and 32%, 53%, 15% were FIGO stages IB, IIA-B, and IIIA-B respectively. All patients received external beam radiation with concurrent cisplatin followed by MR-guided PDR (47%) or HDR (53%) brachytherapy with 59% intracavitary and 41% combined intracavitary/interstitial techniques. There was no difference in total score at baseline compared to end of treatment (p=0.50), but reductions in distress were observed at 6 weeks, 3 mos and 6 mos after treatment compared to baseline (p=0.03, p=0.008 and p=<0.001, respectively). There was a significant improvement in distress over time for each patient reflected in the change in slope (mean slope: -0.79; 95% confidence interval: -1.31, -0.27; p=0.004). There was also a significant improvement in the MCID for total score from baseline over time (p=0.04).

Conclusion

Cervical cancer patients experience significant distress at diagnosis and during definitive CRT that significantly improves over time after treatment to an extent that is expected to be clinically meaningful for patients as defined by the MCID. Prospective collection of cervix cancer specific patient-reported outcomes should be incorporated into routine clinical practice to better inform areas of need and survivorship planning.

P1 Exploring the use of virtual reality as a supplemental educational tool in traditional first day teaching for patients receiving external beam radiation therapy to the pelvis

Kalaina Johnson, Brian Liszewski, Merrylee McGuffin

Purpose

Due to the uniqueness of radiotherapy treatment, most new patients have little knowledge of radiotherapy treatment procedures. Patient education for external beam radiation therapy (EBRT) is traditionally delivered in verbal and/or written form. These education methods may not provide a full picture of the technical aspects of treatment. The purpose of this pilot study was to create and evaluate a prototype 360degree Virtual Reality (VR) video outlining the technical aspects of EBRT to the pelvis as a supplement to traditional education methods.

Methods

A prototype VR video was filmed to simulate the delivery of one fraction of image-guided EBRT to the pelvis from the patient's point of view. Storyboarding and scripting were used to ensure the technical aspects of treatment and standard new patient education protocols at our institution were addressed. The video overlaid with an audio narration track, edited for time and formatted for viewing through a smartphone VR headset. Patients having a radical course of image-guided EBRT to the pelvis were approached in clinic to participate in a focus group evaluating the prototype VR video. Focus groups led by an independent facilitator allowed participants to view and discuss the prototype VR video with relation to the patient education they received prior to treatment. Discussions were recorded, transcribed and subjected to thematic analysis.

Results

All patients were accrued from a single academic cancer centre in a large metropolitan area. In total, 15 patients were approached, 9 consented to participate and 2 were withdrawn (unable to attend a focus group). Of the remaining 7 participants, 3 were male and 4 were female, ranging in age from 54 to 67 years (μ=61, SD=4.89). Thematic analysis revealed 71% (5/7) of participants felt the traditional patient education met their needs. However, 86% (6/7) mentioned the education did not capture all the elements of treatment. Participants identified potential benefits could include an increased understanding of the treatment process, specifically the spatial and acoustic aspects of treatment, as well as the potential to reduce anxiety in new patients. Participants also recommended changes, such as including 2-dimensional elements in the VR video and improvements which would make the viewing experience more realistic. Timing was also important, with 86% (6/7) of participants recommending VR video viewing prior to the first day of treatment.

Conclusion

Overall, patient education at our centre was found to be adequate by most participants. Supplementing traditional education with VR video has the potential to improve upon existing methods, increasing understanding of treatment and decreasing anxiety. Next steps include implementing participant feedback and testing the VR video in the setting of a randomized controlled education study.

P2 Validation of a viability assay for assessing radiation response and investigating drug/radiation combinations

Meghan Lambie, Venkata Manem, Benjamin Haibe-Kains, Scott V. Bratman

Purpose

Radiotherapy (RT) is frequently used either alone or in combination with chemotherapy for curative treatment of squamous cell carcinomas (SCC) originating from the head and neck, lung, esophagus, and cervix. Treatment outcomes for SCCs are heterogeneous, in part due to variable degrees of resistance to ionizing radiation and modest benefit of existing radiosensitizing drugs. Preclinical research into intrinsic cancer cell radiosensitivity biomarkers and novel radiosensitizing drugs has been hampered by a lack of robust high throughput assays of radiation response. We sought to validate a recently published high throughput viability assay as a surrogate of clonogenic survival and extend its use to drug-radiation combinations.

Methods

Clonogenic assays-the gold standard for assessing radiation survival in vitro-and viability assays were performed on 19 SCC cell lines (16 head and neck, 3 esophageal). The clonogenic assay was performed according to published procedures (Franken et al. Nat. Protoc, 2006) with colonies counted using ImageJ. The viability assay was adapted from Abazeed et al. (Cancer Res., 2013). Cells were seeded with a range of densities in 96 well plates then treated with a range of radiation doses (0, 2, 4, and 8 Gy); viability was measured using CellTitre Glo reagent after 9 days. Agreement between clonogenic and viability assays was measured using modified concordance index (C-index) and Pearson correlation. For the addition of drug, cells were allowed to adhere to plates for 2 hours
before drug administration. Cells were irradiated 16 hours later again at a range of doses (0, 2, 4, and 6 Gy for drug analysis), and then quantified as above. All assays were performed with technical and biological triplicates.

Results

There was a high degree of agreement between the area under the curve with the clonogenic assay and the viability assay (C-index = 0.80, p = 3.03x10-7; Pearson r = 0.70, p = 1.10x10-3). Significant concordance was also seen at 2 Gy and 4 Gy dose points (Pearson r = 0.62 and 0.73 respectively), however not at 8 Gy (Pearson r<0.5). The viability assay decreases the overall time for the experiment, as it has a 9-day endpoint rather than the 14 days typical for the clonogenic assay. The viability assay also eliminates cell counting time, as results can be analyzed in minutes. Survival curves with and without radiation with clinically utilized chemotherapeutic drugs cisplatin and paclitaxel were developed which showed an additive effect for drug combinations, demonstrating the ability of the assay to be combined with chemotherapeutic agents and allows for the investigation into dose-response effects.

Conclusion

The viability assay recapitulates the clonogenic assay within our cohort of SCC cell lines. Novel higher throughput methods to analyze radiation response will allow for a more efficient measure of drug and radiation combinations.

P3 Loss of RSPO3 as a potential mechanism of greater invasiveness in prostate cancer

Aruz Mesci, Xiaoyong Huang, David Shin, Christianne Hoey, Jessica Ray, Paul Boutros, Stanley Liu

Purpose

To investigate a potential role of RSPO3, a protein previously implicated as an oncogene in several other cancers, in prostate cancer behaviour.

Methods

We use gene expression and clinical outcome data from a cohort of prostate cancer patients to show a correlation between RSPO3 expression and biochemical relapse-free survival. Then, we utilize shRNA-mediated knockdown technology with in vitro assays such as proliferation, clonogenic survival, Matrigel invasion to characterize the functional consequences of RSPO3 loss. Finally, we assess changes in various cell signaling pathways with RSPO3 loss using Western Blotting to further investigate possible mechanisms of RSPO3 action.

