Reduced Intubation Rates Following Whole-Lung Low-Dose Radiation Therapy (LD-RT) in Patients With COVID-19-Related Pneumonia

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Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Materials/Methods: A chart review identified 283 patients (204 male and 79 female) who received liver SBRT from 2014-2019. Univariate logistic regression models were used to identify demographic, clinical, and dosimetric factors associated with the development of rib fractures post liver SBRT. All statistical tests were two-sided and the null hypothesis was rejected for P < 0.05.

Results: The median follow-up was 12.2 months (range: 3-78.8 months). With respect to primary site, 81% were primary liver tumors and 19% metastases. SBRT doses ranged from 60 Gy in 5 fractions to 30 Gy in 5 fractions. The most commonly used doses were: 40 Gy in 5 fractions (29%), 45 Gy in 5 fractions (23%), 50 Gy in 5 fractions (18%), 35 Gy in 5 fractions (9%), 48 Gy in 3 fractions (8%), and 30 Gy in 5 fractions (5%). Mean PTV volume was 141 cc (range: 3.7-1304 cc). A total of 22 patients (8%) experienced rib fractures. Of these patients, three (17.6%) and one (6%) underwent two and three liver SBRT courses, respectively. The earliest rib fracture was seen 3 months after SBRT and the latest time point at which any rib fracture developed was 27 months. Female gender (2.29; 95% CI: 0.98-5.30; P = 0.032), increasing BED$_{30}$ Gy (1.01; 95% CI: 1.00-1.01; P = 0.016), and BED$_{30}$ Gy (1.02; 95% CI: 1.01-1.04; P = 0.009) were associated with an increased probability of developing rib fractures. Increasing distance from the PTV to the chest wall was associated with a lower probability of developing rib fractures (OR: 0.69; 95% CI: 0.52-0.88; P = 0.007). Mean distance from PTV to chest wall was 2.2 cm (range: 0 - 9.5 cm). Furthermore, increasing D30cc to the chest wall (OR: 1.09; 95% CI: 1.05-1.15; P < 0.001), maximum chest wall dose (OR: 1.1; 95% CI: 1.06-1.15; P < 0.001), V40Gy (OR: 1.08; 95% CI: 1.04-1.14; P < 0.001), V30Gy (OR: 1.02; 95% CI: 1.02-1.03; P < 0.001), V20Gy (1.003; 95% CI: 1.00-1.006; P = 0.016), V10Gy (1.002; 95% CI: 1.00-1.004; P = 0.05) were associated with an increased probability of developing rib fractures. Undergoing more than one course of SBRT to the liver (P = 0.34), PTV volume (P = 0.55), mean chest wall dose (P = 0.94), left versus right side tumors (P = 0.69) and BMI > 30 (P = 0.36) were not associated with the development of rib fractures.

Conclusion: Rib fractures after liver SBRT are a rare event and were observed in 8% of patients. Clinicians should continue to utilize well-established dose constraints and minimize radiation dose delivery to the chest wall.


2031
Clinical Outcomes in Patients Undergoing Coronary Brachytherapy for Restenosis of Coronary Vessels Previously Treated With Drug Eluting Stents

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Purpose/Objective(s): Coronary brachytherapy has been shown to be a potential option for patients that require reintervention following in-stent restenosis (ISR) of a drug eluting stent (DES). The purpose of this study is to assess long-term clinical outcomes in patients undergoing coronary brachytherapy with high-dose-rate (HDR) beta radiation after ISR of a DES in native and grafted vessels.

Materials/Methods: This is a single institution retrospective review of 55 patients that underwent coronary brachytherapy after ISR of a previous DES between January 2015 and June 2017. Each patient underwent cardiac angioplasty with standard percutaneous techniques. A prescribed dose of 23 Gy was delivered to vessels with diameter ≥3.4mm and 18.4Gy in those less < 3.4mm. The primary clinical endpoints were freedom from reintervention and major adverse cardiac events (MACE), defined to be myocardial infarction, progressive congestive heart failure (CHF), or target vessel reintervention.

Results: A total of 61 treated vessels in 55 patients were eligible for analysis with a median follow up time of 49.7 months. No brachytherapy-related complications were observed during the follow up period. Of the 61 vessels, 20 (33%) were grafted and 41 (67%) were native vessels. Overall, there were 29 (47%) patients with ISR requiring reintervention of the previously treated vessel, and 46 (75%) patients that experienced at least one documented MACE. In the graft vessel subgroup, 10 (50%) required reintervention and 15 (75%) experienced a MACE. In the native vessel subgroup, 19 (46%) required reintervention and 31 (51%) experienced a MACE. The overall median times to reintervention and MACE were 11.1 months and 9.1 months, respectively. The median time to a MACE for grafted vessels was 16.8 months compared to 7.0 months in native vessels. The median time to reintervention for grafted vessels was 13.78 months and 8.13 months for native vessels.

