
بسم الله الرحمن الرحیم

20th Congress of Iranian Society of Medical Oncology & Hematology

بیستمین کنگره سراسری انجمن پزشکان انکولوژی و هماتولوژی ایران (سال ۱۴۰۰)

IRANIAN SOCIETY OF MEDICAL ONCOLOGY AND HEMATOLOGY
ISMOH

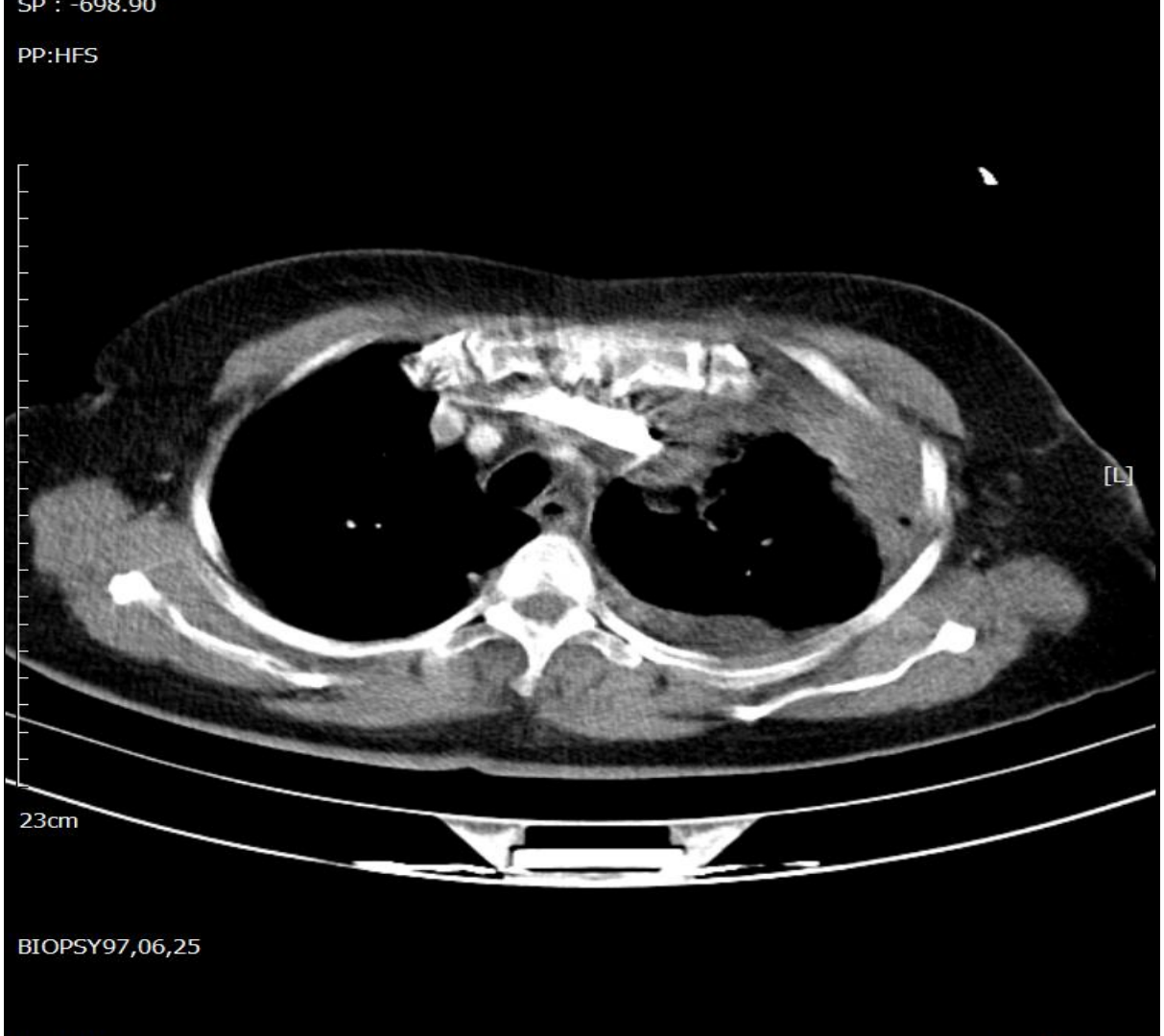
Lung Cancer Panel Discussion

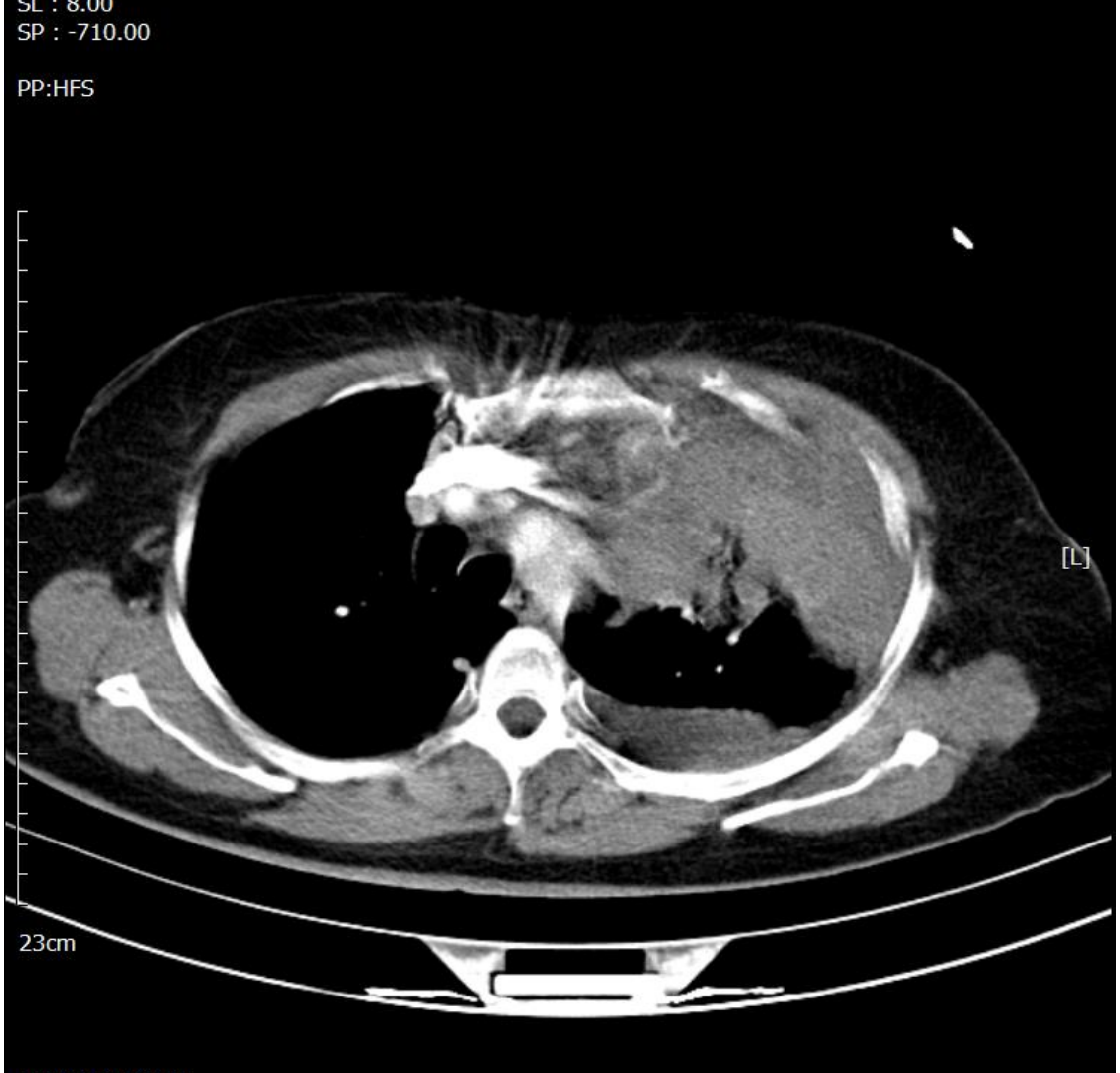
Panel Moderator: Dr. Sharareh Seifi
Panel Members:Dr. Farnaz Taslimi, Dr. Adnan Khosravi, Dr. Sara Haseli, Dr. Mitra Rezaee, Dr. Babak Salimi, Dr. Kambiz Sheikhi, Dr. Atefeh Abedini

A 65 years old non-smoker woman presented with 3 months productive cough and dyspnea in 1397.

P/E: decreasing lung sound.
P.M.Hx: DM+, HTN+

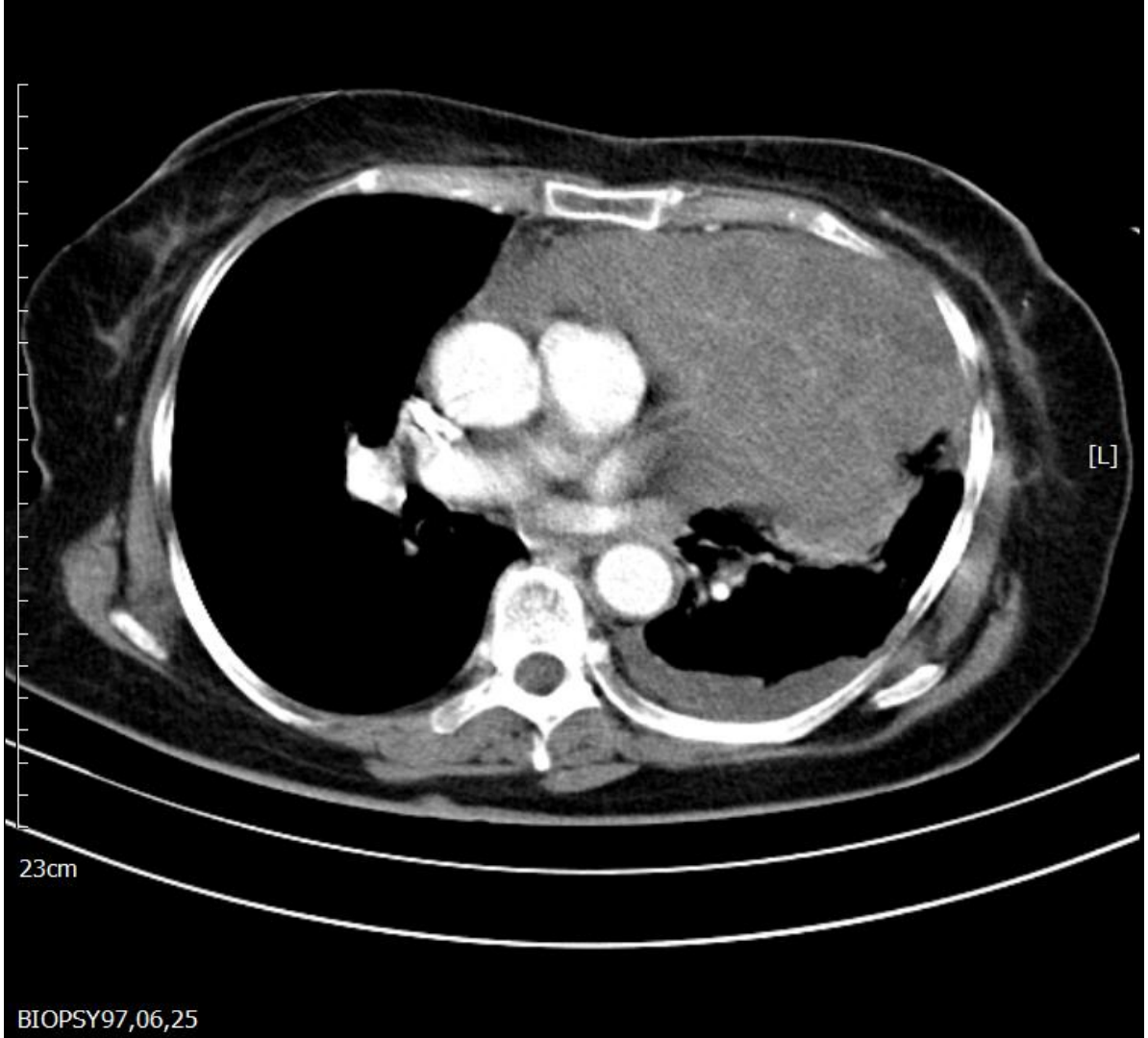
Chest CT/Scan was showing:

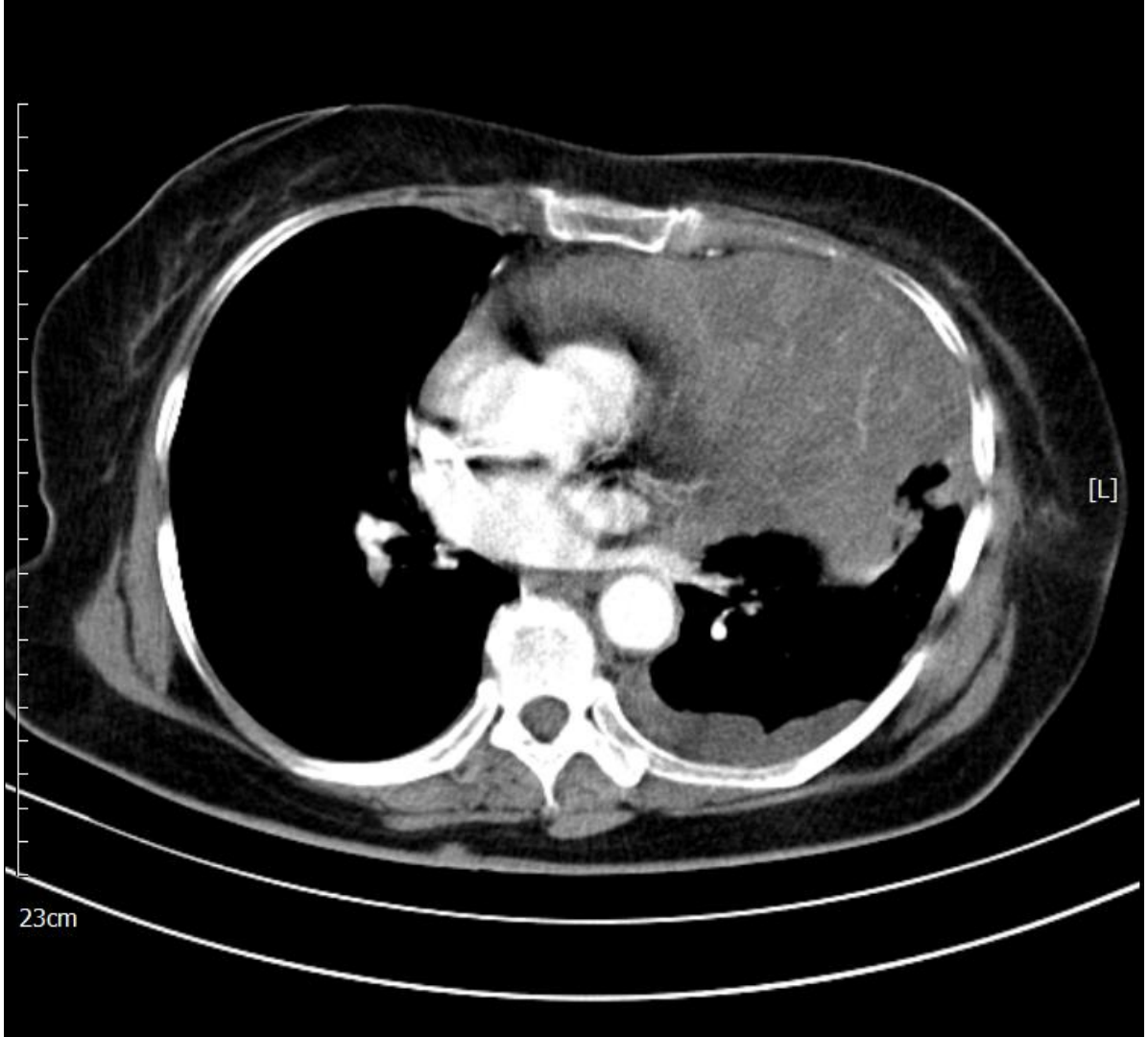

SP : -698.90
PP:HFS
[L]
23cm
BIOPSY97,06,25

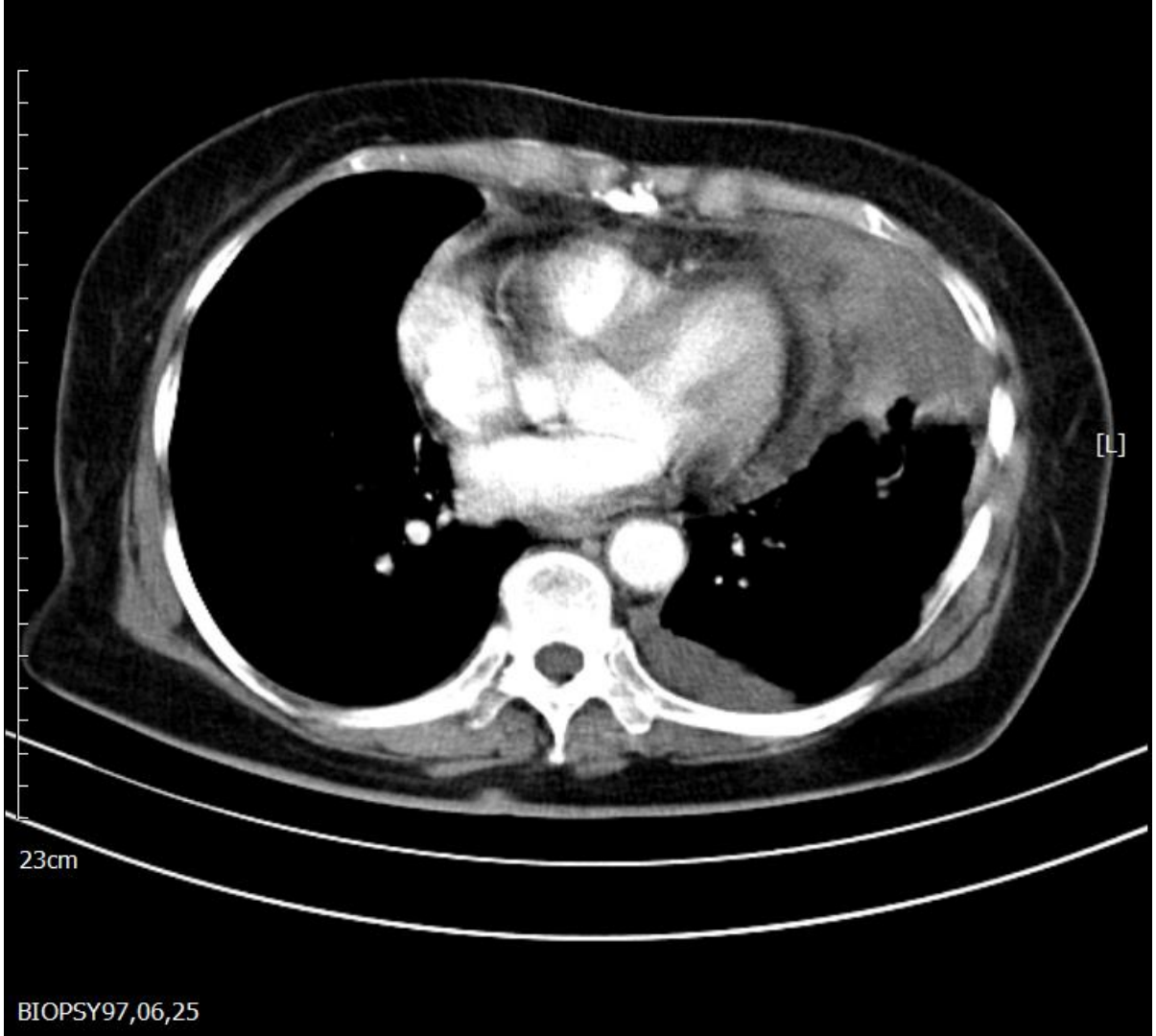

SL : 8.00
SP : -710.00
PP:HFS
[L]
23cm

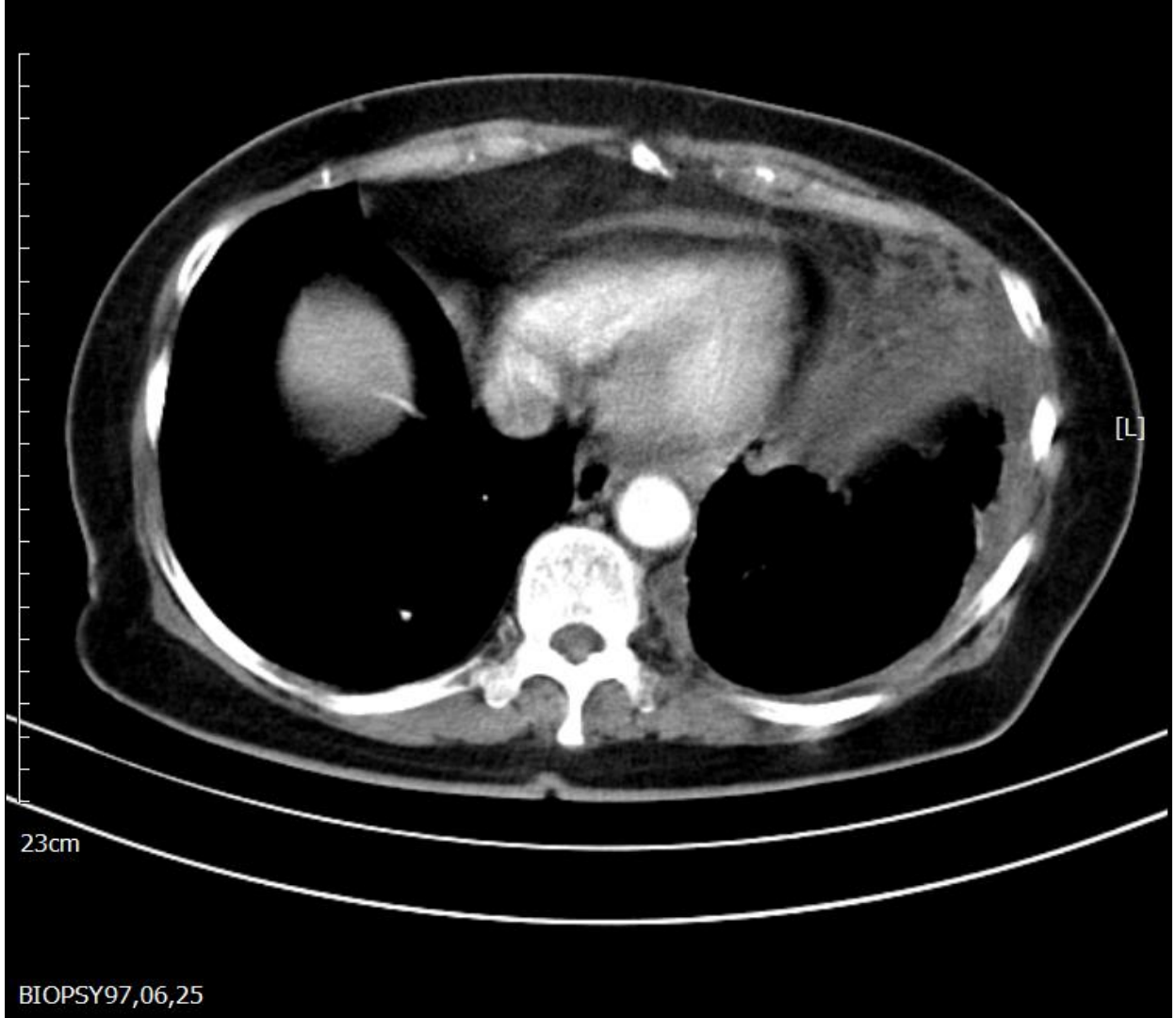

SP : -721.10
PP:HFS
[L]
23cm


[L]
23cm
BIOPSY97,06,25

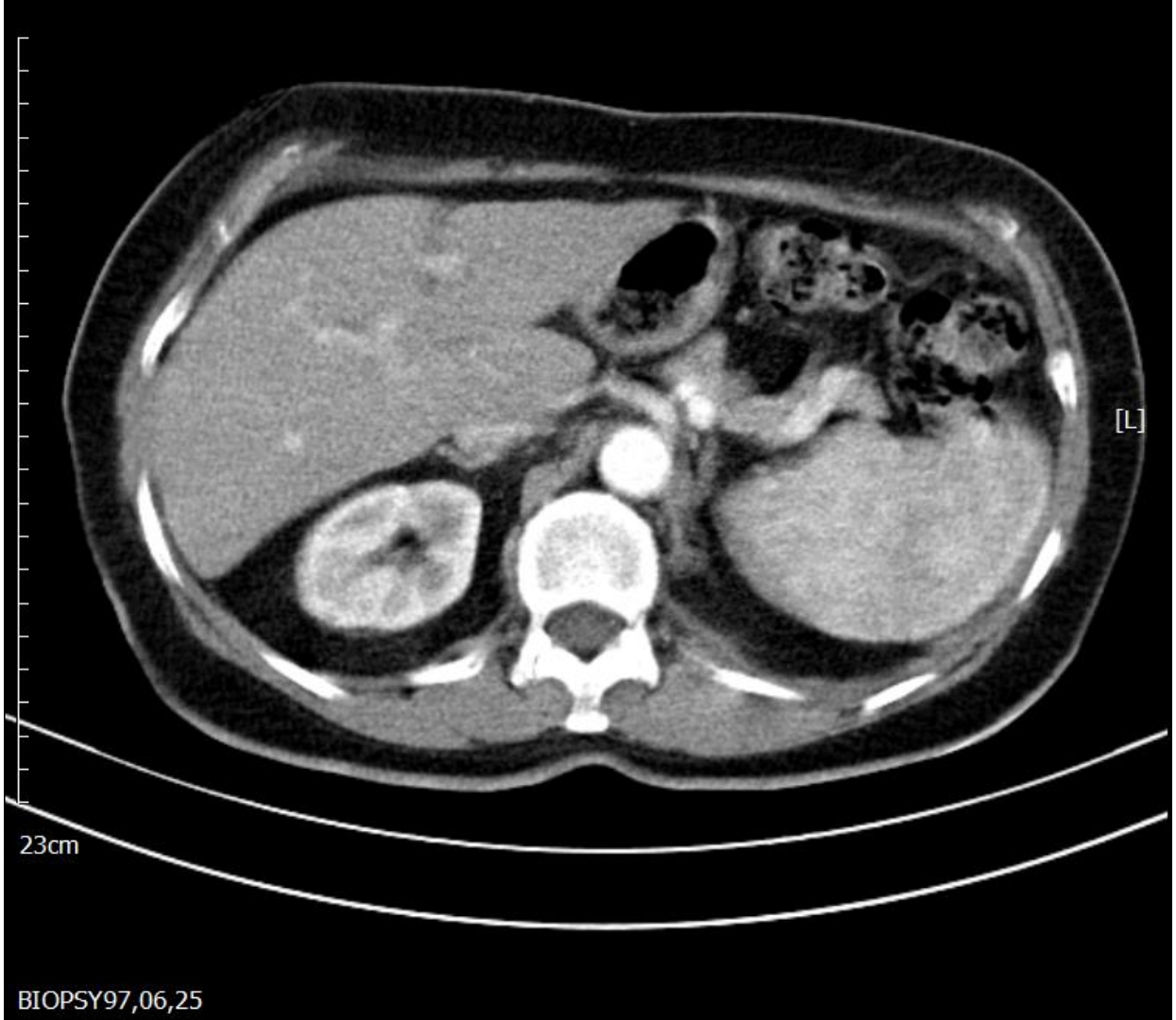

[L]
23cm
BIOPSY97,06,25


[L]
23cm


[L]
23cm
BIOPSY97,06,25


[L]
23cm
BIOPSY97,06,25


[L]
23cm
BIOPSY97,06,25


[L]
23cm
BIOPSY97,06,25

Next step?

1-bronchoscopy?
2-CT guided biopsy?

Bronchoscopy and CT guided core biopsy were done.

Pleural fluid cytology was negative for malignancy.

Pathology report:

شماره پرونده: 159002

Cell block

Lab No. 97-2561C

SPECIMEN:

Bronchoalveolar lavage.

(Smear and cell block).

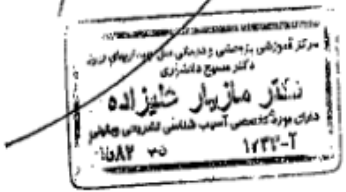
MICROSCOPIC EXAMINATION:

Support below diagnosis.

DIAGNOSIS:

Negative for malignancy.

M.Bahadori M.D ..... M.PoorAbdollah M.D ..... A.Dorudinia M.D .....
M.Alizadeh M.D ..... M.Rezaee M.D.....



تاریخ درخواست : ۲۶/۸/۹۷
تاریخ گزارش: ۱۵:۳۲ ۲۹/۸/۹۷
شماره پرونده : 159002

Pathology

Lab No. 97-2804

SPECIMEN :

TransBronchial lung biopsy.

CLINICAL DATA :

CT file: Mass in left lung. Bronchoscopic file: No abnormality.

MACROSCOPIC:

The specimen received in formalin and consists of five irregular fragments of creamy soft tissue totally measuring 0.4x0.2x0.2cm. (Totally submitted in 1 block)

MICROSCOPIC:

Sections support the following diagnosis.

DIAGNOSIS:

TransBronchial Lung Biopsy:

-Plenty of parietal pleural tissue.

-One fragment of lung with no significant pathologic changes.

-Detached respiratory epithelial cells.

نام بیمار : زهرا صادق
سن : ۶۵ ساله
تاریخ درخواست : ۲۹/۸/۹۷

پرسنل فعال : کامبیز سیمی
تاریخ مراجعه : ۲۱/۸/۹۷
تاریخ گزارش: ۰۸:۳۸ ۰۵/۹/۹۷
شماره پرونده : 159002

Pathology

Lab No. 97-2860

SPECIMEN :

Left lung mass, core needle biopsy.

CLINICAL DATA :

History of dyspnea and hemoptysis.

CT file: Mass in left lung.

MACROSCOPIC:

The specimen received in formalin and consists of multiple filliform tan soft tissue fragments totally measuring 5cm in length and 0.1cm in diameter. Totally submitted in 1 block.

MICROSCOPIC:

H&E stained sections and IHC for TTF1(+) and TG(-) support the following diagnosis.

DIAGNOSIS:

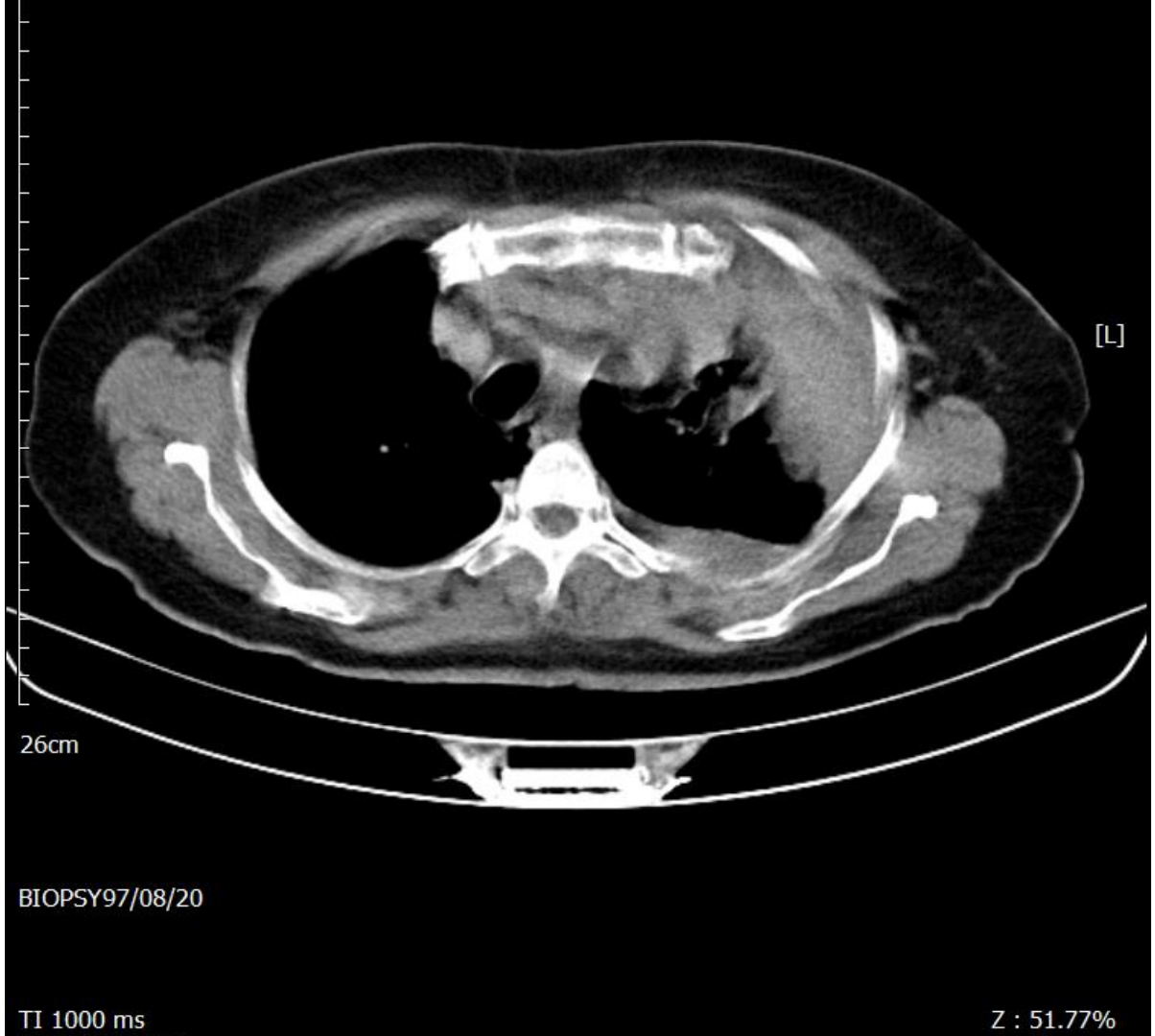
Left lung mass, core needle biopsy:

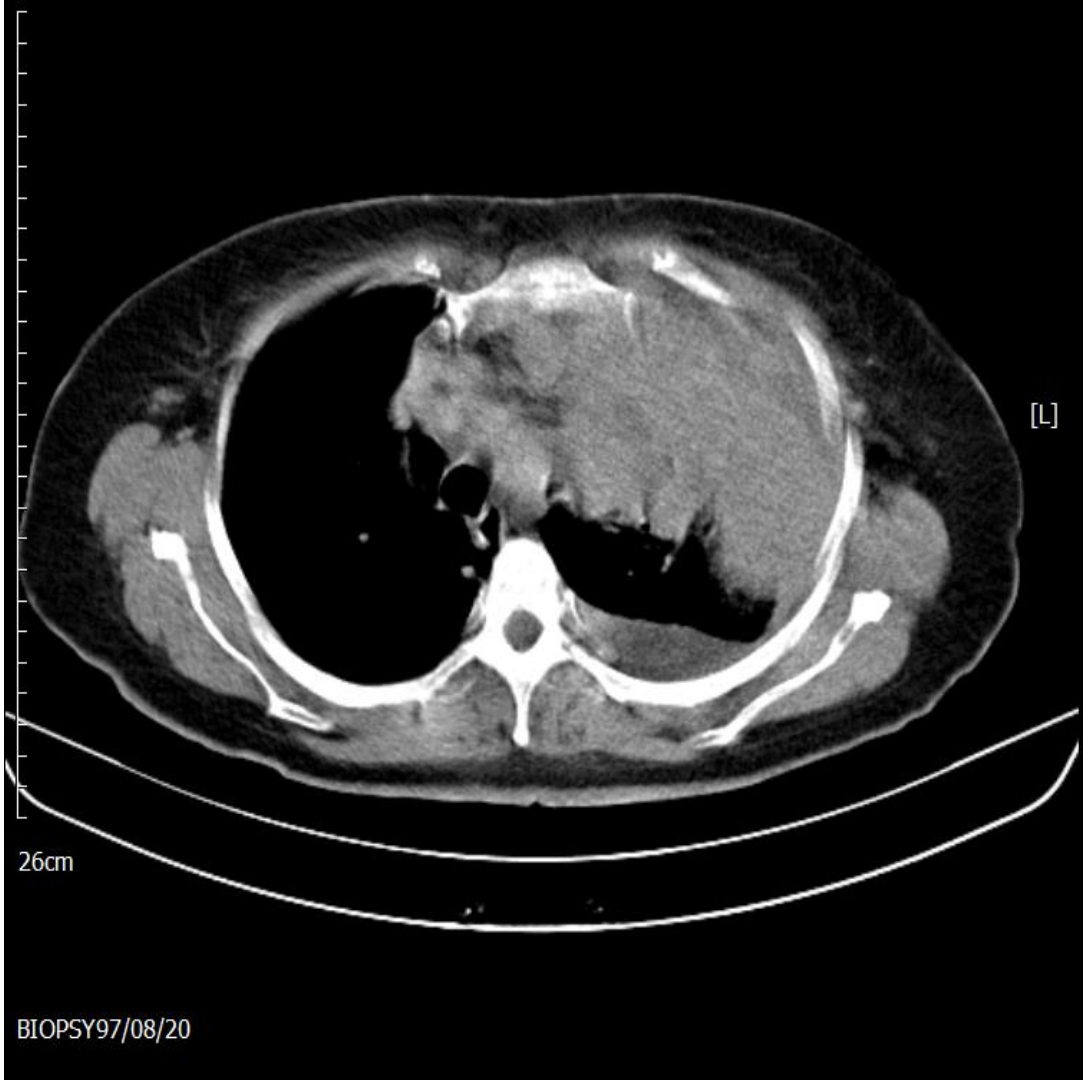
-Primary lung adenocarcinoma; predominantly lepidic and micropapillary pattern.

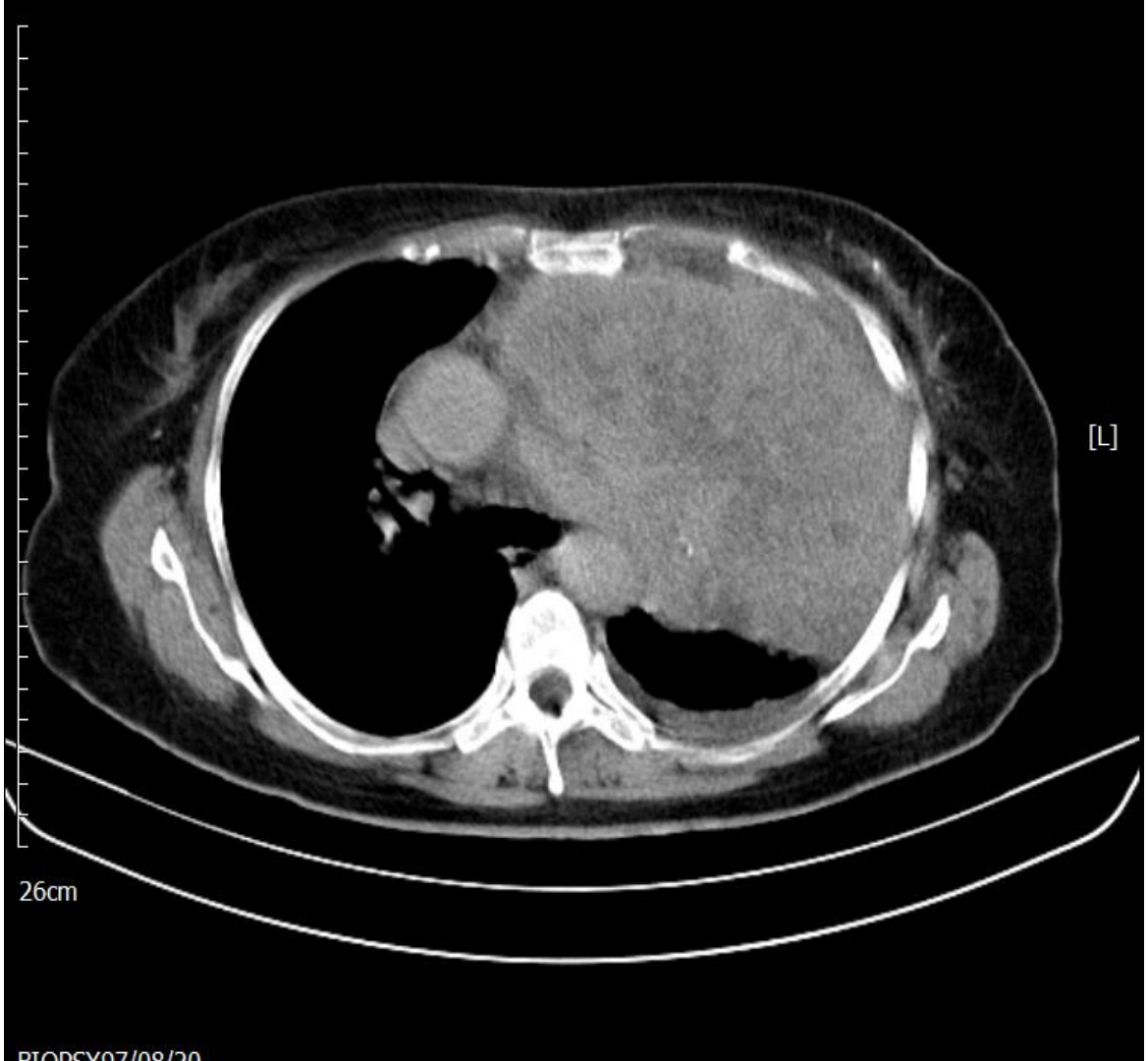
ICD-0 Code C34.9 M-8140/3

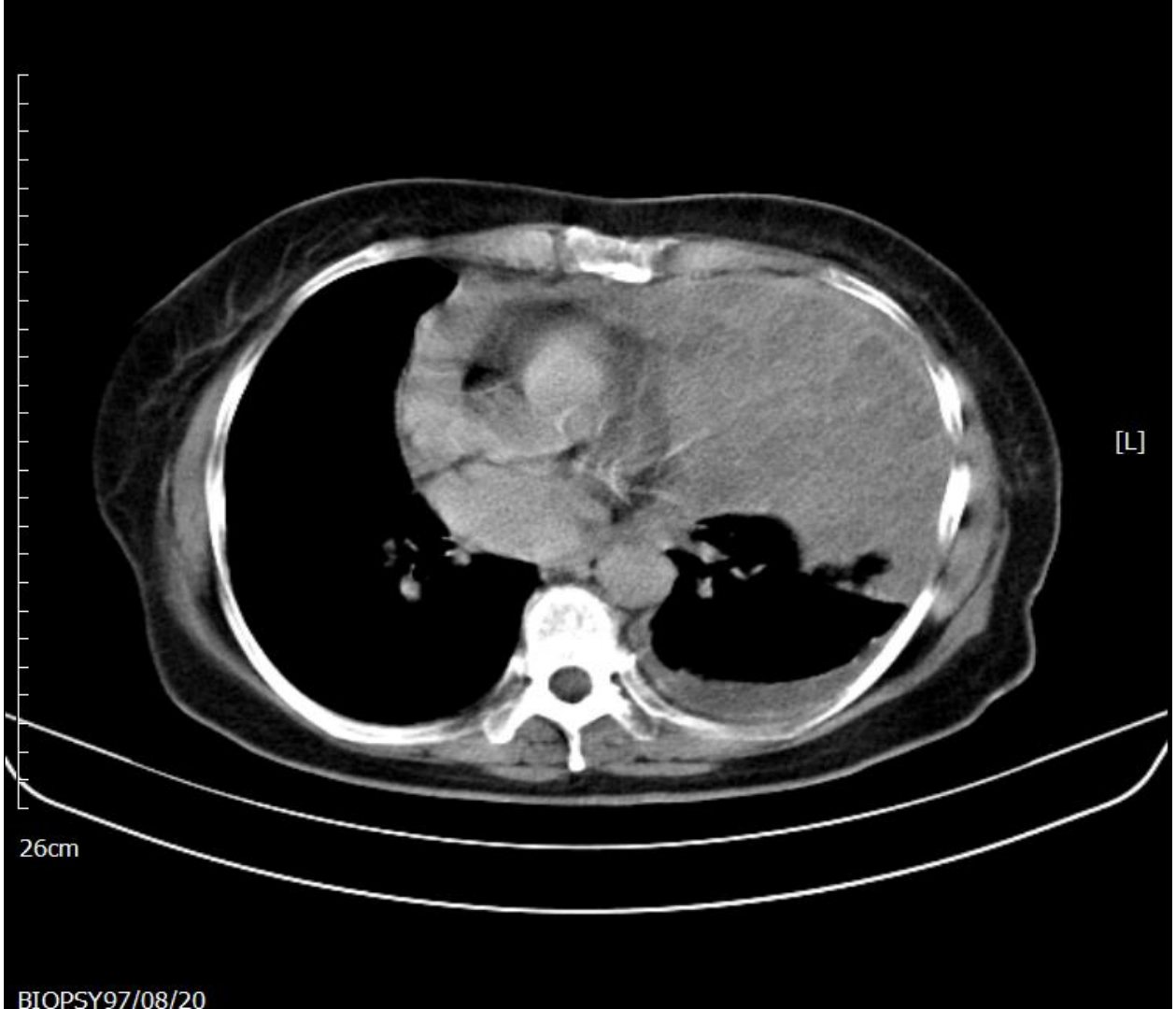
What do you do ?

