Ablative Radiation Therapy For Inoperable Cholangiocarcinoma

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THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Facts about radiation treatment

- High doses (2x the standard) are able to ‘ablate’ solid tumors
  - 15-25 treatments is best to protect surrounding organs if they are close
- Equivalent dose – 100 Gy (new) vs 50 Gy (old)

Facts about Cholangiocarcinoma treatment

- Operable tumors – resection can be curative
  - If not cured, patients live a lot longer
- For inoperable tumors
  - Chemotherapy alone is the standard
  - Gemcitabine and cisplatin
- The role of radiation is not established, but emerging

Challenges in Cholangiocarcinoma

- Proximity of duodenum, stomach colon
- Sparing (often diseased) liver
- Organ motion
  - Respiratory motion
  - Day to day differences

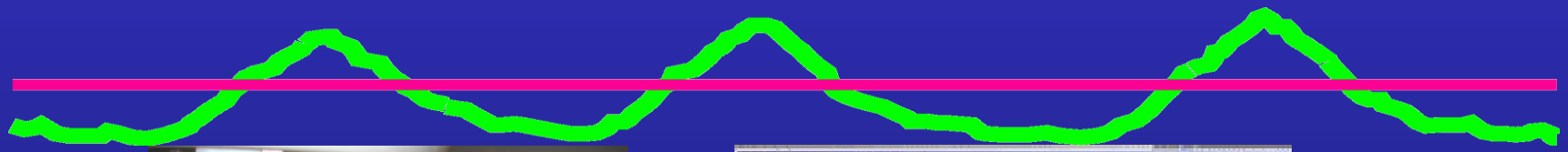
Solutions/Innovations

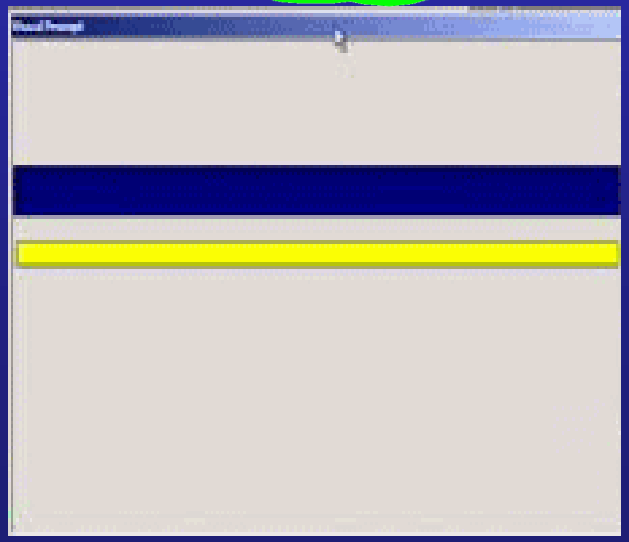
- Gating: Inspiration Breath Hold
  - Varian RPM
  - Feedback-guided Breath Hold
- Image guidance: Diagnostic quality CT
  - CT on rails

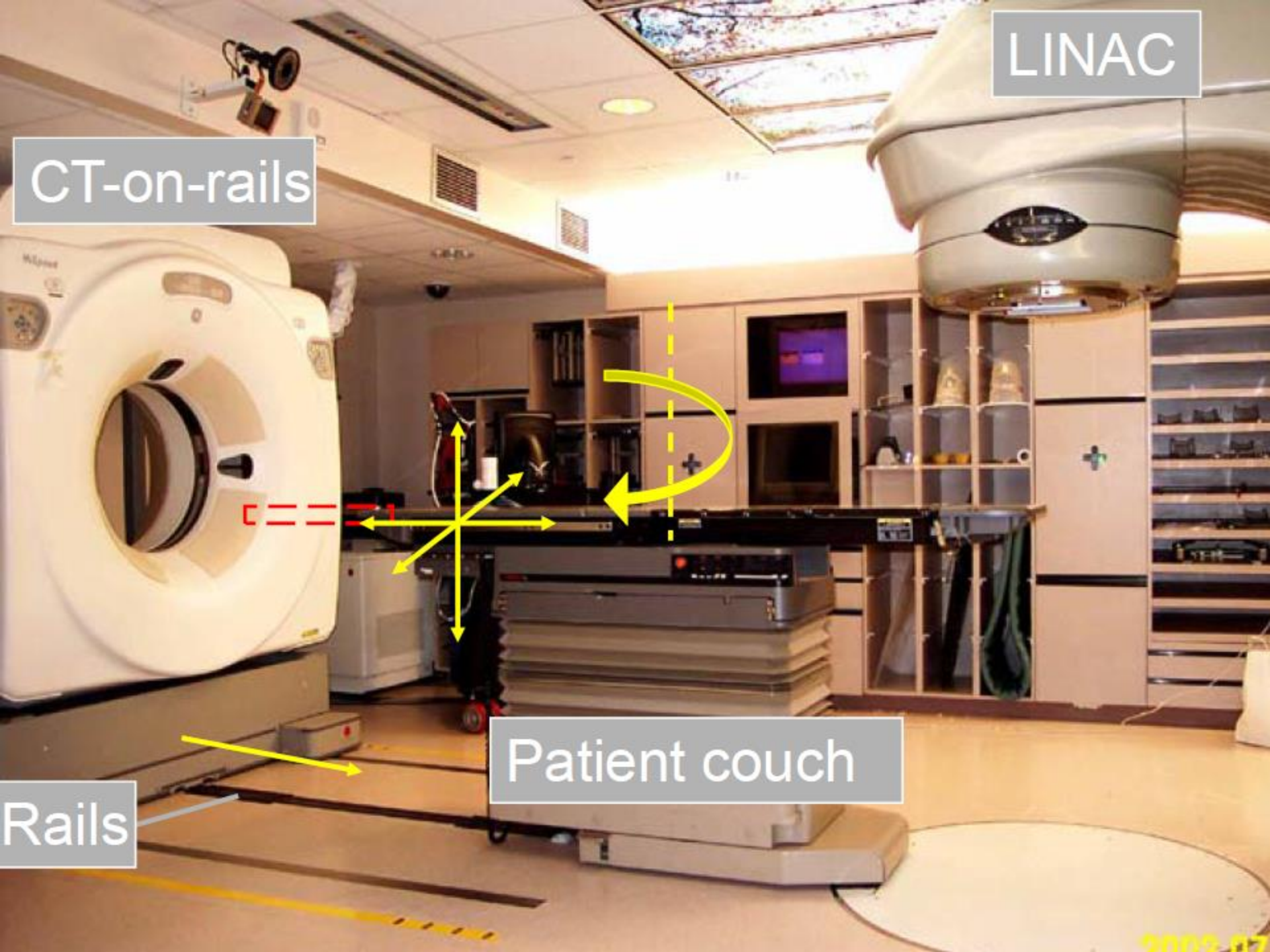
The treatment is complex - very few centers have the ability to do this well for all tumors

