Radiation Oncology
UNIVERSITY OF TORONTO

# UTDRO RESEARCH DAY 2022

*PROGRAM GUIDE*

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## THANK YOU

**A big thank you to everyone who has helped to organize and run UTDRO Research Day 2022!**

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Michael Milosevic, William Tran

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Andrea McNiven, Charmainne Cruje, Jennifer Croke, Jennifer Kwan, Joelle Helou, Marianna Petruccelli, Marianne Koritzinsky, May Tsao, Meghan Ward, Olga Pidhirska, Shane Harding

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# UTDRO RESEARCH DAY – CO-CHAIR WELCOME

## On behalf of the organizing committee, welcome to the University of Toronto, Department of Radiation Oncology (UTDRO) Research Day 2022!

We are excited to showcase the extraordinary work that our trainees in radiation oncology, medical physics, radiotherapy and basic radiation sciences are undertaking in our department.

We hope that this program will initiate thoughtful dialogue and synergize new collaborations within the UTDRO clinical and academic community. This meeting is aimed to provide a cross-section of our research accomplishments and highlight the diverse and innovative work that our trainees have been involved in over the past year.

Today, we also honour Dr. Richard Hill, who was a highly valued member of UTDRO, a brilliant scientist and a thoughtful mentor who generously dedicated his time to ensure the success of his trainees.

We also welcome Dr. Ananya Choudhury, PhD, MRCP, FRCR, as our keynote speaker. Dr. Choudhury is Chair and Honorary Consultant in Clinical Oncology at The University of Manchester and The Christie NHS Trust, UK. She leads a multidisciplinary program in personalized radiotherapy, including MR-guided treatment and translational radiobiology.

Dr. Choudhury's keynote will examine recent advancements in radiation technology and the often-lacking resources required to successfully implement them. Drawing on her vast clinical expertise, she will address how we can overcome the limitations inherent in healthcare systems by working together as a global radiotherapy community.

Finally, we would like to extend a special thanks to all our faculty members and UTDRO staff for their continued support and participation. We hope that you enjoy the program!

Sincerely,

**Mike Milosevic,** MD, FRCPC
Professor and Vice Chair, Research

**William T. Tran,** MRT(T), MSc, PhD
Assistant Professor

# UTDRO RESEARCH DAY – SCHEDULE

Details: May 16, 2022, 12:00 pm – 4:00 pm
Location: Zoom

| Time | Total Length | Main Room | |
|---|---|---|---|
| **12:00 PM** | 10 mins | *UTDRO Chair Welcome* - **Fei-Fei Liu, UTDRO Chair**<br>*Opening Remarks, Tribute to Richard Hill, Keynote Introduction* - **Michael Milosevic, UTDRO Vice Chair Research** | |
| **12:10 PM** | 45 mins | *Keynote Speaker*<br>Global Radiotherapy: How Can We Level the Playing Field? - **Dr. Ananya Choudhury, PhD, MRCP, FRCR** | |
| **12:55 PM** | 10 mins | *Break* | |
| **Time** | **Total Length** | **Stream A** | **Stream B** |
| **01:05 PM** | 40 mins | ***Oral Presentations: Section 1***<br>*(Moderated by Shane Harding)* | ***Oral Presentations: Section 2***<br>*(Moderated by Jennifer Croke)* |
| | | 1. The Role of PRDX4 in Regulating Immune Responses Through DNA Damage in Pancreatic Cancer<br>**Lucie Malbeteau** | 5. Mature Local Control and Reirradiation Rates Comparing Spine Stereotactic Body Radiotherapy to Conventional Palliative External Beam Radiotherapy<br>**K. Liang Zeng** |
| | | 2. Circulating HPV DNA Kinetics Predict Clinical Outcomes in a Large Cohort of Radiotherapy-Treated p16-Positive Oropharyngeal Cancers<br>**Eric Zhao** | 6. Five-Fraction Stereotactic Ablative Radiotherapy to the Pelvis and Prostate with Focal Intra-Prostatic Boost: Outcomes of the 5STAR Clinical Trial<br>**Rohann Correa** |
| | | 3. Measurement of Tumor Hypoxia in Patients with Non- Small Cell Lung Cancer Using PET with 18F-FAZA<br>**Avipsa Das** | 7. Clinical Outcomes of Dose-Painted Radiotherapy in Muscle Invasive Bladder Cancer<br>**Inmaculada Navarro** |
| | | 4. Unilateral Versus Bilateral Radiotherapy for HPV Positive Oropharyngeal Carcinoma: Impact on Long Term Symptom Burden<br>**Ionut Busca** | 8. Evaluating Magnetic Resonance Imaging (MRI)-only Simulation and Planning for Fiducial-Based Prostate Stereotactic Body Radiotherapy (SBRT)<br>**Allan Hupman** |
| **1:45 PM** | 10 mins | ***Rapid-fire Presentations 1: Posters 1 – 7***<br>*(Moderated by Shane Harding)* | ***Rapid-fire Presentations 2: Posters 8 – 14***<br>*(Moderated by Jennifer Croke)* |
| **1:55 PM** | 10 mins | ***Break*** | |

# UTDRO RESEARCH DAY – SCHEDULE [CON'T]

Details: May 16, 2022, 12:00 pm – 4:00 pm
Location: Zoom

| Time | Total Length | Stream A | Stream B |
|---|---|---|---|
| **2:05 PM** | 40 mins | ***Oral Presentations: Section 3***<br>*(Moderated by Andrea McNiven)* | ***Oral Presentations: Section 4***<br>*(Moderated by Moderated by Lori Holden)* |
| | | 9. Daily Adaptive Replanning with Dose Accumulation for Prostate Ultra-Hypofractionated Radiotherapy Using Machine Learning Automated Planning on CBCT<br>**Maryam Golshan** | 13. Investigation of Dose Distribution of Uniformly and Non- Uniformly Loaded Generic and Notched Eye Plaques with Monte Carlo Simulations<br>**Oleksii Semeniuk** |
| | | 10. Feasibility of Machine Learning Automated Treatment Planning for Magnetic Resonance Guided Radiation Therapy in Prostate Cancer<br>**Aly Khalifa** | 14. Management of Radiotherapy Patients with Cardiovascular Implantable Electronic Devices: A National Survey of Multi- Disciplinary Radiation Oncology Professionals<br>**Amir Safavi** |
| | | 11. Individualized Prediction of Distant Metastases Risk in Oral Cavity Carcinoma: A Validated Predictive-Score Model<br>**Badr Id Said** | 15. Final Results of an International Delphi Consensus Study Regarding the Optimal Management of Radiation Pneumonitis<br>**Indu Voruganti** |
| | | 12. Automatic Segmentation for Targets and OARs in Cervical High Dose Rate (HDR) Brachytherapy via Deep Learning Techniques<br>**Ruiyan Ni** | 16. The Effects of a Curriculum Change on Peer Mentorship Among Radiation Oncology Residents<br>**David Mak** |
| **2:45 PM** | 10 mins | ***Rapid-fire Presentations 3: Posters 15 – 20***<br>*(Moderated by Andrea McNiven)* | ***Rapid-fire Presentations 4: Posters 21 - 26***<br>*(Moderated by Lori Holden)* |
| **Time** | **Total Length** | **Main Room** | |
| **2:55 PM** | 5 mins | *Closing Remarks and Poster Hall Opening*<br>**William Tran, Program Co-Chair** | |
| **Time** | **Total Length** | **Breakout Rooms** | |
| **3:00 PM** | 1 hour | *Poster Hall* | |
| **4:00 PM** | | *Event End* | |

# UTDRO RESEARCH DAY – POSTERS

**Rapid-fire Presentation:** May 16, 2022, 1:45 pm – 1:55 pm [Posters 1 – 16]
**Poster Hall:** May 16, 2022, 3:00 pm – 4:00 pm
**Location:** Zoom

***Rapid Fire Presentations 1: Posters 1 – 7*** *(Stream A)*

| Poster # | Abstract Title | Presenter |
|---|---|---|
| **1** | Safety and Efficacy of Stereotactic Body Radiotherapy for Ultra-Central Thoracic Tumours | **George Li** |
| **2** | Dosimetric Outcomes for Adaptive Prostate SBRT on MR-Linac: The Time Taken for Contouring and Re-planning Makes a Difference | **Eyesha Younus** |
| **3** | Review of 20 Years of Adult Medulloblastoma Treatment at a High-Volume Center – Chemotherapy Prescription Trends and Survival | **Marissa Sherwood** |
| **4** | Commissioning of the Elekta Symmetry 4D Cone Beam Mode | **Eric Christiansen** |
| **5** | Unanticipated Radiation Re-planning for Stage III Non-small Cell Lung Cancer | **Melinda Mushonga** |
| **6** | Predictive Factors for Survival and Radiation Necrosis in Patients with Recurrent High-Grade Glioma Treated with Re-Irradiation | **Daniel Palhares** |
| **7** | Selection of a Stereotactic Radiosurgery Technique Using a Target Volume Regularity Index | **Charmainne Cruje** |

***Rapid Fire Presentations 2: Posters 8 – 14*** *(Stream B)*

| Poster # | Abstract Title | Presenter |
|---|---|---|
| **8** | Evaluating Multidisciplinary Peer Review: A Retrospective Study of Plan Modifications in Radical and Palliative Intent Radiation Therapy Treatments | **Adrian Cozma** |
| **9** | Frameless Cobalt60-Based Hypofractionated Stereotactic Radiosurgery (HSRS) for Brain Metastases: Impact of Dose and Volume | **Michael Yan** |
| **10** | Impact of MGMT Promoter Methylation Status on Tumor Dynamics during Weekly Adaptive Radiotherapy for Glioblastoma | **John Hudson** |
| **11** | Estimating Prevalence of Oligometastases at Initial Staging of Neuroendocrine Tumors- Findings from a 68Ga DOTATATE PET (Ga68PET) Population-Based Registry | **Sarah Murad** |
| **12** | Perspectives of Patients with Metastatic Lung Cancer on Symptom Screening and Patient-Reported Symptom Trajectory Data | **Amir Safavi** |
| **13** | Outcomes of Extracranial Oligorecurrence after Prior Metastases Directed Stereotactic Body Radiotherapy for Oligometastatic Disease | **Jonathan Peng** |
| **14** | A Total Inverse Planning Paradigm: Prospective Trial Evaluating the Performance of a Novel 3D-Printed Head Immobilization Device Generated from MR Imaging | **Paola Anna Jablonska** |

# UTDRO RESEARCH DAY – POSTERS [CON'T]

**Rapid-fire Presentation:** May 16, 2022, 2:45 pm – 2:55 pm [Posters 15-26]
**Poster Hall:** May 16, 2022, 3:00 pm – 4:00 pm
**Location:** Zoom

***Rapid Fire Presentations 3: Posters 15-20*** *(Stream A)*

| Poster # | Abstract Title | Presenter |
|---|---|---|
| **15** | Early Clinical Effectiveness, Toxicity, and Quality of Life Outcomes of Magnetic Resonance Imaging-Guided Stereotactic Ablative Radiotherapy: A Systematic Review | **Amir Safavi** |
| **16** | Daily Assessment of On-Treatment Tumour Regression by Cone Beam CT Suggests Prognostic Dynamic Biomarkers in Nasopharyngeal Cancer | **Eric Zhao** |
| **17** | Early Institutional Experience of Ultra-Hypofractionated Breast Radiotherapy in a Large Academic Cancer Centre | **Hiba Othman** |
| **18** | The Modern Management of Large Brain Metastases: A Review | **Bryce Thomsen** |
| **19** | Tumour Specific Growth Rate as a Predictor of outcomes in Oligo-Progressive Disease Treated with Stereotactic Body Radiotherapy | **Inmaculada Navarro** |
| **20** | Salvage Interstitial Brachytherapy for Treatment of Recurrent Endometrial Cancers in The Vagina: 7-Year Single Institution Experience | **Marissa Sherwood** |

***Rapid Fire Presentations 4: Posters 21 – 26*** *(Stream B)*

| Poster # | Abstract Title | Presenter |
|---|---|---|
| **21** | Clinical Outcomes of Metastatic Breast Cancer Patients Post Hypo-fractionated Ablative Liver Radiotherapy | **Melinda Mushonga** |
| **22** | Development and validation of an automated dose-of-the-day method for MRI-guided SBRT of UGI patients | **Oleksii Semeniuk** |
| **23** | Graphical User Interface (GUI) Development for Deep Learning Assisted Algorithm for Catheter Reconstruction During MR-Only Gynecological Interstitial Brachytherapy | **Kaiming Guo** |
| **24** | Optimization of Catheter Placement for Transperineal Interstitial Gynaecological Brachytherapy | **Jill Bennett** |
| **25** | Partial Breast Re-Irradiation Using Ultra Hypofractionation: A Phase 2 Multi-Institutional, International Study | **Fadwa Abdel Rahman** |
| **26** | Timing of Radiation Pneumonitis in patients receiving Immune checkpoint inhibitors | **Melinda Mushonga** |

# UTDRO RESEARCH DAY ABSTRACTS – ORAL PRESENTATIONS

*Oral Presentations: Section 1*

## 01 The Role of PRDX4 in Regulating Immune Responses Through DNA Damage in Pancreatic Cancer

*Lucie Malbeteau, Pallavi Jain, Bradley Wouters, Marianne Koritzinsky*

### PURPOSE

Pancreatic cancer could climb to the second leading cause of cancer death by 2030, due to a rising incidence rate coupled with a 5-year overall survival lower than 8%. This poor clinical outcome is explained by late detection and lack of effective therapeutic options. A minority of patients with ductal adenocarcinoma (PDAC) undergo surgery, while most patients present with locally advanced or metastatic disease that is treated with chemotherapy alone. Radiotherapy (RT) is an emerging treatment modality on the heels of better image guidance, but remains rarely curative. PDAC is also resistant to immune therapy, in part due to the immunosuppressive pancreatic tumor microenvironment (TME). This resistant tumor phenotype is driven by scarce tumor-infiltrating effector T cells along with a prominent infiltrate of immunosuppressive macrophages that promote T cell dysfunction. Our current work aims to reactivate the suppressive immune infiltrate using RT to then improve PDAC sensitivity to immunotherapy. Local DNA damage induces site-specific cancer cell death, but recent studies have also reported a broader RT-dependent effect, priming tumor-specific T cells. Specific fractionation regimens were shown to initiate cancer cell-intrinsic production of type-I interferons (IFNs), resulting in radiation-induced activation of anti-tumor T cells that mediate abscopal responses in experimental tumor models.

### METHOD

We unveiled that perturbating redox homeostasis by targeting the antioxidant protein peroxiredoxin 4 (PRDX4) render pancreatic cancer cells vulnerable to RT. PRDX4 loss enhanced reactive oxygen species (ROS) abundance that sensitized PDAC cells and tumors to ionizing radiation. We now hypothesize that the ROS and DNA damage that accompanies PRDX4 targeting can activate innate immunity signaling, synergize with RT, and be further exploited with immune checkpoint inhibition.

### RESULTS

We demonstrate that cell death induced by PRDX4 depletion in human pancreatic cancer cells is accompanied by DNA damage and accumulation of cytosolic DNA, a potent primer for immune therapy. Consistently, PRDX4 knockdown results in the transcriptional upregulation of inflammatory-related genes, including type I-IFNs, cytokines, and interferon-stimulated genes (ISGs). Importantly, this induction is dependent on STING, the critical regulator of the innate immune responses, as treatment with an inhibitor, or STING knockdown, substantially blunts their upregulation. We show the same significant “rescue” phenotype when the transcription factor NFκB, a downstream STING effector, is knocked down.