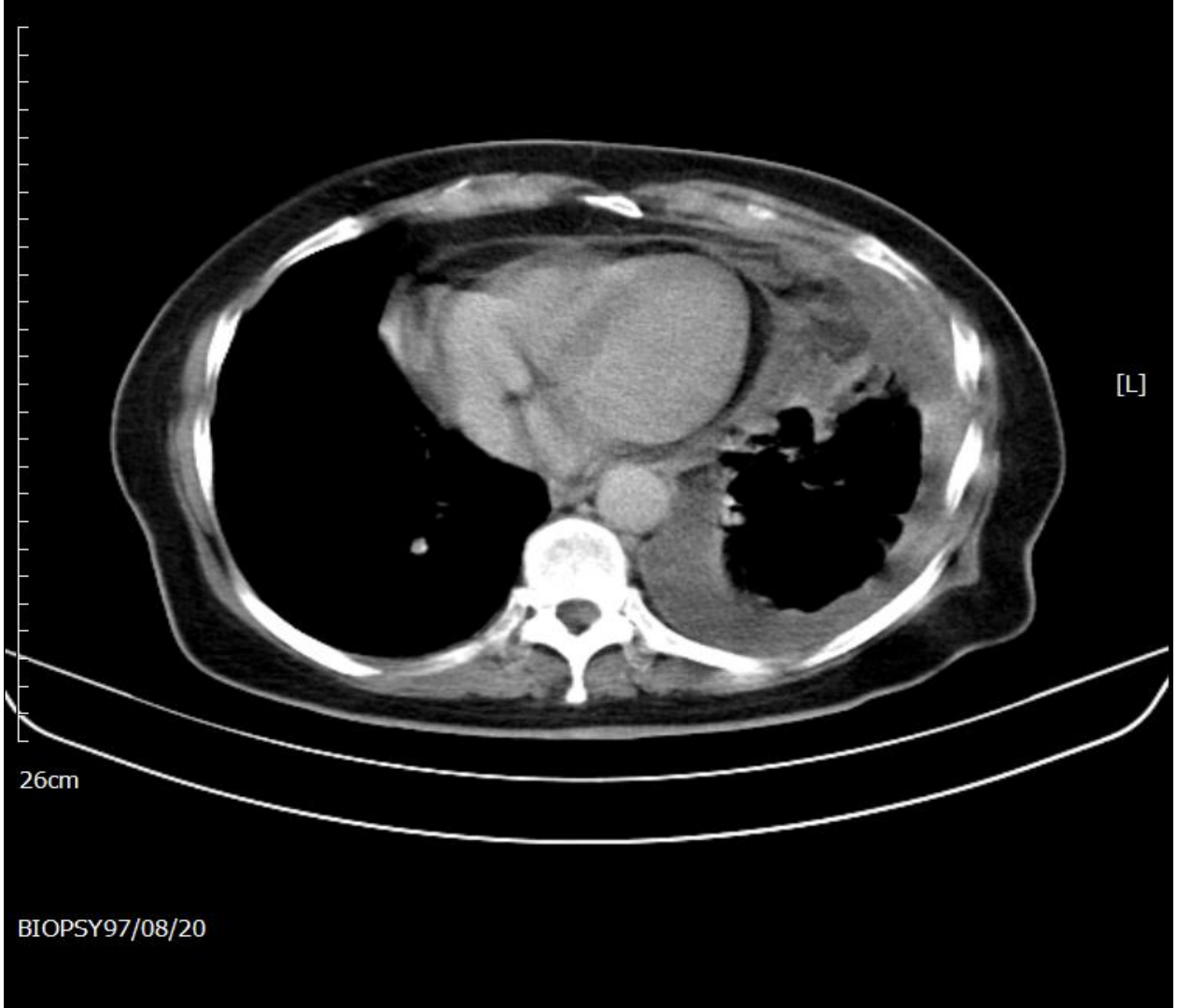
Staging?
Molecular study?

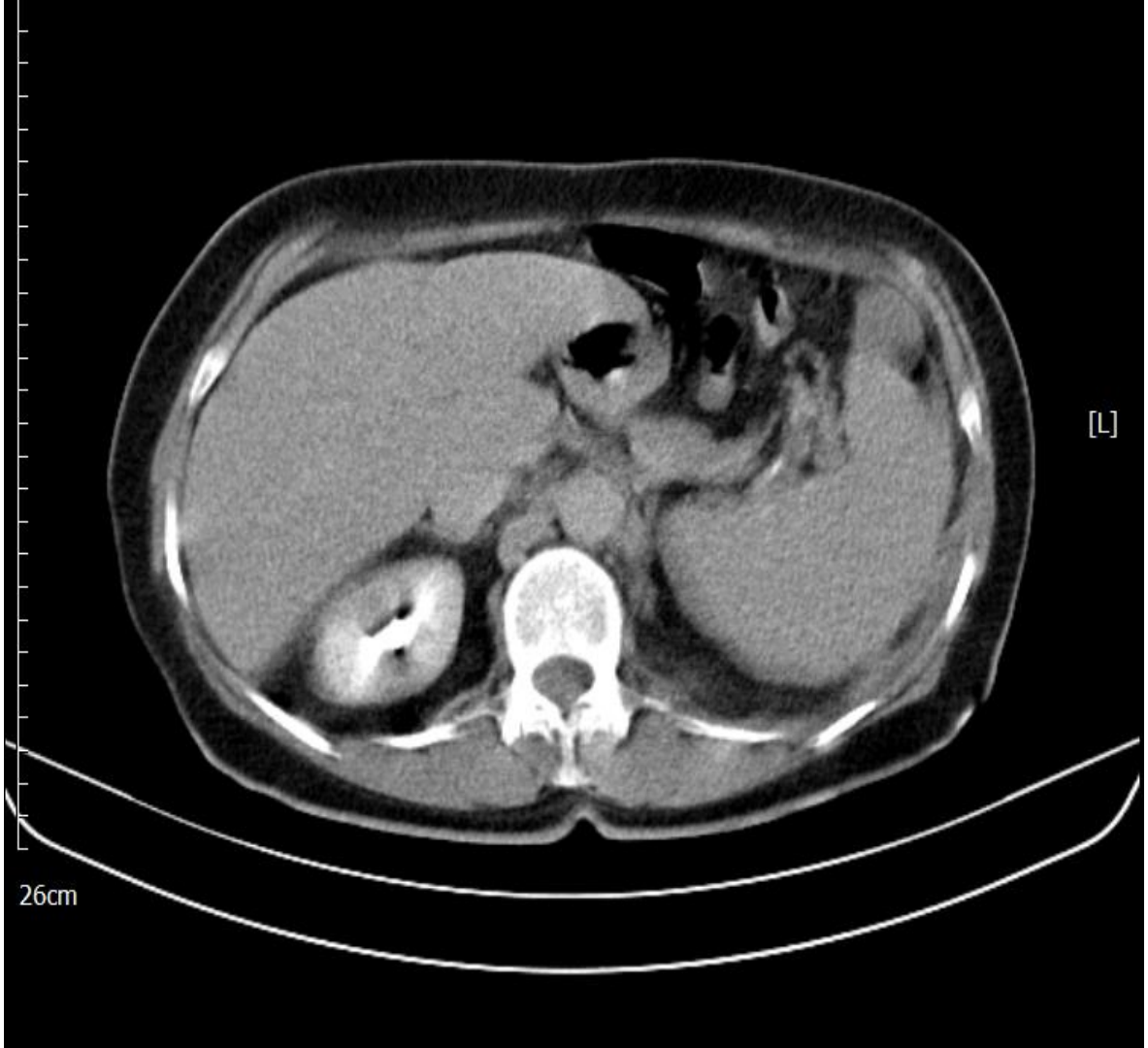

[L]
26cm
BIOPSY97/08/20
TI 1000 ms
Z : 51.77%


[L]
26cm
BIOPSY97/08/20


[L]
26cm


[L]
26cm
BIOPSY97/08/20


[L]
26cm
BIOPSY97/08/20

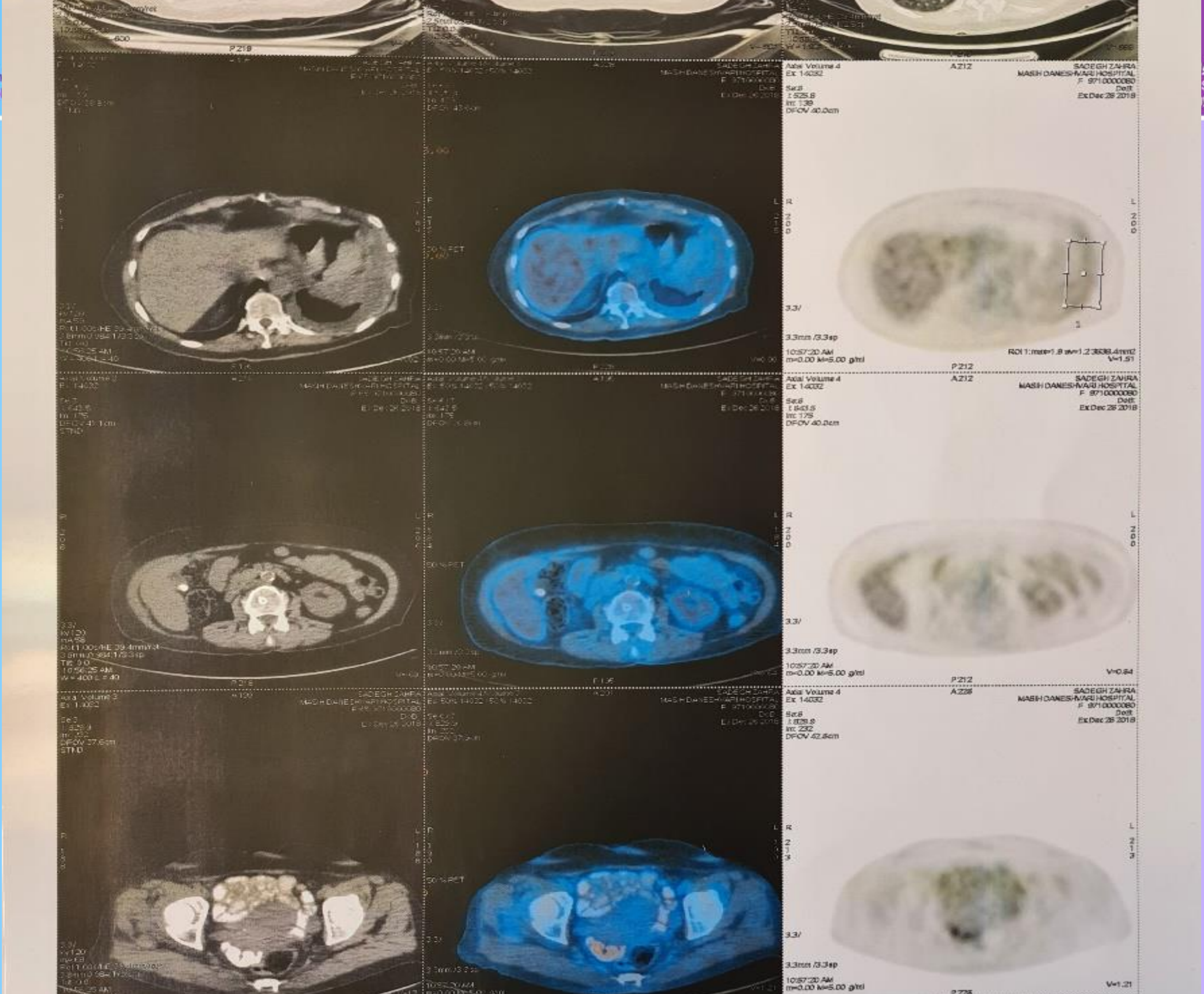

[L]
26cm

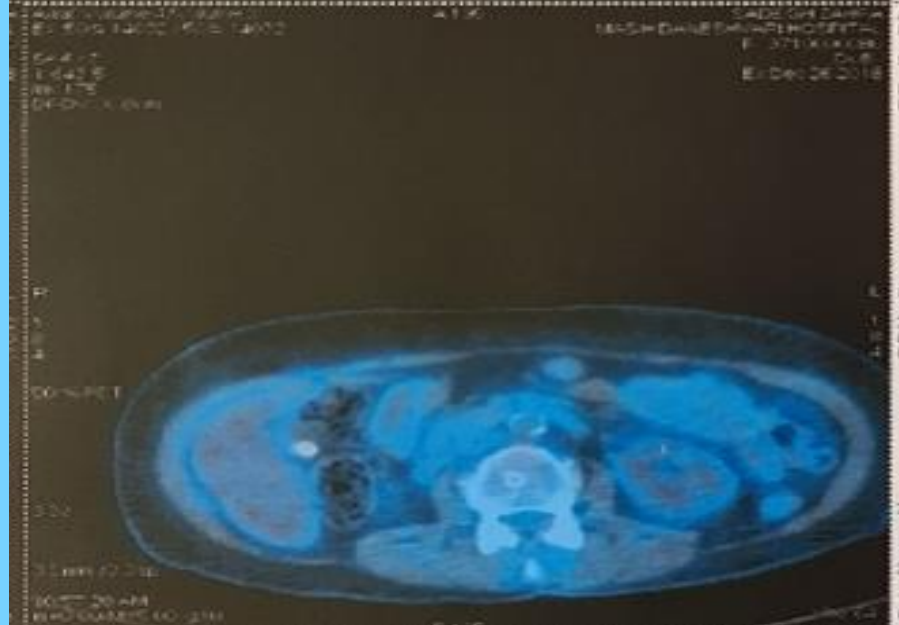
Brain MRI:Nl

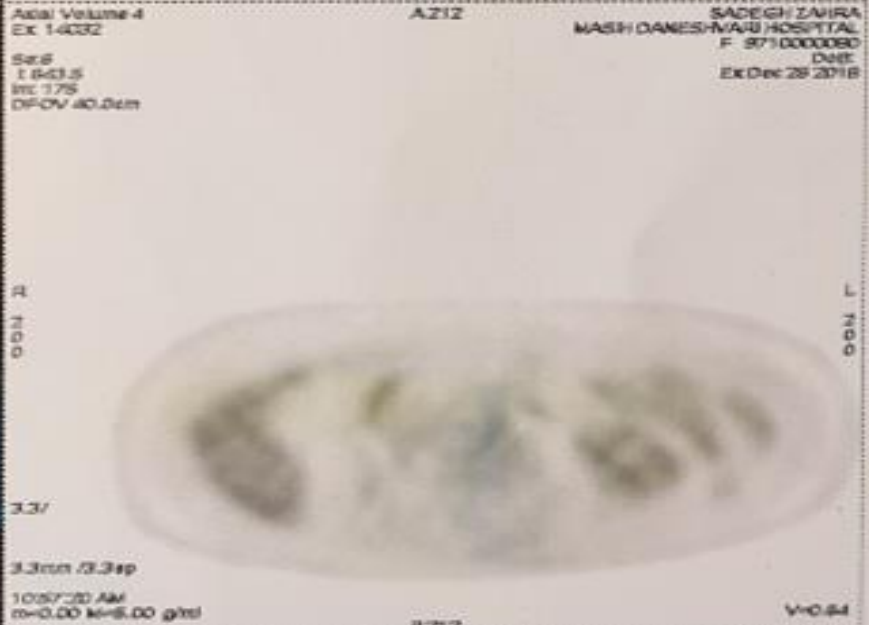
PET/CT Scan :

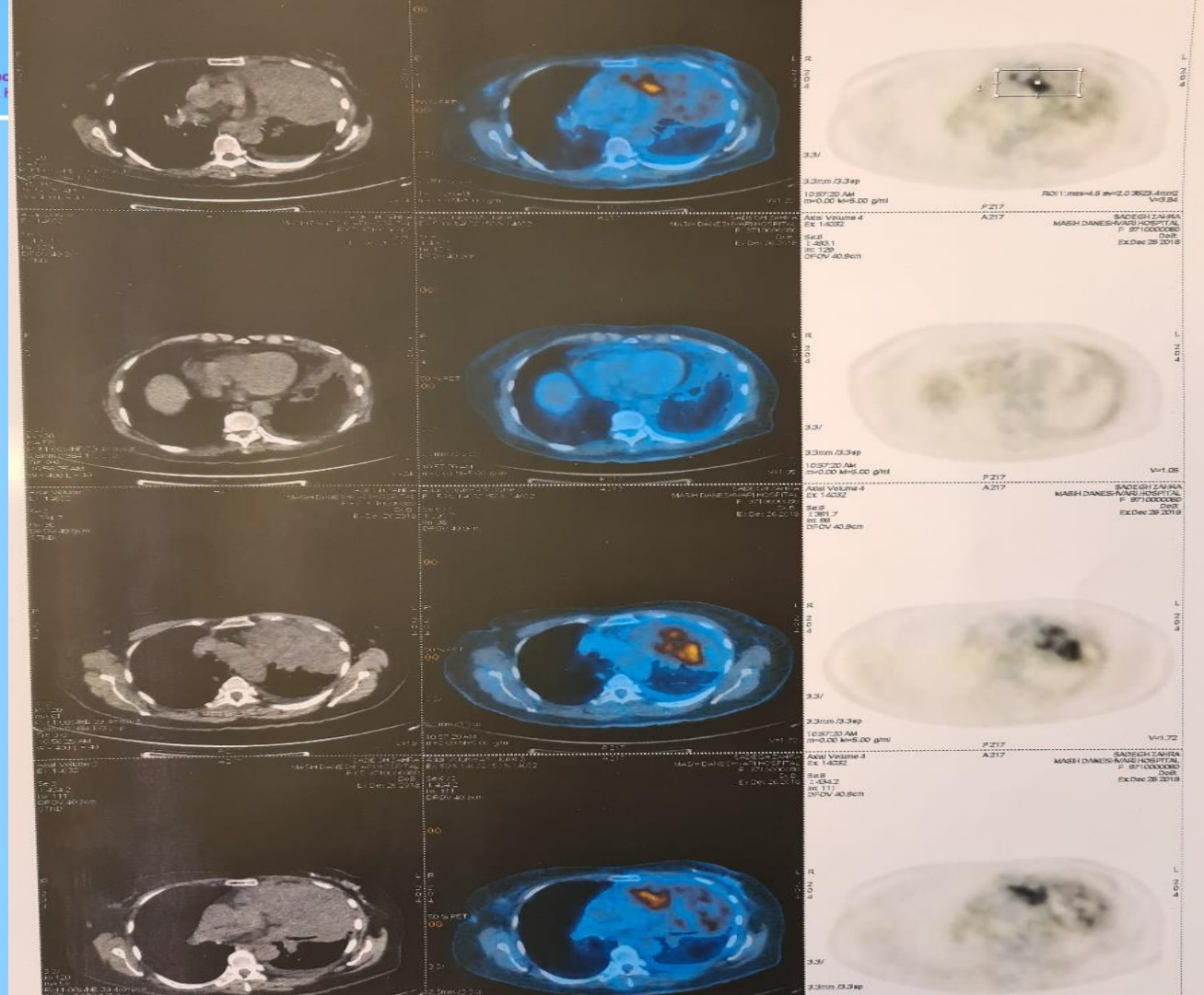
Congress of Iran
of Medical Oncol

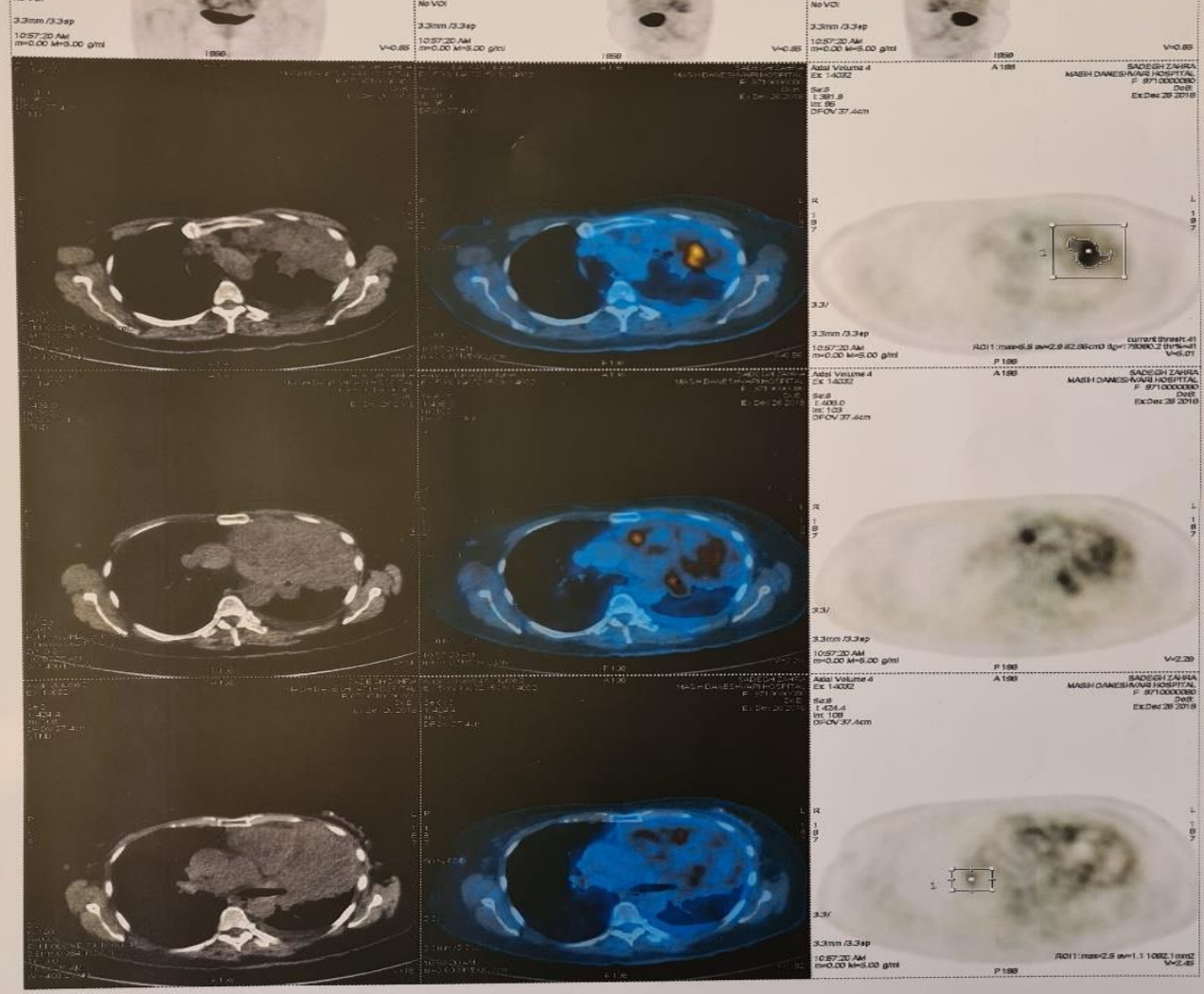
انجمن هماتولوژی و انکو
Society of Medical
y and Hematology

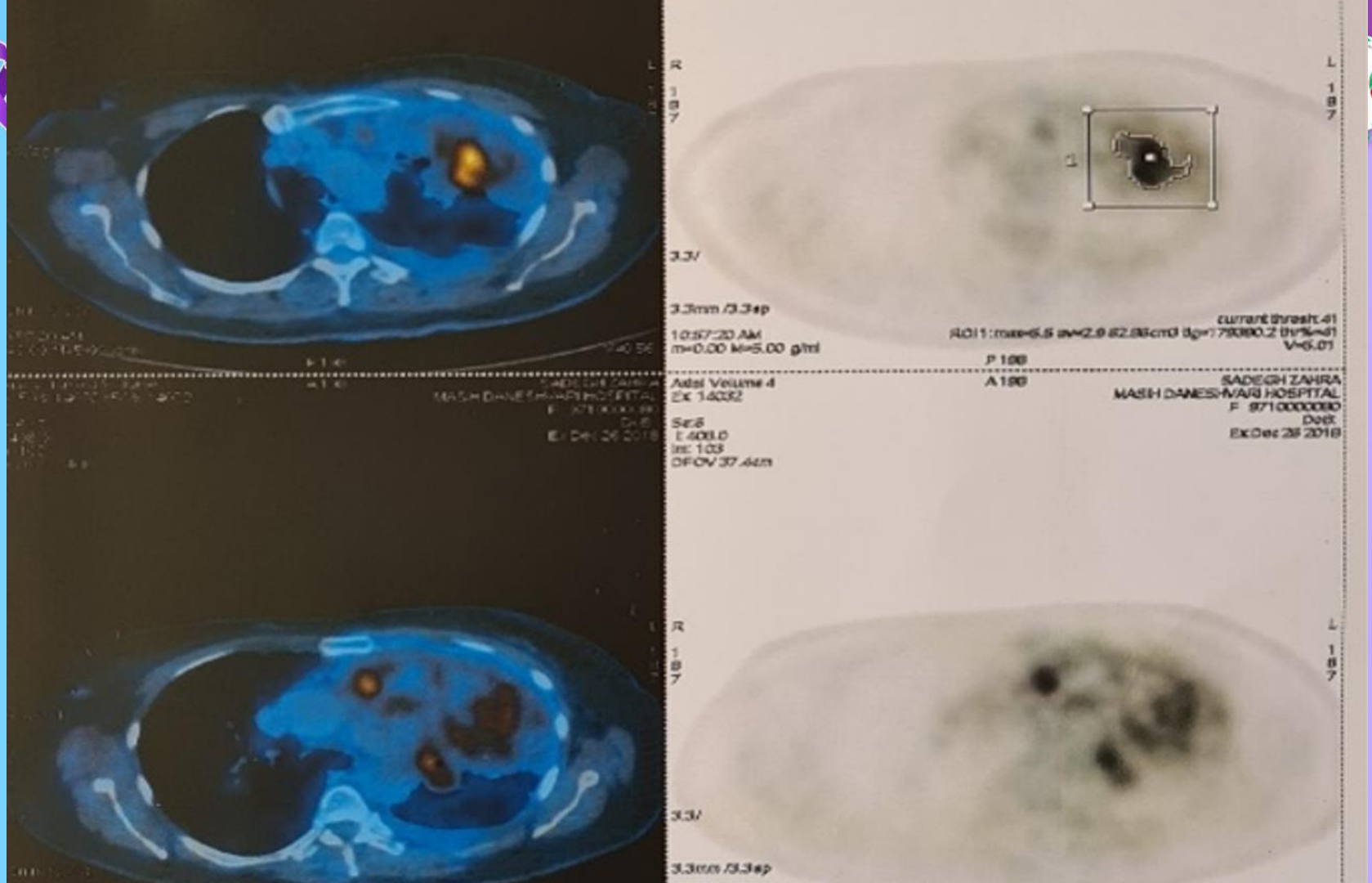











R
L
3.3mm /3.3sp
SADEGH ZAHRA
MASIH DANESHVARI HOSPITAL

Age: 65 Y/O

Exam Date: 12 / 26 / 2018 (m/d/y)

جنسیت: مونث

سن: ۶۵ سال

تاریخ اسکن: ۱۳۹۷/۱۰/۰۵

PET/CT FROM VERTEX TO MID-THIGH
With Discovery 690 GE (General Electric), 64 Slice CT & Time-of-flight (ToF)

HISTORY: **Lung Cancer**
QUESTION: **Treatment Response Evaluation**

TECHNIQUE:

Sixty minutes following administration of 257 MBq of FDG intravenously a partial body integrated PET-CT scan from vertex to proximal thighs was acquired. Sections were reconstructed in three standard orthogonal planes.

For anatomic referencing and for transmission correction purposes an unenhanced low dose CT was acquired and fused images were also generated.

BRAIN:

There is no midline shift or intracranial hemorrhage. The lateral ventricles are normal. The cerebellum and brainstem are intact. The basal cisterns are patent. The skull is intact.

Physiological FDG-uptake of the brain is seen.

NECK:

The major salivary glands of the neck are normal. The epiglottis & aryepiglottic folds, true & false vocal cords, and supra & subglottic airways are intact. The thyroid lobes have normal size & texture. No cervical lymphadenopathy is detected.

Physiological FDG-uptake of the neck is seen.

CHEST:

Lobar consolidation with heterogeneous increased metabolic activity in left upper lobe is seen, extending to left lower lobe with prominent interstitial marking (SUVmax= 5.5).

Ipsilateral hypermetabolic pleural thickening with minimal effusion is also detected (SUVmax= 1.9).

Normal variant azygos fissure is seen.

Chest wall is unremarkable. Heart size is normal.

Physiological FDG-uptake of the heart is noted.

Age: 65 Y/O
سن: ۶۵ سال

Exam Date: 12 / 26 / 2018 (m/d/y)
تاریخ اسکن: ۱۳۹۷/۱۰/۰۵

ABDOMEN & PELVIS:

Gallstone is seen.

The liver has normal size. There is no intra or extrahepatic bile duct dilatation.
The spleen and pancreas are intact. The kidneys and adrenal glands are normal.
The abdominal aorta is normal in caliber.
There is no lymphadenopathy within the abdomen.
The visible genital organs are normal. Rectum & pararectal fossa are intact. The visualized bowel loops are normal.
There is no lymphadenopathy within the pelvis.
Physiological FDG-uptake of the kidneys and the bladder are seen.

MUSCULOSKELETAL:

Normal FDG activity is seen in the axial skeleton. No blastic or lytic lesion is noted on CT.

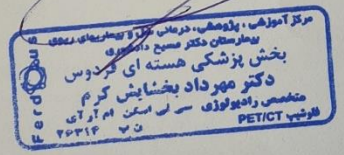
CONCLUSION:

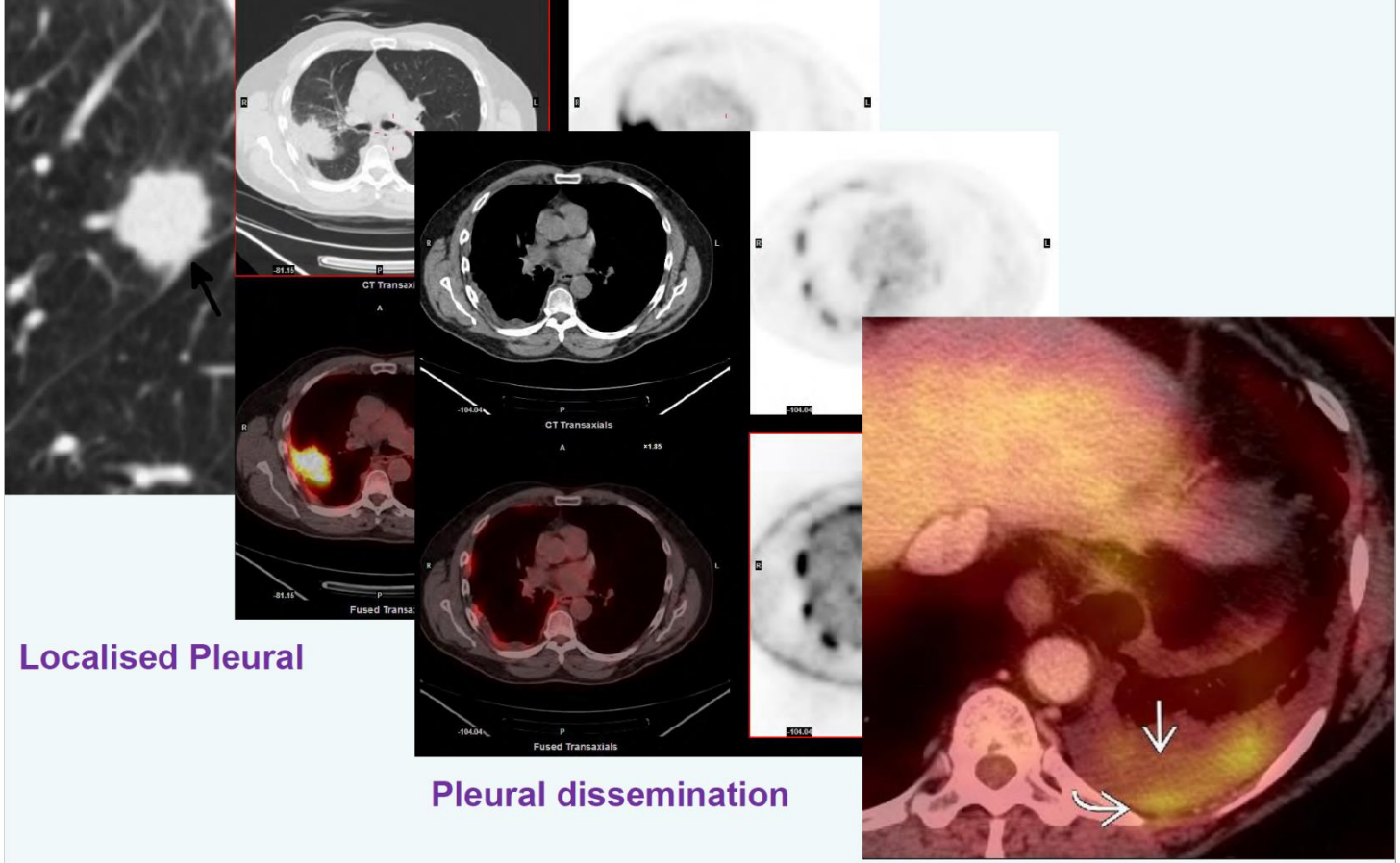
- **Lobar consolidation with heterogeneous increased metabolic activity in left upper lobe is seen, extending to left lower lobe with prominent interstitial marking.**
- **Ipsilateral hypermetabolic pleural thickening with minimal effusion is also detected.**

Type: F. P. Mohebi: 12/27/2018 10:33 AM

Mehrdad Bakhshayesh-Karam M.D.
Professor of Radiology
PET-CT Fellowship

Farahnaz Agha-Hosseini M.D..
Nuclear Physician





Localised Pleural

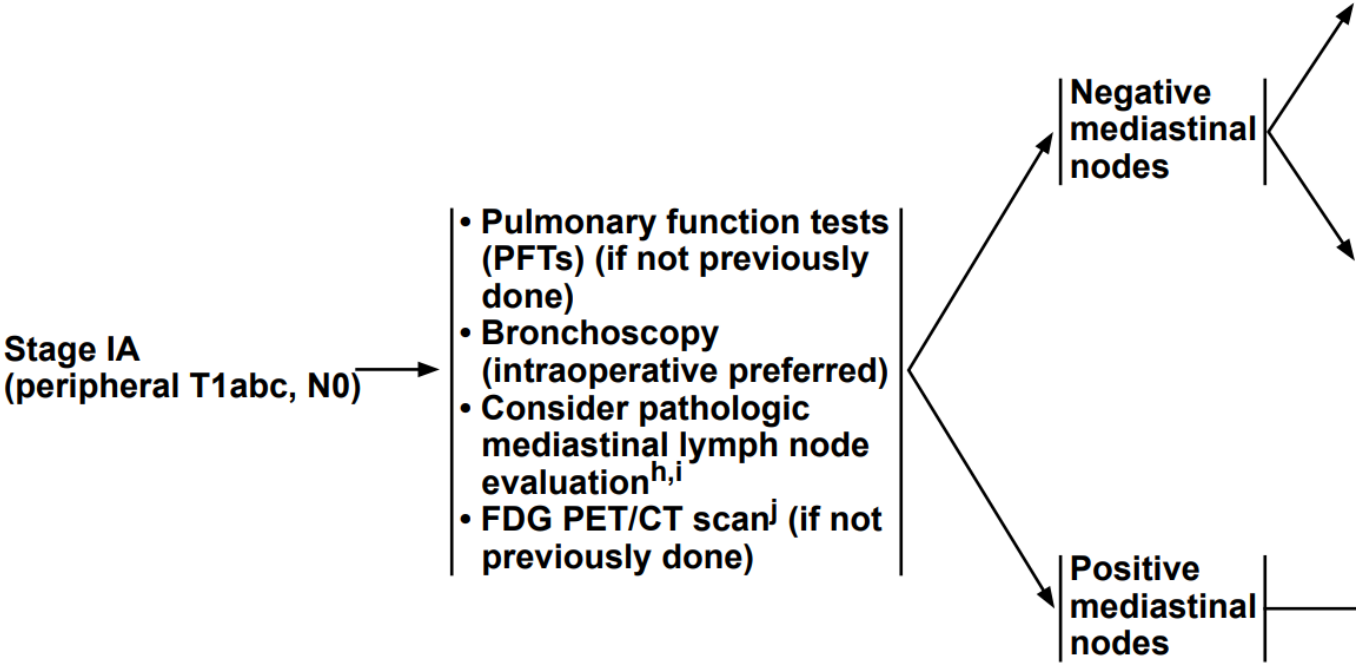
Pleural dissemination

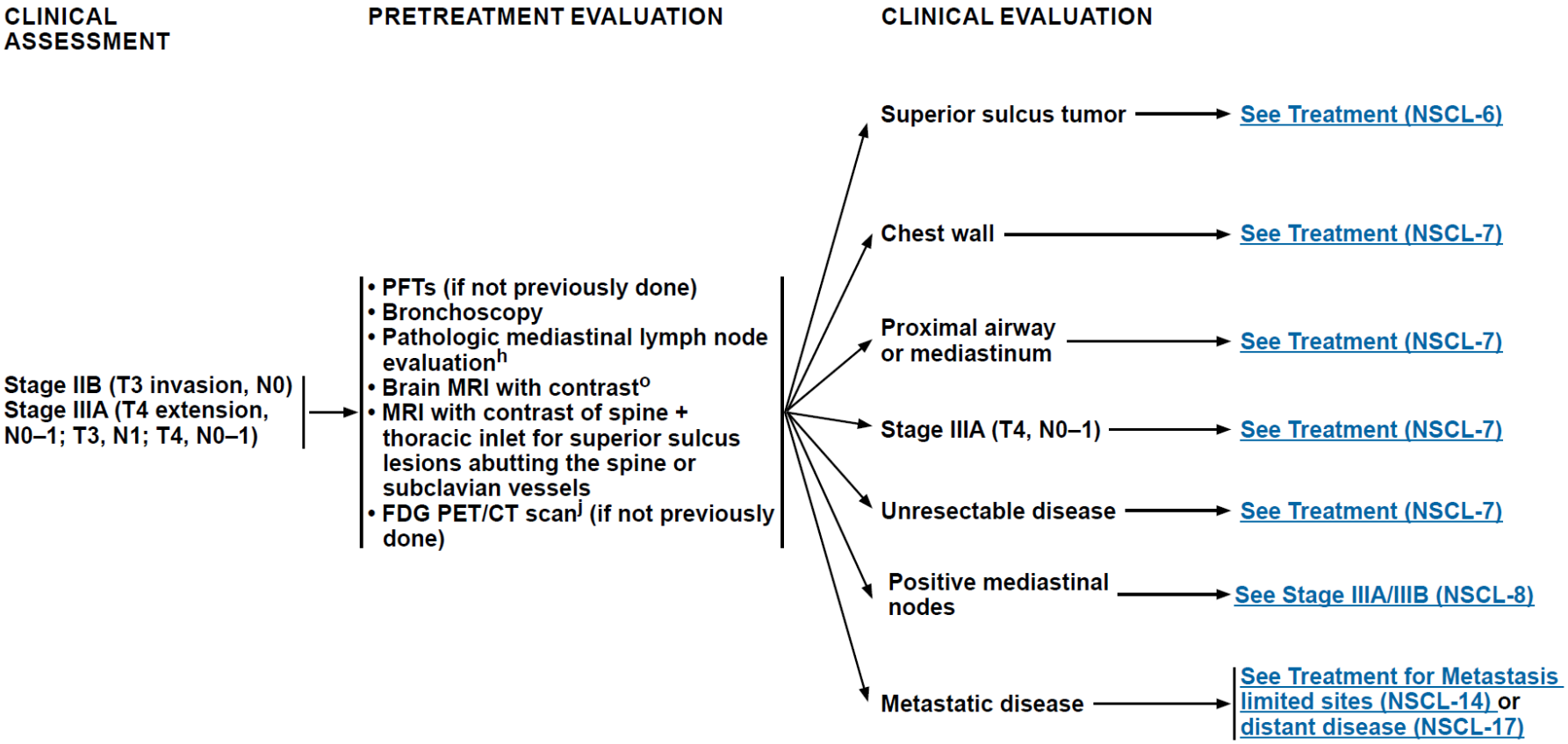
Malignant Effusion

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022
Non-Small Cell Lung Cancer

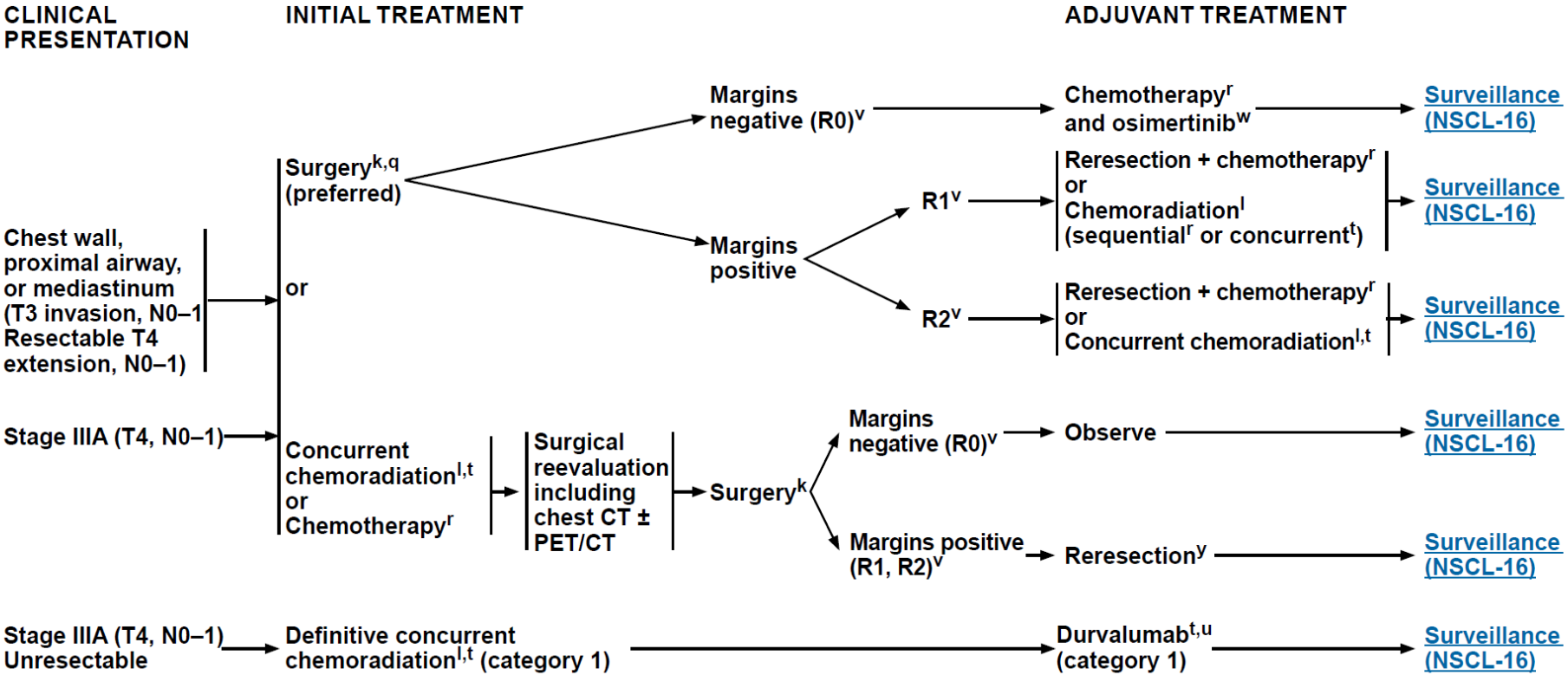
CLINICAL ASSESSMENT **PRETREATMENT EVALUATION[g]**




CLINICAL ASSESSMENT
PRETREATMENT EVALUATION
CLINICAL EVALUATION
Stage IIB (T3 invasion, N0)
Stage IIIA (T4 extension, N0–1; T3, N1; T4, N0–1)
• PFTs (if not previously done)
• Bronchoscopy
• Pathologic mediastinal lymph node evaluation[h]
• Brain MRI with contrast[o]
• MRI with contrast of spine + thoracic inlet for superior sulcus lesions abutting the spine or subclavian vessels
• FDG PET/CT scan[j] (if not previously done)
Superior sulcus tumor
See Treatment (NSCL-6)
Chest wall
See Treatment (NSCL-7)
Proximal airway or mediastinum
See Treatment (NSCL-7)
Stage IIIA (T4, N0–1)
See Treatment (NSCL-7)
Unresectable disease
See Treatment (NSCL-7)
Positive mediastinal nodes
See Stage IIIA/IIIB (NSCL-8)
Metastatic disease
See Treatment for Metastasis limited sites (NSCL-14) or distant disease (NSCL-17)

NCCN Guidelines Version 6.2021
Non-Small Cell Lung Cancer

NCCN Guidelines Index
Table of Contents
Discussion



She admitted in oncology ward to start neoadjuvant chemotherapy after thoracosurgeon consult.