Results

In a cohort of prostate cancer patients, lower levels of RSPO3 expression correlates with lower biochemical relapse-free survival. Functionally, shRNA-mediated loss of RSPO3 in prostate cancer cell lines paradoxically decreases proliferation but increases invasiveness. There is no significant change to clonogenic survival. Western Blot analysis shows an increased level of SAPK signaling with RSPO3 downregulation. Further experiments to characterize the mechanism of RSPO3 action are underway.

Conclusion

In prostate cancer, loss of RSPO3 protein may result in a more aggressive phenotype.

P4 Evaluating the kinetics and thermodynamics of Gafchromic (EBT3) films in the context of radiation dosimetry of megavoltage beams

Eric Da Silva Daniel Crawford, Darrick V. Heyd, David Beachey

Purpose

Radiochromic film, specifically Gafchromic EBT3 film, is often used for the purpose of performing absolute dosimetry of megavoltage beams. Gafchromic EBT3 film offers the advantage of being self-developing and providing dosimetric information with high spatial resolution. Such film works on the basis of a polymerization reaction of monomers within the active layer emulsion which results in a colored product which changes in optical density over a period of time. The optical density of this layer, and thus the film, relates directly to absorbed radiation dose. Being based on a polymerization reaction, the degree of polymerization, and thus the measured optical density, is dictated by the thermodynamics and kinetics of the reaction. The purpose of this work was to assess the thermodynamics, chemical kinetics and thus the equilibrium conditions of the EBT3 active layer over a period of time in order to assess the accuracy and precision of the films as based on the chemical reaction of the active layer with a focus on its chemical stability over time.

Methods

Gafchromic EBT3 films were irradiated using orthovoltage and clinical MV beams of a LINAC as to deliver 0-100 Gy of radiation dose to the films. The optical density of the films was monitored by scanning the films in a flatbed scanner in absorption mode and with a scanning UV-VIS spectrometer. The optical density was monitored using the red, green, and blue channels over a period of 14 days. Films irradiated under identical conditions were assessed using confocal Raman micro-spectroscopy whereby the emulsion layer was probed in situ using both 782 and 514 nm lasers. Measurements were made over the same period of time. The chemical thermodynamics and kinetics of the irradiated emulsion layer was assessed using the acquired Raman spectra using a method similar to that developed and described by Da Silva and Rousseau (2008) [Phys. Chem. Chem. Phys. 10: 4606].

Results

The EBT3 films presented rapid darkening and change in the red, green and blue absorption bands within a 20 hour period independent of the absorbed dose to the films. Raman measurements indicated that the chemical reaction progressed for the period of study indicating that under the given environmental conditions that chemical equilibrium within the emulsion layer may not have been reached. The changes observed over the study period in the kinetic and thermodynamic parameters were followed by changes in the absorption characteristics of the films which indicate a dynamic chemical system prone to a partial shift back to the original pre-exposure system.

Conclusion

Gafchromic EBT3 films were found to be prone to shifts in the chemical equilibrium within the active layer with associated potential for changes in the absorption characteristics with time towards the pre-exposure system.

P5 Lymph node ratio as a predictor of distant metastases in major salivary gland carcinomas

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Purpose

To investigate the prognostic value of lymph node ratio (LNR, number of positive lymph nodes[LN]/total number of excised LN) on distant metastases (DM) and overall survival (OS) in patients (pts) with major salivary gland carcinoma (SGC).

Methods

An REB-approved retrospective review was conducted for SGC patients treated at our institution with curative surgery and neck dissection (>=6 dissected LN)+/-adjuvant treatment in 2000-2015. Patients, treatment and outcomes data were collected from our institutional maintained databases. Staging was reviewed according to the AJCC-UICC 8th edition. High risk pathology was defined with histologic grade and WHO histologic criteria, and included: adenoid cystic carcinoma (ACC), salivary duct carcinoma, SCC, G2/3 adenocarcinoma, G2/3 mucoepidermoid carcinoma (MEC), G2/3 carcinoma ex-pleomorphic adenoma, carcinosarcoma, undifferentiated (small-, large-cell or lymphoepithelial) carcinoma and G3 of other histologic subtypes. Distant control (DC) and OS were analyzed with competing risk and Kaplan-Meier methods respectively. LNR (continuous variable) was subjected to multivariable analysis (MVA) for DM and OS (adjusted for age, gender, primary SGC subsite, pathologic stage, high-risk pathology, lymphovascuar invasion [LVI], perineural invasion [PNI], extranodal extension [ENE] and surgical margin status). The optimal cutpoint of LNR that maximized the difference in outcomes was determined using maximally selected rank statistics. Subgroup analysis was performed for patients with pN+.

Results

A total of 204 pts were identified: median age: 56 yr (16-91); median follow-up: 5.2 yr (0.4- 17.6); parotid gland primary tumor location: 168 (82%); high risk pathology: 151 (74%); pT3-4: 132 (65%), pN+: 99 (44%); LVI: 49 (26%); positive microscopic surgical margin: 103 (52%); ENE: 37 (19%). PORT was used in 195 pts (96%); and adjuvant concurrent chemotherapy in 11 (5%). Of 2,725 LNs evaluated, 328 (12%) were pN+. The median number of dissected LN was 23 (6–101). For pN+ pts, the median number of involved LN was 3 (1-65) and median LNR was 14% (1%–100%). High-risk pathology and LVI were associated with high LNR ($p<0.001$ for both). On MVA LNR was independently correlated with DM (HR:1.18, 95%CI: 1.07-1.30, $p<0.001$) and OS (HR:1.16; 95%CI: 1.06-1.28, $p=0.002$) and so did LVI+ (DM: HR:2.54, 95%CI: 1.38-4.70, $p=0.003$) and OS (HR:2.50; 95%CI: 1.33-4.70, $p=0.004$), positive margins (DM: HR:2.47, 95%CI: 1.31-4.65, $p=0.005$) and OS (HR:2.59; 95%CI: 1.35-4.95, $p=0.004$),. The optimal cut-off point for LNR was 8%; 5-yr DC: 42% vs 88%, $p<0.001$; 5-yr OS: 44% vs 89%, $p<0.001$ for LNR ≥8% vs <8%. In a subgroup analysis of patients with pN+, LNR remained predictive for DM (HR:1.24, 95%CI: 1.14-1.35, $p<0.001$) and OS (HR 1.27, 95%CI: 1.16-1.38, $p<0.001$).

Conclusion

High LNR is associated with a higher risk of DM and lower OS. LNR should be evaluated in future prospective studies for intensified therapy or surveillance schedule in patients with SGC.

P6 Prostate treatment in a MRI-Linac for patients with bilateral hip implants

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Purpose

The MRI-Linac offers a distinct advantage of imaging soft tissue using MRI for target delineation and MV imaging for metal implant delineation. This study was designed to assess the dosimetric implications of treating a patient with a bilateral hip implant in a MRI-Linac (Elekta AB, Stockholm, Sweden).

