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Preliminary Approach to Implementing a COVID-19 Thoracic Radiation Therapy Program

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JSW is on the Clinical Advisory Board for TAE Life Sciences
JSW is on the board of directors for Coquí Pharma

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Abstract
The value of low dose whole thoracic radiation therapy (LD-WTRT) for SARS-CoV-2 (COVID-19) pneumonia is unknown. Should ongoing clinical trials demonstrate that LD-WTRT proves effective for COVID-19 pneumonia recovery, widespread rapid implementation will be helpful globally. Our aim was to outline a pragmatic process for safe and efficient administration of LD-WTRT to patients with COVID-19 pneumonia that
could be implemented successfully in a community hospital setting based upon participation in the PreVent clinical trial of LD-WTRT.

Introduction
Radiation therapy with low doses of x-rays was historically used to treat pneumonia in the 1920s to 1940s (1-3). Due to the advent of penicillin and increasing concerns about radiation injury, its use for non-neoplastic disease diminished sharply after World War II. The COVID-19 pandemic presents a clinical scenario where low dose radiation therapy may again provide a benefit for patients with certain types of pneumonia (4-6).

Recent and ongoing trials are investigating the efficacy and safety of low dose whole thoracic radiation therapy (LD-WTRT) to treat COVID-19 pneumonia (7-14). If LD-WTRT is shown to be efficacious, radiation oncology practices will have to adapt new procedures into their workflow to efficiently ensure the safety of both cancer center patients and staff. Here we aim to outline a pragmatic process with which to safely administer LD-WTRT to patients with COVID-19 pneumonia.

The PreVent trial is a multicenter phase II clinical trial randomizing patients to best supportive care, 0.35 Gy, or 1.0 Gy of LD-WTRT. In this report, we outline the feasibility of implementing a LD-WTRT program based upon participation in the PreVent clinical trial.

Materials & Methods
Data Access and Patient Screening

We worked with inpatient nursing operations and IT to access patient data. We designed an auto-populated spreadsheet (15) to screen current inpatients for identifying information, admission date, confirmed COVID-19 PCR positive test results, and oxygen use. The radiation oncologist screened patients for eligibility at 5 AM to ensure adequate time for chart review. Criteria for eligibility are shown in Table 1.

Chart Review

Electronic medical record (EMR) review was done for hospitalized patients deemed appropriate for LD-WTRT per discussion with the primary medical team. Information including presenting symptoms, treatment to date, whether they met protocol eligibility criteria, and diagnostic imaging was reviewed. Chest x-rays were available, but we looked for prior chest CT scans to estimate field size and potential virtual simulation for treatment.

Communication and Evaluation Before Enrollment

For potentially eligible patients, we contacted the hospitalist to review eligibility for consideration of LD-WTRT based upon clinical need and safety of transportation. If approved, radiation oncology consultation and screening for interest as well as eligibility for LD-WTRT was done via telehealth. The patient’s nurse logged into teleconference software (16) with a hospital-linked smart tablet, donned PPE, and brought the tablet to the patient for virtual consultation.
A focused history was taken to assess duration of pulmonary symptoms or fever (<9 days per protocol), ability to lie still in the supine or prone position for the time necessary for positioning and radiation treatment, and patient interest in the protocol. The historical rationale, the trial, and reason for offering LD-WTRT was reviewed in a 30-45 minute evaluation without physical examination.

Ineligible patients were reassured that they were receiving standard therapy currently. For patients interested in the protocol, consent was obtained. The signature page was photographed and sent securely to clinical trials staff via mobile phone. Physical examination was then performed.

*Coordination for Transportation*
To minimize risk of infection, LD-WTRT only took place at the end of the day, after the cancer center completed treatment of scheduled radiotherapy patients on the less active of two linear accelerators in the department. A member of the Infection Prevention team traveled the route from the patient unit to Radiation Oncology to ensure a safe path. Security unlocked and secured access along the transport route, through a back entrance used for patients either hospitalized or coming by ambulance. Nursing was called to coordinate transport to the Radiation Oncology department. If the patient required high-flow oxygen, respiratory therapy provided a non-rebreather mask to the patient prior to transport with medical floor nursing support if needed. The service engineer was notified to prevent unscheduled work on the linear accelerator.
**Treatment Planning**

The patient was registered in the radiation oncology EMR (ARIA, Varian Medical Systems) and placed on a protocol-specific care path. Per protocol, CT simulation was not permitted to minimize potential departmental contamination. Diagnostic chest CT and x-ray data from the current hospitalization were used to design estimated AP/PA fields. CT scan import into the Eclipse treatment planning system (TPS) permitted confirmation of dose distribution. The carina was contoured to help with pre-treatment localization and set-up.