Feedback Guided Gated Breath-hold (FGBH)

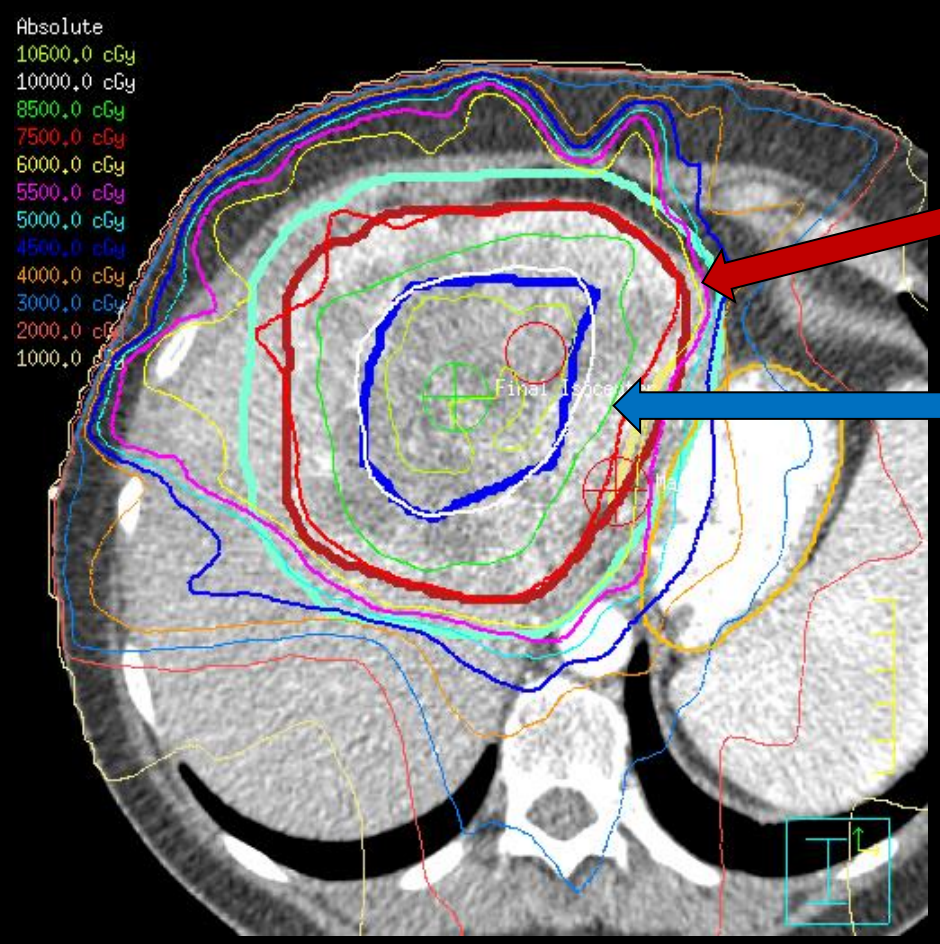
- Patient to voluntarily holds their breath within the gate (visual feedback helps this process)
- Turn the beam on when the patient is holding their breath in the gate.
- CBCT or CT-on-rails can be done during FGBHs