Methods

A patient with a bilateral titanium hip implant was chosen for hypo-fractionated SBRT treatment of the prostate with a prescription of 3500 cGy in 5 fractions. The electron density of the metal implant was overridden in the Monaco treatment planning system (TPS) Research Version 5.19.3. Treatment plans were generated using (i) a 6-field conventional beam arrangement avoiding entrance through the prostheses and (ii) a 7-field beam arrangement with evenly distributed beams around the target volume including two beams partially entering through the prostheses. The dose was calculated using the Monte Carlo dose calculation algorithm, GPUMCD. Concentric rings with 2 mm, 4 mm, and 8 mm radial distances from the hip implants were created to record D0.1cc to the bone surrounding the implant. Plans were optimized both with and without the presence of the magnetic field.

Results

For the plans optimized using beams entering through the prosthesis, the D0.1cc was 1525 cGy, 1554 cGy, and 1619 cGy, at 2, 4 and 8 mm radial distances from the implant, respectively. The D0.1cc values were similar for plans optimized with and without the presence of the magnetic field. A target volume conformity index (CI) of 1.04 was achieved for the MRI-Linac plan (with magnetic field and evenly-distributed beams) compared to the plan with no magnetic field and conventional beam arrangement (CI = 1.21).

Conclusion

The maximum dose to the bone surrounding the prosthetic implant was recorded to be well within the published dose limit (30 Gy for a 5-fraction regimen) for bone necrosis. Patients with bilateral hip implants are generally treated with beams avoiding entrance through the hip implants which makes it difficult to achieve acceptable dose constraints for OARs and dose conformity for the target. Treatment of such patients in the MRI-Linac in combination with a Monte Carlo TPS would provide a bi-fold advantage in terms of improved imaging for both soft tissue and high density implants and improved dosimetry using a more flexible beam arrangement. We have demonstrated that clinically-acceptable treatment plans with good target conformity are achievable for patients with bilateral hip implants in the presence of the magnetic field of the MRI-Linac.

P7 Patient-reported acute fatigue in elderly breast cancer patients treated with and without regional nodal radiation

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Purpose

Although regional nodal irradiation (RNI) improves outcomes in breast cancer (BC) patients, it is associated with increased toxicity. Therefore, controversy still exist surrounding its indications. The purpose of this study was to evaluate and compare patient-reported acute fatigue in elderly BC patients with and without regional nodal radiation (RNI).

Methods

Elderly breast cancer patients (≥ 65 yrs) treated with adjuvant radiotherapy (RT) between 2012 and 2017 were identified from a prospective database. The validated Edmonton Symptom Assessment System (ESAS) questionnaire, which assesses fatigue, was completed prior to (baseline), during, at end of RT and first follow-up (6-12 weeks). Symptoms are rated on a 10-point Likert scale, with higher scores indicating higher fatigue. Patients and treatment characteristics were also recorded. Patients were divided into two cohorts: those who received RNI (cohort 1) and those who did not (cohort 2). A minimal clinically important difference (MCID) was defined using an anchor of ≥1-point compared to baseline. The proportion of patients reporting a change in fatigue at the end of RT was evaluated. Univariate and multivariable logistic regression were conducted to assess the association between RNI and MCID after adjusting for potential confounders. To test the robustness of the results, dynamic changes of fatigue scores over time were compared between the cohorts using a general linear mixed model after assuming individual patient with random effect. A two-tailed p-value ≤ 0.05 was considered statistically significant.

Results

Of the 1204 patients, 654 completed the ESAS at baseline and end of RT and were considered for this analysis (cohort 1 = 137, cohort 2 = 511). Mean age at diagnosis was similar between the groups: cohort 1 71± 6 vs. cohort 2 72± 5 years (total 72± 4). Overall, cohort 1 had higher stage and reception of chemotherapy (69% vs. 16%). Mean baseline fatigue was higher for cohort 1 vs. 2 (2.5 ± 2.4 vs. 2.1 ± 2.3, p=0.03). On univariate and multivariable analyses, RNI was not associated with an increased odd of MCID for fatigue at the end of RT (44% vs. 47%; OR: 0.89, 95 % CI: 0.61-1.30, p=0.56). After adjusting for confounders (age, duration of RT, endocrine therapy), higher baseline fatigue (OR: 0.86, 95% CI 0.80-0.92, p<0.001) and receipt of chemotherapy (OR: 0.53, 95 % CI:0.34-0.83, p=0.006) were the only factors associated with decreased odds of MCID. Dynamic changes showed a significant worsening of fatigue scores over time (p<0.001) with no difference between the cohorts (p=0.42); both experienced parallel worsening of fatigue levels over time (cohort*time p=0.18).

Conclusion

The addition of RNI in elderly BC patients is not associated with a significant worsening of patient-reported fatigue. Therefore, RNI should be considered in elderly BC patient with adverse factors.

P8 Impact of immobilization on interfractional errors for upper extremity soft tissue sarcoma radiation therapy

Aran Kim, Valerie Kelly, Winnie Li

Purpose

Due to the rare nature and presentation of upper extremity soft tissue sarcomas (UE STS) and the high mobility of associated anatomy, various patient positioning strategies are employed for radiation treatment. Limited analyses have been performed to assess the effectiveness of the different immobilization methods used. The purpose of this study is to measure the interfractional setup errors associated with UE STS using cone beam computed tomography (CBCT), and to identify and compare the different immobilization methods used regarding their accuracy and reproducibility.

Methods

Retrospective data collection was performed under institutional ethics approval. All patients treated with daily CBCT guidance for UE STS during 2014-2015 were identified and triaged based on type of immobilization. After defining an optimal region-of-interest (ROI) for image registration, daily CBCT images were automatically registered to reference CT images to quantify translational and rotational discrepancies. Means and standard deviations were calculated.

Results

Seventeen UE STS patients met inclusion criteria: 13 were treated for shoulder/axilla/upper arm, and 4 for arm/elbow/forearm. 3 main types of immobilization were identified: vacuum cradles with custom thermoplastic shells, vacuum cradles alone, and no immobilization accessories used. Patient repositioning occurred if translational and rotational displacements were larger than 1cm and 5° respectively, as per institutional guidelines. Patient repositioning rates were 18% for vacuum cradle with thermoplastic shells, 15% for vacuum cradles only, and 6% for no immobilization accessories. Mean translational displacements in right/left, superior/inferior, and anterior/posterior directions were -0.04±0.33cm, 0.32±0.33cm, and 0.12±0.25cm for vacuum cradle with thermoplastic shell; 0.25±0.10cm, -0.07±0.22cm, and 0.00±0.17cm for vacuum cradle alone; and 0.14±0.15cm, 0.08±0.45cm, and -0.01±0.24cm for no immobilization. For all patients, rotational displacements in the pitch, roll and yaw were 0.15±1.99°, 0.31±2.11°, and -0.21±1.76° respectively.

Conclusion

Large interfractional errors, especially in the rotational axes, were observed, regardless of immobilization strategy. This study reinforces the need for better immobilization techniques for upper extremity STS. Limitations include small study population and unequal representation of different parts of the upper extremity. Further research is required.

