

# Radiation Pneumonitis Secondary to Treatment with Y-90 for Hepatocellular Carcinoma

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## Background

Hepatocellular carcinoma (HCC) is 4<sup>th</sup> leading cause of cancer-related mortality globally<sup>1</sup>

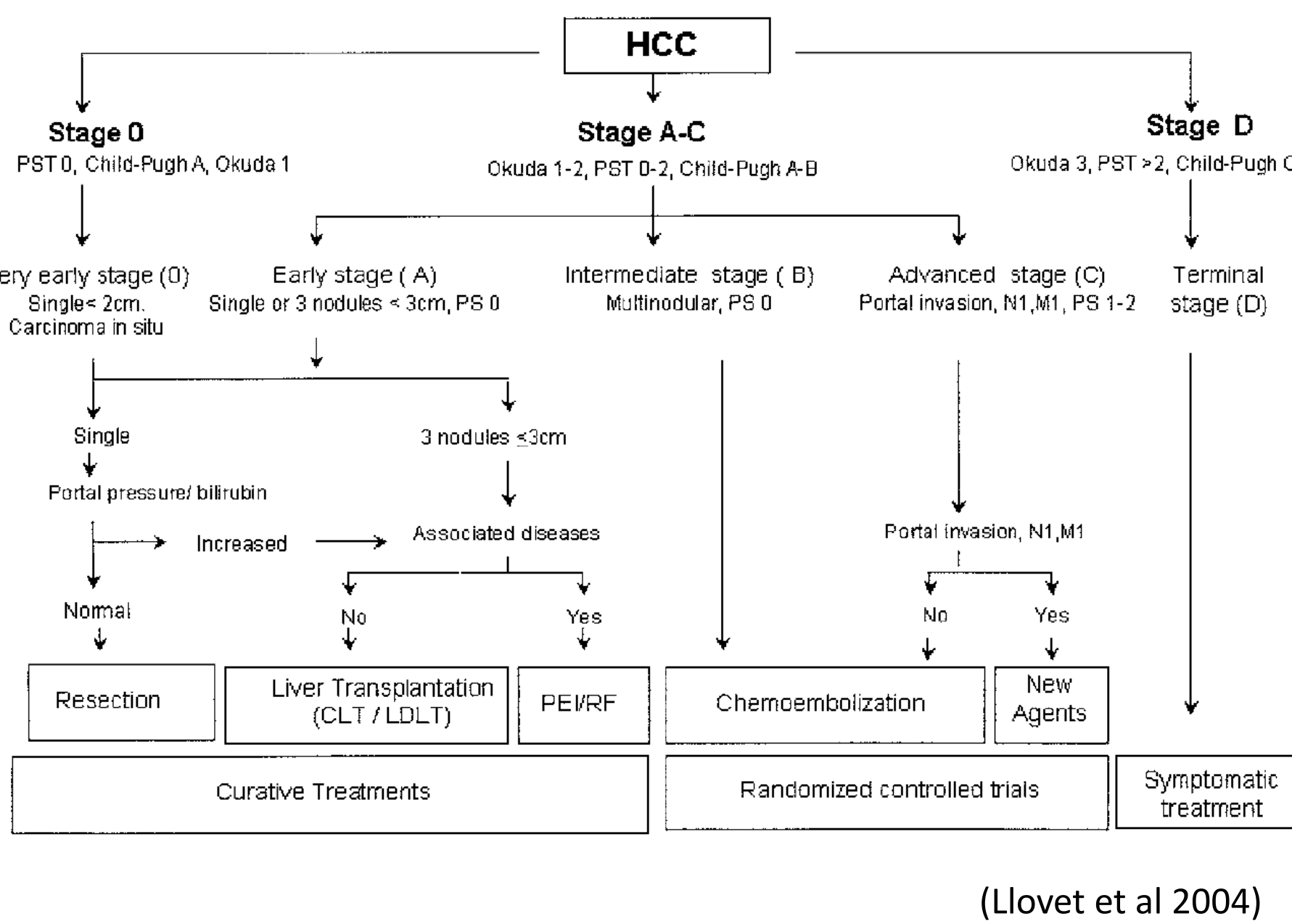
### Treatment for HCC

<b>Within Milan criteria</b> - Single tumor < 5 cm or - 2-3 tumors not exceeding 3 cm, and - No vascular invasion	Liver transplant for unresectable HCC
<b>Outside Milan criteria</b>	<b>Locoregional therapy</b> - Radiofrequency ablation (RFA) - Transarterial chemoembolization (TACE) - Transarterial radioembolization (TARE)

### TARE

- Delivers yttrium-90 (Y-90), high energy beta particle emitting radio-isotope, directly to tumor through hepatic artery
- Good safety profile because it provides lethal dose to tumor, minimizes toxicity to surrounding tissue
- Rare complication: radiation pneumonitis, with an incidence of less than 1%, in patients with HCC<sup>1</sup>

### Barcelona-Clinic Liver Cancer staging classification



### Liver Imaging Reporting and Data System (LIRADS)

LR-1	Definitely benign
LR-2	Probably benign
LR-3	Intermediate probability of malignancy
LR-4	Probably HCC
LR-5	Definitely HCC
LR-M	Malignant but not HCC specific
LR-TIV	Tumor in vein

## Case 1

62 year old male with history of decompensated cirrhosis secondary to hepatitis C virus complicated by HCC

- HCC diagnosis: 2.9 x 2.0 x 2.6 cm LI- RADS 5 lesion , 3.1 X 2.8 X 3.0 cm LI-RADS 5 lesion
- Treatment: BCLC class B – Y-90 with bridge to transplant

### Initial course:

- Treated with Y-90 twice, 1 month apart between sessions