### CONCLUSION

Taken together, these data demonstrate that PRDX4 depletion associates with an inflammatory phenotype dependent on STING signaling. Going forward, we will combine PRDX4 loss with regimens of radiation that are aligned with literature (e.g., 3x8Gy, 5x7Gy and 1x10Gy) to assess synergizing effects on STING activation and immune secretion in human cells. As such, exploiting vulnerable redox homeostasis via PRDX4 targeting to specifically modulate components of the TME can help to determine how to utilize RT to override PDAC resistance to immunotherapy and improve patient outcomes.

# 02 Circulating HPV DNA Kinetics Predict Clinical Outcomes in a Large Cohort of Radiotherapy-Treated p16-Positive Oropharyngeal Cancers

*Eric Y. Zhao, Ariana Rostami, Zhen Zhao, Shao Hui Huang, John Cho, John de Almeida, Meredith E. Giuliani, David P. Goldstein, Ezra Hahn, Kathy Han, Andrew J. Hope, Ali Hosni, John Kim, Fei-Fei Liu, Geoffrey Liu, Jolie Ringash, Brian O'Sullivan, Lillian Siu, Anna Spreafico, John N. Waldron, Scott V. Bratman*

## PURPOSE

Human papillomavirus (HPV) driven oropharyngeal cancer (OPC) has heterogeneous outcomes with 5-year recurrence of up to 30% after definitive (chemo-)radiotherapy (CRT/RT). Circulating HPV DNA (ctDNA) is a convenient dynamic biomarker that can be repeatedly measured for risk stratification and response monitoring. Understanding of HPV ctDNA kinetics during treatment and its association with clinical and treatment factors is nascent. We characterized HPV ctDNA kinetics in the largest-to-date cohort of RT- or CRT-treated OPC.

## METHOD

Among 262 patients with p16 positive, stage I-III (TNM-8) OPC treated with standard of care curative-intent RT (n=107) or CRT (n=155), blood samples were collected at baseline (pre-treatment), week 4 of RT (mid-treatment), and 3-month follow-up (post-treatment). Early-treatment (end of week 1) blood draws were also performed in a subset of patients (n=92) with detectable baseline ctDNA. Copies of HPV-16 ctDNA were quantified using a previously validated multiplex droplet digital PCR assay and normalized to plasma volume. Primary outcome was recurrence-free survival (RFS) and secondary outcomes were progression-free survival (PFS) and overall survival (OS).

## RESULTS

With median follow up of 42.0 months (range: 3.5-77.5), 3-year RFS was 90%. Pre-treatment HPV ctDNA was detected in 220 (84%) patients and ranged from 0.32 to 2.4x10^5 copies/mL in plasma. Baseline ctDNA level was moderately associated with T category (median copies/mL: 350 in T1-2 and 730 in T3-4, $p = 0.011$) and strongly associated with N category (N0: 83, N1: 357, N2: 609, N3: 5903, $p < 0.001$). Among patients with detectable pre-treatment ctDNA, clearance (undetectable ctDNA) occurred in 3.5%, 14.3%, and 90.7% of early-, mid-, and post-treatment samples, respectively. Clearance at each timepoint was consistently associated with longer RFS, PFS, and OS, though the study was only powered to detect significant differences at post-treatment. 3-year RFS, PFS, and OS were 93.0%, 91.0%, and 93.6% respectively if ctDNA was cleared post-treatment, versus 67.9%, 54.2%, and 53.8% if ctDNA was not cleared. Improved RFS was associated with lower ctDNA levels (adjusted for disease stage) at early-treatment (HR: 1.37, 95% CI: 1.01-1.86, $p = 0.046$) and post-treatment (HR: 1.30, 95% CI: 1.08-1.56, $p = 0.0047$), but not at pre- or mid-treatment. An increase (peak) in ctDNA level from pre-treatment to early-treatment was associated with inferior RFS ($p=0.18$), PFS ($p=0.03$), and OS ($p=0.03$).

## CONCLUSION

Detectability of HPV ctDNA during and post-treatment is prognostic of recurrence and survival in RT-treated p16+ OPC. Quantitative ctDNA levels at early-treatment and post-treatment are prognostic, independent of disease stage. Early-treatment ctDNA kinetics show promise as a potential dynamic biomarker of treatment response.

# 03 Measurement of Tumor Hypoxia in Patients with Non-Small Cell Lung Cancer Using PET with 18F-FAZA

*Avipsa Das, Alexander Sun, Angela Lin, Brandon Driscoll, Doug Vines, Jessica Weiss, Amy Liu*

## PURPOSE

Tumor hypoxia is believed to be one of the contributors for treatment failure in non-small cell lung cancer (NSCLC), but has not been extensively evaluated as a prognostic/predictive factor in lung cancer. Hypoxia tracer 18F-FAZA provides a non-invasive method of hypoxia imaging. This prospective study aims to evaluate the feasibility and potential benefits of using FAZA-PET scans to assess NSCLC tumor hypoxia.

## METHOD

Patients diagnosed with stage II–III NSCLC have been recruited in this ongoing study, starting from January 2015. We report on the initial 27 patients. All patients have been imaged with 18F-FAZA PET before initiation of curative radiotherapy, along with standard 18F-FDG PET for staging workup. The maximum standard uptake value (SUVmax) of 18F-FAZA PET images, hypoxic volume (HV), Tumormax/Bloodmean (T/B) ratio and hypoxic fraction (HF) were described for primary and nodal tumors. Recurrence free survival (RFS) and overall survival (OS) were calculated from radiotherapy completion date to any recurrence (local/regional/ distant) and date of death from any cause, respectively. Spearman correlation was used to explore potential correlation and agreement among several variables such as: primary and nodal tumor volume, 18F-FAZA/hypoxia and 18F-FDG parameters, and clinical outcomes.

## RESULTS

Intra-lesional hypoxia were identified in 21/27 (78%) patients for primary tumor volume, 14/27 (52%) patients for nodal tumor volume, and 22/27 (81%) patients overall. Larger primary tumor volume is correlated with higher T/B ($p=0.01$) and higher HF ($p=0.01$). Primary tumors with higher T/B ratio also had higher HF ($p<0.0001$). The same correlations also apply to nodal disease. Nodal FAZA SUVmax is correlated with primary FAZA SUVmax ($p<0.0001$). After a median follow up of 21 months, RFS and OS at 2 years is 57% and 61%, respectively. Higher nodal volume is significantly associated with poorer overall and recurrence free survival, and time to distant recurrence.

## CONCLUSION

Intra-lesional hypoxia in NSCLC primary and nodal tumors can be detected by 18F-FAZA PET. Initial results are encouraging. Ongoing trial accrual and long term follow-up of our patient cohort will provide more information with regards to the imaging and clinical value of 18F-FAZA PET. This study may eventually lead to using 18F-FAZA PET as a guiding tool to escalate dose to the hypoxic region of lung tumors.

# 04 Unilateral Versus Bilateral Radiotherapy for HPV Positive Oropharyngeal Carcinoma: Impact on Long Term Symptom Burden

*Ionut Busca, John de Almeida, Shao Hui Huang, Jie Su, Wei Xu, Madeline Li, Scott Bratman, John Cho, Meredith Giuliani, Ezra Hahn, Andrew Hope, John Kim, Brian O'Sullivan, Jolie Ringash, John Waldron, Ali Hosni*

**PURPOSE**

Bilateral neck radiotherapy (RT) is often required for oropharyngeal carcinoma (OPC) patients while unilateral neck RT is only used for selected small well-lateralized primary tonsillar tumors with no/minimal ipsilateral nodal disease. Our purpose is to compare long-term symptom burden following unilateral vs bilateral RT in patients with oropharyngeal carcinoma (OPC).

**METHOD**

A retrospective review was conducted for patients with T1-3 N0-2b (AJCC 7th edition), HPV positive tonsillar cancer treated with IMRT from 2012 to 2017. Patient-reported symptom burden was collected at point of care using the MD Anderson Symptom Inventory (MDASI) at baseline, RT-end (3 weeks pre or post final RT fraction), 3 weeks – 3 months, 3 – 6 months, 6 – 12 months, 12 - 24 months, and 24 - 36 months post RT. Within each period, the latest record was chosen if there were multiple records available for one patient. MDASI symptom scores (ranging from 0 = "not present" to 10 = "as bad as you can imagine") were compared between unilateral vs bilateral RT groups at each time point using Wilcoxon Rank-Sum tests and linear mixed effect model.

**RESULTS**

A total of 256 patients were eligible, of whom MDASI scores were available in 125, including 22 (18%) with unilateral and 103 (82%) with bilateral neck RT. Median age was 59 years, and 95 (76%) were male. The differences in "Dry Mouth" scores from baseline to 6 months and from baseline to 36 months were significantly better (lower) in the unilateral RT group on mixed effect model analysis [mean 2.48 (95% CI: 1.43 – 3.53) vs 4.1 (95% CI: 3.48 – 4.72), $p = 0.0028$] and [mean 2 (95% CI: 1.02 - 3) vs 3.1 (95% CI: 2.53 – 3.67), $p = 0.04$] respectively, when accounting for other variables; these differences meet a conventional threshold for clinical importance. MDASI change scores in other domains were similar between the two groups (all $p > 0.05$). Mean MDASI raw scores were highest at RT-end for all domains with improvement by 2 years for most symptoms. The unilateral RT group had significantly better (lower) raw MDASI scores in "Dry Mouth" at baseline (mean 0.3 vs 1.4, $p = 0.045$) and 6 months post RT (mean 2.6 vs 5.4, $p < 0.001$). "Swallowing" raw scores were also statistically significantly better (lower) in the unilateral RT group at 6 months post-RT (mean 2.1 vs 3.5, $p = 0.047$).

**CONCLUSION**

Patients receiving unilateral RT fare better with "Dry mouth" by 6-month and 36-month and possibly with "Swallowing" by 6-month post RT compared to patients receiving bilateral RT.

# 05 Mature Local Control and Reirradiation Rates Comparing Spine Stereotactic Body Radiotherapy to Conventional Palliative External Beam Radiotherapy

*K. Liang Zeng, Sten Myrehaug, Hany Soliman, Zain A Husain, Chia-Lin Tseng, Jay Detsky, Mark Rushin, Eshetu G Atenafu, Christopher D Witiw, Jeremie Larouche, Leodante da Costa, Pejman Jabehdar Maralani, Wendy R Parulekar, Arjun Sahgal*

**PURPOSE**

Stereotactic body radiotherapy (SBRT) improves complete pain response for painful spinal metastases compared to conventional external beam radiotherapy (cEBRT). We report mature local control and reirradiation rates in a large cohort of patients treated with SBRT vs. cEBRT enrolled previously in the Canadian Clinical Trials Group Symptom Control (SC).24 phase II/III trial.

**METHOD**

137/229 (60%) patients randomized to 24 Gy in 2 SBRT fractions or 20 Gy in 5 cEBRT fractions were retrospectively reviewed. By including all treated spinal segments, we report on 66 patients (119 spine segments) treated with SBRT, and 71 patients (169 segments) treated with cEBRT. The primary outcomes were MR based local control and reirradiation rates for each treated spine segment.

**RESULTS**

The median follow-up was 11.3 months (IQR:5.3-27.7 months), and median OS in the SBRT and cEBRT cohorts were 21.6 and 18.9 months (p=0.428), respectively. The cohorts were balanced with respect to radioresistant histology and presence of “Mass” (paraspinal and/or epidural disease extension). Risk of local failure after SBRT vs. cEBRT at 6, 12 and 24 months were 2.8% vs. 11.2%, 6.1% vs. 28.4% and 14.8% vs. 35.6%, respectively (p<0.001). cEBRT (HR:3.48, 95%CI:1.94-6.25, p<0.001) and presence of “Mass” (HR:2.07, 95%CI:1.29-3.31, p=0.002) independently predicted local failure on multivariable analysis. The 1-year reirradiation rates and median times to reirradiation after SBRT vs. cEBRT, were 2.2% vs 15.8% (p=0.002) and 22.9 months vs. 9.5 months respectively. Radioresistant histology (HR:2.66, 95%CI:1.43-4.94, p=0.002) and cEBRT (HR:2.34, 95%CI:1.14-4.78, p=0.002) independently predicted for reirradiation. 8/12 iatrogenic vertebral compression fractures (VCFs) were after SBRT and 4/12 after cEBRT; Grade 3 toxicities were isolated to the SBRT cohort (5/12).

**CONCLUSION**

Risk of local failure and reirradiation is lower with SBRT compared to cEBRT for spinal metastases. Although the iatrogenic VCF rates were within expectations, Grade 3 VCF were isolated to the SBRT cohort.

# 06 Five-Fraction Stereotactic Ablative Radiotherapy to the Pelvis and Prostate with Focal Intra-Prostatic Boost: Outcomes of the 5STAR Clinical Trial

*Rohann Correa, Melanie Davidson, Stanley K. Liu, William Chu, Chia-Lin (Eric) Tseng, Patrick Cheung, Danny Vesprini, Hans T. Chung, Gerard Morton, Ananth Ravi, Renee Korol, Andrea Deabreu, Zeeba Bhounr, Nicole Mittmann, Alice Dragomir, Hima Musunuru, Liying Zhang, Andrew Loblaw.*

**PURPOSE**

Focal boost of the dominant intraprostatic lesion (DIL) improves oncological outcomes in unfavorable-risk prostate cancer (PCa). We hypothesized that MRI-directed DIL boost could be safely and tolerably integrated with 5-fraction stereotactic ablative radiotherapy (SABR) targeting the prostate and pelvic lymph nodes.

**METHOD**

This single-institution, phase I/II trial enrolled men with high-risk and unfavorableintermediate PCa (NCT02911636). Patients underwent MRI to delineate the DIL and planning CT with urethrogram. Treatment consisted of 25 Gy to the elective pelvic lymph nodes & seminal vesicles, 35 Gy to the prostate, and up to 50 Gy DIL boost in 5 weekly fractions. Implanted fiducials, endorectal immobilization (GULok), and pre-treatment cone beam CT were utilized. Patients also received androgen deprivation therapy (ADT, 6-18 months). The primary outcome was grade ≥3 genitourinary (GU) or gastrointestinal (GI) toxicity (CTCAE v4.0). Secondary outcomes included quality of life (QoL) and biochemical failure defined by the Phoenix criteria.

**RESULTS**

Thirty men (63.3% high-risk, 23% grade group 5) were enrolled between January and August 2017. All patients received ADT. The DIL received a median D90% of 48.3 Gy. At median follow-up of 55.1 months (interquartile range: 52.8-59.5), there were no grade ≥ 3 toxicities. Cumulative incidence of worst acute grade 2 GU & GI toxicity was 56.7% and 16.7%, respectively. Cumulative incidence of late grade 2 GU & GI toxicity was 73.3% and 20.0% with prevalence of 50.0% and 13.3%, respectively. Mean nadir PSA (±standard deviation, SD) was 0.056 ng/mL (±0.096), achieved at a median of 16.7 months (1.9-23.4) post-treatment. At last follow-up, mean PSA was 0.22 ng/mL (±0.31). A single patient experienced biochemical failure (3.3%) in the form of an out-offield, non-regional nodal recurrence. QoL data collection is ongoing using patient-reported outcomes and will be presented subsequently.

**CONCLUSION**

The 5STAR trial met its primary endpoint, demonstrating safety and tolerability of integrated focal DIL boost with pelvic & prostate SABR for unfavorable-risk PCa. Our encouraging oncological efficacy data are among the first to be reported at medium-term (4-5 year follow-up) using this particular treatment strategy. These results support further investigation in a randomized setting.

