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

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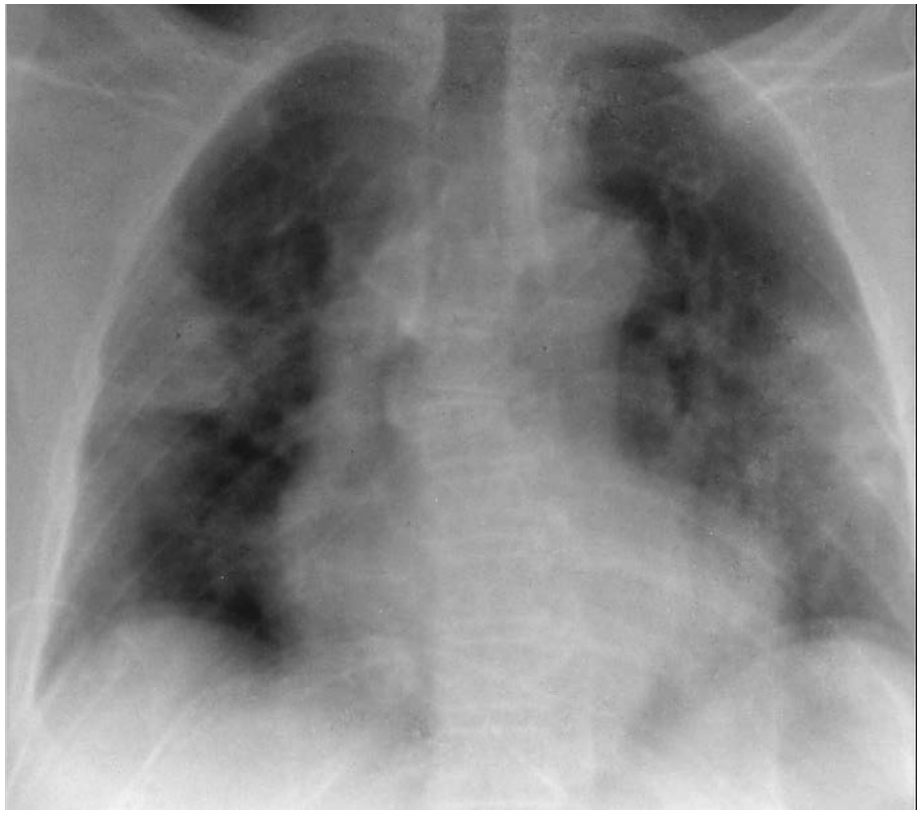
Disclosure

- Employment Disclosure: Emory University

- Founder of CureRaysTM, 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)

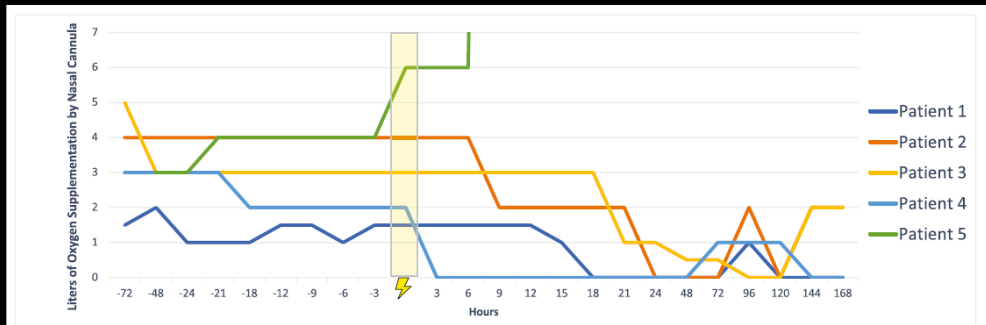
- **Eligible patients** were SARS-CoV-2 positive, hospitalized, bilateral radiographic consolidations & required supplemental oxygen (i.e., **severe ARDS**)
- **Intervention**: 1.5 Gy whole-lung LD-RT
- **Primary & Secondary Endpoints**: Safety (Phase 1) and Efficacy (Phase 2)
- Phase 1 included outcomes 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 ≥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**)