The anatomic target was the entire thorax to include the lungs bilaterally with an estimated 1.5 to 2 cm margin in all directions. In the absence of clear lung imaging, the superior and lateral borders were identified as 2 cm beyond the outer aspect of the ribs. The inferior border was identified at the T12-L1 interspace. The only method of blocking allowed was via the primary LINAC jaws; no multileaf collimator leaves were used. In the event of superior-inferior dimension collimator limitations, we favored covering the lung bases and diaphragmatic recesses over coverage of the lung apices.

Patients randomized to a protocol dose of 0.35 or 1.0 Gy had treatment prescribed to midplane along the central axis without heterogeneity corrections using 6-18 MV photons, accounting for separation at the level of the carina as identified on orthogonal KV/KV, cone beam CT or MV imaging. Isocenter was set at the carina for localization and to permit taking a separation at the central axis.
**Treatment Delivery**

Any equipment in the linear accelerator vault not being directly used by the patient was covered with a plastic sheet, placed inside a cabinet, or removed from the room. The treatment team consisted of “HOT” and “COOL” members. Two “HOT” therapists and the physician donned PPE and entered the treatment vault to set the patient up on the linac couch. The patient was positioned supine with arms in a comfortable position. Prone positioning was permitted if needed for patient safety or comfort. If a diagnostic CT was used for planning, the patient was set up in the same position as the diagnostic CT. A “COOL” therapist remained in the control room, closed the vault door, and maintained audio and visual contact with the “HOT” team members at all times. After the “HOT” team members doffed their PPE and exited the treatment vault, the physician and one therapist converted from “HOT” to “COOL” in the control area with the linac console, while the remaining “HOT” therapist donned clean PPE in preparation for post treatment re-entry.

Kilovolt x-ray images were then acquired. The carina was identified and the patient was aligned to bony anatomy on the AP image. Vertical depth was identified on the lateral image and shifts were made to this point. Following isocenter placement, three MV images: central superior, inferior right lateral, and inferior left lateral were taken to verify all field borders (Figure 1). If these actions could not be accomplished from outside the treatment vault due to limitations of the linear accelerator, a “HOT” team member would
re-enter the treatment vault to perform couch movements. Once the patient’s position was confirmed by the “COOL” therapist and physician, the patient received treatment.

After the patient was transported back to the hospital floor, the “HOT” therapists placed a “DO NOT ENTER” sign on the linac vault door. All three therapists and the physician then doffed their PPE following recommended procedures. Environmental Services and Housekeeping were contacted to request room decontamination. Security was notified to close the department.

Results

Using this approach, we were able to minimize COVID-19 exposure to the members of our healthcare team and other patients on treatment, and successfully deliver LD-WTRT to a patient with COVID-19 pneumonia. Zero staff and other patients contracted COVID-19 from this process. Treatment planning time to incorporate a diagnostic CT for virtual simulation, creating a DRR, and MU calculations was 20 minutes. Patient time in the department was <40 minutes, setup for verification on the couch was 15 minutes, and treatment delivery was 12 seconds (for a 1Gy dose in our patient’s case).

Discussion

Here, we outline an approach for minimizing the exposure of patients undergoing radiation treatment for cancer to COVID-19 by delivering LD-WTRT at the end of the
day. An alternative approach to minimize exposure between these different patient populations undergoing radiation treatment would be to deliver LD-WTRT during the day using a separate LINAC dedicated to these protocols.