P9 Creation of a high-fidelity computer-based simulation to improve resident competency in radiotherapy treatment plan evaluation

Jenna Adleman, Jeff Winter, Thomas Purdie, Andrea McNiven, Jennifer Croke

Purpose

Treatment plan evaluation is a core competency for radiation oncology (RO) and medical physics (MP) residents. Gaps in teaching and assessing plan evaluation have been identified in residency training. The purpose of this project was to create and implement an interactive plan evaluation case bank for RO and MP residents to improve competency.

Methods

A needs assessment was performed to inform case selection, case bank development and accompanying software. Current and former residents were asked to assess their confidence in various aspects of plan evaluation using a 10-point Likert scale (1=least confident, 10=most confident). In parallel, a list of clinically unacceptable plans (with corresponding acceptable plans) from January 2011-June 2013 was compiled and categorized by clinical site, reason for rejection, detectability and relevance. Cases were reviewed for consensus by two ROs and two MPs. An interactive web-based DICOM-RT tool was used to query and interact with the case bank database. A companion software tool, acting as an interactive simulation platform, was created to allow user interaction with the database.

Results

Thirty participants (68%) responded to the needs assessment: 13 current RO (6 junior, 7 senior), 10 former RO, 3 current MP and 4 former MP residents. Opportunities for improving plan evaluation were identified with the following mean confidence scores: assessment of target coverage (6.6±2.5), doses to OARs (6.2±2.4), conformity (5.7±2.5), overall plan acceptability (5.5±2.3) and ability to suggest improvements (4.9±2.1). Extracted themes for case bank development included incorporating diverse clinical sites, common cases, target coverage and OAR assessment, DVHs, conformity and provision of immediate feedback. Of the 218 clinically unacceptable plans, 50 were included in the case bank. These cases were categorized, anonymized and imported into the case bank database. Additional acceptable and unacceptable plans were generated to augment the case bank where required. The companion simulation software platform was implemented and tested to ensure proper functionality. The simulation platform describes each clinical scenario and allows residents to enter their assessment, error classification and suggested corrective action (if applicable). The simulation platform then provides immediate feedback, including error description, correction strategy and link to the corrected plan.

Conclusion

An innovative, interdisciplinary plan evaluation case bank has been created to address an identified learning gap in RO and MP training. The format improves fidelity of the simulation by allowing interaction with the images and plan in 3D, incorporation of feedback to residents and visualization of the corresponding clinically acceptable plan. This case bank can be leveraged as a teaching and assessment tool in competency based medical education. Future work will evaluate resident satisfaction with and effectiveness of the case bank as a learning tool.

P10 Tumor-targeted dose escalation for localized prostate cancer using MR-guided HDR brachytherapy (HDR) or integrated VMAT (IB-VMAT) boost: Dosimetry and early toxicity analysis

Noelia Sanmamed, Cynthia Ménard, Jenny Lee, Alejandro Berlin, Tim Craig, Bernadeth Lao, Alex Rink, Andrew Bayley, Charles Catton, Mary Gospodarowicz, Padraig Warde, Peter Chung

Purpose

To report dosimetry and early toxicity outcomes of tumor-targeted dose-escalation delivered by integrated VMAT (IB-VMAT) or MR-guided HDR brachytherapy (HDR) boost for prostate cancer.

Methods

Patients diagnosed with localized prostate cancer, with at least 1 identifiable intraprostatic lesion (> 5mm and <33% total prostate volume) on multiparametric MRI (mpMRI) were enrolled in a prospective non-randomized phase II study. All patients received VMAT to the prostate alone (76 Gy in 38 fractions) plus a GTV boost: IB-VMAT (95Gy in 38 fractions) or MR-guided HDR (10Gy single fraction). GTV was delineated on mpMRI and deformably registered to planning CT scans. CTV76 included prostate plus 5mm margin around the GTV avoiding OARs (penile bulb, urethra, rectum/bladder wall). PTV76 was CTV + 5mm AP/ SI and 3mm LR. PTV95 was GTV + 5mm AP/ SI and 3mm LR (IB-VMAT). PTV10 was GTV(s) + 2 mm SI and 1mm AP/RL (HDR). Comparative dosimetry using EQD2 assuming α/β 3 Gy was performed. For HDR, deformable registration to account for anatomical distortion was used to estimate EQD2 and then summed with the external beam dose. Toxicity data was prospectively collected (CTCAE v.4.0).

Results

80 patients were enrolled, 40 received IB-VMAT and 40 HDR boost. PTV76 (means) were 93.2cc and 90.2 cc, PTV (GTV) volume was 11.7 cc and 3.2 cc for IB-VMAT and HDR, respectively Dosimetric results are: GTV D99 105.3 Gy (SD 2.8) in the VMAT arm and 103.1 Gy (SD 6.7) for HDR arm, D0.1cc 111.7 Gy (2.8) and 416.7 Gy (100.5); PTV76 D99 71.6 Gy (1) and 72.7 Gy (2), D0.1cc 112.2 Gy (1.7) and 467.9 Gy (174.5). OARs doses were rectal wall D0.5cc 79.4 Gy (5.0) and 82.6 Gy (4.8) respectively, bladder wall D0.5cc 77.2 Gy (5.9) and 76.2 Gy (4.9), and urethra D0.5cc 87.4 Gy (7.0) and 85.7 Gy (6.6). Median follow-up was 24 months (range 6-36). Acute grade 2 GU toxicity was 40% and 42.5% in IB-VMAT and HDR, while GI toxicity was 7.5% and 10%, respectively. One IB-VMAT patient developed grade 3 GU acute toxicity (urinary retention). Of 69 patients with >12 months follow up (33 IB-VMAT and 36 HDR boost), 18.1% (IB-VMAT) and 19.4% (HDR) developed grade 2 GU toxicity, while grade 2 GI toxicity rates were 6% (IB-VMAT) and 2.7% (HDR). Late grade 3 toxicity was observed in 2 patients (IB-VMAT): 1 GU (hematuria attributable to a new bladder cancer) and 1 GI (rectal ulcer in the context of concurrent HIV antiviral therapy). Deterioration in sexual function occurred in 20% IB-VMAT and 12.5% HDR patients. No statistically significant difference in toxicity was found between both groups.

Conclusion

Our early results suggest comparable dosimetry to OARs and rates of Grade 2 toxicity between the two boost techniques. HDR boost achieved higher mean and max GTV doses than IB-VMAT. Further follow-up will determine long-term outcomes.

P11 Dose reconstruction for lung cancer patients with gross anatomical changes during radiotherapy

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Purpose

To assess the dosimetric effect of gross anatomical changes (e.g., atelectasis, pleural effusion) occurring during radiation treatment (RT) of locally advanced lung cancer using dose reconstruction with the goal of informing future decision making around replanning. Our secondary objective was to investigate the impact of replanning on the agreement between planned and delivered doses.