- After 2 months, patient developed dry cough with pleuritic chest pain, dyspnea on exertion, fatigue, and malaise
- Prescribed prednisone 20 mg for 4 days and benzonatate for symptomatic relief

### First Evaluation:

- Initial work up: CXR showed bilateral airspace opacities and consolidations in upper lobes
- CT chest: **bilateral perihilar and central ground glass opacities, concerning for pneumocystis carinii pneumonia, multifocal pneumonia or active tuberculosis (Figure 1)**
- Infectious work up: AFB, beta-D glucan, aspergillus antibody, cryptococcus antibody, histoplasma antigen, and fungal culture of sputum were negative
- 1<sup>st</sup> Bronchoscopy
  - Normal bronchial mucosa and anatomy
  - BAL: cytology negative for malignancy, GMS negative for pneumocystis jirovecii, AFB stain negative for TB
- Patient was discharged home with plans for repeat outpatient bronchoscopy

### Second presentation:

- Presented for outpatient repeat bronchoscopy with biopsy, however was hypoxic to 85% on room air and continued dry cough and dyspnea on exertion

### Second evaluation:

- CXR: redemonstrated bilateral consolidations
- 2<sup>nd</sup> Bronchoscopy
  - Normal bronchial mucosa and anatomy
  - BAL: cytology negative for malignancy; AFB stain, fungal culture, CMV culture and bronchial culture negative
  - Lung biopsy: poorly oriented fragments of alveolar and respiratory mucosa with anthracotic pigment deposition
- Steroids and antibiotics were deferred given unclear etiology of CT findings
- Re-review of initial CT chest: findings more consistent with fibrosis rather than active infection.

