PLANETS
Cancer Charity

University Hospital Southampton
NHS Foundation Trust

# *Interventional Radiology in NETS*

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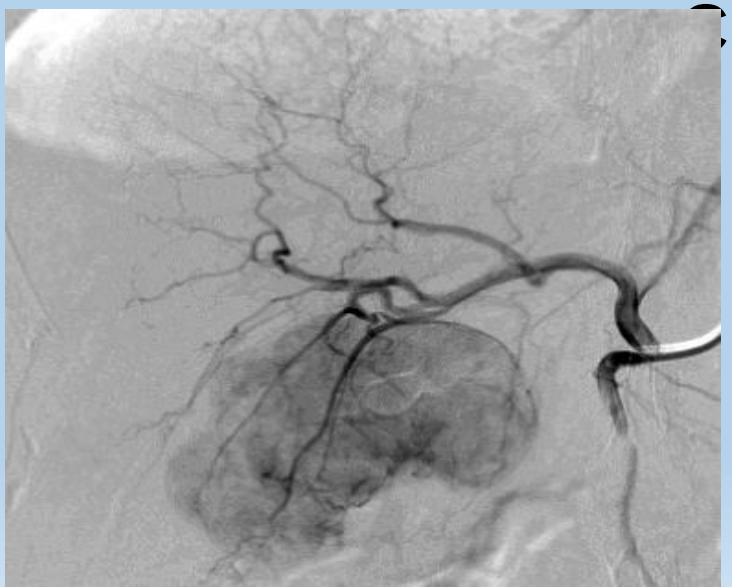
Consultant Interventional Radiologist



IASIOS ACCREDITED CENTRE
INTERNATIONAL ACCREDITATION SYSTEM FOR INTERVENTIONAL ONCOLOGY SERVICES

# Interventional Radiology – Who are we ?

# The great big of Minimally Invasive, Image-guided Procedures #MIIPs as EMOJIS and HASHTAGS

## What parts of the body can be treated by Interventional Radiologists? #WithoutaScalpel

liver

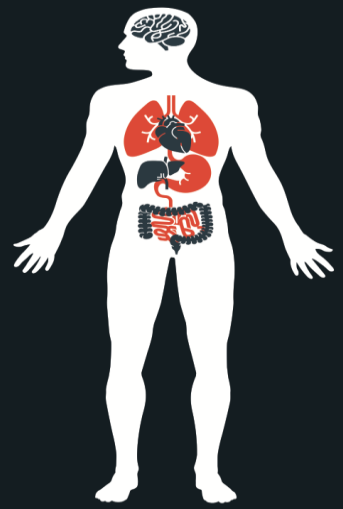
kidneys

lungs

intestine

stomach

spine



brain

gallbladder

uterus

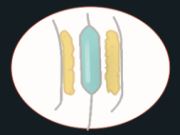
legs

spleen

prostate

## What can the Interventional Radiology (#irad) team do through a pinhole in the skin?

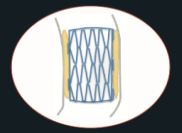
Dissolve blood clots #stoptheclot



Open blocked blood vessels #PTA

Stop internal bleeding #embolization

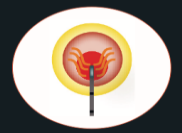
Freeze tumors #cryoablation



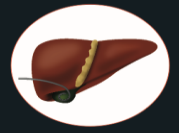
Keep vessels open #PAD #stent

Prevent amputation #CLI #CLIfighters

Take tissue samples #biopsy



Kill tumors with energy #radiofrequency



Treat infection #cholecystostomy

Send patients home with just a band-aid #qualityof life #patientsfirst #empowered

Stop aneurysms from bursting #coiling #aneurysm

Poison tumors #TACE #theCancerSnipers

Shrink fibroids #UFE #DontLoseURU

Stop pain from spinal fractures #vertebroplasty

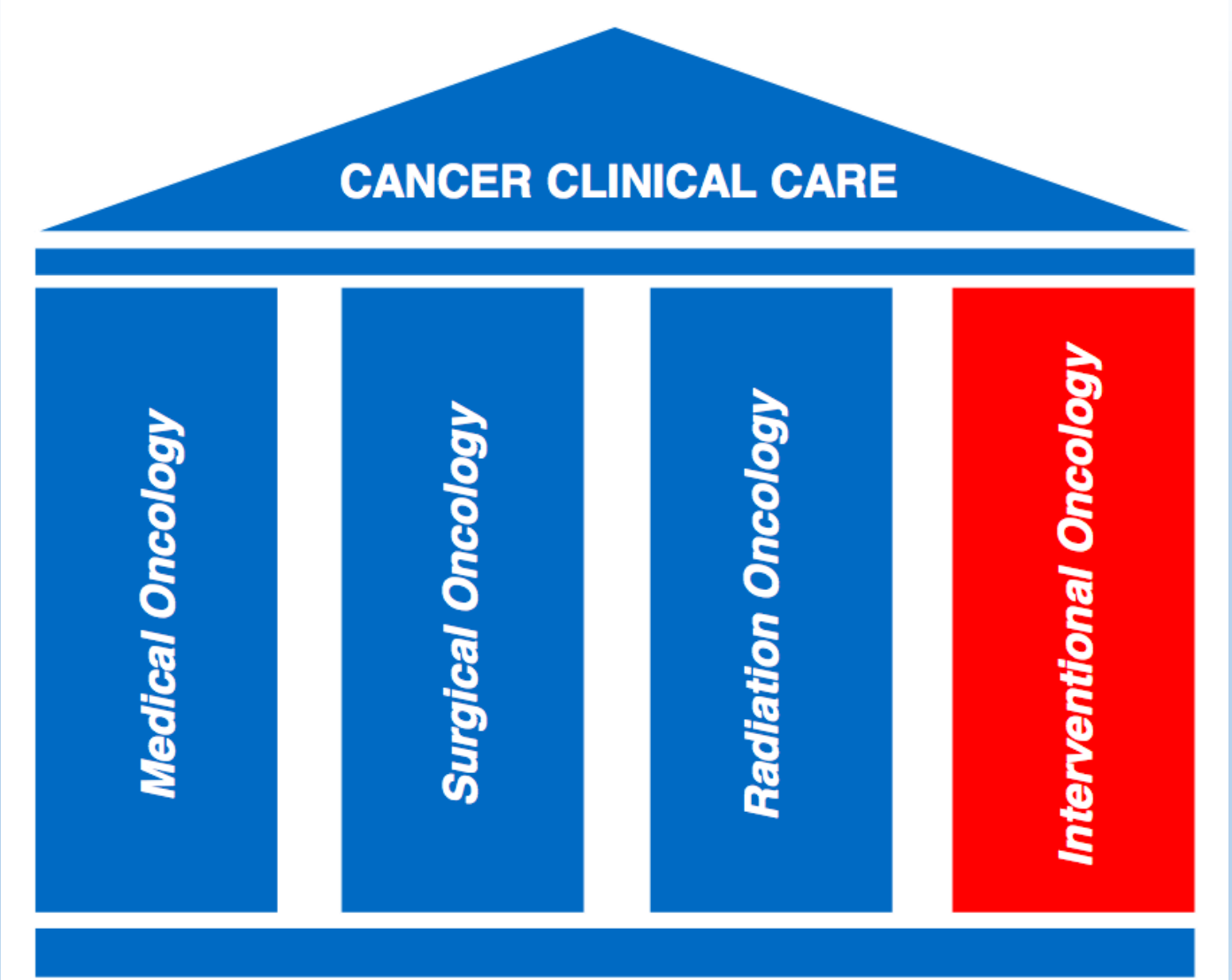
Suppress the hunger hormone #nanoblock

Shrink an enlarged prostate #PAE

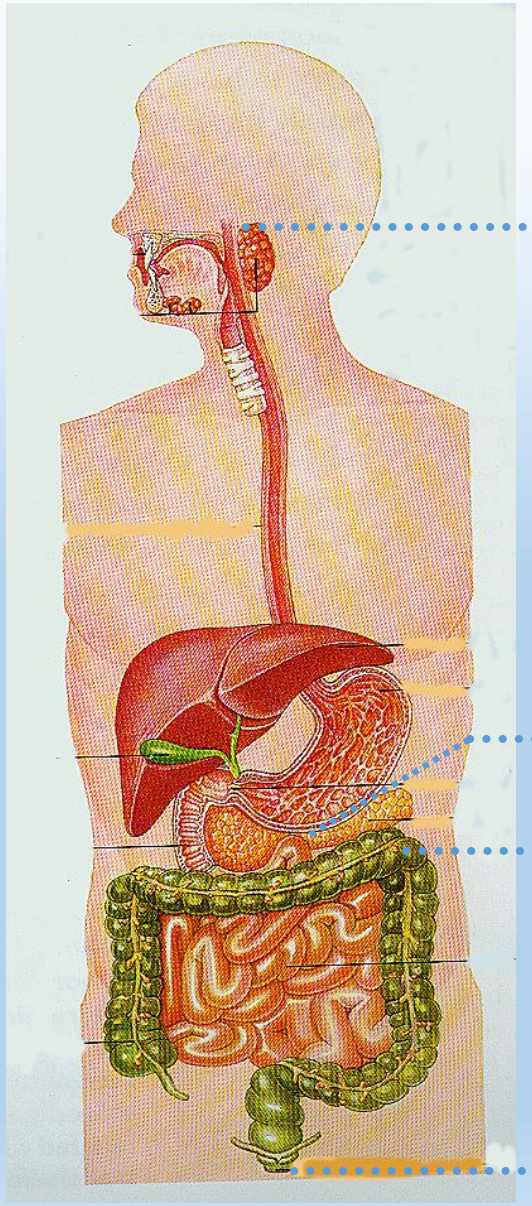
Stop blood clots from traveling to the lungs #DVT #PE #filterout

the Interventional Initiative

# Interventional Oncology



# Type, Distribution and Frequency of GEPNET



| | Relative frequency | Function | Histology |
|---|---|---|---|
| **Foregut** | 30% | Functional | Islet cell |
| **Midgut** | 60% | Functional | Carcinoid |
| **Hindgut** | <10% | Non-functional | Carcinoid |

# Grades of Neuroendocrine Neoplasms – WHO 2017

| Grade | Differentiation | Miotic Count/Ki-67 |
|---|---|---|
| 1 (low) - NET | Well differentiated | <2 mitoses/10 HPF<br><3% Ki-67 index |
| 2 (Intermediate) - NET | Well differentiated | 2-20 mitoses/10 HPF<br>3-20% Ki-67 index |
| 3 (high) - NET | Well differentiated | >20 mitoses/10 HPF<br>>20% Ki-67 index |
| 3 (high) – Neuroendocrine Carcinoma (NEC) | Poorly differentiated | >20 mitoses/10 HPF<br>>20% Ki-67 index |
| Mixed Neuroendocrine Non-Neuroendocrine Neoplasm (MiNEN) - See text | | |

# Background

- Neuroendocrine tumours from gastro-pancreatic origin (GEP-NET) can be responsible for liver metastases.

- Metastases can be the dominant part of the disease
  - ➢ Tumour burden
  - ➢ Symptoms related to liver metastases

- Liver metastases constitute the most frequent metastatic site.

# Background

- ENETS recommends - only G1 and G2 tumours are potential candidate for liver-directed (locoregional) therapies.

- G3 carcinomas  are candidates for systemic treatment due to the rapid progression of the disease and usually widespread metastases.

# Goals for IA therapy

- Reduction in tumour burden
- Potential conversion to resectable status
- Control of hormonal symptoms (when somatostain analogues fail)

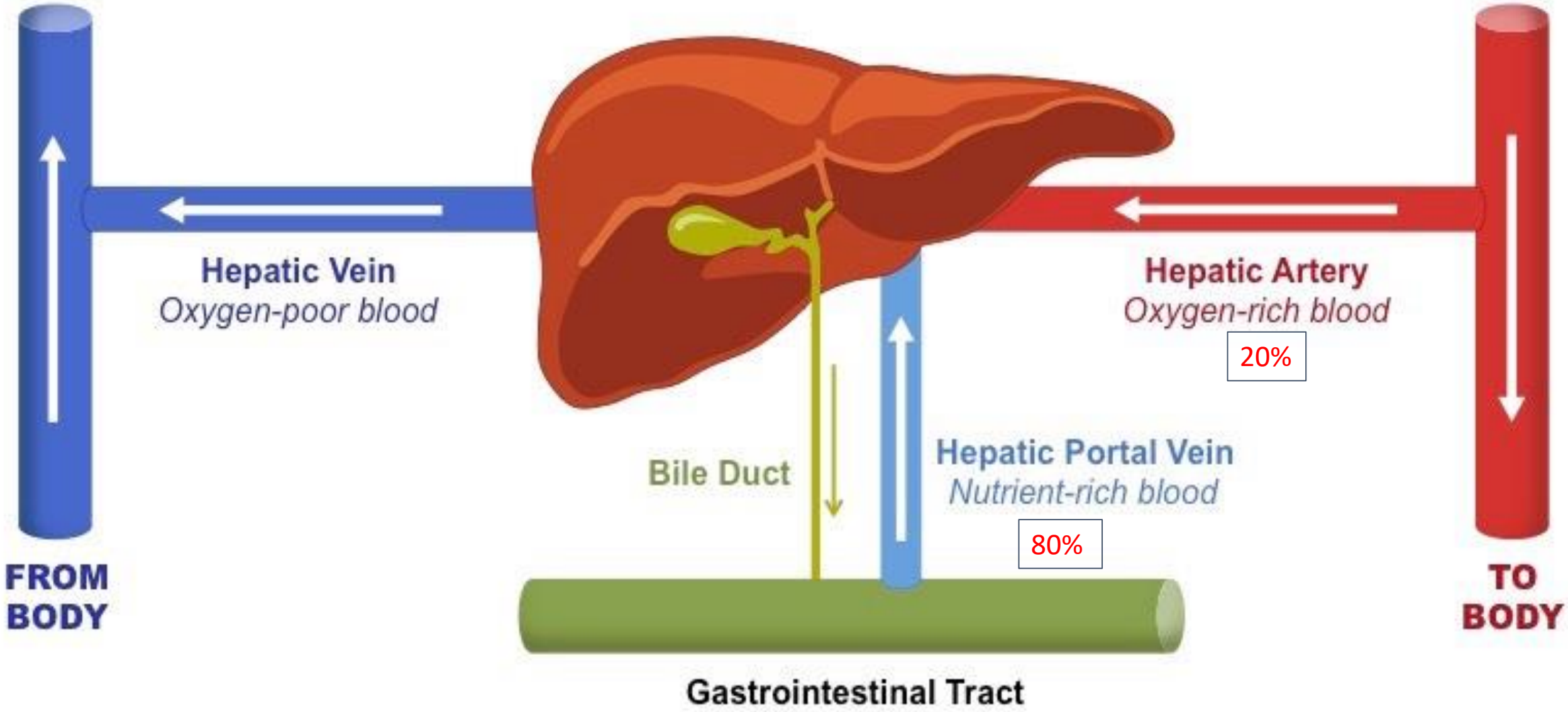
# IA Therapies

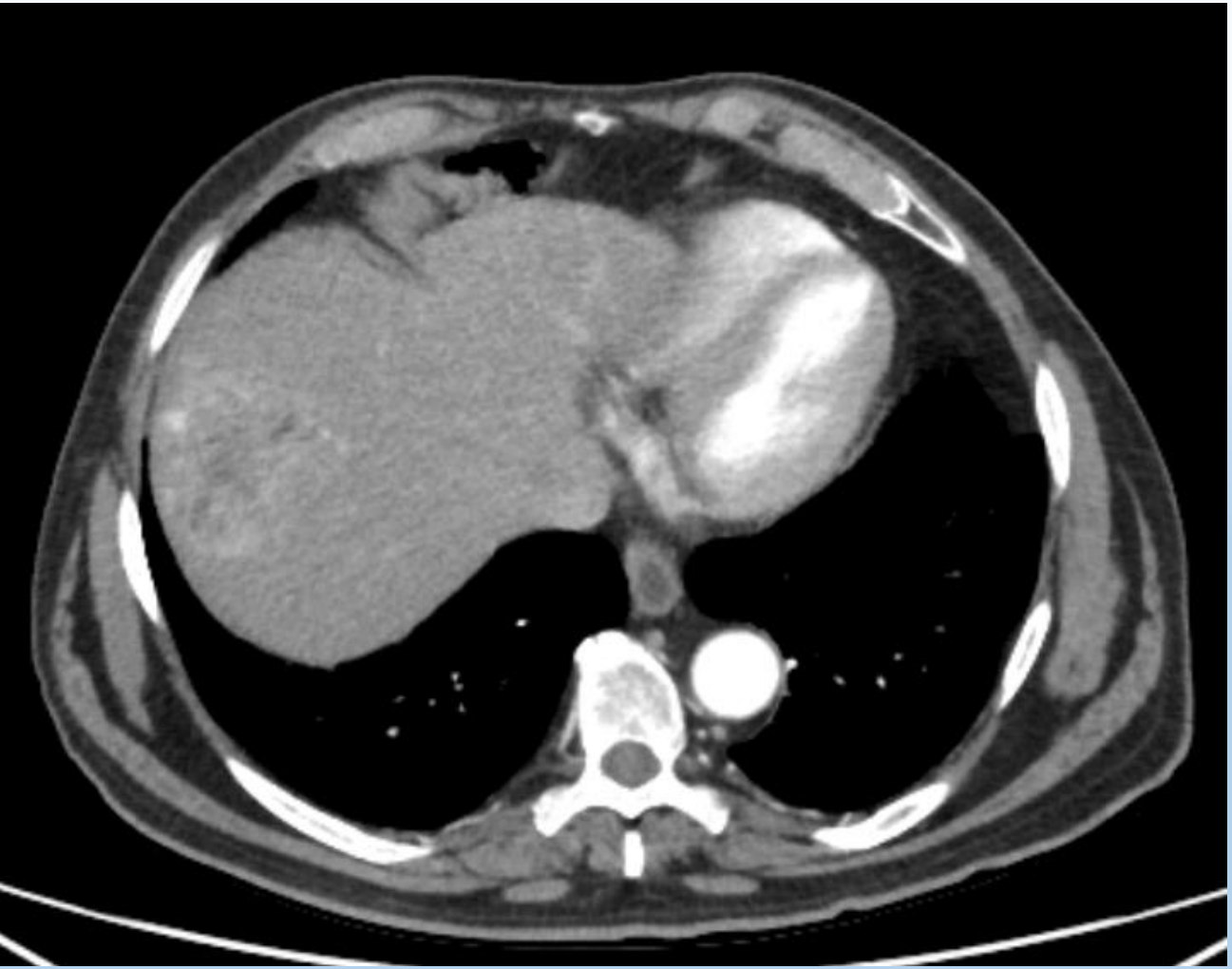
- Trans arterial chemoembolisation (TACE)
- Tran arterial embolisation (TAE)
- Selective Internal Radiation Therapy (SIRT)

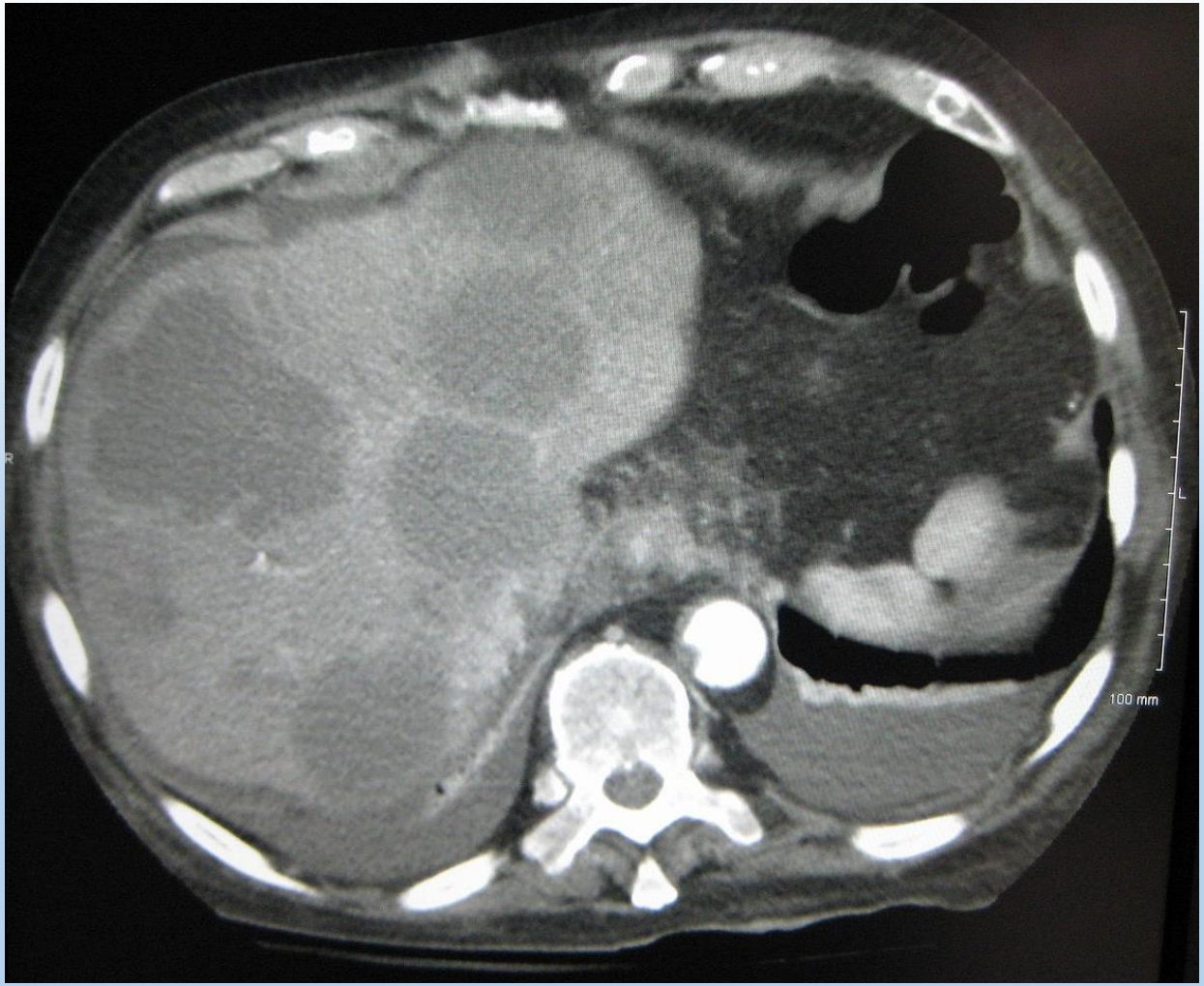
- Ablation

# Rationale for IA therapy

- Normal liver has a dual vascular supply including 20% inflow from the hepatic artery and 80% inflow from the portal vein.
- This differential supply allows IA treatment as primary and metastatic liver lesions take their blood supply from HA.
- NET especially arterialised compared to other mets (mCRC/Breast). Good target for IA therapy.


Hepatic Vein
Oxygen-poor blood
Hepatic Artery
Oxygen-rich blood
20%
Bile Duct
Hepatic Portal Vein
Nutrient-rich blood
80%
FROM BODY
TO BODY
Gastrointestinal Tract

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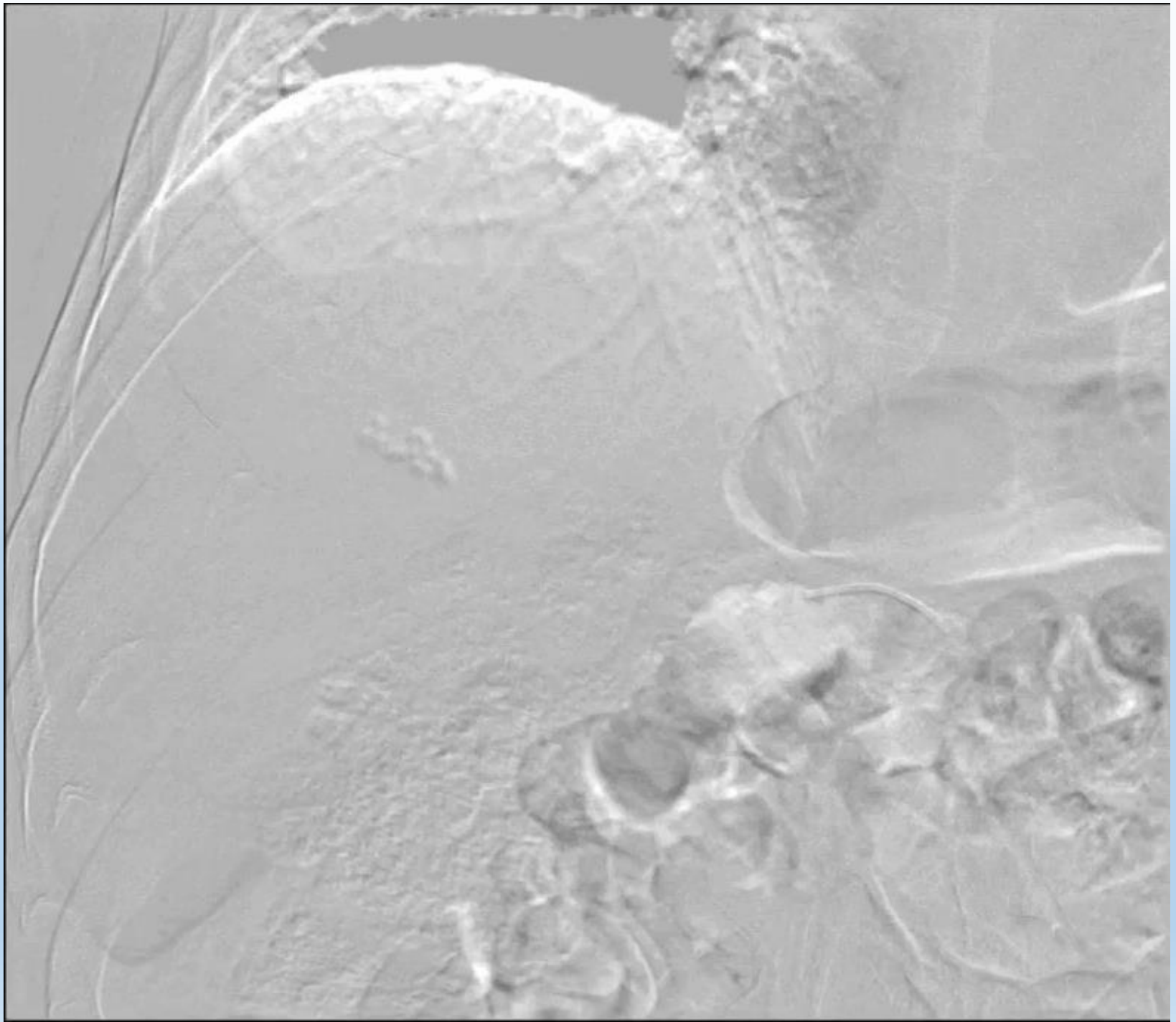