# 07 Clinical Outcomes of Dose-Painted Radiotherapy in Muscle Invasive Bladder Cancer

*Inmaculada Navarro, Shinthujah Arulanantham, Zhihui (Amy) Liu, Michael Tjong, Vickie Kong, Tony Tadic, Victor Malkov, Neil Fleshner, Girish Kulkarni, Alexandre Zlotta, Charles Catton, Alejandro Berlin, Peter Chung, Srinivas Raman*

## PURPOSE

Trimodality therapy (TMT) is an evidence-based alternative to radical cystectomy in muscle invasive bladder cancer (MIBC); however, there is limited data on dose-painted radiotherapy (RT) protocols. We report the outcomes of a partial boost technique used at our institution for definitive RT in MIBC.

## METHOD

This was a single institution retrospective study of cT2-4N0M0 MIBC patients that were treated with external radiation treatment (EBRT) to the bladder and underwent a partial boost to the tumor bed between April 2003 and November 2020. The tumor bed target delineation was guided by either intravesical injection of Lipiodol or through fusion of the pre-treatment imaging to the planning CT simulation. The majority of cases were treated with contemporary techniques with IMRT/VMAT planning introduced in 2008 and daily image-guidance implemented in 2006. Kaplan-Meier was used for Overall survival (OS) and progression-free survival (PFS). Cumulative incidence function (CIF) was used to estimate local recurrence (LR), regional recurrence (RR) and distant metastasis (DM). Univariable and multivariable cause-specific hazard model was used to assess factors associated with LR.

## RESULTS

123 patients were analyzed. The median age was 73 years (65 - 81) and the 81% had T2-disease. 41.5% received neoadjuvant-chemotherapy and 76.4% received concurrent-chemotherapy. IMRT/VMAT-planning techniques were used in 74%. Lipiodol injection for was used in 54%. The median follow-up was 35 months. The median EQD2 prescription dose to the boost volume was 66Gy (52.1, 70) and 46Gy (34, 52.5) to the remaining bladder. Late high-grade (G3-G4) genitourinary and gastrointestinal toxicity was 9% and 3%. At 5-year, OS and PFS were 78% (69.2-87.8) and 45.8% (36.8-57.1). The CIF of LR was 42.5% (32.3, 52.6), of whom 28.9% (19.2-38.5) were at site of original involvement, and 21.4% (12.3-30.5) were muscle-invasive. 32 out of 46 (69.5%) had isolated LR with no RR or DM. Seven patients underwent salvage cystectomy. There were no statically significant factors associated with LR on univariate or multivariate analysis.

## CONCLUSION

Partial boost technique in MIBC is associated with good disease control and high rates of cystectomy free survival. These results are comparable to other institutional series using whole bladder RT protocols. Prospective trials are required to compare oncological and toxicity outcomes between these techniques.

# 08 Evaluating Magnetic Resonance Imaging (MRI)-only Simulation and Planning for Fiducial-Based Prostate Stereotactic Body Radiotherapy (SBRT)

*Allan Hupman, Joe A Presutti, Ananth Ravi, Ling Ho, Andrew Loblaw, Melanie TM Davidson*

## PURPOSE

Commercial packages deriving synthetic computed tomography (sCT) images from MRI images are becoming available for radiotherapy planning. This study evaluates the suitability of the Philips MRCAT (Magnetic Resonance for Calculating Attenuation) Prostate package for prostate SBRT.

## METHOD

Five prostate SBRT patients underwent CT and MRI simulation (which included images for contouring, sCT-generation, and fiducial identification). Since MRCAT-sCT only exhibit 5 Hounsfield unit (HU) bins (air, fat, water/muscle, spongy and cortical bone), we compared HUs from MRCAT-sCT to CT in a voxel-wise fashion. A histogram of CT values was plotted around each MRCAT-sCT bin and its peak value extracted. Dose was compared using prostate SBRT dose-volume evaluation metrics, and gamma analysis (1%/1mm, with thresholds= 10%, 20%, 50%, 80%, 90%, to highlight lower and higher dose disagreements). All calculations used a single CT-to-density table and accounted for differences in body contour and rectal gas. Gamma analysis was constrained within the overlap region between CT and MRCAT-sCT external contours. Structures that differed in density between MRCAT-sCT and CT were density-overridden in the MRCAT-sCT plan to match the average cohort CT-density values, to assess the impact of density mismatch on dose. Namely, fiducials (due to their absence on MRCAT-sCT) were set to 2g/cc and bones to 1.2g/cc.

## RESULTS

HUs for soft tissues (fat and muscle) were similar between MRCAT-sCT and CT. However, MRCAT-sCT underestimated the HUs of compact bone by ~7.5%, resulting in an average bone density decrease of ~3.5%. Identical plans computed on CT and MRCAT-sCT had reasonable dosimetric agreement (gamma pass rates at 1%/1mm/10% were > 99%). However, when excluding low doses with a 90% threshold, gamma pass rates dropped as low as 82%, indicating disagreement at higher doses. This was reflected in DVH metrics for targets and in high-dose metrics for adjacent organs-at-risk (OAR). Accounting for fiducials improved the gamma pass rate by 3% at 1%/1mm/90% (range 0.1-9.8%) while also overriding the bone density brought all values > 99%. After the density corrections, target DVH metrics were all within 1% and OAR metrics within 1% or 0.3cc compared to their CT counterparts.

## CONCLUSION

Higher doses are particularly important for prostate SBRT because they have been linked to the toxicity of adjacent OARs. Achieving good dose accuracy is thus critical to the safe clinical implementation of an MRI-only planning approach. We showed that while the MRCAT-sCT derived from the MRCAT Prostate package results in reasonable dosimetry, improvements in the accuracy of higher doses could be achieved with density adjustments. While fiducials need to be incorporated manually, a new CT-to-density table could alternatively be introduced to improve the bone density assignment. Additional patients will be required to further validate these observations to enable their incorporation into our MRI-only planning workflow for prostate SBRT.

# 09 Daily Adaptive Replanning with Dose Accumulation for Prostate Ultra-Hypofractionated Radiotherapy Using Machine Learning Automated Planning on CBCT

*Maryam Golshan, Aly Sherif Khalifa, Jeff Winter, Jason Xie, Alejandro Berlin, Chris McIntosh, Tom Purdie, Victor Malkov, Tony Tadic*

## PURPOSE

In prostate cancer radiotherapy, anatomical changes over the course of treatment will impact the delivered dose. With online adaptive radiotherapy, it is possible to generate a novel treatment plan at each fraction based on the CBCT imaging used for daily image guidance. Our objective here is to establish a novel pipeline for daily adaptive replanning for ultra-hypofractionated prostate radiotherapy using machine learning (ML) automated planning and dose accumulation.

## METHOD

We retrospectively demonstrated daily adaptive replanning with dose accumulation for ten patients with prostate cancer treated with 4270 cGy in 7 fractions using daily iteratively-reconstructed cone-beam computed tomography (CBCT). A clinical expert contoured CTV and organs-at-risk on all CBCTs and we generated daily plans for 3 and 7 mm PTV margins using ML planning. We used a hybrid intensity/structure-based algorithm for CT-to-CBCT deformable image registration (DIR) and dose accumulation. We evaluated geometric and dosimetric DIR accuracy by comparing spatial and DVH differences between propagated and manual contours for CTV, bladder, and rectum. We compared accumulated daily replanning with the reference plan using DVHs.

## RESULTS

We successfully executed automated daily replanning and dose accumulation across all fractions. DIR demonstrated excellent geometric accuracy with Dice similarity coefficients of 0.97±0.01, 0.99±0.01 and 0.97±0.02 for CTV, bladder and rectum. Mean distance-to-agreement for CTV, bladder and rectum were 0.3±0.3, 0.2±0.1 and 0.4±0.4 mm. Dosimetric evaluation of DIR showed DVH differences of 8±13 cGy for CTV D95%, 9±21 cGy for rectum D1cc, 33±46 cGy for rectum D35%, and 4±11 cGy for bladder D1cc (scaled to 7 fractions).

For 3 mm margins, the reference PTV V95% was 99.7±0.1% and adapted/accumulated CTV V95% was 100±0.001%. For 3 mm margins, rectum V90% and V75% were 6.6±1.9% and 11.4±2.6% on the reference CT and 3.4±1.3% and 7.6±1.9% for adapted/accumulated plans. The same trend existed for organs-at-risk and targets for 7 mm margin.

## CONCLUSION

In this study, we created and validated a novel pipeline for investigating the value of ML automated planning for CBCT-based online adaptive prostate radiotherapy. Evaluation of the DIR demonstrated excellent spatial alignment and dosimetric accuracy. Adapted plans showed improved rectum sparing while maintaining target coverage. In future, with this automated pipeline, we will be able to investigate different strategies for ML-driven online adaptation, such as varying PTV margins.

# 10 Feasibility of Machine Learning Automated Treatment Planning for Magnetic Resonance Guided Radiation Therapy in Prostate Cancer

*Aly Khalifa, Jeff Winter, Inmaculada Navarro, Chris McIntosh, Thomas G. Purdie*

## PURPOSE

Atlas-based machine learning (ML) provides an interpretable automated radiation therapy (RT) planning framework by allowing direct comparison of the automatically generated RT plan to the patients selected from the training dataset as the basis of dose prediction (i.e., the atlases). However, ML models require large datasets for training, impeding their adoption in new clinical settings. Here, we investigated whether a computed tomography (CT) based ML model could be repurposed for magnetic resonance (MR) guided RT of prostate cancer.

## METHOD

We retrospectively collected contoured CT and MR imaging from 55 prostate cancer patients treated on a 1.5T MR-linac. For each patient, we automatically generated hypofractionated (60 Gy in 20 fractions) RT plans on both images using clinically validated ML that was trained on CT imaging only. Equivalence between CT and MR plan doses was assessed using institutional dose-volume criteria (two-one-sided t-tests, equivalence threshold of 5% of each criterion's limit). Differences in the passing rates of criteria were also assessed (Exact McNemar tests). Anatomical variation was quantified by the amount of overlap between the planning target volume (PTV) and the rectum and bladder. We estimated the expected dose differences due to anatomical differences using linear regression analysis, both for anatomical differences between CT and MR images, and between RT plans and their respective selected atlases.

## RESULTS

Dose equivalence between CT and MR plans was demonstrated for all dose-volume criteria except for the dose to 30% and 50% of the bladder volume. Respectively, the median bladder doses were 519 cGy and 381cGy higher on MR plans. However, these dose differences did not cause a statistically significant difference in dose-volume criteria pass rates for the bladder. Differences in the amount of PTV overlap between MR and CT images moderately correlated ($r > 0.7$, $p < 0.001$) with differences in dose-volume metrics. Similarly, differences in overlap between a patient and their selected atlases correlated ($r > 0.7$, $p < 0.001$) with the dose difference between them.

For the dose to 30% of the bladder volume, the regression analyses revealed that MR-CT anatomical differences accounted for a 52 cGy increase, and that plan-atlas anatomical differences accounted for a 180 cGy increase. This left 288 cGy of the 519 cGy of the observed difference between CT and MR plans unexplained by anatomical variation. Similar trends were observed for the dose to 50% of the bladder volume.

## CONCLUSION

Approximately 45% of the dose differences observed when applying a CT-based ML to MR imaging was attributable to anatomical variation. The largest source of anatomical variation was within the training set of atlases, rather than between CT and MR imaging. Despite the increased bladder doses, MR plans remained within acceptable dose limits.

# 11 Individualized Prediction of Distant Metastases Risk in Oral Cavity Carcinoma: A Validated Predictive-score Model

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**PURPOSE**

We aimed to develop and validate a risk-scoring system for distant metastases (DM) in oral cavity carcinoma (OCC).

**METHOD**

In this IRB-approved retrospective study, OCC patients treated at 4 tertiary cancer institutions with curative surgery+/- postoperative radiation/chemo-radiation (PORT/PO-CRT) were divided into discovery and validation cohorts (randomly selected in 3:2 ratio). Staging was reviewed based on TNM 8th edition. Predictors of DM identified on multivariable analysis in discovery cohort were used to develop DM risk-score model to classify patients into risk groups using Contal and O'Quigley method for cut-off optimization. The utility of risk classification was subsequently evaluated in validation cohort. C-index was used to assess predictive ability of the continuous risk score.

**RESULTS**

Overall, 2749 patients were analyzed (table 1). Predictors (risk score coefficient) of DM in discovery cohort were: pT3-4 (0.4), pN+ (N1: 0.8; N2: 1.0; N3: 1.5), histologic grade 3 (G3, 0.7) and lymphovascular invasion (LVI, 0.4). The DM risk groups were defined by cumulative sum of risk score coefficients: high risk (sum>2), intermediate risk (sum=1-2), and standard risk (sum<1). In the discovery cohort, 5-yr DM for high vs intermediate vs standard risk groups was 33% vs 19% vs 6%, p<0.001 (C-index=0.79). Similarly, in the validation cohort, 5-yr DM for high vs intermediate vs standard risk groups was 36% vs 23% vs 7%, p<0.001 (C-index=0.77). When applied to entire study population, this predictive model showed excellent discriminative ability in predicting DM only without locoregional failure (29% vs 18% vs 3%, p<0.001), late (>2 yr) DM (11% vs 5% vs 3%; p<0.001), DM in patients treated with surgery only (26% vs 11% vs 6%, p<0.001), PORT (37% vs 23% vs 7%, p<0.001), and PO-CRT (42% vs 29% vs 9%, p<0.001). Finally, 5-yr OS for high vs intermediate vs standard risk groups in the overall cohort was 24% vs 38% vs 66%, p<0.001.

**CONCLUSION**

A predictive-score model for DM utilizing pT3-4, pN1/2/3, G3 and LVI demonstrated a validated utility in identifying patients at higher risk of DM who may be evaluated for individualized risk-adaptive treatment escalation and/or surveillance strategies.

# 12 Automatic Segmentation for Targets and OARs in Cervical High Dose Rate (HDR) Brachytherapy via Deep Learning Techniques

*Ruiyan Ni, Sejin Kim, Benjamin Haibe-Kains, Alexandra Rink*

## PURPOSE

Brachytherapy is an important component in managing cervical cancer and improves survival rates over external beam radiotherapy alone by delivering a high radiation dose to the tumor region while sparing the surrounding organs at risk (OARs). Magnetic Resonance Imaging (MRI) is the preferred imaging modality for cervical HDR brachytherapy, recommended due to superior soft tissue contrast. Accurate segmentation of target tumor and OARs is the prerequisite of the treatment planning; however, the manual delineation is the most time-consuming aspect of a cervix brachytherapy procedure and may lead to high intra- and inter-observer variation. To overcome these difficulties, this study aims to achieve the automatic segmentation of targets and OARs for MRI-guided HDR brachytherapy using deep learning (DL) techniques.

## METHOD

A dataset of 48 T2-weighted MR images (acquired axially) of cervix region was built from 13 cervical cancer patients undergoing brachytherapy. These MR images were manually contoured by radiation oncologists during brachytherapy treatment. An end-to-end automatic segmentation framework was developed based on a novel self-adapting U-Net-based method, called nnU-Net ('no-new-Net'). 3D full-resolution U-Net architecture was manually selected to preserve the image quality and the automated configuration was used for preprocessing, network training, and postprocessing. The network was trained on 42 cases from 11 patients for 200 epochs and applied to four OARs (bladder, rectum, sigmoid, and small bowel) and high-risk clinical target volume (HR-CTV). We did five-fold cross-validation during training to eliminate the overfitting and each fold contained two/three patients. The segmentation performance was evaluated by two standard metrics, i.e., volumetric Dice Similarity Coefficient (DSC) and 95th percentile of Hausdorff distance (HD95), and two novel methods, including surface DSC and added path length (APL) for assessing time-saving and clinical applicability of the auto-generated contours. All results are reported as mean ± standard deviation.