### Remaining disease course:

- Had recurrence of original LIRADS 5 lesion, and decision was to proceed with TACE
- Hepatic angiography during pre-treatment planning – **prominent arterial portal fistula (Figure 2)**

## Case 2

61 year old male with history of decompensated cirrhosis secondary to HCV complicated by portal vein thrombosis and unresectable HCC

- HCC diagnosis: infiltrative 7 cm LIRADS 5 with tumor thrombus
- Treatment: BCLC class C – Y-90

### First Pretreatment Evaluation

- 99mTc-MAA scan: 7.8% shunting from right hepatic artery to lung

### First Y-90 treatment

- Y-90 given: 131.8 Gy delivered to right hepatic artery
- Post-nuclear medicine scan: no radiotracer activity in extrahepatic organs or tissues

### First Post-treatment course

- 1 month later: MRI - 2 new HCC lesions and tumor thrombus
- Treated with TACE and sorafenib
- 2 months later: MRI - LR-TR equivocal with likely post-treatment changes
- 6 months later: MRI – viable tumor with possible invasion of vein, concerning for recurrence

### Second Pretreatment Evaluation

- 99mTc-MAA scan: 22.67% shunting from right hepatic artery to lung

### Second Y-90 treatment

- Y-90 given: 119.9 Gy delivered to right hepatic artery

### Second Post-treatment course

- 3 months later: **CT chest – bilateral predominantly peripheral peribronchial consolidations with associated mild traction bronchiectasis and scattered nodular opacities in the left upper lobe, which could be consistent with organizing pneumonia, radiation pneumonitis from prior Y-90, or COVID (Figure 3)**
- COVID test was negative. Patient determined to have radiation pneumonitis secondary to Y-90. He was asymptomatic and discharged home without any treatment