What is your preferred regimen?

Pemetrexed + cisplatin
Paclitaxel+carboplatin
Vinorelbine +cisplatin
Erlotinib
PDL1 inhibitor

Neoadjvant chemotherapy could be considered in:

- T4N0 tumours where nodal disease had been excluded by invasive methods when a R0 resection is considered to be feasible; after induction therapy, when there has been nodal downstaging and a pneumonectomy can be avoided.

- Neoadjuvant chemotherapy is thought to convey a number of benefits :
- I. Reduction in tumour size;
- II. Increased operability;
- III. Eradication or prevention of micro-metastases;
- IV. Better tolerability;
- V. The possibility that it is more effective when the blood supply remains intact prior to surgery;
- VI. Better compliance with medication in the preoperative period.

J Thorac Dis. 2014 May; 6(Suppl 2): S224–S227

Potentially resectable stage IIIA

- The main objectives of induction therapy are:
  - to eradicate subclinical metastases and mediastinal lymph node disease
  - to improve local control of the disease
  - to increase resectability
  - to reduce the magnitude of surgical resection

- Surgical resection after induction therapy is indicated when imaging tests rule out extrathoracic disease progression, functional assessment after induction therapy indicates that the patient can tolerate resection, restaging techniques confirm an improvement of the mediastinal status and the type of resection ensures a complete resection but avoids a pneumonectomy.

Magem et al. CTO 2019

Neoadjuvant Chemotherapy

Table 2 Randomized trials of main neoadjuvant chemotherapy in NSCLC

Study name	Study type	Setting	Number of patients	Disease stage	Drug(s)	Response rate, %	P value/HR (95% CI)	3-yr DFS, %
NATCH	Phase III	Adjuvant/ neoadjuvant	624	IA–II	CBDCA-PTX	53.3	0.176/0.92 (0.81–1.04)	38.3
IFCT 0002	Phase III	Neoadjuvant/ perioperative	528	I–II	CBDCA-PTX; CDDP-Gem	52.3/49.2	0.63/1.06 (0.84–1.33)	56.1
LU22/NALVT/ EORTC	Phase III	Neoadjuvant	519	I–III	Platinum-based	49	0.86/1.02 (0.80–1.31)	NS
ChEST	Phase III	Neoadjuvant	129	I–IIIA	CBDCA-Gem	35.4	0.03/0.70 (0.50–0.97)	52.9

NSCLC, non-small cell lung cancer; ChEST, chemotherapy in early-stages NSCLC trial; CBDCA, carboplatin; CDDP, cisplatin; CI, confidence interval; CT, chemotherapy; Gem, gemcitabine; HR, hazard ratio; NS, not stated; PTX, paclitaxel; yr, years; NSCLC, non-small cell lung cancer.

Indini A, Journal of Thorac Dis 2020.

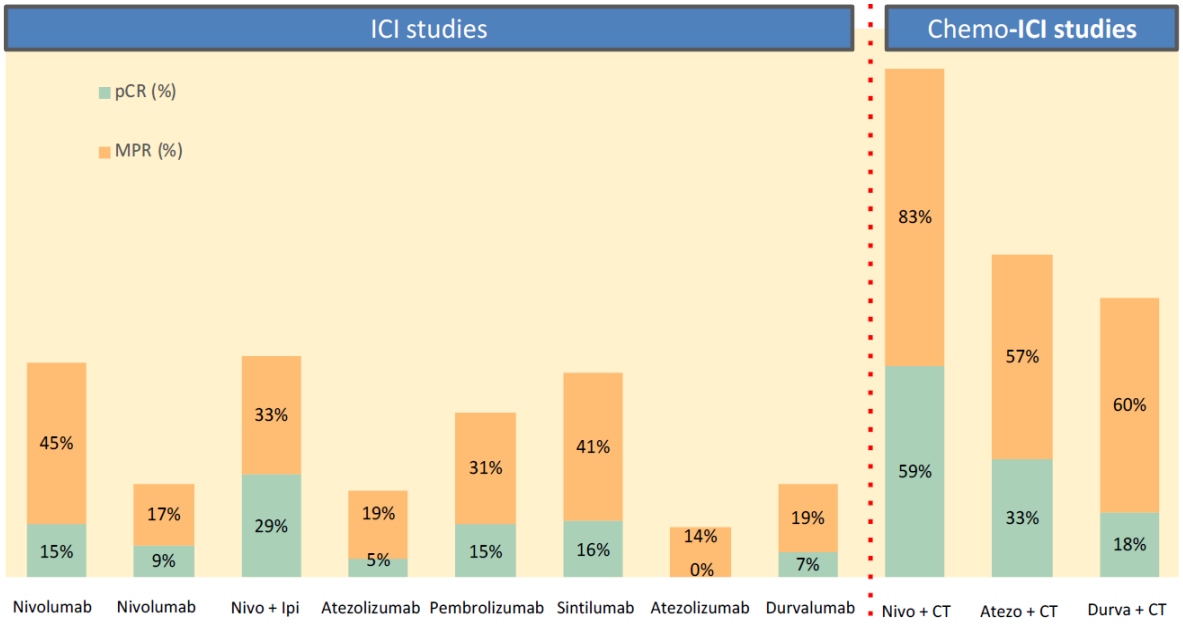
Ongoing Trials of neoadjuvant immunotherapy for NSCLC

NEOADJUVANT IO MONOTHERAPY

Trial	Nº patients	Stage	Drug (Nº doses)	Primary Endpoint	Pathological Response	
Forde et al (2018)	22	I-IIIA	Nivolumab(2)	Safety-Feasibility	MPR: 45%	pCR:13%
Reuss J et al (2020)	9	IB-IIIA	Nivo+Ipi (3-1)	Safety-Feasibility		pCR:33%
Cascone T et al. NEOSTAR (2019)	44	I-IIIA	Nivo/+/-Ipi (3-1)	MPR	MPR:19% MPR:44%	pCR:10% pCR:38%
Gao S et al. (2020)	40	I-IIIB	Sintilimab (2)	Safety	MPR:40.5%	pCR:16%
Kwiatkowski et al LCMC3 (2019)	101	IB-IIIA	Atezolizumab (2)	MPR	MPR:19%	pCR:5%
Bar J et al (2019) MK3475-223	14	I-II	Pembrolizumab (1-2)	Safety	MPR:40%	.
IoNESCO (2020)	50	IB-IIIA	Durvalumab (3)	% of R0	MPR:18.6%	.
Besse B et al Princeps (2020)	30	I-IIIA	Atezolizumab (1)	Tolerance	MPR:14%	.

Courtesy of M. Provencio. ES06.01

Neoadjuvant ICI trials in early-stage NSCLC



	Forde et al.	NEOSTAR		LCMC3	MK3475-223	Li et al.	PRINCEPS	IONESCO	NADIM	COLUMBIA	SAKK 16/14
N	22	23	21	101	15	40	30	50	46	14	67
Stage	I-IIIA	I-IIIA		IB-IIIA	I-II	IB-IIIA	I-IIIA	IB-IIIA	IIIA	IB-IIIA	IIIA (N2)
Surgery	95%	96%	81%	89%	87%	93%	100%	92%	90%	79%	82%
RR	10%	22%	19%	7%	NR	20%	7%	9%	74	57%	58%

Benitez et al. Clinical Cancer Research 2020

Neoadjuvant erlotinib in EGFR – mutated stage IIIA-N2 patients

- pts stage IIIA-N2 17 Chinese centers screened
- 72 pts randomized

	neoadjuvant erlotinib *42dd pre – 1y postop*	cisplatin + gemcitabine *2 cycles pre – 2 cycles postop*	
ORR	54.1%	34.3%	*OR 2.26*
surgery	31 pts – 83.8%	24 pts – 68.6%	
LN downstaging	13%	4.2%	
PFS	21.5 mos	11.4 mos	*HR 0.39*

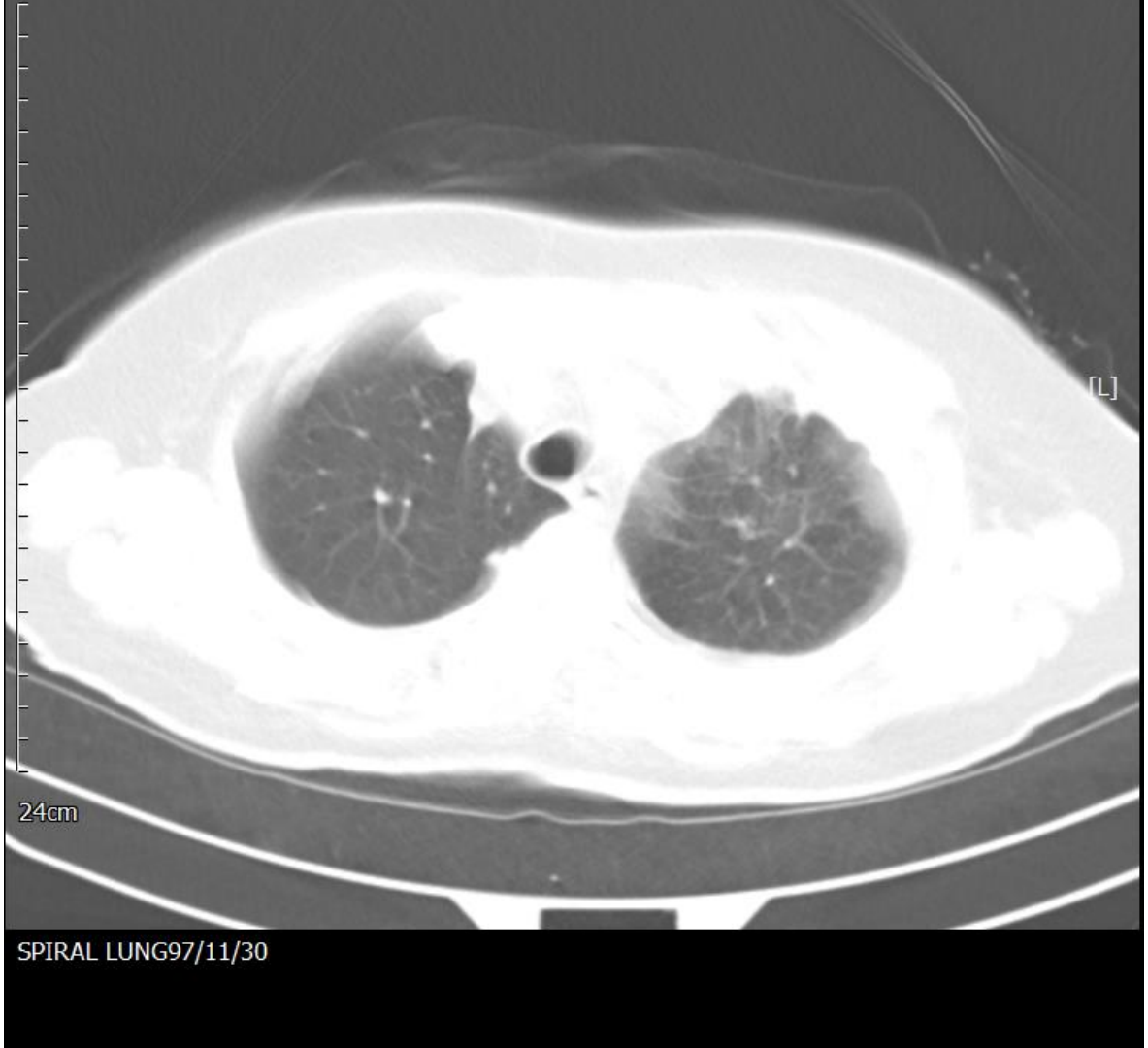
- no OS data
- EGFR-mutated stage IIIA-N2 erlotinib ↑ ORR and PFS

EMERGING - CTONG 1103. Zhong WZ et al. J Clin Oncol 2019; 37:2235-45

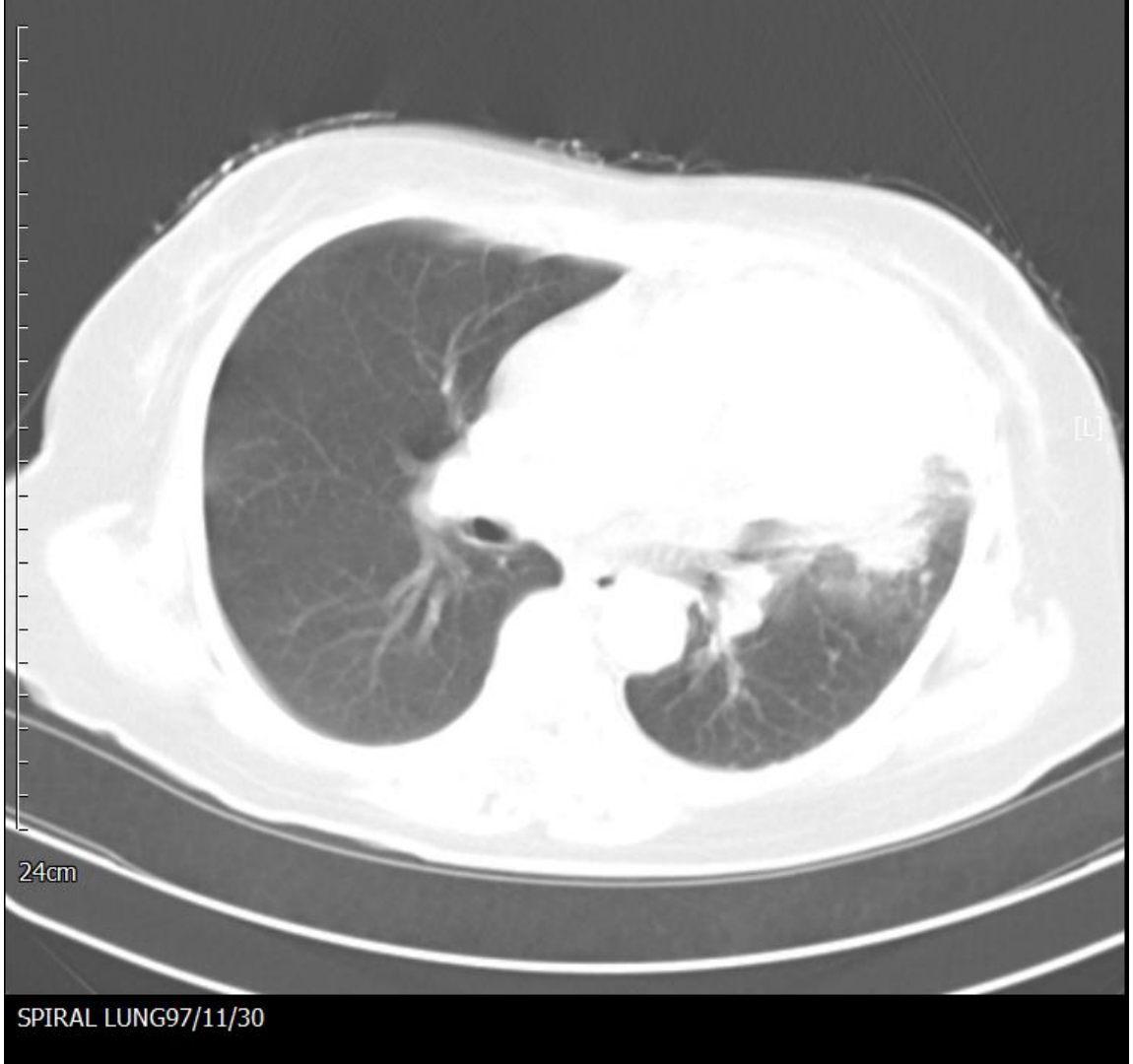
Patient received 4 cycle of pemetrexed + carboplatin.

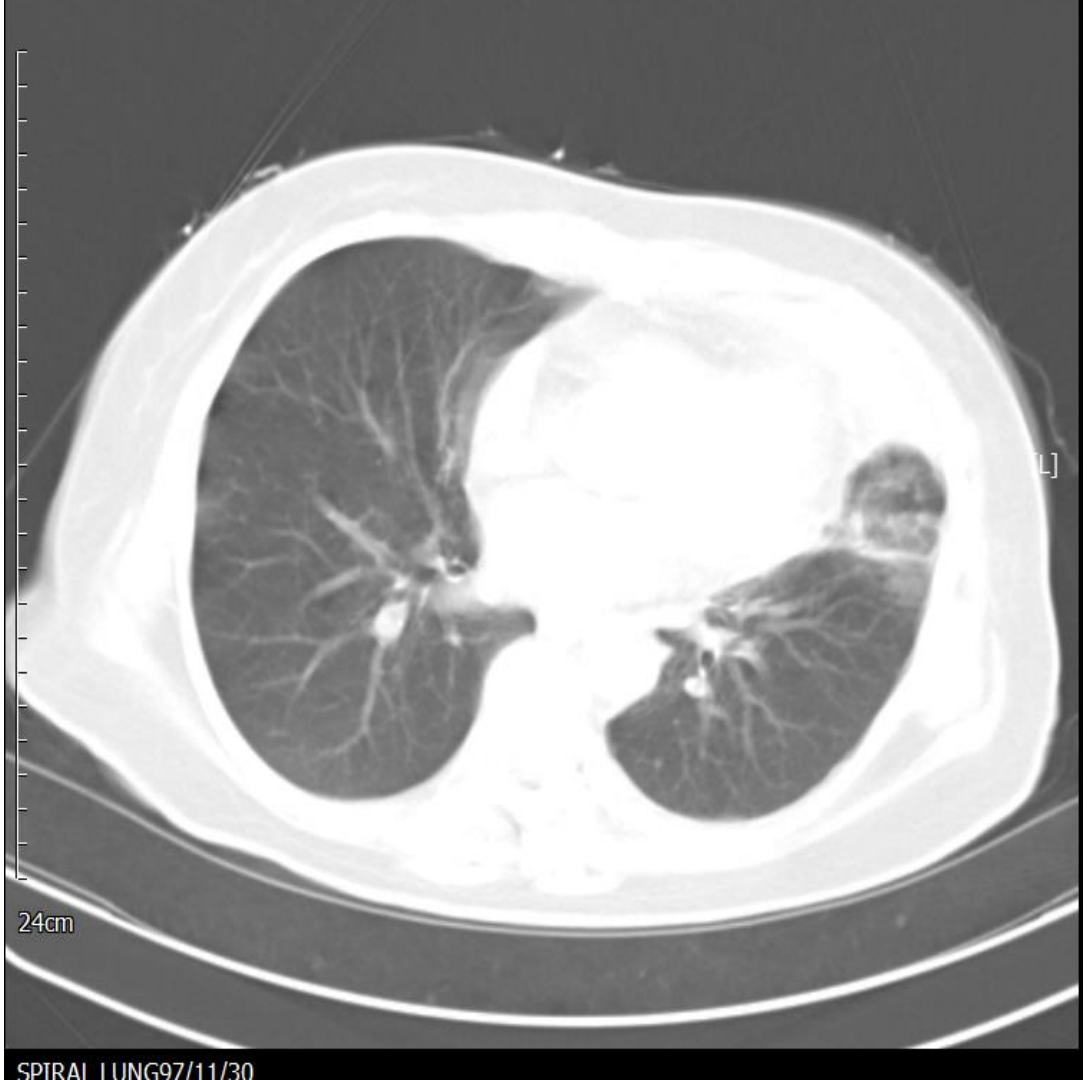
CT scan showed :