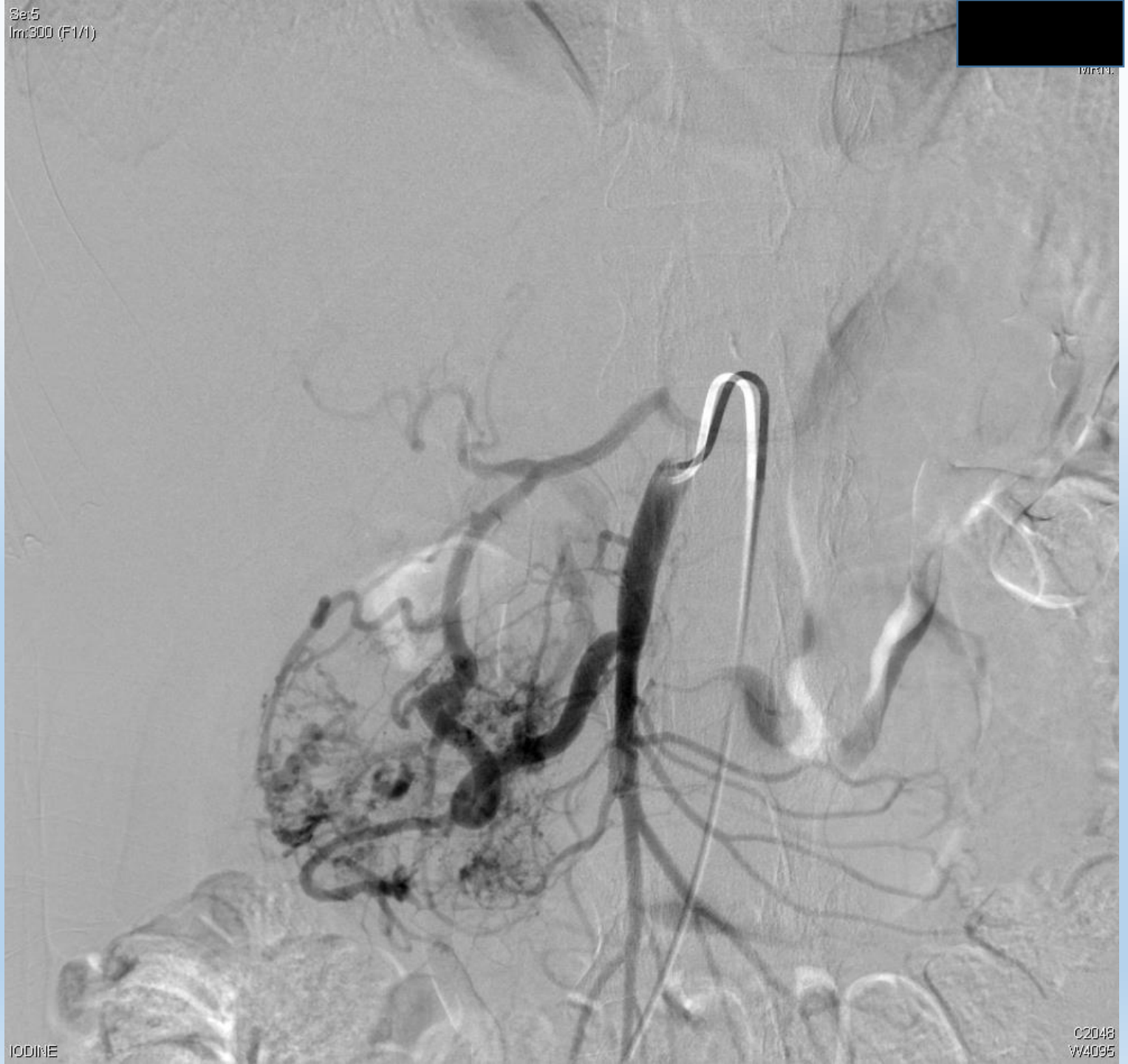
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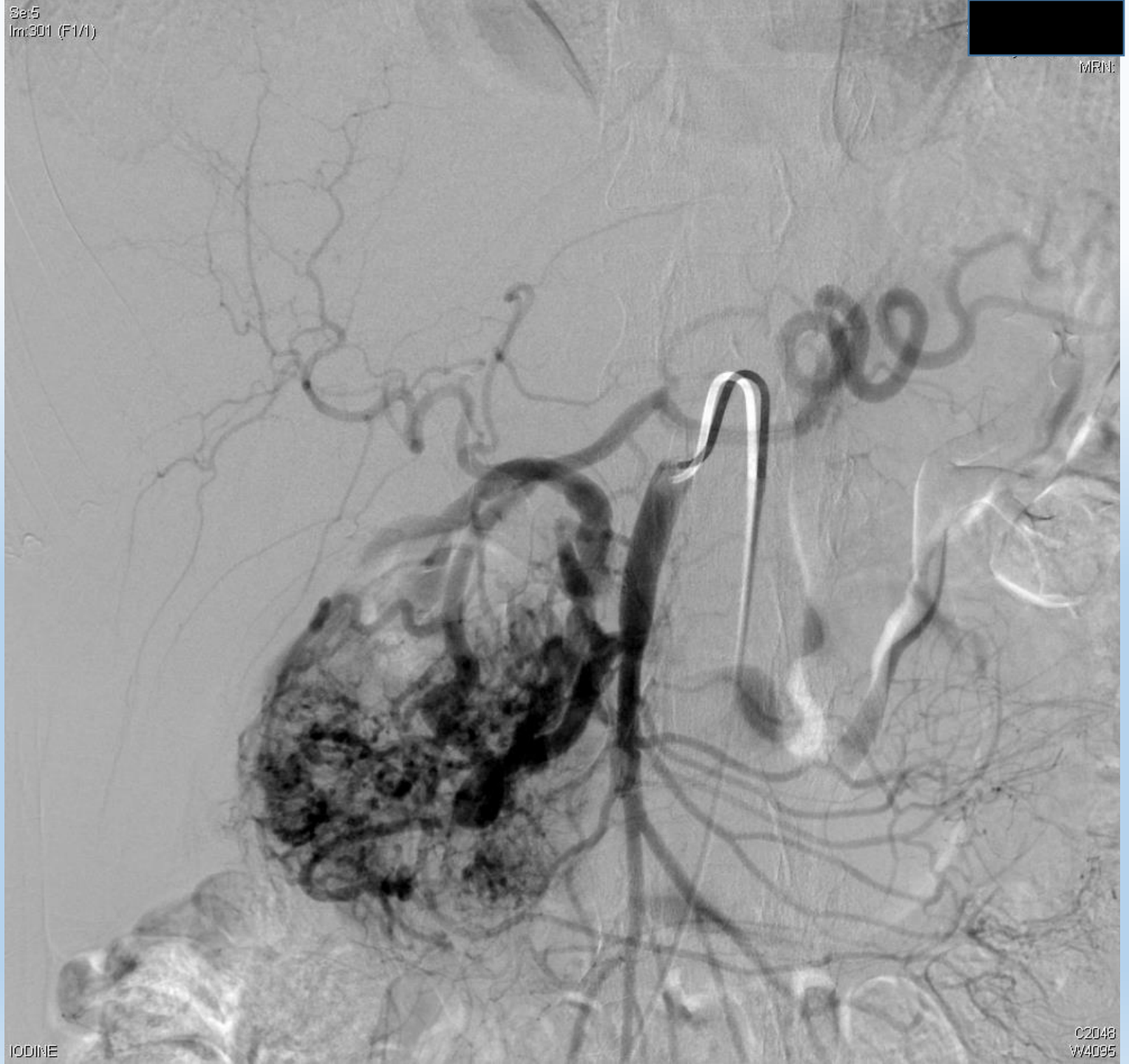
Im:300 (F1/1)
IODINE
C2048
W4095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MRN:
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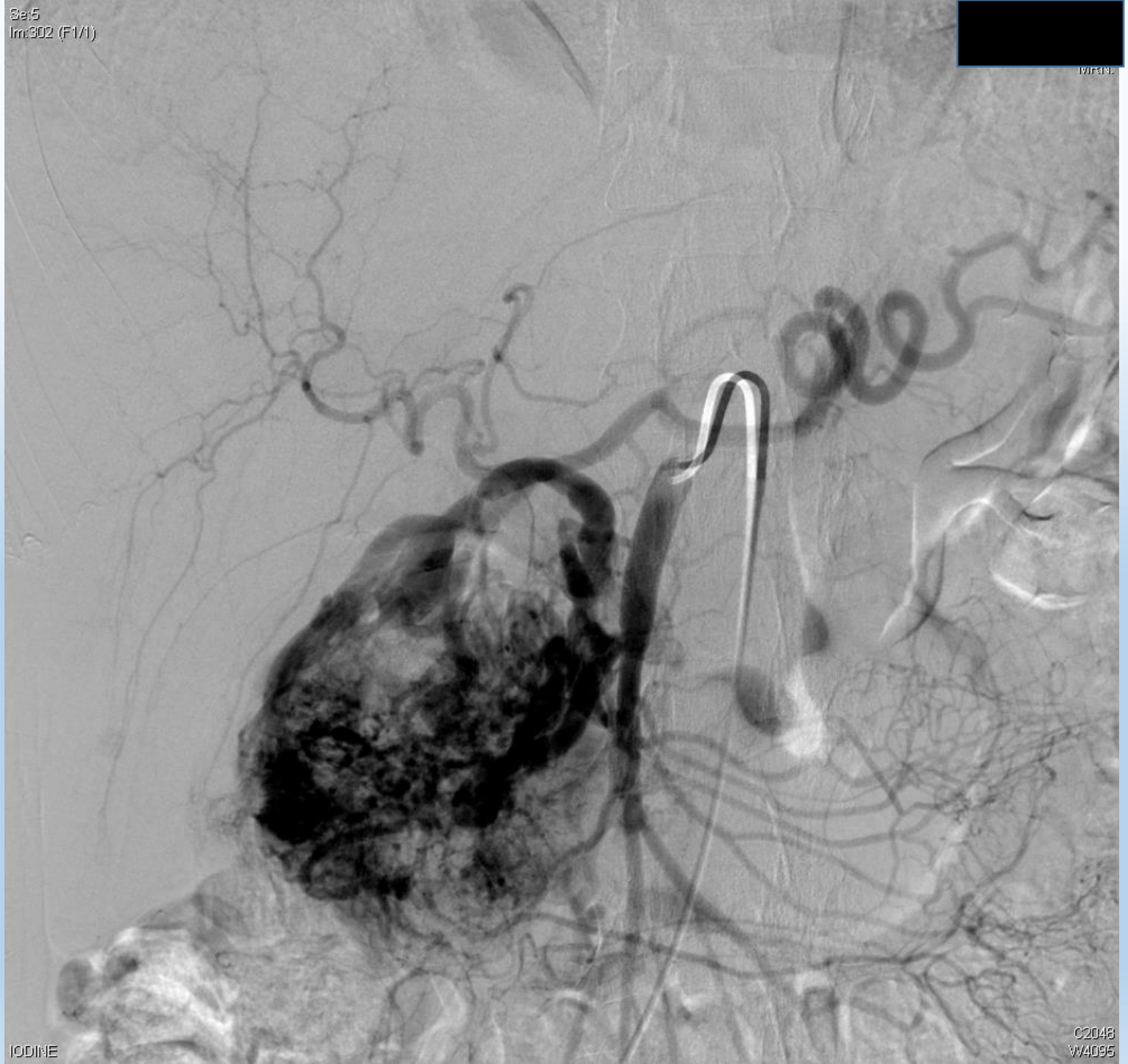

Se:5
Im:302 (F1/1)
IODINE
C2048
W4095

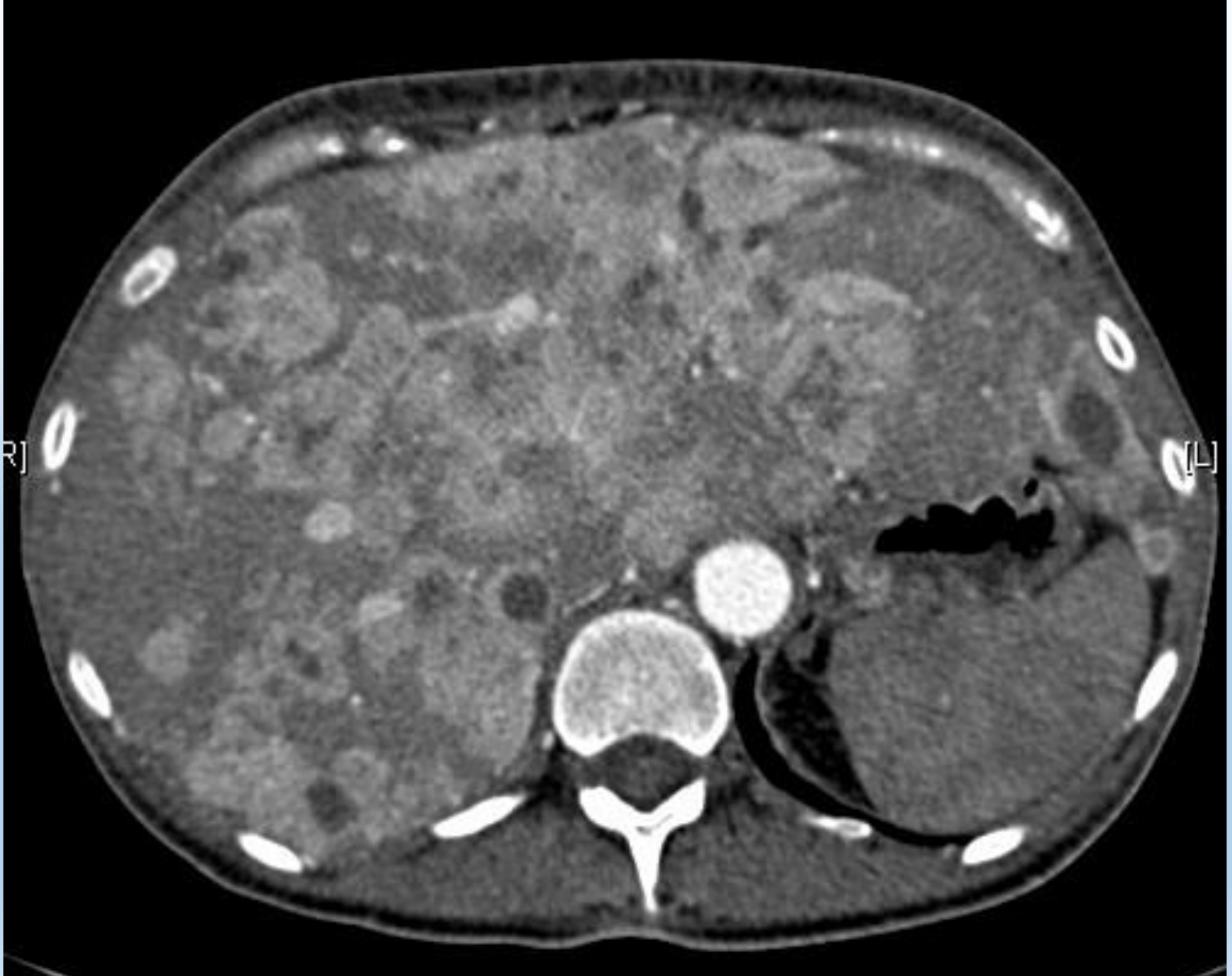
# Patient Selection - Contraindications

Absolute

- Poor liver function (Bili >20, low albumin, ascites)
- Poor performance status (ECOG >2)
- PVT (main v segmental)

Relative

- Arterial dissection or inability to exclude extra hepatic supply
- Disease burden >50%
- Biliary Enteric anastomosis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# At UHS

- MDT discussion (Surgeon, Endocrinologists, Radiologist, CNS, Nuclear med and Oncologists)
- Patient referred to IR for TAE/TACE
- Seen in IR clinic with IR CNS

- Pre admission for Octreotide infusion as per protocol
- GA

# Protocol for Perioperative Management of Patients with Neuroendocrine or Carcinoid Tumours

| | Non-functioning | Previous History of carcinoid syndrome/well controlled carcinoid on depot octreotide | Active carcinoid syndrome | Active carcinoid syndrome with symptomatic/significant Carcinoid heart disease |
|---|---|---|---|---|
| Surgical or IR procedure unrelated to neuroendocrine tumour | **A** | **A** | **B** | **C** |
| Minor surgical intervention/biopsy/ablation of neuroendocrine tumour | **A** | **B** | **C** | **D** |
| Major Surgery on metastatic deposits or bulky primary tumour or embolic therapy or cardiac surgery | **B** | **C** | **D** | **E** |

**A** no octreotide required
**B** octreotide 100mcgs IV on induction
**C** octreotide 12.5mcgs/hr IV infusion for 8-12 hours pre-operatively, continued for 12-24 hours post procedure *(octreotide 300mcgs in 250mls of 0.9% saline at 10mls/hr)*
**D** octreotide 25mcgs/hr IV infusion for 24 hours pre-operatively and continued for 24-48 hours post operatively *(octreotide 600mcgs in 250mls of 0.9% saline at 10mls/hr)*
**E** octreotide 50mcgs/hr IV infusion for 24 hours pre-operatively and continued for 72 hours post operatively *(octreotide 1200mcgs in 250mls of 0.9% saline at 10mls/hr)*

*Regardless of chosen regimen: if signs of carcinoid syndrome (dry flushing, tachycardia, hypotension and wheeze caused by release of serotonin from tumours) are observed the patient should be given bolus octreotide 100mcgs IV to be repeated as required: this is the mainstay of treatment (continue or start background infusion 50mcg/hr).*
***If haemodynamic instability is encountered support from critical care/ICU should be requested urgently.***
Drugs to consider using in a carcinoid crisis: hydrocortisone, ranitidine, chlorpheniramine (reduce histamine release)

- Hypotension: IV fluids, consider phenylephrine or noradrenaline or vaspopressin
- Hypertension: optimise analgesia and anaesthesia (fentanyl/propofol), consider magnesium or GTN infusion in acute setting

AVOID DRUGS THAT CAUSE HISTAMINE OR SEROTININ RELEASE: thiopentone, suxamethonium, atracurium, morphine, tramadol, dopamine, isoprenaline

WESSEX NET GROUP

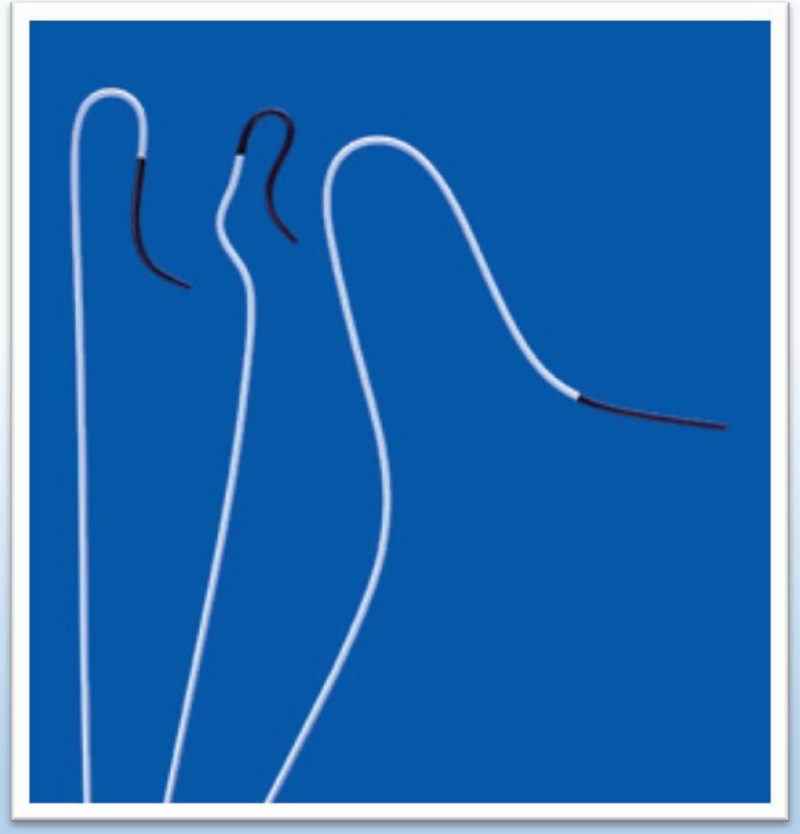
# Post Procedure

- Overnight inpatient stay (1-3 days)
- Continue Octreotide as per protocol
- Advice re: post embolization syndrome
- Home with analgesia/antiemetics
- Phone review IR CNS day 3 and 7
- Clinical and CT review at  8 weeks/MDT
- ? Re treat

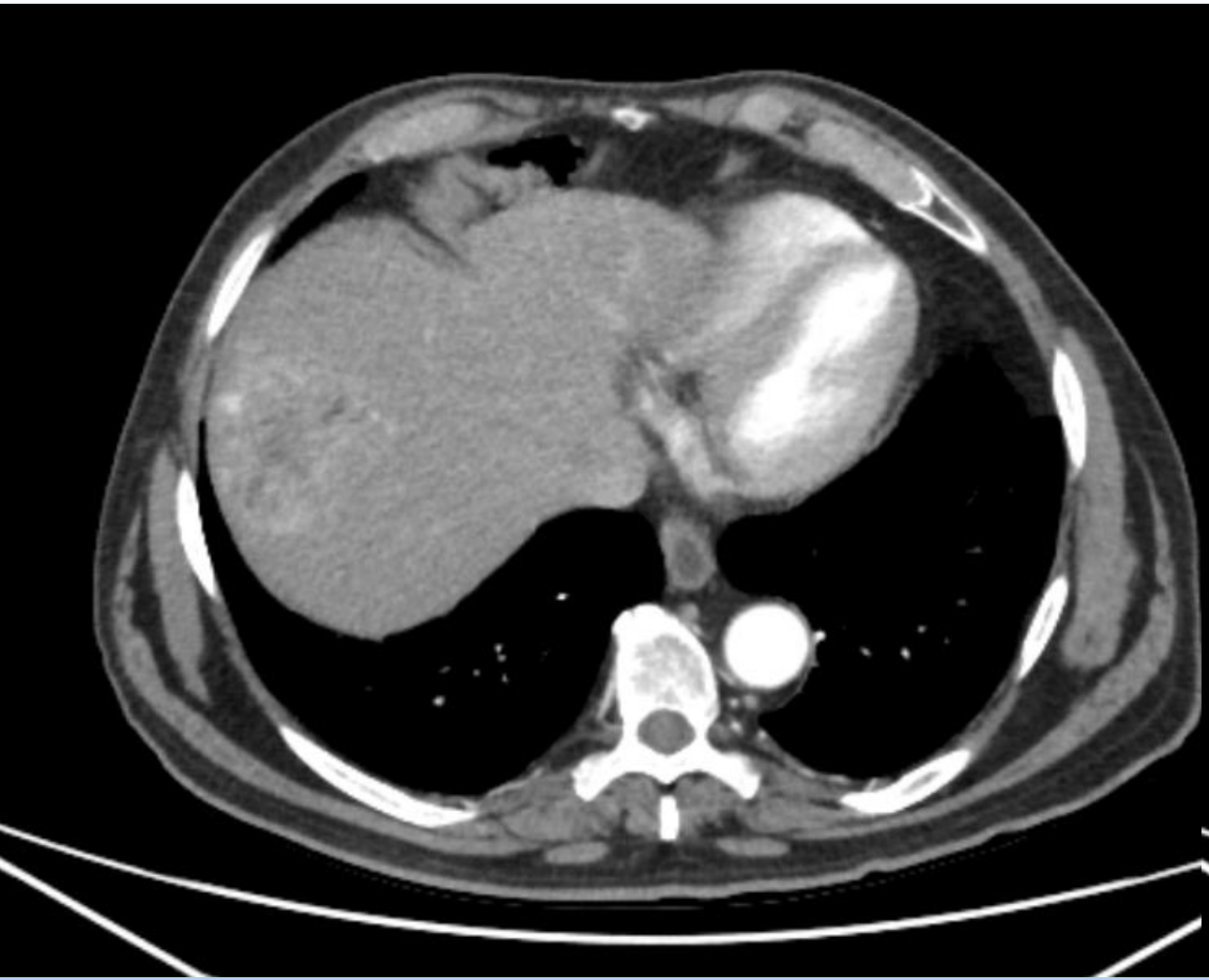
# Principles of Treatment

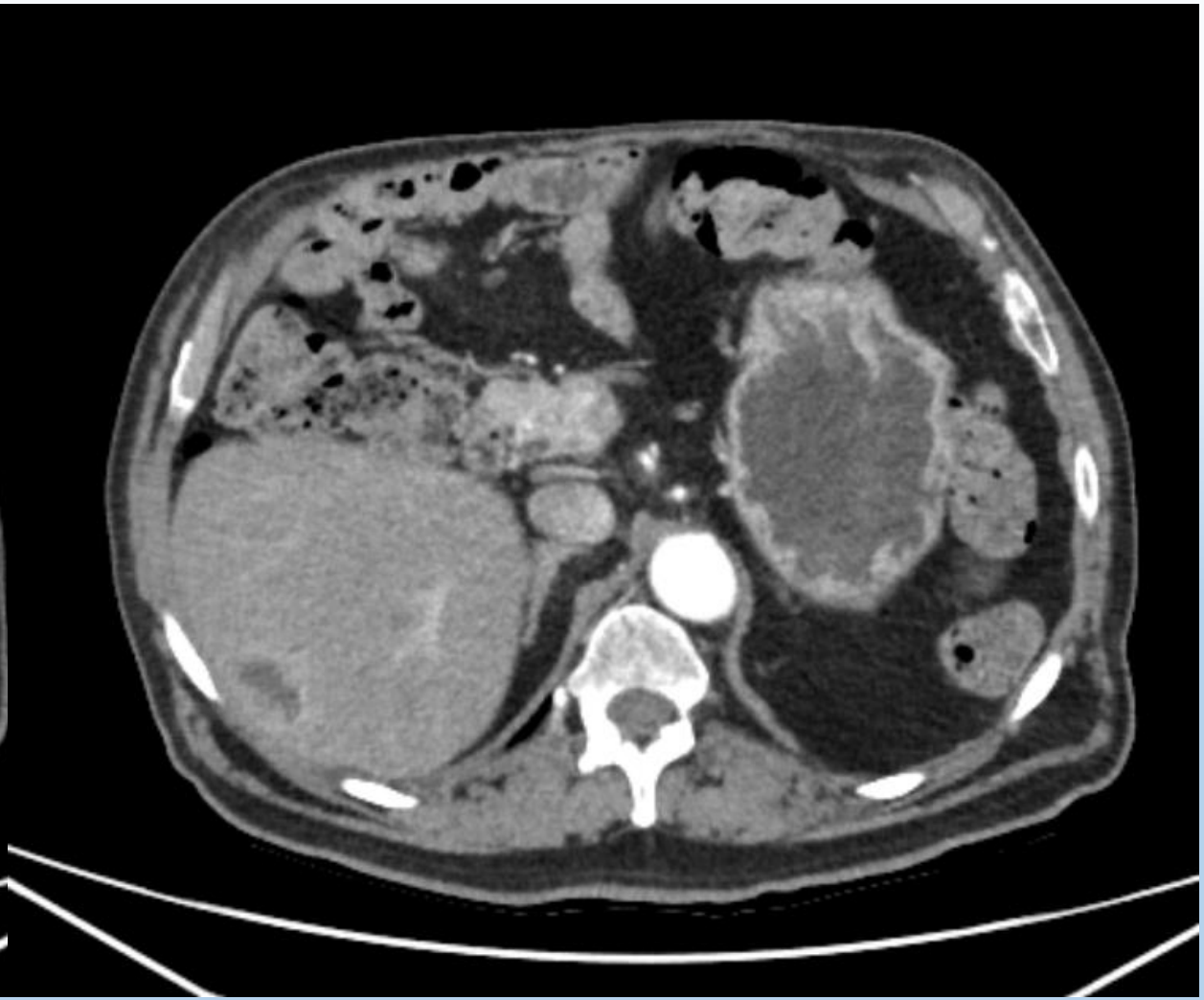
- Normal background liver
- Selective vs Lobar
- For disease vol >50% - segmental treatments.
- For Bilobar disease – Lobar treatments 4-6weeks apart.
- PVT or Biliary enteric anastomosis – consider oil based (Lipiodol)
- Endpoint – sluggish antegrade flow v stasis