## RESULTS

The preliminary results of the automatic segmentation showed that the volumetric DSCs for the 6 test cases were 0.87 ± 0.03 (bladder), 0.83 ± 0.03 (rectum), 0.64 ± 0.08 (sigmoid), 0.6 ± 0.2 (small bowel), and 0.6 ± 0.1 (HR-CTV). HD95 (mm) were 5 ± 3 (bladder), 7 ± 2 (rectum), 27 ± 9 (sigmoid), 39 ± 19 (small bowel), and 16 ± 5 (HR-CTV). Surface DSC and APL (cm) across all contours were 0.5 ± 0.1 and 900 ± 500, respectively. With the novel self-configuration method, our model demonstrated comparable performance with previous studies despite the very limited dataset size. More accurate and robust results could be expected with more clinical data extracted.

## CONCLUSION

We have proposed a DL-based automatic segmentation approach for cervical cancer targets and OARs in MR-guided brachytherapy. This method holds great potential to improve contouring efficiency without clinically significant loss of accuracy and thus, improving plan accuracy and decreasing dosimetric uncertainty.

# 13 Investigation of Dose Distribution of Uniformly and Non-Uniformly Loaded Generic and Notched Eye Plaques with Monte Carlo Simulations

*Oleksii Semeniuk, Victor Malkov, Robert Weersink*

## PURPOSE

Princess Margaret Cancer treats over 100 patients with choroidal melanomas annually using eye plaque brachytherapy, with plaque loadings using sources of different activities. For complex treatments close to the optic nerve, a combination of notched plaques and asymmetric source distribution are used to target the tumour while minimizing dose to the optic nerve. Current dose calculations use TG43 are inadequate for tumour and optic nerve dosimetry. Here we investigate the effect of non-uniform loading on dose distribution for generic and notched eye plaques using Monte Carlo simulations.

## METHOD

Using EGSnrc Monte Carlo (MC) simulations, we investigate eye plaque dose distributions in water and in an anatomically representative in silico eye phantom. Simulations were performed in accordance with the TG-43 formalism and compared against full MC simulations which account for inter-seed and inhomogeneity effects due to tissue and the presence of the plaque.

## RESULTS

Uniformly and non-uniformly loaded plaque dose distributions in water showed virtually no difference between each other. Comparing normalized dose profiles along the central axis for standard TG43 vs. full MC, TG43 overestimated the dose in the first few millimeters, while relative dose profiles matched at longer distances. More pronounced changes in the relative dose distributions were observed in the lateral directions. The full width at half maximum dose profile for generic eye plaques is ~10% lower using full MC vs TG43 due to the inclusion of tissue and plaque inhomogeneities. Our simulations show that the lateral dose contraction favorably impacts the dose distribution for both uniformly and non-uniformly loaded 16 mm plaques: TG43 overestimates the dose to the organs at risk, while underestimating the target coverage.

## CONCLUSION

With individual normalization of MC and TG43, TG43 calculations overestimate the lateral dose distribution of both generic and notched eye plaques, leading to the dose overestimation for the organs at risk (optic nerve, iris, lens, etc.) and to underestimation of target coverage. The dose matching along the central axis for the non-uniformly loaded plaques to that of uniformly loaded ones, was found to be sufficient for providing a comparable coverage and can be clinically used in eye-cancer-busy centers. Our MC models of generic and notched plaques models will be further evaluated for treatment planning of patient-specific eye lesions. Of particular interest is for asymmetrically loaded and notched plaques that are used to treat tumours close to the optic nerve, where MC models will provide more accurate dosimetry to this sensitive structure compared to currently used TG-43 methods.

# 14 Management of Radiotherapy Patients with Cardiovascular Implantable Electronic Devices: A National Survey of Multi-Disciplinary Radiation Oncology Professionals

*Amir H. Safavi, Alyaa H. Elzibak, Andrew Warner, Elysia K. Donovan, Jay S. Detsky, Alexander V. Louie*

**PURPOSE**

This study aimed to characterize the contemporary management of Canadian radiotherapy (RT) patients with cardiovascular implantable electronic devices (CIEDs), in light of updated American Association of Physicists in Medicine (AAPM) guidelines.

**METHOD**

A 22-question, web-based survey, informed by recommendations from the AAPM TG-203 report, was developed to elicit the demographics, knowledge, and management practices of participants regarding CIEDs in RT. The survey was piloted locally to optimize content validity, face validity, and usability, prior to distribution to study participation. The survey was emailed by the Canadian Association of Radiation Oncology, Canadian Organization of Medical Physicists, and Canadian Association of Medical Radiation Technologists to their respective memberships in January 2020. Survey responses were anonymously collected from January-February 2020. Descriptive statistics were calculated for responses to multiple choice, linear scale, and short-answer questions. Frequency analyses were performed to identify the most common responses to free-text questions. Statistical comparisons were made using Chi-square and Fisher's exact tests. A p value threshold of 0.05 was used for statistical significance.

**RESULTS**

In total, 155 surveys were completed by 54 radiation oncology (RO), 26 medical physics (MP), and 75 radiation therapy (RTh) respondents in academic and community (49%) practices across all provinces. The majority of respondents (77%) had managed >10 patients with CIEDs in their career. Most respondents (70%) reported using risk-stratified institutional management protocols. Respondents used manufacturer recommendations, rather than AAPM or institutionally recommended dose limits, when the manufacturer limit is 0 Gy (44%), 0-2 Gy (45%), or >2 Gy (34%). The majority of respondents (86%) reported an institutional policy to refer to a cardiologist for CIED evaluation both prior to and after completion of RT. The three most common scenarios in which respondents would not refer patients with CIEDs for pre-RT cardiology evaluation were 1) CIED located far from the field (23% of all respondents, 39% of RO respondents), 2) emergency RT (15% of all respondents, 24% of RO respondents), and 3) recent CIED check (8% of all respondents, 11% of RO respondents). Cumulative dose to CIED, pacing dependence, and neutron production were considered as part of risk stratification for device malfunction by 83%, 81%, and 56% of ROs, respectively. Dose and energy thresholds for high-risk management were not known by 45% and 52% of respondents, with ROs and RThs significantly less likely to report thresholds than MPs ($p < 0.05$). Although 59% of respondents felt comfortable managing patients with CIEDs, community respondents were significantly less likely to feel comfortable than academic respondents ($p < 0.05$).

**CONCLUSION**

The management of Canadian RT patients with CIEDs is characterized by variability and uncertainty. National consensus guidelines are needed to improve provider knowledge and confidence in caring for this growing population.

# 15 Final Results of an International Delphi Consensus Study Regarding the Optimal Management of Radiation Pneumonitis

*Indu Voruganti, Cicely Cunningham, Lorraine McLeod, Stephen Harrow, Alexander V. Louie.*

**PURPOSE**

There is a lack of consensus around the diagnosis, management and follow-up of radiation pneumonitis (RP). A Delphi consensus process was conducted in this area.

**METHOD**

In round 1, open questions were distributed to 31 clinicians treating thoracic malignancy. In round 2, participants rated agreement/disagreement with statements derived from round 1 answers using a 5-point Likert scale. Consensus was defined as ≥75% agreement. Statements which did not achieve consensus were modified and re-tested in round 3.

**RESULTS**

Response rate was 74% in round 1 (n=23/31; 17 oncologists, 6 respirologists); 82% in round 2 (n=19/23; 15 oncologists, 4 respirologists); and 100% in round 3 (n=19/19). Thirty-eight of 64 round 2 statements achieved consensus; a further 11/26 statements achieved consensus in round 3. In round 2, there was agreement that risk stratification/mitigation should consider patient factors; the importance of minimising RP risk through treatment planning; the basis for diagnosis of RP; and that oncologists and respirologists should be involved in treatment. Treatment should involve oral steroids with consideration of gastroprotection, starting with 60 mg PO prednisolone or equivalent, for a duration of 2 weeks, with a taper of 10 mg in the daily dose per week, or for severe pneumonitis, IV methylprednisolone for 3 days before PO. Key statements achieving consensus in round 3 were: “There is uncertainty about the clinical significance of whether pneumonitis is radiation- or drug induced, and further research is needed to understand this area,” and “Although there are guidelines for the review schedule of patients receiving immunotherapy, it is unclear how these could be modified for patients also receiving radiotherapy.”

**CONCLUSION**

Consensus was achieved on many aspects of RP diagnosis and management. Further research is needed, particularly around pneumonitis in those receiving both radiotherapy and immunotherapy. These data will inform the development of final consensus statements providing practical guidance on diagnosis and management of RP.

# 16 The Effects of a Curriculum Change on Peer Mentorship Among Radiation Oncology Residents

*David Y. Mak, Janet Papdakos, Joanne Alfeiri, Jennifer Croke, Paris-Ann Ingledew, Shaun K.Loewen, Meredith Giuliani*

**PURPOSE**

Peer mentorship is the educational, professional, and personal support provided amongst trainees within a similar level of training. While peer mentorship has shown to benefit academic success and professional growth, little data has examined contextual factors, such as curricular change, that may affect the accessibility, content, and quality of these relationships. This study aims to explore peer mentorship among Radiation Oncology (RO) resident physicians following the implementation of a new nationwide, competence-based RO residency curriculum, known as Competency by Design (CBD).

**METHOD**

Two cohorts of Canadian RO residents in English programs were invited to participate - one being the final academic year before CBD implementation (non-CBD cohort entering training in July 2018), and the other being the inaugural CBD academic year (CBD cohort entering training in July 2019). Residents participated via convenience sampling and engaged in semi-structured interviews to elicit their thoughts and perceptions on the impact of curriculum change on peer mentorship. Interviews were conducted until data saturation, meaning that no new ideas or themes were emerging from the data. Interviews were audio-taped, de-identified and transcribed. Iterative data collection was conducted in parallel with thematic analysis methods, using both deductive and inductive analysis, to generate themes to describe findings.

**RESULTS**

Between April and December 2021, 14 interviews were conducted with 6 non-CBD (32% response rate) and 8 CBD (53% response rate) residents, at which point thematic saturation was achieved. Participants represented 8 out of 10 eligible English RO training programs across Canada. Three major themes were identified: (i) the CBD-cohort identified fewer opportunities for peer mentorship in navigating formal evaluation processes, and in discussing uncertainties about the later stages of residency training; (ii) peer mentorship tended to thrive when able to occur as spontaneous in-person interactions; and (iii) there was minimal impact on specialty-specific learning.

**CONCLUSION**

Findings from this study identified that inaugural RO residents of a new curriculum experienced uncertainty around new training objectives, and that peer mentorship was most impactful as informal and in-person interactions. Our findings suggest that the unintended consequences of curriculum change on resident peer mentorship may be mitigated from improved orientation and communication about stage-specific training objectives, and to provide increased opportunities for informal activities amongst residents.

# UTDRO RESEARCH DAY ABSTRACTS – POSTER PRESENTATIONS

*Poster Presentations: Section 1*

## 01 Safety and Efficacy of Stereotactic Body Radiotherapy for Ultra-Central Thoracic Tumours

*George J. Li, Hendrick Tan, Humza Nusrat, Hanbo Chen, Joe Chang, Jeevin Shahi, Ian Poon, May Tsao, Yee Ung, Patrick Cheung, Alexander V. Louie.*

**PURPOSE**

While stereotactic body radiotherapy (SBRT) is increasingly utilized in the management of ultra-central thoracic tumours, concerns regarding the potential for significant toxicity remain. We sought to evaluate the toxicity and efficacy of SBRT in these tumours at our institution.

**METHOD**

Patients with ultra-central lung tumours or nodes treated at our institution with SBRT between 2009 and 2019 were retrospectively reviewed. Ultra-central location was defined as having the planning target volume (PTV) overlapping or abutting the central bronchial tree and/or esophagus. Per institutional policy, patients were planned with homogenous dose distributions, with target coverage objectives of ITV V100 >99%, PTV V95 >99%, and PTV Dmax <105%. All SBRT plans were reviewed in radiation quality assurance rounds by a team of dosimetrists and radiation oncologists. The primary endpoint was SBRT-related grade ≥3 toxicities, defined using the Common Terminology Criteria for Adverse Events (CTCAE) V5.0. Secondary endpoints included grade ≥2 toxicities, local control (LC), progression-free survival (PFS) and overall survival (OS). Competing risks analysis was used to estimate LC. Kaplan-Meier method was used to estimate PFS and OS.

**RESULTS**

A total of 160 patients who received 169 ultra-central courses of SBRT were included, with a median follow-up of 21.6 months. The median age was 69 years, and most patients were of good performance status (94%, ECOG 0-2). The most frequent tumour histologies were NSCLC (42%) and RCC (26%). Treatment intent was most commonly for oligoprogression (46%) and oligometastasis (31%), followed by primary lung cancer (18%). SBRT prescription doses ranged from 30-55Gy in 5 fractions (BED10 range 48-115 Gy). The most common prescription was 50Gy in 5 fractions (44%). Thirteen (8.1%) patients experienced grade ≥3 toxicity and 26 (16.2%) experienced grade ≥2 toxicity. There was 1 case of grade 4 esophagitis and 2 cases of grade 4 pulmonary toxicity (bronchopleural fistula and bronchial obstruction). There was 1 possible treatment related death (pneumonia/pneumonitis). The 1- and 2-year LC rates were 94.7% and 87.6%, respectively. Median PFS was 8.7 months (95% confidence interval [CI], 7.4-10.5), with 1- and 2-year PFS being 35.5% and 23.7%. Median OS was 3.7 years (95% CI, 2.7-not reached), with 1- and 2-year OS being 77.5% and 66.1%.

**CONCLUSION**

In one of the largest case series of ultra-central thoracic SBRT reported to date, homogenously prescribed SBRT plans were associated with relatively low major toxicity and encouraging LC rates across a variety of treatment indications. Future work to evaluate predictors of major toxicity is planned.

# 02 Dosimetric Outcomes for Adaptive Prostate SBRT on MR-Linac: The Time Taken for Contouring and Re-planning Makes a Difference

*Eyesha Younus, Andrew Loblaw, Patrick Cheung, William Chu, Chia-Lin Tseng, Danny Vesprini, Jay Detsky, Stanley Liu, Hans Chung, Melanie TM Davidson, Matt Wronski, Mark Ruschin*

## PURPOSE

To investigate whether online-adaptive MR-Linac session time for prostate SBRT counteracts some of the advantages of plan adaptation.

## METHOD

Our institution has treated 40 prostate cancer patients on 1.5 Tesla MR-Linac with 40Gy/5-fractions to the clinical target volume (CTV) and 36.25Gy to the planning target volume (PTV). The CTV is the prostate and proximal 1 cm of seminal vesicles and the PTV is a 4mm expansion of the CTV. During daily online adaptation, the physician re-contours relevant structures on the anatomy-of-the-day captured by localization MRI (MR-loc), and the pre-plan is adapted to the shape (ATS) of the current anatomy on MR-loc (plan=ATS-loc). To assess the anatomical changes during re-contouring/re-planning (average time=25 min), a verification MRI (MR-ver) is acquired prior to beam-on to ensure that prostate is within PTV. Offline we generate two comparison plans per fraction: (1) a rigid-shift Adapt-to-Position (ATP) plan mimicking a conventional image-guidance approach but calculated on daily anatomy (plan=ATP-loc); (2) recalculation of ATS-loc on MR-ver (plan=ATS-ver). Dosimetry is compared fraction-by-fraction and on the accumulated dose over all fractions (DA) using the following planning tolerances: CTV V40Gy >95%; CTV D99% > 36.25Gy (PTV dose); bladder V39.5Gy < 3cc; rectum V38Gy < 1.5cc and Dmax < 42Gy.