Methods

We retrospectively identified 11 patients with gross changes identified on treatment, 6 of which were replanned. To estimate the dose actually delivered, we performed dose reconstruction in RayStation (v6, RaySearch Laboratories, Stockholm, Sweden). This involved dose calculation on daily CBCTs and deformable image registration (DIR) to map the reconstructed dose onto the corresponding plan or replan CT. For each fraction, we compared DVH metrics between the planned and reconstructed delivered dose. Key OAR dose statistics compared included maximum dose for the spinal canal, V40 for heart, V20 for lung and the mean lung dose. For patients that were replanned, we assessed whether the replan impacted the agreement between planned and delivered OAR doses. We also compared the agreement between planned and delivered doses between the cohorts with and without replanning. Statistical tests were performed with Student's two-tailed t-test ($p < 0.05$ considered significant).

Results

We successfully reconstructed dose for all patients except for one replanned case with large changes that could not be recovered using deformable registration. We qualitatively assessed DIR accuracy and excluded fractions with gross registration errors. Across all patients and fractions, the mean differences between the planned and delivered dose metrics were 0.9 ± 2.4% (mean ± STD error) for spinal canal maximum dose, -0.4 ± 0.7% for the heart V40, -1.3 ± 0.5% for lung V20 and -1.5 ± 0.5% for mean lung dose. Within treatment courses replanned, no significant differences existed before and after the new plan with regards to the agreement between planned and delivered doses. Moreover, no significant differences in this agreement existed between treatment courses replanned versus those that were not.

Conclusion

We demonstrated the value of dose reconstruction for lung patients with gross anatomical changes. We found that the agreement between planned and delivered dose metrics for the spinal canal, heart and lung did not vary considerably throughout treatment, even in the presence of large anatomical changes, or whether the cases were replanned or not. We are currently exploring quantification of inherent uncertainties in accumulating dose in this challenging cohort, including impact of DIR quality, CBCT dose calculation and lung tissue deformation.

P12 Intrafraction tracking for spinal SBRT and motion assessment on an Elekta Linac

Daniel Markel, Daniel Letourneau, Harald Keller, David Shultz

Purpose

Spine stereotactic body radiation therapy (SBRT) uses ablative levels of radiation to treat tumors and high-risk post-operative regions. Due to the large doses and dose gradients surrounding the spinal cord, tight positioning tolerances of 1 mm and 1° are used for these patients, however movement during treatment remains unaccounted for. Recent development on the Elekta linac/XVI platform allows for the acquisition of an intra-fraction CBCT dataset during arc treatment delivery. The encompassing purpose of this work is to develop a framework for real-time vertebrae tracking using the intra-fraction CBCT projections to assess intra-fraction motion for SBRT treatments at our center. Our framework involves in plane tracking of spinal vertebrae during SBRT treatment through registration of intra-fraction CBCT projections compared to simulated projections created from the planning CT. Initial phantom results to assess the accuracy of our framework is presented here.

Methods

Simulated projections were created with the SimpleRTK Python package using a pre-treatment CT acquired with a GE CT simulator. In order to study the efficacy of our framework, projections of a custom solid water anthropomorphic torso phantom were acquired intra-fractionally during the delivery of a 12Gy VMAT plan. These were acquired for presets using 40 and 160 mA currents and exposure times of 40 ms per projection acquired every 1°. Registration was performed with SimpleITK using a mutual information metric and a regular gradient descent optimizer. Patient setup errors were introduced by applying known shifts to the planning CT in 3D along the X and Y axes of the kV panel. This shifted volume was then re-projected and the resulting registration accuracy with real projections was quantified as a function of angle and displacement.

Results

Registration accuracy for the 40 mA current preset using the anatomical phantom at isocenter was found to be 0.82 ± 0.29 mm for displacements up to 3.2 mm and 1.3 ± 1.5 mm for up to 8.2 mm in the X direction. Accuracy in the Y axis was found to be 0.51±0.21 mm up to 1 cm in displacement. The use of a 160 mA current to improve image quality only improved mean registration accuracy by 0.02 mm and 0.04 mm in the X and Y axes. Registration accuracy only exceeded these values when components of the hexapod couch not accounted for in the simulated projections occluded the spine. The registration time was found to be 0.7 seconds per projection and 1.7 seconds to simulate a single projection which can be pre-calculated.

Conclusion

The proposed framework demonstrates feasibility in terms of accuracy and speed for real-time tracking of vertebrae. Additional improvement involving further post-processing and isolation of the spine are ongoing. Furthermore, a prospective study of paraspinal patient data is planned.

P13 Automatic contour propagation of organs-at-risk on serial MRIs and dosimetric implications in glioblastoma patients undergoing chemo-radiation

Sangjune Laurence Lee, James Stewart, Young Lee, Sten Myrehaug, Arjun Sahgal, Mark Ruschin, Chia-Lin Tseng

Purpose

Changes in brain anatomy during chemo-radiation (CRT) for glioblastoma (GBM) can be visualized with magnetic resonance imaging (MRI). The objective of this study is to investigate the anatomical changes that occur in organs-at-risk (OAR) on serial MRIs during CRT for GBM patients, and to determine the feasibility of automatic OAR contour propagation and its dosimetric implications for the purpose of an adaptive workflow in MR-guided radiotherapy.

Methods

Fourteen GBM patients treated with 60 Gy in 30 fractions of CRT underwent serial multiparametric MRIs on days 0, 10, 20 of treatment (D0, D10, and D20) and 1 month post last fraction (P1M). OARs including the brainstem, globes, lenses, optic nerves, and optic chiasm were manually contoured at each time point on the contrast-enhanced T1-weighted MRI and compared to propagated contours generated based on the STAPLE deformable image registration algorithm. The Dice similarity coefficient (DSC) was used to quantify changes in manual versus propagated contours. Dosimetric comparison between the manual and propagated contours with respect to maximum point doses (Dmax) of OARs was performed using the reference D0 treatment plan. Statistical differences were determined using the Wilcoxon signed-rank test.

Results

The mean DSC between the manual and propagated OAR contours varied from OAR to OAR (range 0.63 – 0.95) across all time points. The mean DSC +/- standard deviation (SD) across all patients and time points for the brainstem was 0.95 +/- 0.01. For the optic chiasm, the mean DSC +/- SD was 0.77 +/- 0.15. The mean difference in Dmax for each OAR, between the manual contours at each time point compared to the D0 contours, ranged from 5-375 cGy. For the brainstem, the differences were 21 +/- 90 (p=0.68), 53 +/- 112 (p=0.19), and 99 +/- 205 cGy (p=0.01) at D10, D20, and P1M, respectively. For the optic chiasm, the differences were 81 +/- 471 (p=0.90), 64 +/- 433, (p=0.58) and 138 +/- 909 cGy (p=0.26) at D10, D20, and P1M, respectively. The mean difference in Dmax for each OAR, between the manual and propagated contours, ranged from 0.3-704 cGy. For the brainstem, the differences were 25 +/- 116 (p=0.59), 33 +/- 77 (p=0.27), and 61 +/- 137 cGy (p=0.09) at D10, D20, and P1M, respectively. For the optic chiasm, the differences were 59 +/- 566 (p=0.67), 512 +/- 671, (p<0.01) and 441 +/- 915 cGy (p=0.03) at D10, D20, and P1M, respectively.