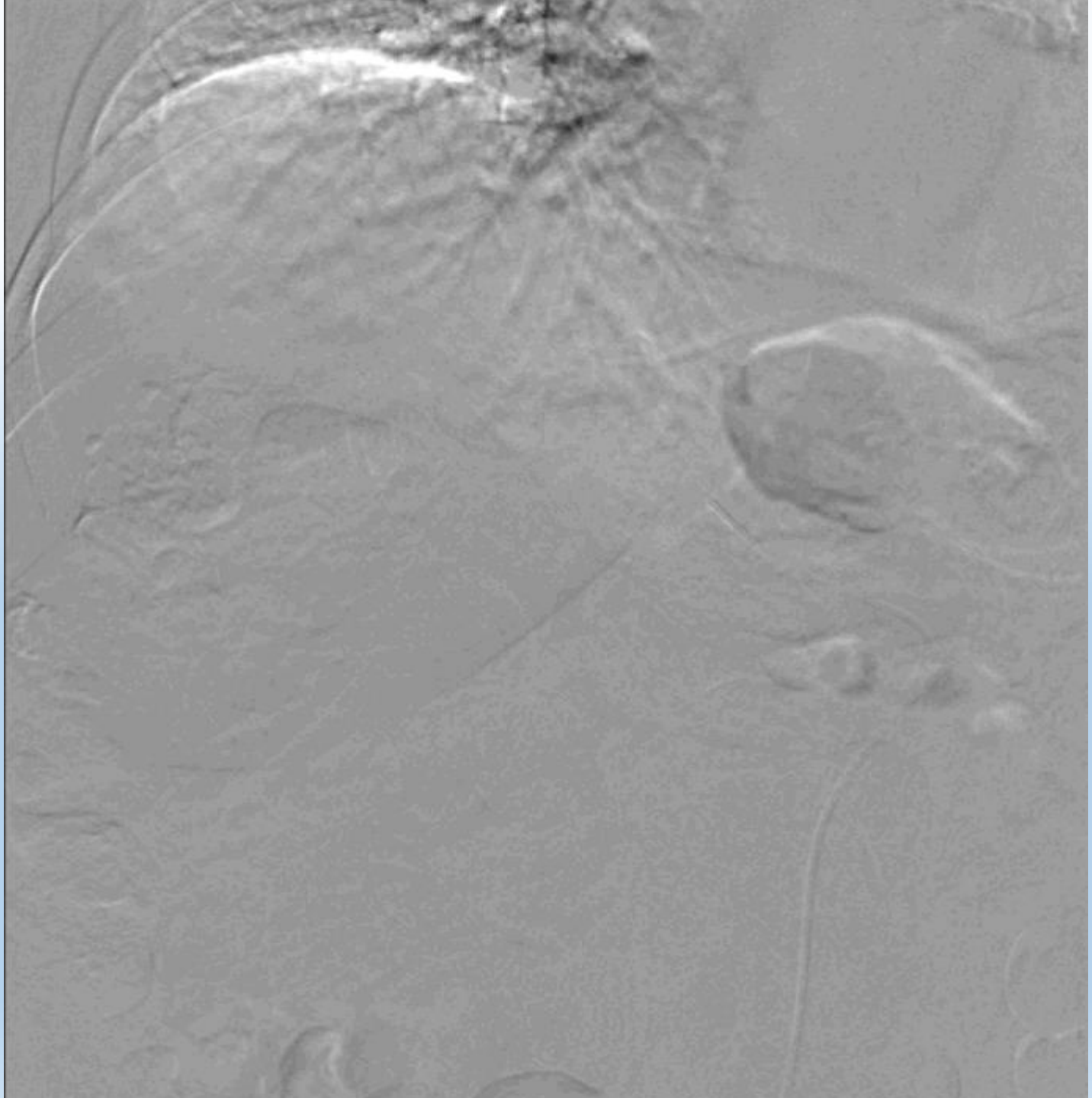
# Technical Aspects

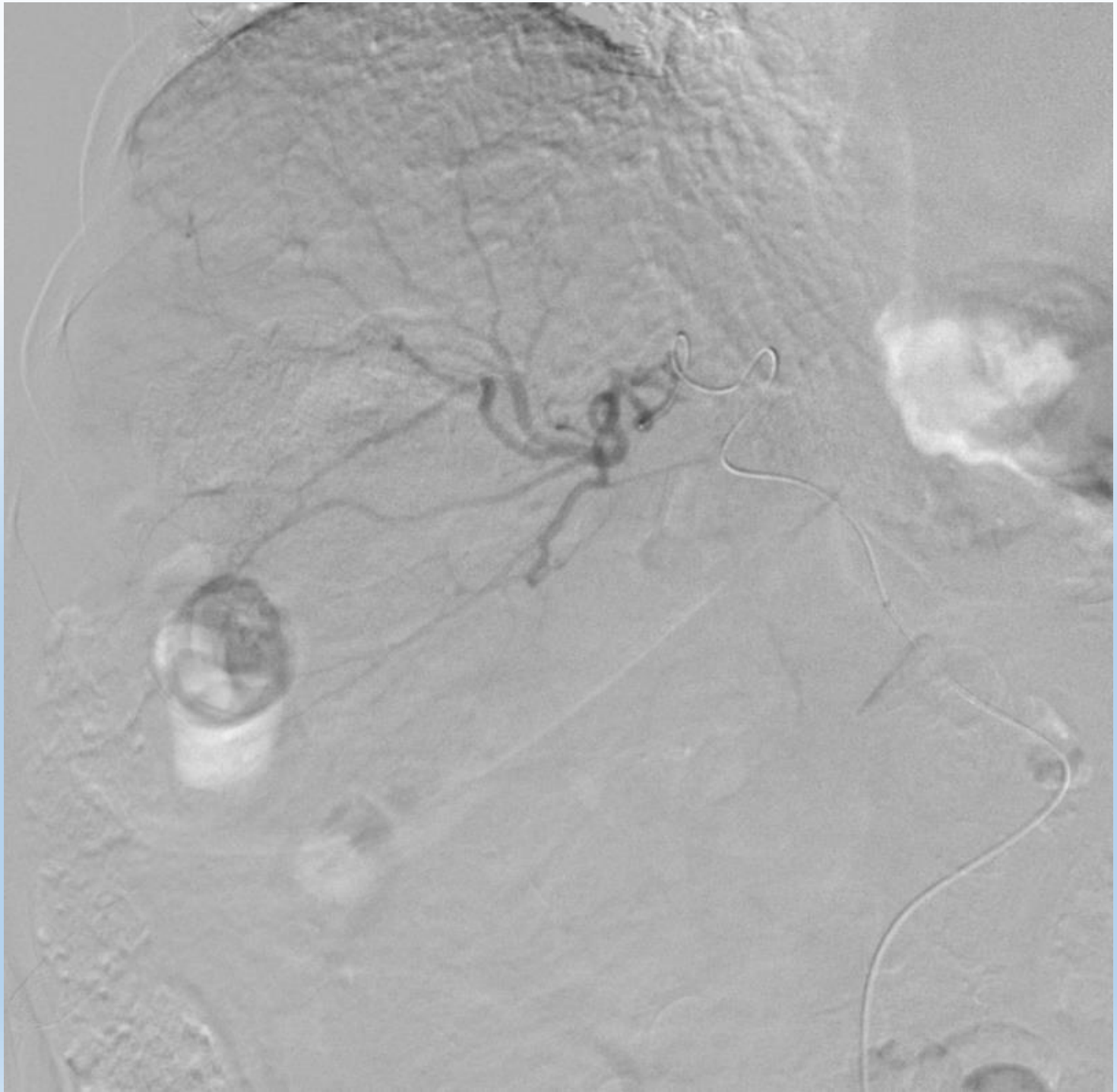


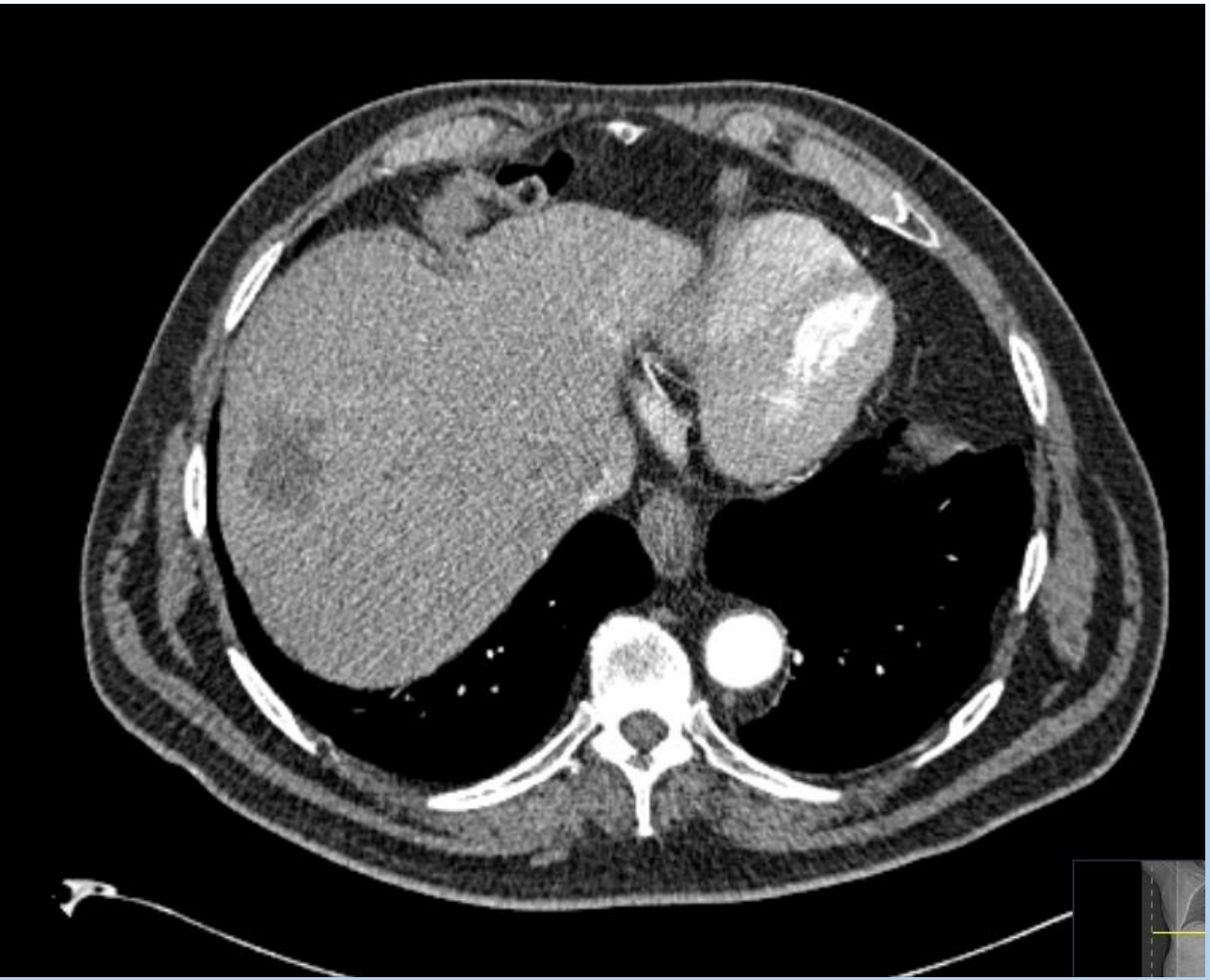
- Right CFA. US guided
- 4/5Fr sheath
- Access to Coeliac axis with base catheter
- Microcatheter and microwire to more selective hepatic arterial branches.
- Rotational CT
- Haemostasis : manual compression /6F angioseal closure.