## RESULTS

35 fractions (given 2-3 times per week) in 7 patient cases were included in the analysis thus far. In a fraction-by-fraction comparison: CTV V40Gy > 95% was achieved in 97% (34/35), 71% (25/35), and 47% (16/35) of the ATS-loc, ATP-loc, and ATS-ver plans respectively while CTV D99% > 36.25Gy was achieved in 100% (35/35), 86% (30/35), and 57% (20/35). ATP-loc experienced 14 violations in 105 total constraints assessed over all fractions and subjects, which is 10 more violations compared to ATS-loc (4/105), while ATS-ver had 9/105 violations. On DA plans, CTV D99% > 36.25 Gy was achieved for all 7 patients and all 3 techniques, and only 1 OAR violation occurred on ATP-loc and ATS-ver.

## CONCLUSION

The time required for adaptation results in anatomical changes (e.g. bladder filling), which affects the dosimetric outcomes achieved on the localization MRI as seen by superimposing that plan on the verification MRI. Nevertheless, online adaptation still provided favorable OAR dosimetry compared to rigid adaptation, or ATP. The full benefit of the ATS scheme will be realized by making ATS more time efficient. More data will be required to validate the current observed trends and their impact on accumulated dose.

# 03 Review of 20 Years of Adult Medulloblastoma Treatment at a High-Volume Center – Chemotherapy Prescription Trends and Survival

*Marissa Sherwood, Seth Climans, Ronald Ramos, Normand Laperriere, Warren Mason*

## PURPOSE

Medulloblastomas are WHO grade 4 tumors and represent less than 1% of adult brain malignancies. Standard of care is maximal safe resection follow by craniospinal and primary site radiation – the role for chemotherapy has been unclear. The objective of this study was to review 20-year chemotherapy prescribing trends in adult medulloblastoma patients at a high-volume center, with secondary objectives assessing overall and progression free-survival. We hypothesized that primary chemotherapy (concurrent or adjuvant) would be associated with prolonged survival and that patients treated in the most recent decade would have received chemotherapy more often.

## METHOD

A retrospective review was performed of adult medulloblastoma patients at a high-volume center from 1999-01-01–2020-12-31. Eligible patients were 18 years and older with a pathologic diagnosis of medulloblastoma – those with supratentorial primitive neuroectodermal tumors were excluded. Descriptive statistics were used to present population data and Kaplan–Meier estimators for survival analysis.

## RESULTS

Forty-three patients were eligible; median age was 30 and male: female ratio was 2:1. Desmoplastic and classical histologies were the most common. Molecular subgroup was available for 6 patients, with SHH predominating. Of all patients, 47% (23/49 were classified as high risk – most commonly due to large cell/anaplastic histology or large residual. Only 10 (20%) received primary chemotherapy, 70% of which had high risk disease. Of the patients who received primary chemotherapy, 30% went on to receive chemotherapy for recurrence or metastases; of the entire population, this was only 39%. Primary regimens were mainly cisplatin/lomustine/vincristine, while recurrence regimens were often cisplatin/etoposide. The majority who received primary chemotherapy were treated from 2010–2020. Median overall survival was 7.8 years (95% CI 5.7–∞), with 1-, 5-, and 10-year survival 95.8%, 67.5% and 42.2% respectively. Overall survival was marginally better for those who did not receive primary chemotherapy (8.5 years) vs those who did (7.4 years). The main chemotherapy toxicity was hematologic and neuropathy - 90% of primary chemotherapy patients experienced toxicity

## CONCLUSION

This study reviewed 20 years of treatment trends for a group of adult medulloblastoma patients at a high-volume center. We found only a small proportion of patients received chemotherapy as their primary treatment with surgery and radiation. Patients who received primary chemotherapy had marginally worse overall survival – perhaps due to baseline worse clinical status not captured by the definition of high vs. intermediate risk disease. Despite calls for adjuvant chemotherapy for all adult medulloblastoma patients, there is clinical equipoise and future randomized trials are needed.

# 04 Commissioning of the Elekta Symmetry 4D Cone Beam Mode

*Eric Christiansen, Cathy Neath, Aaron Vandermeer*

## PURPOSE

The purpose of this work is to commission the Symmetry 4D cone-beam CT (CBCT) image acquisition mode, available on Elekta linacs, for potential clinical use in image-guided radiation therapy. The accuracy of this mode in capturing the complete range of tumour motion and in correcting for errors in patient setup is evaluated.

## METHOD

The Symmetry mode of CBCT imaging gives a set of phase-binned 4D-CBCT images. This is accomplished by using a slower gantry speed than for 3D-CBCT, allowing for the acquisition of projections at each phase of the respiratory motion. Each phase may be viewed independently to evaluate that the ITV created during planning remains appropriate. The 4D-CBCT image may also be used to correct the patient setup by performing registration to the reference CT image. In this work, the Quasar respiratory motion phantom was used to simulate the patient's respiratory motion. A custom 3D-printed insert was fabricated to represent a tissue-density lung tumour, and placed inside a low-density cedar cylinder representing the lung, which is driven by an electric motor. Motion amplitude, frequency, and imaging parameters were varied to evaluate the effect of each on the resulting 4D-CBCT images. Reference 4D-CT images were also acquired. The motion amplitude observed in the 4D-CBCT was compared to the amplitude set on the motor. Registration accuracy was determined using high-density surface markers visible in the reference and CBCT images.

## RESULTS

For nearly every tested combination of motion parameters, the 4D-CBCT acquired over 3 min and using the S20 FOV gave the smallest difference from the actual - measured amplitude, with an average difference of 1.3 mm (range: 0-6.0 mm). The exception to this was for 20 mm amplitude and 6 bpm, for which the 1 min acquisition and S10 FOV gave the smallest difference at 5 mm. The average registration error for different imaging parameter combinations ranged from 0.2 to 0.4 mm. The registration error for any combination of motion and imaging parameters was no greater than 0.5 mm, except for the 20 mm amplitude, 6 bpm acquired over 1 min, for which the error was 1.4 mm. 4D-CBCT images acquired with motion amplitudes of 5 and 10 mm at 6 bpm featured severe reconstruction artifacts. These artifacts persisted for the 5 mm amplitude up to 12 bpm.

## CONCLUSION

Given the presence of reconstruction artifacts for 6 bpm, it is recommended not to use the 4D-CBCT image acquisition mode at or below this respiratory frequency. The optimal set of imaging parameters is a 3 min acquisition and S20 FOV. For frequencies greater than 6 bpm, the 4D-CBCT images can be expected to capture the entire tumour range of motion to within 0.7 mm, and accurately register the patient to within 0.3 mm.

# 05 Unanticipated Radiation Re-planning for Stage III Non-small Cell Lung Cancer

*Melinda Mushonga, Patrick Cheung, Alexander Louie, Yee Ung, Ian Poon, Liying Zhang, May Tsao*

## PURPOSE

Technological advancements in the planning process have facilitated more efficient complex radiotherapy (RT) adaptation in cancers where changes in motion and anatomy during treatment may occur, such as in stage III non-small cell lung cancer (NSCLC). The primary objective of this study was to identify factors associated with unanticipated RT re-planning in Stage III NSCLC. Secondary objectives were to examine survival and cumulative incidence of local, regional and distant recurrence.

## METHOD

In this single-institution ethics-board approved study, all stage III NSCLC patients from January 1, 2016, to December 31, 2019, treated with radical intent RT were analyzed. Descriptive statistics were performed, including the frequency of RT re-planning and reason for re-planning. Logistic regression analysis was used to identify predictive factors associated with re-planning. Variables significant on univariate modelling, with a P value < 0.05, were selected for multivariate modelling. Overall survival was determined using the Kaplan-Meier method. Cumulative incidence of local, regional, and distant recurrence was determined using the competing risk method.

## RESULTS

There were 144 patients with Stage III NSCLC meeting study criteria, of which 18% (n=26) required re-planning. The most common reason for re-planning was due to volume changes (target shift or enlargement) on cone beam computed tomography (CBCT) (n=20, 77%), followed by failure to meet planning constraints (n=6, 23%). On univariate analysis, patients with a larger superior -inferior (SI) dimension of the primary and nodal planning target volume (PTV) was associated with a higher incidence of re-planning [Odds ratio (OR) 1.17, 95% CI 1.03-1.35 p = 0.02). Larger PTV (primary and nodal) was also associated with higher incidence of re-planning on univariate analysis [(OR) 2.48, 95% CI 1.21-5.38, p= 0.02). On multivariable analysis, only larger PTV (primary and nodal) were statistically predictive of re-planning. The actuarial median OS was 36.3 months (95% CI 27.7-66.5). The cumulative incidence for local, regional, and distant recurrence at 2 years were 18% (95% CI 12-25%), 19% (95% CI 13-26%), and 38% (95% CI 30-46%), respectively.

## CONCLUSION

A larger SI dimension of the PTV, as well as larger PTV are associated with a higher odds ratio of re-planning. Survival and recurrence outcomes for this group of patients are similar to the outcomes reported in the literature.

# 06 Predictive Factors for Survival and Radiation Necrosis in Patients with Recurrent High-Grade Glioma Treated with Re-Irradiation

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**PURPOSE**

To analyze the predictors of survival and radiation necrosis in adult patients (pts) with recurrent high-grade gliomas (rHGG) who have undergone re-irradiation (ReRT).

**METHOD**

All adult pts with rHGG who had ReRT from 2009 to 2020 at one institution were retrospectively reviewed. Demographic, clinical, dosimetric, and radiological data were obtained from the electronic medical records. The primary outcome was to identify predictors of overall survival (OS) and radiation necrosis (RN). The secondary outcome was to identify patterns of failure after ReRT, which was defined as in-field, marginal or distant if > 95% of the recurrence volume was in the 80% isodose line (IDL), between 80%-20% IDL, or outside 20% IDL, respectively. OS, progression-free survival (PFS), and RN were estimated by the Kaplan-Meier method. Toxicity was recorded according to CTCAE V5.0.

**RESULTS**

Were included 79 pts with a median age of 52 yrs (range, 19-79), 62% were male, 85% had grade 4 glioma at presentation and 98% at ReRT. IDH was wildtype/mutated/unknown in 73%/11%/15% of pts. 92% had concurrent/adjuvant temozolamide at the primary treatment. 34% had re-resection prior to ReRT. 16% had concurrent bevacizumab at ReRT. The most common fractionation schedules at the primary treatment were 40Gy/15Fx (9%) and 50-60Gy/28-33Fx (91%), and at ReRT were 17-24Gy/1Fx (9%), 20-35Gy/5Fx (38%), 25-35Gy/10Fx (48%) and 36-54Gy/18-30Fx (5%). The median cumulative equivalent dose in 2 Gy fractions (EQD2, a/b=2) was 103Gy (range, 81-216). The median OS and PFS were 9.9 (95% CI 8.3-11.6) and 4.1 mos (95% CI 3.6-5.4), respectively. The OS and PFS rate at 6/12 months were 69.6%/34.2% and 29.1%/7.5%, respectively. The prognostic factors for OS on multivariate analyses (MVA) were interval from initial treatment to first progression ≥16.3mos (HR=0.35, 95% CI 0.20-0.59, p<0.001), re-resection prior ReRT (HR=0.43, 95% CI 0.25-0.73, p=0.002), ECOG ≥1 at ReRT (HR=1.90, 95% CI 1.10-3.30, p=0.022) and PTV volume at ReRT ≥112cc (HR=2.63, 95% CI 1.55-4.44, p≤0.001). Toxicities G2 and G3 were 22% (8.8% RN) and 5% (2.5% RN), respectively. Concurrent use of bevacizumab (p<0.001) and EQD2 ≤98 Gy (p<0.001) were predictors for lower incidence of RN on MVA. Exploratory analysis suggested three risk groups for RNs based on cumulative EQD2: ≤100Gy (RN = 4%), 100-111Gy (RN = 13%), and ≥111Gy (RN = 20%). The failures after ReRT were in-field, marginal or distant in 67%, 6%, and 27% of pts who had follow-up MRI, respectively.

**CONCLUSION**

Re-irradiation is a safe and effective treatment for GBM. We describe predictive factors for OS and RN to guide patient section. Focus on pts with the most favorable OS may aid in identifying pts most likely to benefit from ReRT.

# 07 Selection of a stereotactic radiosurgery technique using a target volume regularity index

*Charmainne Cruje, Yizhen Wang*

## PURPOSE

This work proposes the use of a target volume regularity index (RI) to decide between using HDMLCs or cones to deliver stereotactic radiosurgery (SRS) treatments to the brain. Instead of preparing two plans (i.e. one HDMLC plan and a separate SRS cone plan to treat the same target volume) followed by selecting the more conformal plan between the two, one plan can be prepared based on the calculated RI, which can expedite the planning workflow of SRS treatments.

## METHOD

In this study, 50 retrospective brain treatment cases were planned and treated using Varian SRS cones. Treatment planning was done in iPlan RT, then imported in Varian Eclipse V13 for treatment using a Varian TrueBeam linac. Plan conformity was calculated using the ratio of V95% to the PTV (i.e. conformity index or CI), and the ratio of V50% to V100% (i.e. gradient index or GI). The closer CI and GI are to 1, the better the plan quality.

All cases were replanned using HDMLCs with the VMAT technique in Varian Eclipse V13. Plan conformity was compared between SRS cones and HDMLC by identifying changes in CI vs. RI, CI(cone)-CI(HDMLC), and GI vs. RI. The RI was calculated by normalizing the surface area of the PTV-equivalent sphere to the surface area of the PTV (e.g. RI = 1 for spherical PTVs, RI « 1 for highly irregular targets).

## RESULTS

Lower CIs were observed when HDMLCs are used instead of SRS cones at lower RI, indicating better plan quality. Higher GIs were calculated when HDMLCs are used. Greater differences in CIs were observed at lower RI. Our centre considers a CI difference of 0.2 a significant improvement in dose conformity to the PTV, which interpolates to a RI of 0.96.

## CONCLUSION

HDMLCs result in higher plan conformity to all targets at the expense of slower dose falloff. A threshold RI of 0.96 was identified, below which HDMLCs produce more conformal plans than SRS cones. The selection of a SRS technique using the target volume RI can potentially streamline the planning workflow of SRS treatments.

# 08 Evaluating Multidisciplinary Peer Review: A Retrospective Study of Plan Modifications in Radical and Palliative Intent Radiation Therapy Treatments

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## PURPOSE

Multidisciplinary peer review of radiation therapy treatment plans is recognized as an integral component to improving quality and safety. Our institution has established a goal of 100% peer review completion for all radiation therapy treatment plans, of both radical and palliative intent. This study investigates whether treatment intent influences the rate of plan modifications (PM) arising from peer review recommendations, and whether the timing of when peer review is conducted may modulate any effect.

## METHOD

Peer review primarily focused on target volume, dose, and fractionation. Pertinent clinical and treatment plan characteristics were extracted, including intent (radical/palliative), whether the treatment plan followed institutional protocol or not, and anatomical target site. The primary endpoint was PM rate, defined as any change implemented following recommendations from peer review. All treatment plans peer reviewed between November 2015 – November 2016 (cohort 1) and November 2016 – November 2017 (cohort 2) were analysed. Between the 1st and 2nd cohort, a new institutional policy was introduced requiring peer review to occur prior to commencement of treatment planning. To evaluate the effect, we developed a causal model involving intent as the exposure variable, PM as the outcome variable, and both target site and protocol treatment, as confounding variables. Logistic regression analysis was used to describe the relationship between the variables influencing the PM decision process.

## RESULTS

A total of 3807 radiation therapy treatment plans involving 2608 patients were included in the analysis. Among the initial cohort (1740 treatments, 1195 patients), plans with palliative intent were 35% less likely to have a PM (OR = 0.65, CI = 0.49 - 0.86) compared to those with radical intent. However, following the policy change, in the second cohort (2067 treatments, 1413 patients), the probability of PM for plans with either palliative or radical intent was equally likely (OR = 1, CI = 0.76 – 1.31).

