

# Low-Dose Radiation Therapy and Severe COVID-19-Related Pneumonia

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# Disclosure

- Employment Disclosure: Emory University
- Founder of CureRays™, a start-up manufacturer of commercial products to offer COVID-19 treatments with low-dose radiation therapy



# RESCUE 1-19 (First LD-RT Trial in the World)

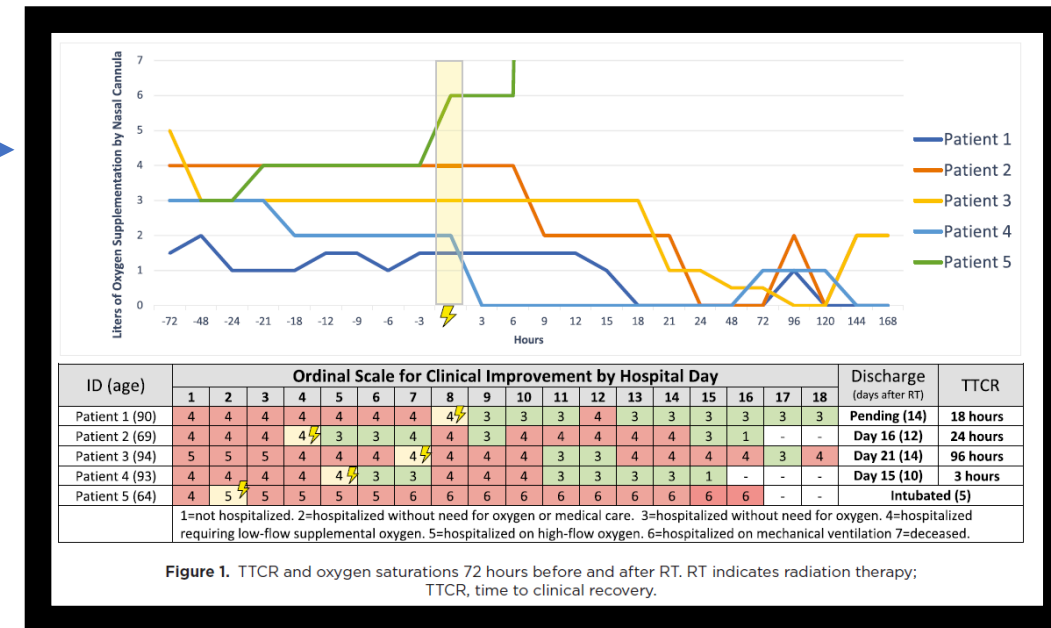
- **Eligible patients** were SARS-CoV-2 positive, hospitalized, bilateral radiographic consolidations & required supplemental oxygen (i.e., **severe ARDS**)
- **Intervention:** 1.5 Gy whole-lung LD-RT
- **Primary & Secondary Endpoints:** Safety (Phase 1) and Efficacy (Phase 2)
- **Phase 1** included outcomes in first 5 patients with preplanned interim 7-day analysis (PMID: **32986274**)
- **Phase 2** included outcomes in all 10 patients @ day 28 compared with age- and comorbidity-matched controls.
- **Efficacy endpoints:** time to clinical recovery (TTCR), radiographic improvement on serial x-rays, and biomarkers response
- Two-sample t-tests, chi-square tests, univariate Cox proportional hazard models, cumulative incidences, and hazard ratios were reported.