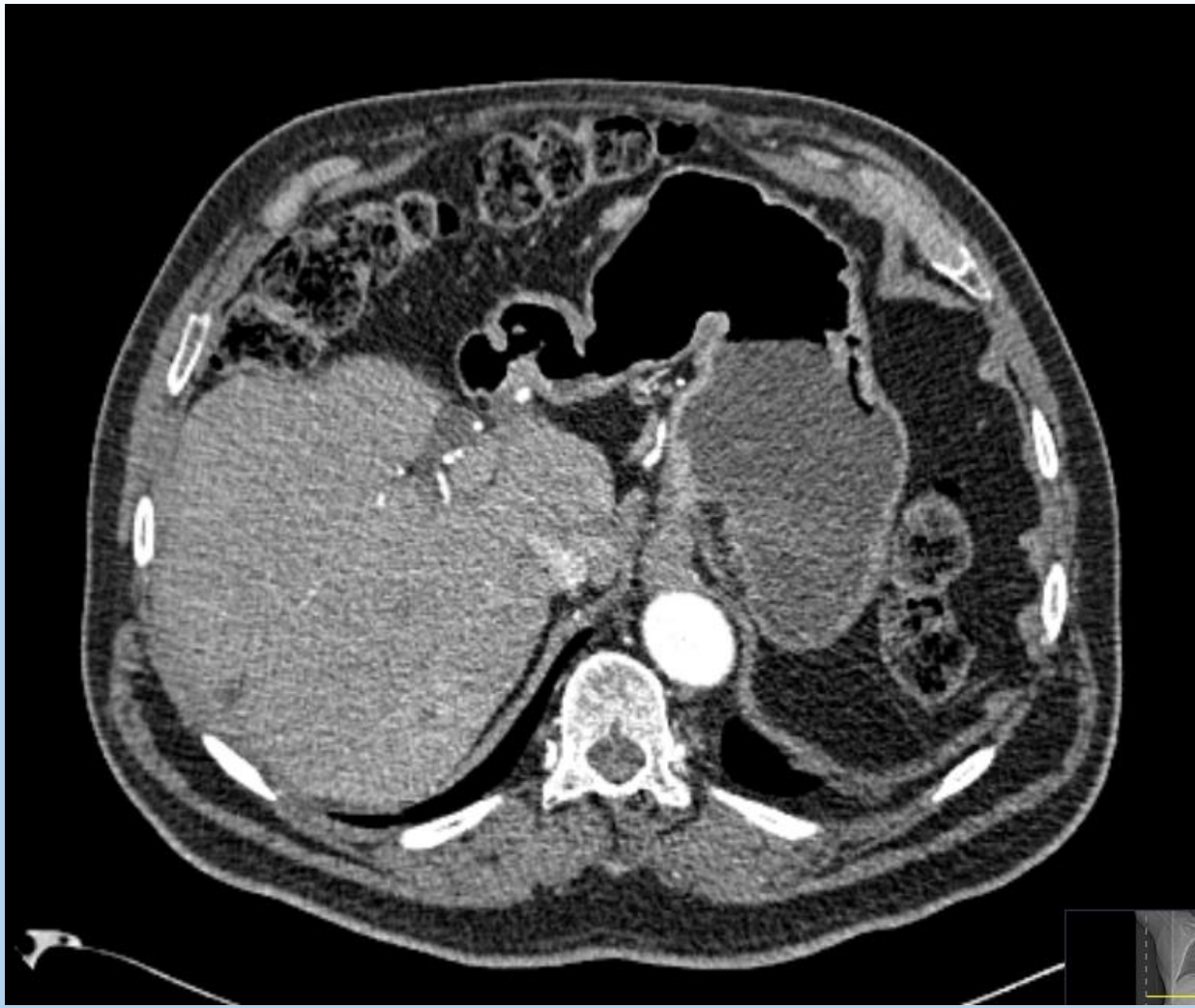


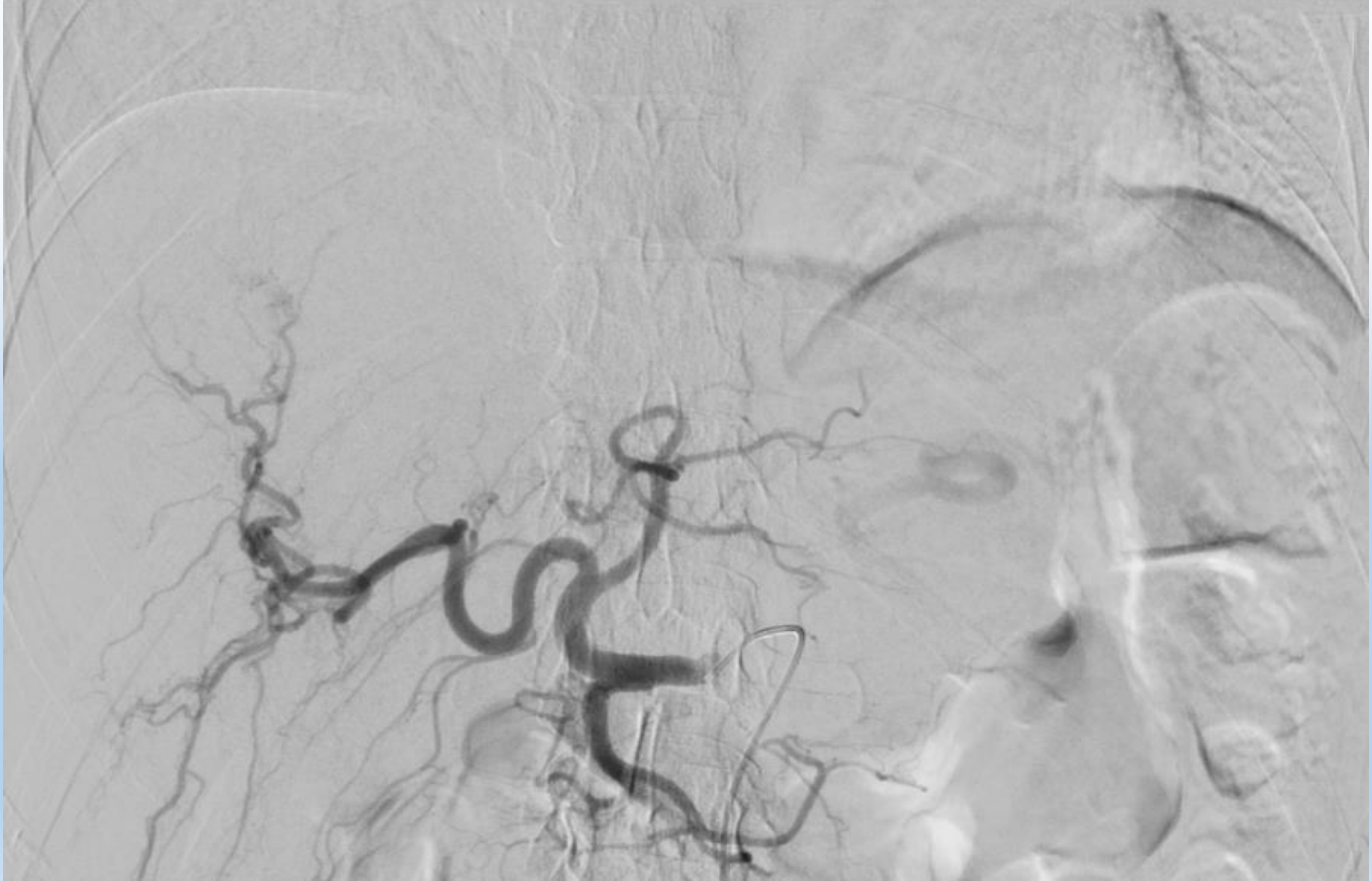


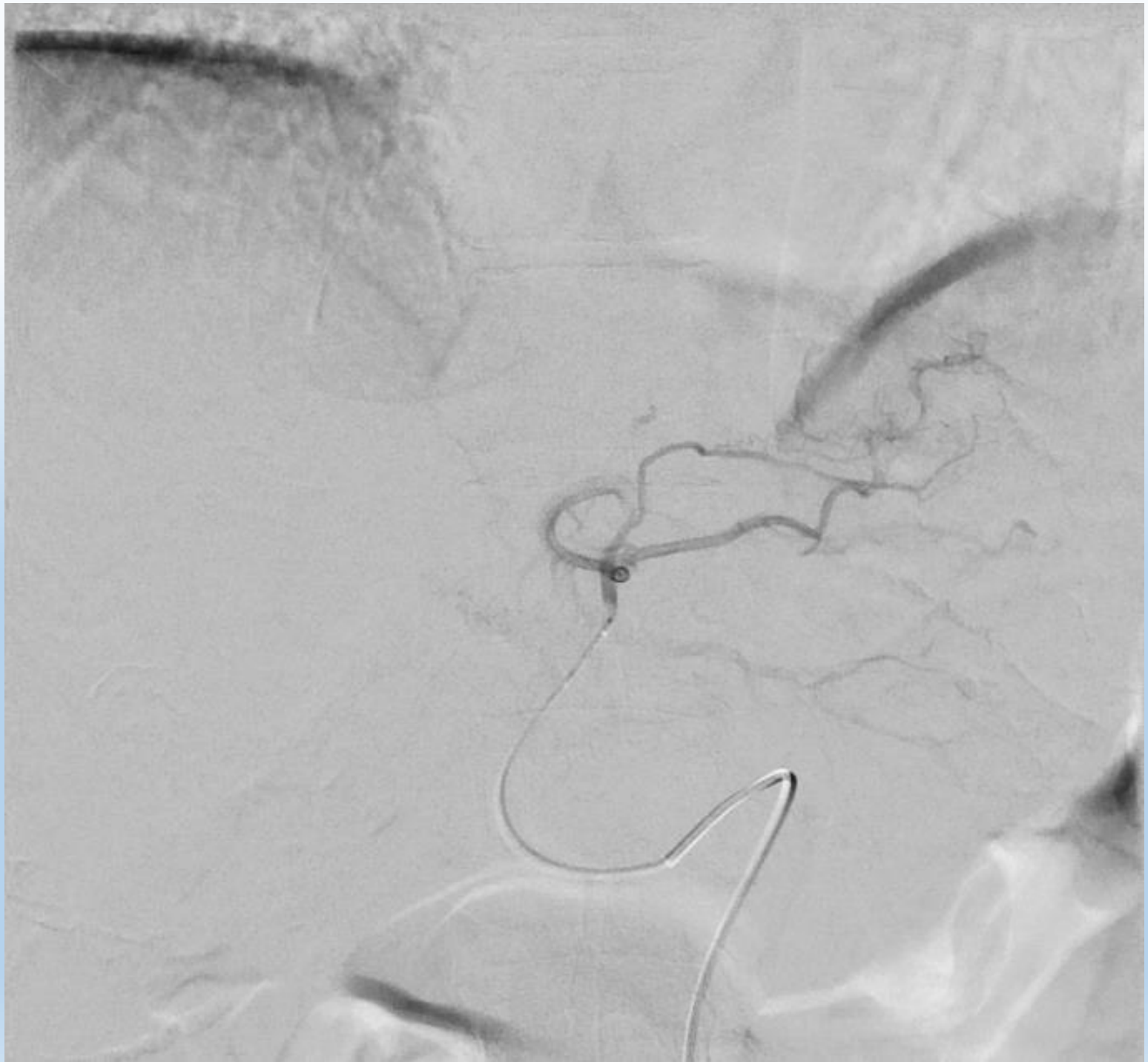


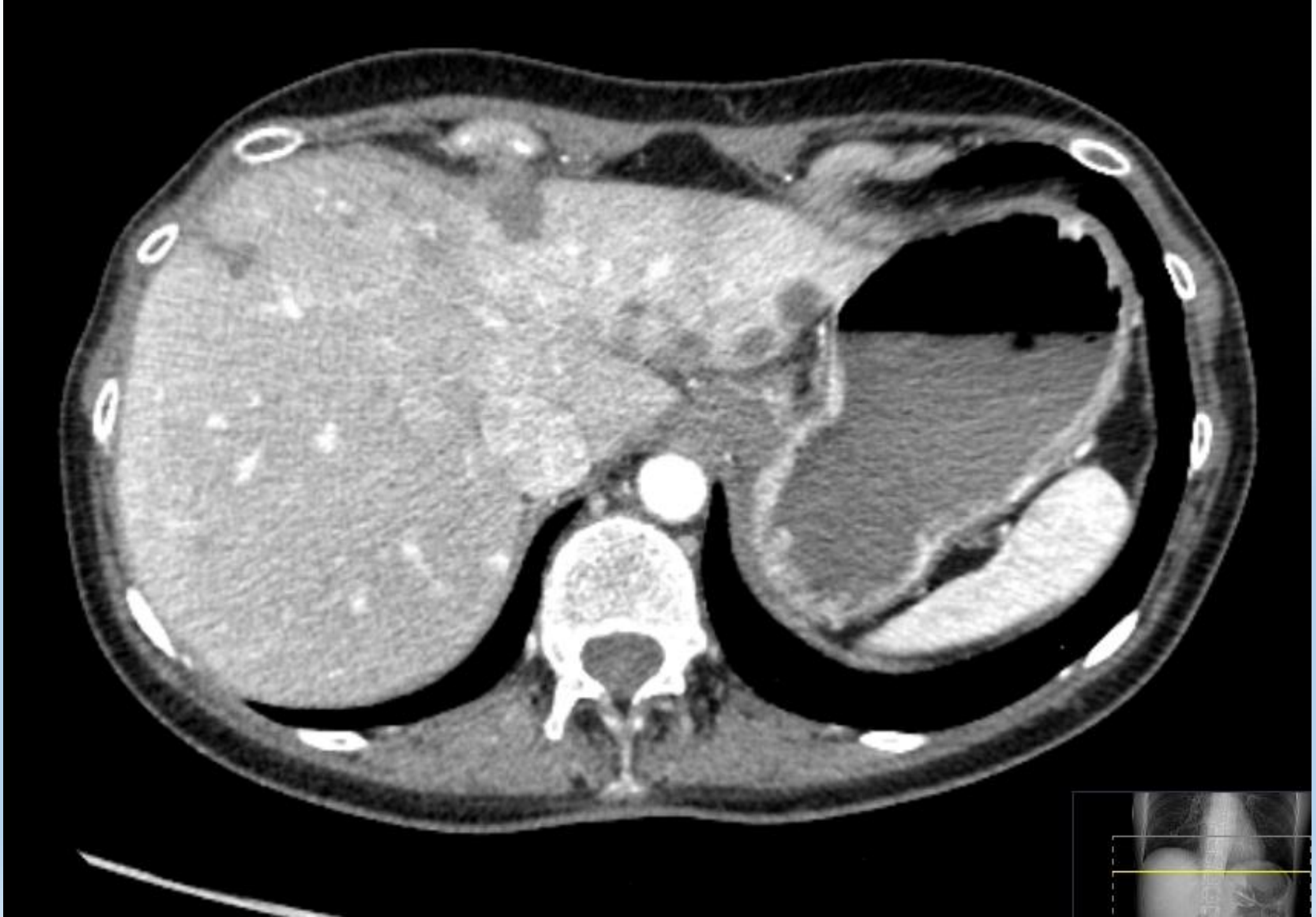


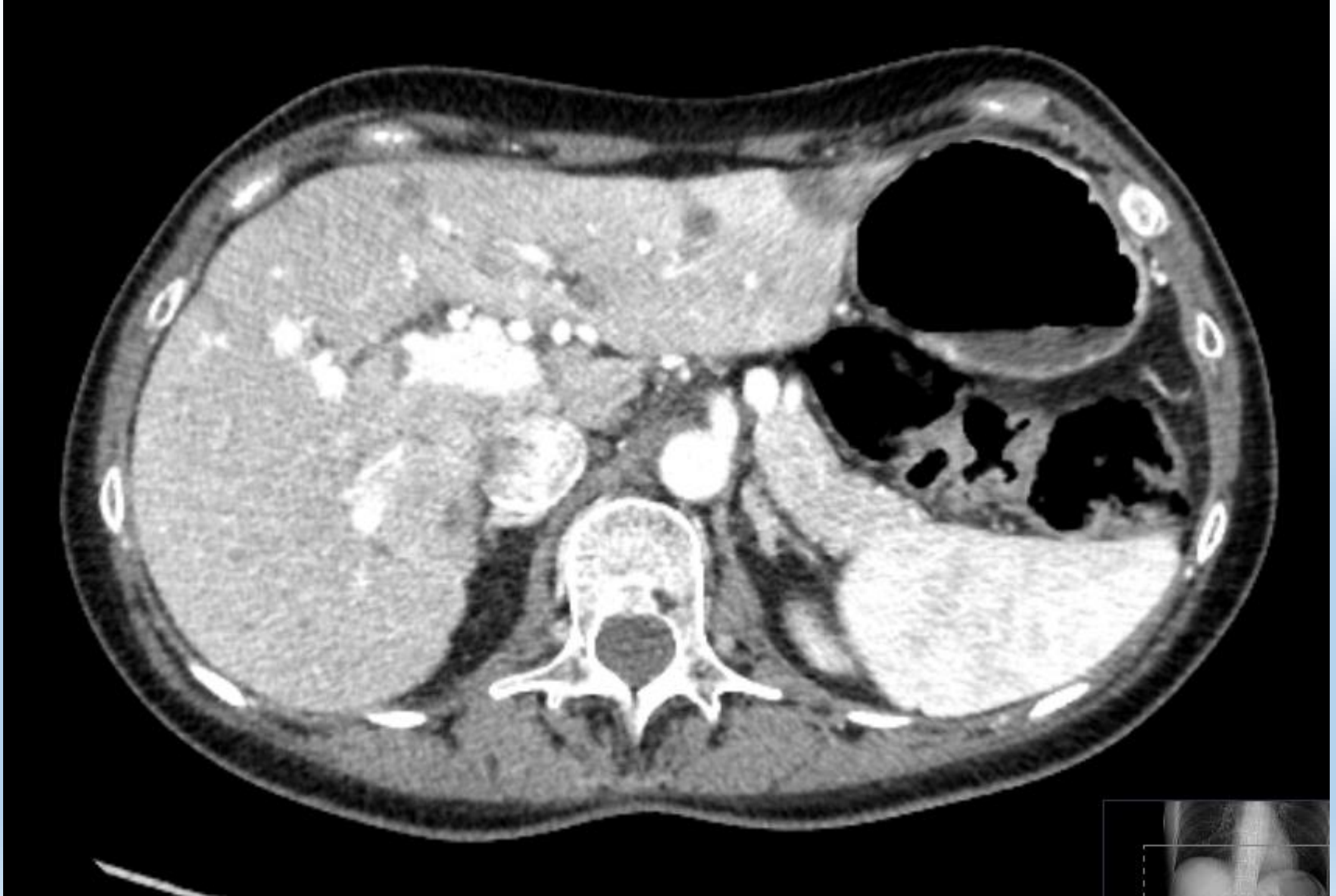


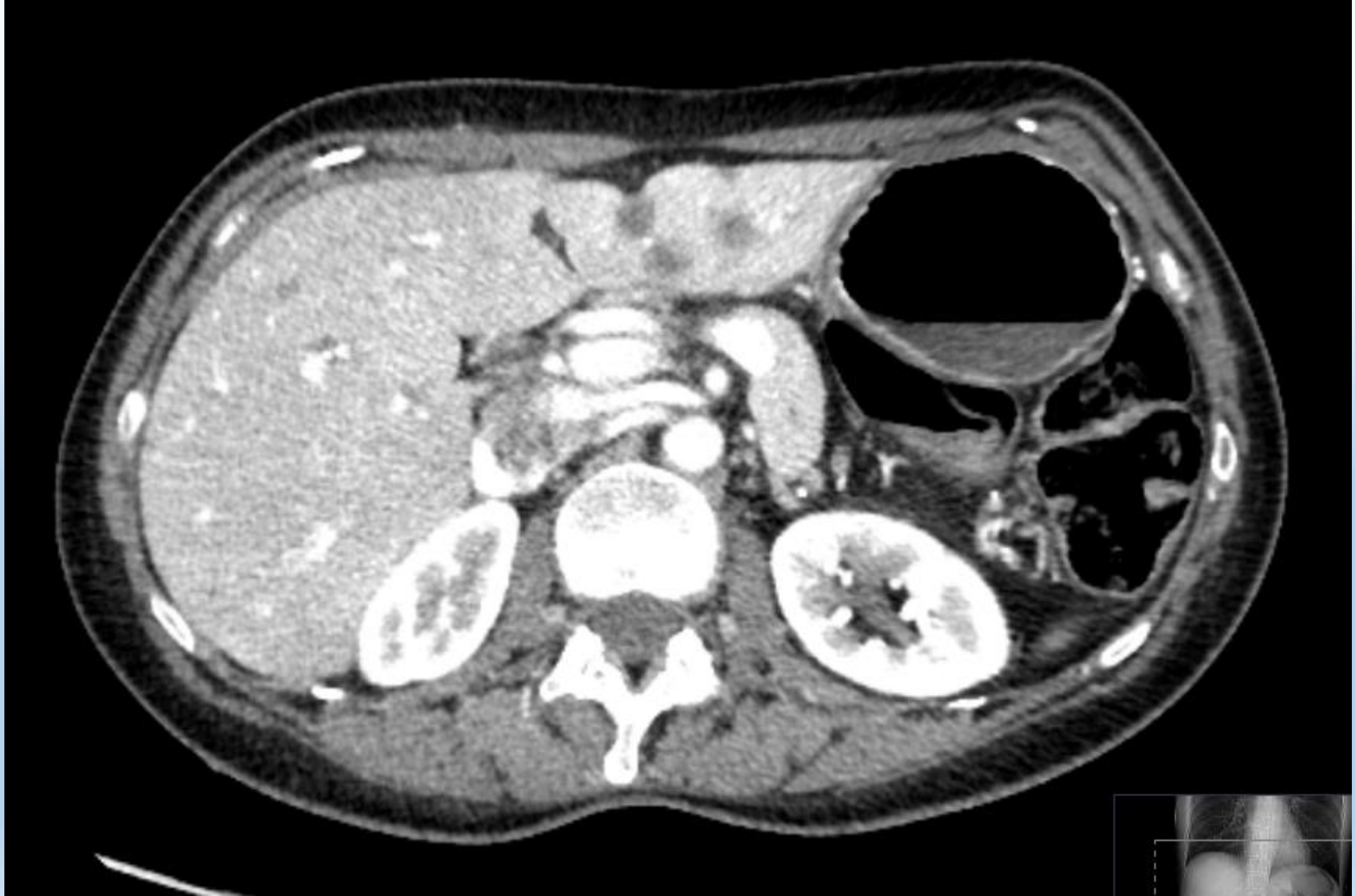


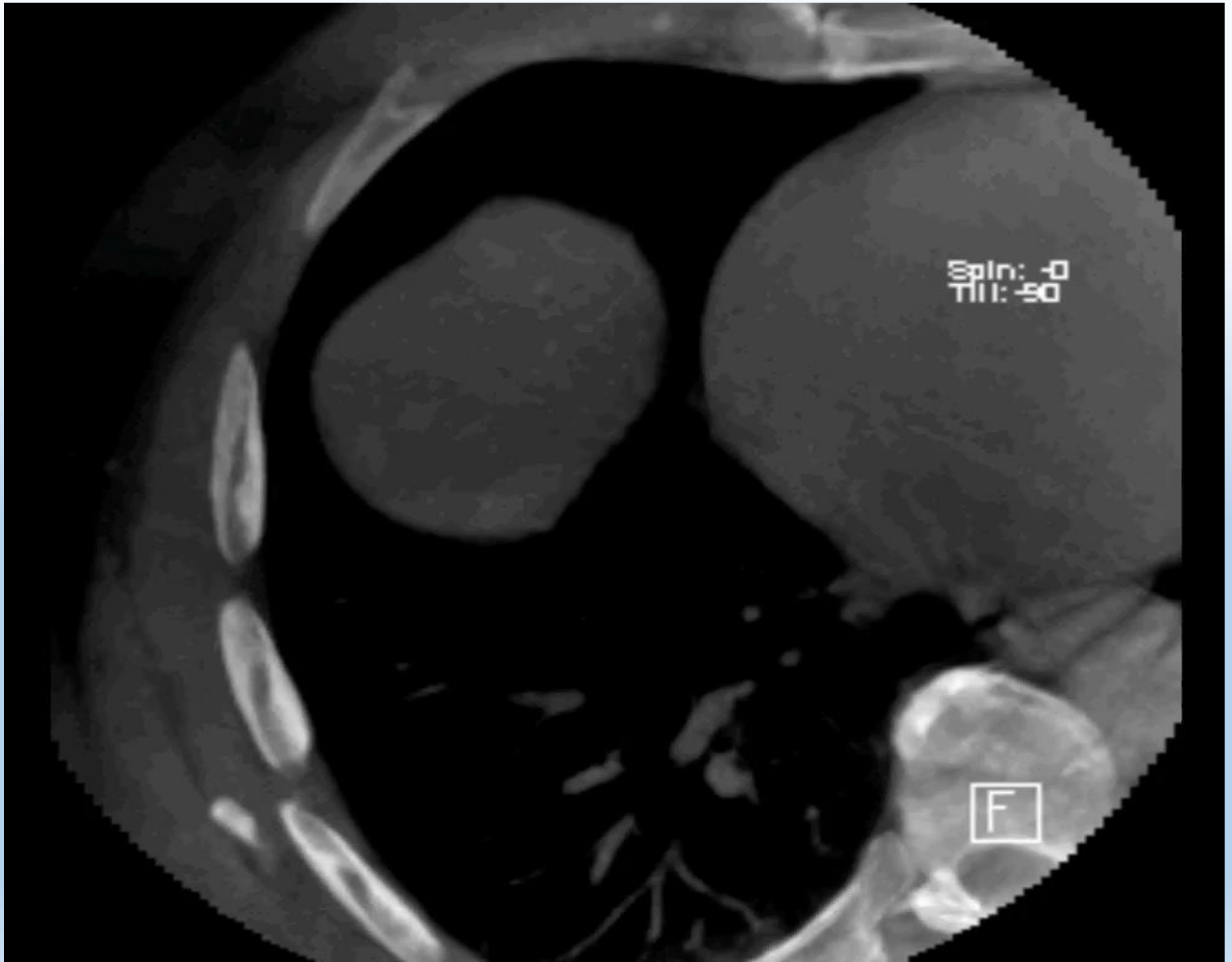








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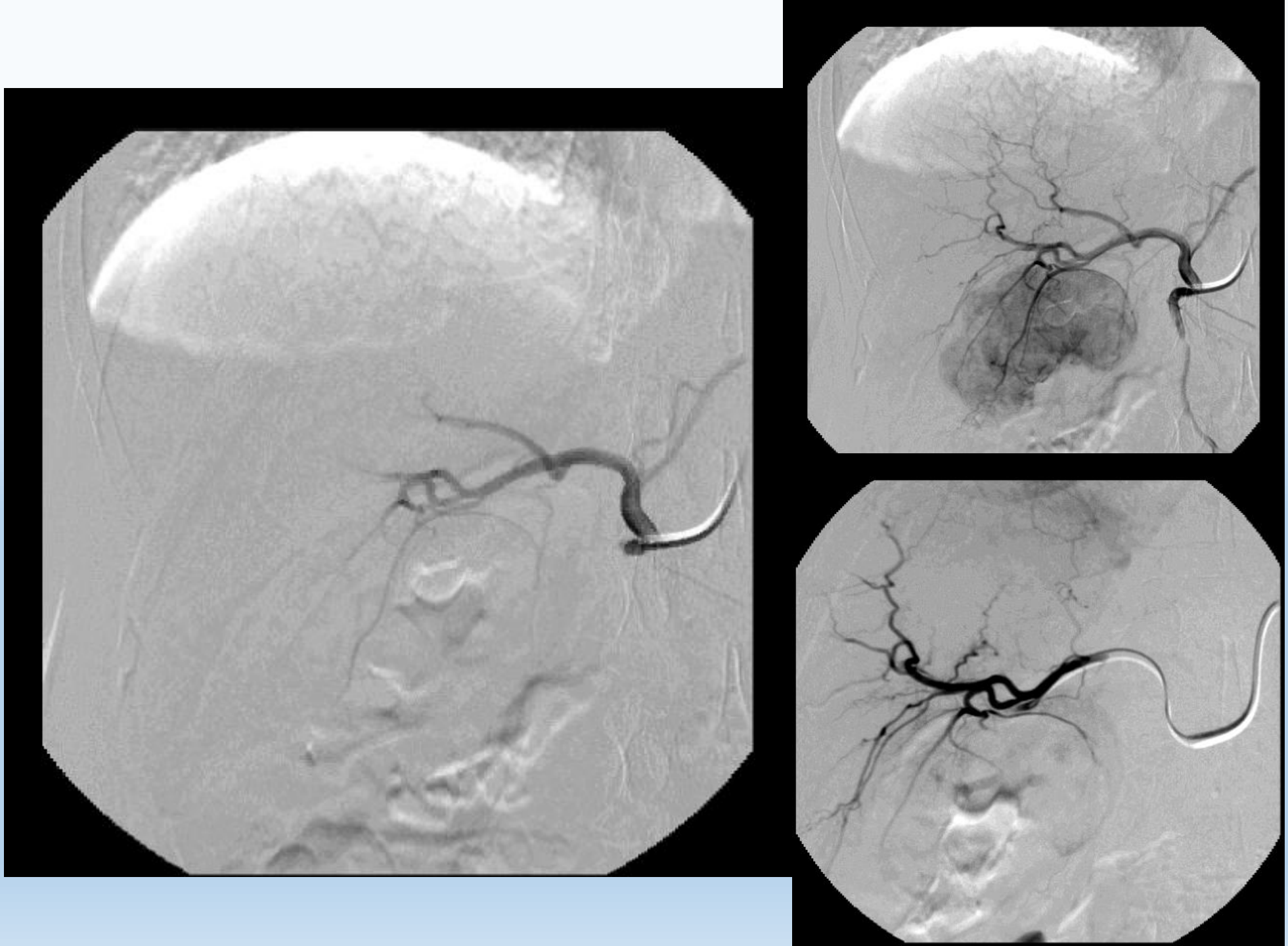
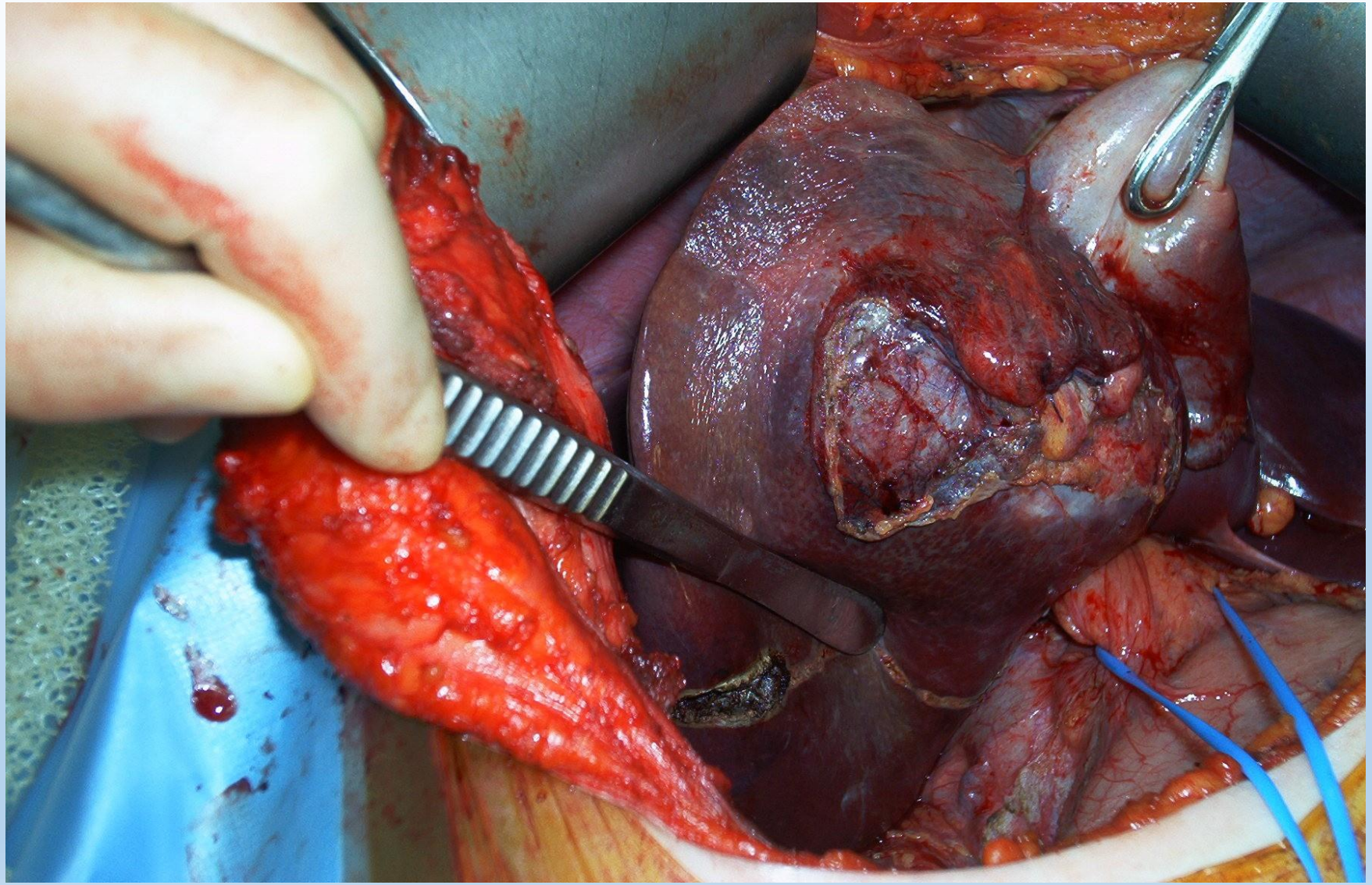
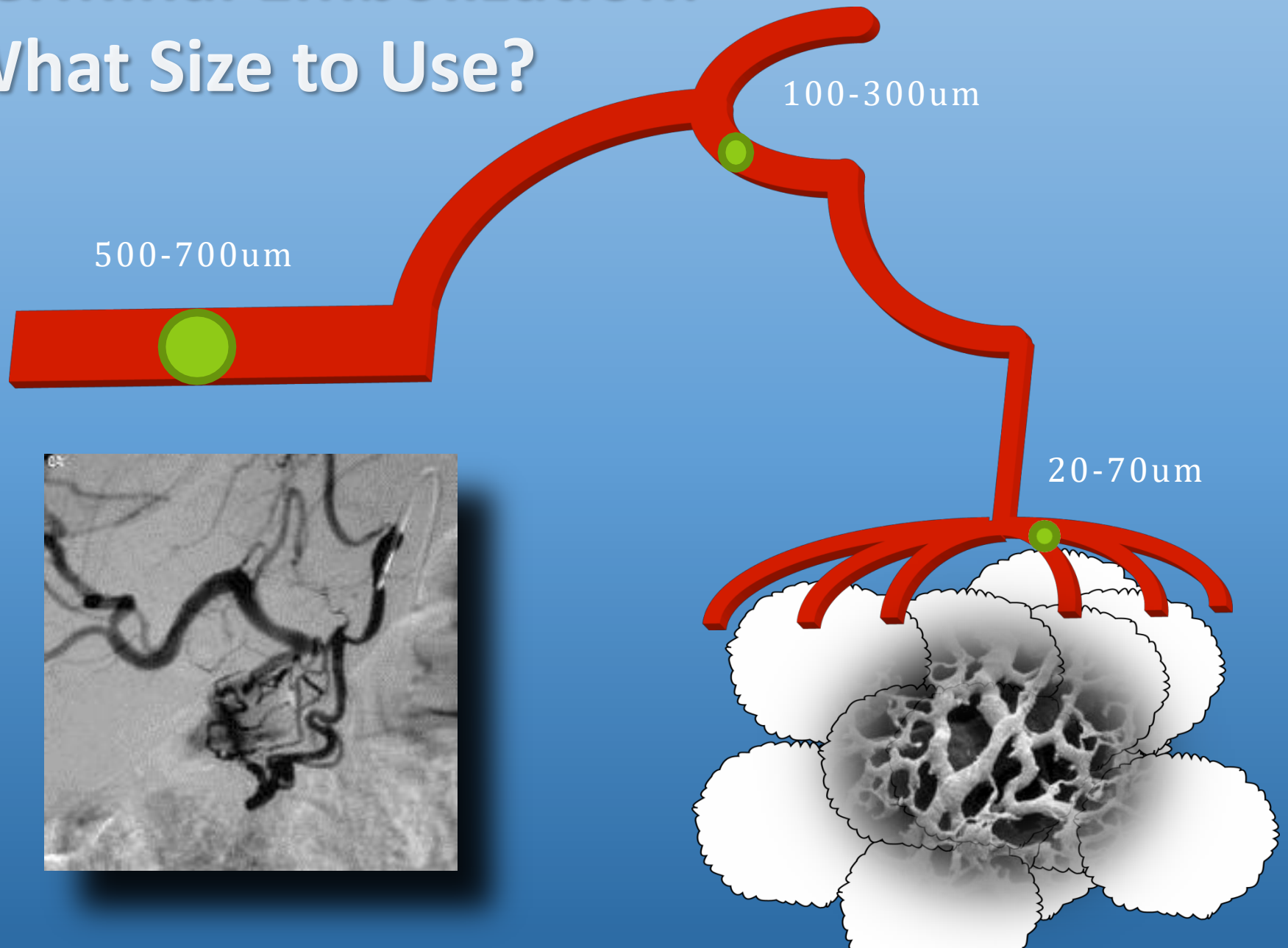


# Bulky segment 5 NET



# Terminal Embolization: What Size to Use?



# Aggressive Cytoreduction for Liver mets

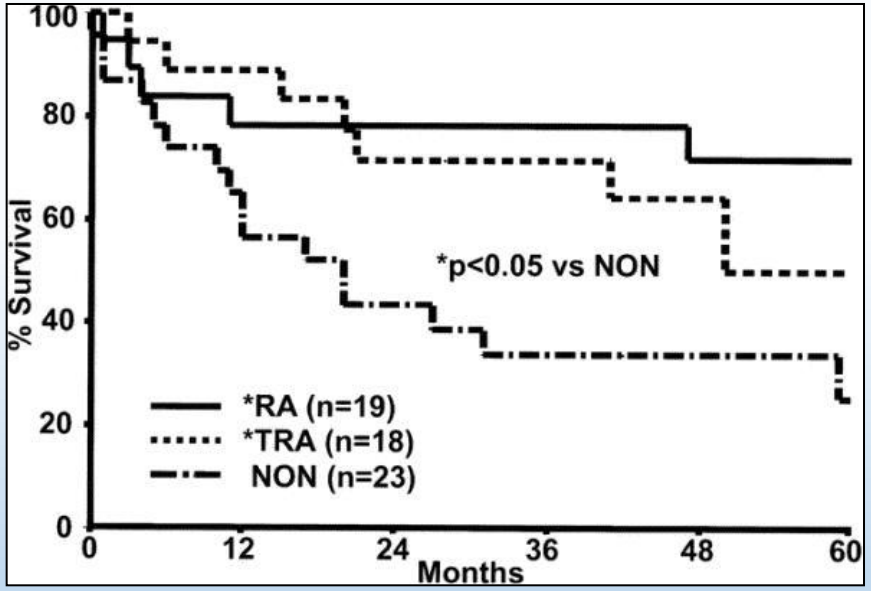
The case for symptomatic embolisation is proven
90% response

Surgical paper from Indiana

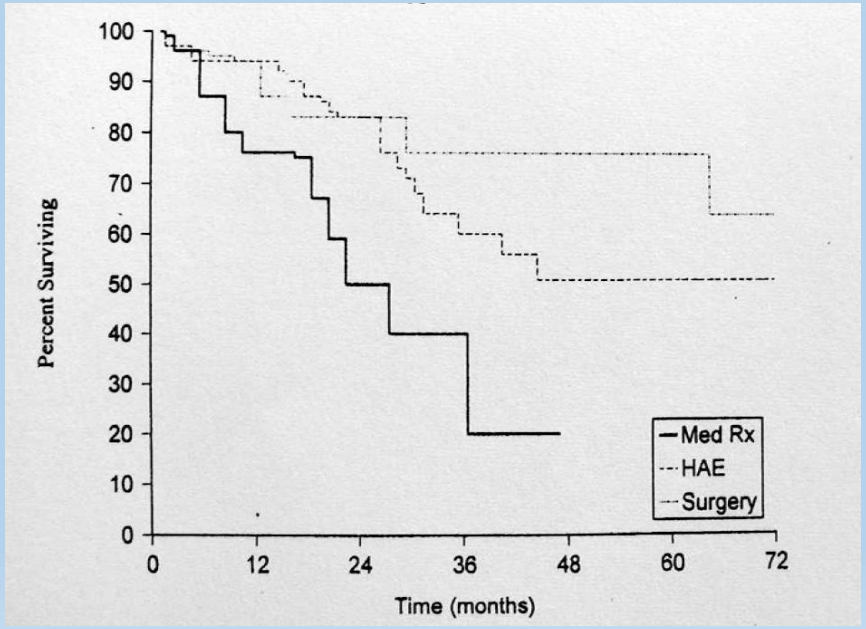
“aggressive management of NET hepatic metastases does improve survival and TACE increases the patient population eligible for this strategy.”

60 Patient retrospective

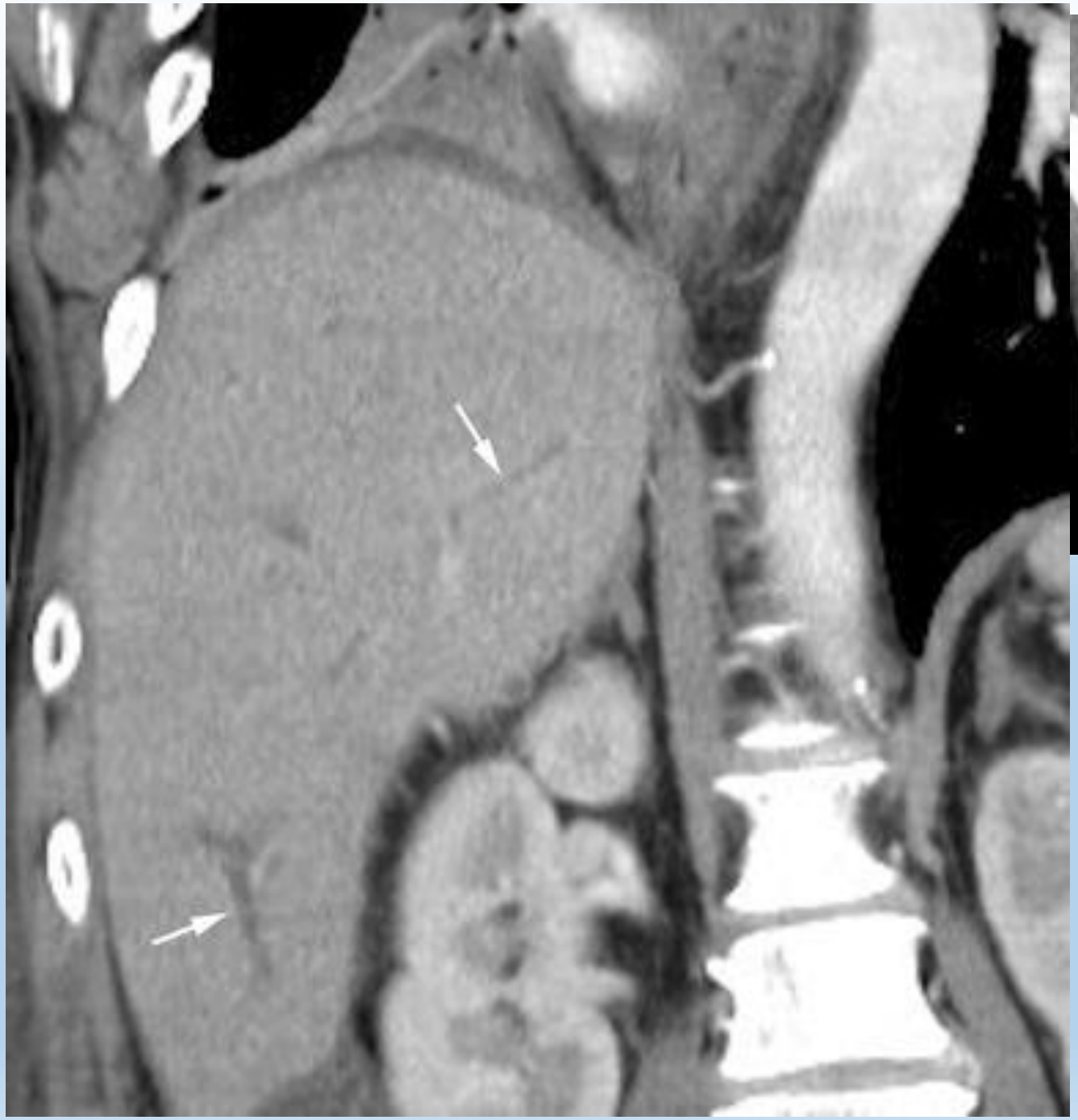
Chamberlain study
- 85 pts, liver mets from NET
- Surgery
- Medical tx