## CONCLUSION

We found that treatment plans of palliative intent were initially 35% less likely to be modified than those of radical intent, however, this difference was nullified by the change in timing of when peer review occurred in the treatment planning process. This may be explained by possible biases against PM in palliative treatments where the perceived clinical impact may not be felt to outweigh the additional work required. Earlier integration of peer review within the treatment planning process may contribute to reducing potential intent bias in decision making regarding peer review recommendations.

# 09 Frameless Cobalt60-Based Hypofractionated Stereotactic Radiosurgery (HSRS) For Brain Metastases: Impact of Dose and Volume

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## PURPOSE

Frameless, gated, image-guided, Cobalt60-based hypofractionated stereotactic radiosurgery (Co60-HSRS) is a novel technical paradigm in the treatment of brain metastases that allows for both the dosimetric benefits of the Co60 based stereotactic radiosurgery (SRS) platform as well as the biologic benefits of fractionation. We report mature local control and adverse radiation effect (ARE) outcomes following 5 fraction Co60-HSRS for intact brain metastases.

## METHOD

All patients with intact brain metastases treated with 5-fraction Co60-HSRS between 2017-2020 were retrospectively reviewed. Patients were typically selected for HSRS as opposed to single fraction SRS if the metastases were larger (>2cm diameter), were in eloquent areas, or were in proximity to another lesion receiving HSRS. Survival estimates were determined per patient using Kaplan Meier methods, and LC as well as ARE rates were determined per lesion using competing risk methods. Univariable competing risk regression using Fine and Gray's methods were performed, and subsequent multivariable (MVA) regression using a backwards step-wise selection technique generated the final adjusted models.

## RESULTS

In total, 299 metastases in 146 patients were identified. The median radiologic and clinical follow-up was 10.6 (range 0.5-49.9) and 10.7 months (range 0.5-47.6), respectively. The median maximum tumor diameter and volume were 1.7 cm (range, 0.2-3.9) and 2.4 cubic centimeters (cc) (range, 0.004-24.92), respectively. The median total dose and prescription isodose was 27.5Gy (range, 20-27.5) in 5 daily fractions and 52% (range, 45-93), respectively. The median overall survival (OS) was 12.7 months (95% confidence interval [CI], 9.11-17.85), and the 1-year local failure rate was 15.2% (95% CI, 11.4-19.6). MVA identified a total dose of 27.5Gy vs. ≤25 Gy (hazard ratio [HR] 0.59, $p = 0.042$), and prior chemotherapy exposure (HR 1.99, $p = 0.015$), as significant predictors of LC. The 1-year ARE rate was 10.8% and the symptomatic ARE rate was 1.8%. MVA identified a gross tumor volume of ≥4.5cc (HR 7.29, $p < 0.001$) and a mean intra-tumoral dose of ≥39Gy (HR 3.17, $p = 0.034$) as significant predictors of symptomatic ARE.

## CONCLUSION

Moderate total doses in 5 daily fractions of Co60-HSRS were associated with high rates of LC and a low incidence of symptomatic ARE. A prescription dose of 27.5Gy was superior with respect to local control versus ≤25 Gy in 5 daily fractions. Target volumes of 4.5cc or larger as well as a mean dose >39Gy, were associated with higher rates of symptomatic necrosis. Further study will help refine the optimal dosimetric constraints for Co60-HSRS.

# 10 Impact of MGMT Promoter Methylation Status on Tumor Dynamics during Weekly Adaptive Radiotherapy for Glioblastoma

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## PURPOSE

Adaptive MRI-guided radiotherapy (RT) on a 1.5T MR-Linac using a reduced clinical target volume (CTV) of 5mm instead of the 15mm standard for glioblastoma (GBM) is currently being evaluated on the UNITED clinical trial (NCT04726397). We present a preliminary comparison of morphological changes during a course of adaptive RT with concurrent temozolomide between tumors with MGMT promotor methylation (MGMT-m) and those that are MGMT promoter unmethylated (MGMT-um).

## METHOD

The first 30 patients with GBM (all IDH wildtype) enrolled on the UNITED trial were analyzed. RT consisted of 60 Gy in 30 fractions (n=12) or 40 Gy in 15 fractions (n=18) (Fx). Expansions on the gross tumor volume (GTV) consisted of a 5 mm CTV with the provision to include FLAIR hyperintense areas at-risk and a 3 mm planning target volume (PTV). A pre-treatment reference plan was developed from a standard planning MRI (FxRef) followed by weekly on-line fully adaptive re-planning at Fx1, Fx6, Fx11, etc., based on a gadolinium contrast-enhanced MRI acquired on the MR-Linac. Remaining fractions were image-guided by pre-beam-on onboard non-contrast MRI, to ensure stability of the treatment volumes. The GTV and CTV were quantified by their absolute volumes, volumes relative to the FxRef and the maximum linear distance from the edges of the reference contour at FxRef to the weekly adapted contours (migration distance, dmig). MGMT promoter methylation status was explored as a fixed effect in a linear mixed statistical model.

## RESULTS

The median changes in GTV relative to FxRef at Fx1, Fx6, Fx11, Fx16, Fx21, and Fx25 in MGMT-um tumors (n=12) were 10.3%, 9.2%, 10.6%, 14.5%, 18.0% and 17.3%, respectively, while for MGMT-m (n=18) were 3.4%, 0.0%, -8.6%, -11.3%, -11.3% and -5.6% (p=0.021). A similar significant trend was observed with the CTV. With a median time interval of 6 days (range, 1-18 days) between FxRef and Fx1, the GTV increased by over 10% in 58% of MGMT-um tumors compared to only 33% of MGMT-m tumors. MGMT-um tumors had significantly larger maximum dmig compared to tumors with MGMT-m, with a median dmig of 9.6 mm vs. 5.8 mm, respectively (p=0.018). The maximum GTV migration distance was greater than 5, 10 and 15 mm in 83%, 50% and 17% of MGMT-um tumors but only 56%, 11% and 0% for MGMT-m tumors, respectively.

## CONCLUSION

MGMT-um GBM exhibited significant changes in morphology and migration distance between the time of treatment planning to the first treatment fraction, as well as throughout a course of RT. In this population, our results support a greater frequency of imaging and plan adaptation when applying personalized reduced CTV margins.

# 11 Estimating Prevalence of Oligometastases at Initial Staging of Neuroendocrine Tumors- Findings from a 68Ga DOTATATE PET (Ga68PET) Population-Based Registry

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## PURPOSE

Well differentiated neuroendocrine tumors (NET) have a long natural history. Determining the prevalence of oligometastases (OM) in NET would guide novel treatment and clinical trial designs. The Ontario PET-NET registry (OntPNR) is a population-based registry (since April 2019) of patients (pt) approved for Ga68PET fulfilling the provincial access criteria. The objective was to describe the prevalence of OM disease at initial staging of well-differentiated NET.

## METHOD

A retrospective analysis of the OntPNR was conducted. DICOM images, reports and registry data were used. Staging cohort (SC) included pts with localized primary NETS and/or limited metastases (mets) where definitive surgery is planned. OM is defined as 1-5 metastatic lesions following Ga68PET.

## RESULTS

Between May 2019 and Nov 2021, 1,084 pts underwent Ga68PET. Of the 326 pts in the SC, M:F 1:1; grade 1 (159; 49%) & Ki67 low at <6% (189; 58%) M1 (151; 46%). The most common primary sites were midgut (121; 37%) pancreatic (73; 22.4%) and unknown primaries (57; 17.5%). The primary tumors were previously removed prior to Ga68PET staging scan in 49 (15%) patients. Metastases were present in 151/326 pts (46.3%).

OM were identified in 30/326 (9.2%) pts [20 (13.2%) in the liver only and 10 (6.6%) extra-hepatic]. Median number of mets was 2 (Range 1-5). The most common mets site was liver (20; 67%), followed by bone (7; 23%) and peritoneal deposits (4: 13%). Pts in the OM cohort are more likely to be males (21/30; 70% OM vs 159/326; 49% SC); and had unknown primaries (8/30; 27% OM; 57/326; 17.5% SC).

## CONCLUSION

OM occurred in 9.2% of NET pts with apparent localized primary NETs and or limited metastases where definitive surgery is planned, and staged with Ga68 DOTATATE PET CT. This estimate does not include pts who are OM that are induced (post treatment) or during follow up. Expansion of the definition of OM (e.g. up to 10 metastatic lesions) could further enhance our understanding of the pattern of NET spread. These population based results can serve as the basis for epidemiological investigations and clinical trials planning.

# 12 Perspectives of patients with metastatic lung cancer on symptom screening and patient-reported symptom trajectory data

*Amir H. Safavi, Emily Bryson, Victoria Delibasic, Frances C. Wright, Ambika Parmar, Natalie Coburn, Alexander V. Louie*

**PURPOSE**

Symptom screening and collection of patient-reported outcome (PRO) data are increasingly prevalent in the care of patients with metastatic non-small cell lung cancer (mNSCLC). We explored the perspectives of patients with mNSCLC on symptom screening and utilization of symptom trajectory PRO data for patient education.

**METHOD**

Ten patients with mNSCLC were selected by convenience sampling at a Canadian tertiary cancer centre to participate in a qualitative study. Baseline participant and treatment characteristics were obtained via chart review. Semi-structured interview guides were designed by a multidisciplinary team of lung cancer and PRO investigators. One-on-one interviews were conducted with each participant by two investigators from August 6, 2021, to October 27, 2021. Interviews were audio-recorded and transcribed verbatim. Anonymized transcripts underwent inductive coding by two investigators and thematic content analysis was performed from August 6, 2021, to February 6, 2022.

**RESULTS**

Participants were 50% female and had a median age of 68 years (56-77). Sixty percent of participants had smoking histories. Median time since diagnosis was 28.5 months (6-72). The most common treatments were palliative radiotherapy (80%) and EGFR inhibitors (60%). Participants identified a knowledge gap regarding expected symptom trajectory through treatment and recovery. Participants sought symptom trajectory information from a variety of sources, including informational websites and informational documents from pharmaceutical companies as the most common sources. Seven themes were identified in total. Three themes were identified regarding symptom screening: 1) symptom screening is useful for symptom self-monitoring and disclosure to the healthcare team, 2) symptom screening tools are variably utilized by participants and their healthcare providers, and 3) screening of additional quality-of-life domains (smoking-related stigma, sexual dysfunction, and financial toxicity) is commonly desired. Four themes were identified regarding symptom trajectory PRO data for patient education: 1) symptom trajectory data provide reassurance and motivation to improve symptoms, 2) symptom trajectory data should be disclosed after an oncologic treatment plan is developed, 3) symptom trajectory data should be communicated via in-person discussion with accompanying patient-education resources, and 4) communication of symptom trajectory data should include reassurance about symptom stabilization, acknowledgement of the variability in patient experience, and strategies to improve symptoms.

**CONCLUSION**

Symptom screening tools require more standardized utilization and should include common quality-of-life concerns of patients with mNSCLC. Symptom trajectory PRO data derived from routine screening should inform novel knowledge translation tools to satisfy an unmet need for patient education.

# 13 Outcomes of Extracranial Oligorecurrence After Prior Metastases Directed Stereotactic Body Radiotherapy for Oligometastatic Disease

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## PURPOSE

The Consortium of Oligometastatic Research (CORE) database consists of 1033 patients who presented with either synchronous or metachronous oligometastatic disease and were treated with ablative therapy to all sites. Of this cohort, a subset of patients had subsequent extracranial oligometastatic recurrence. These patients represent a unique cohort and we aim to report their outcomes in an effort to appropriately select patients who would benefit from further ablative therapy.

## METHOD

A retrospective review of patients in the CORE database was conducted. Oligorecurrent disease was defined as ≤5 new metastases after having previously received ablative treatment to all known sites of oligometastatic disease. Our primary endpoint was time to widespread progression (WSP), estimated using competing risk analysis where death was the competing risk. Widespread progression was defined as developing metastatic dissemination not amenable to further ablative treatment, inclusive of developing ≥6 new sites of extracranial metastases or a malignant effusion. WSP was measured from the date of initial diagnosis and from the date of first oligorecurrence. Secondary endpoint was estimated overall survival (OS) using Kaplan-Meier method.

## RESULTS

A total of 375 patients had oligorecurrent disease and 233 received further ablative therapy to all metastatic sites. Of the 233 patients, 83 had a subsequent oligorecurrent event and 57 received further ablative therapy to all metastases. Of the 375 patients, 161 developed widespread progression by last follow up. The median time to widespread progression from initial diagnosis was 80.7 months (95% CI: 68.2-90.9) and from first oligorecurrence was 55.1 months (95% CI: 33.3-not reached). The 2 year and 5 year WSP rates from initial diagnosis were 11.0% (95% CI: 7.6-14.3) and 40.6% (95% CI: 34.3-46.9) and from first oligorecurrence were 38.8% (95% CI: 33.6-43.9) and 52.5% (95% CI: 45.3-59.8). The median OS was 44.8 months (95% CI 37.0-51.0). The 1 year, 2 year and 5 year OS rates were 85.0% (95% CI: 81.9-89.1), 69.8% (95% CI: 64.9-74.6) and 33.3% (95% CI: 25.5-41.1) respectively.

## CONCLUSION

Individuals who recur in a limited number of sites appear to represent a favorable subgroup of metastatic patients. In this retrospective cohort, oligorecurrent patients demonstrate favourable natural histories with regards to time to widespread progression and overall survival, and may benefit from further metastases directed ablative therapy.

# 14 A total inverse planning paradigm: prospective trial evaluating the performance of a novel 3D-printed head immobilization device generated from MR imaging.

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**PURPOSE**

Immobilization is crucial for reproducible positioning during CNS radiotherapy (RT). Current RT planning processes require redundant dedicated imaging studies resulting in added healthcare costs. Innovative approaches may increase the value of care. The aim of this study was to prospectively deploy and assess the performance of a total inverse planning paradigm in which a patient-specific 3D-printed immobilization device is generated from MR imaging, allowing for the creation of a reproducible and tolerable positioning device for patients undergoing CNS RT.

**METHOD**

Patients undergoing LINAC-based CNS RT (primary brain tumor or resected brain metastases) were prospectively enrolled (IRB #18-5753; NCT04114786). MR and CT simulations were conducted as per standard practice, the latter including a moulding session to generate a conventional thermoplastic mask (T-mask). In the investigational arm, an in-house designed 3D-printed mask (3Dp-mask) was generated from MR images to recreate natural head positioning during MR acquisition and allow coupling with the LINAC table during RT delivery. Differences in inter-fraction motion were compared between patients treated with the conventional (T-mask) versus the investigational (3Dp-mask) paradigm. Adverse events and tolerability were assessed using a patient-reported questionnaire after conventional moulding session, and by the end of the first and last weeks of treatment for both arms.

**RESULTS**

The trial will enroll a total of 40 patients (20 on each arm). At time of this preliminary analysis, 12 (T-mask) and 10 patients (3Dp-mask) have completed CNS RT and all study evaluations. Median time from simulation to ready-to-treatment was 5 (range 1 -7) and 7 days (range 6-11) for the conventional and investigational arms, respectively. The average time to complete the 3Dp-mask design and printing was 38.5 hours (range 34-42). Inter-fraction set-up motion average was overall comparable (R/L, p=.412; A/P, p=.024 greater motion with the T-mask, and S/I, p=.009, greater motion with the 3Dp-mask). The majority (80%) of patients reported no or mild discomfort with the 3Dp-mask, compared to 67% of those treated with T-mask (p=0.5). No patients in the investigational arm, but four (33%) in the conventional group reported the standard T-mask being “discomforting” or “distressing” at some point during study evaluations (p=0.05).