Conclusion: Coronary brachytherapy is a suitable treatment modality for patients with recurrent ISR. The current data demonstrates that it is a safe and effective approach in both native and grafted vessels in patients who have failed multiple prior interventions with DES. We observed the freedom from reintervention was longer for grafted vessels compared to native vessels. A similar result was observed in freedom from a MACE. Further prospective studies are needed to validate and expand on these findings.


2032
Reduced Intubation Rates Following Whole-Lung Low-Dose Radiation Therapy (LD-RT) in Patients With COVID-19-Related Pneumonia

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Purpose/Objective(s): Low-dose radiotherapy (LD-RT) is a well-established treatment for multiple human inflammatory conditions. Whole-lung LD-RT may be effective in COVID-19-related pneumonia. LD-RT treatment of 0.5 or 1.5 Gy to the bilateral lungs on a prospective, combined phase III, multi-site, single-institution trial. Patients were followed for 28 days or until discharge and compared to controls blindly matched by age, comorbidity, duration of symptoms, and disease severity. Eligible patients were confirmed by SARS-CoV-2 positive PCR, unable to wean from oxygen at enrollment, and had radiographic consolidations. Patients were enrolled into 5 cohorts stratified by treatment variables and severity of illness: LD-RT alone vs. LD-RT with concurrent drug therapies, non-intubated vs. intubated status, and low (1.5 Gy) vs. lower (0.5 Gy) radiation dose. Qualitative aims were to establish safety and explore efficacy. Quantitative endpoints were continuous, categorical, and time-to-event, and included clinical recovery, intubation, radiographic changes, and biomarker responses. Intubation endpoints are reported for all cohorts using the log-rank test and Kaplan-Meier method.

Results: Outcomes of 80 patients were available for analysis at study closure. In total, 40 of 70 planned patients (57% trial enrollment) received
whole-lung LD-RT between April 24 and December 7, 2020 and were compared to 40 matched controls. Cohorts 1&2: Ten non-intubated patients received 1.5 Gy without concurrent COVID-directed drug therapies (10 of 10 planned, 100% cohort enrollment) and were compared to matched controls. Intubation rates were 40% in controls compared to 10% following LD-RT (P = 0.11). Cohort 3: One intubated patient received 1.5 Gy (1 of 20 planned, 5% cohort enrollment). Cohort 4: Twenty separate non-intubated patients received 1.5 Gy with concurrent dexamethasone/ remdesivir (20 of 20 planned, 100% cohort enrollment) and were compared to matched controls. Intubation rates were 32% in controls compared to 14% following LD-RT (P = 0.09). Cohort 5: Nine patients received 0.5 Gy with concurrent drug therapies (9 of 20 planned, 45% cohort enrollment) and were compared to matched controls. Zero controls required intubation compared to 11% following LD-RT (P = 0.32). Among all non-intubated patients and matched controls combined (n = 78), mechanical ventilation was required in 28% of controls compared to 12% following LD-RT (reduced 57%, P = 0.05). The trial was prematurely closed due to observed reproducibility of efficacy. A randomized trial is now ongoing.

**Conclusion:** In the first, prospective, phase II/II trial of radiotherapy for COVID-19-related pneumonia, a single treatment of whole-lung LD-RT reduced intubation rates by 57% compared to controls in patients receiving supportive care with or without drug therapies (P = 0.05).


### 2033

**Impact of Response to Neo-Adjuvant Therapy to Primary Rectal Cancer on Lung Metastases Treated With SABR**


**Purpose/Objective(s):** We assessed outcomes in patients undergoing stereotactic ablative radiotherapy (SABR) to lung oligometastatic disease (OMD) of rectal origin in terms of overall survival (OS), progression free survival (PFS) and local control (LC). We assessed if LC and local failure (LF) of lung metastases (LM) is related to primary rectal cancer (PRC) histological response to neo-adjuvant therapy (NAT) to determine if this can act as a biomarker for local response.

**Materials/Methods:** We undertook a retrospective review of patients with LM from rectal adenocarcinoma treated with SABR at two institutions, with at least 6 months follow up (FU). Data were collected from paper and electronic patient records. Statistical methods used were descriptive analysis, Kaplan Meier, log-rank test and Cox regression.