## Figures

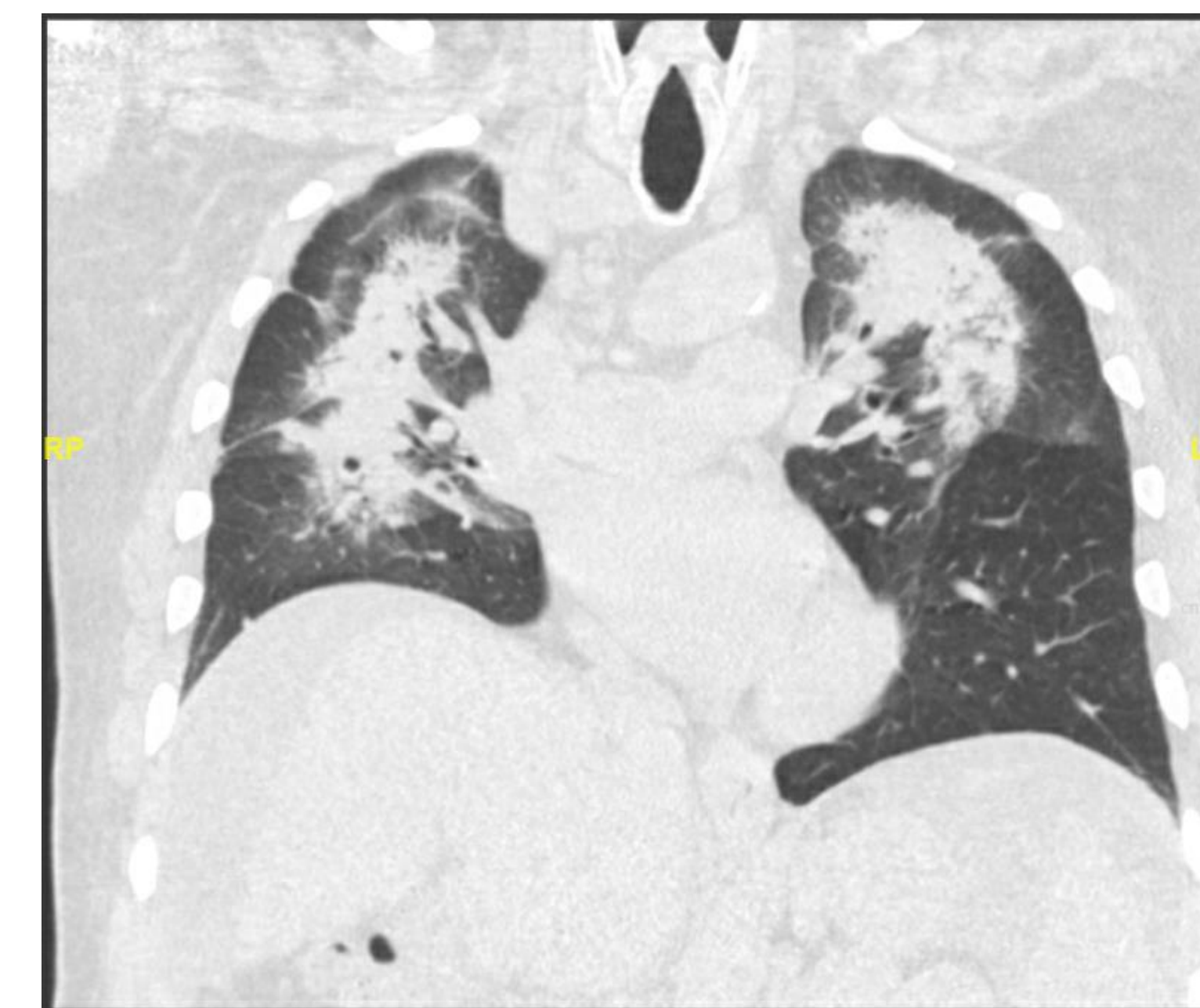


Figure 1: CT chest of case 1; 2 months post Y-90



Figure 2: Hepatic angiography – prominent arterial portal fistula (yellow arrow)