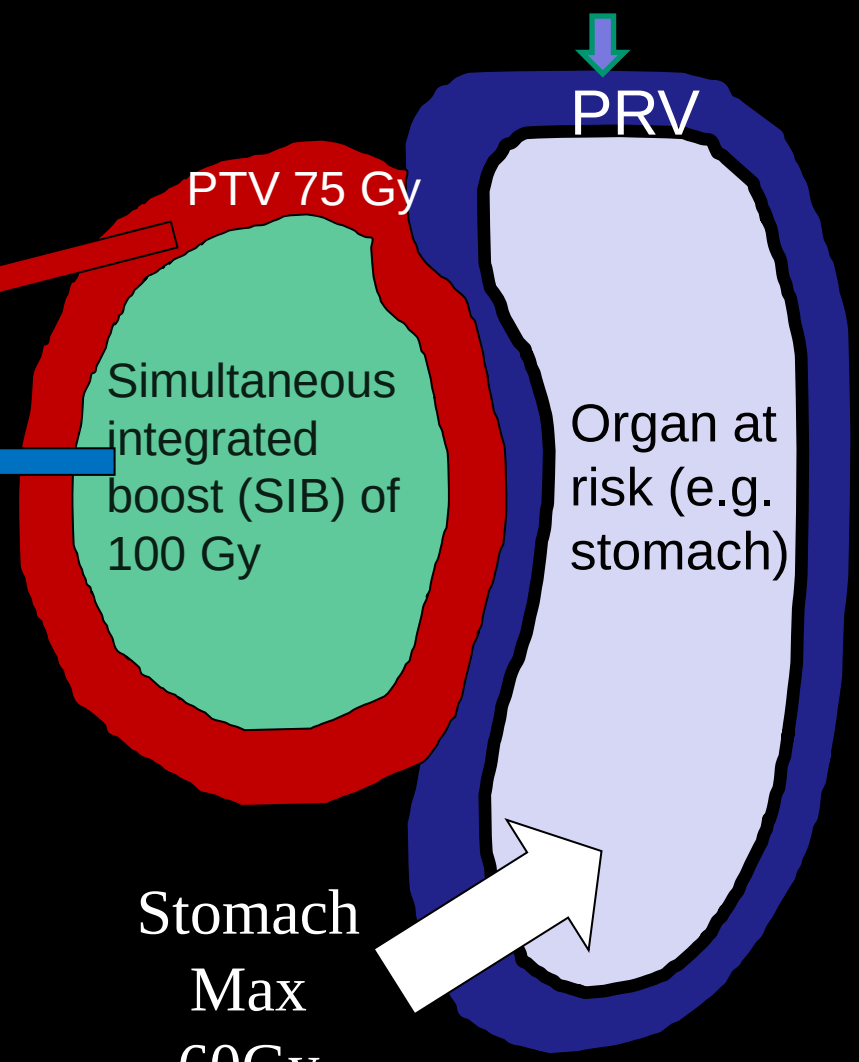





LINAC
CT-on-rails
Patient couch
Rails

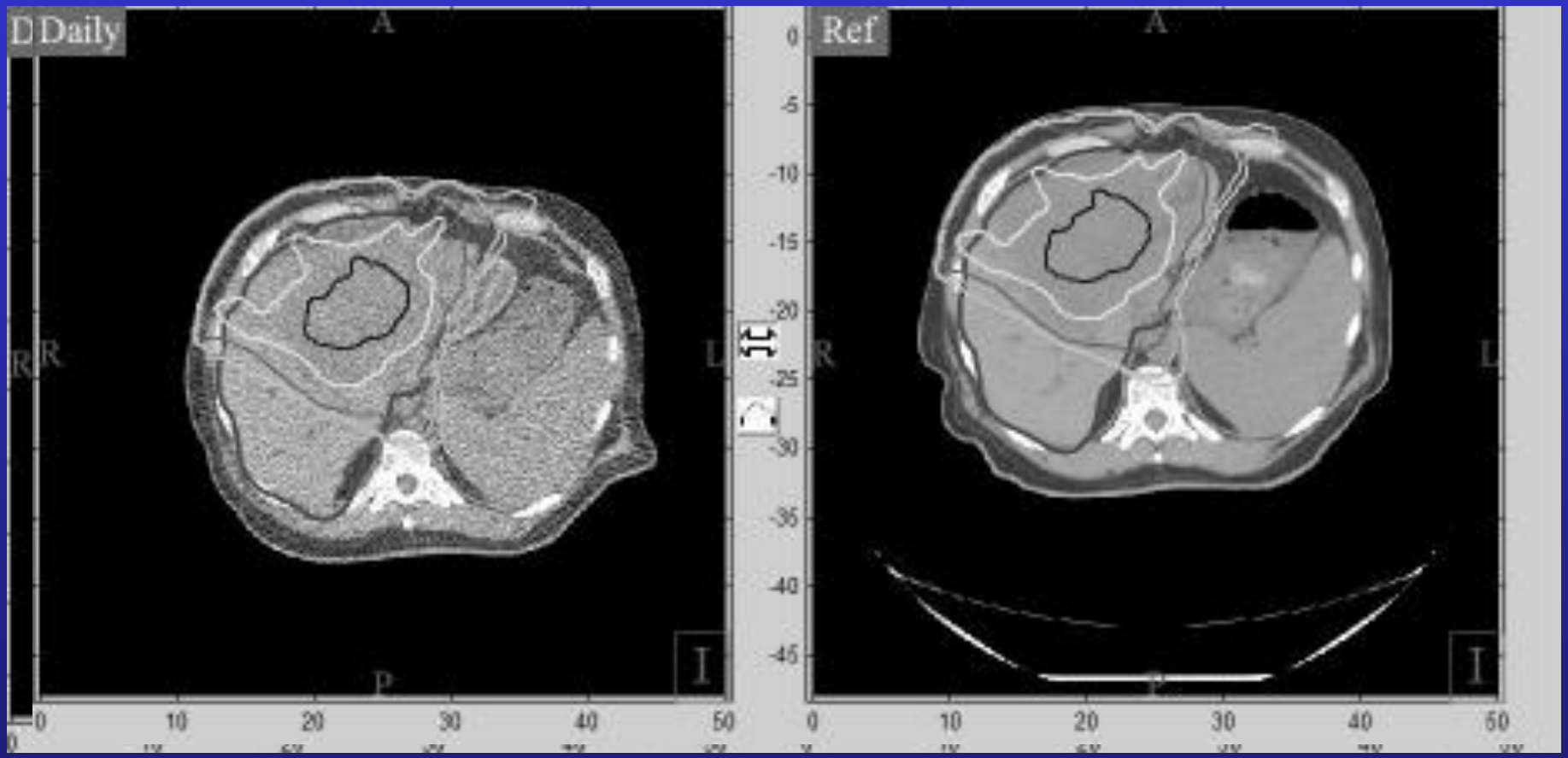
Radiation treatment plan and illustration of the Simultaneous Integrated Boost/Protection (SIB/SIP) technique