Conclusion

Significant anatomical changes and resultant changes in OAR Dmax occur over the course of CRT for GBM. Automatic contour propagation using deformable image registration in an MR-guided radiotherapy workflow is feasible. The performance of contour propagation varies depending on the OAR and implications in dosimetric differences warrant further investigation.

P14 Dosimetric study on patient transfer between Varian Clinac iX and TrueBeam Linacs

Shima Yaghoobpour Tari, Michelle Nielsen, Grace Zeng

Purpose

Varian Clinac iX and TrueBeam have different head designs and MLC control systems. TrueBeam's primary collimators are thicker and it contains an anti-backscatter filter, affecting beam profiles at the shoulder regions. TrueBeam MLC leaf positioning is more accurate than the Clinac iX, which influences dosimetric leaf gap (DLG) and leaf transmission. The objective of this study was to characterize the dosimetric differences in treatment planning and delivery between these two machines in order to assess the potential impact of patient transfer in a center with limited resources.

Methods

10 pelvis 6MV VMAT plans with large field size, 10 prostate 6MV VMAT plans with regular field size and 9 field-in-field breast plans with mixed 6MV and 16MV were planned and measured on an iX unit and a TrueBeam unit. Treatment planning system (TPS) is Varian Eclipse version 11. TrueBeam and iX beam models were based on Varian reference data along with in-house optimized DLG and transmission values. A cylindrical solid water phantom with multiple ion-chamber insert positions was used to measure the absolute dose in target regions. Measurements were compared against the TPS calculations for two models.

Results

The average measured dose differences between the iX and TrueBeam models for prostate and pelvis plans were 0.2% and 1% for high dose region and 0.7% and 0.1% for low dose region, respectively. The average calculated dose differences between the two machines were 1.4% and 1.8% for high dose region and 1.9% and 1.9% for low dose region, respectively. The TrueBeam dose was lower than the iX dose for all calculated and measured plans largely due to the lower TrueBeam DLG and leaf transmission values for VMAT plans. The maximum differences between the calculated dose for one machine and the delivered dose on the other machine were 1.2% and 1.6% for high dose region and 1.8% and 1.4% for low dose region, respectively. For breast plans, the average measured dose difference between two machines was 2.3% and the average calculated dose difference was 1.1%. The TrueBeam measured and calculated dose were cooler than the iX machine mainly because of the anti-backscatter filter. The maximum difference between the calculated dose for one machine and the delivered dose on the other machine was 1.9% for breast plans.

Conclusion

Systematic dosimetric differences were observed between the TrueBeam and iX units for both treatment planning and delivery. These differences were found to be small and of limited clinical significance suggesting that patient transfer is justifiable at our centre.

P15 Neurological death is common in patients with EGFR mutant non-small cell lung cancer

Matthew Ramotar, Sierra Barnes, Mark Doherty, David Shultz

Purpose

Patients with EGFR mutant non-small cell lung cancer (EGFRmNSCLC) have a high incidence of brain metastases (BM). We sought to determine the rate of neurologic death in EGFRmNSCLC patients diagnosed with brain metastases.

Methods

A single-institution prospectively managed database identified 204 patients with EGFRmNSCLC treated for brain metastases between 2000 and 2016. We estimated actuarial survival rates using the Kaplan-Meier method. The incidence of neurologic death (ND) was determined using a competing risks analysis. ND was correlated to clinical and treatment variables using Fisher's exact test. Survival was calculated from the date of BM diagnosis. We defined neurologic death as death due to brain metastases or leptomeningeal disease.

Results

Fifty-six percent of patients had BM at the time of initial diagnosis. The initial BM treatment was up front stereotactic radiosurgery (SRS), whole brain radiation therapy (WBRT), or tyrosine-kinase inhibitor (TKI) alone in 22, 60, and 18 percent of patients, respectively. Two-year rates of OS in these subgroups were 64%, 38%, and 50%, respectively (p=0.016). The 5-year rate of neurologic death was 38%. Thirty-four percent died of non-neurologic causes, 8% died of unknown causes, and the remaining patients were alive at last follow-up. Median survival (MS) was 19 months; MS in patients who died of non-neurologic causes and neurologic causes was 23, and 15 months, respectively. Of age, staging, BM at diagnosis, history of TKI therapy, initial treatment of BM, staging at diagnosis, and leptomeningeal disease at diagnosis (LMD), only LMD was significantly associated with ND (p=0.047).

Conclusion

Neurologic death due to EGFRmNSCLC BM was more common in our cohort than has been previously reported, highlighting the need for dedicated studies focused on the best management of BM in this population.

P16 Three-dimensional-guided perineal-based interstitial brachytherapy in primary vaginal cancer: A systematic review of local control and toxicities

Yonathan Weiss, Lucas Mendez, D D'Souza, Ananth Ravi, Lisa Barbera, Eric Leung

Purpose

Systematic review to evaluate local control and toxicities of perineal-based interstitial brachytherapy (P-ISBT) in primary vaginal cancers treated with three-dimensional (3D) image-based planning.

Methods

Systematic review of the literature using the PRISMA guideline was conducted through a search of Medline, EMBASE and Cochrane databases. This search resulted in 20 relevant manuscripts plus one manuscript found outside of the search. Selected studies evaluated the role of P-ISBT in vaginal tumours treated using 3D planning. 6 of 21 manuscripts contained sufficient information for LC and toxicity calculations. Data were extracted by at least two investigators.

Results

A total of 252 vaginal cancer patients were treated with P-ISBT and planned with 3D image-based planning. Clinical outcomes could be identified for 112 patients and ranging from stage I to IVA and in majority of cases stage II-III. Most patients received 45–50.4 Gy EBRT to the pelvis followed by a P-ISBT boost with a range of median EQD2 between 23.8 and 33.8Gy, with majority of patients receiving 28-30 EQD2Gy. Total dose to patients were in a narrow range in median EQD2Gy (72.2 - 78.4). Patients were treated with either HDR, LDR, or PDR techniques, and a small number (2) received HDR plus PDR. Overall LC was 85% (95/112) with a median follow-up ranging from 17 to 45 months. Half of the patients (49%) had a median follow-up of at least 35 months. No significant procedure-related complications were reported. Combined late gastrointestinal, genitourinary and vaginal grade 3 and 4 toxicity was 11.6%.

Conclusion

Promising LC rates were found in patients with vaginal cancers treated with perineal ISBT with 3D image-based planning. In this systematic review, tumours were most often stage II or III and yet a LC rate of 85% was found. P-ISBT with 3D planning seems to be an effective and safe treatment for primary vaginal tumours, though further investigation is required to optimize treatment given institutional variations in technique, planning and treatment protocol.