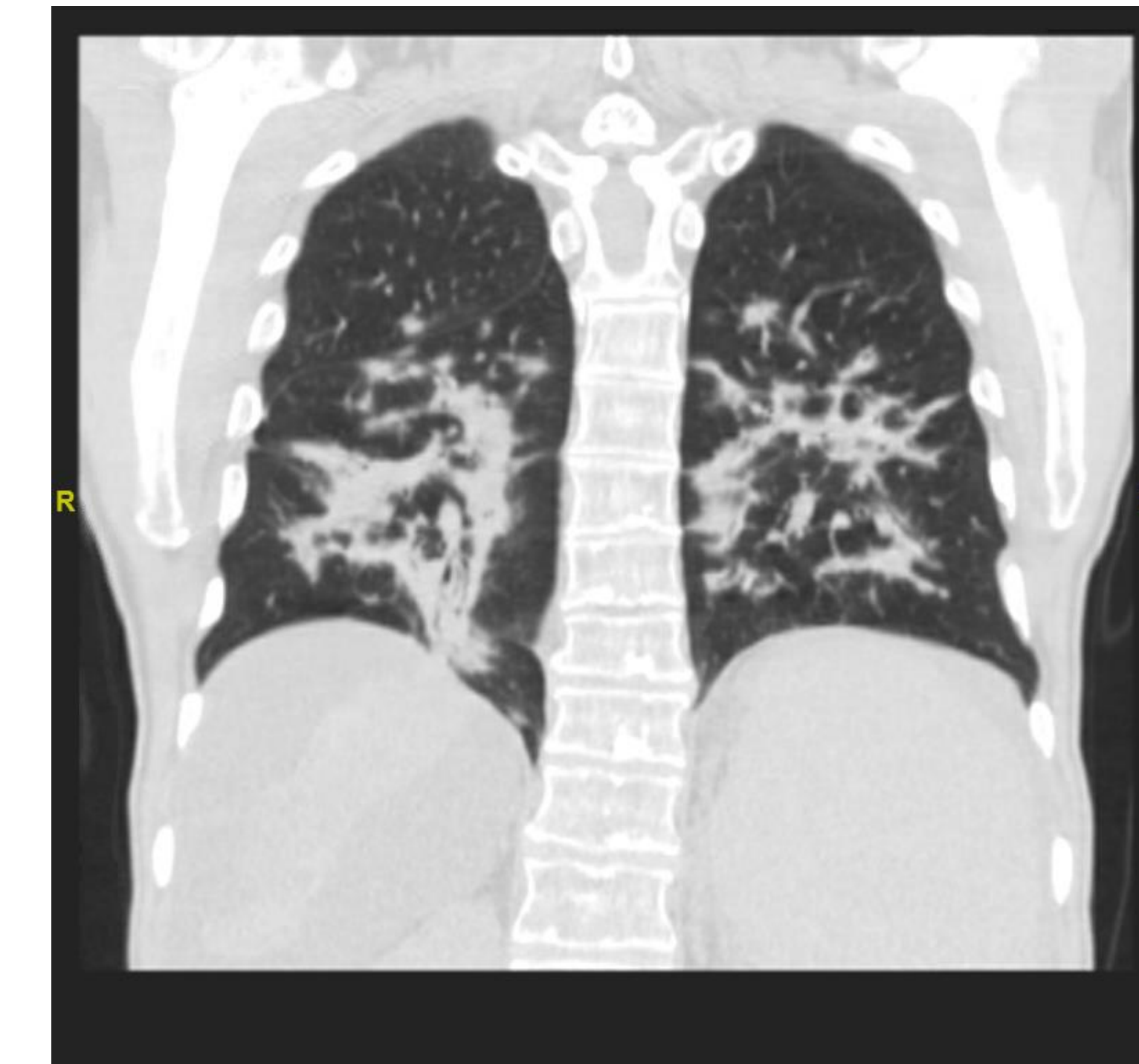


Figure 3: CT chest of case 2; 3 months after second treatment with Y-90

## Discussion

Radiation pneumonitis

- Typical presentation**
  - Symptoms: dry cough, exertional dyspnea
  - Restrictive ventilator pattern on pulmonary function testing
  - Respiratory status: range from mild hypoxia to severe respiratory failure<sup>3</sup>
- Timing:** onset usually 1-2 months, but as late as 6 months after treatment with Y-90<sup>3,4</sup>
- Imaging (CT chest):** bilateral ground glass opacities and ill-defined patchy opacities with relative peripheral and hilar sparing<sup>3,4</sup>
- Histology findings:** presence of radioactive globules or scattered microspheres is diagnostic; can be nonspecific generalized inflammation<sup>5</sup>
- Other work up:** rule out cardiac and infectious etiologies that may demonstrate ground glass opacities<sup>3</sup>
- Treatment:** steroids – no standardized dose or duration<sup>3</sup>
- Risk factors:** high lung shunting fraction (LSF), aggressive nature of disease (such as HCC) leading to collaterals and arteriovenous shunts
  - Case 1: presence of arterial portal fistula
  - Case 2: LSF noted to be 22.67%

Reducing risk of radiation pneumonitis

- Hepatic angiography and 99mTc-MAA can be performed to estimate LSF<sup>3,4</sup>

LSF	Reduce radiation dose by
10-15%	20%
16-20%	40%
>20%	Avoid altogether

- Lungs should not receive more than 30 Gy in a single dose or more than 50 Gy over multiple doses<sup>3,4</sup>

## Conclusion

TARE is a useful interventional radiology technique and an alternate local therapy to treat HCC. High lung shunt fraction and dose of radiation to the lungs are linked to radiation pneumonitis. It is not only appropriate to perform pre-treatment planning with hepatic angiography and 99Tc-MAA to approximate the lung shunt fraction, but also important to time it as close as possible to a patient's treatment session given the highly vascular nature of HCC and subsequent risk of developing new collateral blood vessels and more arteriovenous shunting. Although the incidence of radiation pneumonitis is less than 1%, it is important to identify this complication as respiratory failure can result and treatment with steroids can be initiated in the appropriate candidates.

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