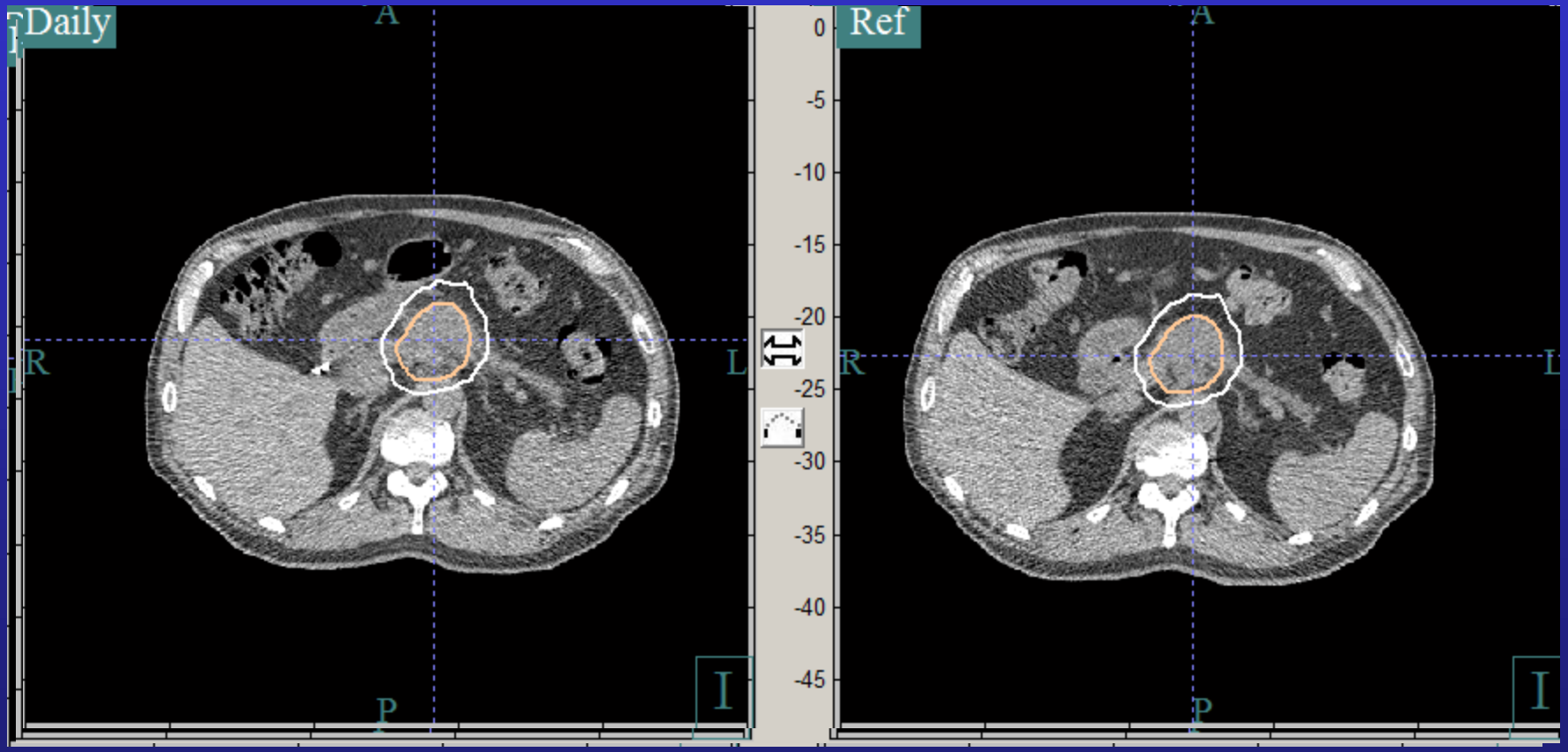


Stomach Max 60Gy

CT on rails vs Sim CT



CT guidance- Monitoring Stomach Position Hfx XRT PancCa

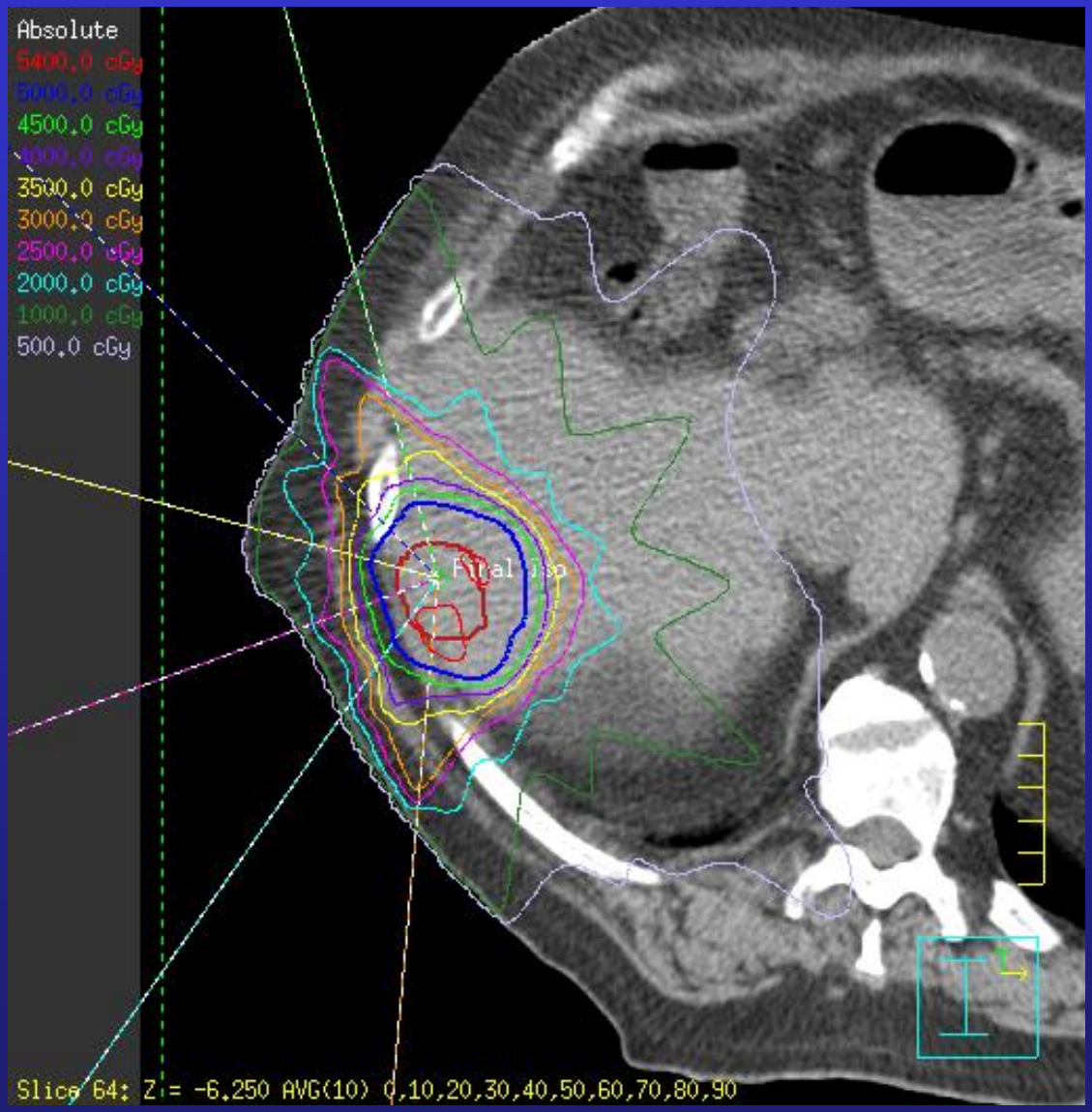


67.5 Gy - 15 fx - 45Gy

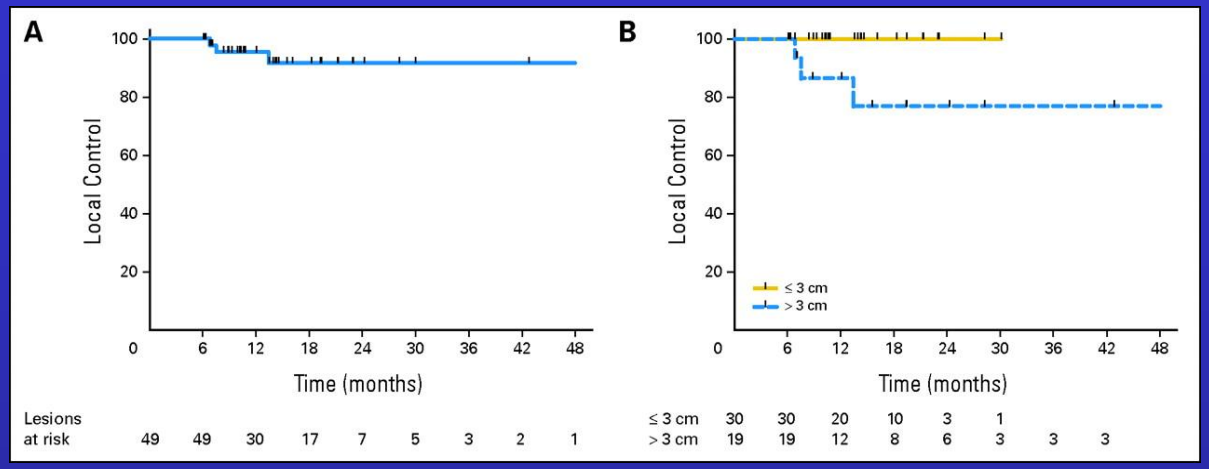
Outline- Ablative Liver XRT

- SBRT for small mets
- Why patients die of liver tumors
- Intrahepatic Cholangiocarcinoma results