# Results

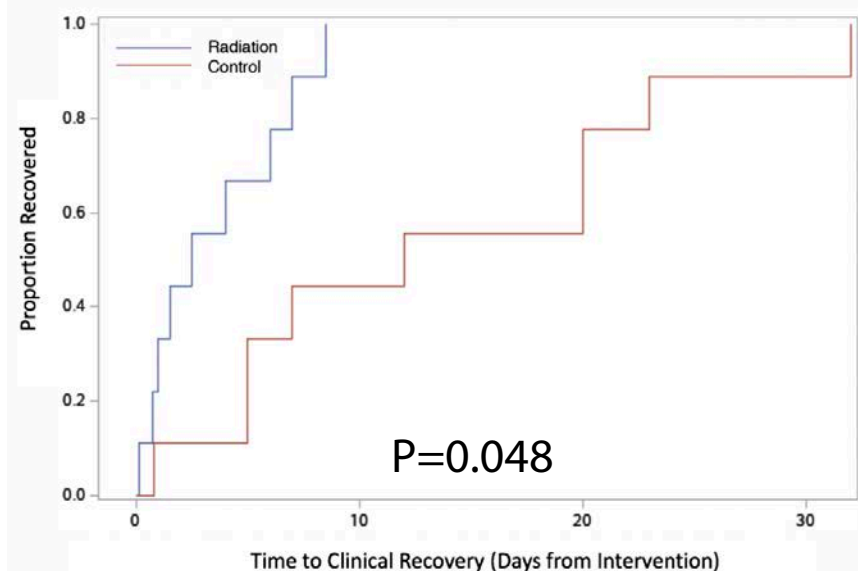
- Ten patients received whole-lung LD-RT between April 24 and May 24, 2020 and compared with ten matched controls treated with best supportive care and COVID-directed therapies
- **Primary endpoint: 7 Day interim** →
- **Secondary Endpoints: Median TTCR was 12 days in controls compared to 3 days in the LD-RT cohort (HR 2.9, p=0.05)**
- Median time to hospital discharge was 20 versus 12 days in LD-RT (p=0.19)
- Intubation rates were 40% versus 10%, in favor of LD-RT (p=0.12)
- 28-day overall survival was 90% for both cohorts
- Age  $\geq 65$  was associated with lower oxygen requirement and shorter TTCR in the LD-RT cohort (p=0.01) but not the control cohort (p=0.40)
- Inflammatory, cardiac, hepatic biomarkers, and serial radiographs also were favored of LD-RT

LD-RT was safe (PMID: 32986274)