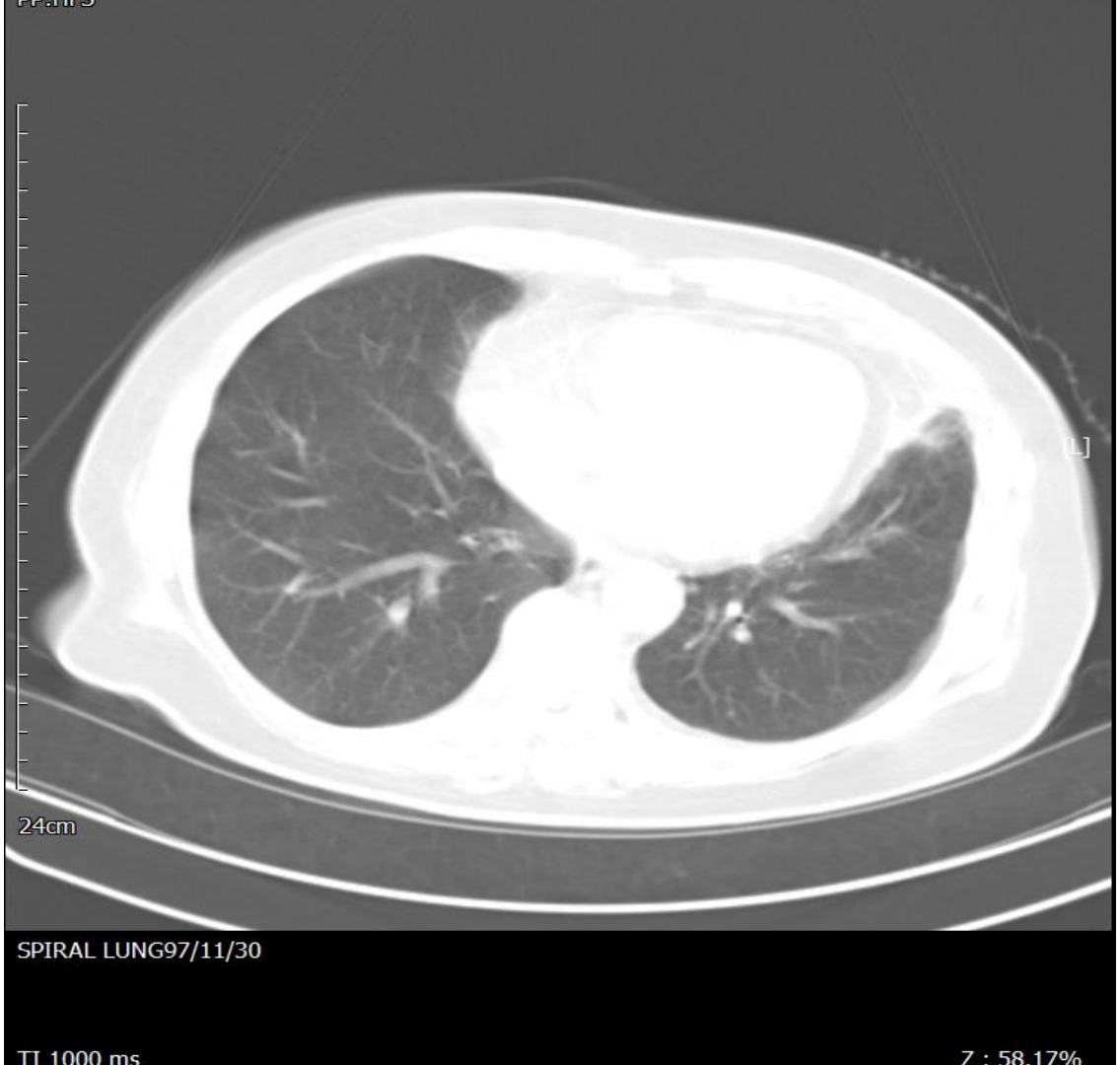
11/97

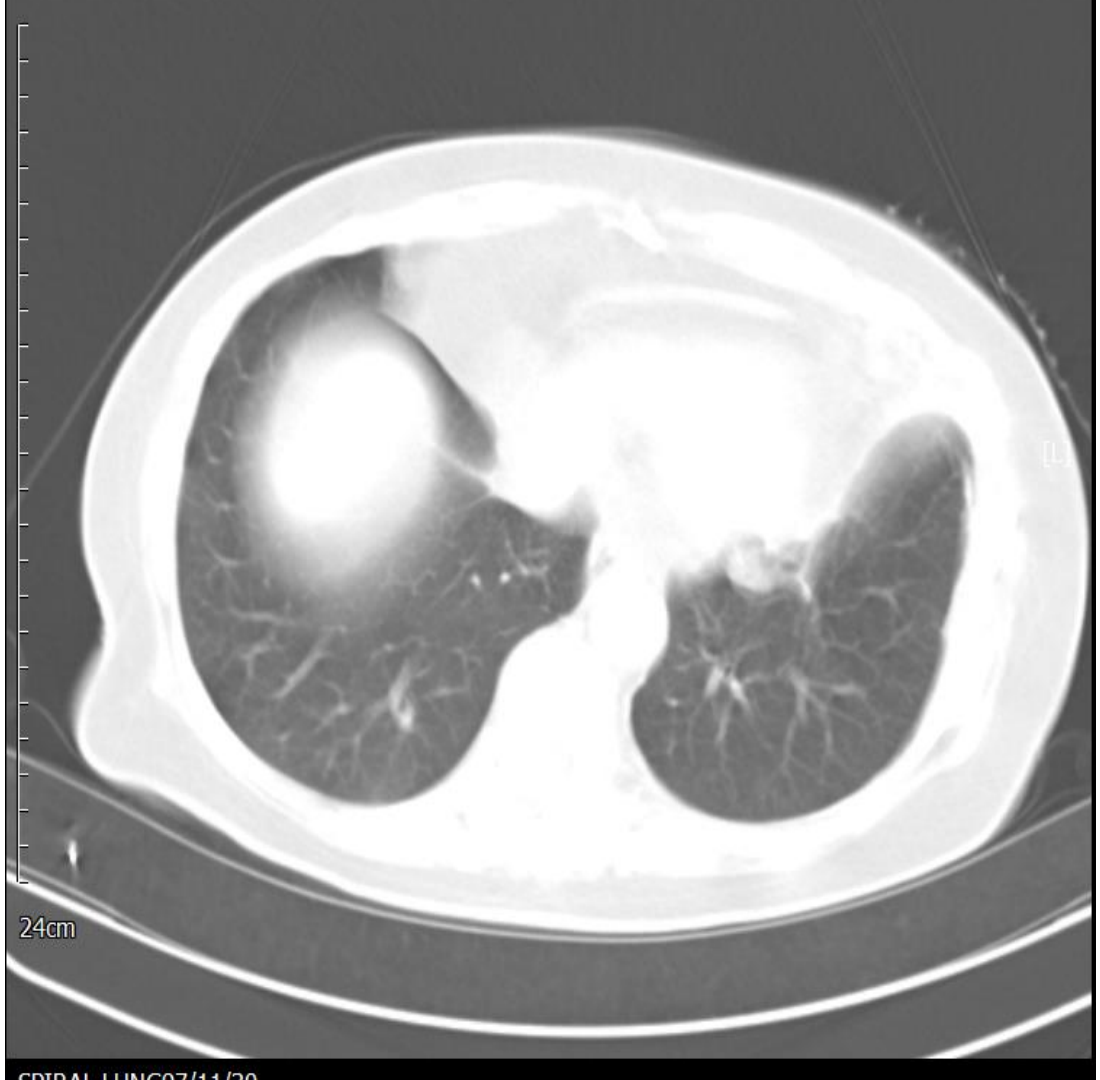

[L]
24cm
SPIRAL LUNG97/11/30

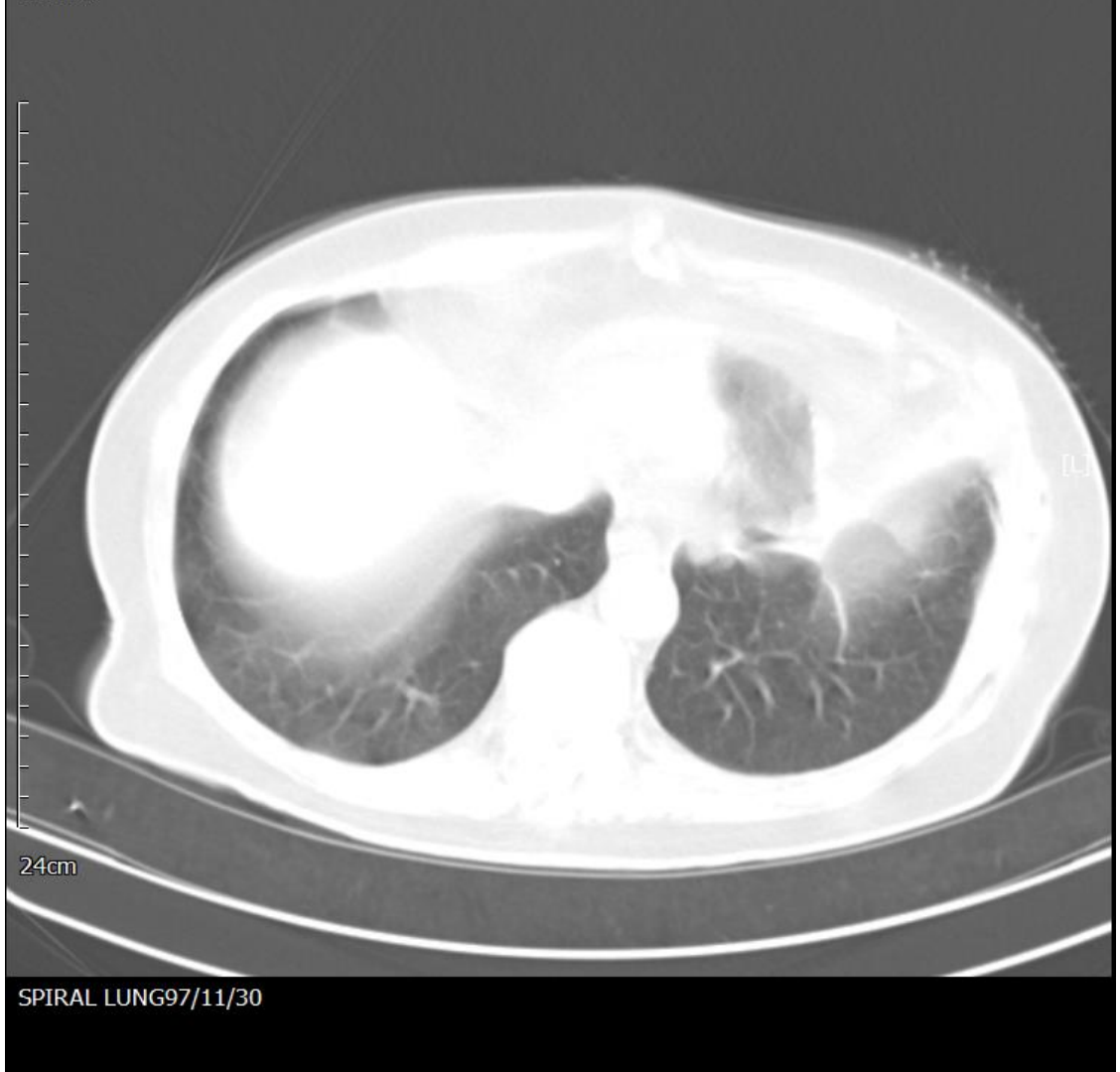

24cm

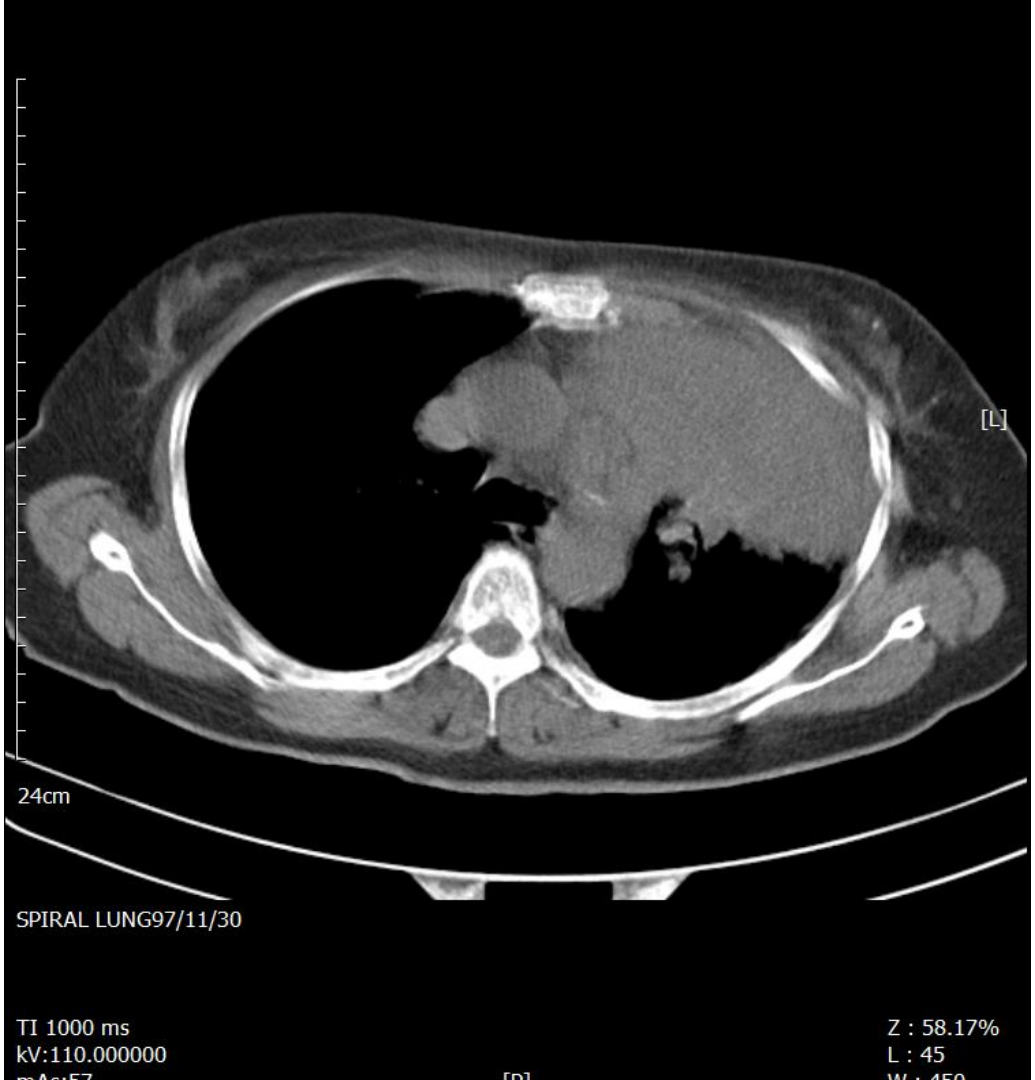

24cm
SPIRAL LUNG97/11/30

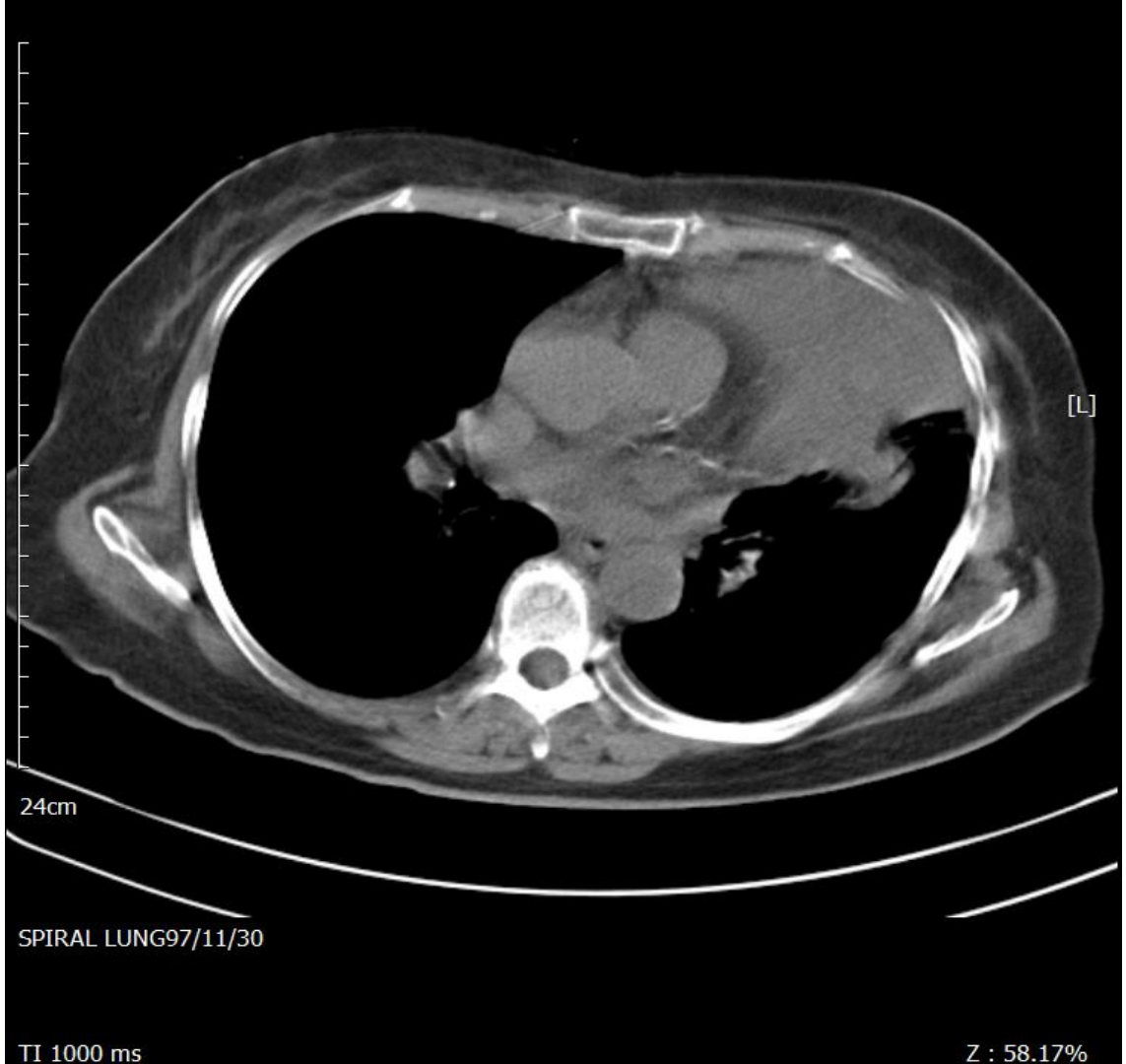

[L]
24cm
SPIRAL LUNG97/11/30

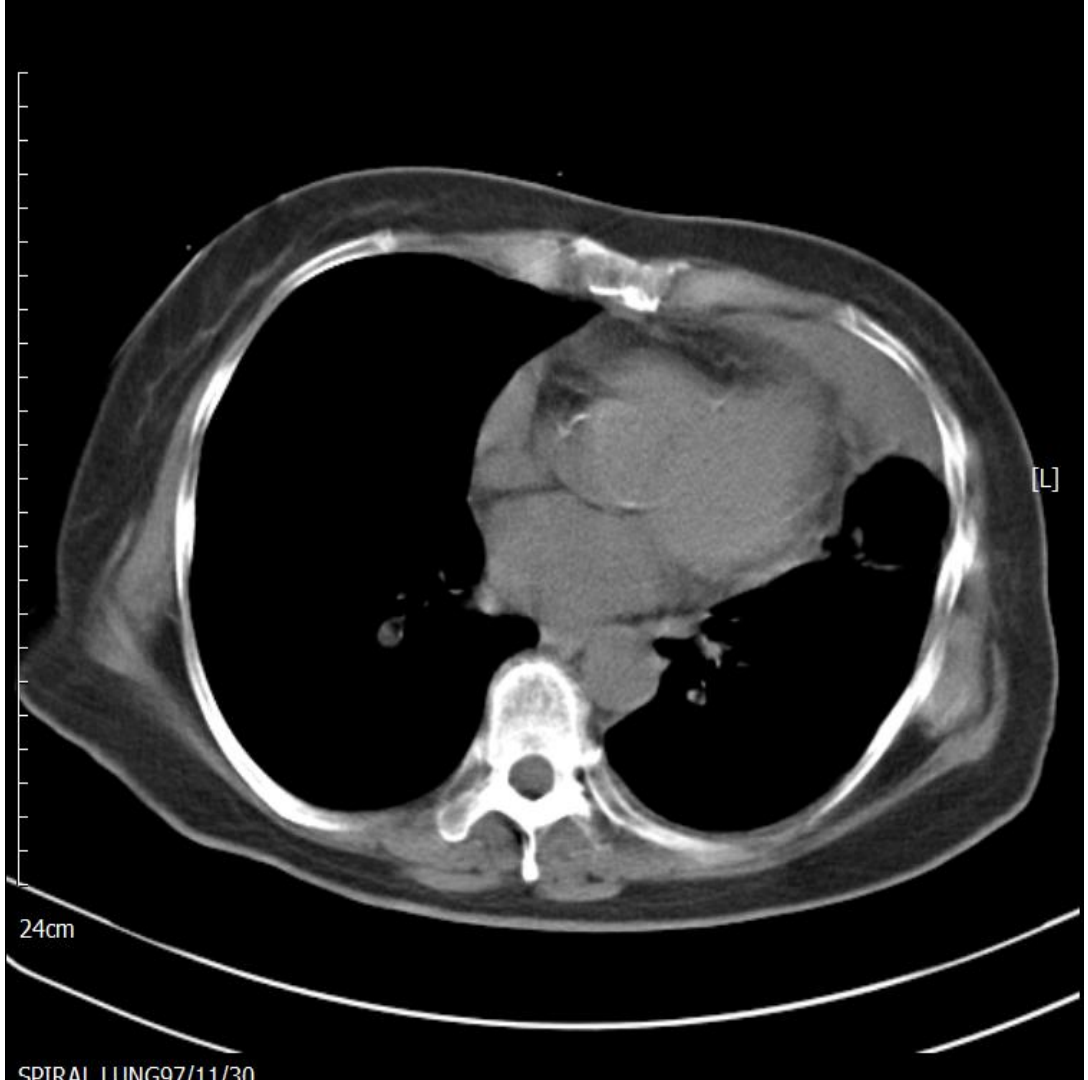

[L]
24cm
SPIRAL LUNG97/11/30
TI 1000 ms
Z : 58.17%

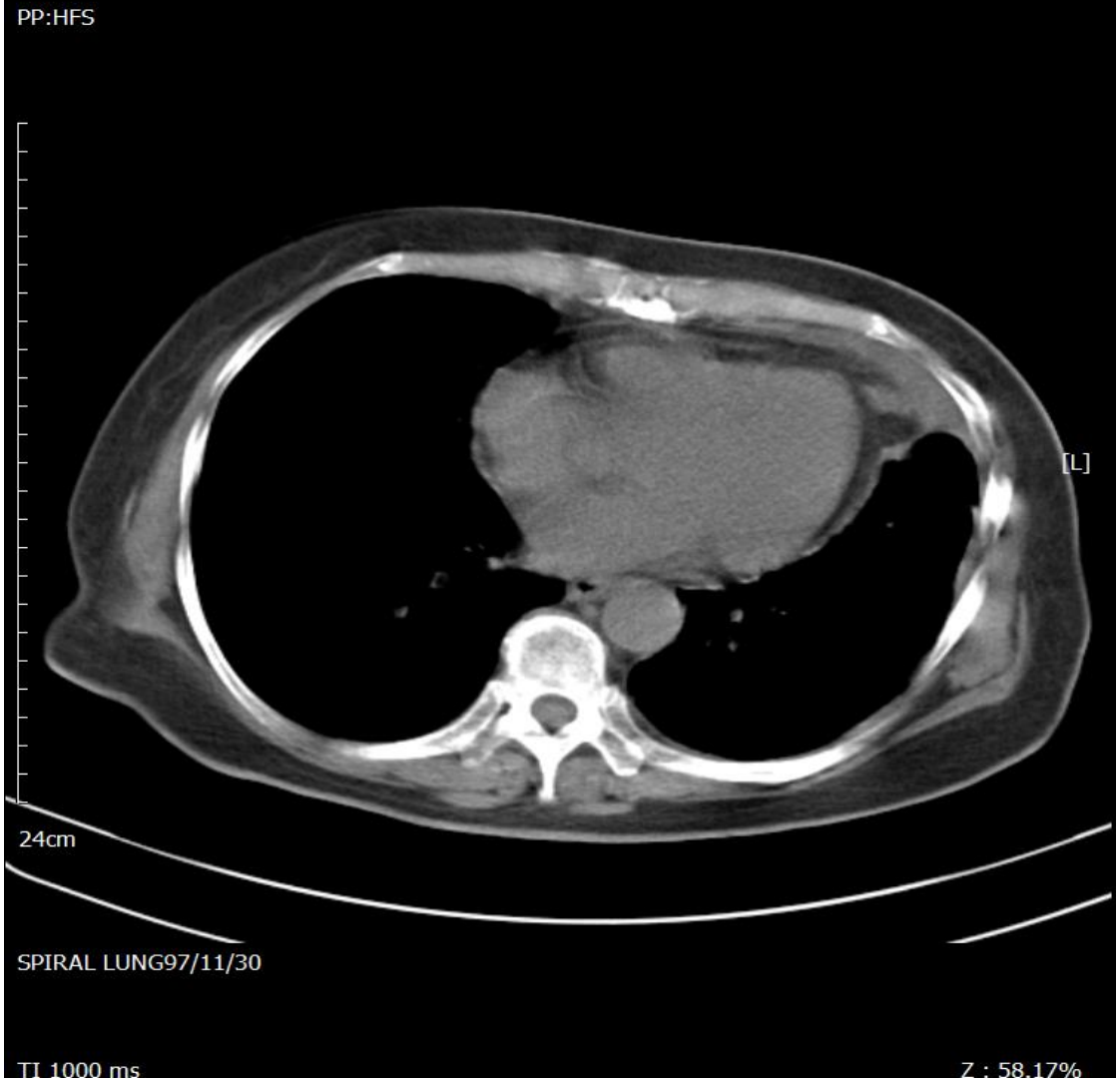

24cm


24cm
SPIRAL LUNG97/11/30

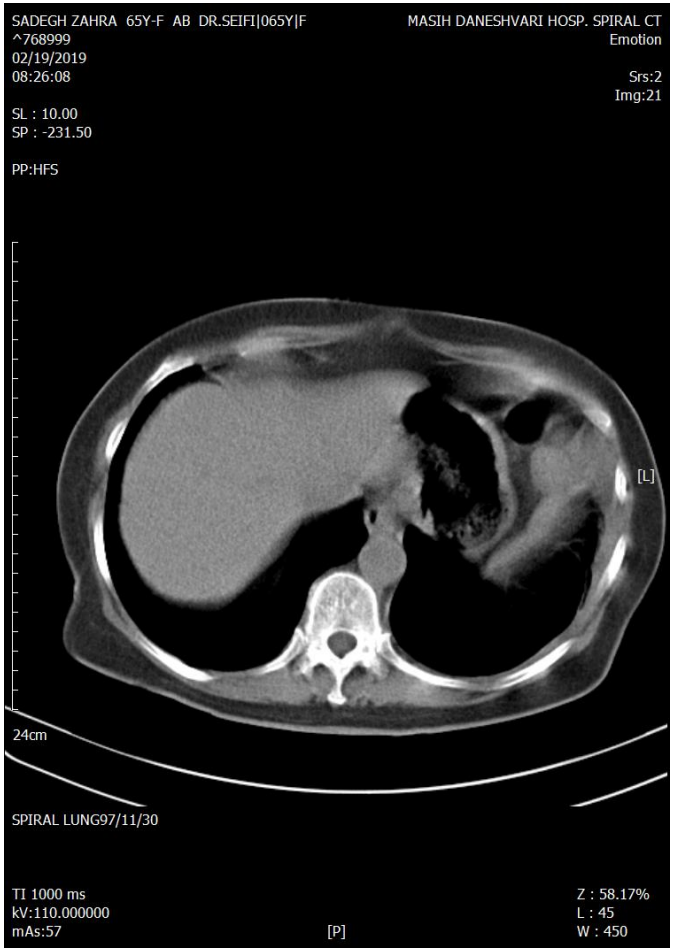

[L]
24cm
SPIRAL LUNG97/11/30
TI 1000 ms
kV:110.000000
Z : 58.17%
L : 45


[L]
24cm
SPIRAL LUNG97/11/30
TI 1000 ms
Z : 58.17%


[L]
24cm
SPIRAL LUNG97/11/30


PP:HFS
[L]
24cm
SPIRAL LUNG97/11/30
TI 1000 ms
Z : 58.17%

Title


SADEGH ZAHRA 65Y-F AB DR.SEIFI|065Y|F
^768999
02/19/2019
08:26:08
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:21
SL : 10.00
SP : -231.50
PP:HFS
[L]
24cm
SPIRAL LUNG97/11/30
TI 1000 ms
kV:110.000000
mAs:57
[P]
Z : 58.17%
L : 45
W : 450

Next step?

Consultation with thoracic surgeon was requested.

The tumor was unresectable.

What is your plan?

Consultation with radio-oncologist was requested.

She received mediastinal radiation.

Approaches to Improve Outcomes for stage III NSCLC

Strategy	Outcome
Induction chemotherapy prior to chemo-RT	Negative
Consolidation chemotherapy after chemo-RT	Negative
Addition of targeted therapy after chemo-RT	Negative
Addition of targeted therapy to chemo-RT	Negative
Prophylactic cranial RT after chemo-RT	Negative

Vokes et al. J Clin Oncol 2007; Hanna et al. J Clin Oncol 2008; Bradley et al. Lancet Oncol 2015; Cheema et al. Curr Oncol 2019.

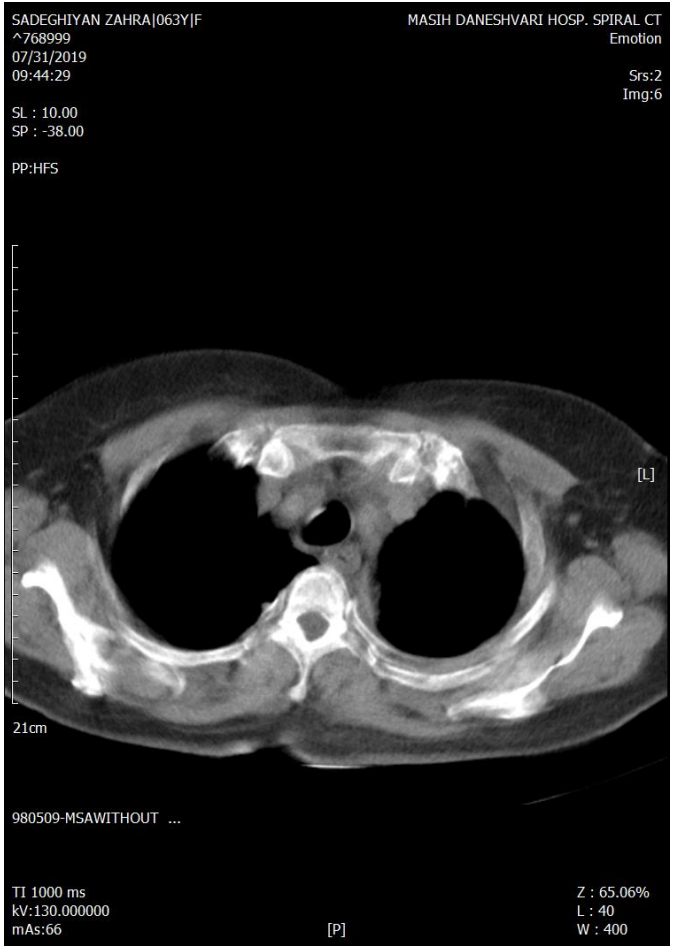
Overview of Guidelines of treatment for Unresectable Stage III NSCLC: ESMO

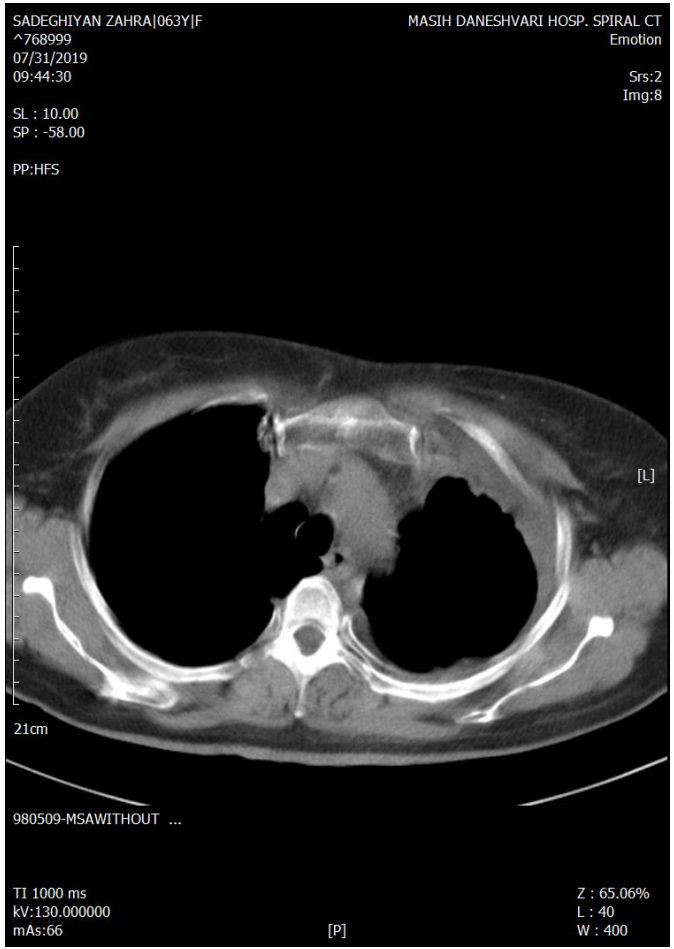
- Concurrent chemo-RT is the treatment of choice in patients evaluated as unresectable in stages IIIA and IIIB [Level I, A evidence]
- 60 to 66 Gy in 30 to 33 daily fractions is recommended for concurrent chemo-RT [I, A]
- In the stage III disease chemo-RT strategy, 2 to 4 cycles of concomitant chemotherapy should be delivered [I, A]
  - There is no evidence for further induction or consolidation CT
- If concurrent chemo-RT is not possible -- for any reason -- sequential chemotherapy followed by definitive RT represents a valid and effective alternative [I, A]

Postmus et al. Ann Oncol 2017: ESMO Guidelines. NSCLC

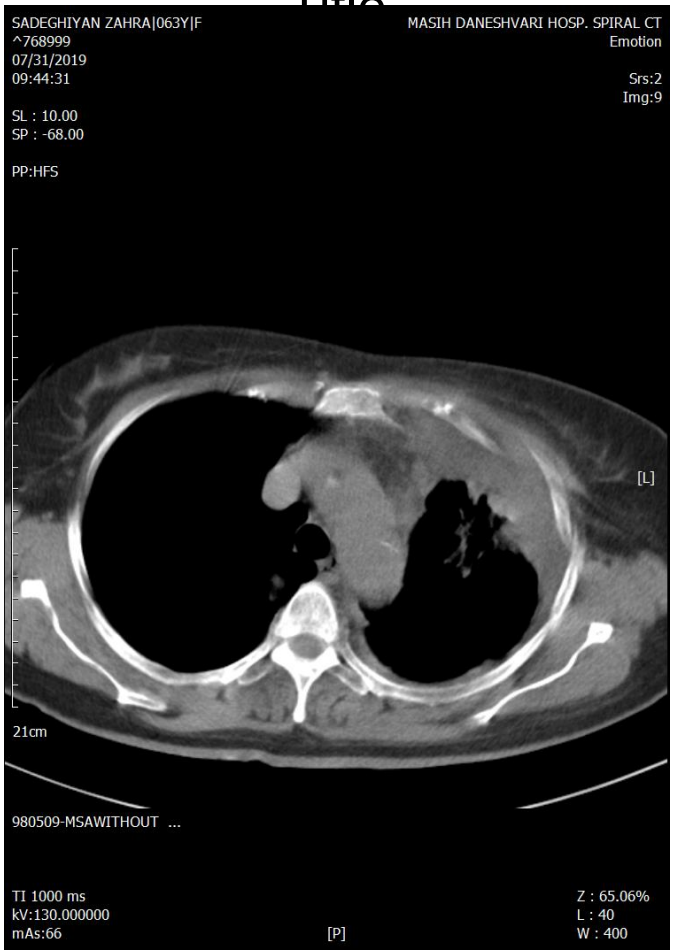
05/98

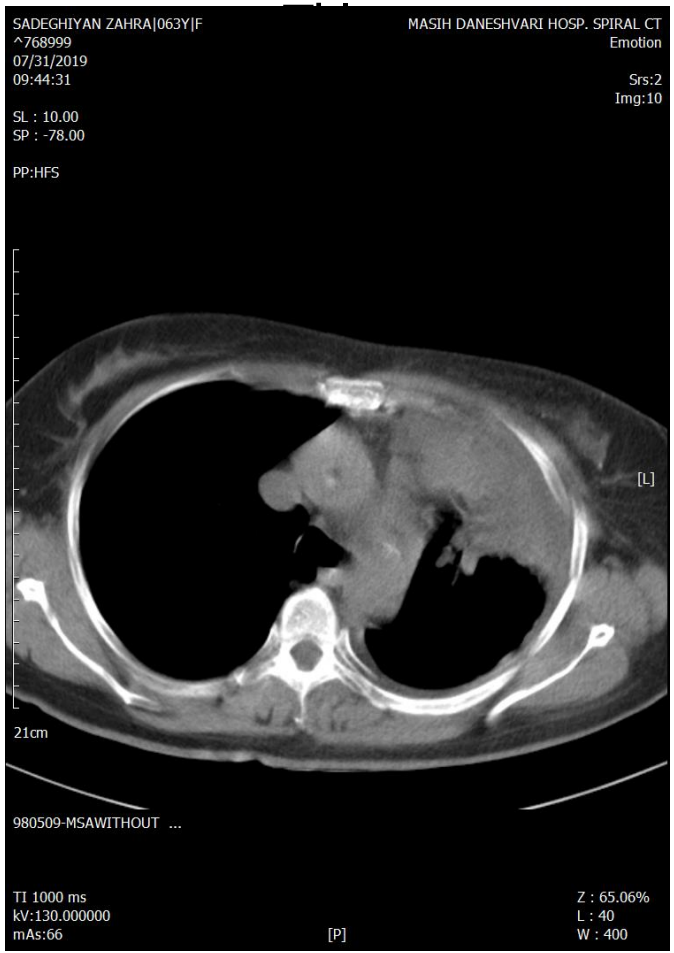
After irradiation


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:44:29
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:6
SL : 10.00
SP : -38.00
PP:HFS
[L]
21cm
980509-MSAWITHOUT ...
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 65.06%
L : 40
W : 400

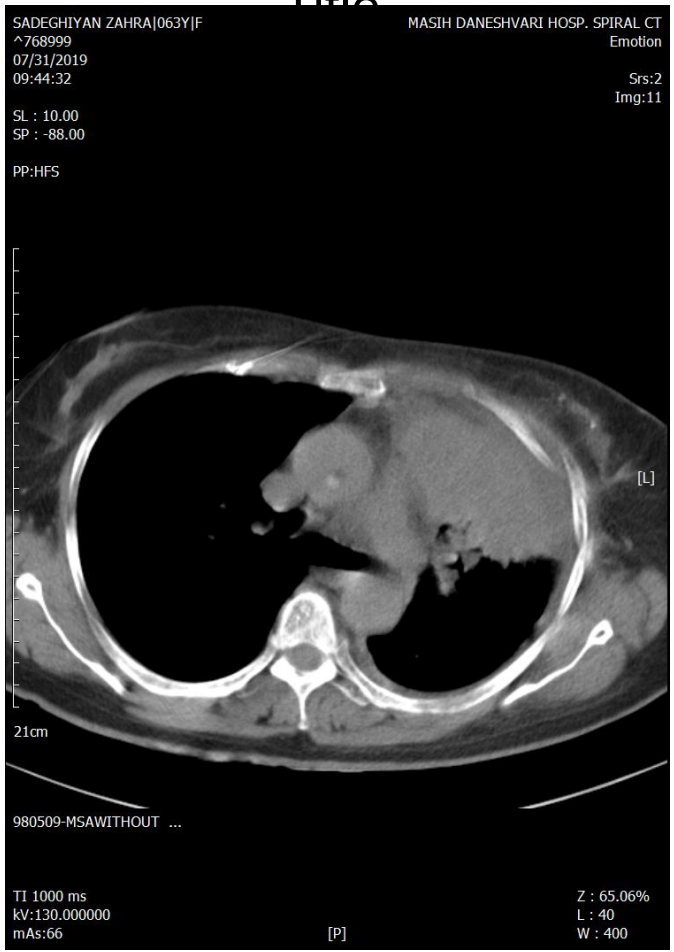

SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:44:30
SL : 10.00
SP : -58.00
PP:HFS
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:8
[L]
21cm
980509-MSAWITHOUT ...
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 65.06%
L : 40
W : 400

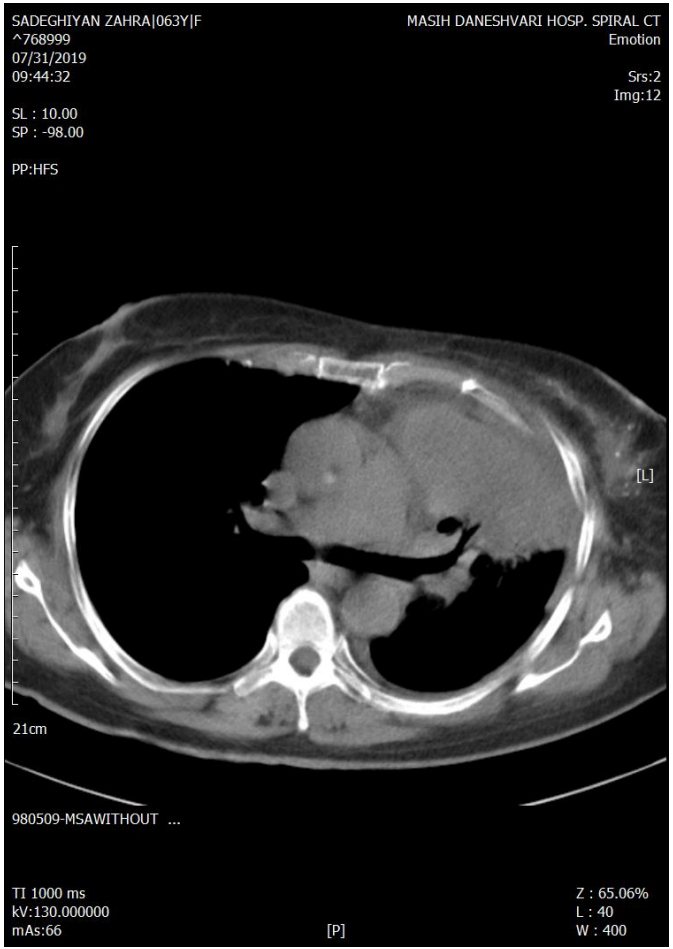
Title


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:44:31
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:9
SL : 10.00
SP : -68.00
PP:HFS
[L]
21cm
980509-MSAWITHOUT ...
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 65.06%
L : 40
W : 400

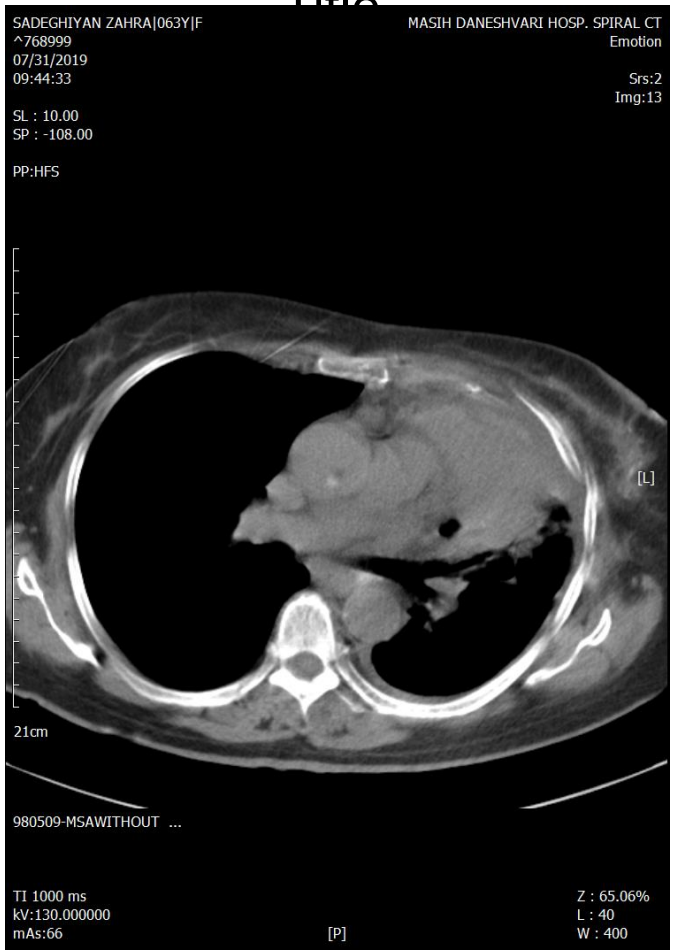

SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:44:31
SL : 10.00
SP : -78.00
PP:HFS
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:10
[L]
21cm
980509-MSAWITHOUT ...
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 65.06%
L : 40
W : 400

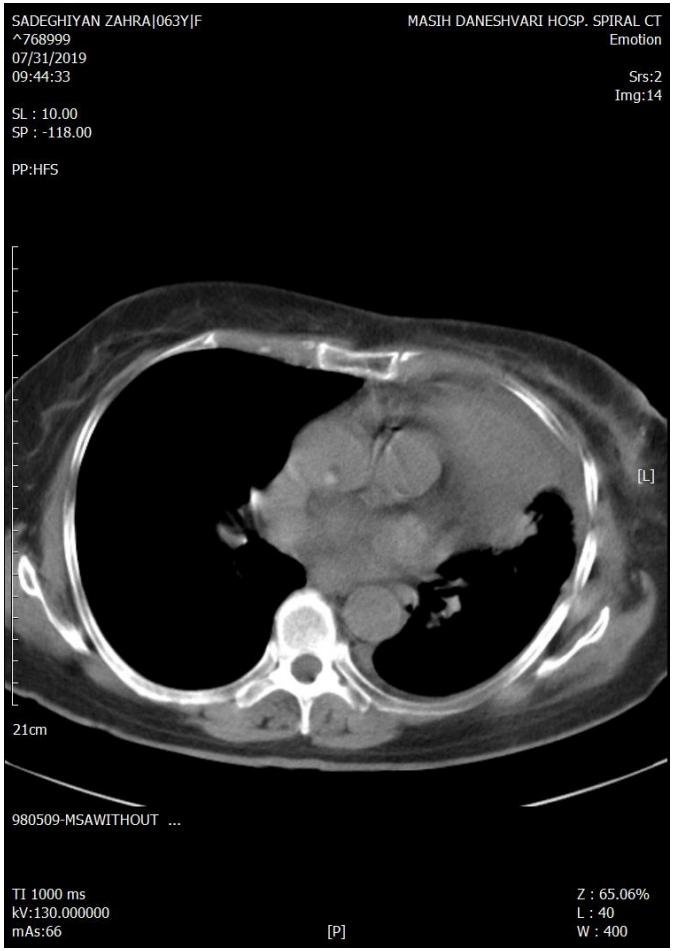
Title


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:44:32
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:11
SL : 10.00
SP : -88.00
PP:HFS
[L]
21cm
980509-MSAWITHOUT ...
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 65.06%
L : 40
W : 400

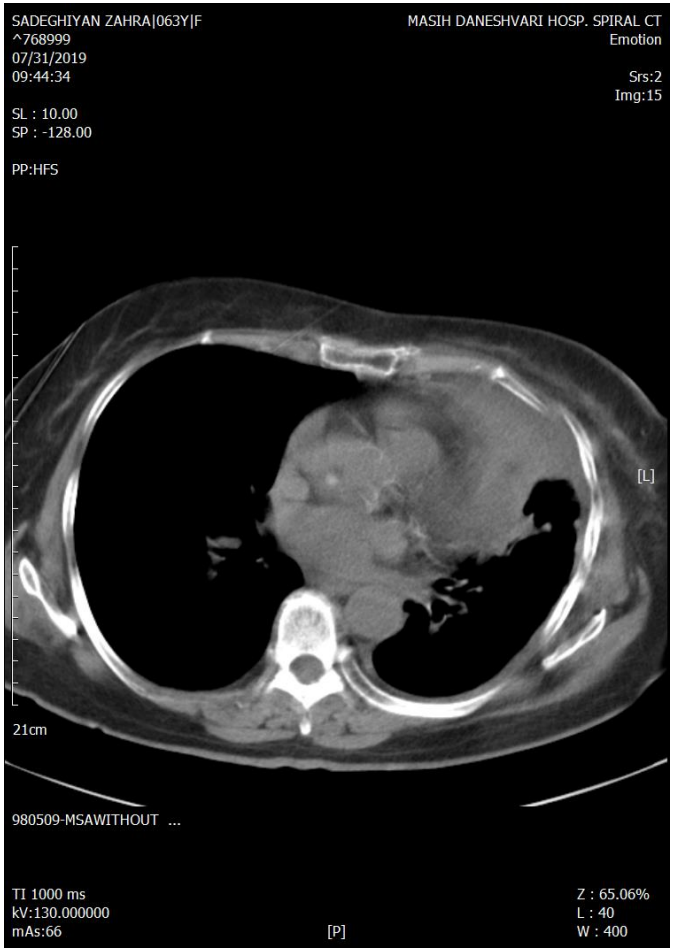

SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:44:32
SL : 10.00
SP : -98.00
PP:HFS
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:12
[L]
21cm
980509-MSAWITHOUT ...
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 65.06%
L : 40
W : 400

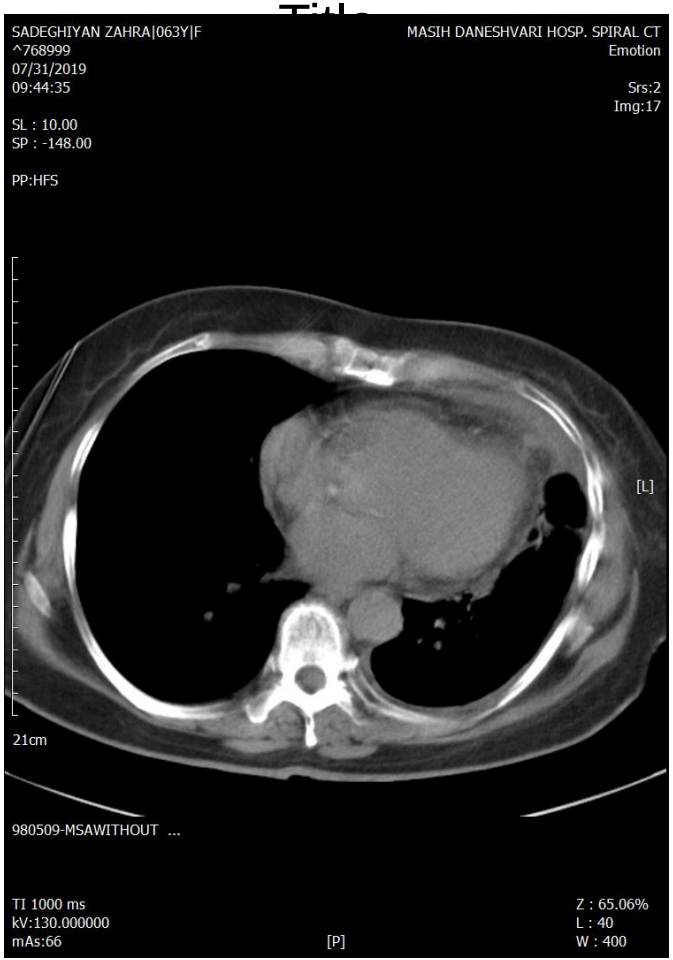
Title

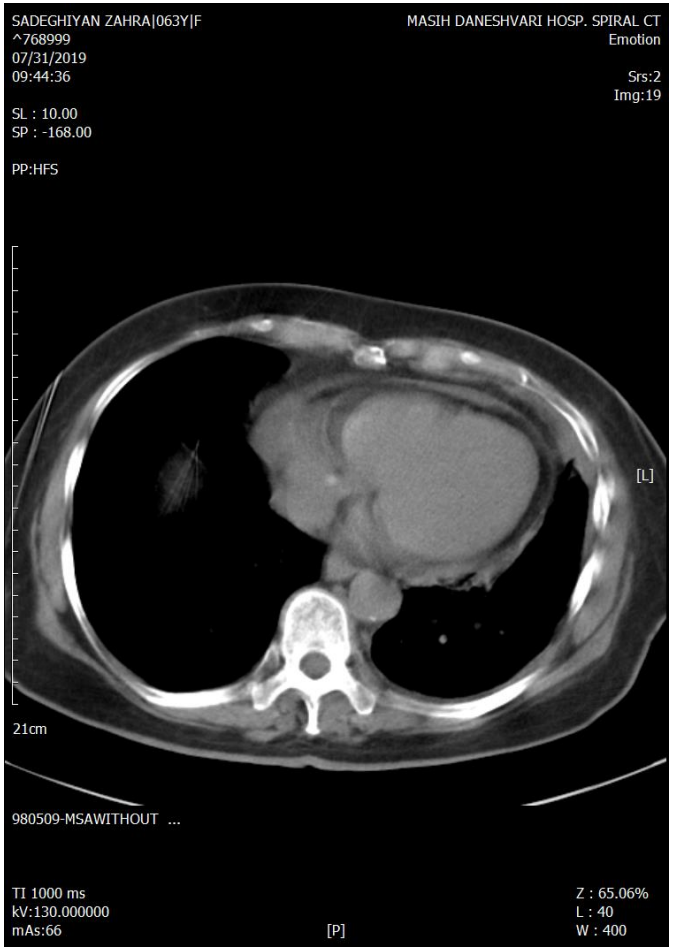

SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:44:33
SL : 10.00
SP : -108.00
PP:HFS
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:13
[L]
21cm
980509-MSAWITHOUT ...
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 65.06%
L : 40
W : 400

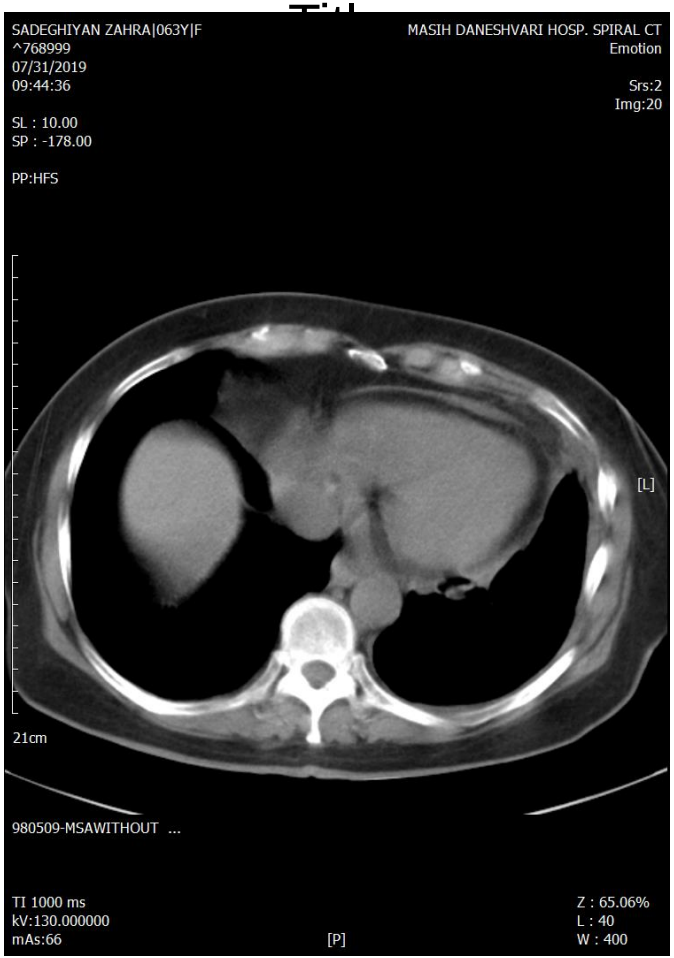

SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:44:33
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:14
SL : 10.00
SP : -118.00
PP:HFS
[L]
21cm
980509-MSAWITHOUT ...
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 65.06%
L : 40
W : 400

Title

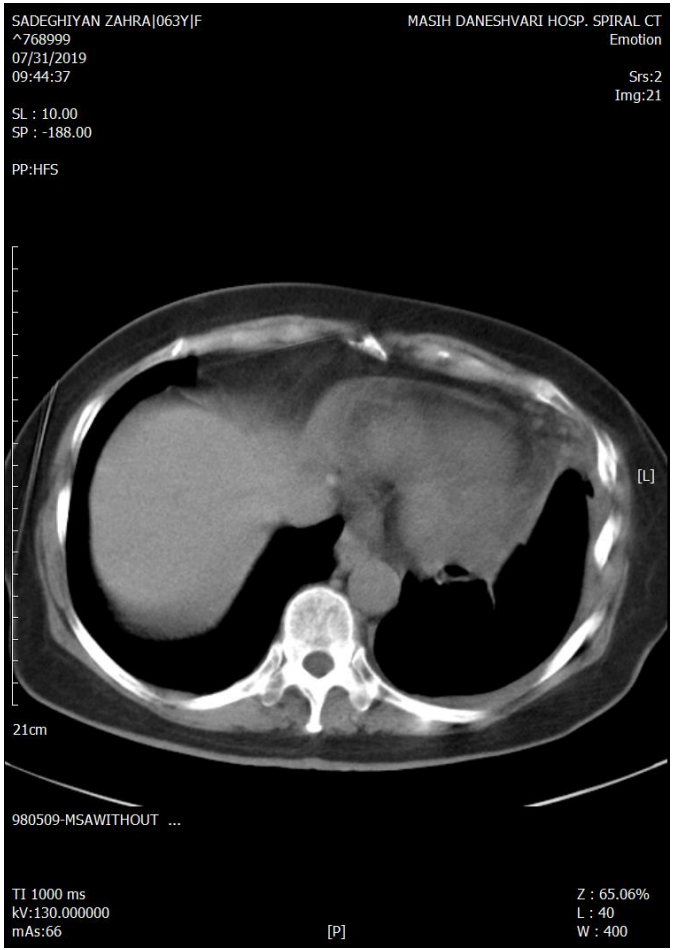

SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:44:34
SL : 10.00
SP : -128.00
PP:HFS
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:15
[L]
21cm
980509-MSAWITHOUT ...
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 65.06%
L : 40
W : 400


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:44:35
SL : 10.00
SP : -148.00
PP:HFS
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:17
[L]
21cm
980509-MSAWITHOUT ...
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 65.06%
L : 40
W : 400