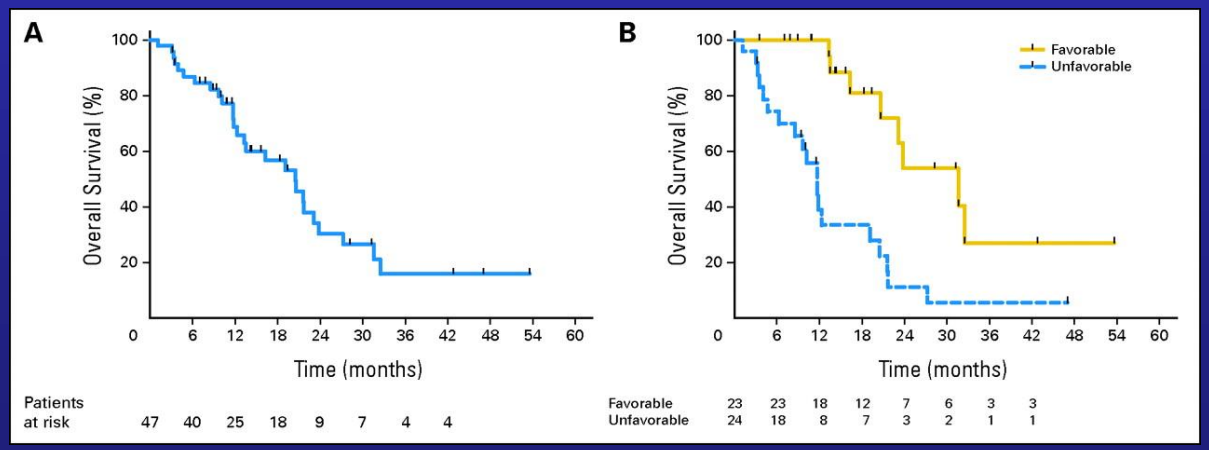
Steriotactic XRT for Liver Metastasis



SBRT for liver mets: OS benefit?



Local control according to maximal tumor diameter.



Overall survival for according to primary site.

Rusthoven K E et al. JCO 2009;27:1572-1578

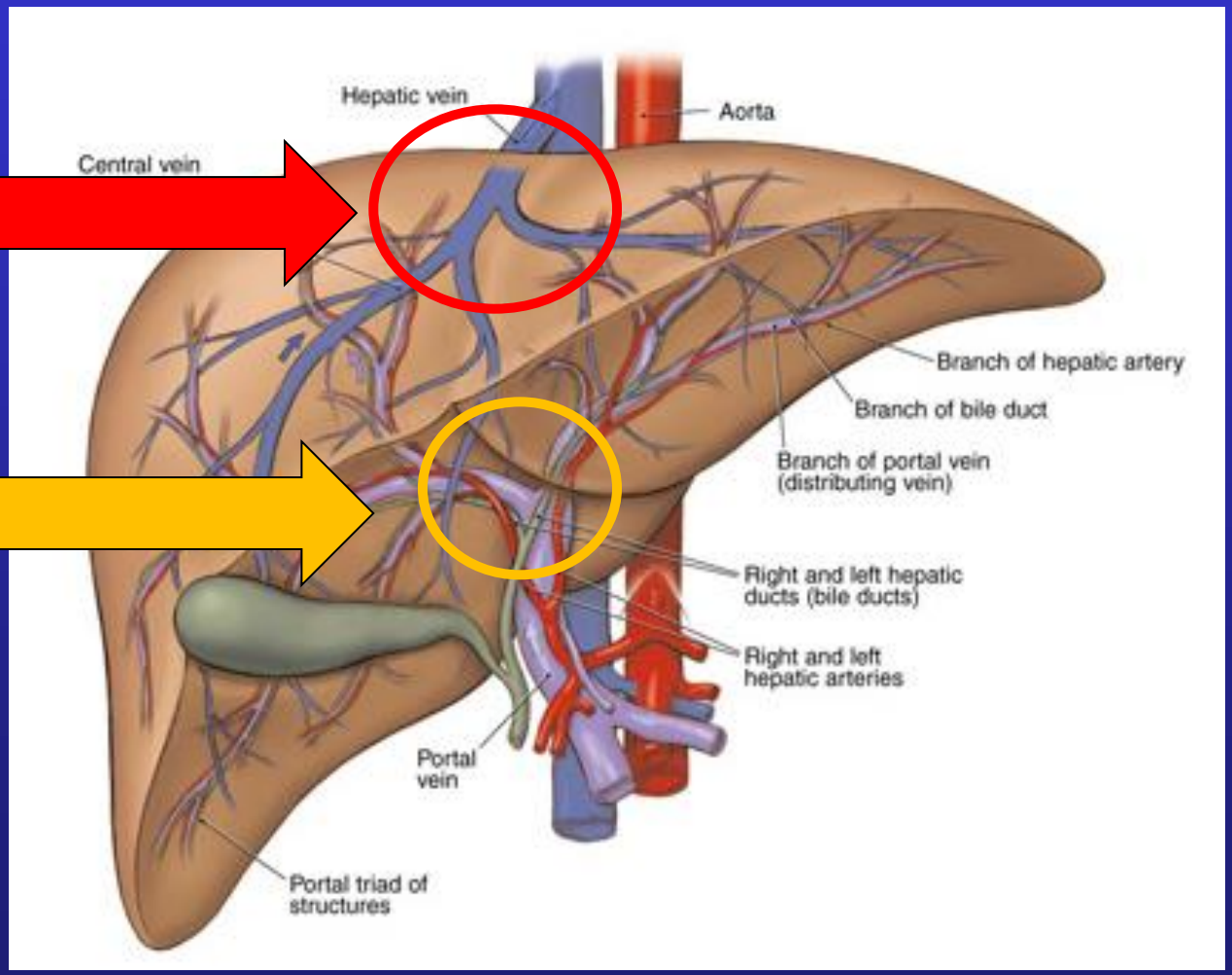
Treatment options for small liver mets

- Surgical resection
- RFA- not near vessels or bile ducts
- SBRT- third option
  - Poorly located tumors
  - More likely OS benefit
- Y-90 embolization