**CONCLUSION**

The proposed total inverse planning paradigm using a 3D-printed immobilization device is feasible, rendering comparable inter-fraction performance while offering a better patient experience compared to the conventional thermoplastic mask. This approach could allow serial workflow processes and potentially significant cost savings. The completed study will be presented at the ASTRO meeting.

# 15 Early Clinical Effectiveness, Toxicity, and Quality of Life Outcomes of Magnetic Resonance Imaging-Guided Stereotactic Ablative Radiotherapy: A Systematic Review

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**PURPOSE**

Magnetic resonance imaging-guided stereotactic ablative radiotherapy (MRgSABR) is postulated to further improve the therapeutic ratio of stereotactic radiotherapy by increasing the certainty of dose delivery. As early phase data on MRgSABR have rapidly accumulated, we systematically reviewed the existing literature to summarize the clinical outcomes, toxicity and patient-reported outcomes following MRgSABR.

**METHOD**

This review was conducted in accordance with consensus guidelines. PubMed, Embase, and Cochrane Library databases were queried from January 2014 to August 2021. Studies in the English language that evaluated local control (LC), overall survival (OS), clinician-reported toxicity and patient-reported quality of life (QOL) outcomes of MRgSABR were included. Reviews or guidelines that did not contribute new results, studies with ≤3 total patients, and studies where MRgSABR results could not be disaggregated from radiotherapy using non-MR platforms were excluded. Results were summarized using medians and ranges.

**RESULTS**

We identified 849 sources, with 34 (1148 patients) meeting all inclusion criteria. Most studies (19/34) were retrospective in nature, with the remaining being prospective single-arm studies. Median follow-up duration ranged from 4 to 25 months. Liver, prostate, and pancreas were the most common sites for MRgSABR studies. Eleven studies reported results on liver MRgSABR (199 patients). LC at 1 year was 86-95% (median: 88%) and LC at 2 years was 73-100% (median: 80%) for liver MRgSABR. OS at 1 year was high at 69-93% (median: 80%), though OS at 2 years was lower at 46-60% (median: 51%). Grade 3 toxicity ranged from 0 to 8% and no grade 4+ toxicity was reported for liver MRgSABR. Six studies reported results for prostate MRgSABR (282 patients). Biochemical control ranged from 75% to 100% at a median follow-up of 6 to 12 months. Grade 3+ toxicity ranged from 0 to 2% and patients reported temporary increases in urinary symptoms during prostate MRgSABR that resolved over time. Six studies reported results for pancreatic MRgSABR (304 patients). OS at 1 year was 59-82% (median: 69%) and OS at 2 years was 38-52% (median: 45%). LC was 57-95% at 1 year (median: 86%) and 59-83% at 2 years (median: 77%). The risk of acute grade 3+ toxicity was 0-4% (median: 1.5%) and the risk of late grade 3+ toxicity was 3-13% (median: 5%) following pancreatic MRgSABR. Remaining studies that reported on a variety of treatment and primary sites showed good LC of 72-96% at 1 year (median: 92%). Grade >3 toxicity was <5% except for lung (8-20%) and head and neck MRgSABR (43%).

**CONCLUSION**

Early data on MRgSABR indicate good LC and tolerability across multiple clinical scenarios, though noticeable toxicity was observed in certain treatment sites. Prospective comparative clinical trials are needed to quantify the improvement in clinical outcomes with MRgSABR relative to non-MR-guided radiotherapy technologies.

# 16 Daily Assessment of On-Treatment Tumour Regression by Cone Beam CT Suggests Prognostic Dynamic Biomarkers in Nasopharyngeal Cancer

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## PURPOSE

Despite advancements in radiotherapy, approximately 30% of nasopharyngeal cancer (NPC) patients develop treatment failure. Dynamic on-treatment biomarkers may provide early evidence of response offering opportunities to adapt treatment. Using daily cone beam computed tomography (CBCT) scans, we measure air volume recovery, an automated surrogate of tumour regression, and report its association with outcomes. We hypothesized that increased air volume recovery is associated with improved recurrence-free survival.

## METHOD

Patients with NPC treated with curative intent were included. Primary gross target volume (GTVp) was propagated from planning CTs to daily CBCTs by rigid registration and a density threshold was applied to measure the air volume in a 5 mm uniform expansion of the GTVp. Air volume was expressed as percent of planning GTVp volume. Missing values were interpolated, air volume trajectories were smoothed by sliding window averaging, and area under the curve (AUC) was calculated to provide a summary metric capturing both magnitude and rate of air volume recovery. Primary endpoint was recurrence free survival (RFS).

## RESULTS

Between 2013 and 2015, 39 consecutive patients with localized or locally advanced NPC underwent radical radiotherapy (n=5) or chemoradiotherapy (CRT) (n=34) to a planned dose of 70 Gy in 35 fractions (Fx). Median AUC of the air volume recovery curve was 2.8 (Range: 0.05-7.4). Patients with above-median AUC had longer RFS (HR=0.28, p=0.045, median follow-up: 83 mo). Exploration of clinical factors associated with air recovery showed that AUC was higher in CRT than RT alone (OR: 1.74±1.60, p=0.04), lower in large tumours with high GTVp volume (OR: -0.037±0.18, p<0.001), and was not correlated with disease stage. Current smokers had 26% lower median AUC than never/former smokers (p=0.132). AUC was lower in patients with detectable end-of-treatment Epstein-Barr virus (EBV) circulating tumour DNA (median AUC 0.99 vs. 2.8, p=0.021). Exploratory post-hoc analysis of air volume velocity (slope of air volume curve) identified two independent putative positive prognostic biomarkers: high mid-treatment slope and negative end-treatment slope. Patients without failure had higher mid-treatment air recovery velocity (Fx 15-22), with Fx 18 velocity yielding the maximal RFS difference (HR: 0.12, p = 0.007). Negative velocity at the end of treatment was associated with improved regional (p=0.033) and distant metastatic (p=0.013) control.

## CONCLUSION

Higher rate and magnitude of tumour regression, inferred by the CBCT surrogate measure of air volume recovery, was associated with improved RFS. In post-hoc analysis, this discovery cohort allowed us to identify promising dynamic biomarkers which might guide treatment adaptation. Validation of these biomarkers is ongoing in a large cohort of NPC patients with mature follow up.

# 17 Early Institutional Experience of Ultra-Hypofractionated Breast Radiotherapy in a Large Academic Cancer Centre

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**PURPOSE**

Ultra-hypofractionated radiotherapy (U-HFRT) is non-inferior to moderate hypofractionation (M-HFRT) for local control following breast-conserving surgery for early-stage breast cancer and is safe in terms of normal tissue toxicity. Our objective was to evaluate early institutional experience of U-HFRT in a real-world setting at a large academic cancer centre.

**METHOD**

Stage 0-II breast cancer patients who received adjuvant whole breast irradiation (WBI) or partial breast irradiation (PBI) between May 2020 and March 2021 were compiled. Patients were divded into 2 cohorts: U-HFRT (26Gy in 5 daily fractions) and M-HFRT (40.05Gy in 15 fractions). Clinical and treatment characteristics were extracted from medical records and displayed using descriptive statistics. Physician-assessed skin toxicity was collected for patients treated with U-HFRT during RT and at follow-up visits using the RTOG radiation morbidity scale. Associations between toxicity and clinical/treatment characteristics were determined using mixed-effects logistic regression, accounting for time. Comparisons between the U-HFRT and M-HFRT cohorts were performed using the Wilcoxon rank sum test (continuous) and Chi-square/Fisher's exact test (categorical).

**RESULTS**

Median age at diagnosis for the entire cohort was 60.5 years: U-HFRT 66.2 years and M-HFRT 55.1 years ($p<0.001$). For the U-HFRT cohort, 70% had hormone-receptor positive invasive breast cancer (70% pT1c, 95% pN0) and 20% had DCIS. WBI/PBI was delivered to 385 patients, of which 188 (49%) received U-HFRT. For these patients, the majority (72%) received WBI, 28% PBI and a boost was used in 26%, compared to 96%, 4% and 47%, respectively, for those treated with M-HFRT ($p<0.001$). Grade 1 RTOG skin toxicity significantly improved over time for patients who received U-HFRT: 37% during RT, 57% within 90 days post-RT and 6% >1-year post-RT ($p<0.001$). Grade 2 toxicity was minimal (5% within 90 days post-RT) and there were no grade 3 toxicities. Age, RT volume (WBI vs. PBI) and chemotherapy were not associated with toxicity for U-HFRT; however, increased toxicity was observed for patients who received a boost ($p<0.001$). Factors associated with increased usage of U-HFRT were older age, use of PBI, no boost and no breast reconstruction ($p<0.001$).

**CONCLUSION**

U-HFRT was rapidly adopted at our institution for early-stage breast cancer and is associated with low rates of reported skin toxicity. The use of U-HFRT was greatest in patients with low-risk breast cancer, consistent with a conservative approach to implementation in a real-world setting.

# 18 The Modern Management of Large Brain Metastases: A Review

*Bryce Thomsen, Hany Soliman*

**PURPOSE**

Our objective was to identify contemporary management options for large brain metastases reported in literature, specifically evaluating local control and risk of toxicity.

**METHOD**

A literature search examining modern management of large brain metastases was performed using ovid-MEDLINE.

**RESULTS**

A total of 18 articles met criteria for review, evaluating single fraction radiosurgery (SRS) and multi-fraction stereotactic radiation therapy in both the definitive and post-operative cavity setting, as well as targeted therapies.

**CONCLUSION**

Multi-fractionated radiosurgery represents a modern and attractive treatment approach in the definitive management of patients with large brain metastases, with equivalent local control and reduced rates of radionecrosis less than 13% in comparison to single fraction SRS. In cases where surgery is indicated, fractionated cavity radiation should be considered for large tumor bed volumes.

More research is needed for the optimal dose and fractionation regimen for optimal tumor control with reduced risk of radiation toxicity, but common regimens include 3-5 fractions while meeting appropriate biologically effective dose (BED) goals. Future areas of interest include targeted therapies in the initial management of brain metastases as well as pre-operative radiation therapy to reduce risk of leptomeningeal disease.

# 19 Tumour Specific Growth Rate as a Predictor of outcomes in Oligo-Progressive Disease Treated with Stereotactic Body Radiotherapy

*Inmaculada Navarro, Joelle Helou, Subin Kuruvilla Thomas, Andrew J. Hope, and Aisling S. Barry*

**PURPOSE**

The aim of this study is to assess the variation and the impact of pre- and post- tumour specific growth rate (SGR) on outcomes of metastatic patients with oligo-progressive (OP) disease treated with SBRT.

**METHOD**

Patients with known metastatic disease and ≤3 radiologically OP were enrolled in a prospective phase II study. For the purpose of this analysis, treated metastases were retrospectively contoured on pre-SBRT diagnostic images (GTV), at time of SBRT (GTV2) and post-SBRT (GTV3). SGR was calculated using the time interval (t=days) and volume changes (GTVx/GTVy) for each metastasis (ln(GTV2/GTV1)/t). Pre-SBRT growth (SGR1) was defined as GTV2–GTV1, and post-SBRT (SGR2) as GTV3 – GTV2. High SGR was defined as greater than the median SGR value for each population. Progression was defined as local failure (LF) or distant progression. The impact of SGR1 and SGR2 (as continuous variables) on LF and progression was evaluated using a subdistribution hazards model to account for the competing risk of death. Cox Proportional Hazard was used to assess the association of SGR1 and SGR2 with overall survival (OS). For patients with multiple lesions, the highest SGR was used for progression and OS analyses.

**RESULTS**

Thirty-four patients with 53 metastases from breast (10, 29.4%), gastro-intestinal (GI) (14, 41.2%) and genito-urinary (GU) (10, 29.4%) cancers were analyzed. Median follow-up was 11.2 (interquartile range (IQR): 8.0-15.9 months). The median volume of GTV1, GTV2 and GTV3 was 3.8 (IQR 0.9 - 6.6)cc, 7.1 (IQR 1.9-15.3)cc and 2.7 (IQR 0.8-7.9)cc. Median SGR1 and SGR2 was 0.007 (IQR 0.003 - 0.013) and -0.009 (IQR -0.01 to -0.001), with median SGR1/SGR2 per histology 0.004 (IQR 0.002 – 0.007)/-0.009 (IQR -0.018 to -0.005) breast, 0.011 (IQR 0.006 – 0.01)/-0.009 (IQR-0.013 to -0.002) GI and 0.007 (IQR 0.001 – 0.015)/-0.01 (IQR-0.013 to -0.001) GU. There was no statistically significant difference seen between histologies and SGR1 (p 0.08) and SGR2 (p 0.77). 52% (27/52) of metastases had a high SGR1 and 43% (22/51) a high SGR2. At 12 months the CIF of LF and progression was 9% (93.3-18.7%) and 10% (95CI 2.4-23.9%) respectively, while the probability of OS was 64%. There was a significant association between SGR1 and the probability of progression (p 0.0013) while no significant association was found with the CIF of LF (p 0.132) or OS (p=0.490). Patients with low vs. high SGR1 had a higher probability of being alive but the difference did not reach statistical significance [SGR1 75% vs. 64% (p 0.29)]. SGR2 did not have a significant impact LF (p=0.245) or OS (p 0.645). There was a trend towards significance with progression (p 0.053).

**CONCLUSION**

Lower SGR measurements seems to have better response after SBRT and may be used in the future for patient selection. These findings require validation in a larger cohort.

# 20 Salvage Interstitial Brachytherapy for Treatment of Recurrent Endometrial Cancers in The Vagina: 7-Year Single Institution Experience

*Marissa Sherwood, Hanbo Chen, Amandeep Taggar, Moti Paudel, Elizbeth Barnes, Liying Zhang, Eric Leung*

## PURPOSE

Interstitial brachytherapy (ISBT) is an effective, accepted treatment for vaginal recurrence of endometrial cancer (EC). This study reviews a large tertiary institution's experience and presents outcomes for recurrent EC in the vagina treated with ISBT.

## METHOD

Patients who underwent salvage ISBT for vaginal recurrence of EC from January 1, 2014 - August 31, 2021, were included. Patients with second primaries or distant metastases at diagnoses were excluded. Initial disease factors, treatment details, recurrence and salvage treatment details were recorded. Actuarial outcomes calculated include overall survival (OS), local (LF), nodal (NF), and distant failure (DF).

## RESULTS

Forty-two patients were included; median age was 67; most initial cancers were adenocarcinoma (81%; 34/42), grade 1 (43%; 16/37), and stage IA (62%; 24/39). Initial treatment included adjuvant external beam radiation (EBRT) (17%), vaginal vault BT (19%), EBRT plus vaginal vault BT (7%) and chemotherapy (12%). Median time from surgery to recurrence was 14 months. At recurrence, 19% (8/42) had lymph node involvement and 7% (3/42) distant metastases. For salvage, 26% (11/42) of patients received ISBT alone, 74% (31/42) EBRT plus ISBT and 29% (12/42) sequential chemotherapy. Thirty-nine cases used interstitial technique while 3 had interstitial technique then multi-channel cylinder for remaining fractions. The most common prescription for salvage ISBT alone was 42 Gy in 6 fractions while in combination with EBRT was 21 Gy in 3 fractions. Mean ISBT HRCTV D90 was 37.56 Gy, mean dose to Rectum D2cc 27.42 Gy and Bladder D2cc 19.85 Gy. Mean ISBT and EBRT HRCTV D90 was 77.65 Gy, mean dose to Rectum D2cc 67. 46 Gy and Bladder D2cc 61.98 Gy. Median follow-up after salvage BT was 20 months (range: 0-84). For patients undergoing salvage EBRT and ISBT, 2-year OS, LF, DF was 85.6%, 24% and 37.6%, respectively. With salvage ISBT alone, 2-year OS, LF, DF was 83.3%, 16.7% and 54.3%, respectively. Four patients received repeat BT for second vaginal recurrence. One patient experienced grade 3/4 late toxicity of radiation proctitis and small bowel obstruction.