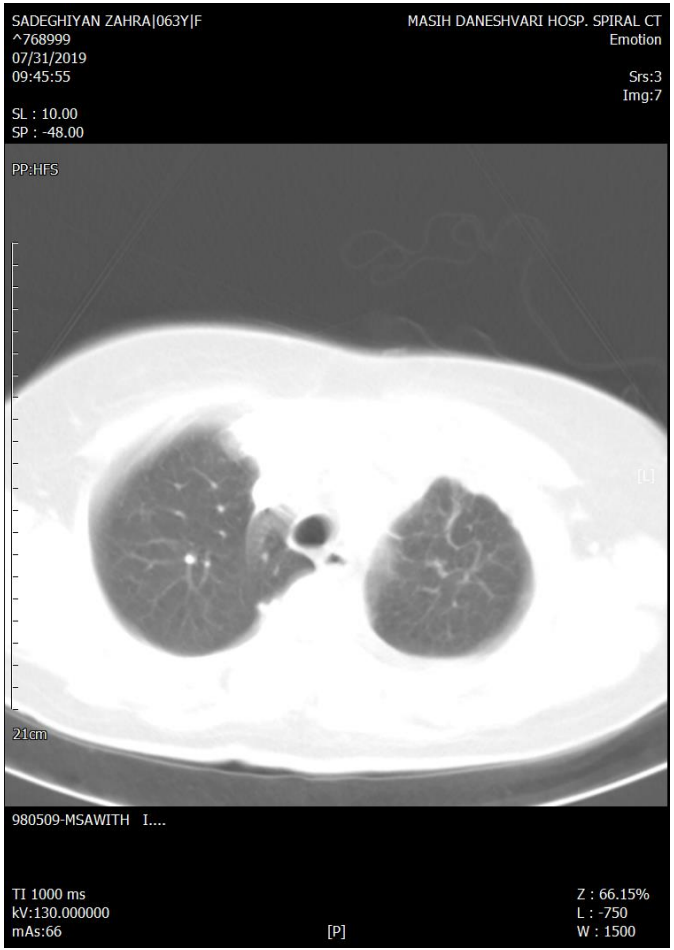

SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:44:36
SL : 10.00
SP : -168.00
PP:HFS
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:19
[L]
21cm
980509-MSAWITHOUT ...
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 65.06%
L : 40
W : 400


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:44:36
SL : 10.00
SP : -178.00
PP:HFS
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:20
[L]
21cm
980509-MSAWITHOUT ...
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 65.06%
L : 40
W : 400

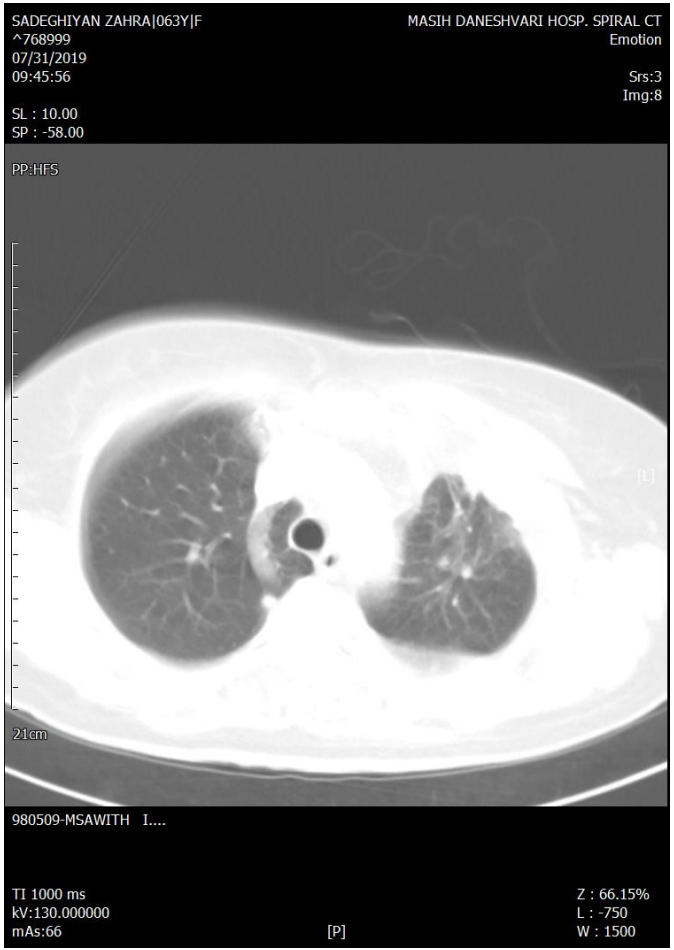
Title


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:44:37
SL : 10.00
SP : -188.00
PP:HFS
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:2
Img:21
[L]
21cm
980509-MSAWITHOUT ...
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 65.06%
L : 40
W : 400

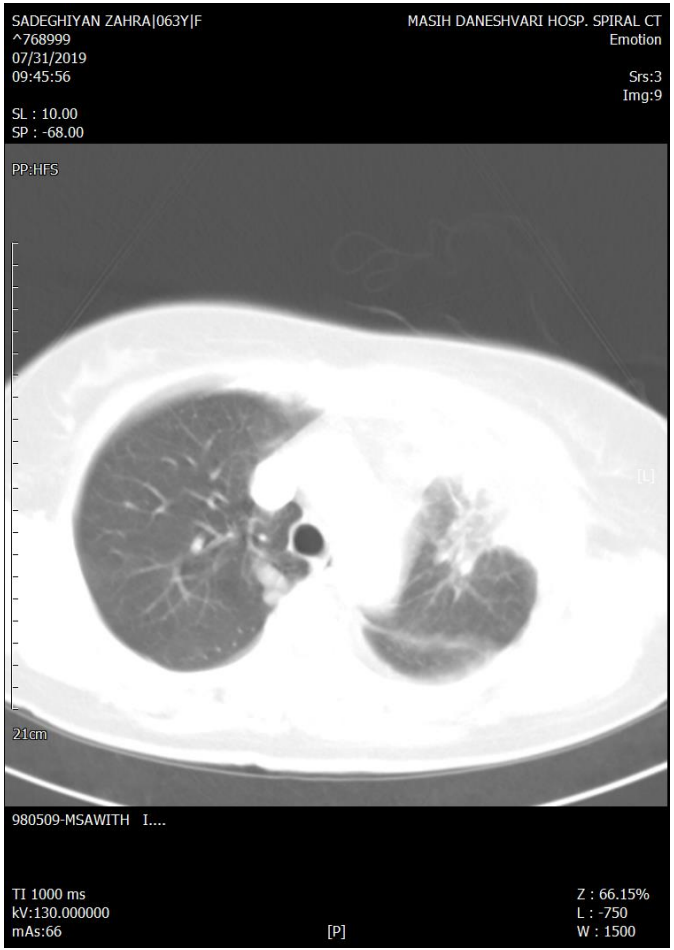
Title


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:45:55
SL : 10.00
SP : -48.00
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:3
Img:7
PP:HFS
21cm
980509-MSAWITH I....
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 66.15%
L : -750
W : 1500

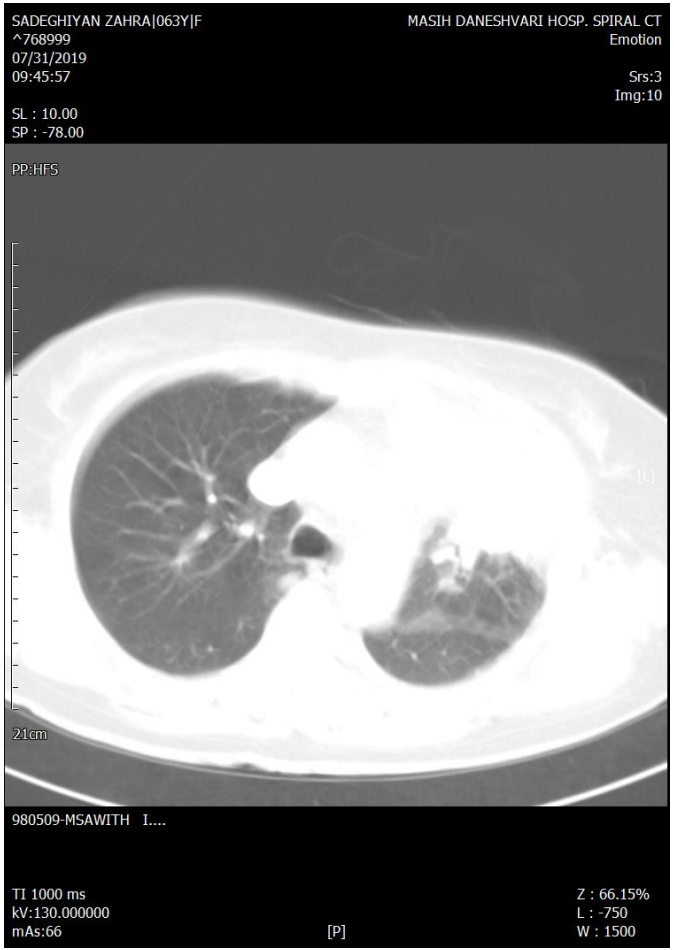
Title


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:45:56
SL : 10.00
SP : -58.00
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:3
Img:8
PP:HFS
21cm
980509-MSAWITH I....
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 66.15%
L : -750
W : 1500

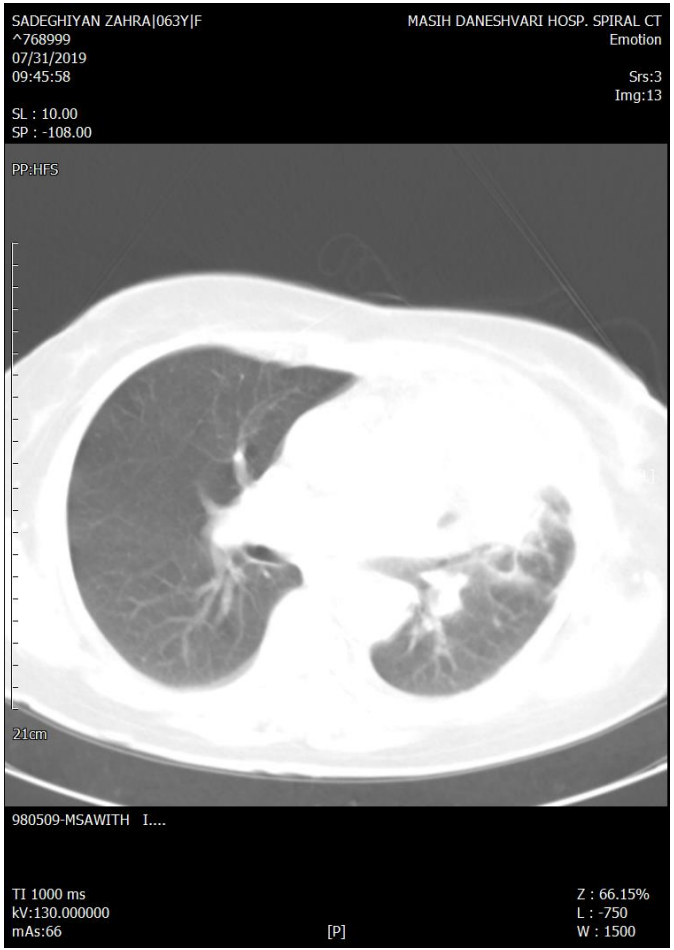
Title


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:45:56
SL : 10.00
SP : -68.00
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:3
Img:9
PP:HFS
21cm
980509-MSAWITH I....
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 66.15%
L : -750
W : 1500

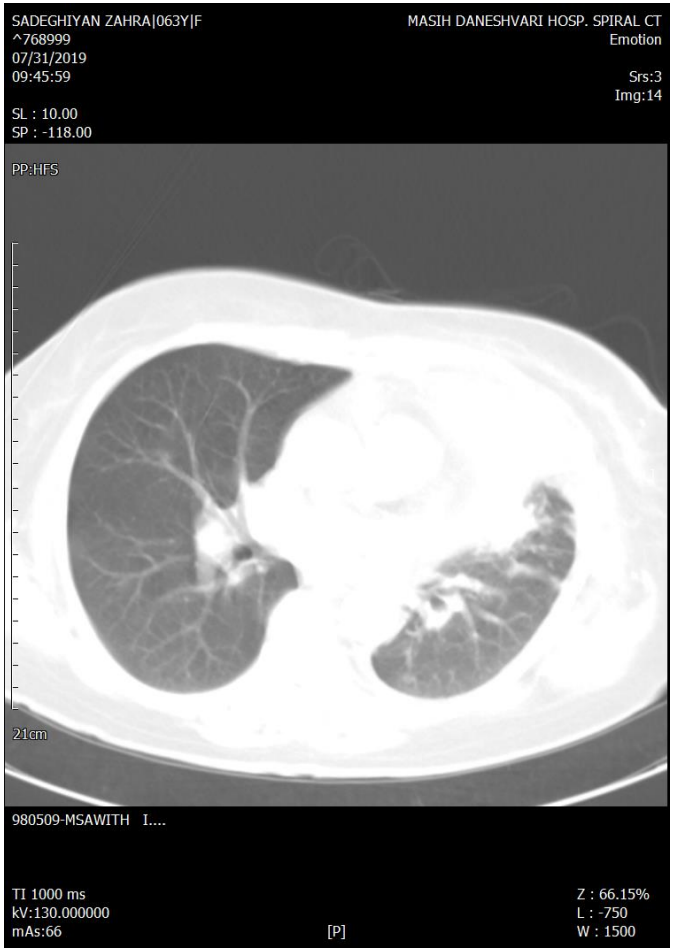
Title


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:45:57
SL : 10.00
SP : -78.00
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:3
Img:10
PP:HFS
21cm
980509-MSAWITH I....
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 66.15%
L : -750
W : 1500

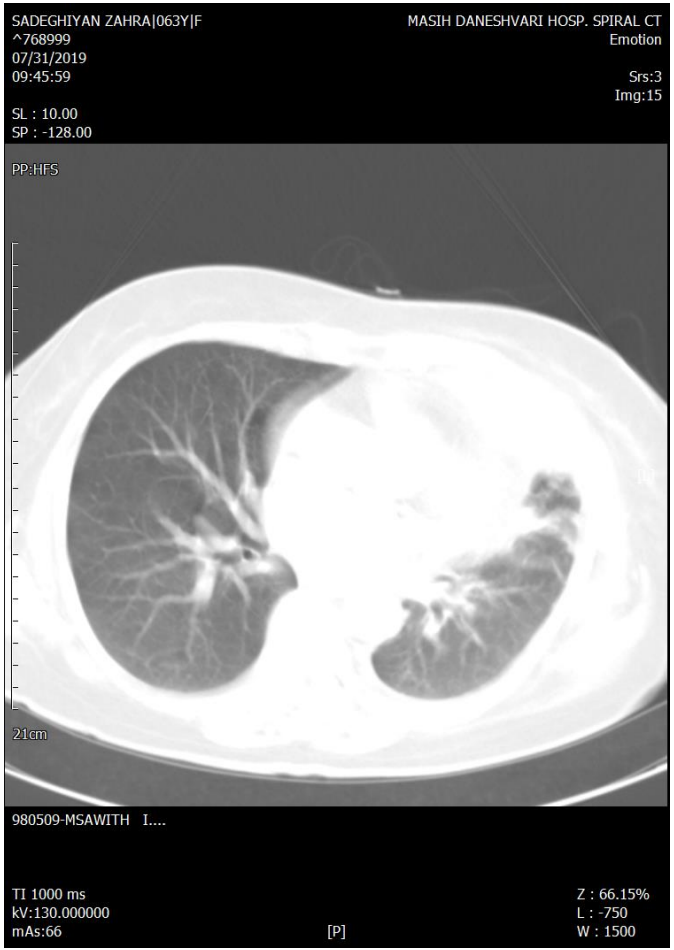
Title


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:45:58
SL : 10.00
SP : -108.00
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:3
Img:13
PP:HFS
21cm
980509-MSAWITH I....
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 66.15%
L : -750
W : 1500

Title


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:45:59
SL : 10.00
SP : -118.00
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:3
Img:14
PP:HFS
21cm
980509-MSAWITH I....
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 66.15%
L : -750
W : 1500

Title


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:45:59
SL : 10.00
SP : -128.00
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:3
Img:15
PP:HFS
21cm
980509-MSAWITH I....
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 66.15%
L : -750
W : 1500

Title


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:46:00
SL : 10.00
SP : -138.00
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:3
Img:16
PP:HFS
21cm
980509-MSAWITH I....
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 66.15%
L : -750
W : 1500

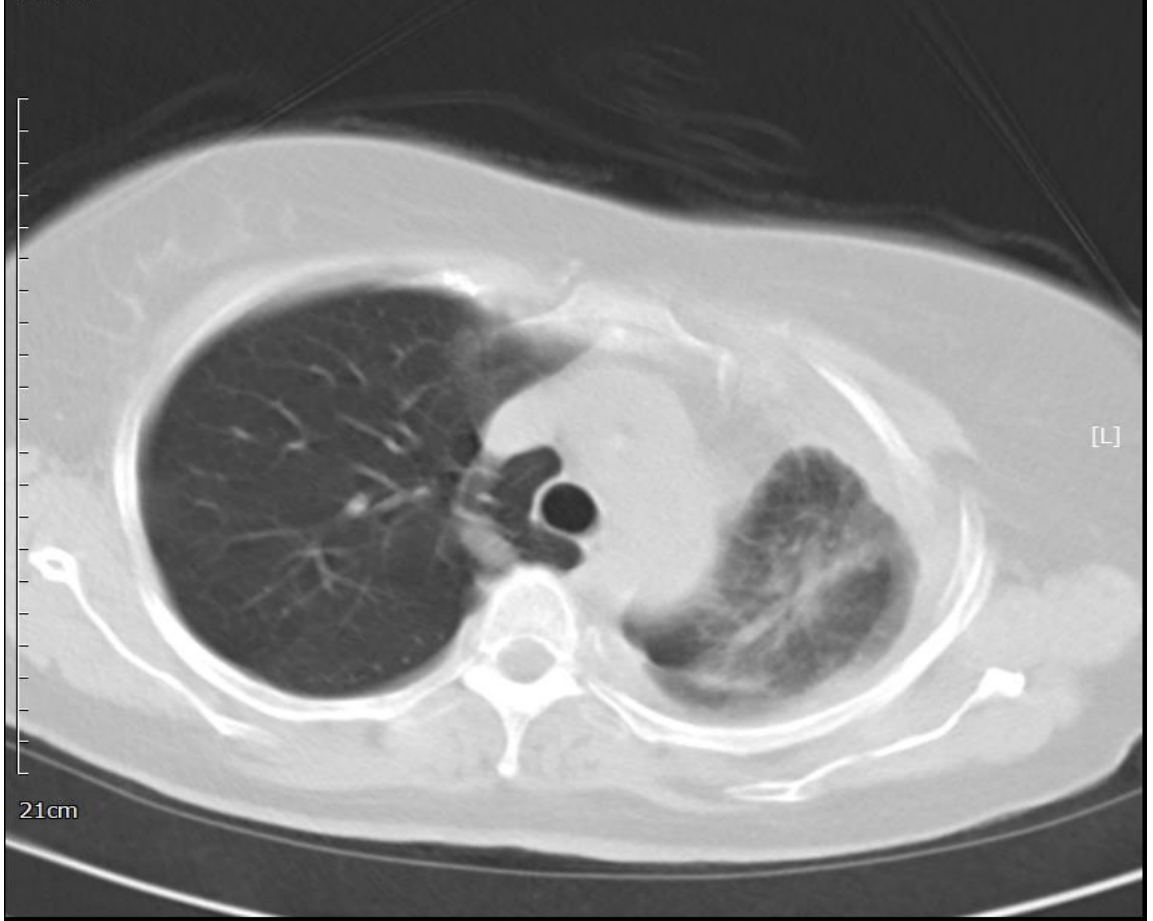
Title


SADEGHIYAN ZAHRA|063Y|F
^768999
07/31/2019
09:46:00
SL : 10.00
SP : -148.00
MASIH DANESHVARI HOSP. SPIRAL CT
Emotion
Srs:3
Img:17
PP:HFS
21cm
980509-MSAWITH I....
TI 1000 ms
kV:130.000000
mAs:66
[P]
Z : 66.15%
L : -750
W : 1500

11/98

- 6 months later

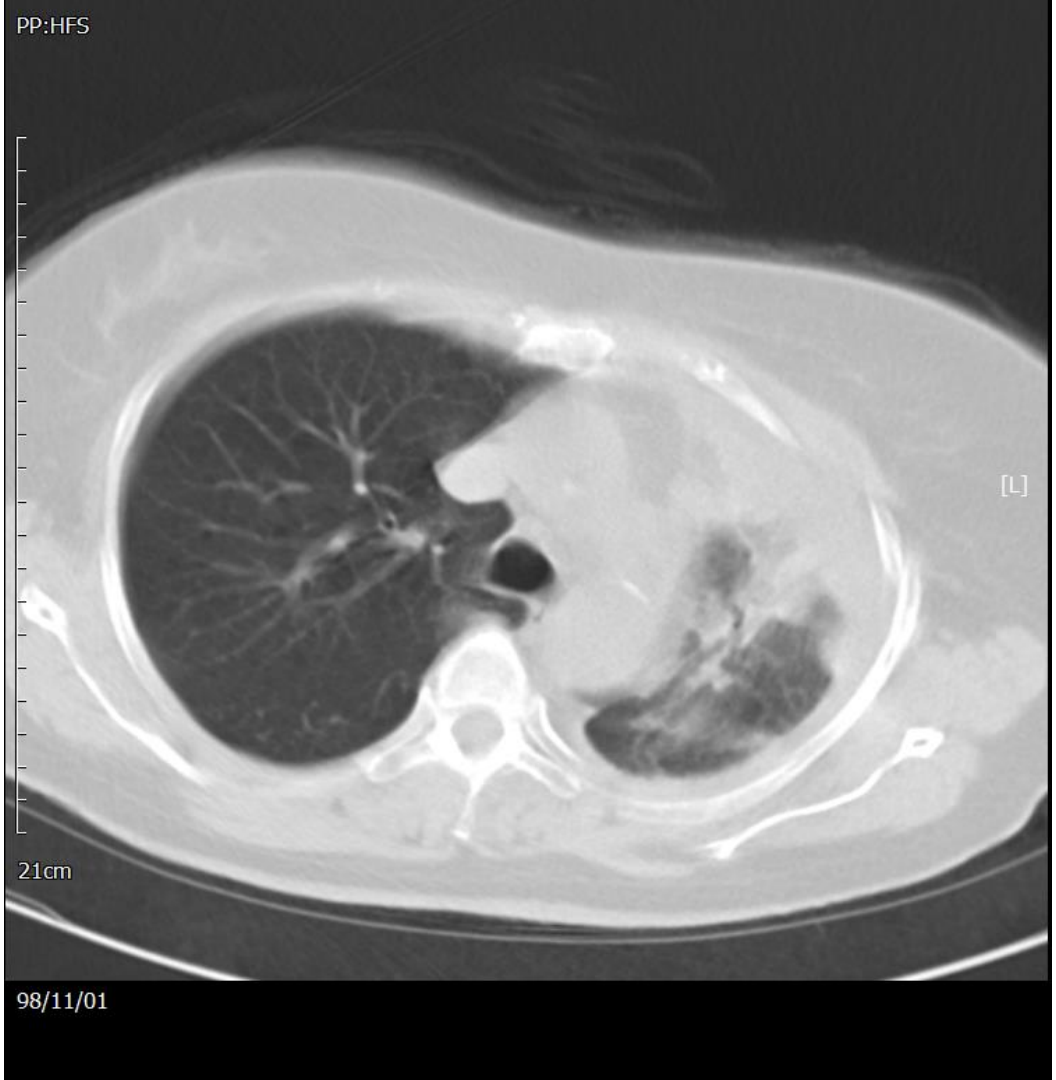

PP:HFS
[L]
21cm
98/11/01

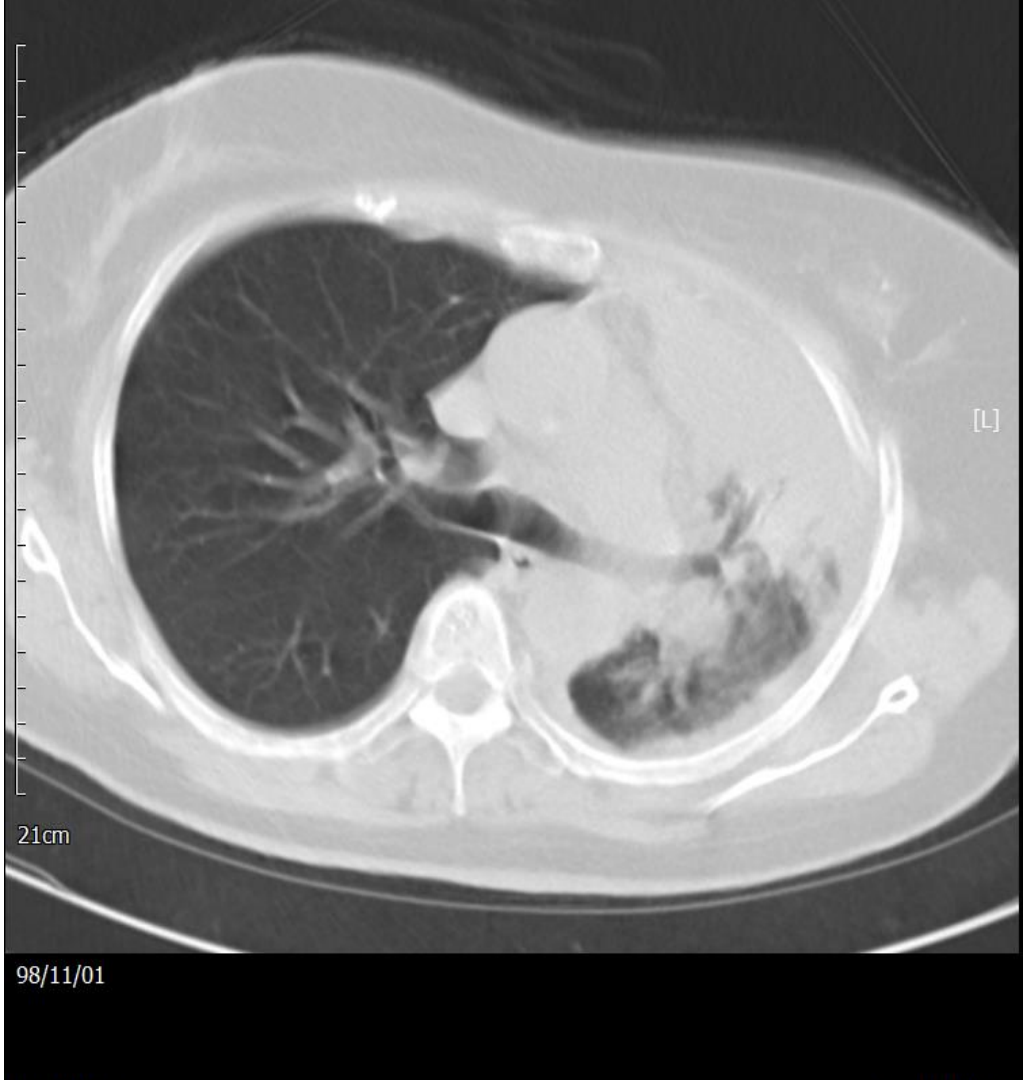


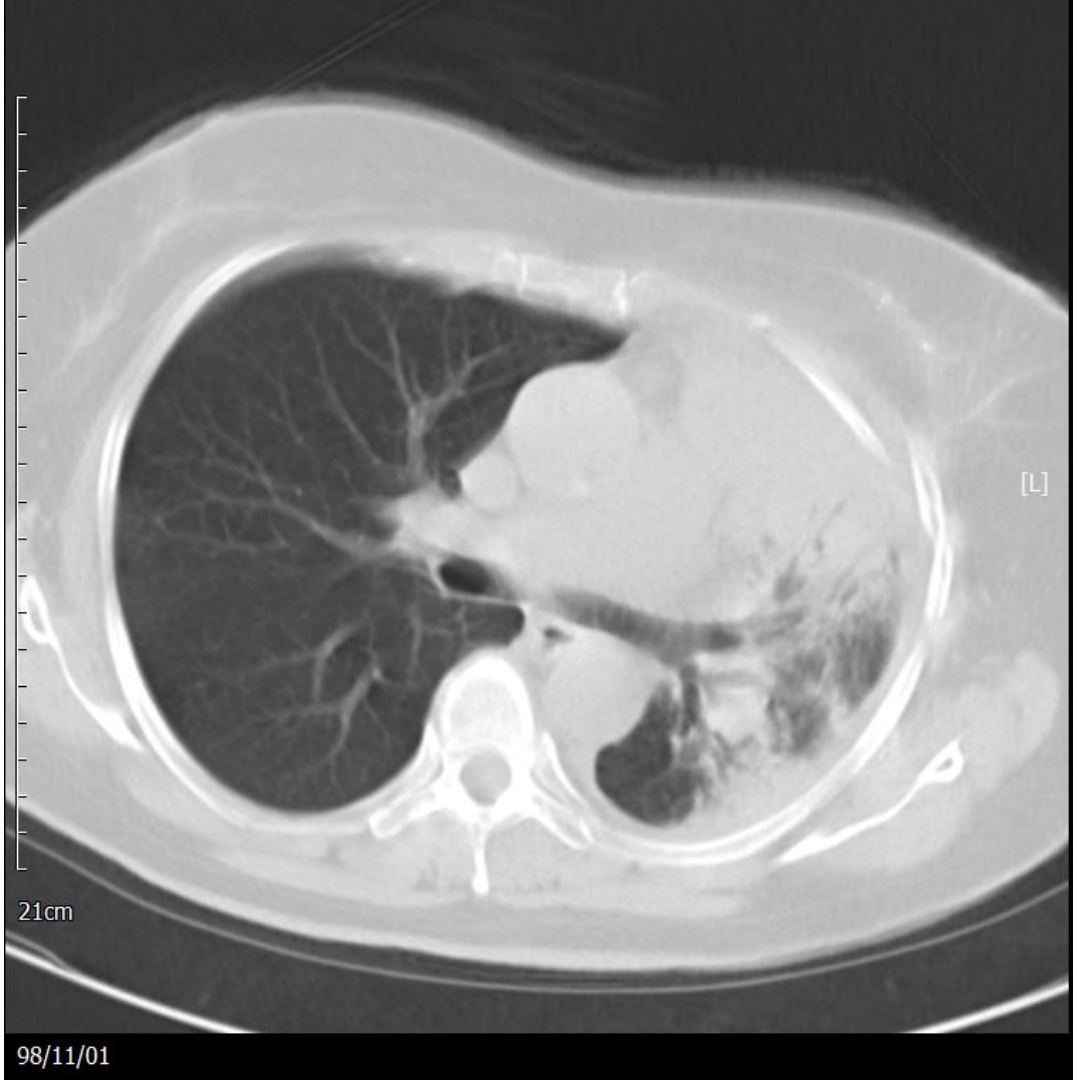
98/11/01

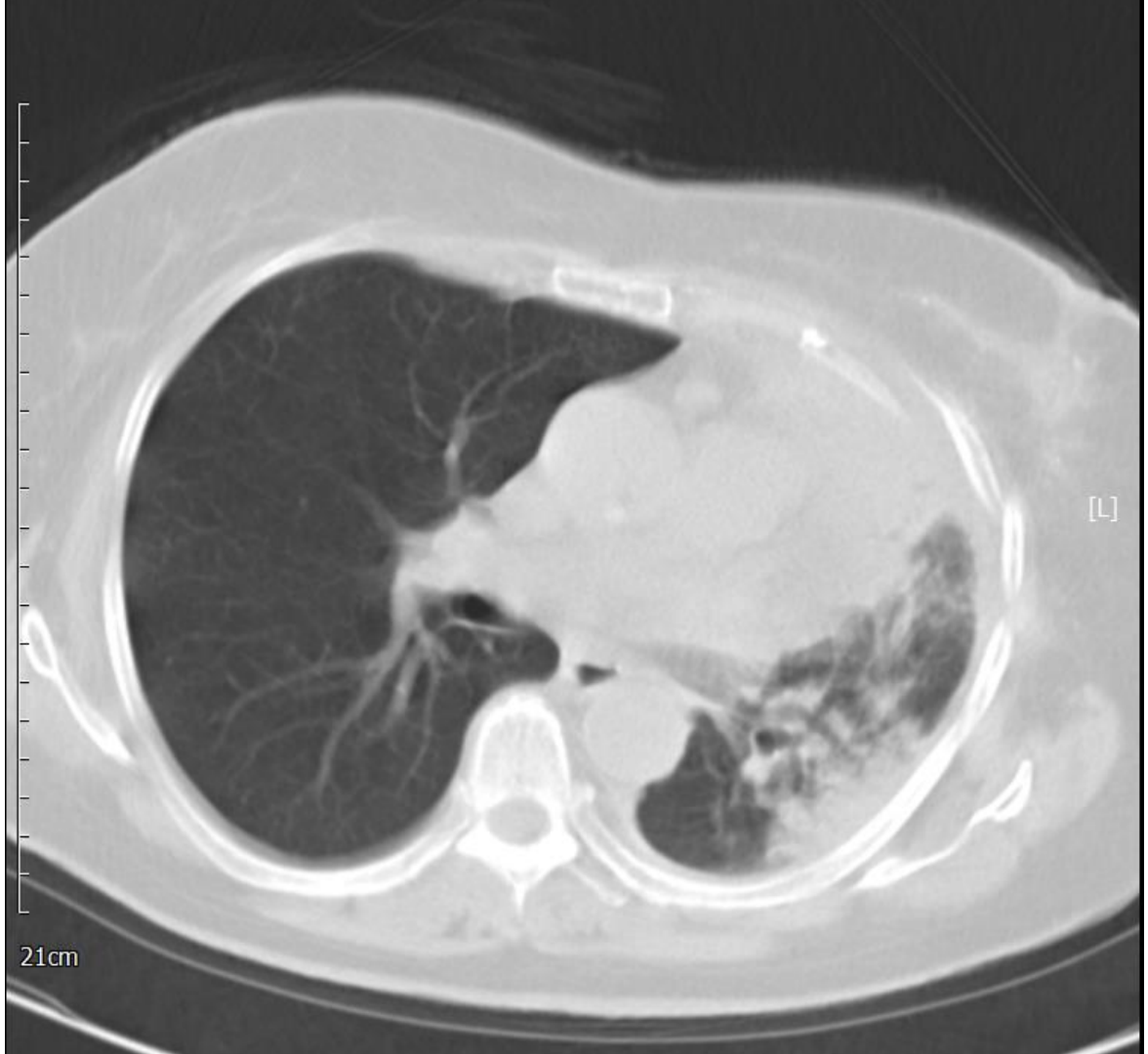
TI 1000 ms
kV:110.000000

Z : 65.93%
L : -500

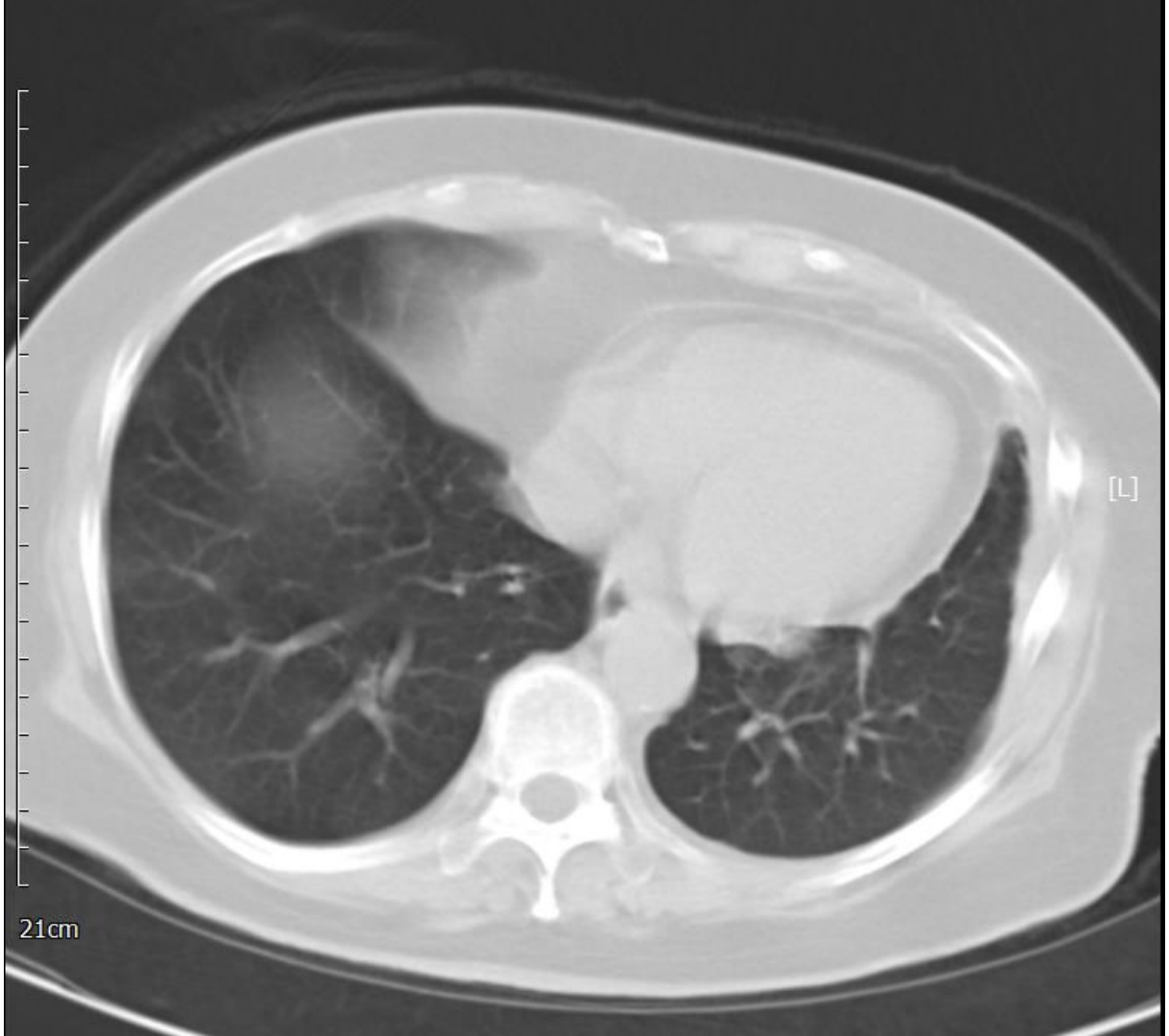

PP:HFS
[L]
21cm
98/11/01

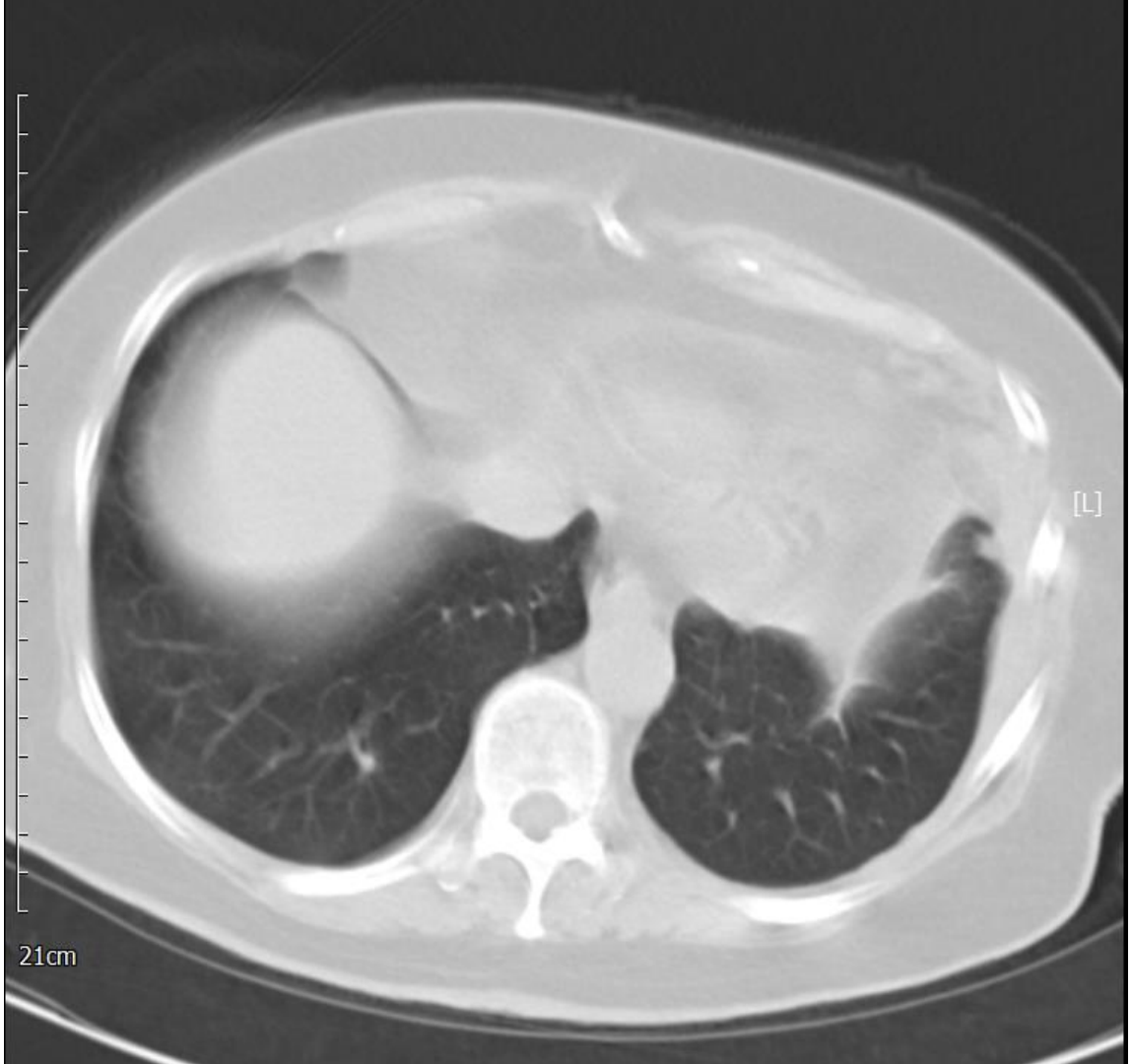

[L]
21cm
98/11/01


[L]
21cm
98/11/01


[L]
21cm


[L]
21cm


[L]
21cm


[L]
21cm

What is your impression?