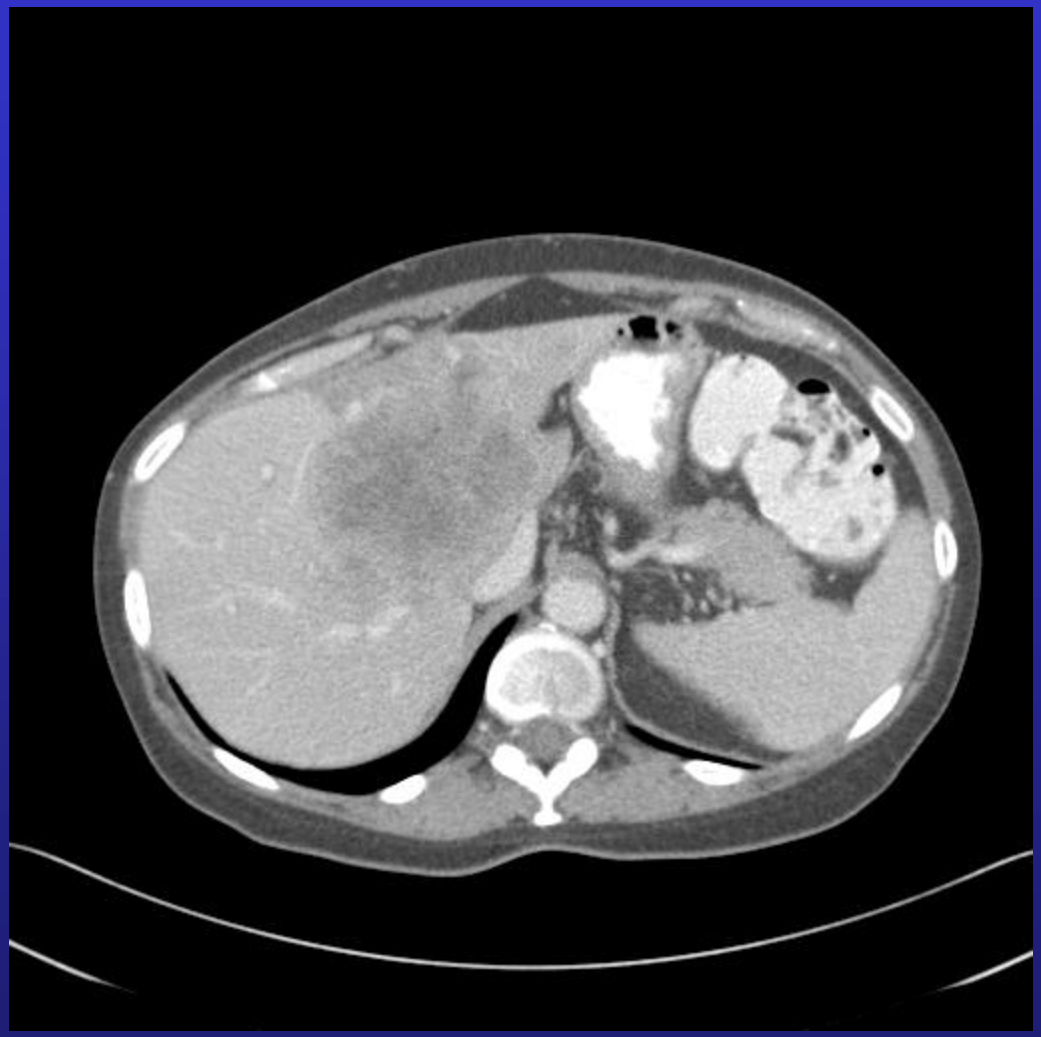
Vascular or biliary tumor extension = mortality