**Results:** A total of 33 patients with 55 LM were treated with SABR between 2013 and 2020. Median age was 69 (40.8-83.1). Median number of lesions per patient was 1 (1-4), 55% had a single LM. The median dose was 50 Gray in a median of 4 fractions. 21 patients with 35 LM had NA therapy to PRC with available histology. 30 patients (91%) were treated for OMD and 3 were treated for oligoprogression of polymetastatic disease. 33% had synchronous metastases at diagnosis. All patients had a controlled primary rectal cancer having undergone definitive surgery. The median FU was 30.6 months (8.3-94). At the last known FU, 23 patients (69.7%) were alive and 10 (30.3%) had died. The median, 1, 2 and 4-yr OS from SABR were 73 months (95% CI 30.9-115), 100%, 91.8% and 67%, respectively. The LC rate was 89%. There was a LF in 6 of 55 LM, with median time to LF of 11.3 months (2.8-36.1). The only variable associated with LC was response [complete (CR) or partial (PR)] of the PRC to NA therapy. The 2 patients who had no response to NAT both suffered LF of a LM (2 of 3 treated LM). In those with CR or PR (21 patients) there was no LF (0 of 32 treated LM). 2 of 10 patients with no NAT also experienced LF (4 of 18 treated LM). There was 1 patient with no rectal histology available, and 1 patient in whom no details of NAT were available. Neither experienced a LF (2 treated LM). The PFS was 5.97 months (1.6-38.5). None of the analyzed variables were associated with PFS, including PET staging prior to SABR or multiple vs single treated metastasis. 22 (67%) patients progressed post SABR. Pattern of progression: 13 out of field lung (OOF) only; 1 local only; 5 distant only; 1 local and distant; 1 local and OOF; 1 OOF and distant; 11 patients (33%) did not develop further OMD or PDM. No patient experienced > G3 acute toxicity, most common being cough and fatigue.

**Conclusion:** This is the largest reported cohort of rectal cancer patients undergoing lung SABR and the only to review LC in terms of response to NAT to PRC. This offers an insight into response and natural history post SABR for LM that can help inform treatment decisions. We have shown that LC is related to PRC response to NAT, which may act as a biomarker for success of lung SABR. This will need to be confirmed by larger studies.


### 2034

**Radiation for Anorectal Cancers in Patients With a History of Prostate Cancer**

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**Purpose/Objective(s):** RT for rectal and anal cancer after prostate cancer RT is usually avoided due to fear of complications, and data on this topic is scarce. Our aim was to evaluate outcomes and toxicity associated with RT in this group of patients.

**Materials/Methods:** We conducted a single institution retrospective study of patients treated with RT for rectal or anal cancer after prior prostate RT from 1/1/1995 - 8/1/2019. Acute and long-term toxicities were collected. Treatment plans were extracted to assess doses to organs at risk and target coverage. Wilcoxon rank sum test was used for correlation between dosimetry and toxicities. Estimated cumulative incidence was used for local progression.

**Results:** We identified 29 patients who received RT after prostate cancer RT, 19 with rectal cancer and 10 with anal cancer. None of those patients had metastatic disease. Prior prostate RT was delivered using low dose rate brachytherapy (LDR) in 15/29 patients with a median dose of 145 Gy (144-160), external beam RT (EBRT) in 10 patients with 79.2Gy/44 or 81Gy/45 fractions (fr), and EBRT + LDR in 4 patients with 50.4Gy/80 110 Gy I-125 or Pd-103 LDR. RT for rectal cancer was delivered most commonly with 50.4Gy/28 fr or 1.5 Gy twice daily fractionation to 30-45 Gy (53% of patients). The most commonly used RT dose for anal cancer was 50Gy/25 fr. Brachytherapy was used in 6 (21%) patients: as a boost after EBRT in 2 patients with anal cancer and alone in 4 rectal cancer patients. Median interval between prostate and anorectal RT was 134 months (6-303). 68% and 80% of rectal and anal cancer patients got concurrent chemotherapy. Table 1 summarizes toxicities associated with anorectal re-RT. Two patients developed fistulas, one was urinary cutaneous after prostate LDR and 50Gy/25fr for rectal cancer, and the other recto vesicular after prostate LDR and 50Gy/25fr for anal cancer; both repaired by extensive surgery. Both patients had more than 10 years between the two RT courses. In 21 patients with available dosimetry, coverage was adequate with a GTV V100% of 98% for rectal cancer patients and 96% for anal cancer patients. There was no significant correlation between toxicities and dosimetric values probably due to the small sample size. The estimated 3-year local progression incidence for all patients was 22%: 11% for rectal cancer, and 4% for anal cancer patients.

**Conclusion:** RT of anorectal cancer after prior prostate cancer RT is feasible but poses a risk of fistulae. Further studies, possibly using