P17 Re-irradiation of primary adult CNS tumors: Outcomes, toxicity and dosimetric factors

Aisha Alqaderi, Fabio Moraes, Alejandro Berlin, Barbara-Ann Millar, Normand Laperriere, Tony Tadic, David Shultz

Purpose

The aim of this study was to evaluate the outcomes, toxicities, and cumulative doses to tumors and critical structures following fractionated re-irradiation of primary brain tumors in adults.

Methods

We reviewed our institutional database for adult patients treated between 2007 and 2017, who received external beam re-irradiation of the brain, defined as overlap of the 25% of prescription isodose volumes. Doses were converted to biologically effective dose, expressed as 2 Gy per fraction equivalent dose (EQD2; $\alpha/\beta = 3$ vs. 10). Toxicity was graded according to CTCAE v4. The Kaplan-Meier method was used for survival analyses.

Results

We identified 58 patients who underwent re-irradiation. The median interval between courses was 4.5 years for WHO grade (G)-I/II, 6.4 years for G-III and 1.2 years for G-IV tumors. The primary diagnoses were meningioma (n= 20), glioblastoma multiforme (n=11), G-III glioma (n=12), G-I/II glioma (n= 9), and others (n=5). The median cumulative prescribed EQD2(α/β 10Gy) was 106.2 Gy (range 74.8-120 Gy). Radiation necrosis occurred in 10 patients following re-irradiation ranging between G1 (n=4) to G3 (n=4). Two of these patients received Bevacizumab and 2 had surgical resection. In total, G≥3 RT-related toxicities were noted in 9 patients, while no G-IV/V toxicities were observed. Twelve- and 24-month overall survival (OS) rates after re-irradiation for G-I/II tumors were 77% and 46%, respectively. For G-III/IV, 12-month OS was 48% and 24-month OS was 29%. Median progression free survival following repeat RT was 10.2 and 6.2 months for G-I/II and G-III/IV tumors, respectively.

Conclusion

Re-irradiation for recurrent primary brain tumors was associated with acceptable rates of toxicity. Re-irradiation for recurrent primary brain tumors was associated with acceptable rates of toxicity. We are currently calculating cumulative doses to critical structures (optic chiasm, cranial nerves, cochlea, brainstem, retina, and hippocampus) and plan to correlate those results to radiation-associated toxicities.

P18 Whole genome characterization of cervical cancer

Jelena Lukovic, Kathy Han, M. Pintilie, N. Chaudary, Jonathan Tsao, R. Quevedo, R. P. Hill, Anthony Fyles, J. Weiss, T. Pugh, Michael Milosevic

Purpose

A number of chromosomal alterations have been identified as important factors in the initiation and progression of cervical cancer. These data, however, are mainly derived from surgical specimens of early stage tumors. The purpose of our study was to analyze the whole genome profile of locally advanced cervical cancers treated with radiotherapy and concurrent cisplatin (RTCT) and to identify recurrent DNA copy number alterations associated with the malignant phenotype.

Methods

Tumor biopsies of locally advanced cervical cancers were obtained at the time of examination under anesthesia, prior to RTCT. All biopsies were reviewed by a gynecologic pathologist. Macro-dissected tumor samples were co-isolated using the Qiagen All-Prep DNA/RNA/miRNA universal kit. DNA samples were submitted for shallow whole genome sequencing where reads were aligned to the hg19 reference genome with an average sequencing coverage of 0.38x. Copy-number was estimated using QDNAseq and ichorCNA by segmenting the genome into genomic bins of 50kb or 1000kb. Age, histology, grade, stage and lymph node status were recorded. Patients were treated with external radiotherapy (45-50 Gy) and concurrent weekly cisplatin (40 mg/m2), followed by pulsed-dose-rate (PDR) brachytherapy (40 Gy). Median follow up was 8.4 (range: 0.2-16.5) years.

Results

121 patients were enrolled in the study from October 1999 to March 2012. They were representative of the cervical cancer population treated with RTCT. The median age was 48.5 (range: 26-84) years. FIGO stage was 1B in 31%, IIA-IIB in 40%, and IIIA-IIIB in 29%. The median percent genome altered (PGA) was 13.2% (range: 0-47.5%). Recurrent copy number amplification events were consistent with previously reported data and include: 11q22.1 (YAP1, BIRC2, BIRC3), 3q26.2 (MECOM, TERC), 1q23.3, 8q24.23 (MYC, PVT2), 20q11.21 (BCL2L1), and 9p24.1 (CD274, PDCDILG2). In contrast to previous reports, locus 7p11.2 coding EGFR was not amplified. Recurrent copy number deletions included: 2q37.1, 2q36.3, 11q23.3, 3p12.3, 19p13.3, and 13q14.11. Previously identified deletions at loci 4q35.2 (FAT1) and 10q23.31 (PTEN) were not seen in our cohort. There were no associations between PGA and any of the baseline clinical factors. There was no association between PGA and disease free survival.

Conclusion

In summary, this study improves our understanding of the genomic landscape in locally advanced cervical cancer. While our findings are similar to those reported previously for earlier stage disease, we also identified potentially important differences that warrant further evaluation. Future analyses will explore relationships between specific chromosomal alterations and gene expression profiles as well as their integrated effects on treatment response and survival. The ultimate goal is to identify genomics biomarkers to aid in the subclassification of disease, prediction of prognosis, and selection of patients who may benefit from treatment intensification.

P19 Dixon-based magnetic resonance imaging for improved detection of brain metastases for radiosurgery planning

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Purpose

Stereotactic radiosurgery (SRS) is the standard treatment for patients with limited brain metastases and good performance status. The current standard MRI pulse sequence for metastasis detection and treatment planning is a post-contrast 3D T1-weighted spoiled gradient echo (SPGR) sequence. MR pulse sequences which provide greater sensitivity for detecting metastases could be advantageous for SRS planning by allowing detection and earlier treatment of smaller metastases, reducing the need for repeat SRS. To this end, we explored the sensitivity of fat saturated Dixon imaging for detection of both intracranial and extracranial metastatic disease and compared this to the standard of care 3D SPGR.

Methods

Twelve patients with known brain metastases were prospectively enrolled and underwent a planning MRI prior to SRS. After contrast administration, images were acquired with a 3D T1-weighted SPGR sequence as well as a two-point 3D Dixon-based spin echo sequence. One neuroradiologist evaluated the SPGR sequence for the presence and number of brain metastases as well as any calvarial metastases. A second neuroradiologist blinded to the results from the SPGR images evaluated the water-only Dixon images in the same manner. The number of parenchymal and calvarial metastases was compared between the two imaging modalities for each patient. In addition, the contrast-to-noise ratio (CNR) between the dominant enhancing lesion and contralateral normal appearing white matter was evaluated for both sequences. The CNR for each sequence was compared using a paired Student's t-test.