HV / IVC confluence

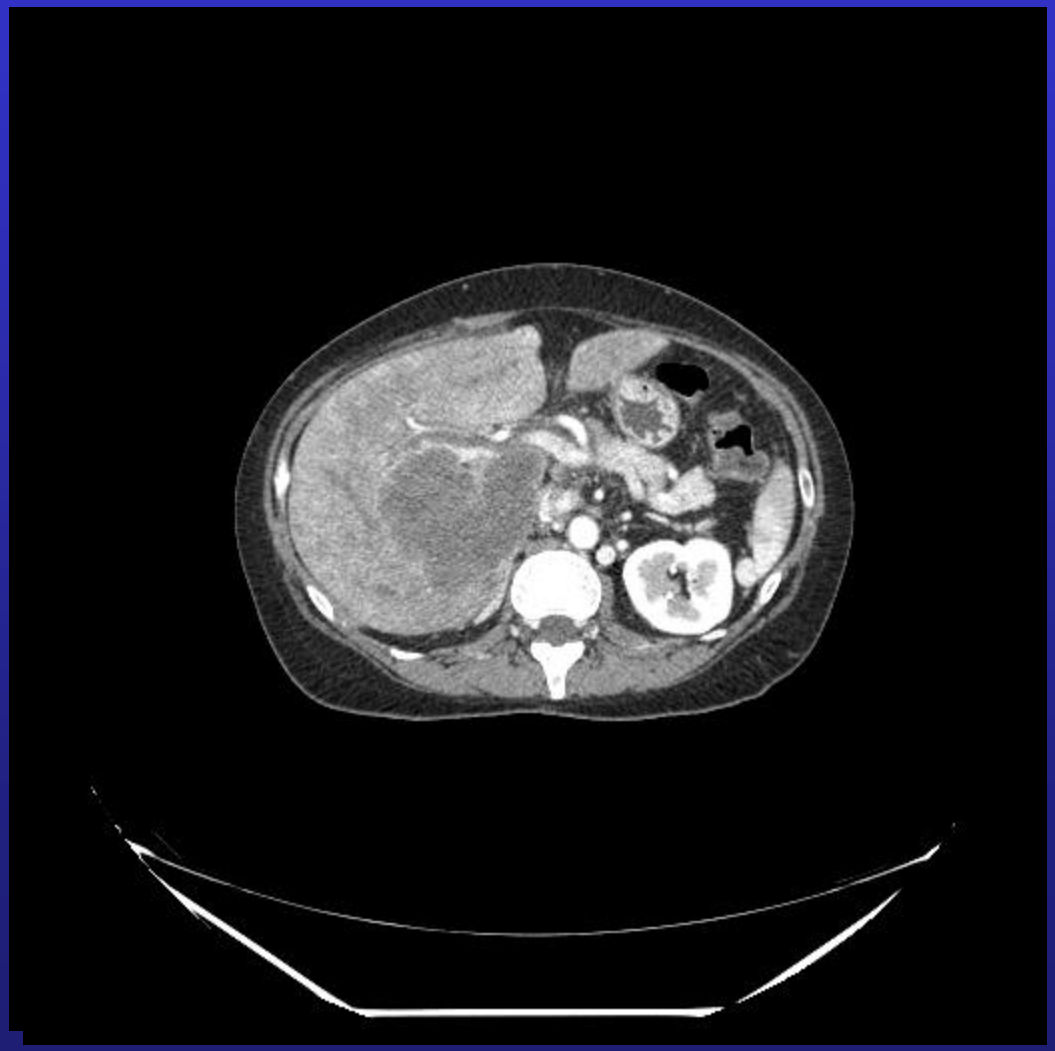
PV and biliary Bifurcation



51 y/o WF IHCa S/P 6 mo Chemo



6 Wks Later - Simulation CT – RT HV Occlusion

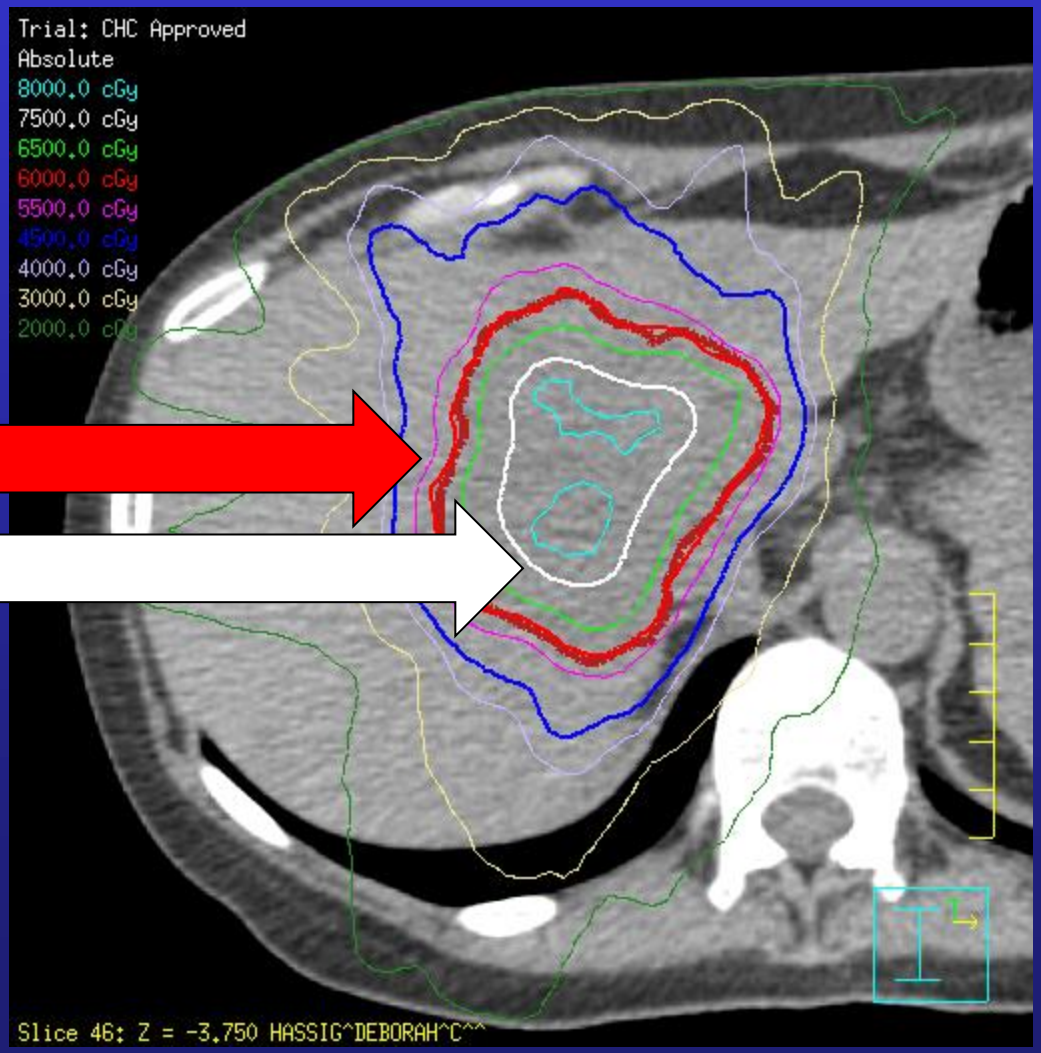


2 Mo Later – S/P Avastin with Response

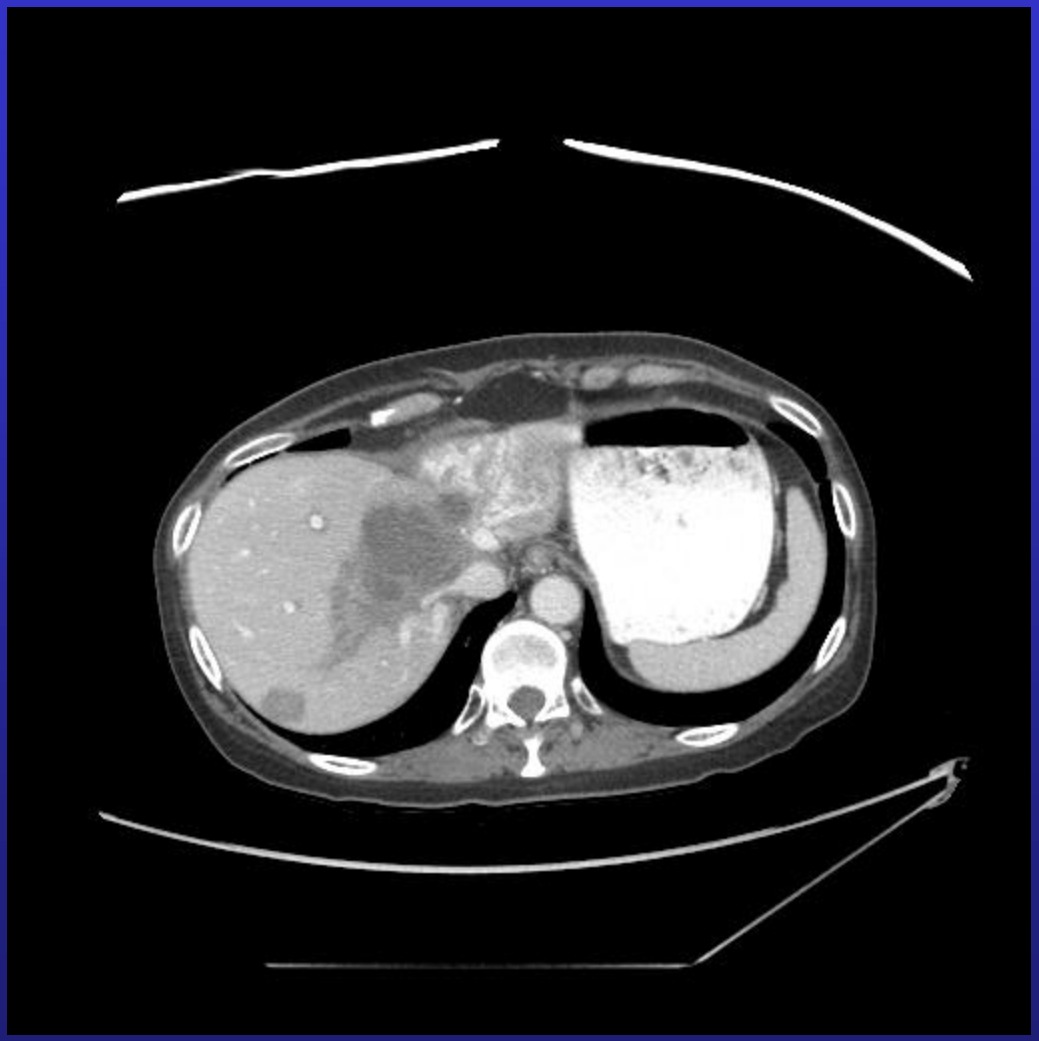
60Gy / 15fx Respiratory Gating + CT image guidance