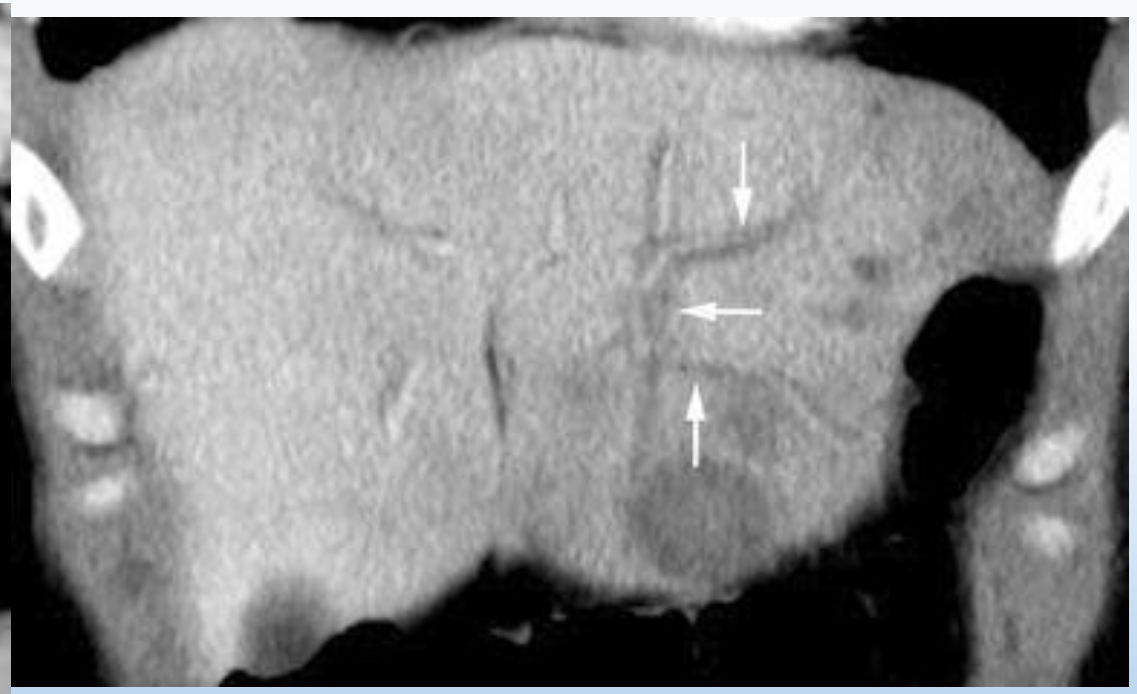


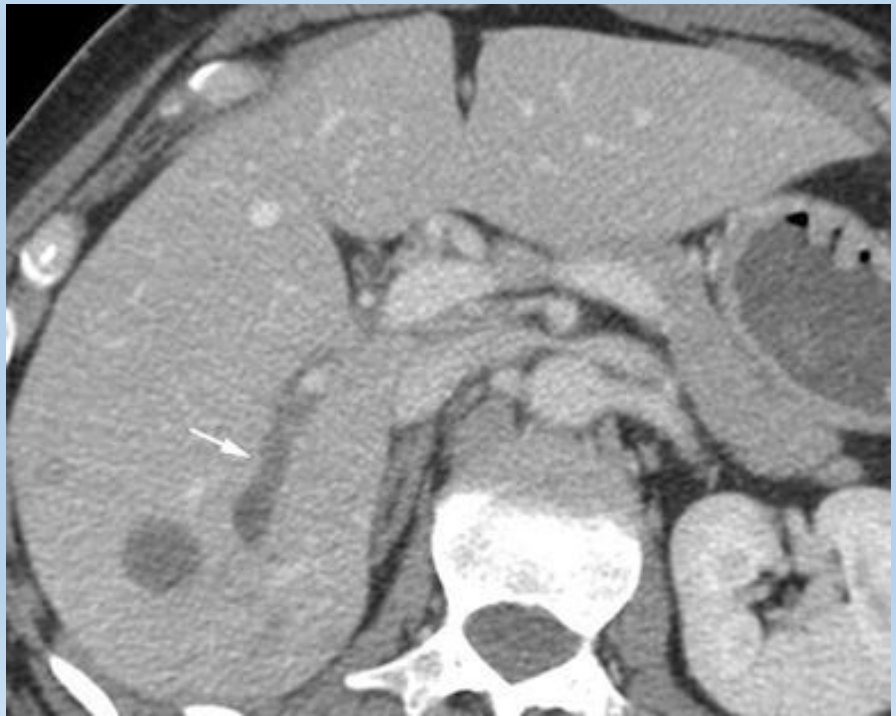

Touzios JG et al, *Annals of Surgery* 2005

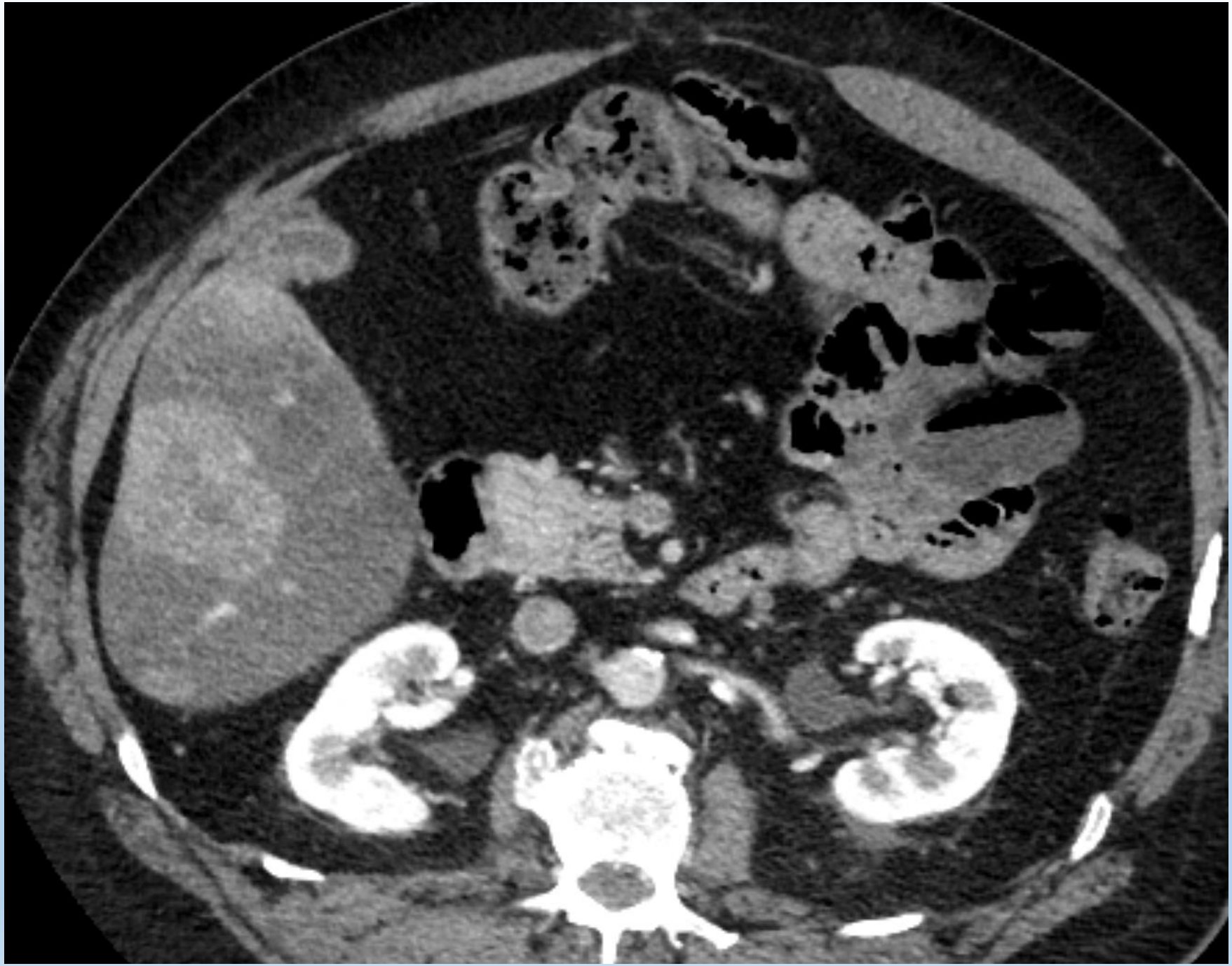


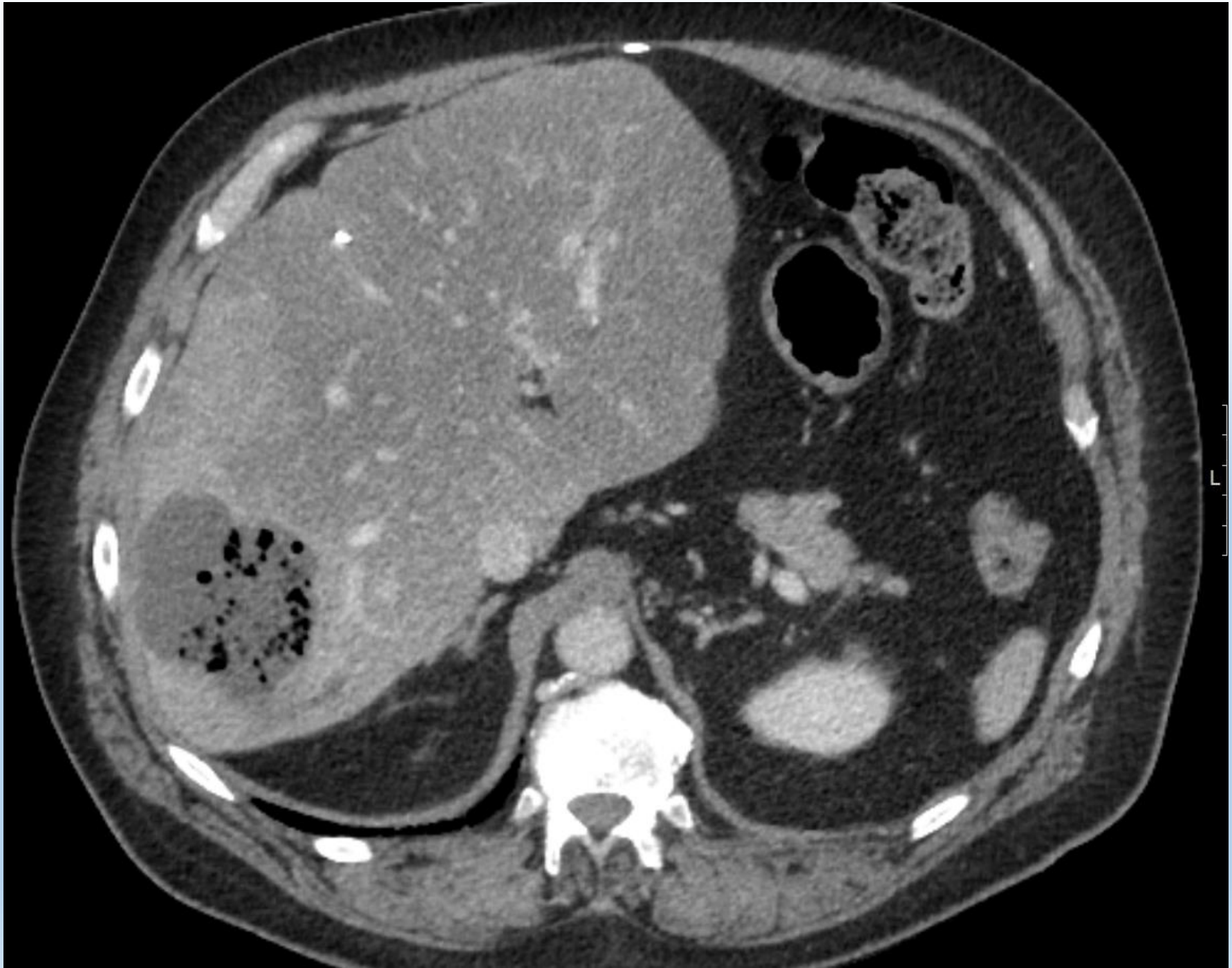

Chamberlin RS, *J Am Coll Surg 2000*

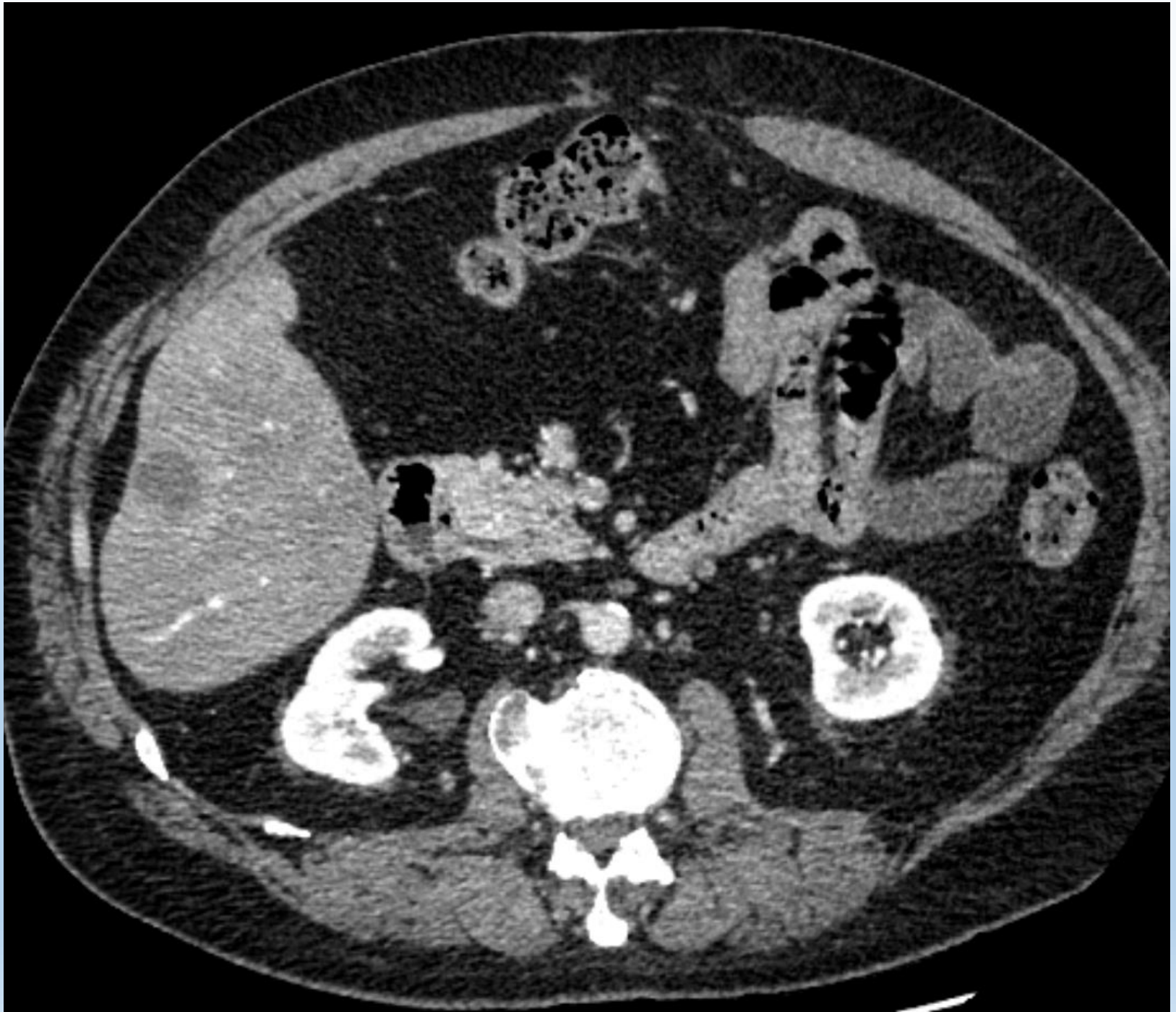












# Quality of Life



## Effects of debulking surgery, transarterial embolisation (TAE) and transarterial chemoembolisation (TACE) on quality of life in patients with metastatic ileal and pancreatic neuroendocrine tumours (NETs)

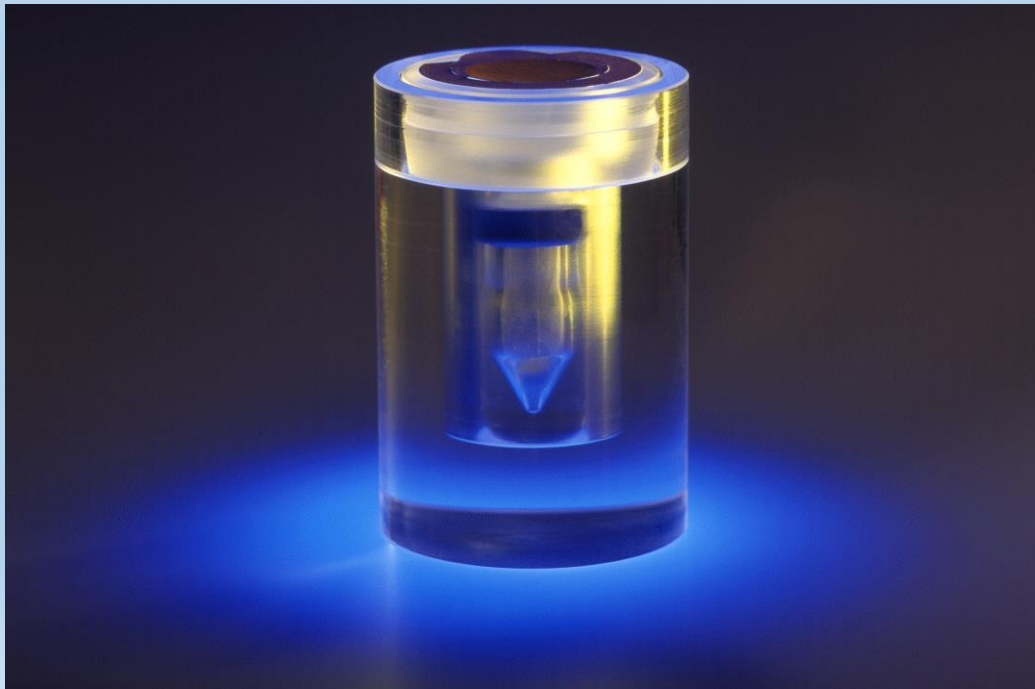
Adam Sinclair [1], Lulu Tanno [2], Emma Jarvis [2], Emma Ramsey [2], Salma Naheed [2], Thomas Armstrong [2], Arjun Takhar [2], John Knight [2], Brian Stedman [2], Sachin Modi [2], Timothy Bryant [2], David Breen [2], Luke Nolan [2], Ma'en Al-Mrayat [2], Neil Pearce [2] & Judith Cave [2]

QOL dips after treatment but back to baseline after 3 months and sustained for 2 years.

# Radioembolisation

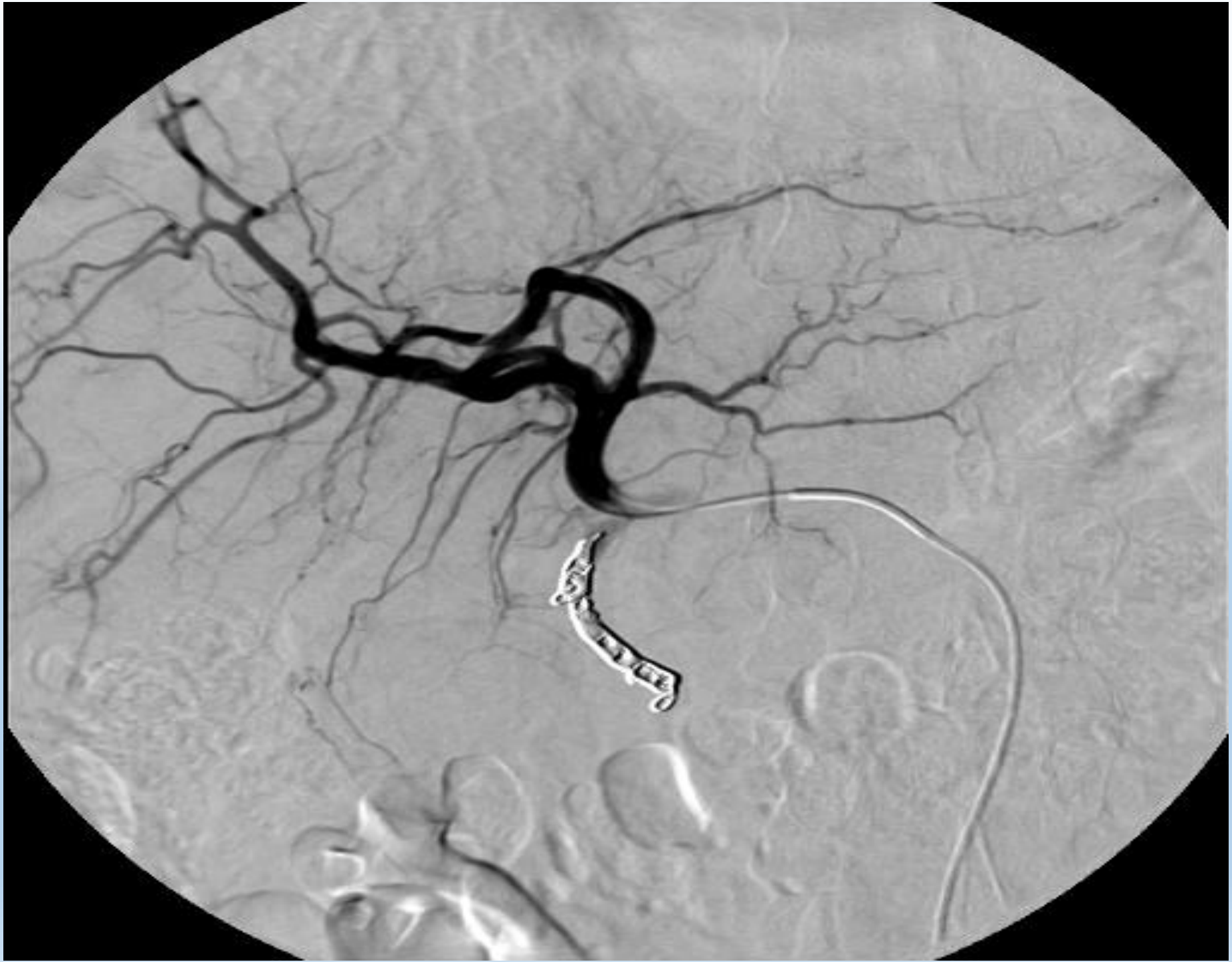
- Radioembolization is also known as transarterial radioembolisation, selective internal radiation therapy, or intraarterial brachytherapy.
- Yittrium 90 (Y90).

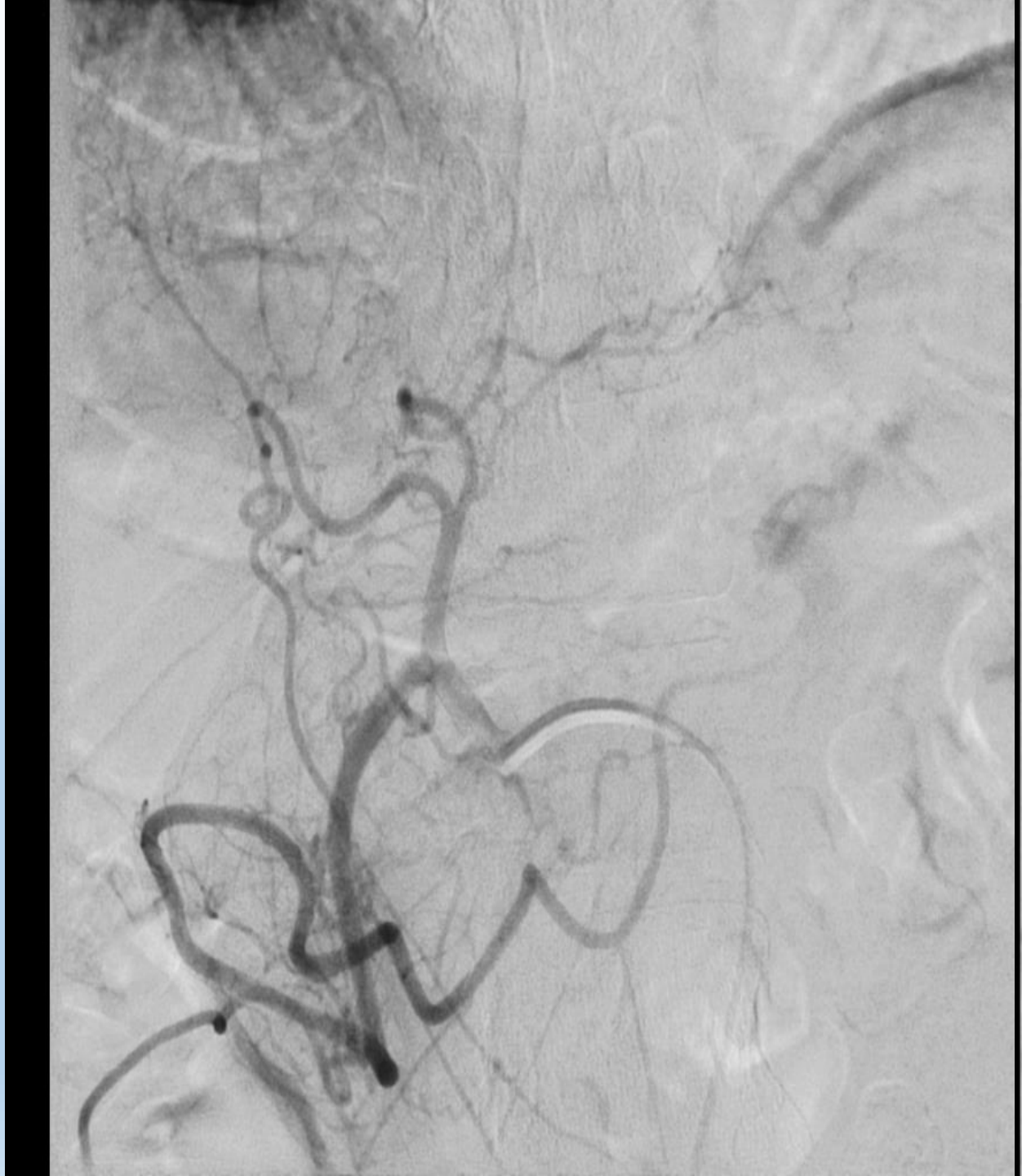
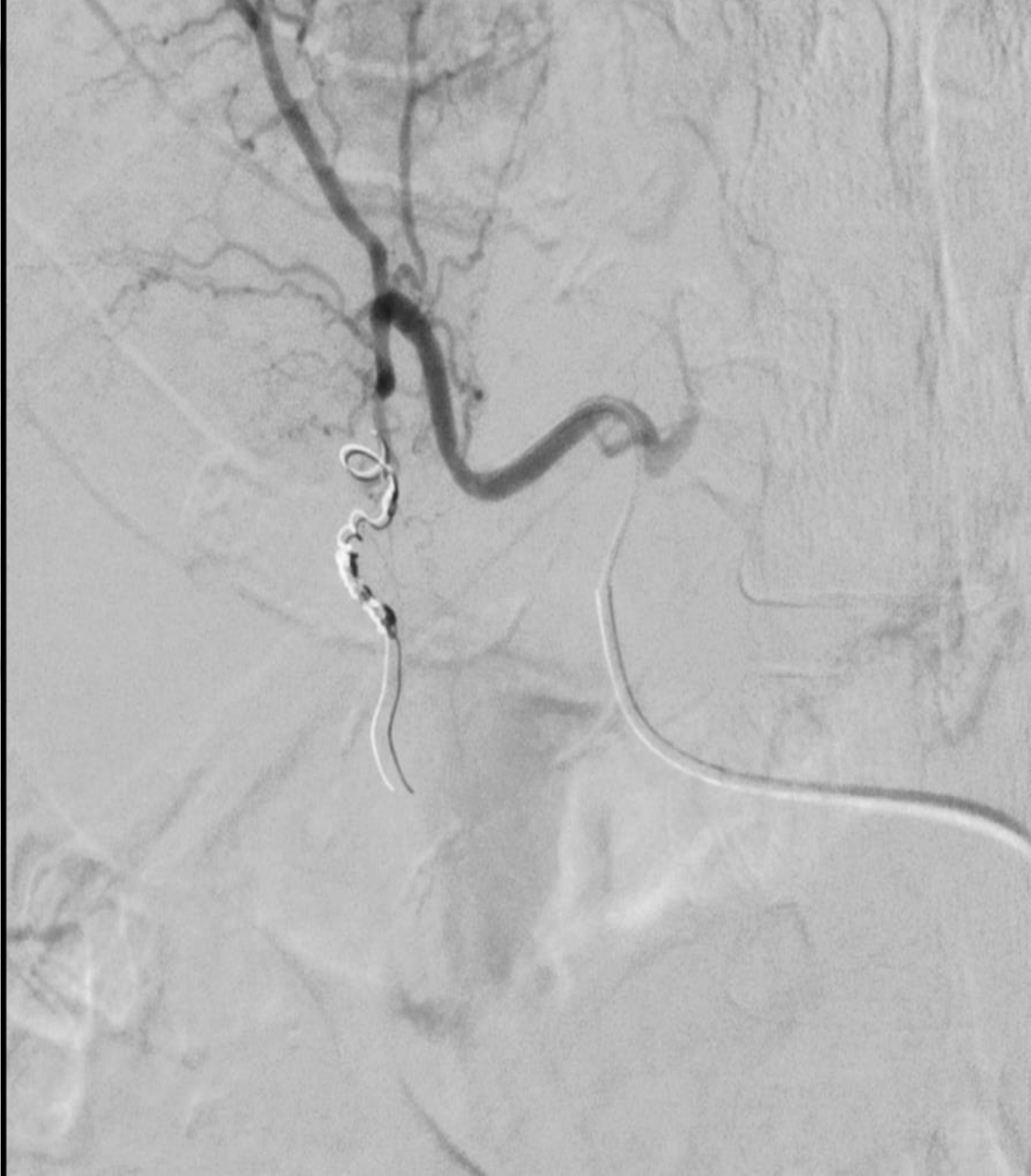
  - *100% pure beta emitter*
  - *Tissue penetration range 2.5 mm (max. 11 mm)*
  - *Decays to $^{90}$Zirconium*
  - *Physical half-life of 64 hrs (2.67 days)*
  - *94% of radiation delivered within 11 days*