LD-WTRT for COVID-19 pneumonia is investigational and there are multiple ongoing trials to evaluate its efficacy, including the PreVent trial. Treating cancer patients on special precautions due to infection (C difficile, MRSA, etc.) is done routinely and radiation therapists already use universal precautions when needed for such situations. Using radiation to treat the infection itself, COVID-19 pneumonia specifically, however, is novel. We found implementing precautions for treatment of COVID-19 pneumonia is feasible when coordinated with the inpatient team. If studies investigating LD-WTRT for this purpose confirm its safety and efficacy, our successful process designed for a community hospital may serve as a potential model for implementation in smaller non-academic facilities. The general process can readily be adapted to larger hospitals including academic facilities. The process described here was implemented in December 2020 which was before the FDA gave emergency use authorization for any COVID-19 vaccine. Thus, no staff had been vaccinated at the time of LD-WTRT delivery. The ability for cancer center patients, treating physicians, and staff to be vaccinated against COVID-19 has made this treatment protocol safer to implement.
References


Radiation Medicine and Protection (2021), doi: 

15. Microsoft Excel


Figure 1. To verify all field borders, three MV images were taken: central superior, inferior right lateral, and inferior left lateral.

Table 1. Inclusion and exclusion criteria as per the PreVent clinical trial.

<table>
<thead>
<tr>
<th>INCLUSION CRITERIA</th>
<th>EXCLUSION CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Laboratory-confirmed diagnosis of SARS-CoV-2 pneumonia</td>
<td>1. Currently requiring mechanical ventilation.</td>
</tr>
<tr>
<td>2. Currently hospitalized with COVID-19</td>
<td>2. Prior thoracic radiotherapy, with the exception of the following:</td>
</tr>
<tr>
<td>3. Age ≥ 50 years</td>
<td>a. Breast or post-mastectomy chest wall radiation (without regional nodal</td>
</tr>
<tr>
<td>4. Symptomatic fever, cough and/or dyspnea for &lt;9 days</td>
<td>irradiation) may be included at the discretion of the site primary investigator, and</td>
</tr>
<tr>
<td>5. Patient or his or her legal/authorized representatives can understand and sign the</td>
<td>b. thoracic skin radiation therapy (without regional nodal irradiation) is</td>
</tr>
<tr>
<td>study informed consent document.</td>
<td>allowed.</td>
</tr>
<tr>
<td>6. Able to be positioned on a linear-accelerator couch for RT delivery</td>
<td>3. Known hereditary syndrome with increased</td>
</tr>
</tbody>
</table>
7. AND at least one of the following risk factors for significant pulmonary compromise:
   a. Fever >102 degrees Fahrenheit during index admission
   b. Respiratory rate of ≥ 26 / minute within 24 hours of screening
   c. SpO2 ≤ 95% on room air within 24 hours of screening
   d. Any patient requiring 4 L/min oxygen therapy to maintain SpO2 <93% within 24 hours of screening
   e. Ratio of partial pressure of arterial oxygen to fraction of inspired <320.

Patients may be enrolled on this trial while concurrently enrolled on other COVID-19 clinical trials.

<table>
<thead>
<tr>
<th>Sensitivity to radiotherapy, including ataxia-telangiectasia, xeroderma pigmentosum, and Nijmegen Breakage Syndrome</th>
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<tbody>
<tr>
<td>4. Known prior systemic use of the following drugs: Bleomycin, Carmustine, Methotrexate, Busulfan, Cyclophosphamide, or Amiodarone</td>
</tr>
<tr>
<td>5. History of or current diagnosis of pulmonary fibrosis, or an alternative pulmonary condition responsible for significant lung compromise at the discretion of the site primary investigator.</td>
</tr>
<tr>
<td>6. History of lung lobectomy or pneumonectomy</td>
</tr>
<tr>
<td>7. Known history of pulmonary sarcoidosis, Wegener’s granulomatosis, systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, polymyositis/dermatomyositis, Sjögren’s syndrome, mixed connective tissue disease, Churg-Strauss syndrome, Goodpasture’s syndrome, or ankylosing spondylitis.</td>
</tr>
<tr>
<td>8. Symptomatic congestive heart failure within the past 6 months including during current hospitalization</td>
</tr>
<tr>
<td>9. History of recent or current malignancy receiving any cytotoxic chemotherapy or immunotherapy within the past 6 months.</td>
</tr>
<tr>
<td>11. History of any solid organ transplant (renal, cardiac, liver, lung) requiring immunosuppressive therapy.</td>
</tr>
<tr>
<td>12. Females who are pregnant or breast-feeding.</td>
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<tr>
<td>13. Inability to undergo radiotherapy for any other medical or cognitive issues.</td>
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