ID (age)	Ordinal Scale for Clinical Improvement by Hospital Day																		Discharge (days after RT)	TTCR
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18		
Patient 1 (90)	4	4	4	4	4	4	4	4	3	3	3	4	3	3	3	3	3	3	**Pending (14)**	**18 hours**
Patient 2 (69)	4	4	4	4	3	3	4	4	3	4	4	4	4	4	3	1	-	-	**Day 16 (12)**	**24 hours**
Patient 3 (94)	5	5	5	4	4	4	4	4	4	4	3	3	4	4	4	4	3	4	**Day 21 (14)**	**96 hours**
Patient 4 (93)	4	4	4	4	4	3	3	4	4	4	3	3	3	3	1	-	-	-	**Day 15 (10)**	**3 hours**
Patient 5 (64)	4	5	5	5	5	5	6	6	6	6	6	6	6	6	6	6	-	-	**Intubated (5)**	
	1=not hospitalized. 2=hospitalized without need for oxygen or medical care. 3=hospitalized without need for oxygen. 4=hospitalized requiring low-flow supplemental oxygen. 5=hospitalized on high-flow oxygen. 6=hospitalized on mechanical ventilation 7=deceased.																			

Figure 1. TTCR and oxygen saturations 72 hours before and after RT. RT indicates radiation therapy; TTCR, time to clinical recovery.

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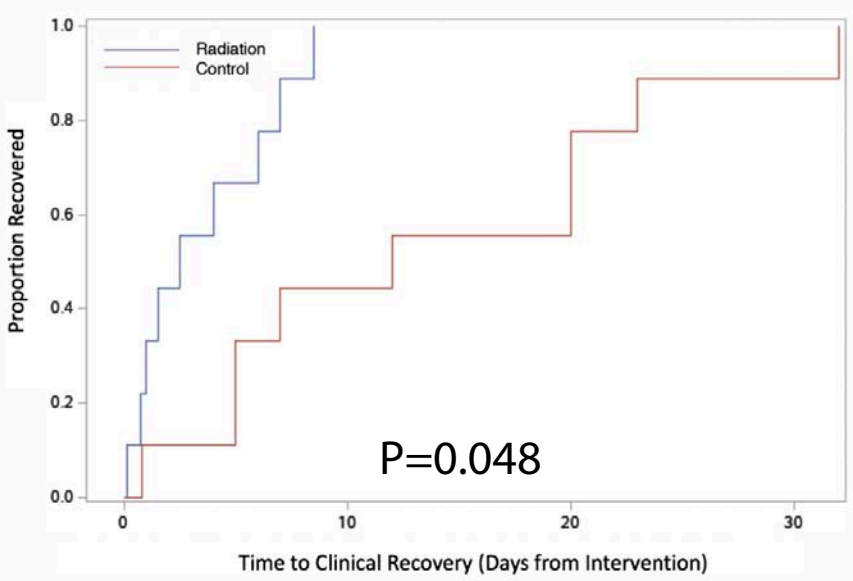
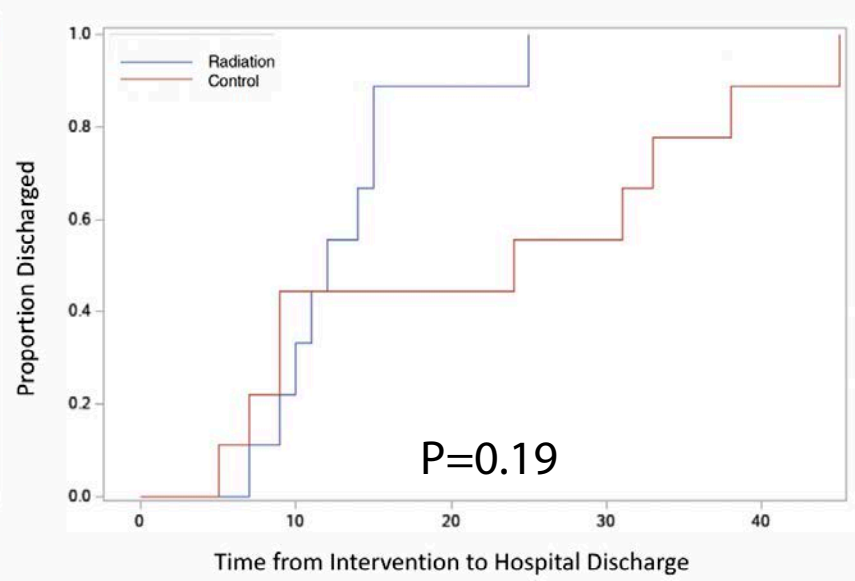
Observed clinical improvements following LD-RT