## CONCLUSION

ISBT is an effective treatment for recurrent EC of the vagina, with acceptable toxicities. Salvage BT alone is an option for patients with previous or contraindication to pelvic radiation.

# 21 Clinical Outcomes of Metastatic Breast Cancer Patients Post Hypo-fractionated Ablative Liver Radiotherapy

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## PURPOSE

The liver is a common site of metastases in breast cancer. Growing data supports the safe and efficacious use of local ablative therapies such as stereotactic body radiotherapy (SBRT) in the setting of liver metastases (LM), but there are limited data describing the metastatic breast cancer (MBCa) population.

## METHOD

A retrospective research ethics board approved study identified MBCa patients who received liver SBRT between 2004 – 2020. Patients were classified according to treatment intent – oligo-metastatic (OM - limited metastatic disease only with primary definitively treated) or oligo-progressive (OP – multi-metastatic with limited progressing disease), and further subdivided according to European Society for Radiotherapy and Oncology and European Organization for Research and Treatment of Cancer OM classifications (induced, repeat, de novo). Outcomes collected included patient demographics, biomarker status (oestrogen receptor (ER)/HER2 positive (+) or negative (-)), local control (LC), overall survival (OS), distant disease-free survival (DDFS), pre-SBRT systemic therapy lines and time to next line systemic therapy. Descriptive statistics and univariate (UVA) and multi-variable analysis (MVA) were performed.

## RESULTS

Thirty MBCa patients with 50Fifty LM treated with SBRT in 30 MBCa patients received SBRT to 50 liver metastases were identified for analysis. Median follow-up was 14.6 months, mean age was 59 (SD 13) years; 53% were ER+/HER2- and 33% HER2+ve. Median lines of pre-SBRT systemic therapy were 2 (0-6) and median time to SBRT from initial diagnosis was 3.1 (0.7 – 15.5) years. The majority ofMost patients were OP (73%) versus OM (27%). Median size of treated LM was 3.1 (1 – 8.8) cm, median SBRT dose delivered 40 (30-60) Gy (biological equivalent dose = 120Gy3) in 5 – 10 fractions, with 100%, 100% and 94% LC at 1-, 3- and 5-years (1 local failure identified at 40 months post SBRT). Median time to next line systemic therapy was 9.9 (1 – 114) months (OM 13.2 vs OP 7.6).

Median OS was 57.7-months; 89% and 63% of patients were alive at 12- and 24-months respectively. On Univariate analysis (UVA), size of the treated LM was significantly associated with survival (HR 1.35, p=0.023), which was not significant on multi-variable analysis (MVA) (p=0.066). There was a trend to significance based on OM/OP classification (HR 4.59, p=0.052) on UVA. 43% of patients developed DDFS; median time to progression post SBRT was 4.8 (0.8 – 114.7) months, OP (vs OM) was significantly associated with DDFS on UVA (HR 3.72, p=0.04) and 'induced' OM disease (versus repeat or de novo) (HR 4.77, p=0.01). Both variables were not significant on MVA.

## CONCLUSION

Liver SBRT in MBCa provides excellent LC, with size of treated LM associated with OS. Further studies assessing the impact of metastatic disease classification, especially the difference in behavior of OM and OP disease on outcomes of patients should be explored.

# 22 Development and validation of an automated dose-of-the-day method for MRI-guided SBRT of UGI patients

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## PURPOSE

To develop and validate an automated procedure for the dosimetric assessment of treatment plan deliveries for upper gastrointestinal cancer sites (liver, pancreas) on an online adaptive MR-Linac system.

## METHOD

The dose-of-the-day (DOTD) procedure was developed using the treatment planning scripting environment in RayStation with data generated in Online Monaco for Unity MR-Linac workflow. The method was applied to 16 patients, receiving 1 or 5 treatment fractions. The key data, including pre-treatment MR images, contours, and dose cloud from the adapt-to-shape online (ATS) plan as well as MR images acquired during treatment delivery (BON), were brought into RayStation for post-processing. An automated scripting pipeline was developed to perform: a) intensity-based deformable image registration (DIR) for ATS-to-BON image sets, b) deformable contour mapping ATS-to-BON, c) transfer rigidly BON contours on ATS, d) derive dosimetric analytics, and e) generate pdf report. The DIR process was validated by expert reviewers. Retrospective test plan re-computations were also performed in Monaco to show that the dose cloud did not change significantly between the ATS and BON data sets and to support the dosimetric analysis performed only with the ATS plan dose.

## RESULTS

The contours free of errors on the ATS examination were accurately mapped to BON and deemed adequate without any manual adjustments. The dose cloud discrepancies between ATS and BON were within ±30 cGy for max point values and ±3 cGy for mean dose. The difference between the clinical goal values for target and OARs (i.e., ΔClinical goal=ATS value - BON value). In most cases, the difference in clinical goal values was within ±50 cGy. The outliers were observed to be present during treatments of both sites (liver and pancreas), regardless of the fractionation regiments. At the same time, they are mostly during the first treatment session, which could be related to the patient getting used to the treatment. Longer overall session time for the single fraction treatments lead to larger absolute changes in the OAR clinical goals.

## CONCLUSION

The intensity-based DIR performed well for ATS-to-BON data and allowed for prompt and reliable contour propagation between intra-faction MR images. Also, the DOTD process was found to be an important clinical tool as it provided the full quantitative assessment of the treatment quality while the patient was still on the bed. Fast execution of the DOTD procedure allows for its use on verification MR scan to pass/fail the online ATS plans prior to the delivery of the treatment. The reported dosimetry intra-fraction differences suggested the need for dose accumulation processes and further plan adaptation based on per session clinical goals.

# 23 Graphical User Interface (GUI) Development for Deep learning assisted algorithm for catheter reconstruction during MR-only Gynecological interstitial brachytherapy

*Kaiming Guo, Amani Shaaer, Moti Paudel*

## PURPOSE

During interstitial high dose rate (HDR) gynecological brachytherapy, magnetic resonance imaging (MRI) offers excellent soft-tissue contrast when contouring targets and organs at risk without any extra radiation. Several catheters are inserted through a standardized template, which is surgically sutured to the patient's perineum. Current approach, manual reconstruction of the implanted plastic catheters, is time-consuming. In order to speed up this process, we have developed a novel deep learning-assisted semi-automatic algorithm to reconstruct interstitial catheters during MR-only interstitial gynecological brachytherapy. The primary aim of this study is to develop a Graphical User Interface (GUI) for digitizing catheters and communicate with Oncentra® Brachy treatment planning system (TPS).

## METHOD

A key component for this semi-automatic catheter detection algorithm is to localize all catheters at the reference slice which is the slice just before the catheters enter into the template and is configured with the help of MR visible reference template attached to the standard template. This process can be completed in this developed GUI using Python 3.6 library. Those localization information will be written into the input files. This input file also requires manual input of measured free length of each catheter, the physical length of catheters sticking out of the standard template which will be used to determine the physical length of catheter inside the patient and to ensure that all catheter lengths are correctly identified. Information in input files are passed to 2D U-Net model to identify all possible catheter markers in a given image slice. Once localized, the true location of a catheter was tracked by finding the extrema, as catheters appear as bright and dark regions in T1- and T2-weighted MR images, respectively. The progress of the program is traced, and the log file can be selected to save. Once digitization complete the marker location will be save to xls file for visualization and analysis, there also an option to directly write the catheter location into Oncentra TPS DICOM plan file. The 3D viewer of reconstructed catheter slices is available in GUI to QA catheter locations slice by slice.

## RESULTS

The GUI is able to digitize the catheters in an average time of 0.55s/catheter/slice for 3 tested patients which is more than 50% time saving compared to conventional manual catheter reconstruction. For example, 160 slices with 15 catheters can be reconstructed in about 22min as opposed to (46 ± 10) min by an expert planner.

## CONCLUSION

The adoption of this GUI in the brachytherapy workflow has potential to improve treatment efficiency by reducing planning time, clinic resources, and manual selection errors. In future, we need to examine GUI with more patients, and test GUI in association with TPS for further evaluation.

# 24 Optimization of Catheter Placement for Transperineal Interstitial Gynaecological Brachytherapy

*Jill Bennett, Cédric Bélanger, Philippe Chatigny, Luc Beaulieu, Alexandra Rink*

## PURPOSE

Cervical cancer is the fourth most common female cancer diagnosis worldwide, and is most often diagnosed in women under the age of 50. The recommended treatment plan for locally advanced cervical cancer includes external beam radiation therapy, chemotherapy, and brachytherapy (BT). Interstitial BT involves the placement of a radioactive source in or close to the tumor using catheters, and is used in cases such as large lesions or lower vaginal involvement. One method of interstitial gynaecological (GYN) BT uses a transperineal catheter template with an intrauterine (IU) tandem. Currently, treatment plans (including dwell times and positions for the radioactive source) are determined based on MRI taken after catheter implantation. This may lead to unused catheters or suboptimal tumor coverage. Each additional catheter also increases the implantation time and tissue injury. Furthermore, changes to patient anatomy due to IU tandem insertion likely render pre-BT diagnostic MRI insufficient for determining optimal catheter placement. For these reasons, we hypothesize that catheter placement optimization based on MRI obtained after placement of the IU tandem and template will improve treatment plan quality and decrease adverse effects.

## METHOD

In retrospective studies, catheter optimization algorithms have produced equivalent or superior treatment plan quality with fewer catheters compared to clinical arrangements. In particular, we will be applying the Centroidal Voronoi Tessellation (CVT) algorithm. CVT is a geometric segmentation algorithm which generates a uniform catheter distribution in the planning region for a set number of catheters. Additionally, CVT produced promising results for prostate cases with simultaneous boost, suggesting that it may be effective for handling multi-dose objectives in cervix cases. This work includes 40 cervical cancer cases previously treated at UHN, where CVT optimization will be used on post-implant BT MRI. The tumor volume as defined on post-implant MRI, minus the organs at risk (OARs), constitute the optimization region for CVT. A GPU-based multicriteria optimizer (gMCO) will then be used to generate treatment plans based on the CVT-determined catheter positions. To accomplish this, existing CVT and gMCO code will be expanded to accommodate GYN templates and OARs. Treatment plan quality will be evaluated using dose volume indices, the homogeneity index (HI), and conformity index (COIN).

## RESULTS

This work is in its preliminary stages. We expect to demonstrate that post-implant MRI used with CVT to find optimal catheter arrangements within the constraints of GYN templates can lead to equivalent or superior treatment plans compared to those generated from clinical catheter placements, while using fewer catheters.

## CONCLUSION

This work aims to lay the foundation for a future prospective study where CVT and gMCO is applied intraoperatively to interstitial BT for cervical cancer. With appropriate adjustments to the MR-guided GYN BT procedure, we hope to improve treatment response and reduce unnecessary tissue injury.

# 25 Partial breast re-irradiation using ultra hypofractionation
# A Phase 2 multi-institutional, international study

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## PURPOSE

Women with local breast cancer (BC) recurrence in the previously irradiated breast have historically been offered mastectomy for local treatment. However, breast-conserving surgery (BCS) followed by re-irradiation with partial breast irradiation (rPBI) has recently been found to be a safe alternative to mastectomy in this setting. Published studies of rPBI have used long fractionation regimens delivered over 3 to 5 weeks, with up to 30 fractions, which can present a challenge for both patients and health systems. This study investigates rPBI using an ultra-hypofractionated 5-fraction regimen, with a primary objective to determine the feasibility of accrual over a 2-year period. Secondary endpoints include acute and late toxicity associated with treatment, the risk of local and distance recurrence, the location of local recurrence (in field or out-of-field), the risk of local recurrence after rPBI requiring mastectomy, invasive breast cancer free survival and overall survival.

## METHOD

Patients > 18 years old with recurrent BC in the ipsilateral breast occurring at least 1 year following completion of prior adjuvant whole or partial breast radiotherapy, with a unifocal tumor < 3.0 cm, resected with negative margins, and clinically node negative will be eligible for this study. The partial breast planning target volume will receive 26Gy in 5.2Gy daily fractions for 5 daily treatments. Fifteen patients will be accrued over 2 years in the setting of a multi-institutional international collaboration involving centres in 4 countries (Canada, Jordan, Brazil, and India).

Statistical Design: This is a prospective single-arm phase II study. Baseline characteristics will be summarized using descriptive statistics. For the secondary endpoints, toxicity associated with treatment will be summarized using frequency and percentage with 95% Clopper-Pearson confidence intervals by grade at each scheduled follow up. Cumulative incidence function will be used to estimate local recurrence, distance recurrence, and local recurrence after rPBI requiring mastectomy, respectively, with death as a competing risk. Location of recurrence will be summarized by frequency and percentage. Kaplan-Meier method will be used to estimate invasive breast cancer free survival and overall survival

## RESULTS

Conduct to Date:
Study Initiative Nov 2021. Study Activation Feb 2022
Funding support: Seed Grant awarded by the Princess Margaret Global Cancer Program, and the Princess Margaret Breast Cancer Program.

## CONCLUSION

Ongoing accrual

# 26 Timing of Radiation Pneumonitis in patients receiving Immune checkpoint inhibitors

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## PURPOSE

Consolidation with Durvalumab is the standard of care in unresectable Stage 3 Non-Small Cell Lung cancer (NSCLC) following radical chemoradiation and pneumonitis is an independent side effect of these therapies. Literature has shown the peak time to development of radiation pneumonitis is 4-8weeks. The purpose of this study was to describe the timing of radiation pneumonitis (RP) by receipt of Durvalumab in patients who received definitive chemoradiation.

## METHOD

In this single institution retrospective study, consecutive patients between 2016 and 2018 with unresectable Stage 3 treated with radical chemoradiation or radical chemoradiation followed by durvalumab were evaluated for development of at least grade 2 radiation pneumonitis based on clinical symptoms and characteristic radiology features. Descriptive analysis including the time from last fraction of radiotherapy to diagnosis of grade 2 radiation pneumonitis was determined. Diagnosis of RP within 2 months of completing radiotherapy was considered early diagnosis. Logistic regression analysis stratified by receipt of Durvalumab of clinical factors predictive of early diagnosis of radiation pneumonitis were evaluated.

## RESULTS

Of the 144 patients with unresectable stage III NSCLC, 31 (22%) developed at least grade 2 radiation pneumonitis after definitive chemoradiation. The median patient age was 67 years (range 41-87). Of these, 12 (39%) received consolidative Durvalumab and most patients over 65 years did not receive Durvalumab 13/20 (65%). The mean time to development of RP was 2.45 months (SD 2.06) in patients who did not receive Durvalumab and 3.90 months (SD 1.91) in patients who received Durvalumab. The mean V5 and V20 lung dose constraints were 60.14% (SD 2.73) and 29.96% (SD 1.82) respectively. By receipt of Durvalumab, age over 65, V5 and V20 lung dose constraints were not predictive of early onset radiation pneumonitis.

## CONCLUSION

Patients on Durvalumab had later onset radiation pneumonitis compared to patients who did not. Traditional dosimetric predictors, i.e. V5 and 20, were not predictive of early onset radiation pneumonitis by receipt of Durvalumab. These results suggest that delaying initiation of Durvalumab may not be necessary in patients with unresectable NSCLC.

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# UTDRO RESEARCH DAY 2022

*THANK YOU*