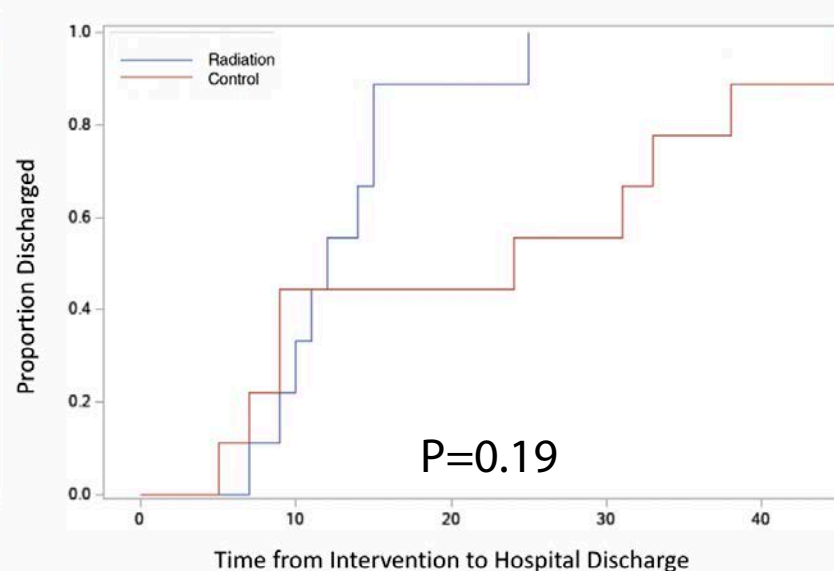


# Observed clinical improvements following LD-RT

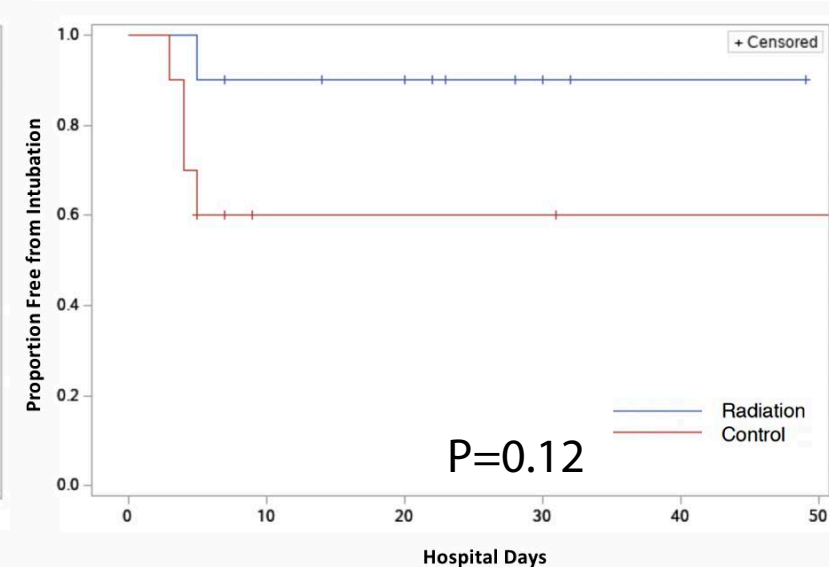
## Time to Clinical Recovery



## Time to Hospital Discharge

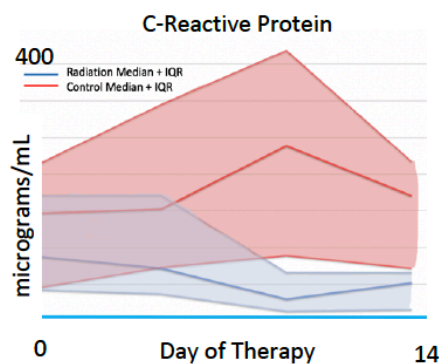


## Intubation Free Rates

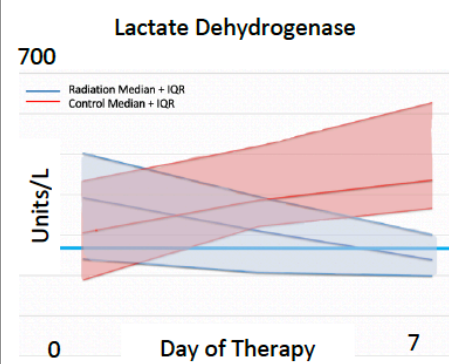


# Observed laboratory improvements following LD-RT

## Inflammation

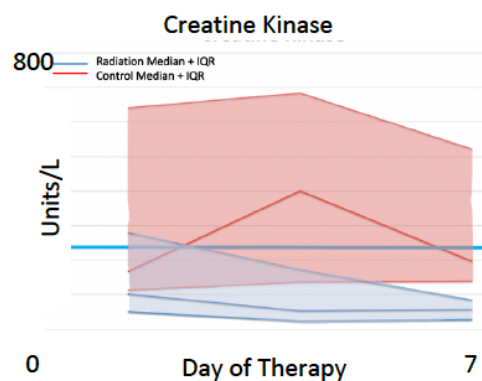


Non-zero change detected	<b>p&lt;0.01</b>
Change superior to pre-LDRT levels	<b>p=0.01</b>
Change superior to controls (red)	<b>p=0.01</b>



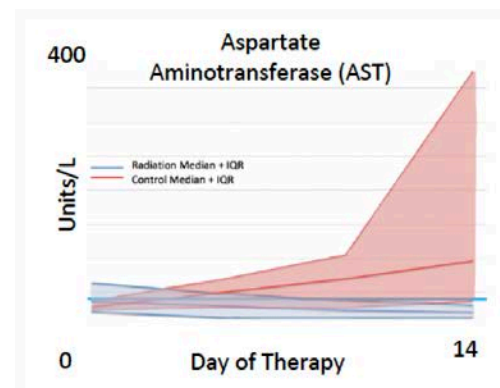
Non-zero change detected	<b>p=0.03</b>
Change superior to pre-LDRT levels	<b>p=0.07</b>
Change superior to controls (red)	p=0.16

## Cardiac Injury

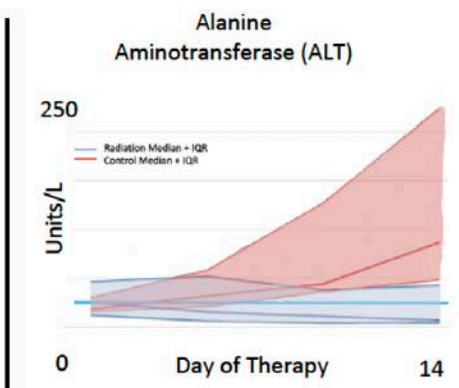


Non-zero change detected	<b>p&lt;0.01</b>
Change superior to pre-LDRT levels	p=0.45
Change superior to controls (red)	<b>p=0.08</b>