Radiation pneumonitis?
Progression?

Radiation Pneumonitis

- Patients who undergo thoracic or neck irradiation for the treatment of malignancy (eg, breast, laryngeal, lung, hematologic) are at risk for radiation pneumonitis and radiation fibrosis.

- Many factors affect the risk for radiation pneumonitis including the ***method of irradiation, the volume of irradiated lung, the total dosage and frequency of irradiation, associated chemotherapy, and possibly the genetic background of the patient***.

- Symptoms caused by subacute radiation pneumonitis usually develop approximately ***four to twelve weeks*** following irradiation, whereas symptoms of ***late or fibrotic radiation pneumonitis develop after six to twelve months***.

- Typical symptoms for both types of lung injury include dyspnea, cough, chest pain, fever, and malaise.

In cases of early or subtle radiation induced pneumonitis, areas of ground-glass opacity may be evident on CT despite a normal chest x-ray.

- The two most common findings are :
- ground-glass opacities and/or
- airspace consolidation

Additional features that are sometimes seen include :

- focal or nodular opacities
- tree-in-bud appearances
- ipsilateral pleural effusion
- atelectasis

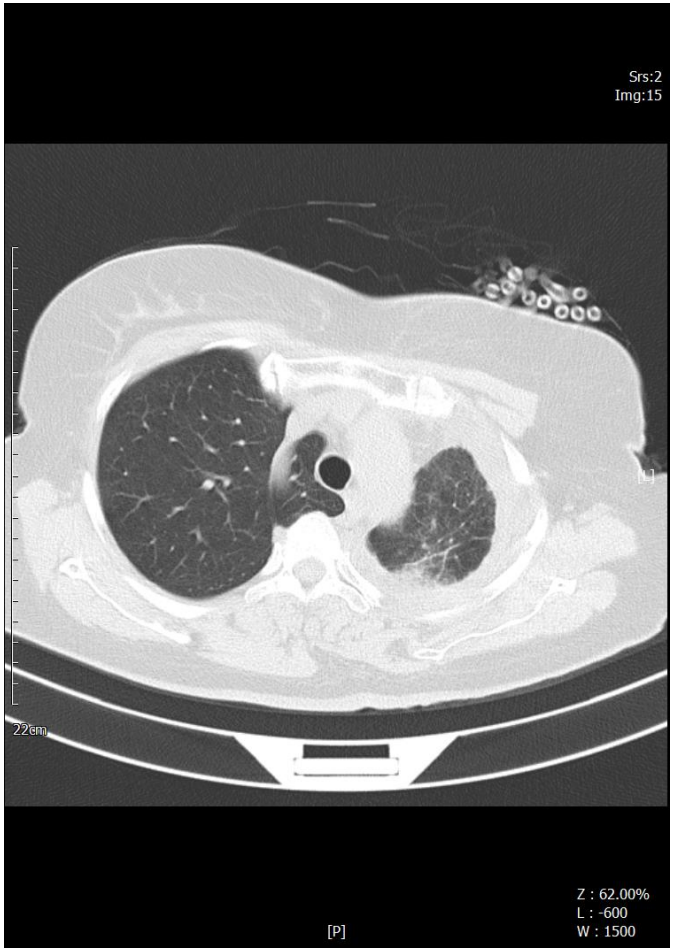
- The diagnosis of radiation pneumonitis is based on the correlation between the onset of symptoms and signs with the timing of irradiation and between the pattern of radiographic changes and the radiation therapy portal.

Careful exclusion of other possible diagnoses, such as

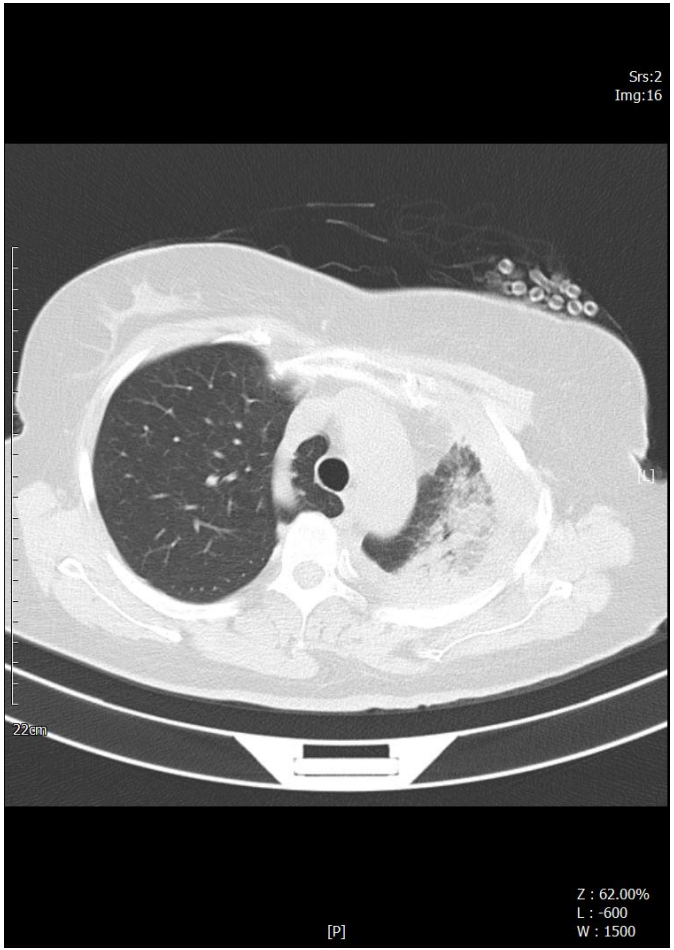
- infection,
- thromboembolic disease,
- drug-induced pneumonitis,
- pericarditis,
- esophagitis,
- tumor progression,
- tracheoesophageal fistula.