Results

The primary site of disease was lung (n=4), breast (n=3), renal cell (n=2), and rectal, melanoma, and esophageal (n=1). The average number of parenchymal metastases in each patient was 9 (range 2 – 35). All lesions detected with SPGR (93 in total) were detected on the Dixon images. There were an additional 18 metastases (in 8 patients) detected on the Dixon images that were all small (2 – 4 mm) and on review not identifiable on the SPGR images. The CNR was significantly higher on the Dixon images (mean = 18.5 ± 9.2) compared to SPGR images (14.1 ± 7.6, $p = 0.0019$). There were nine suspected calvarial metastases detected with the Dixon sequence that were not seen on the SPGR images.

Conclusion

Dixon-based water only post-contrast images provide superior detection of brain metastases compared to standard SPGR approach. The identification of calvarial metastases was also superior using a fat saturated Dixon technique.

P20 Multi-institutional study of salvage irradiation with single-modality interstitial brachytherapy for the treatment of recurrent gynecological tumours in the pelvis

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Purpose

Recurrent gynecological (GYN) tumors can cause significant morbidities for patients with limited options of salvage therapy. Patients who are not candidates for aggressive salvage surgery are often managed with a palliative approach. This study investigates the strategy of high-dose salvage radiation with single-modality interstitial brachytherapy (SM-ISBT) for the management of recurrent GYN pelvic disease at two specialized interstitial brachytherapy centres.

Methods

Patients with gynecological malignancies who had received SM-ISBT for salvage treatment from September 2008 to January 2017 were included. All patient had recurrent gynecological tumors confined to the pelvis with no distant metastasis. Local and regional control, distant metastasis and long-term toxicities were evaluated.

Results

A total of 27 patients with a median follow-up of 20 months (IQR 11-31) after SM-ISBT were included. The primary cancer sites were endometrium (20), cervix (3), vulva (1), vagina (2), rectum (1). All patients had prior pelvic radiation [external-beam radiation (11), brachytherapy (1) or both(15)], and SM-ISBT was delivered as salvage re-irradiation. Median disease-free survival was 20.8 months (IQR 12.1-32.4). SM-ISBT was delivered with a dose of 500 to 700cGy for 3 to 6 fractions over 2 to 19 days, with a median EQD2 of 28.4Gy (range 19-50Gy). Overlap with previous radiation volume was complete (52%), partial (44.5%), or none (3.5%). Median EQD2 in complete, partial, and no overlap group was 26.8, 32.7 and 35.5Gy, respectively (p value=0.59) After SM-ISBT, complete and partial response were achieved in 17 (63 %) and 6 (22.2%) patients, respectively. 2 (7.4%) patient had grade 3 toxicities (both vaginal stenosis), with no patients experiencing grade 4 complications. 10 (37%) patients had grade 1 or 2 toxicities. 17 patients (63%) had recurrence, including local, regional and metastatic in 15 (55.5%), 7 (6%), and 4 (14.8%) patients, respectively. At the last follow up, 17 patients (63%) were alive.

Conclusion

Salvage radiation with SM-ISBT for recurrent GYN malignancies in the pelvis is feasible and safe, and is associated with acceptable rates of toxicities with reasonable local control rates. With limited treatment options available for recurrent GYN tumors in the pelvis, developing strategies to address this morbid local disease is a priority. Prospective multi-institutional studies are warranted to further investigate SM-ISBT as a standard option for salvage GYN treatment.

P21 Global characterization of protein secretion rates in normoxia and hypoxia

Sandy Che-Eun Serena Lee, Saeid Shahidi, Marianne Koritzinsky Sandy

Purpose

Hypoxic tumours are resistant to therapy, leading to poor patient survival. Hypoxic changes such as tumour development, growth, angiogenesis and metastasis lead to an aggressive phenotype. Adverse biological changes stimulated by tumor hypoxia are mediated by cell-surface or secreted proteins. Little is known about how hypoxia affects secretion efficiency of different proteins and therefore ultimately influence differential gene expression in the extracellular space in hypoxia. Definition of the transit kinetics of the proteins through the secretory pathway on a global scale in normoxic and hypoxic environment will create a unique resource to understand differential gene expression in the extracellular space.

Methods

To label all newly synthesized secreted proteins with a short pulse of a non-endogenous amino acid (azido-homoalanine, AHA), precipitation of the proteins and isolation of the AHA-containing proteins from cells and media at various times after the pulse was performed. This allows downstream isolation through incubation with an alkyne-containing biotin that forms a triazole conjugate upon reaction with the azide. This reaction is often referred to as “Click-IT”. Biotin-conjugated proteins can be isolated on a streptavidin resin and can be identified by mass spectrometry.

Results

Here, we established a novel method to determine the transit kinetics of all newly synthesized secreted proteins. We were able to successfully isolate for specific proteins of interest (AHA labeled) and increase the amount of protein of interest (secreted proteins) pulled down in the analysis of the given pilot mass spectrometry data. The pilot mass spectrometry data allowed us to observe over 50 secreted proteins in lysate and media combined. The proteins detected in this dataset were previously proven to have an active role in cancer progression.

Conclusion

We have established a method to determine the secreted proteins that are involved in cancers that are hypoxic in nature. This research aims to provide a fundamental resource of protein kinetics as well as knowledge on protein folding and its transit pathway. This valuable information will establish a novel understanding of protein secretion within the field of proteomics, improving our understanding of translational regulation of extracellular proteins based on differential oxygen conditions.

P22 Utility of a decision aid for accelerated partial breast irradiation in older women with low risk breast cancer

Matthew Neve, Ewa Szumacher, Ines Menjak

Purpose

With an ageing population, an increasing number of older breast cancer patients are being treated. With a range of adjuvant treatments available it can be challenging selecting the most appropriate option. Studies also indicate that senior cancer patients are more likely to be passive in their treatment decision making. Our goal was therefore to improve the comprehension and decision making of senior women regarding their adjuvant therapy options following lumpectomy for low risk breast cancers. This is an educational intervention pilot study with a view to providing future patients with adequate resources to make confident decisions regarding their adjuvant treatments. As such we are testing our education material on patients already undergoing radiation treatment to gain their perspective and feedback.

Methods

Women aged 65 years of age and older with low risk breast cancer as represented in the PRIME II study who were or had already undergone whole breast radiotherapy were identified to take part in this study. Eligible patients were approached and provided with a study package which contained a newly developed educational booklet which outlines adjuvant therapy options following lumpectomy in this age group. A series of self-reported questionnaires developed by the Ottawa Hospital Group were then completed by the patients. These focused on assessing the patient's understanding of the options of 'partial breast irradiation' and 'endocrine therapy alone'. Demographic information regarding our study participants was also obtained.

Results

Preliminary results to date (half of the patients have been accrued n=20) indicate strong support from our study population regarding the usefulness of our educational aid based on our questionnaire and 'Preparation for Decision making' scores (Median score: 43.5/50). Choice: 86% of patients selected partial breast irradiation as their preferred treatment option over endocrine therapy alone). However other parameters used to assess effectiveness (Knowledge, Decision Conflict) proved more variable and difficult to interpret.

Conclusion

While this study is still ongoing, preliminary results indicate that our educational material has been well received by older breast cancer patients, the majority of whom have commented that they believe it will benefit future patients with their decision making. Further study in a randomized controlled trial is warranted.

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