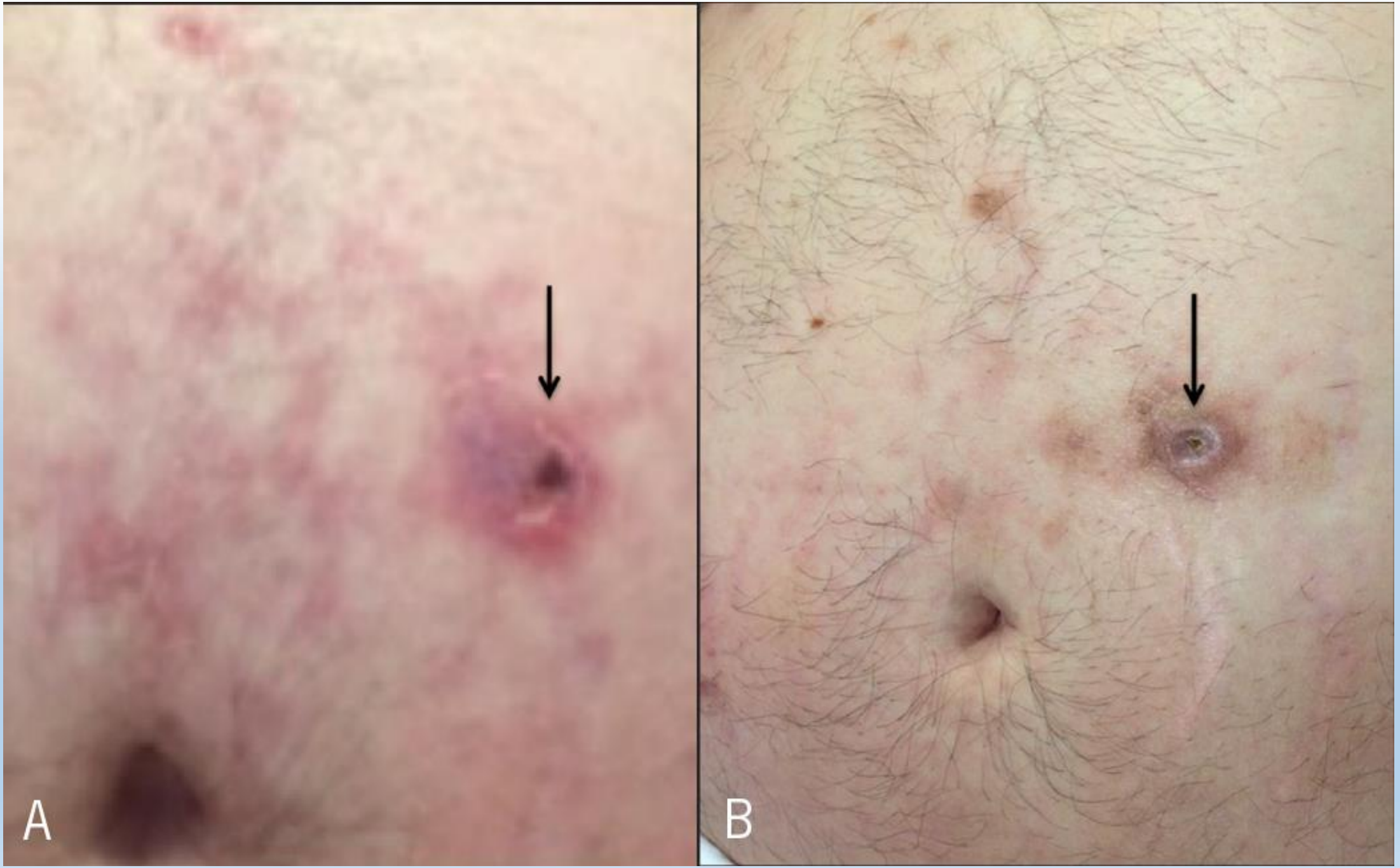


# Angiographic Assessment – Work up

- Day case
- Hepatic angiography
- Determine lung shunt fraction (15% - 30Gy)
- Embolisation of extra hepatic supply
- Treatment strategy
- Deliver $^{99m}$Tc-labeled macroaggregated albumin ($^{99m}$Tc-MAA).
- SPECT/CT within 2 hours



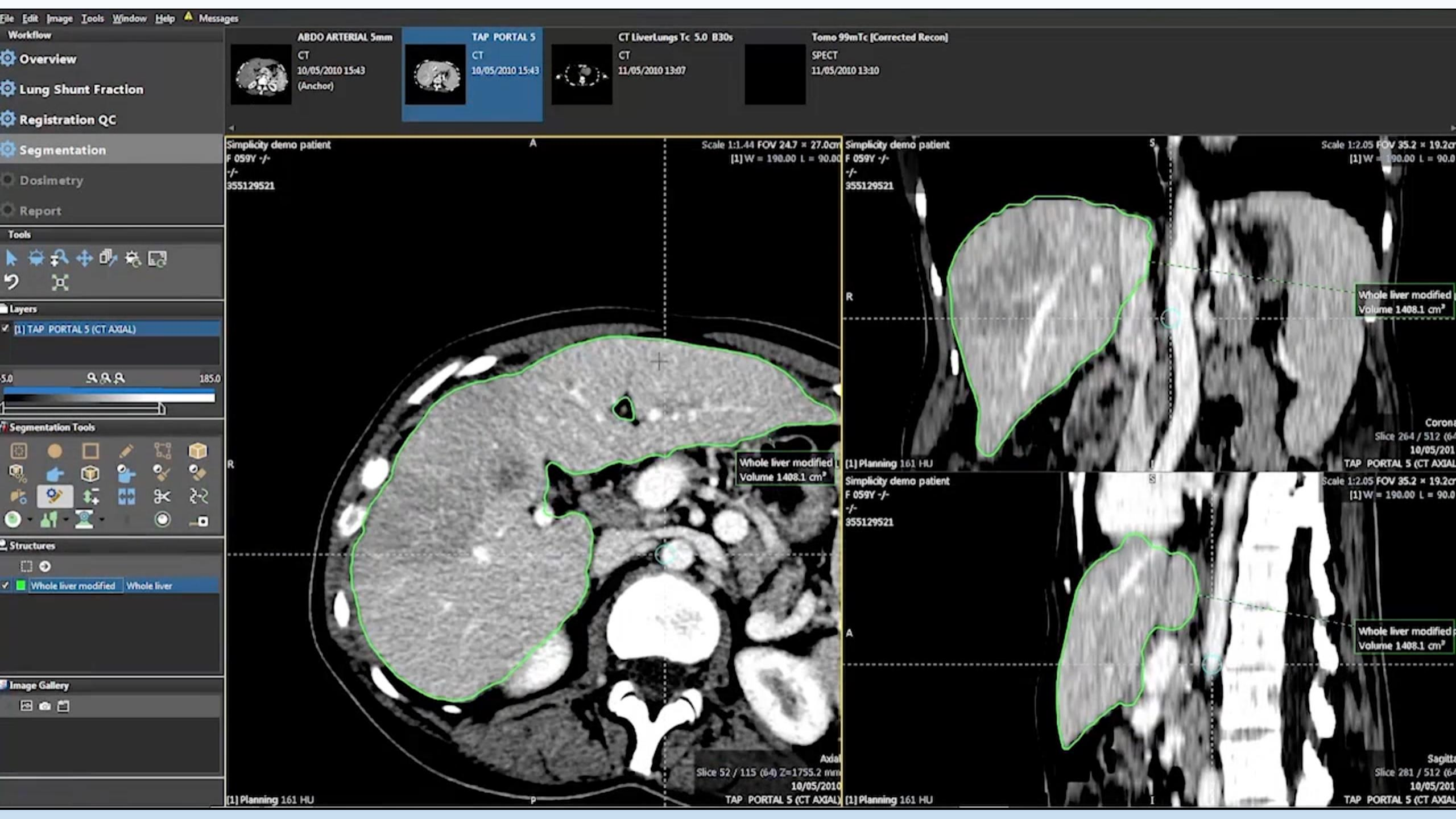



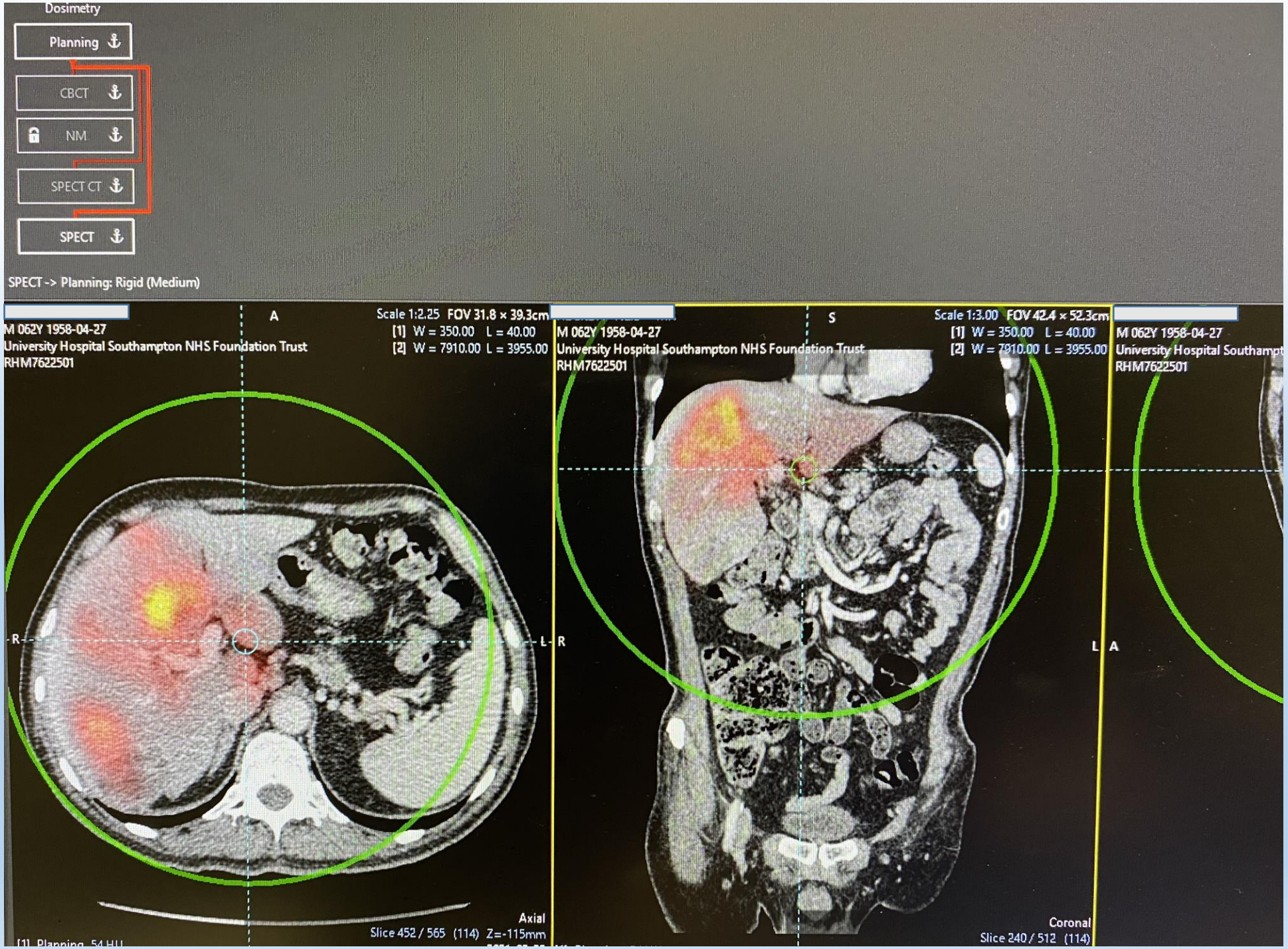

A
B

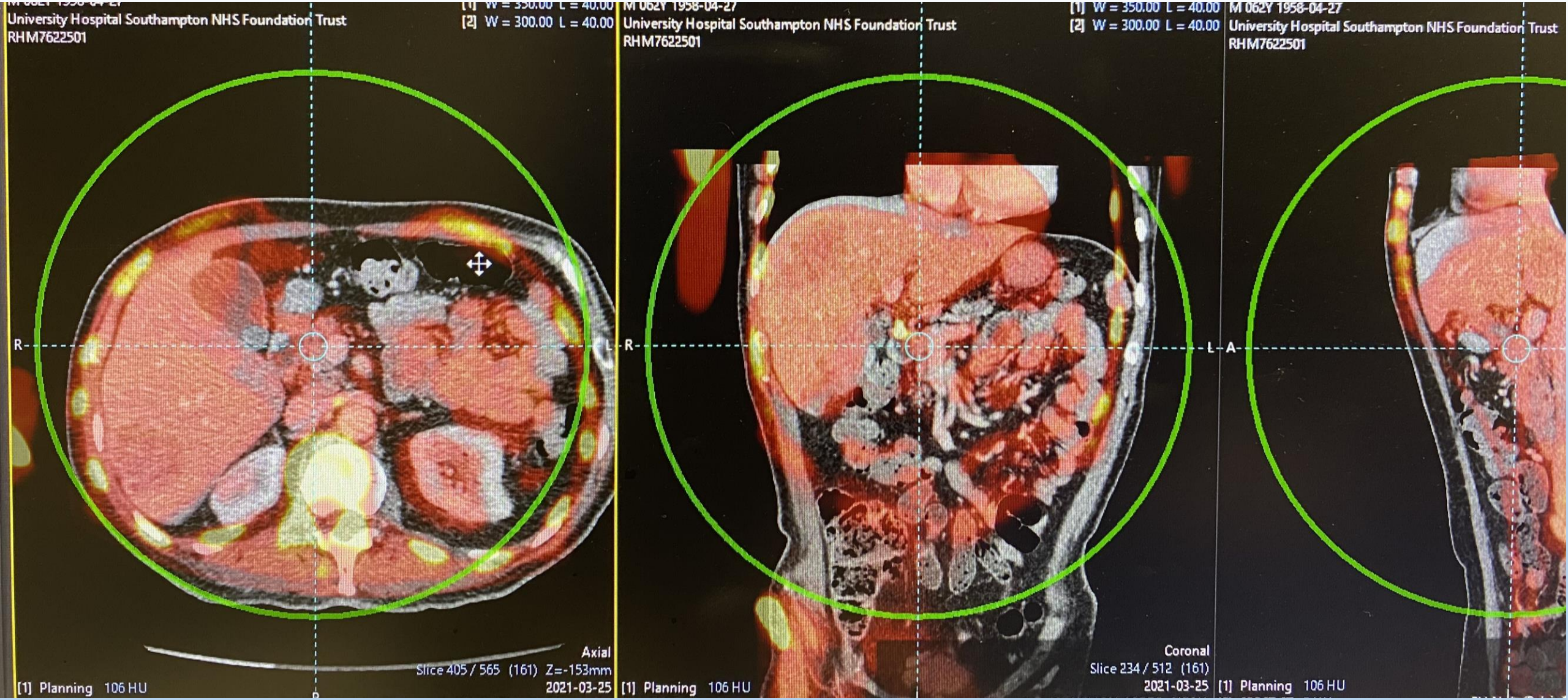
# Dosimetry

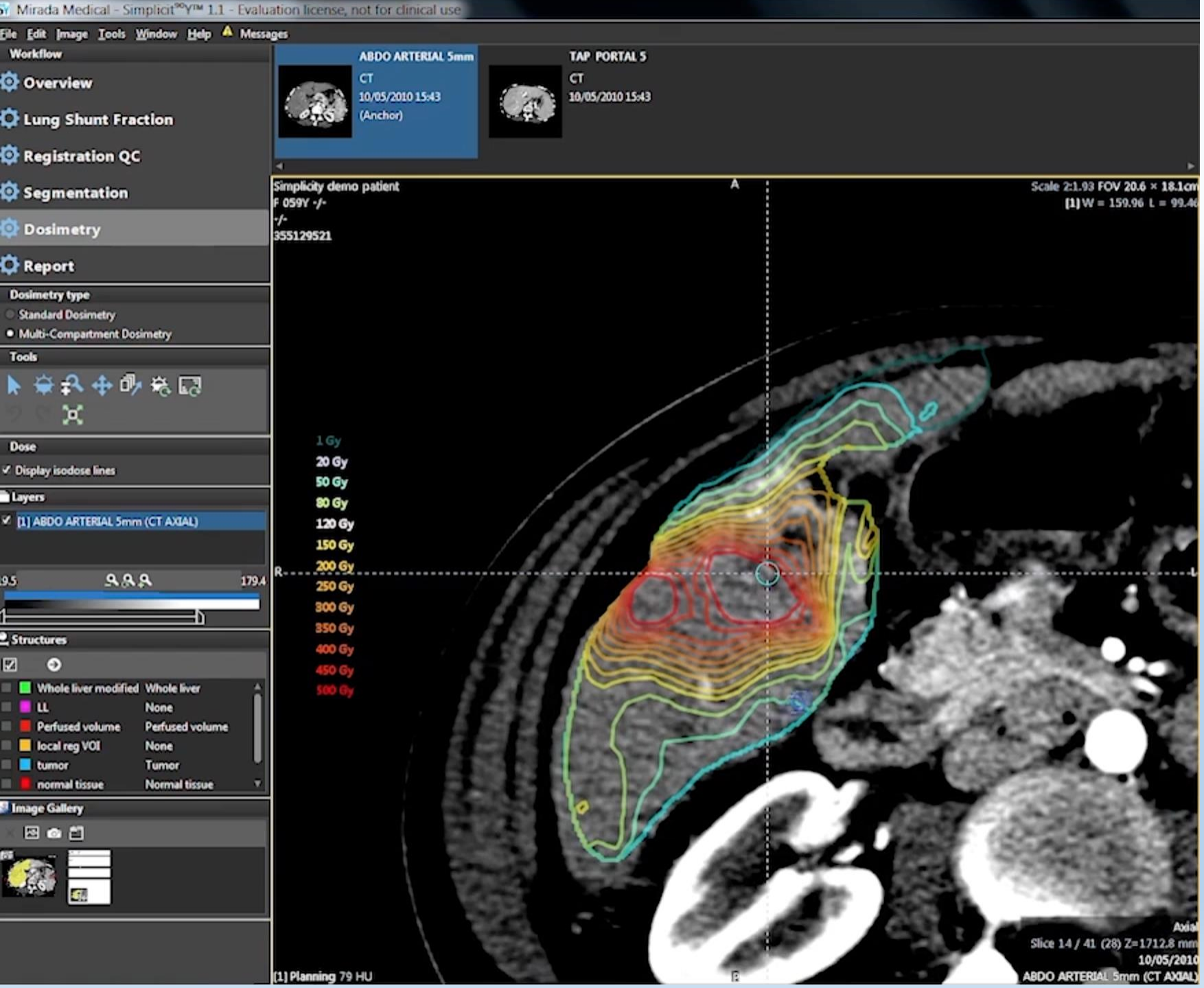
# Dosimetry

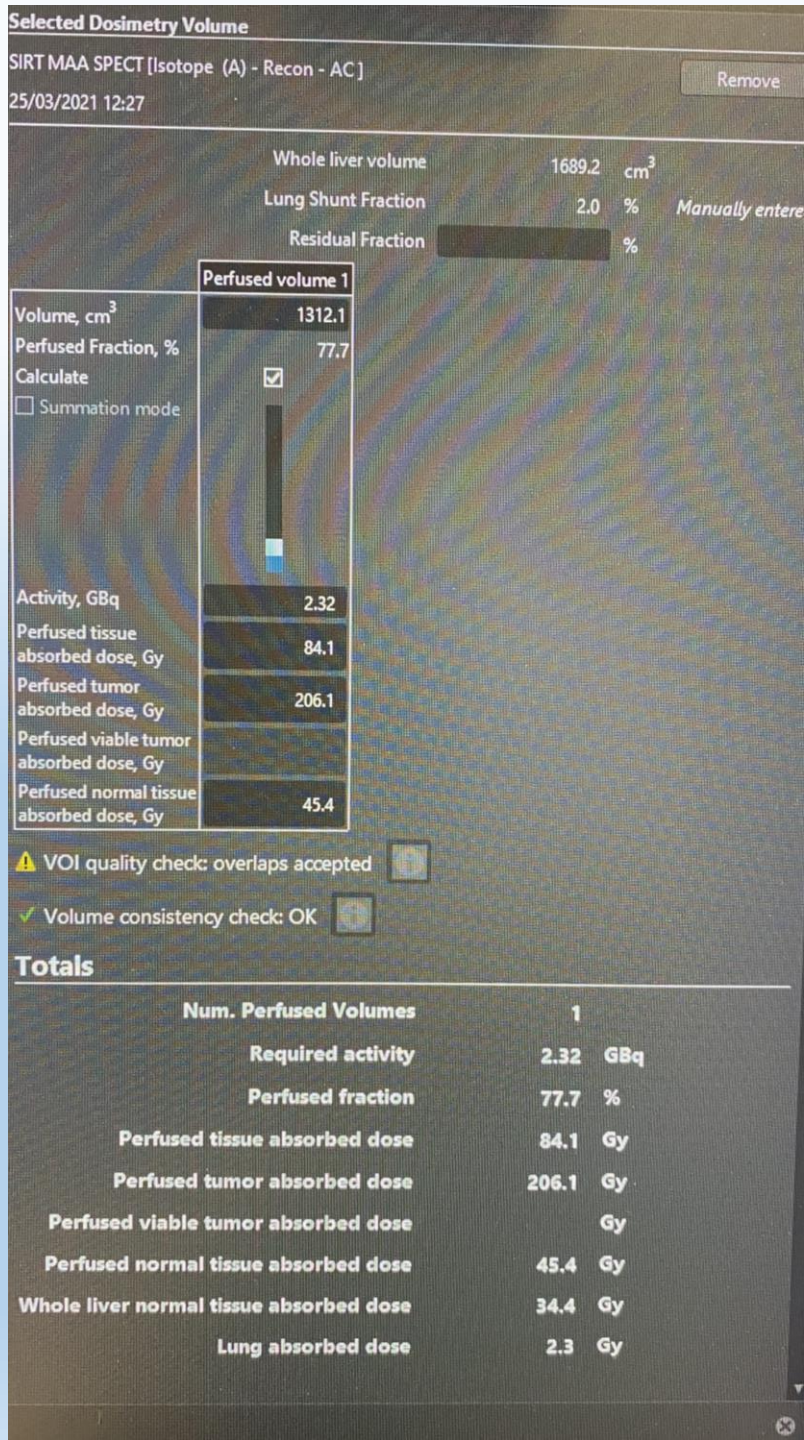
- >120Gy
- Calculate perfused liver volume
- Simplicity Mirada


File Edit Image Tools Window Help Messages
Workflow
Overview
Lung Shunt Fraction
Registration QC
Segmentation
Dosimetry
Report
Tools
Layers
[1] TAP PORTAL 5 (CT AXIAL)
Segmentation Tools
Structures
Whole liver modified
Whole liver
Image Gallery
ABDO ARTERIAL 5mm
CT
10/05/2010 15:43
(Anchor)
TAP PORTAL 5
CT
10/05/2010 15:43
CT LiverLungs Tc 5.0 B30s
CT
11/05/2010 13:07
Tomo 99mTc [Corrected Recon]
SPECT
11/05/2010 13:10
Simplicity demo patient
F 059Y -/-
-/-
355129521
Whole liver modified
Volume 1408.1 cm³
[1] Planning 161 HU
TAP PORTAL 5 (CT AXIAL)


Dosimetry
Planning
CBCT
NM
SPECT CT
SPECT
SPECT -> Planning: Rigid (Medium)
A
Scale 1:2.25 FOV 31.8 x 39.3cm
[1] W = 350.00 L = 40.00
[2] W = 7910.00 L = 3955.00
M 062Y 1958-04-27
University Hospital Southampton NHS Foundation Trust
RHM7622501
R
L
Axial
Slice 452 / 565 (114) Z=-115mm
S
Scale 1:3.00 FOV 42.4 x 52.3cm
[1] W = 350.00 L = 40.00
[2] W = 7910.00 L = 3955.00
M 062Y 1958-04-27
University Hospital Southampton NHS Foundation Trust
RHM7622501
R
L
Coronal
Slice 240 / 512 (114)
M 062Y 1958-04-27
University Hospital Southampt
RHM7622501
L
A


University Hospital Southampton NHS Foundation Trust
RHM7622501
[2] W = 300.00 L = 40.00
R
L
Axial
Slice 405 / 565 (161) Z=-153mm
2021-03-25
[1] Planning 106 HU
M 062Y 1958-04-27
University Hospital Southampton NHS Foundation Trust
RHM7622501
[1] W = 350.00 L = 40.00
[2] W = 300.00 L = 40.00
R
L
Coronal
Slice 234 / 512 (161)
2021-03-25
[1] Planning 106 HU
M 062Y 1958-04-27
University Hospital Southampton NHS Foundation Trust
RHM7622501
A
[1] Planning 106 HU

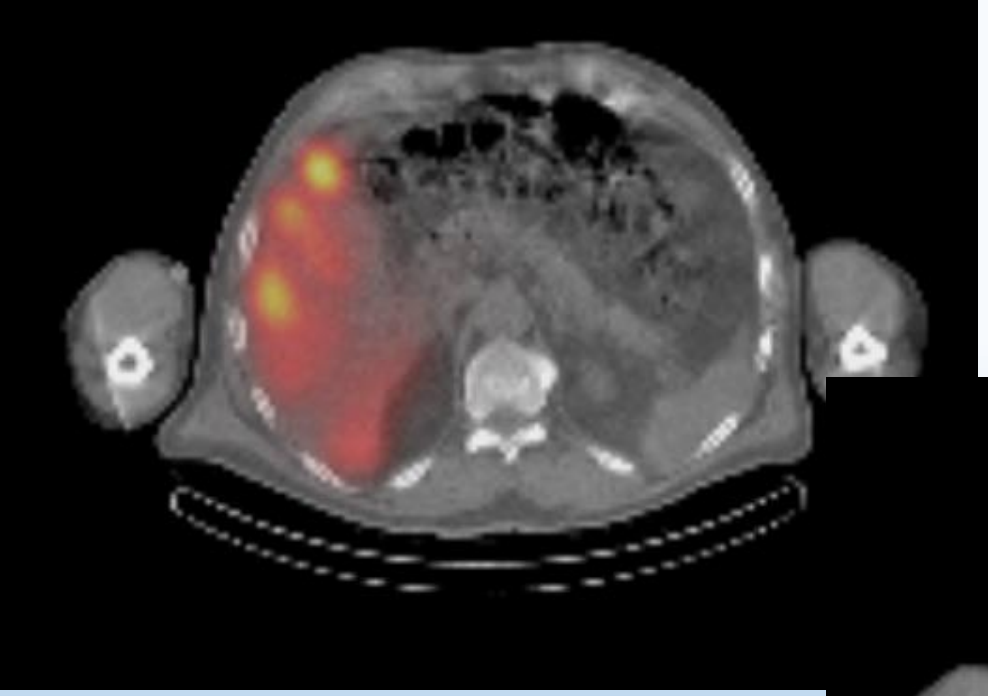

Mirada Medical - Simplicit90Y™ 1.1 - Evaluation license, not for clinical use
File Edit Image Tools Window Help Messages
Workflow
Overview
Lung Shunt Fraction
Registration QC
Segmentation
Dosimetry
Report
Dosimetry type
Standard Dosimetry
Multi-Compartment Dosimetry
Tools
Dose
Display isodose lines
Layers
[1] ABDO ARTERIAL 5mm (CT AXIAL)
Structures
Whole liver modified Whole liver
LL None
Perfused volume Perfused volume
local reg VOI None
tumor Tumor
normal tissue Normal tissue
Image Gallery
ABDO ARTERIAL 5mm
CT
10/05/2010 15:43
(Anchor)
TAP PORTAL 5
CT
10/05/2010 15:43
Simplicity demo patient
F 059Y -/-
-/-
355129521
1 Gy
20 Gy
50 Gy
80 Gy
120 Gy
150 Gy
200 Gy
250 Gy
300 Gy
350 Gy
400 Gy
450 Gy
500 Gy
[1] Planning 79 HU