06/99

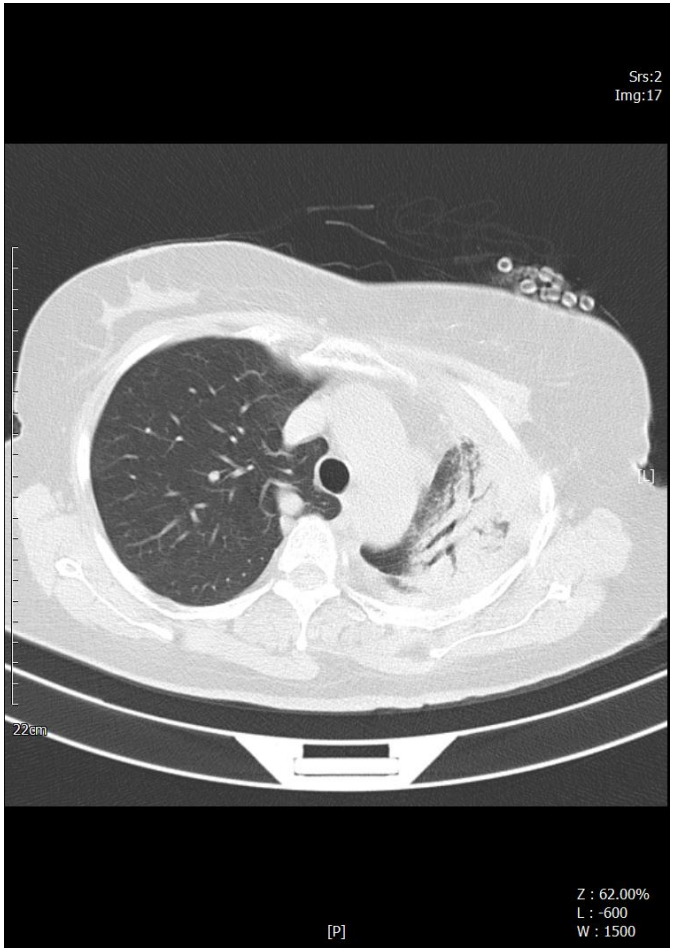
Title



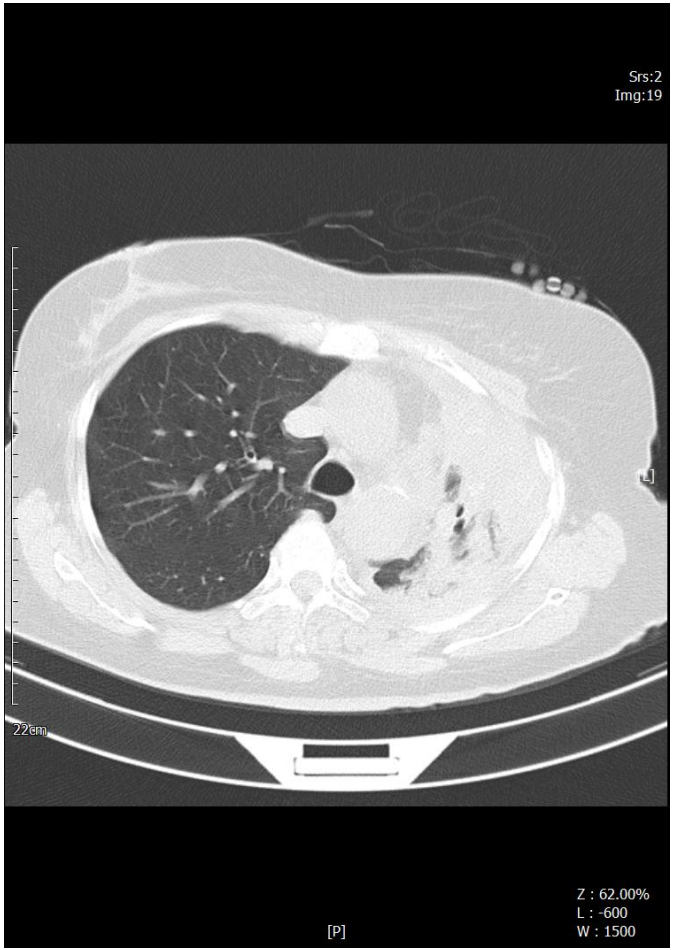
Title



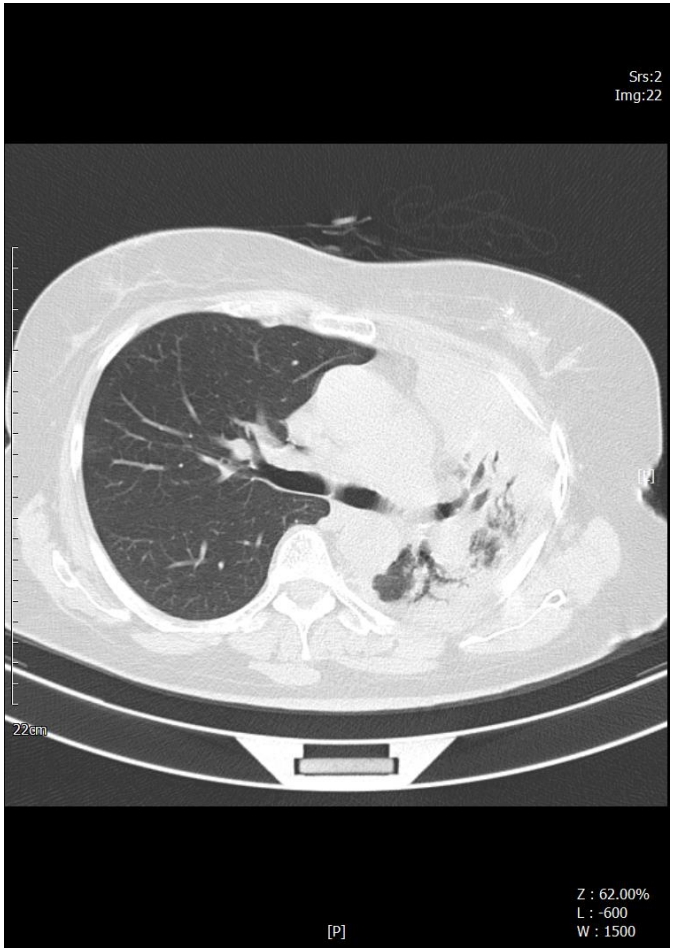
Title



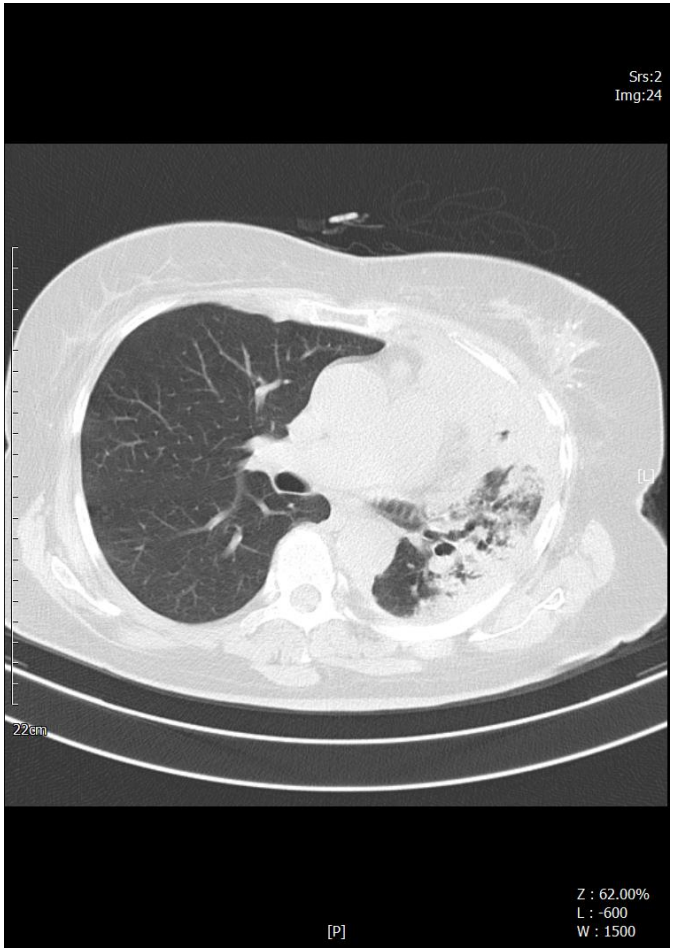
Title



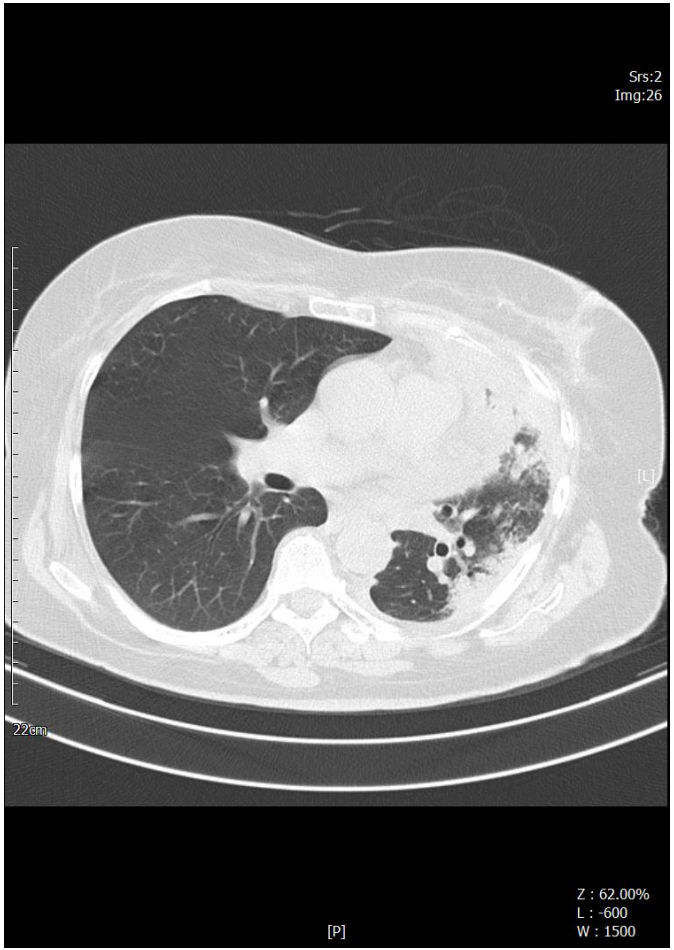
Title



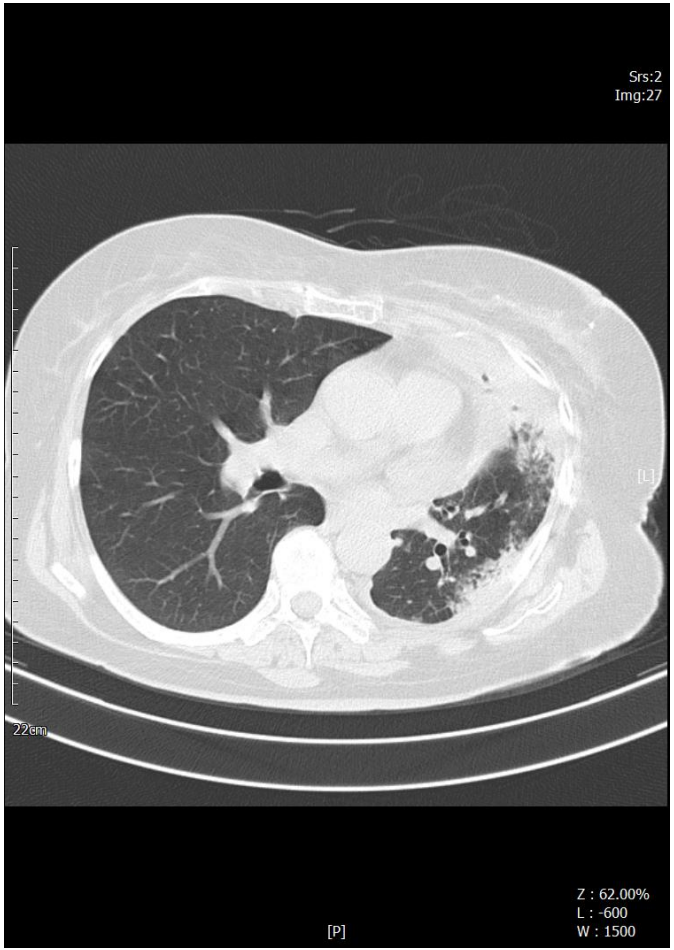
Title



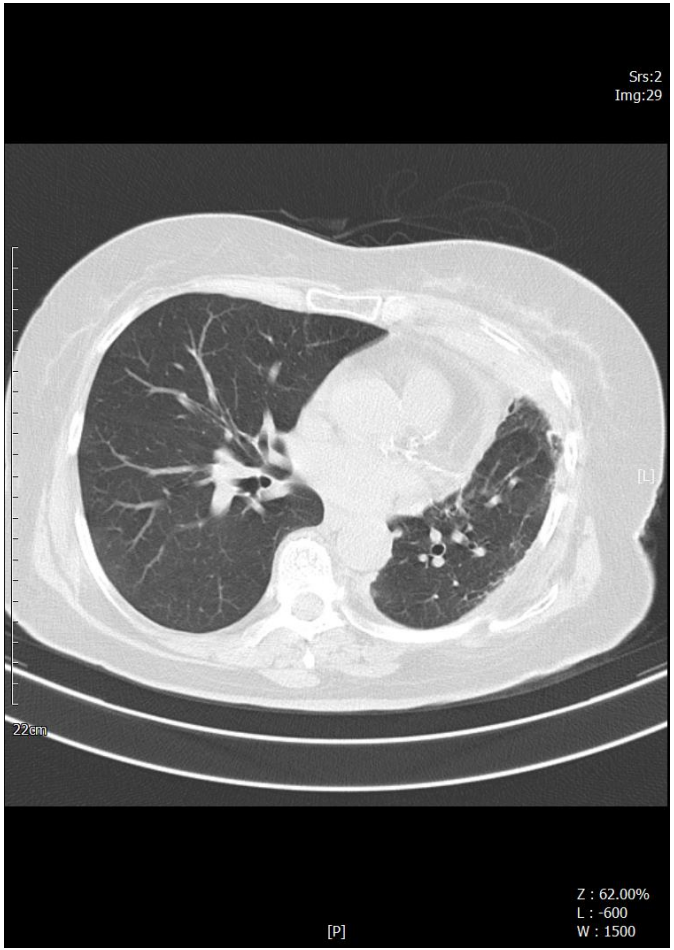
Title



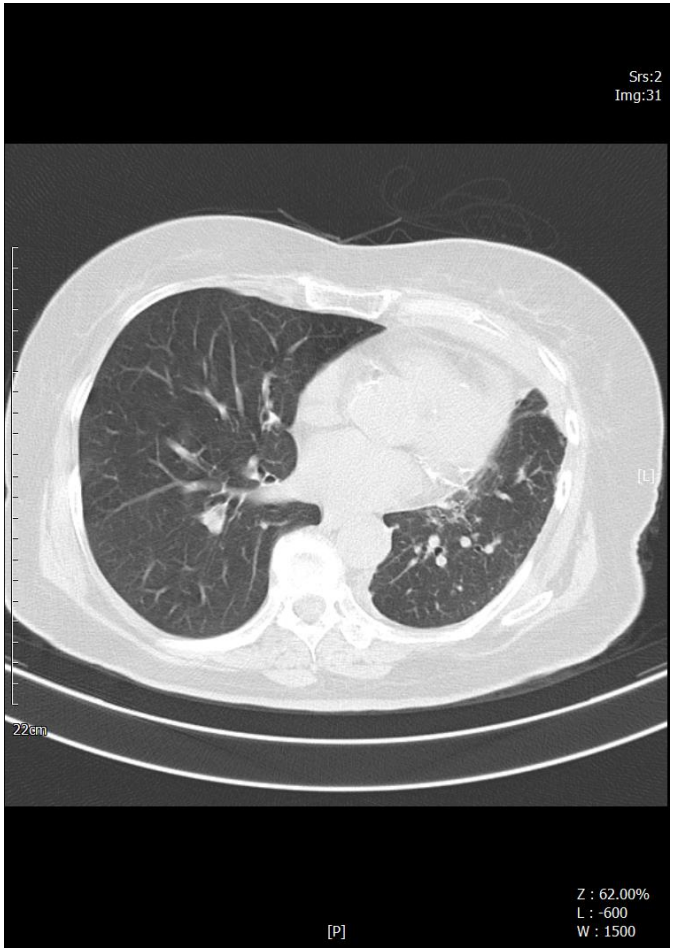
Title



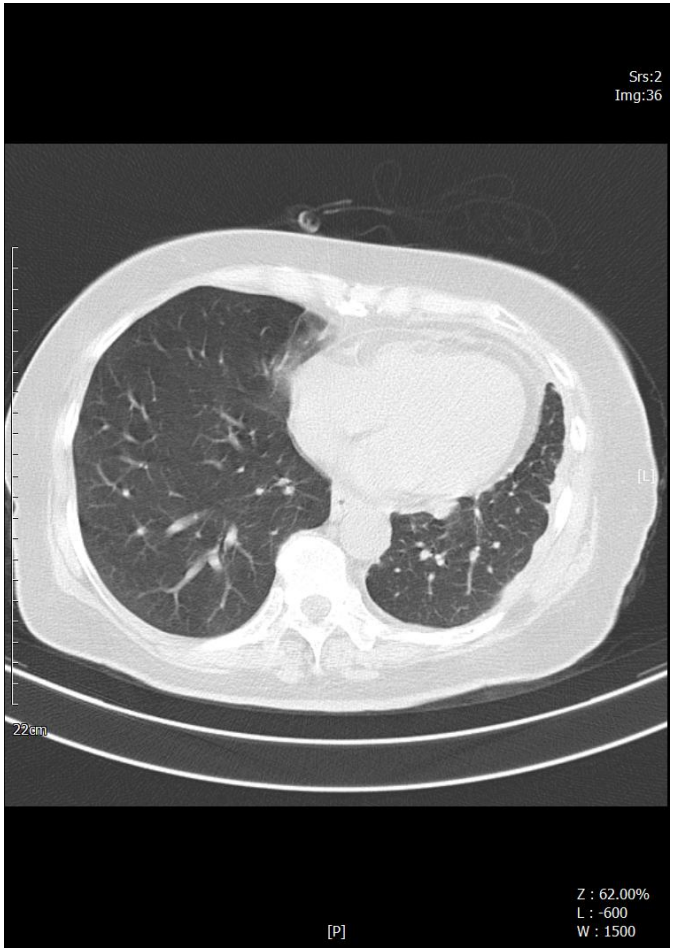
Title



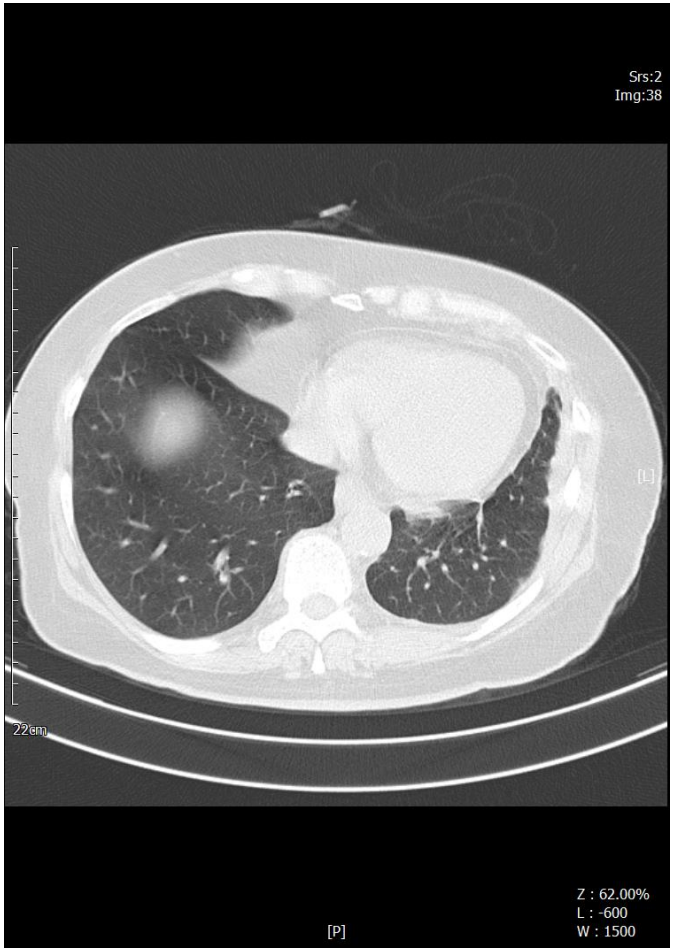
Title



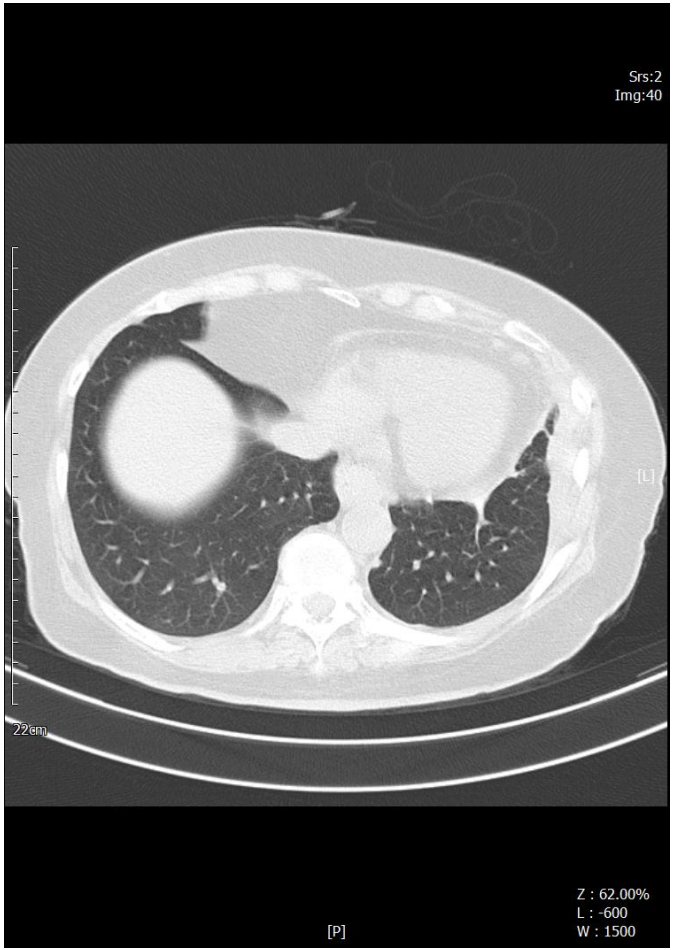
Title



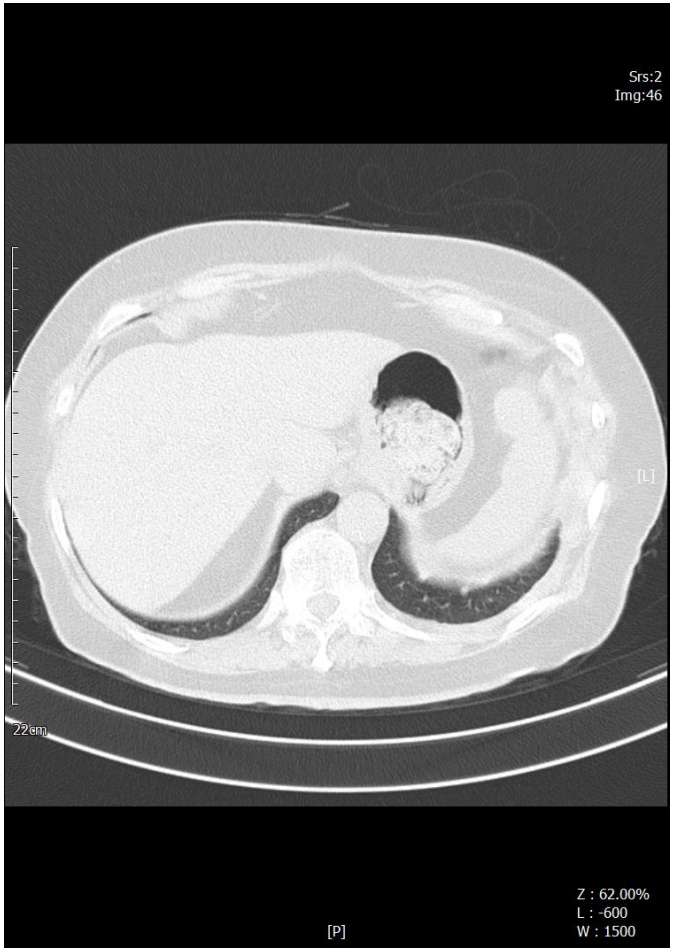
Title



Title

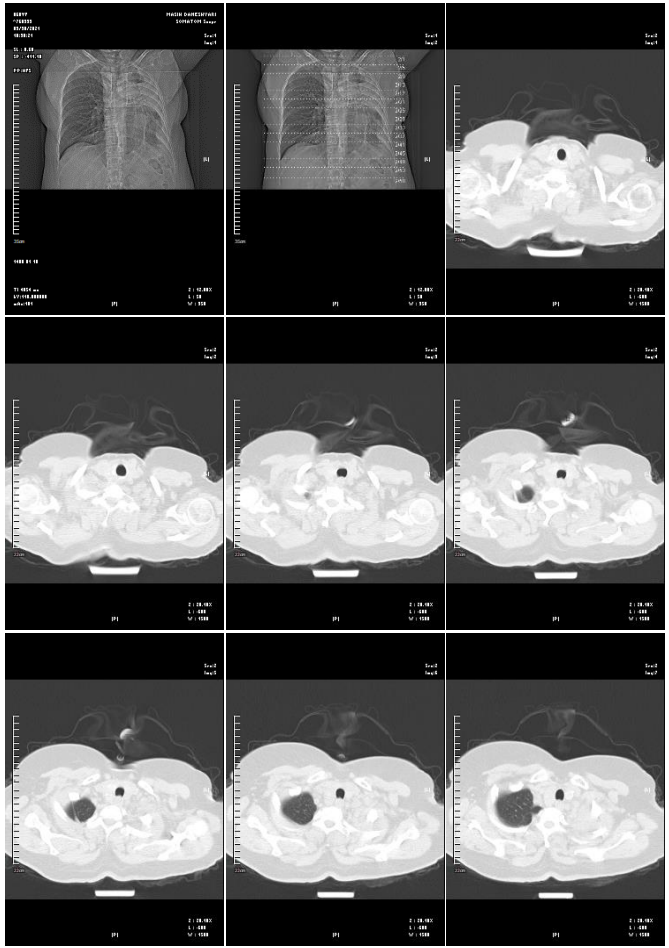


Title

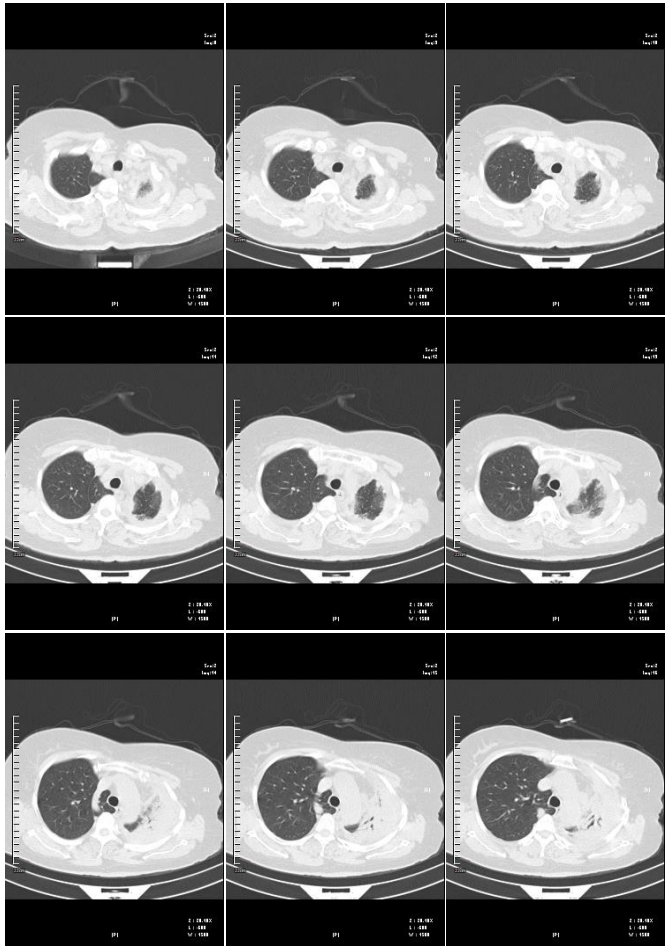


01/1400

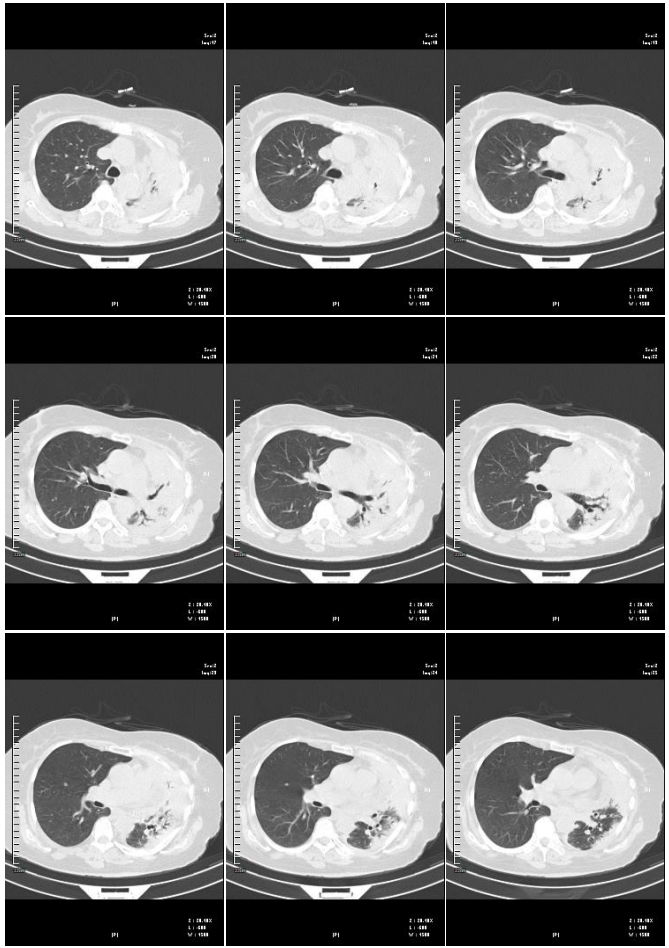
Title



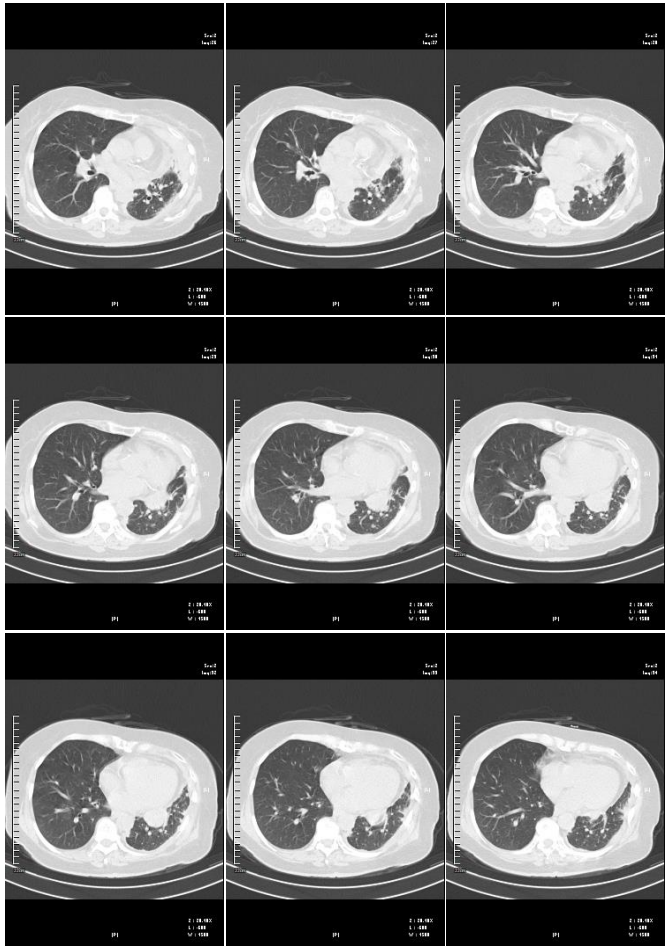
Title



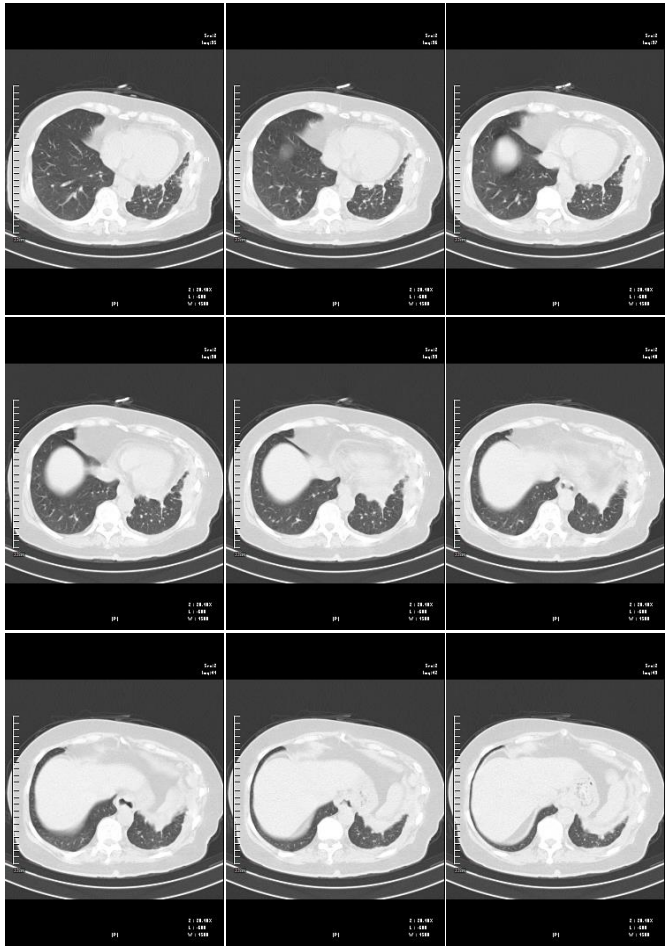
Title



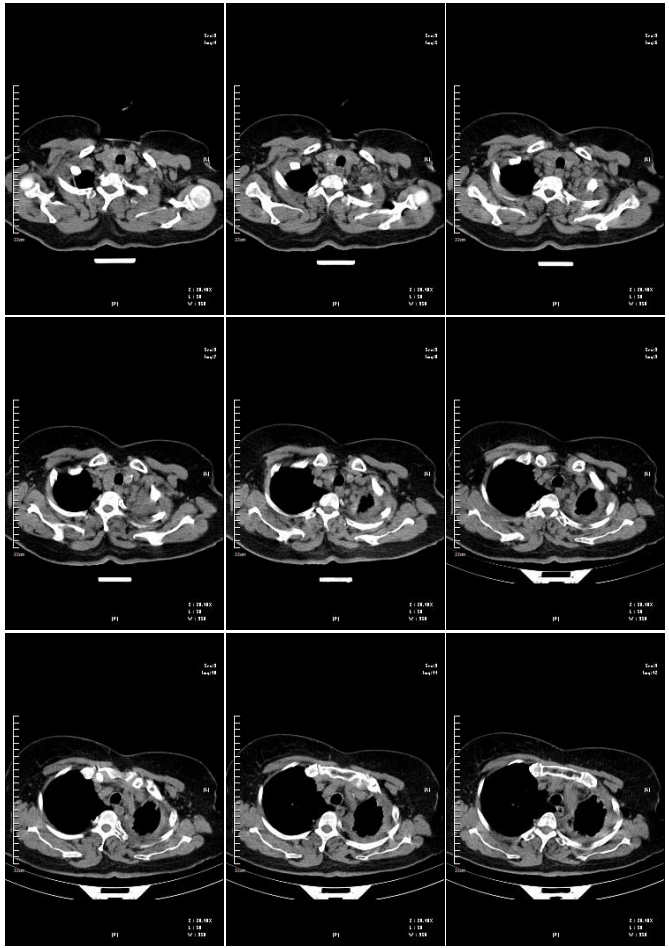
Title



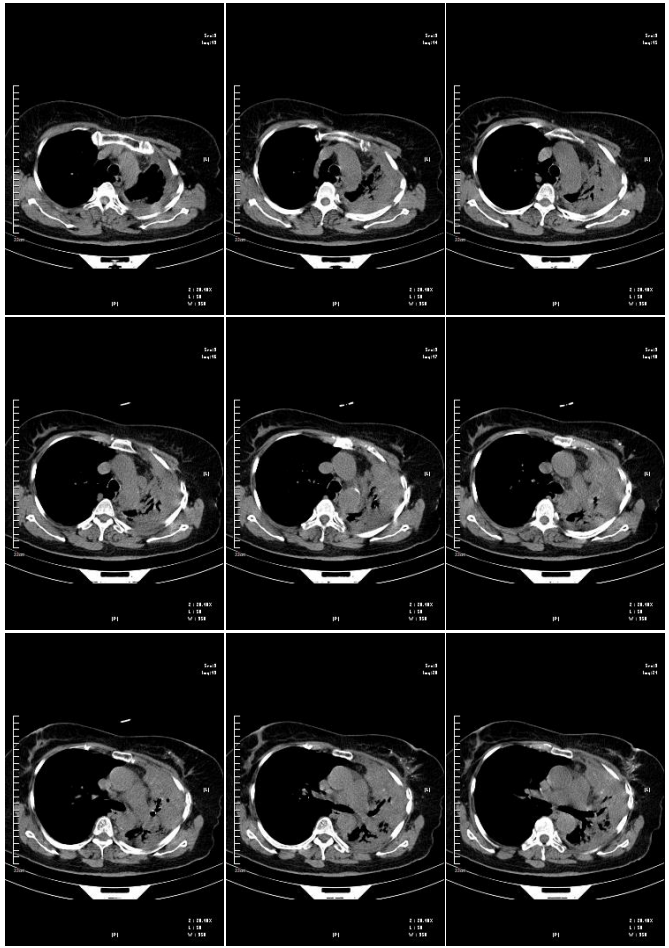
Title



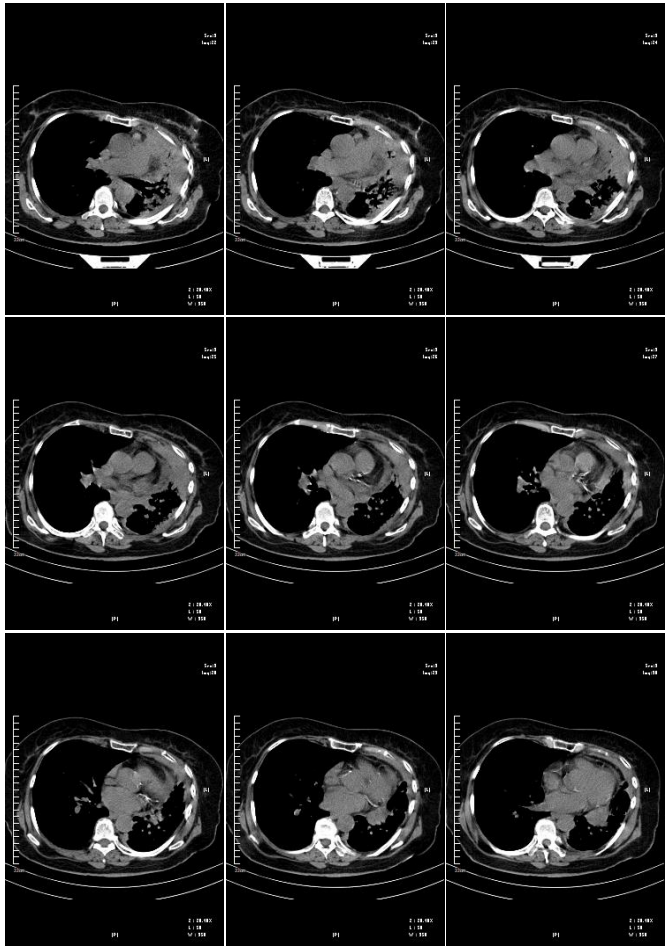
Title



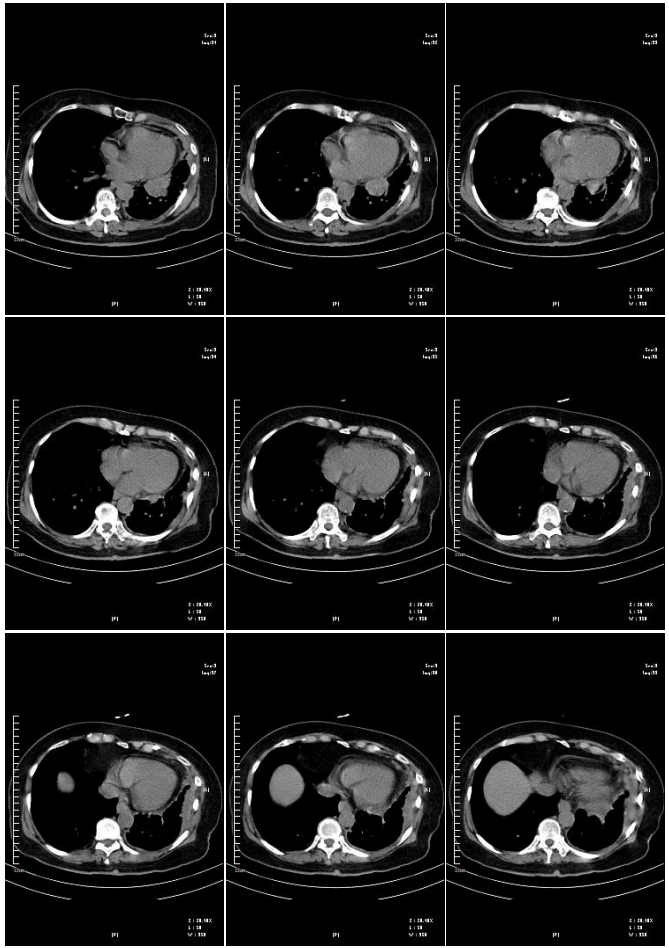
Title



Title



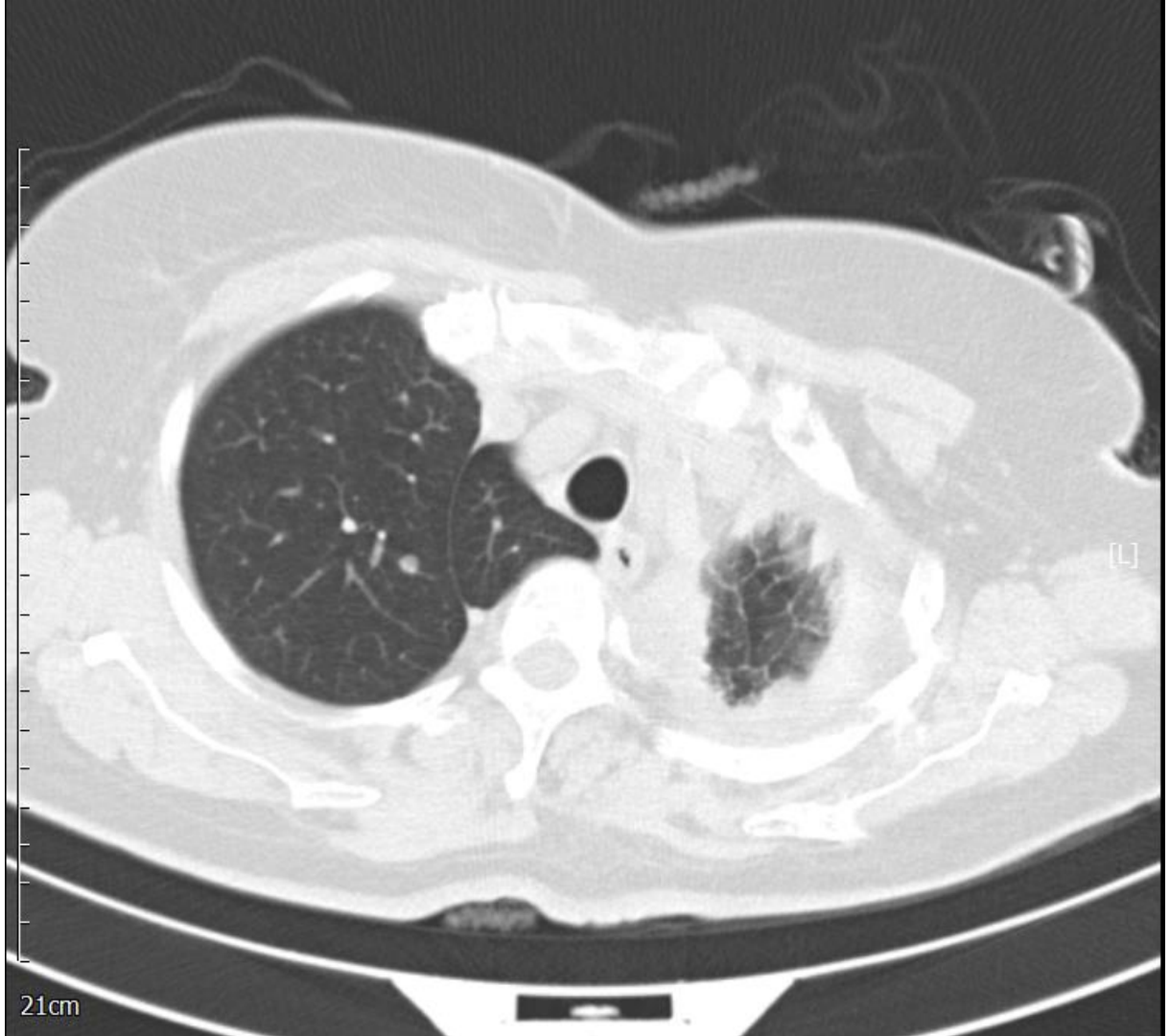
Title

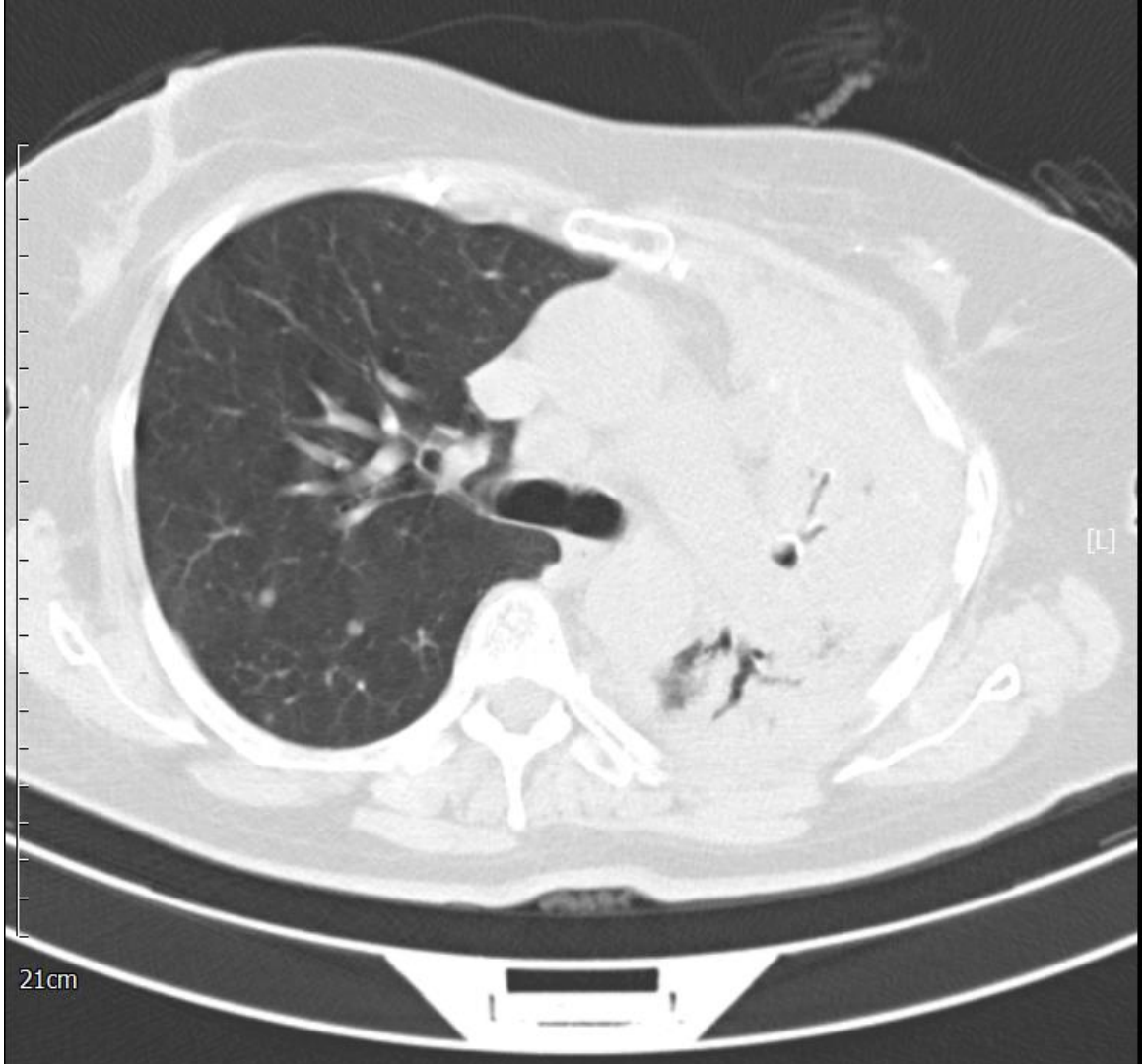


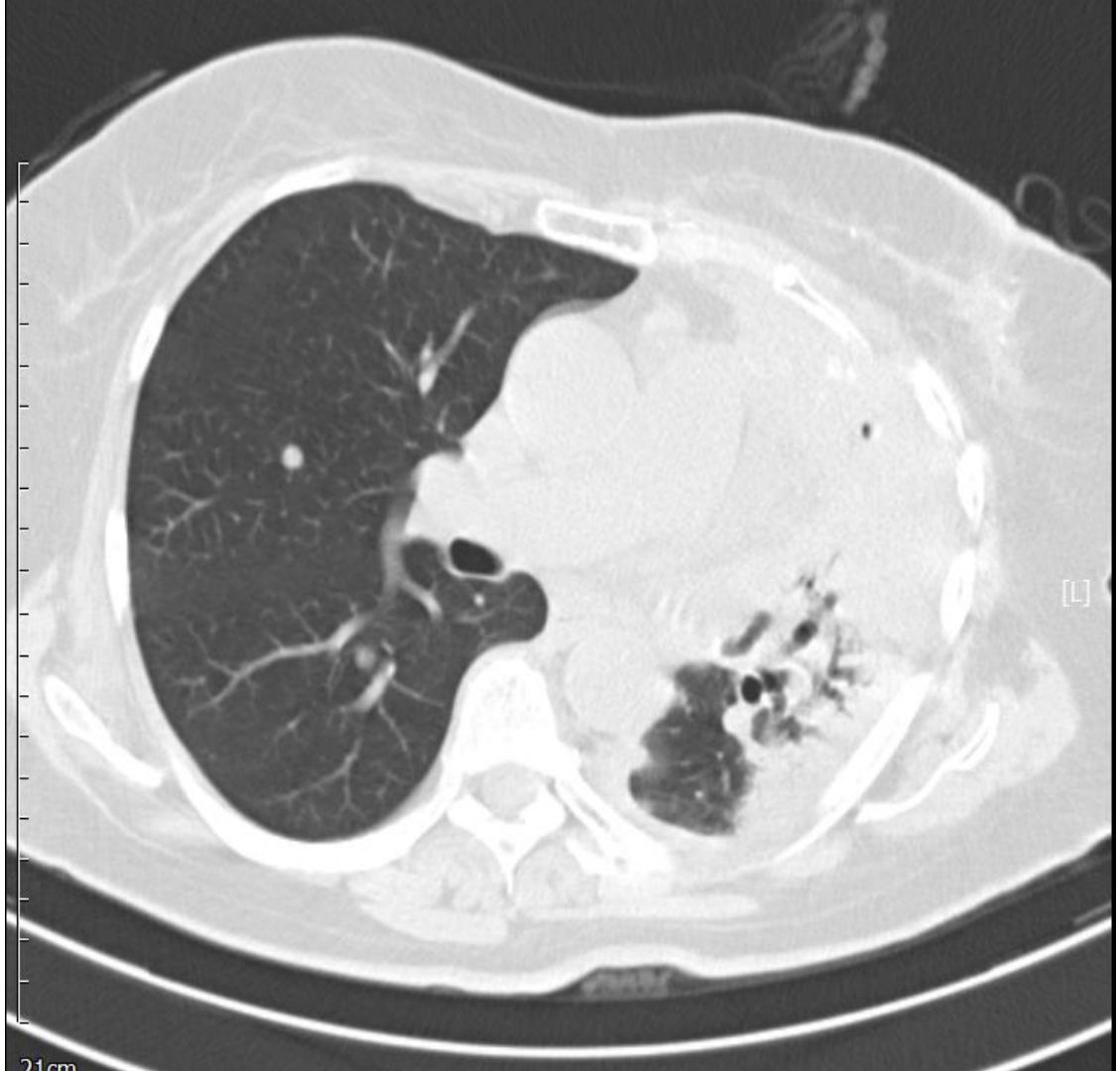
In 07/1400 she had dyspnea and loss of appetite.

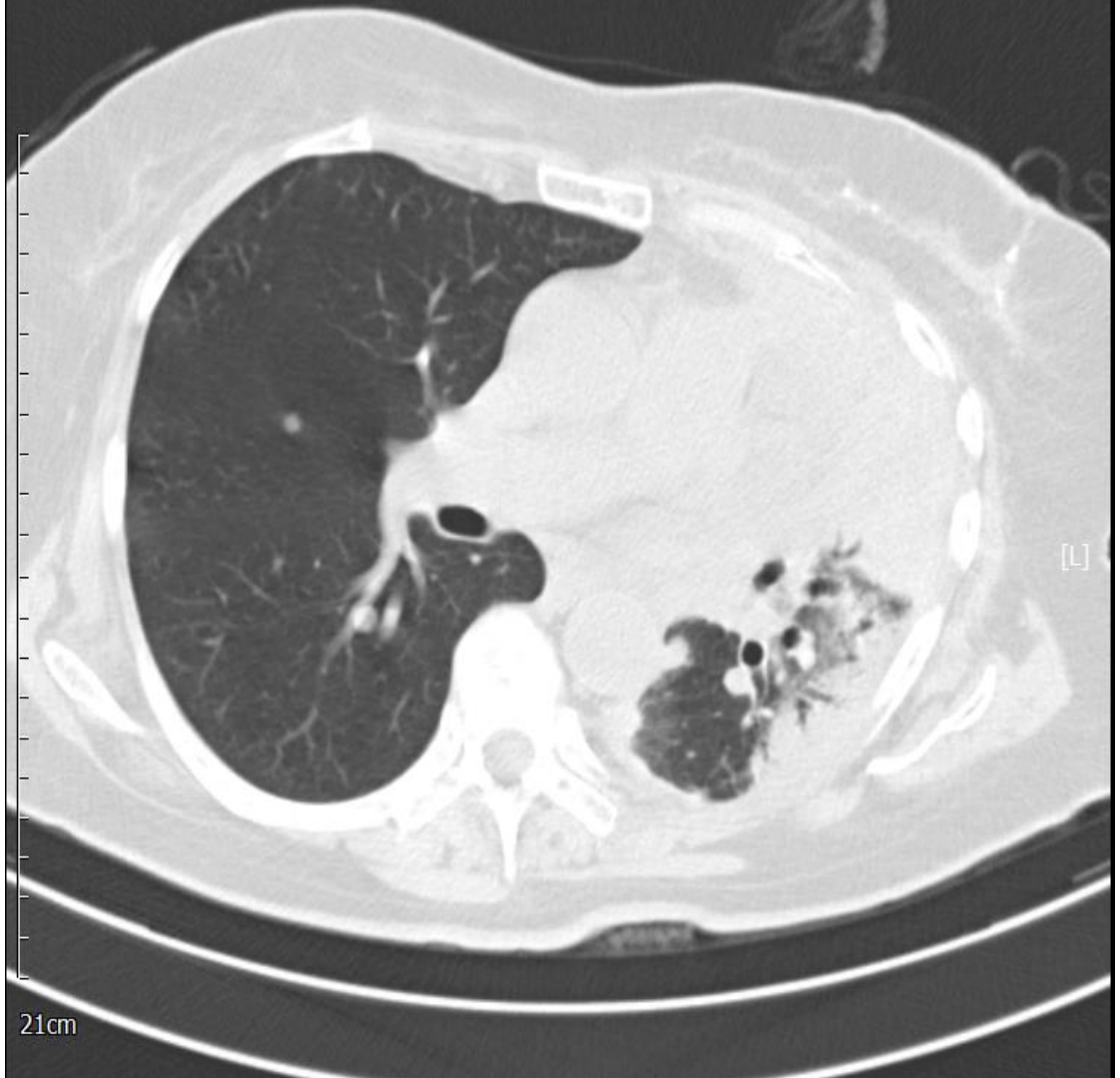
CT scan showed:

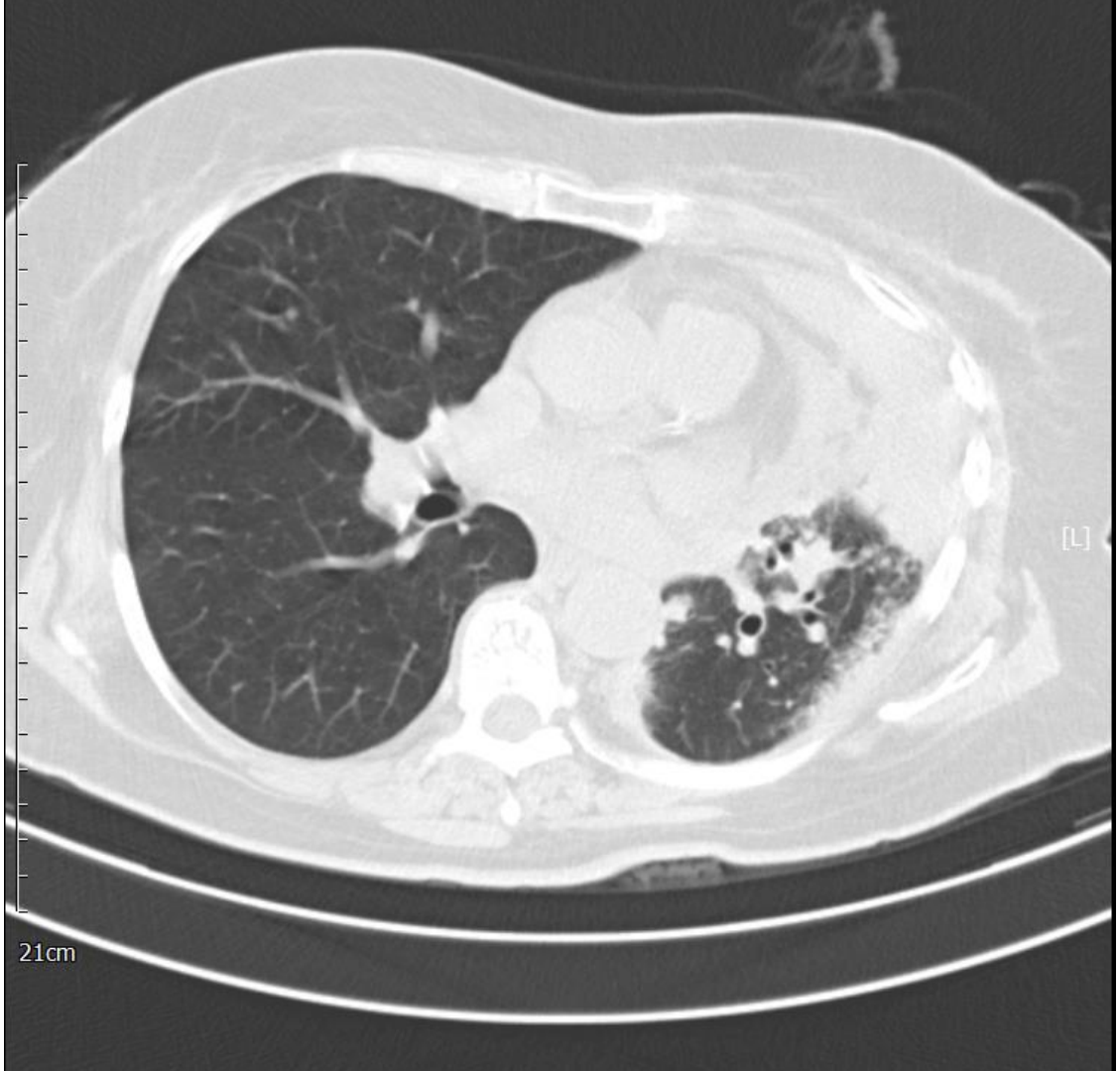
07/1400

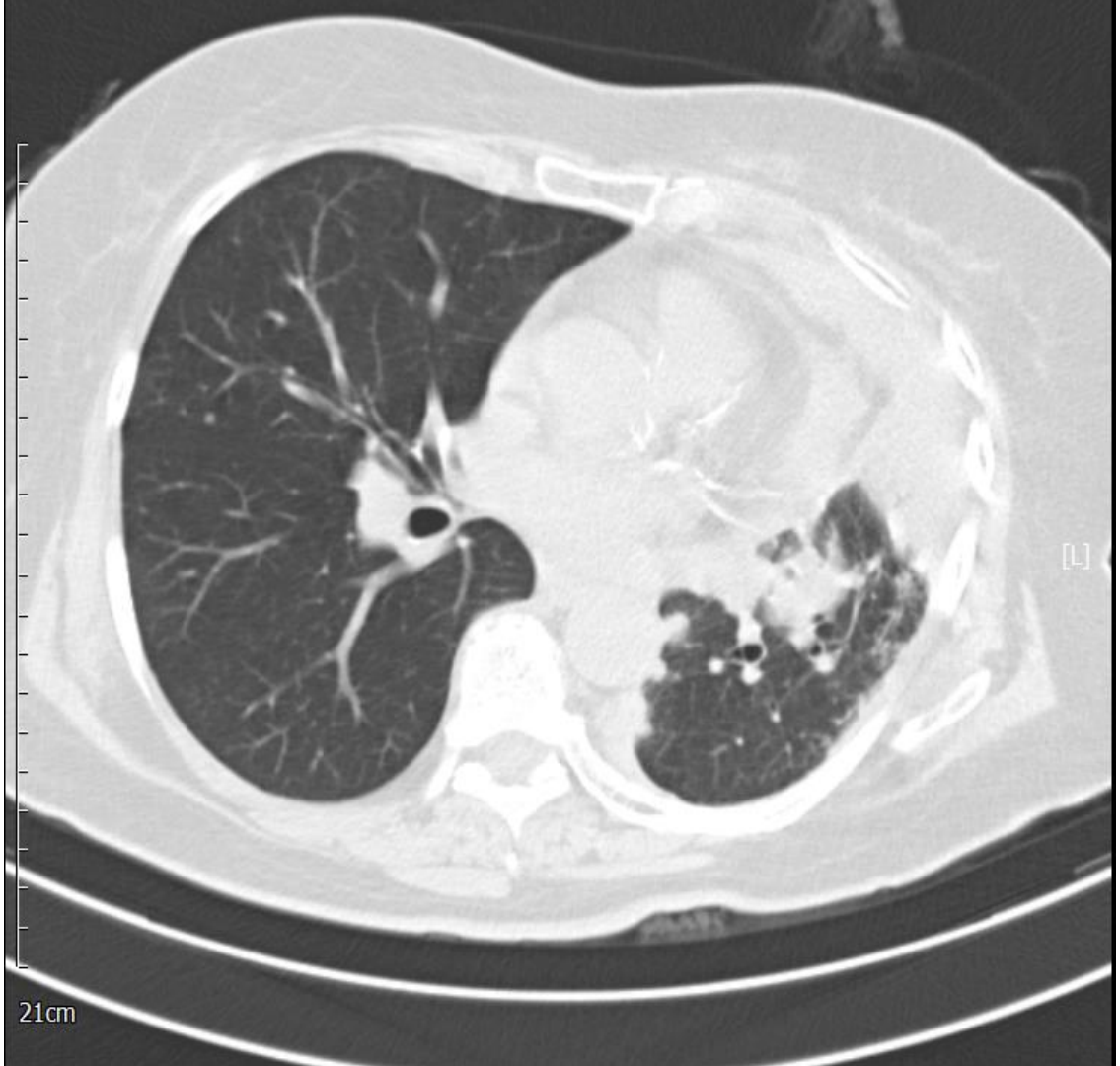

[L]
21cm

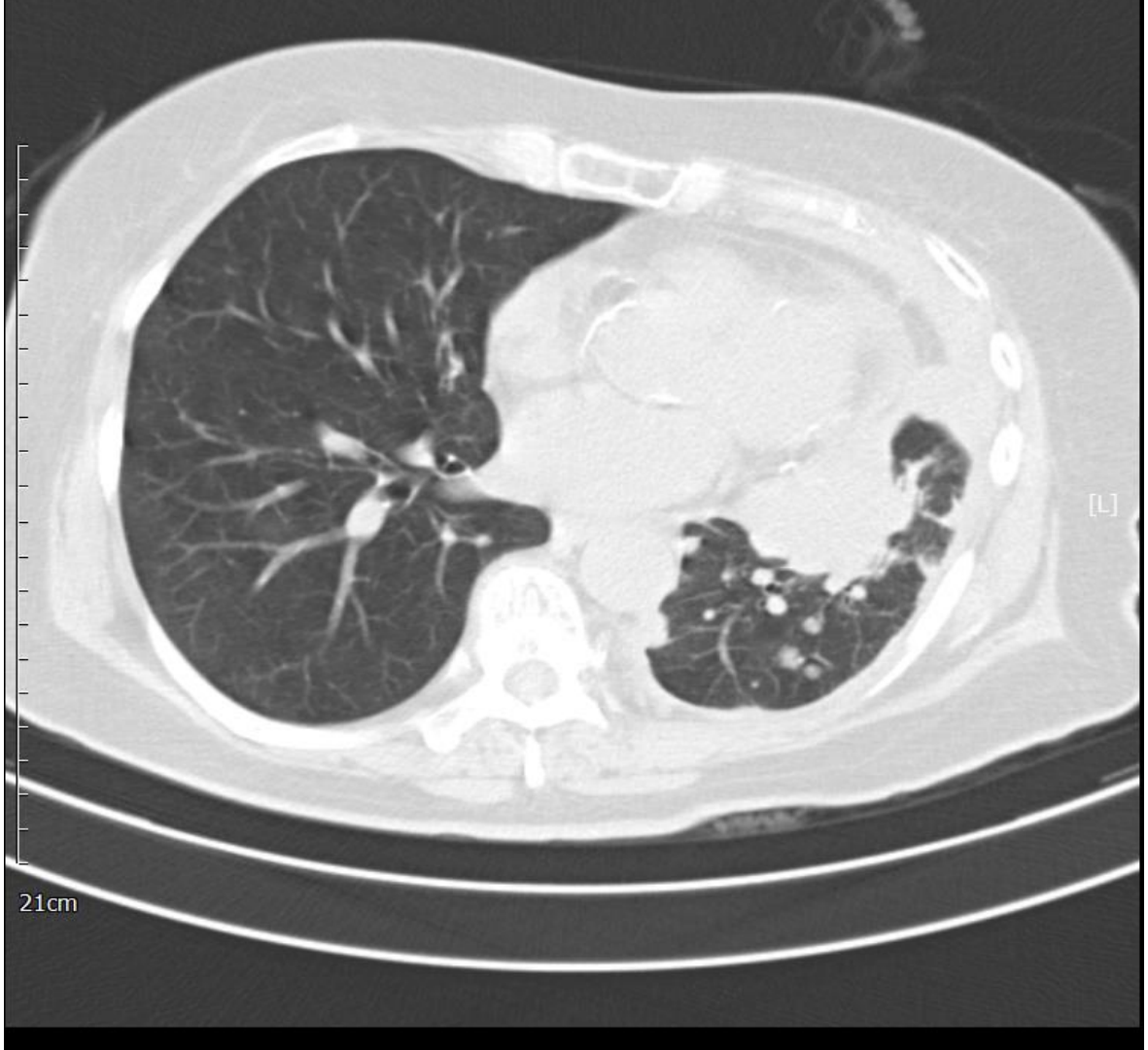

[L]
21cm

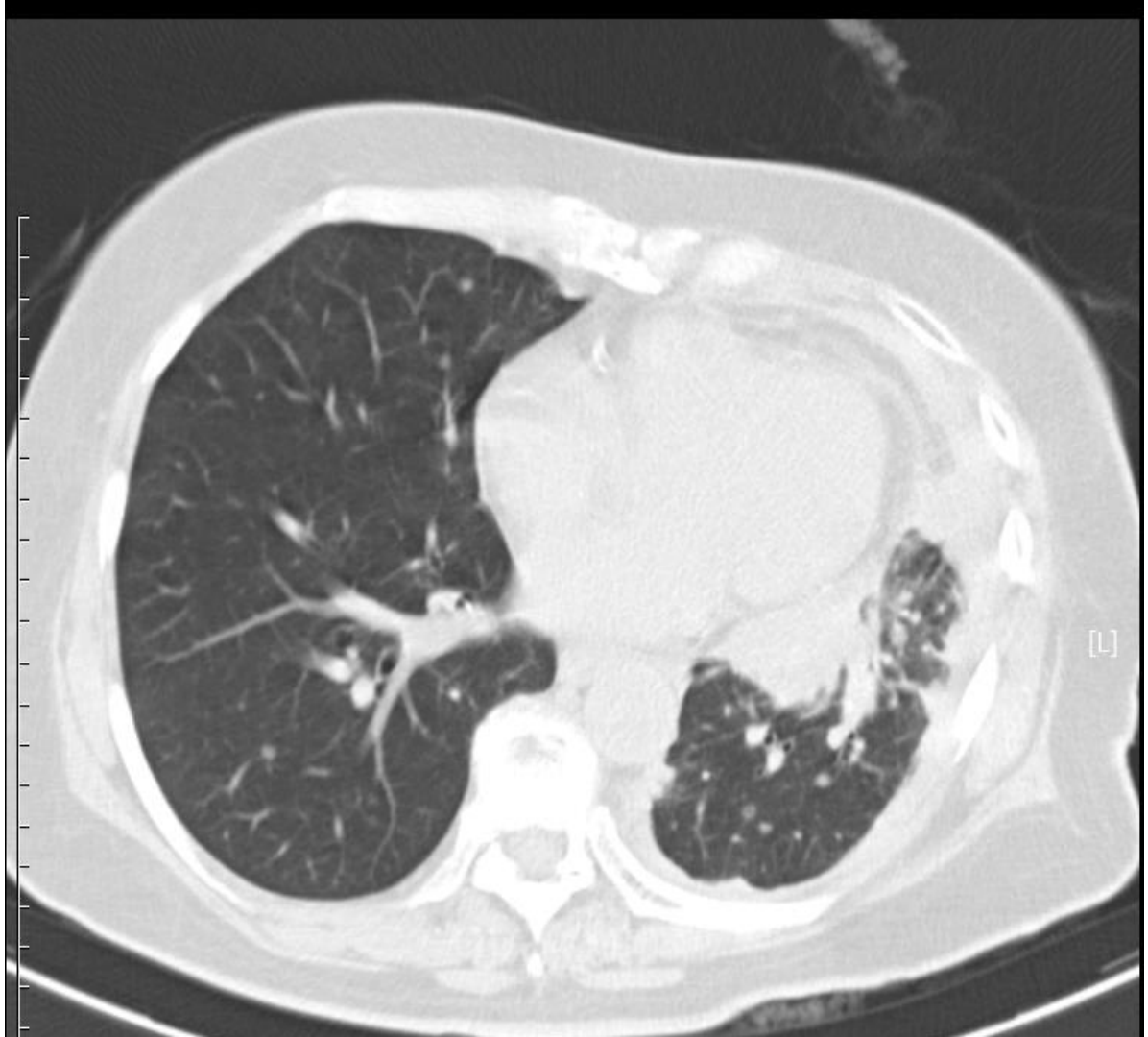

[L]
21cm


[L]
21cm

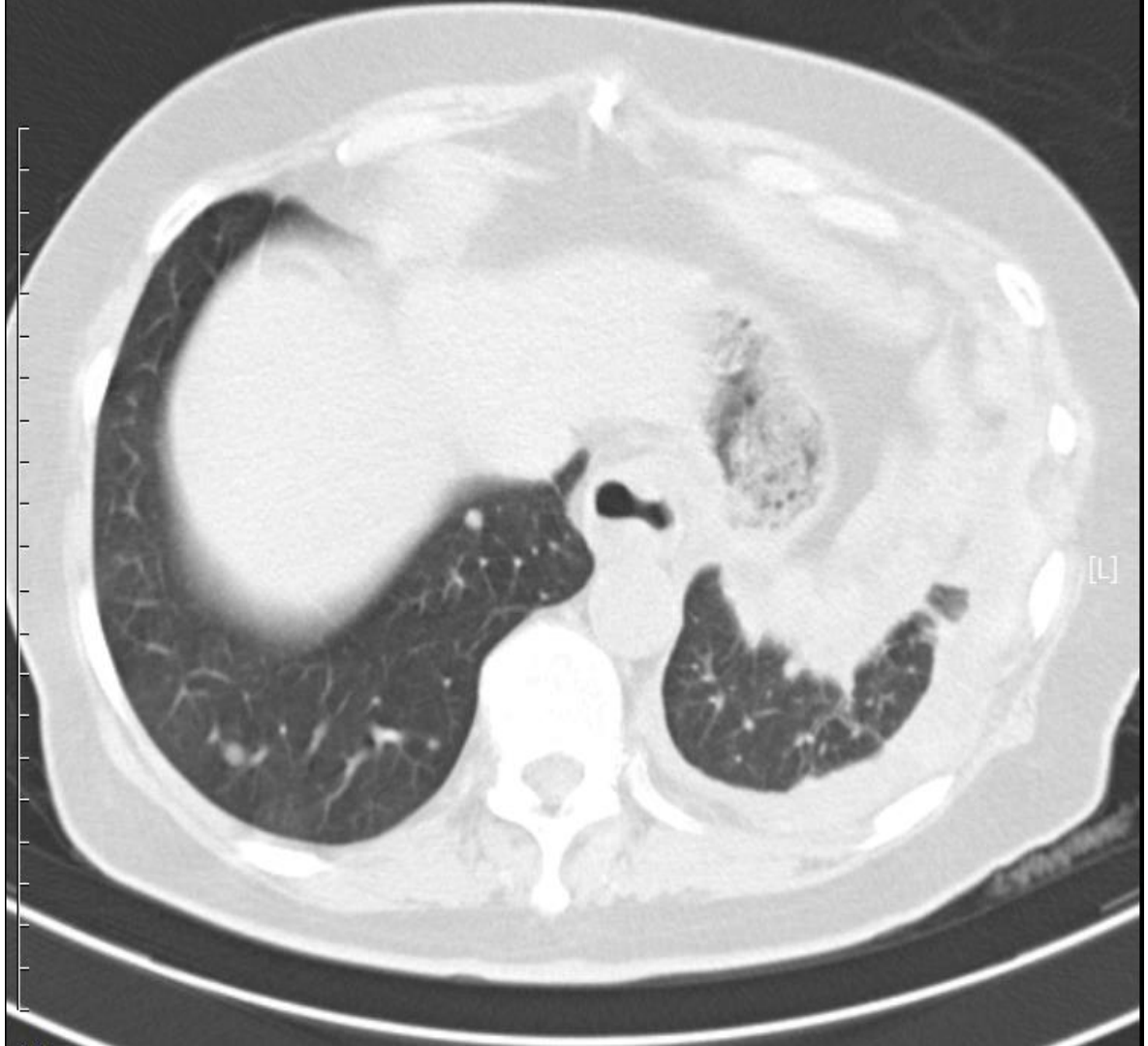

[L]
21cm


[L]
21cm


[L]
21cm


[L]


[L]
21cm


[L]

What is your recommendation ?

All Practical guidelines such as the CAP/IASLC/AMP, ASCO, ESMO and NCCN recommend:

- All patients with advanced nonsquamous NSCLC, regardless of clinical characteristics such as ***age, race, or smoking status***, plus some patients with squamous cell carcinoma such as nonsmokers or those under age 40, should undergo, at a minimum, testing for
- EGFR mutation,
- ALK and ROS1 rearrangements,
- BRAF mutation,
- PDL1 IHC
- with using NGS broader testing:
- such as RET, MET, HER2, and KRAS should also examine

	Nonsquamous Histology	Squamous Cell Carcinoma
Minimum necessary	PD-L1 IHC, EGFR, ALK, ROS1, BRAF	PD-L1 IHC
Recommended*	RET, MET exon 14, HER2, KRAS, NTRK	

Abbreviations: NSCLC, non–small cell lung cancer; IHC, immunohistochemistry; ALK, anaplastic lymphoma kinase; NGS, next-generation sequencing.

*These should be added if testing is done as part of a broad NGS-based panel.

TABLE 1. Recommended Biomarker Tests for Patients With Newly Diagnosed NSCLC

Published in: Nathan A. Pennell; Maria E. Arcila; David R. Gandara; Howard West; *American Society of Clinical Oncology Educational Book* 39531-542.
DOI: 10.1200/EDBK_237863

Molecular study for EGFR mutation was requested.

MP≠ 91

MOLECULAR PATHOLOGY

TEST REQUEST: EGFR Mutation analysis

SAMPLE TYPE: Paraffin embedded block Number 97-2860 from this center.
SAMPLE MORPHOLOGIC CHARACTERISTIC:
A: DIAGNOSIS: primary lung adenocarcinoma; predominantly lepidic and micropapillary pattern.
B: Tumor content: 30 %
C: was the sample dissected to enrich tumor content? No
D: additional morphologic features of note: Positive for TTF1.