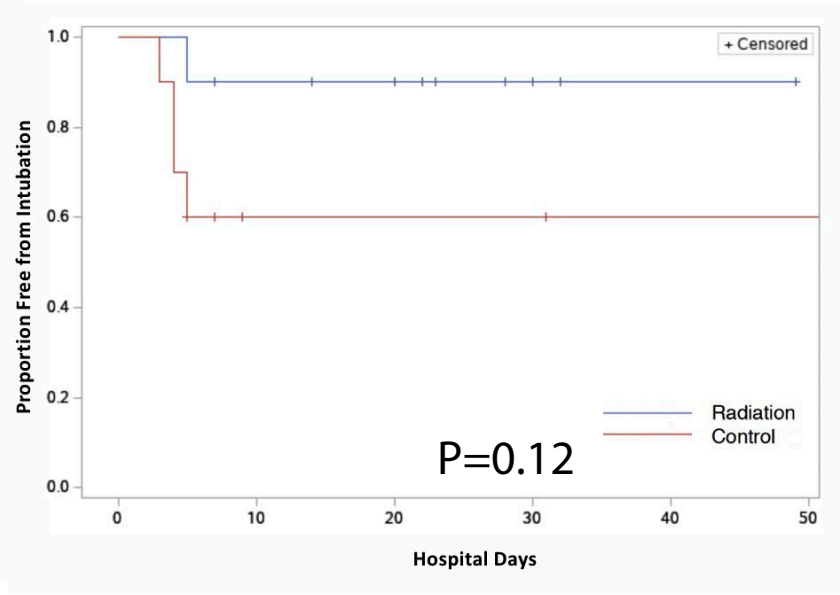
Time to Clinical Recovery



Time to Hospital Discharge



Intubation Free Rates



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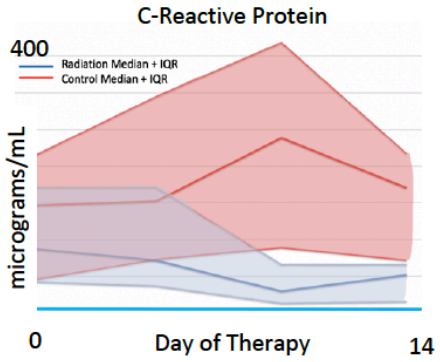
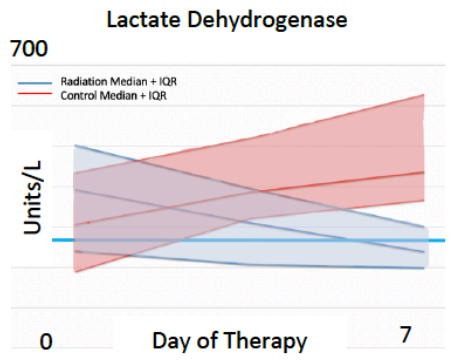
Observed laboratory improvements following LD-RT

Inflammation

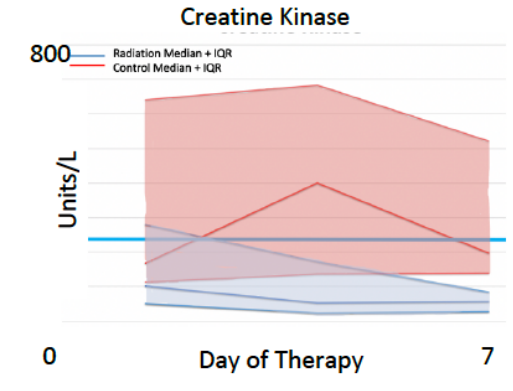


Non-zero change detected	**p<0.01**
Change superior to pre-LDRT levels	**p=0.01**
Change superior to controls (red)	**p=0.01**