## Hepatic Injury



Non-zero change detected	p=0.23
Change superior to pre-LDRT levels	p=0.43
Change superior to controls (red)	<b>p=0.07</b>



Non-zero change detected	p=0.22
Change superior to pre-LDRT levels	p=0.19
Change superior to controls (red)	<b>p=0.04</b>

# Earlier radiographic improvement following LD-RT

ARDS Scale Scores- Control Cohort					
ID	Day 0	Day 1-3	Day 7	Day 14	Day 21
1	2	NA (2)	NA (2)	NA (2)	NA (2)
2	5	5	3	NA (3)	NA (3)
3	3	3	3	3	3
4	2	NA (2)	NA (2)	NA (2)	NA (2)
5	NA	NA	NA	NA	NA
6	3	5	4	NA (4)	NA (4)
7	2	4	4*	5	5
8	4	4	4	NA (4)	NA (4)
9	4	4	4	NA (4)	NA (4)
10	2	2	2	3	2
Mean	3.1	3.9 (3.6)	3.3 (3.2)	3.7 (3.4)	3.3 (3.3)

Controls: 4 of 7 radiographically improved (57%) p=0.04

ARDS Scale Scores- Radiation Cohort					
ID	Day 0	Day 1-3	Day 7	Day 14	Day 21
1	4	2	3	3	2
2	3	3	2	2	NA (2)
3	4	4	2	2	NA (2)
4	5	5	5	NA (5)	3
5	4	5	5	4	NA (4)
6	4	4	4	NA (4)	NA (4)
7	4	2	2	2	NA (2)
8	4	4	4	3	NA (3)
9	4	3	4	NA (4)	NA (4)
10	2	3	2	NA (2)	2
Mean	3.8	3.5	3.3	2.7 (3.1)	2.3 (2.8)

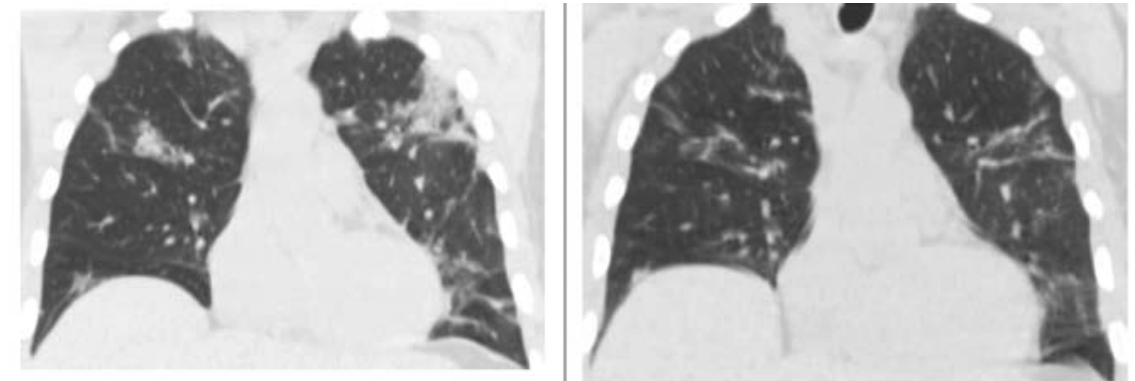
LD-RT: 9 of 10 radiographically improved (90%)



First blinded ARDS score decline



Insufficient radiographs ( $\leq 1$ )



# Conclusion/Summary

- LD-RT for COVID-19 appears to be safe
- LD-RT seems to improve oxygen status, delirium, radiographs, and biomarkers when compared against age and comorbidity matched cohorts
- Confirmatory trials are needed.
- Clinical Trial Registration: NCT04366791

PrePrints and Pubmed References:

<https://www.medrxiv.org/content/10.1101/2020.06.03.20116988v1>

<https://www.medrxiv.org/content/10.1101/2020.07.11.20147793v1>

<https://pubmed.ncbi.nlm.nih.gov/32986274/>