PROCEDURE: Nested –PCR was performed for amplification of Exon 18,19,21 followed by sanger sequencing.

PCR RESULT:

Exon 19: **Deletion of 15 nucleotides at exon 19 (2235-2249) In -frame deletion (746-750) of EGFR gene has been detected**

No mutation has detected in exon 18
exon 21 will be followed.

Next step?

Erlotinib
Afatinib
Osimertinib
Gefitinib
TKI+Antiangiogenesis agent
TKI+Platinum combination CT

Combination Therapy

Further development of EGFR TKIs and use of combinatorial approaches

Two general strategies have been investigated recently

Combination of EGFR TKIs and cytotoxic chemotherapies

- Rationale: Chemotherapy and EGFR TKIs act synergistically to possibly delay resistance; TKIs may also enhance pemetrexed efficacy[a,b]

Combination of EGFR TKIs with anti-angiogenic compounds

- Rationale: very close interaction between EGFR-mediated pathway and VEGFR-mediated pathway[c]

a. Yang Z, et al. *Int J Biol Sci*. 2018;14:204-216; b. Galvani E, et al. *Expert Opin Investig Drugs*. 2011;20:1343-1356; c. Byers LA, et al. *Clin Lung Cancer*. 2007;8(suppl 2):S79-S85.

EGFR-Targeted Tkis + VEGF Inhibitors

Phase 2 Trials

JO25567[a]

- Pts with exon 19 del or exon 21 L858R (N = 152)
- Efficacy data: erlotinib + bevacizumab vs erlotinib alone
  - mPFS: 16.4 mo vs 9.8 mo (*P* = .0005)
  - Follow-up mOS: 47.0 mo vs 47.4 mo (no significant difference)

Phase 2 Trial[b]

- Pts with exon 19 del or exon 21 L858R (N = 88)
- mPFS (erlotinib + bevacizumab vs erlotinib alone)
  - 17.9 mo vs 13.5 mo; HR = 0.81; *P* = .39 (not significantly improved)

a. Yamamoto N, et al. ASCO® 2018. Presentation 9007; b. Stinchcombe TE, et al. *JAMA Oncol*. 2019;5:1448-1455.

Sorting Through the Data

Important to test for *EGFR* mutations

- Positive for mutations → start EGFR TKI therapy

EGFR TKIs

- 3rd generation (osimertinib) superior to 1st generation[a,b]
- 2nd generation (dacomitinib) superior to 1st generation (gefitinib)[c,d]

EGFR TKI Combination Therapy

- EGFR TKI + Chemotherapy: gefitinib + carboplatin + pemetrexed vs gefitinib[e,f]
- EGFR TKI + anti-VEGF: erlotinib + ramucirumab (approved in US and Europe) or bevacizumab + erlotinib[g,h]

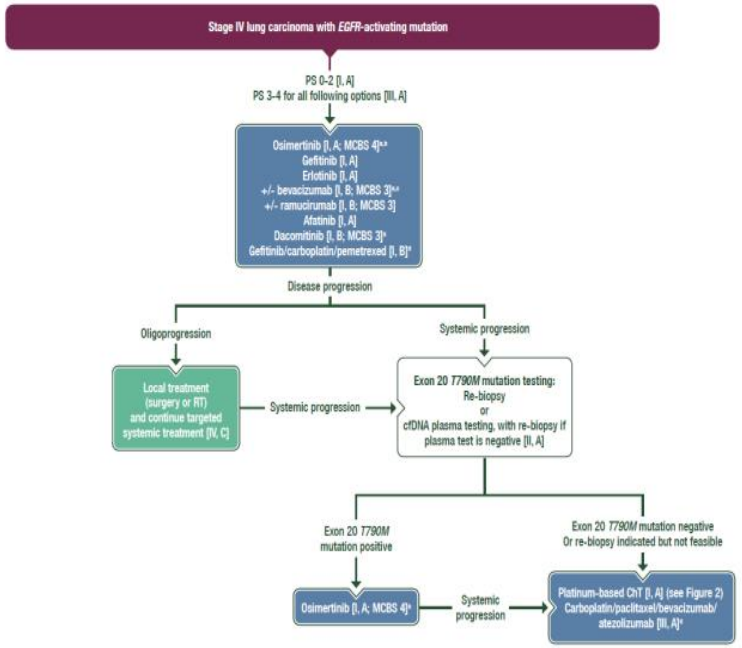
Immunotherapy alone is not a good treatment for patients with *EGFR* mutations[i,j]

a. Soria JC, et al. *N Engl J Med*. 2018;378:113-125; b. Ramalingam SS, et al. *N Engl J Med*. 2020;382:41-50; c. Wu YL, et al. *Lancet Oncol*. 2017;18:1454-1466; d. Mok TS, et al. *J Clin Oncol*. 2018;36:2244-2250; e. Hosomi Y, et al. *J Clin Oncol*. 2020;38:115-123; f. Noronha V, et al. *J Clin Oncol*. 2020;38:124-136; g. Nakagawa K, et al. *Lancet Oncol*. 2019;20:1655-1669; h. Saito H, et al. *Lancet Oncol*. 2019;20:625-635; i. Garassino MC, et al. *Lancet Oncol*. 2018;19:521-536; j. Oxnard GR, et al. *Ann Oncol*. 2020;31:507-516.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Updated version published 15 September 2020 by the ESMO Guidelines Committee

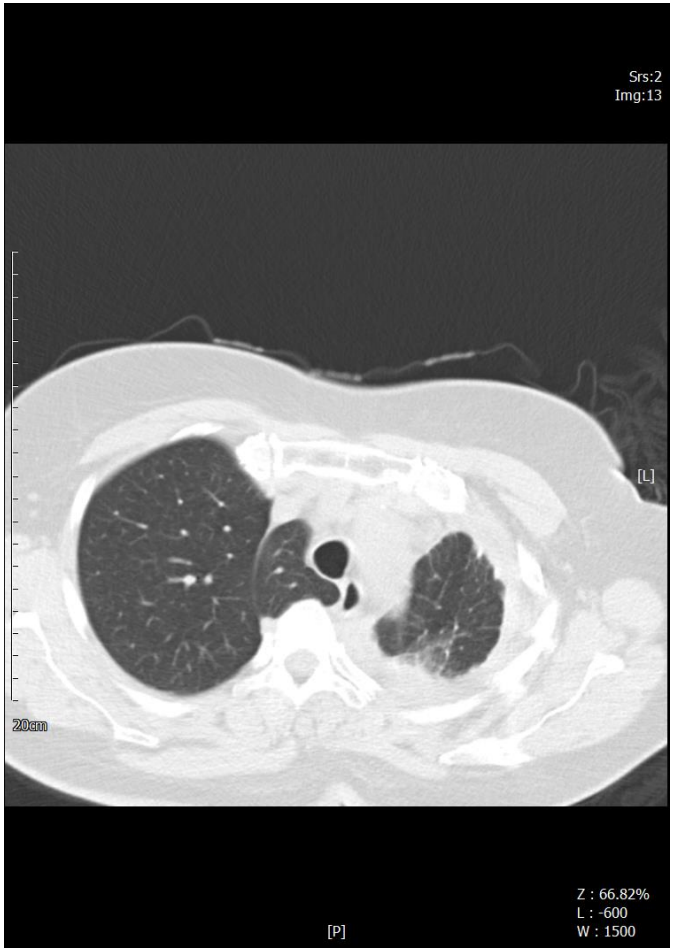
Figure 4. Treatment algorithm for stage IV lung carcinoma with *EGFR*-activating mutation.



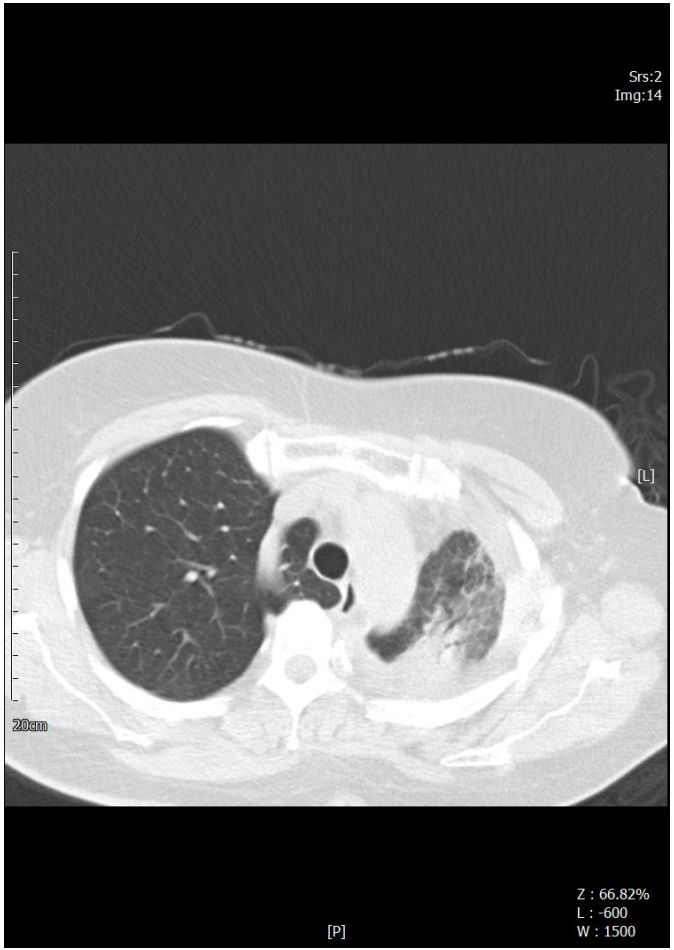
Patient received erlotinib.

CT Scan after one mounth.

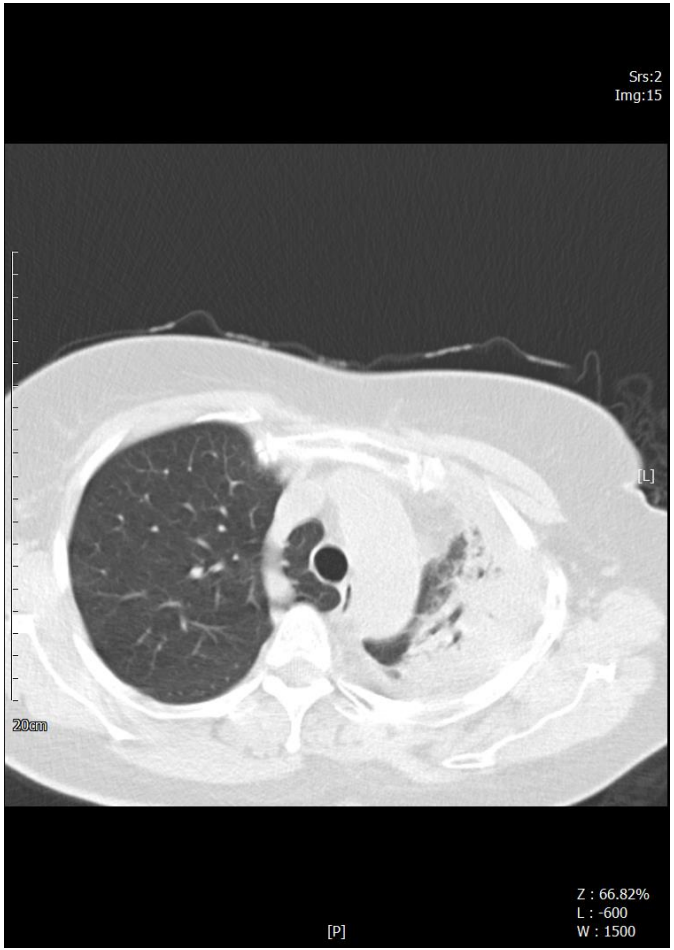
Title



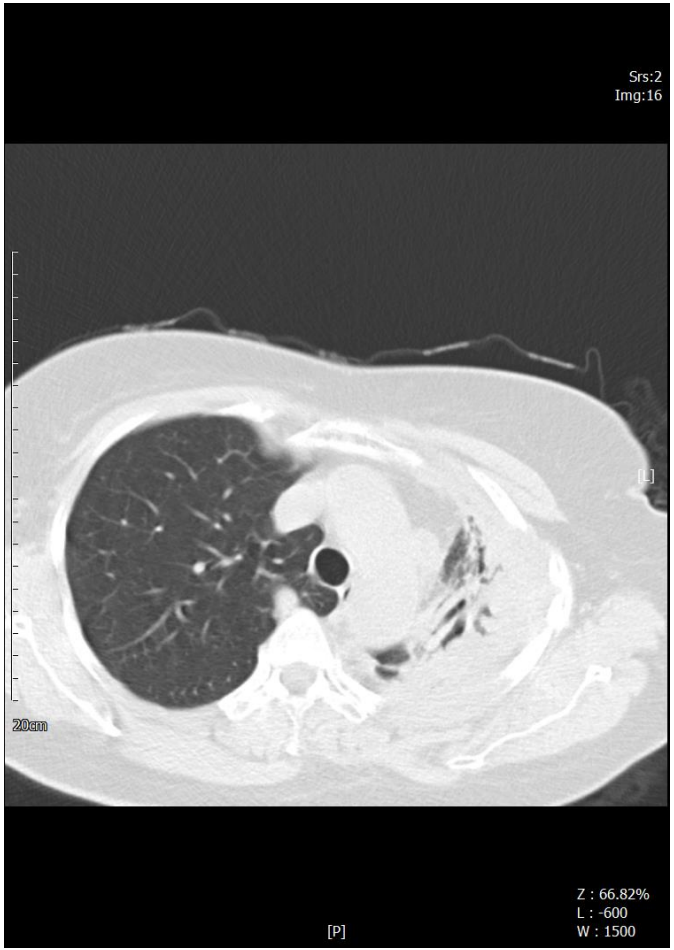
Title

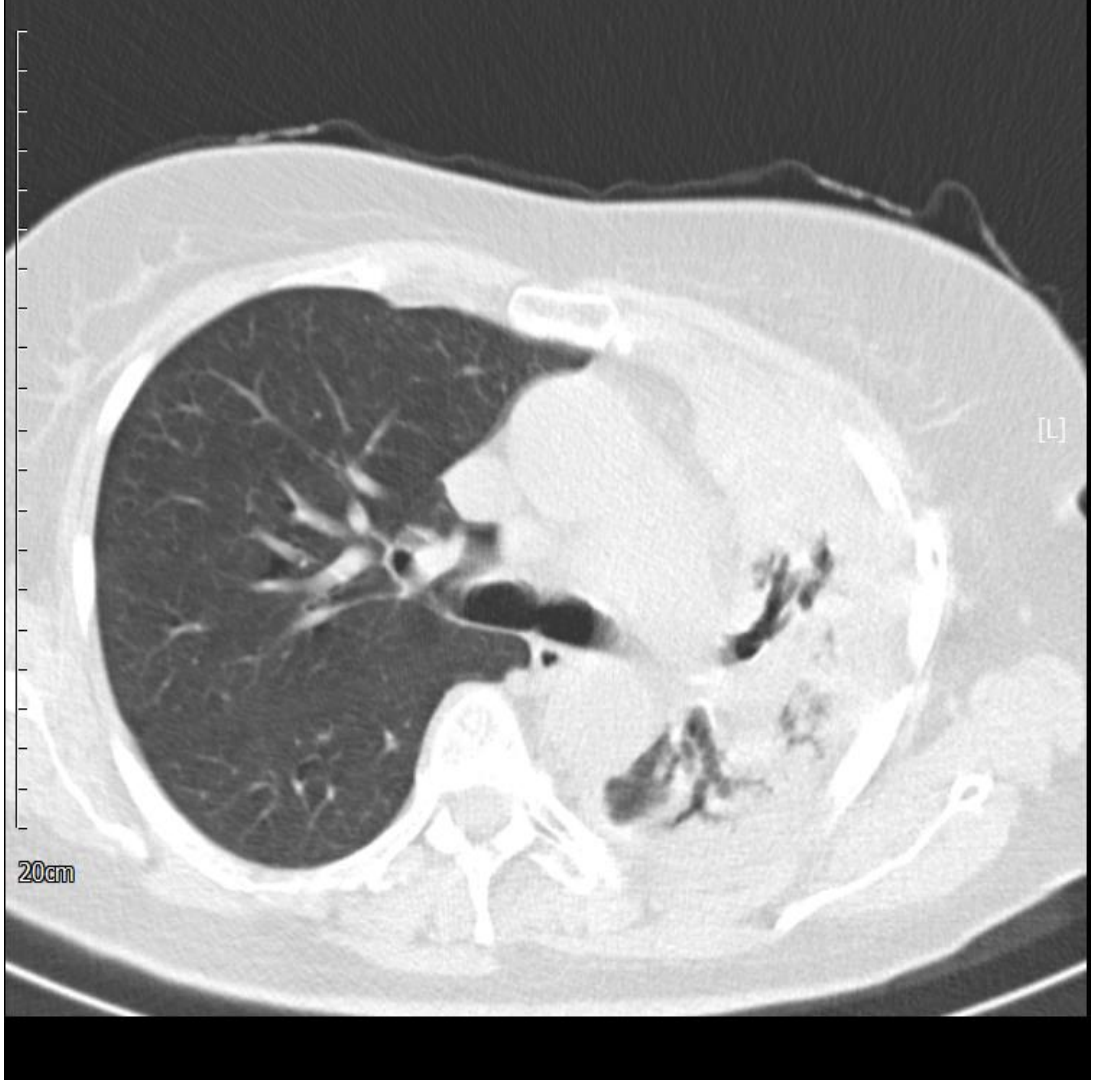


Title

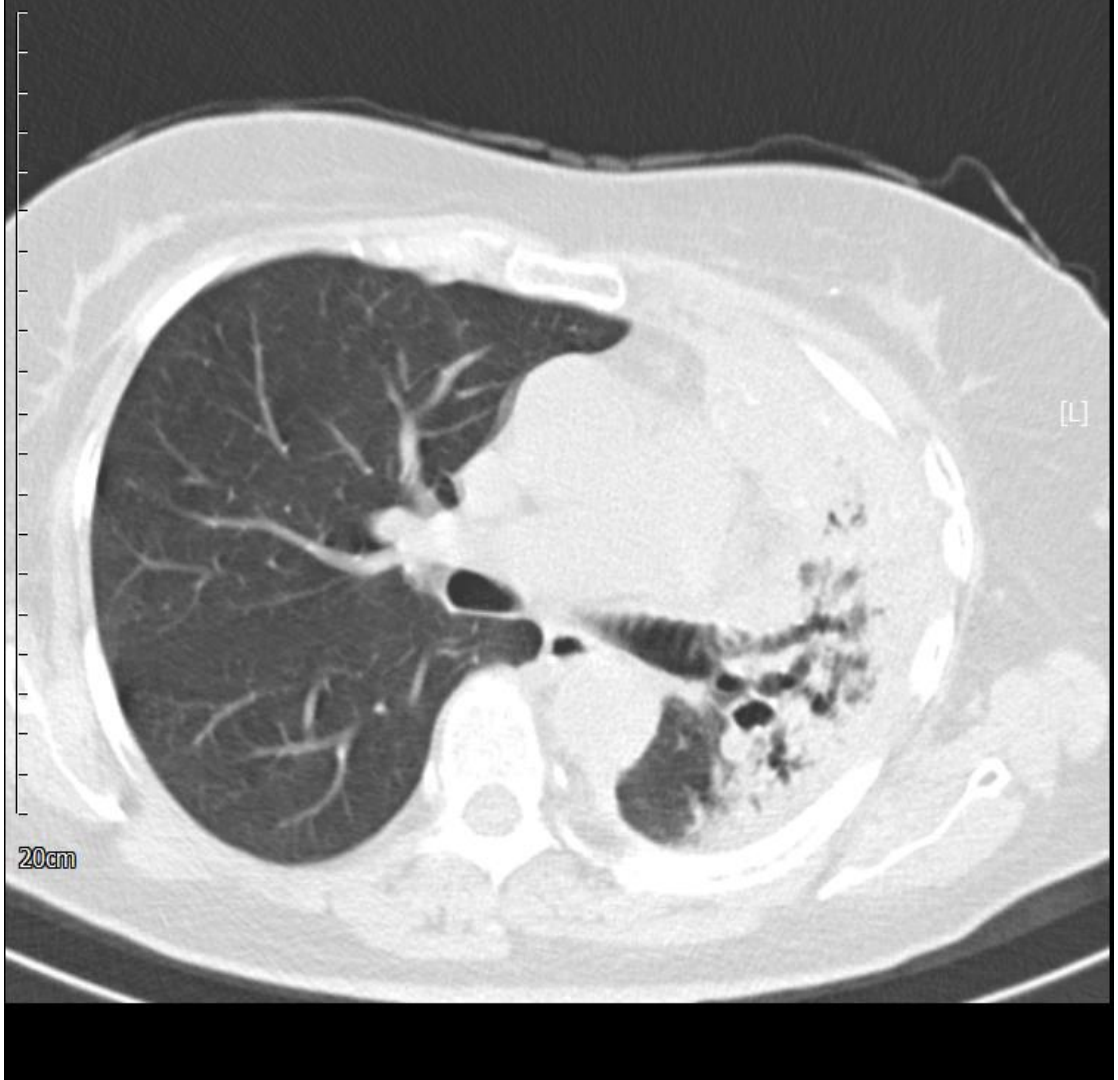


Title



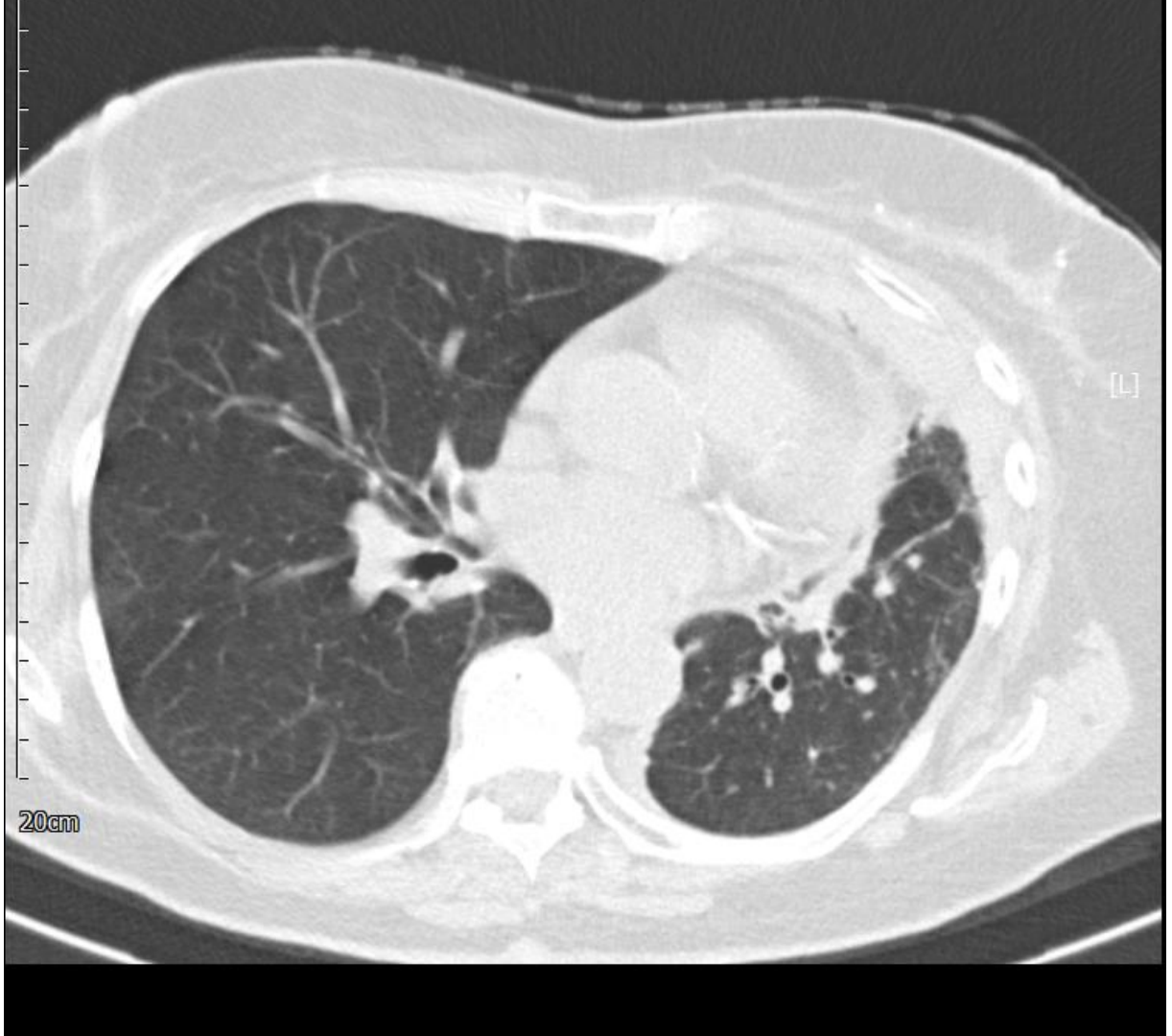

20cm
[L]

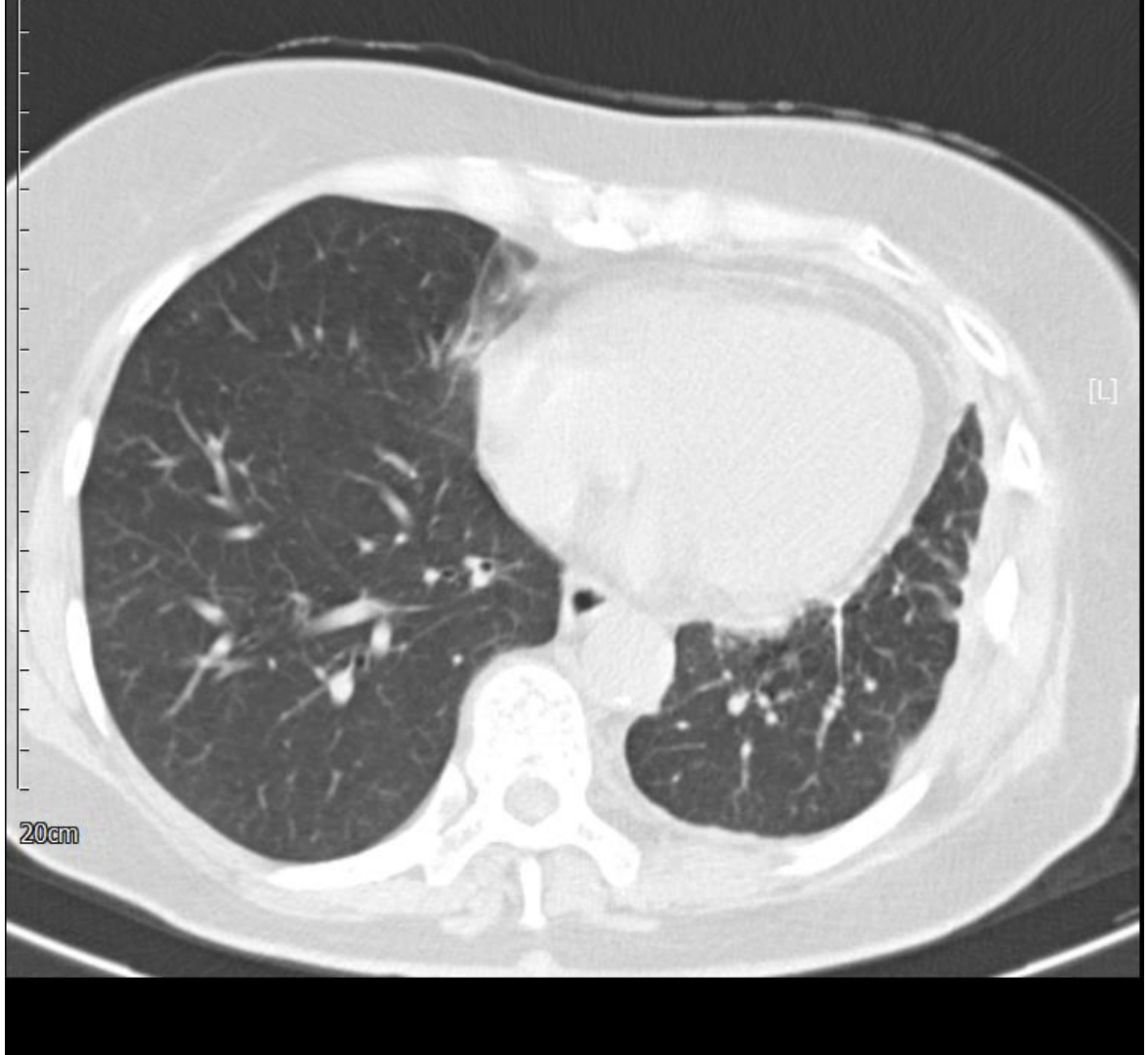

20cm
[L]

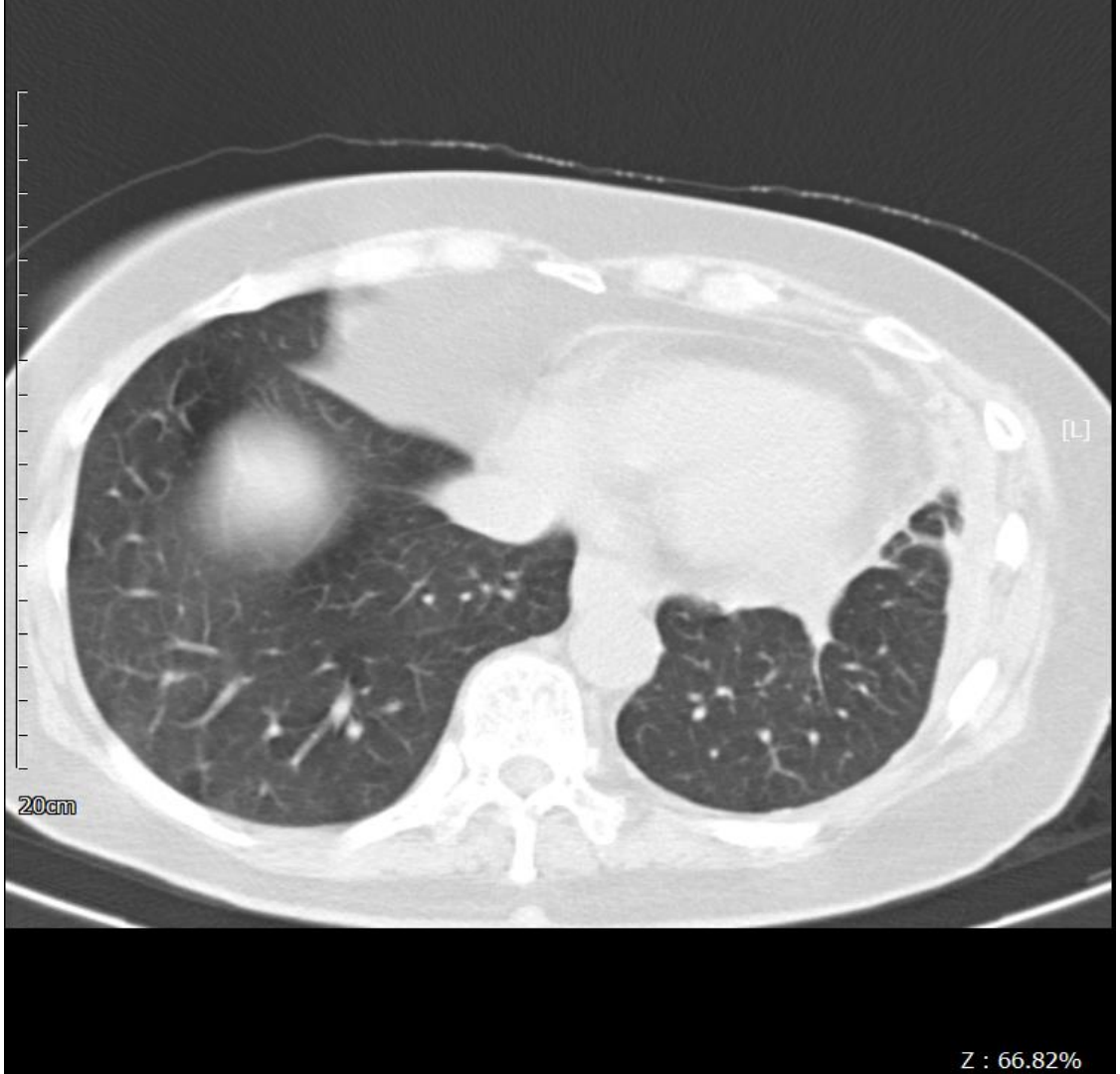

20cm
[L]

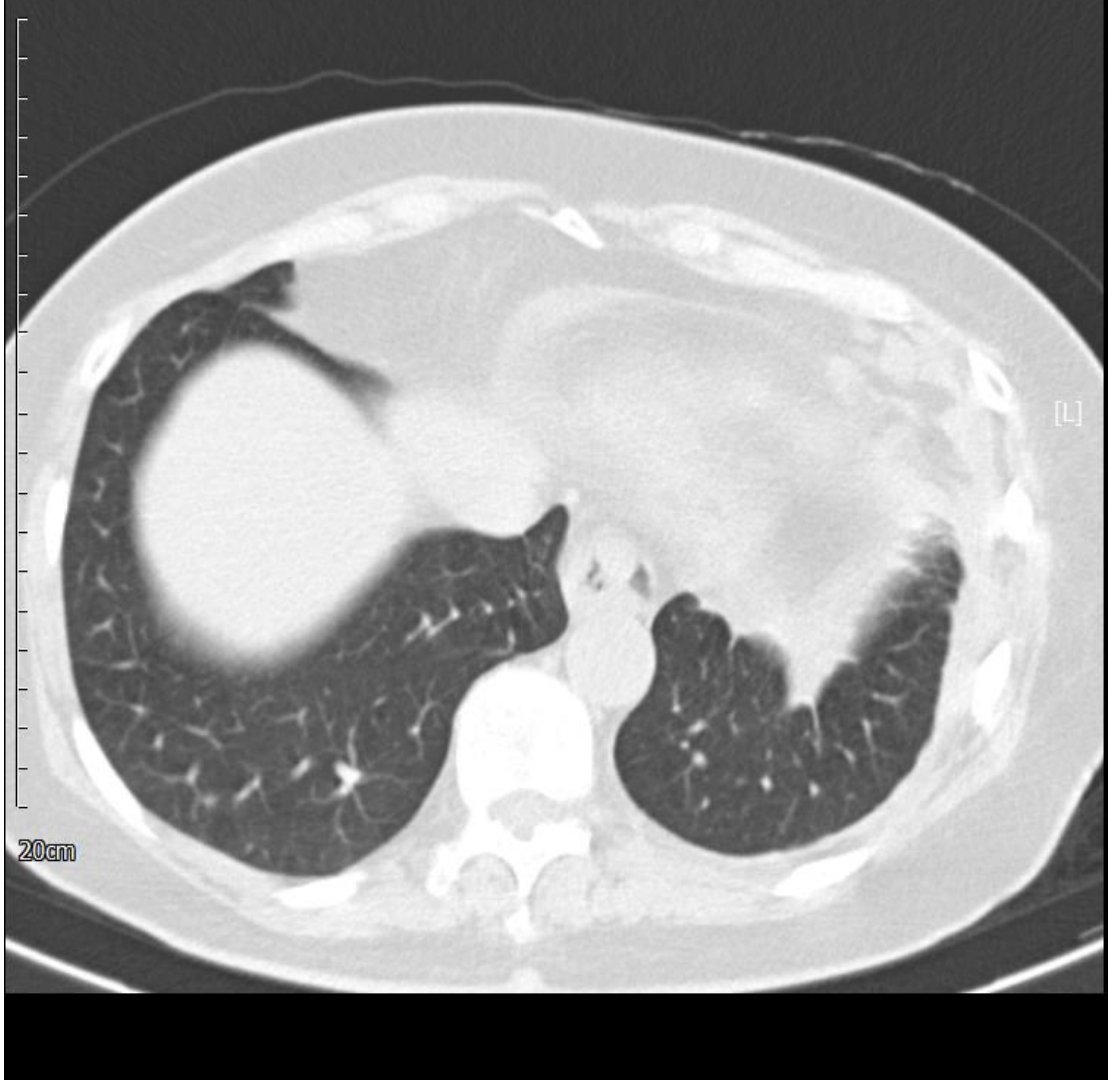

20cm
[L]


20cm
[L]


20cm
[L]


20cm
[L]


[L]
20cm
Z : 66.82%


[L]
20cm

Prevention vs. Treatment of AEs

- Prevention is preferable to treatment
  - Where possible, introduce preventative measures early
  - Regular monitoring of laboratory values (e.g. hepatotoxicity)
- Patient education
  - Early identification of potentially problematic AEs

Management of EGFR TKI AEs

Diarrhea
Incidence: 25-95%[4]
Up to 25% SAE[1]

Study	Drug	All grades (%)	Grade 1–2 (%)	Grade 3–4 (%)
IPASS [6]	Gefitinib	46.6	NS	3.8
First-SIGNAL [7]	Gefitinib	49.7	NS	2.5
NEJ002 [8, 9]	Gefitinib	34.2	33.3	0.9
WJTOG3405 [10, 11]	Gefitinib	54	NS	1
OPTIMAL [12]	Erlotinib	25	NS	1
EURTAC [13]	Erlotinib	57	52	5
LUX-Lung 3 [14]	Afatinib	95	80.6	14.4
LUX-Lung 6 [15]	Afatinib	88.3	82.8	5.4

EGFR epidermal growth factor receptor, *TKIs* tyrosine kinase inhibitors, *NSCLC* non-small cell lung cancer, *NS* not stated

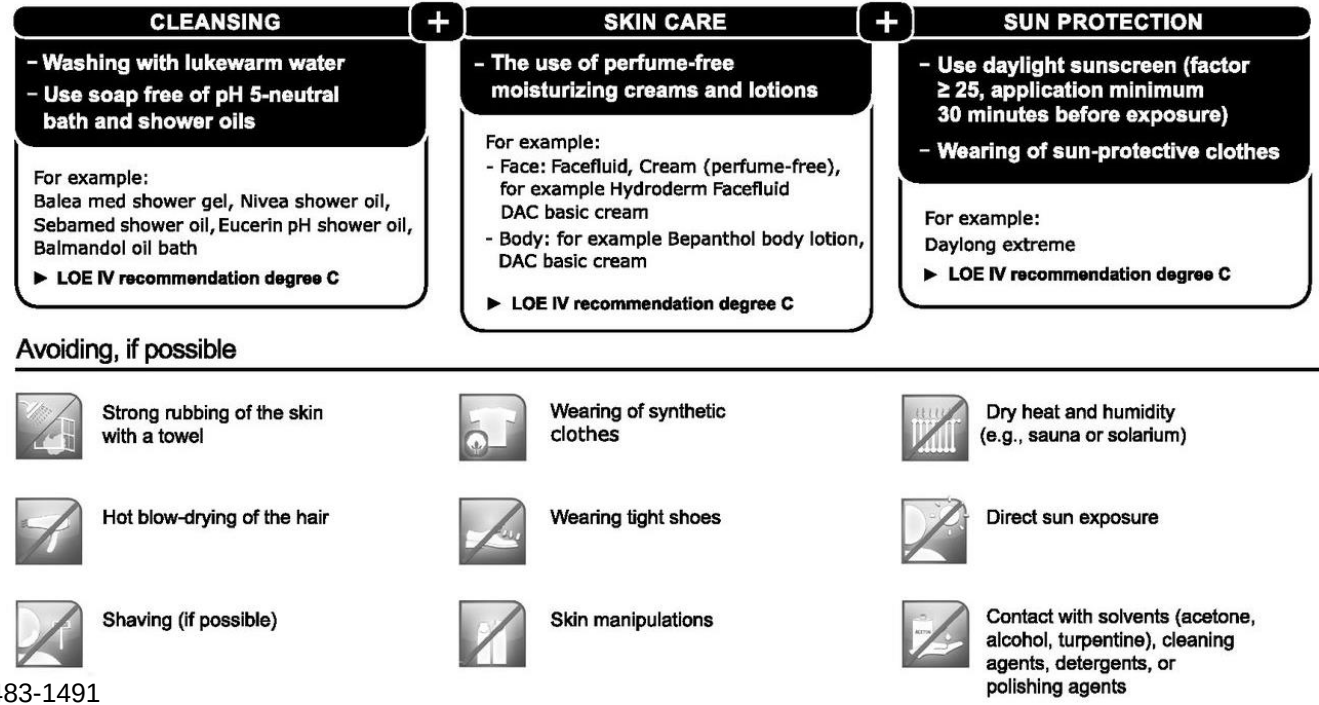
[a] IPASS and FIRST-SIGNAL STUDY also enrolled patients with EGFR wild type tumours

Acne-like Skin Rash (papulopustular eruption, acneiforme dermatitis)
Incidence: 34-89.1% [1-4]
Grade 3/4 incidence: 0-16.2%[1,4]
Image: Grade 4 rash (erlotinib)[2]

[1] Melosky and Hirsh, Front. Onc. **2014**, 4:238; [2] Aw et al. Asia-Pacific JCO, **2018**, 14(1) 23-31; [3] Califano et al. Drugs, **2015**, 75(12) 1335-1348

Prevention of EGFR TKI AEs

- Pro-active management may reduce symptom severity and thus improve compliance.
- Severity and the timing of the onset of the skin rash significantly correlate with the effectiveness of the treatment.
- Early and effective intervention for diarrhea is required.



Melosky et al., **2015**, Curr oncol. 22(2) 123-132
Figure: Hofheinz et al. The Oncologist **2016**;21:1483-1491

Dermatologic toxicity: Note: Management of skin rashes that are not serious should include alcohol-free lotions, topical antibiotics, or topical corticosteroids, or if necessary, oral antibiotics and systemic corticosteroids; avoid exposure to sunlight.

Bullous, blistering, or exfoliative skin toxicity (severe): Discontinue erlotinib.

Severe rash (unresponsive to medical management): Withhold erlotinib; may reinitiate with a 50 mg dose reduction after toxicity has resolved to baseline or ≤ grade 1.

GI toxicity:

Diarrhea: Manage with loperamide; in persistent, severe diarrhea (unresponsive to loperamide) or dehydration due to diarrhea, withhold erlotinib; may reinitiate with a 50 mg dose reduction after toxicity has resolved to baseline or ≤ grade 1.

با تشکر

پایان