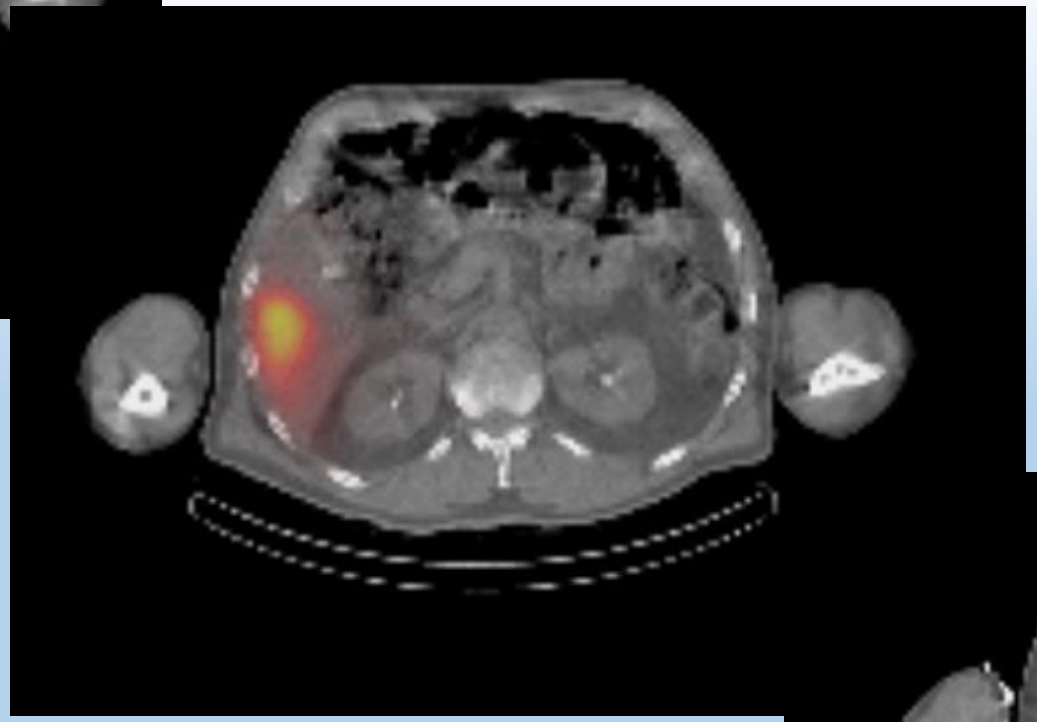

Selected Dosimetry Volume
SIRT MAA SPECT [Isotope (A) - Recon - AC]
25/03/2021 12:27
Remove
Whole liver volume 1689.2 cm3
Lung Shunt Fraction 2.0 %
Residual Fraction %
Manually entere
Perfused volume 1
Volume, cm3 1312.1
Perfused Fraction, % 77.7
Calculate
Summation mode
Activity, GBq 2.32
Perfused tissue absorbed dose, Gy 84.1
Perfused tumor absorbed dose, Gy 206.1
Perfused viable tumor absorbed dose, Gy
Perfused normal tissue absorbed dose, Gy 45.4
VOI quality check: overlaps accepted
Volume consistency check: OK
Totals
Num. Perfused Volumes 1
Required activity 2.32 GBq
Perfused fraction 77.7 %
Perfused tissue absorbed dose 84.1 Gy
Perfused tumor absorbed dose 206.1 Gy
Perfused viable tumor absorbed dose Gy
Perfused normal tissue absorbed dose 45.4 Gy
Whole liver normal tissue absorbed dose 34.4 Gy
Lung absorbed dose 2.3 Gy

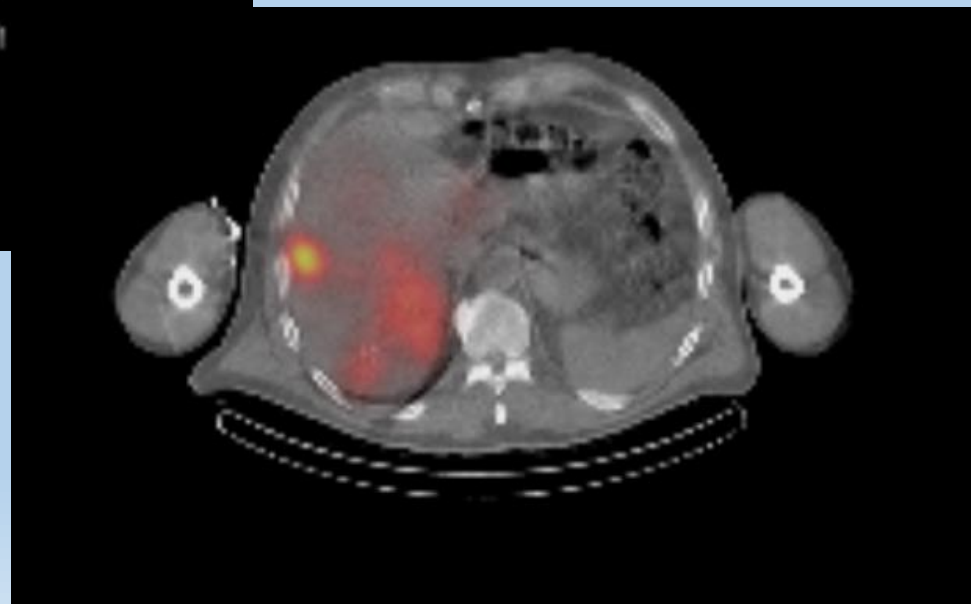
# Radioembolisation

Treatment usually 1-3 weeks after.

- Overnight stay
- Isolation for 24 hours
- Bremsstrahlung SPECT/CT is performed to confirm tumour coverage and evaluate for extrahepatic perfusion
- Angioseal







# Radioembolisation – Complications

- Postembolisation syndrome normal (nausea, pain, fatigue and loss of appetite). 1-2 weeks
- Non target embolization (ulcers and pancreatitis <2%)
- Cholecystitis rare.
- Infection/abscess.
- Radiation hepatitis (elevated bili/alk phos/ascites 4%).

# Radioembolisation – Follow up

- A CT or MRI evaluation of the response after radioembolization can take 2–3 months.
- Tumor necrosis and oedema can result in increased tumor size at 1 month, even when the tumour is responding to treatment.
- CT/MRI at 2-3months.

# Radioembolisation

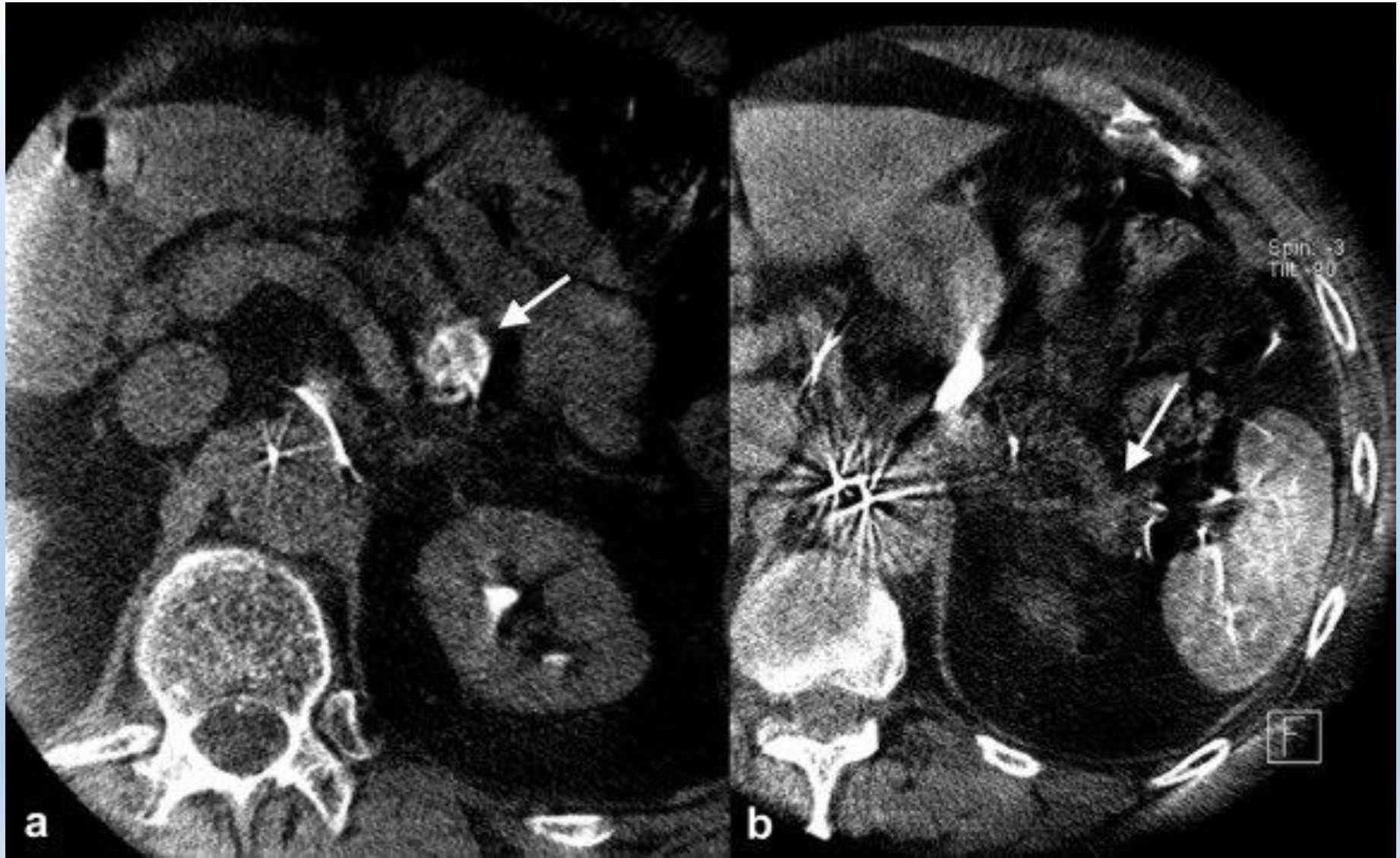
42 Symptomatic patients unresectable NETLM's
Mean activity 1.63Gbq
Recist @ 3 months

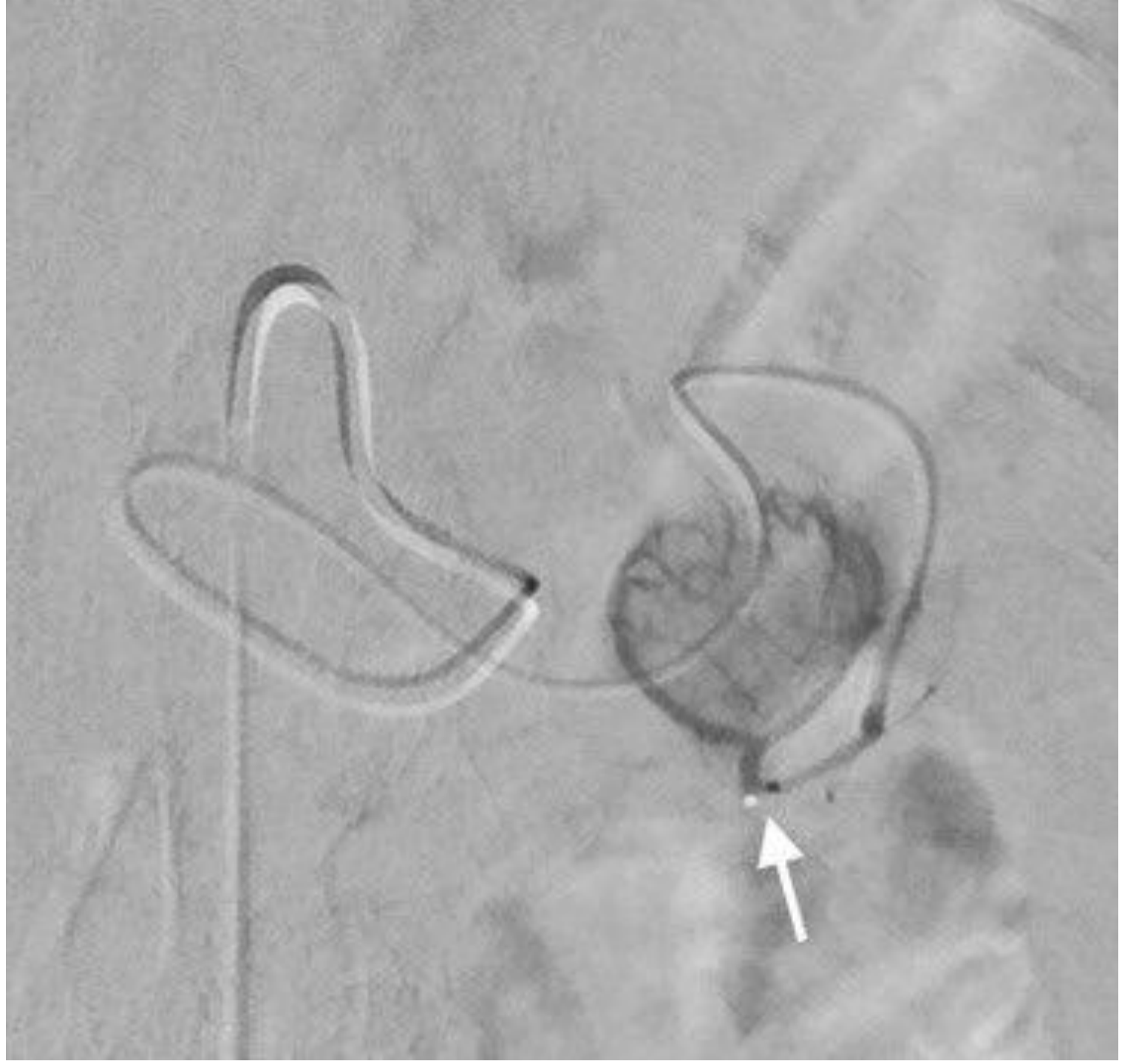
Partial response 22.5%
Stable disease 75%
Progressive disease 2.5%

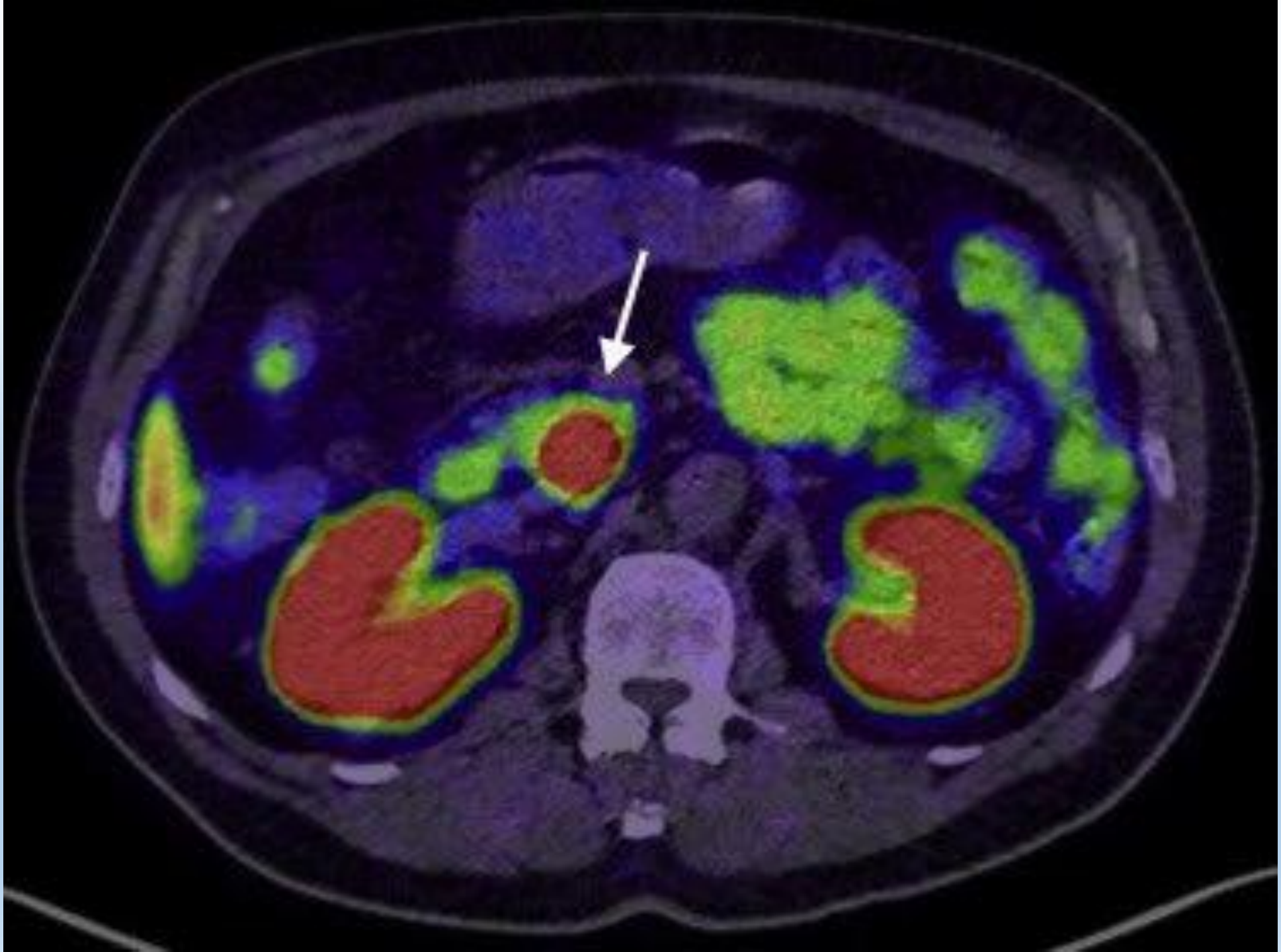
97% patients tumours appeared hypovascular at 3 months
No toxicity > grade 2
Improve symptoms in 36 of 38 patients

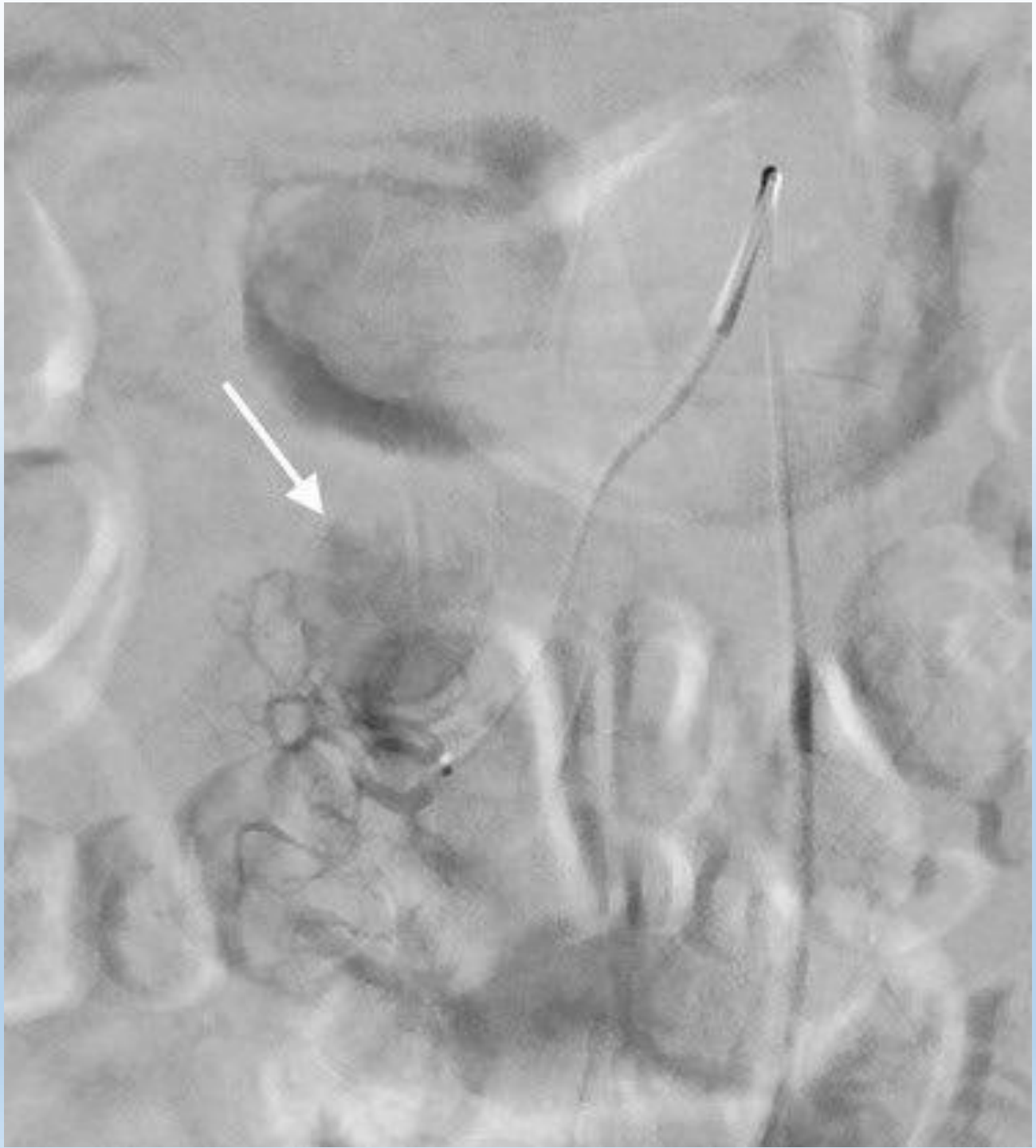
Jakobs, CVIR Epub 2011ç

# Other arterial therapies…





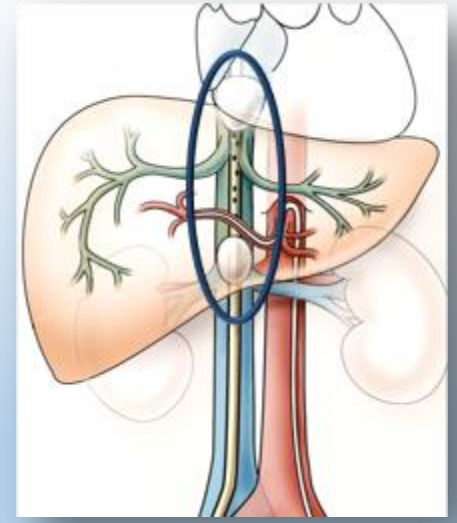




# CHEMOSATURATION Therapy (CS-PHP)

## 3 Procedural Steps

### Isolation



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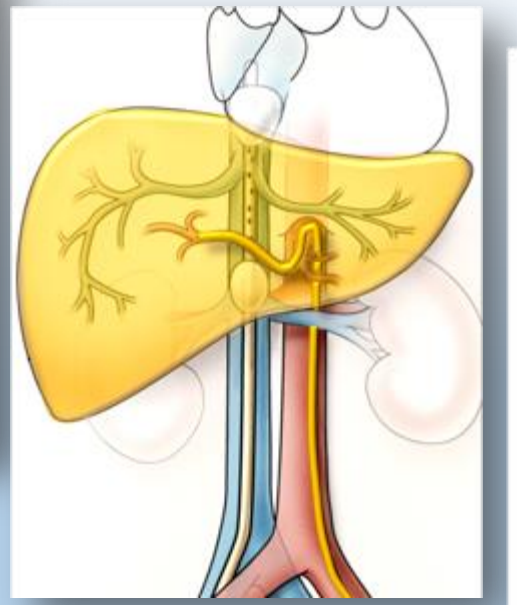

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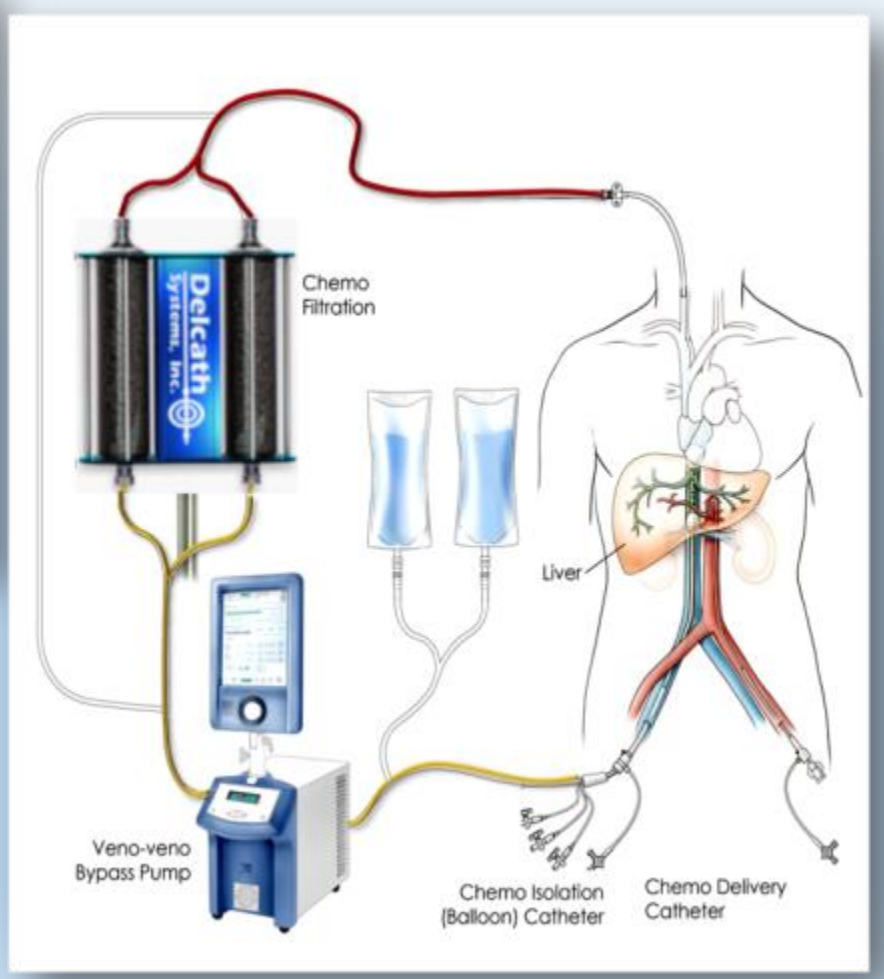