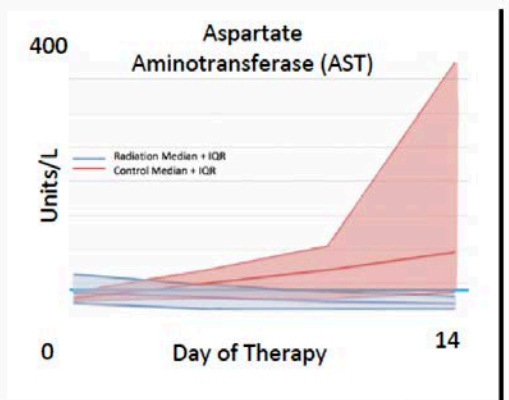
Non-zero change detected	**p=0.03**
Change superior to pre-LDRT levels	**p=0.07**
Change superior to controls (red)	p=0.16

Cardiac Injury

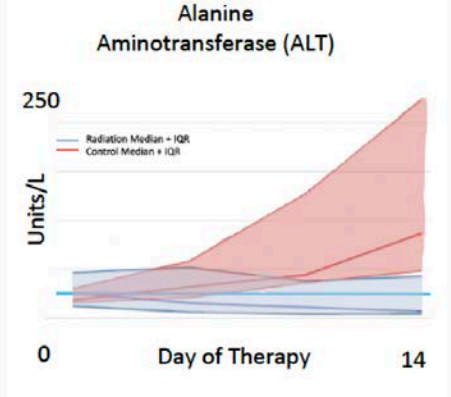


Non-zero change detected	**p<0.01**
Change superior to pre-LDRT levels	p=0.45
Change superior to controls (red)	**p=0.08**

Hepatic Injury



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



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

Earlier radiographic improvement following LD-RT

ARDS Scale Scores- Control Cohort

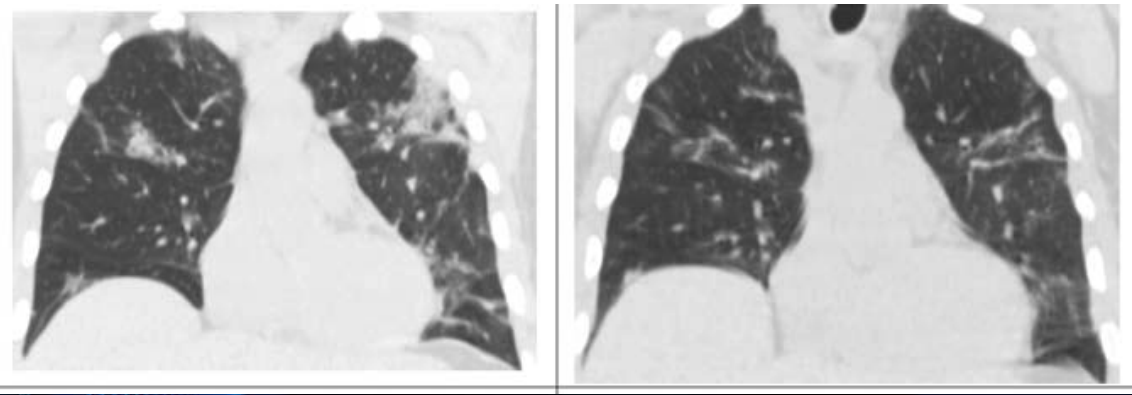
ID	Day 0	Day 1-3	Day 7	Day 14	Day 21
~~1~~	~~2~~	~~NA (2)~~	~~NA (2)~~	~~NA (2)~~	~~NA (2)~~
2	5	5	3	NA (3)	NA (3)
3	3	3	3	3	3
~~4~~	~~3~~	~~NA (3)~~	~~NA (3)~~	~~NA (3)~~	~~NA (3)~~
~~5~~	~~NA~~	~~NA~~	~~NA~~	~~NA~~	~~NA~~
6	3	5	4	NA (4)	NA (4)
7	2	4	4*	5	5
8	4	4	4	NA (4)	NA (4)
9	4	4	4	NA (4)	NA (4)
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 (≤ 1)

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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/