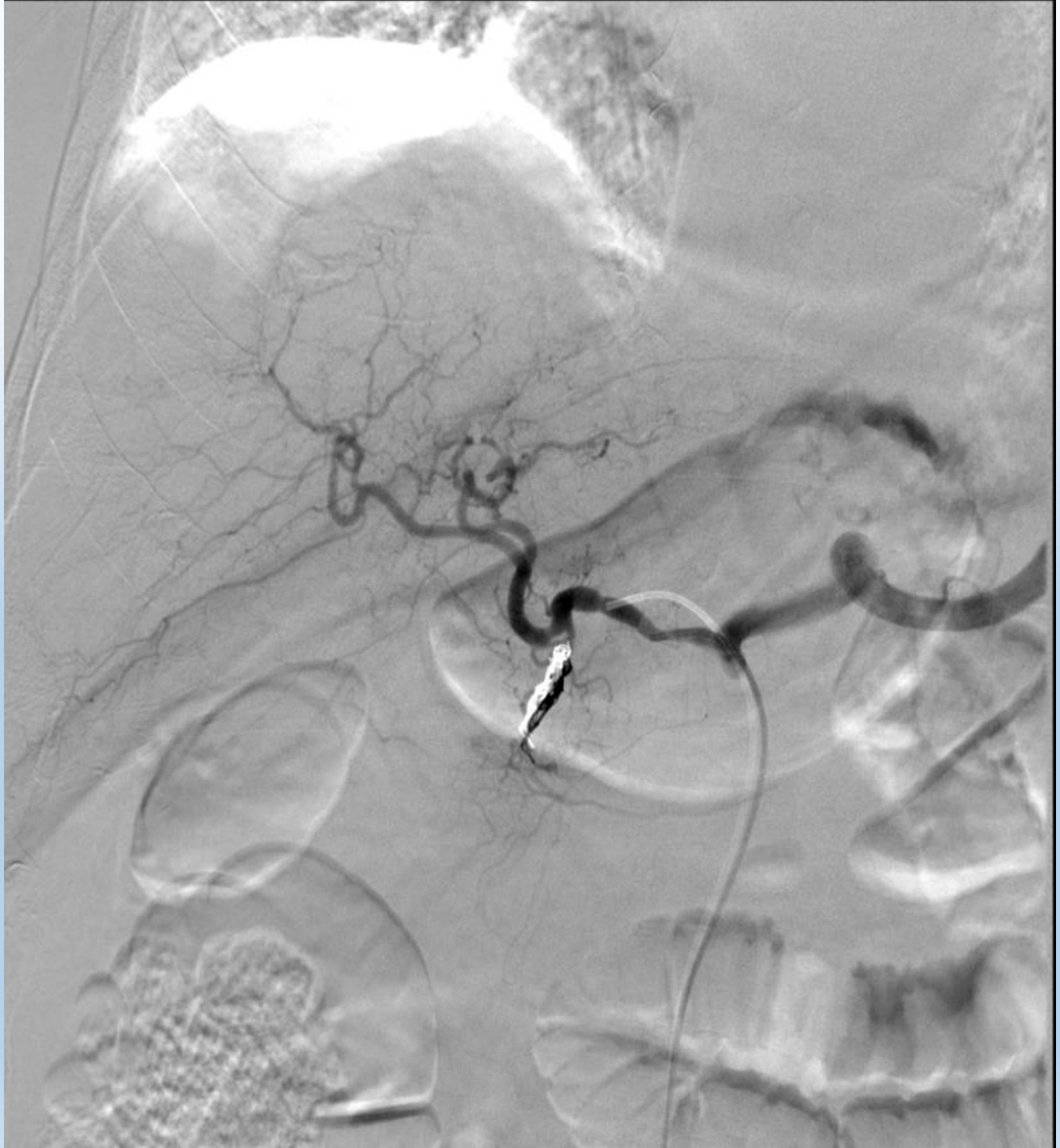

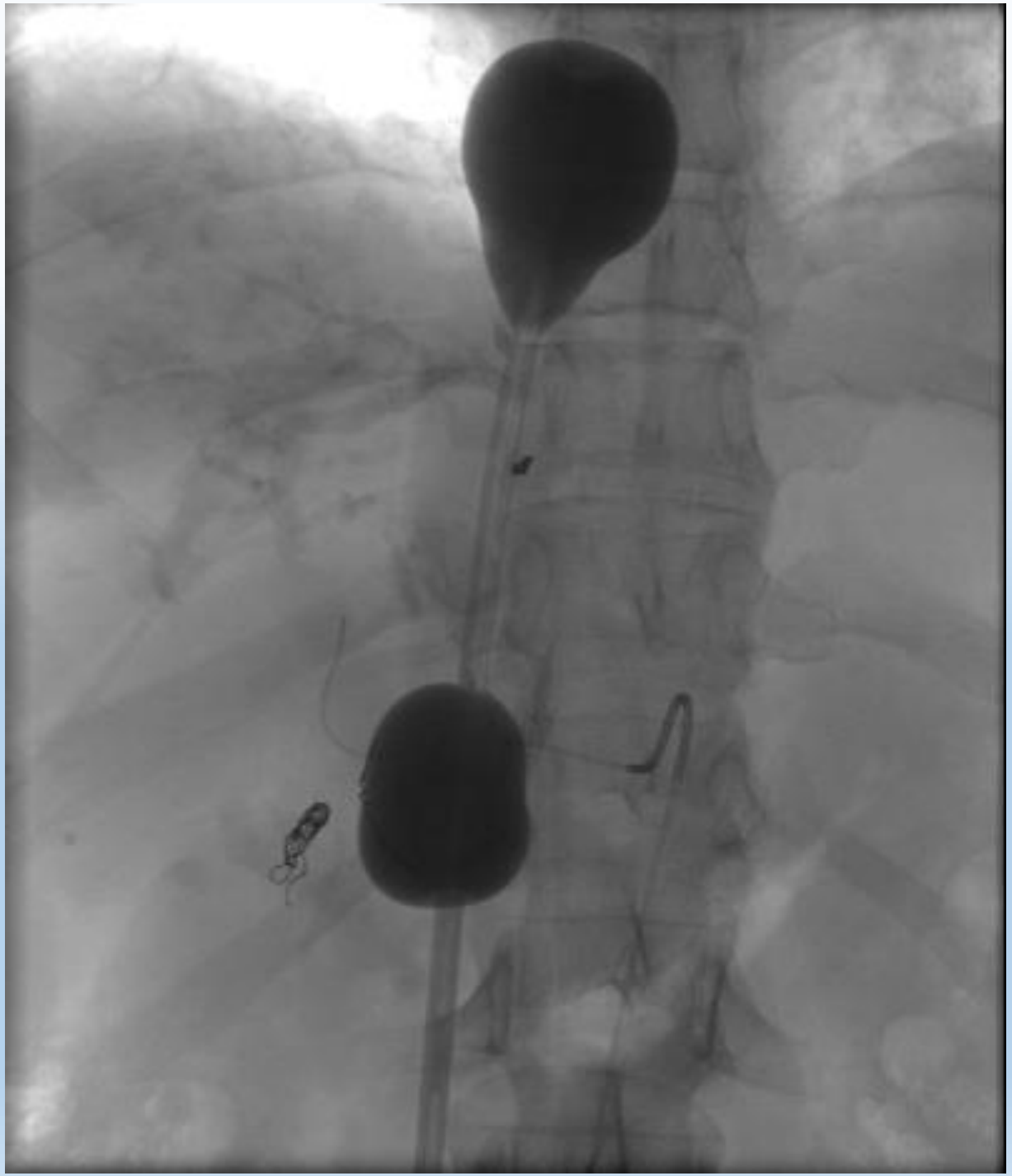

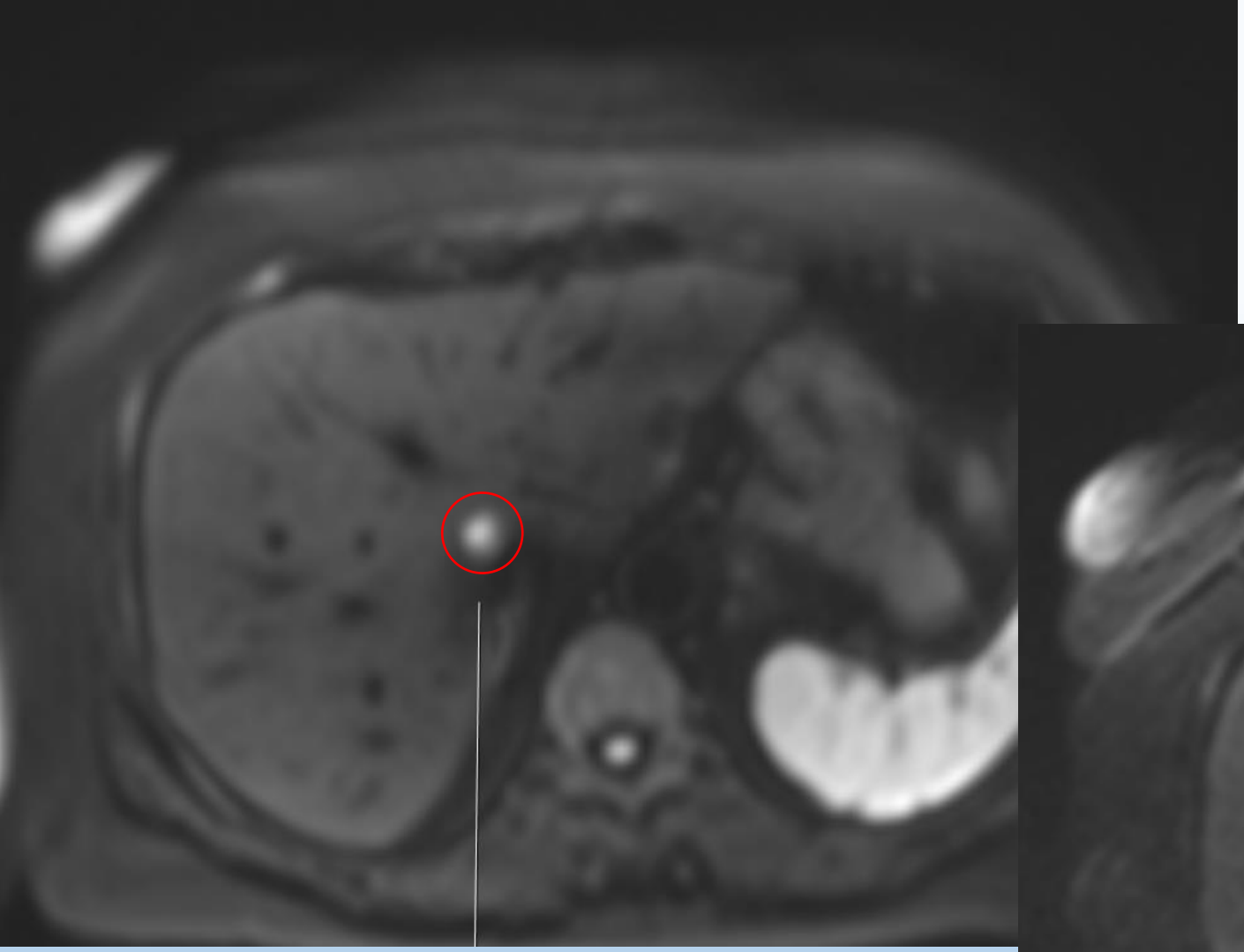

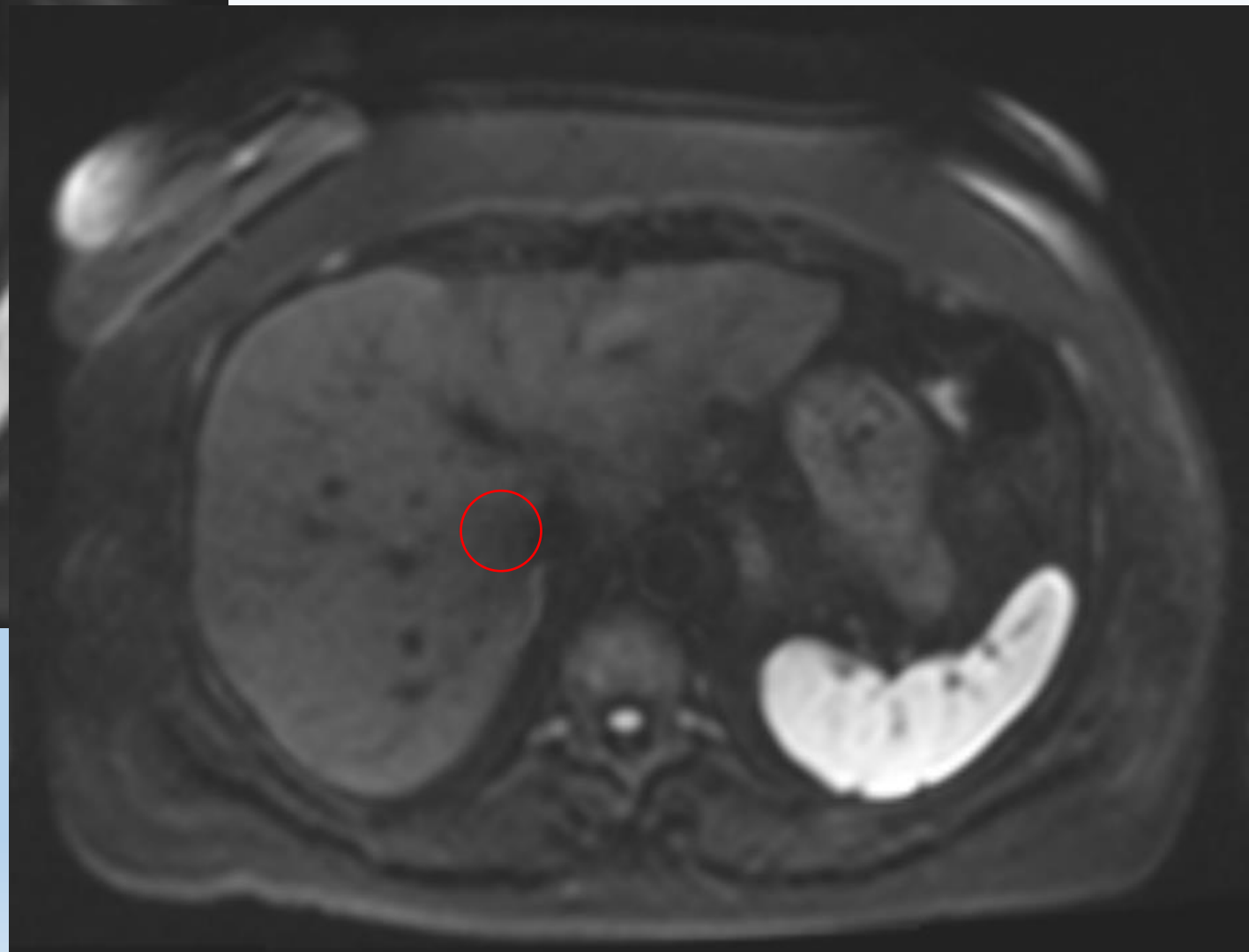

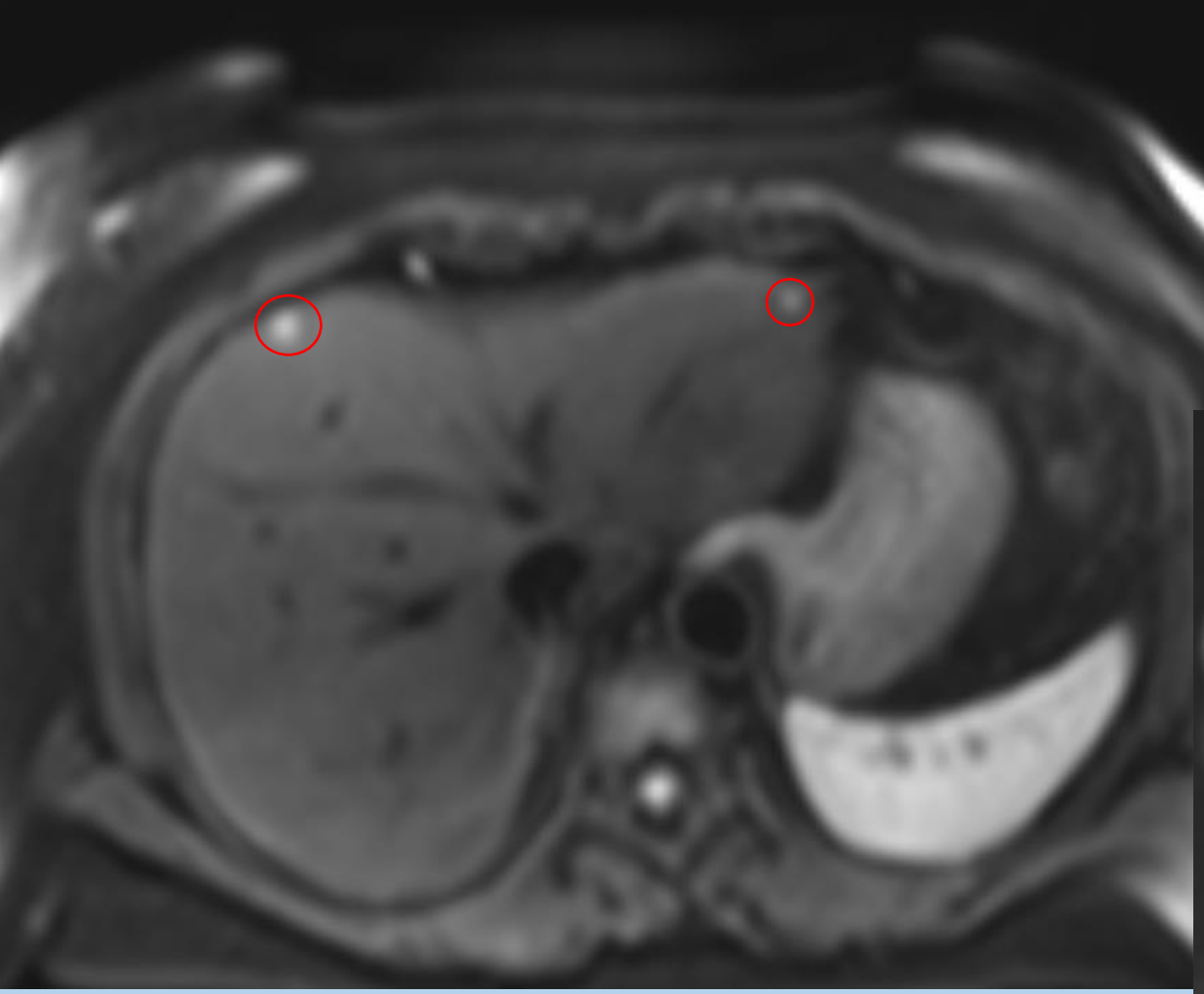

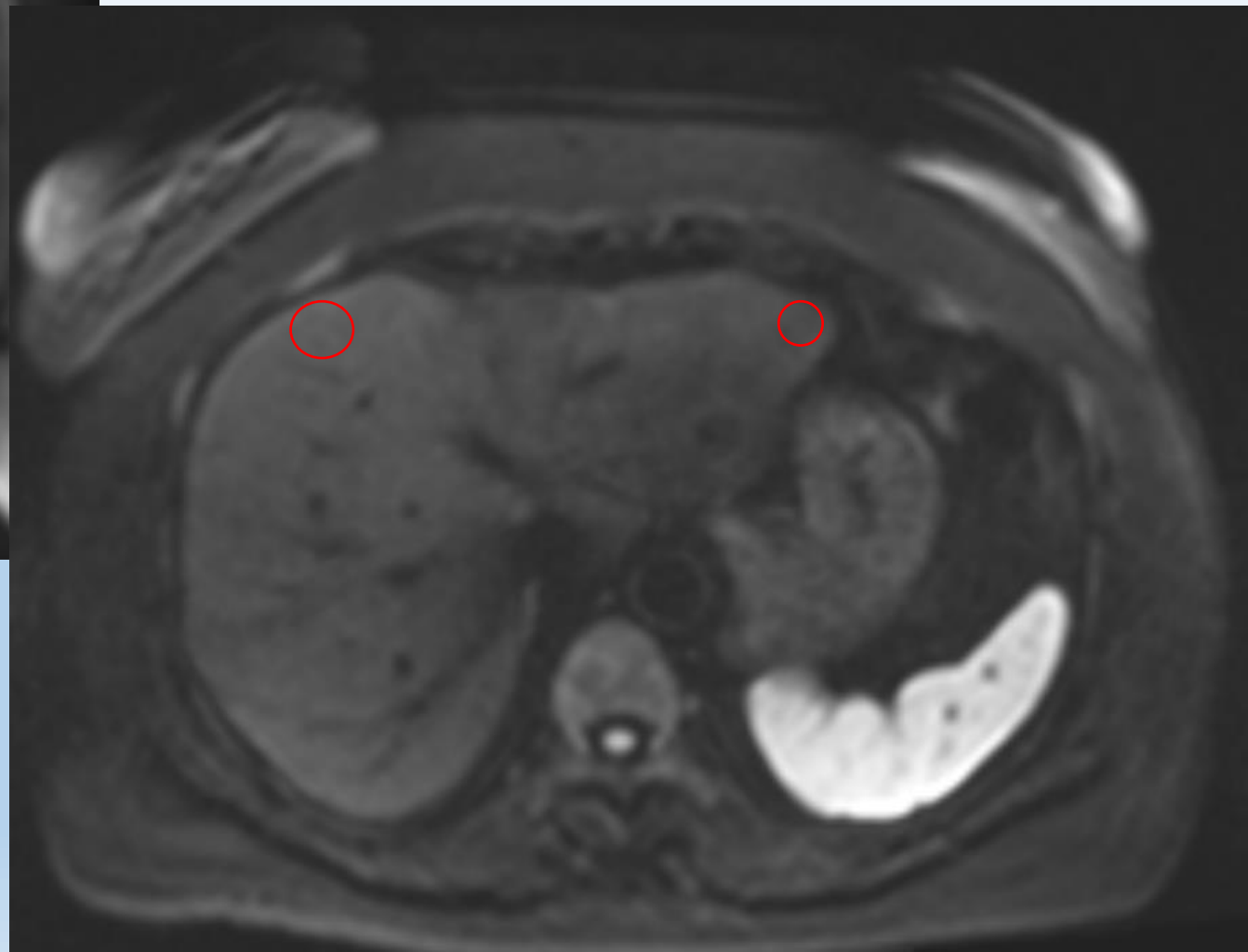

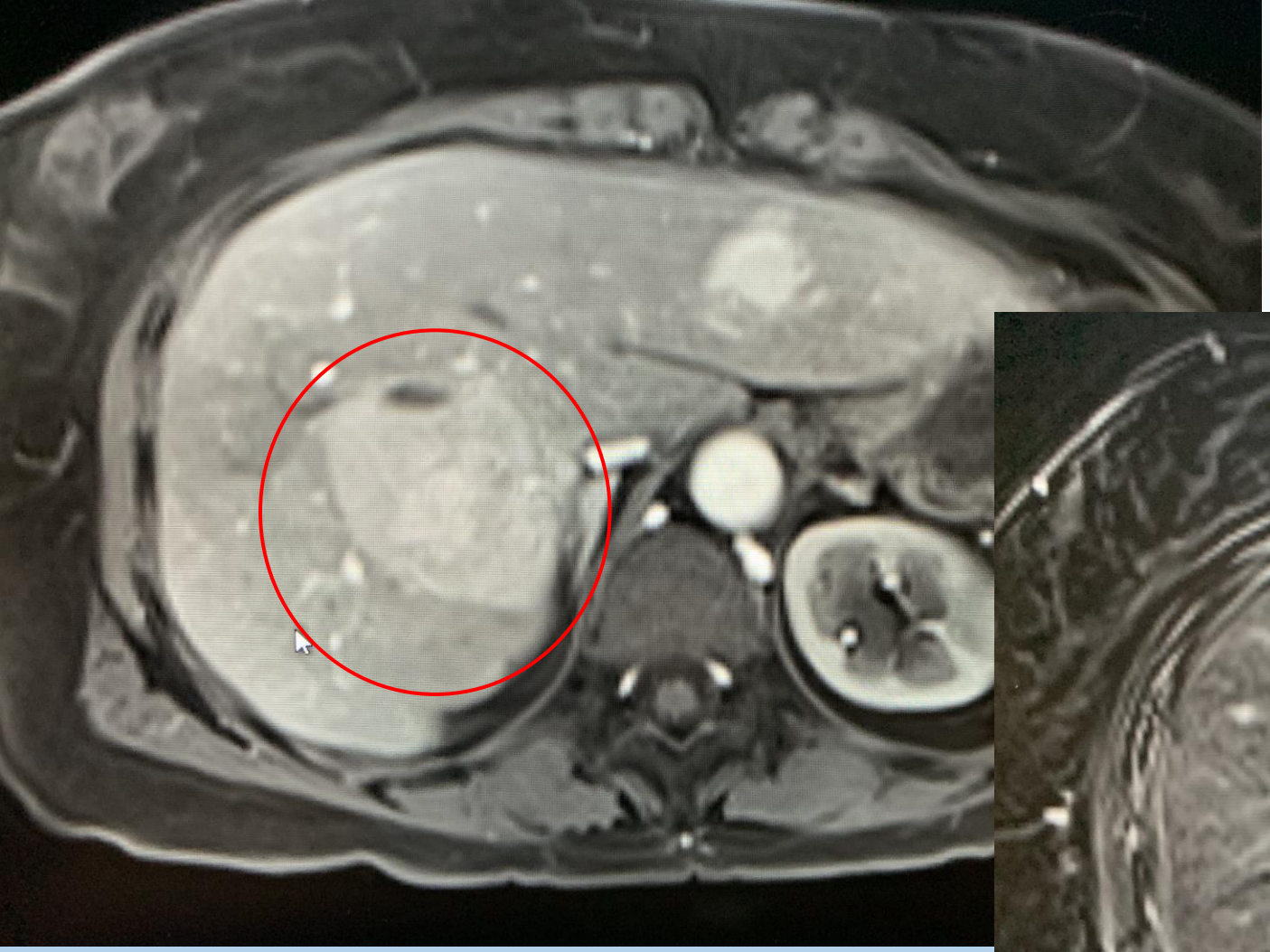

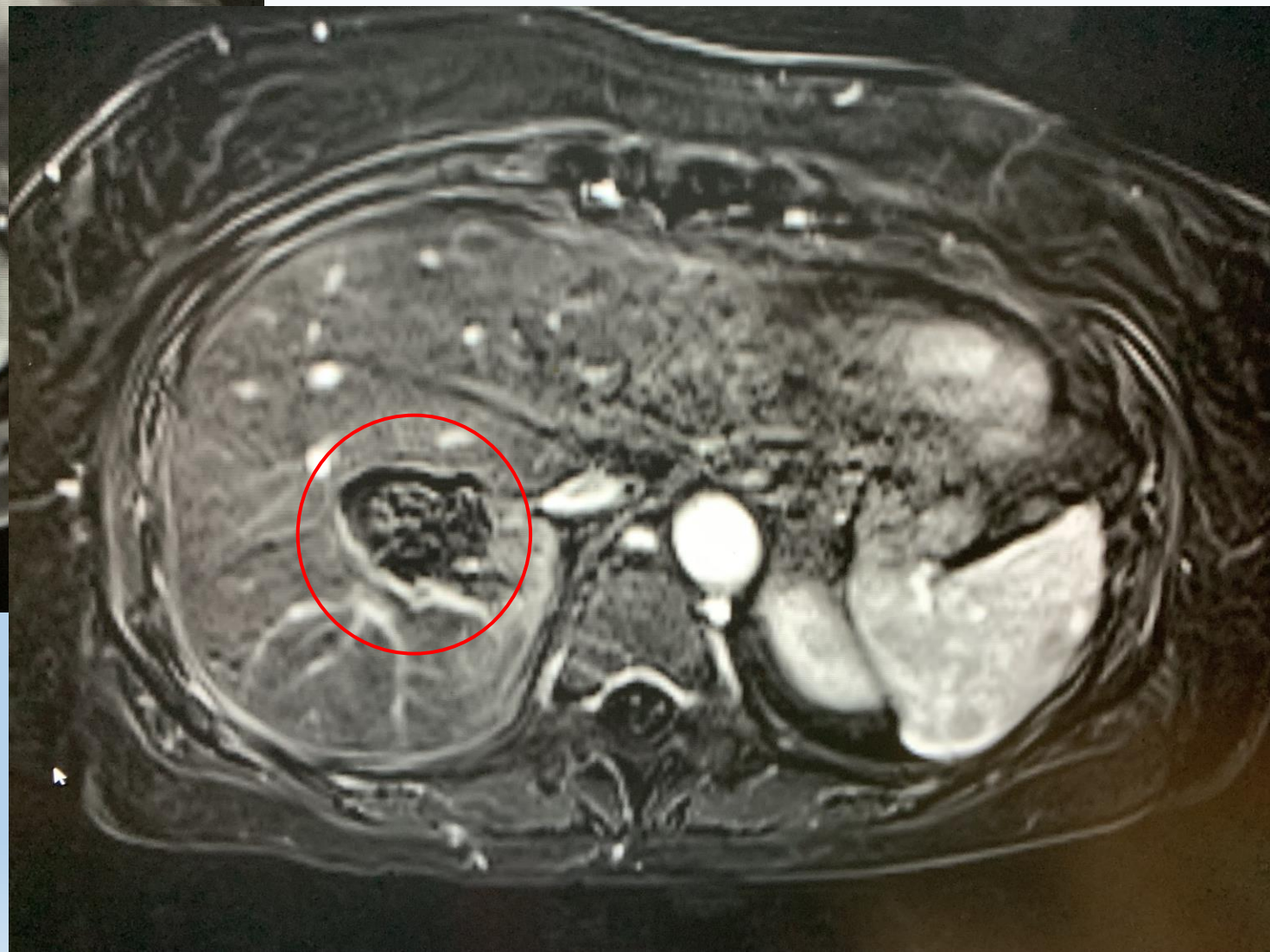


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# Thank you &
# Questions ??