60Gy/15 fx

75Gy/15 fx



4 months after XRT

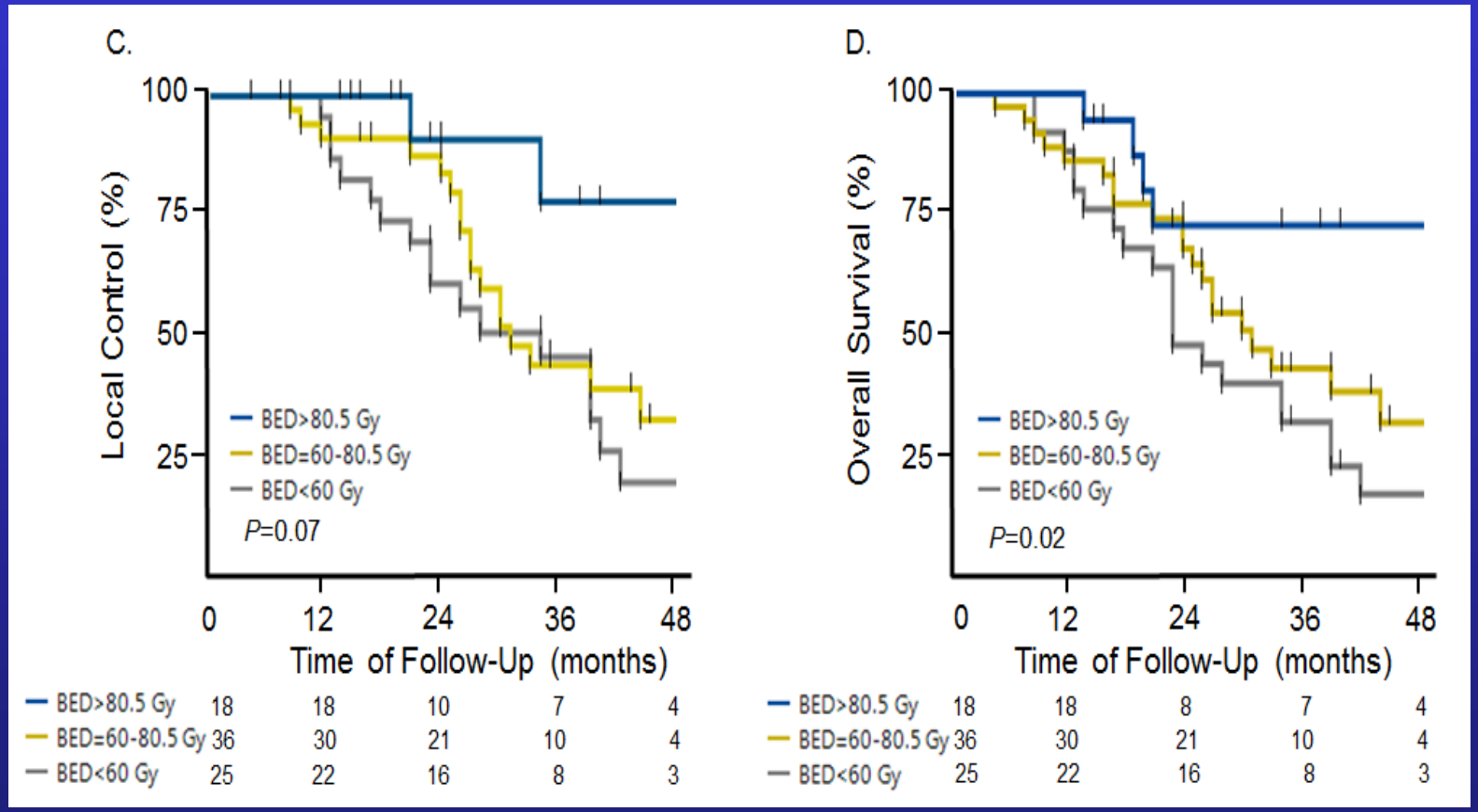


MDACC Results 2002-2014, n=79

Inoperable IHCa/ Definitve XRT

- Worse prognosis than operable tumors
  - Larger
  - Node+
  - Metastatic
- RT doses range 35-100 Gy
- 50 (63%) concurrent CTX
  - Capecitabine most common

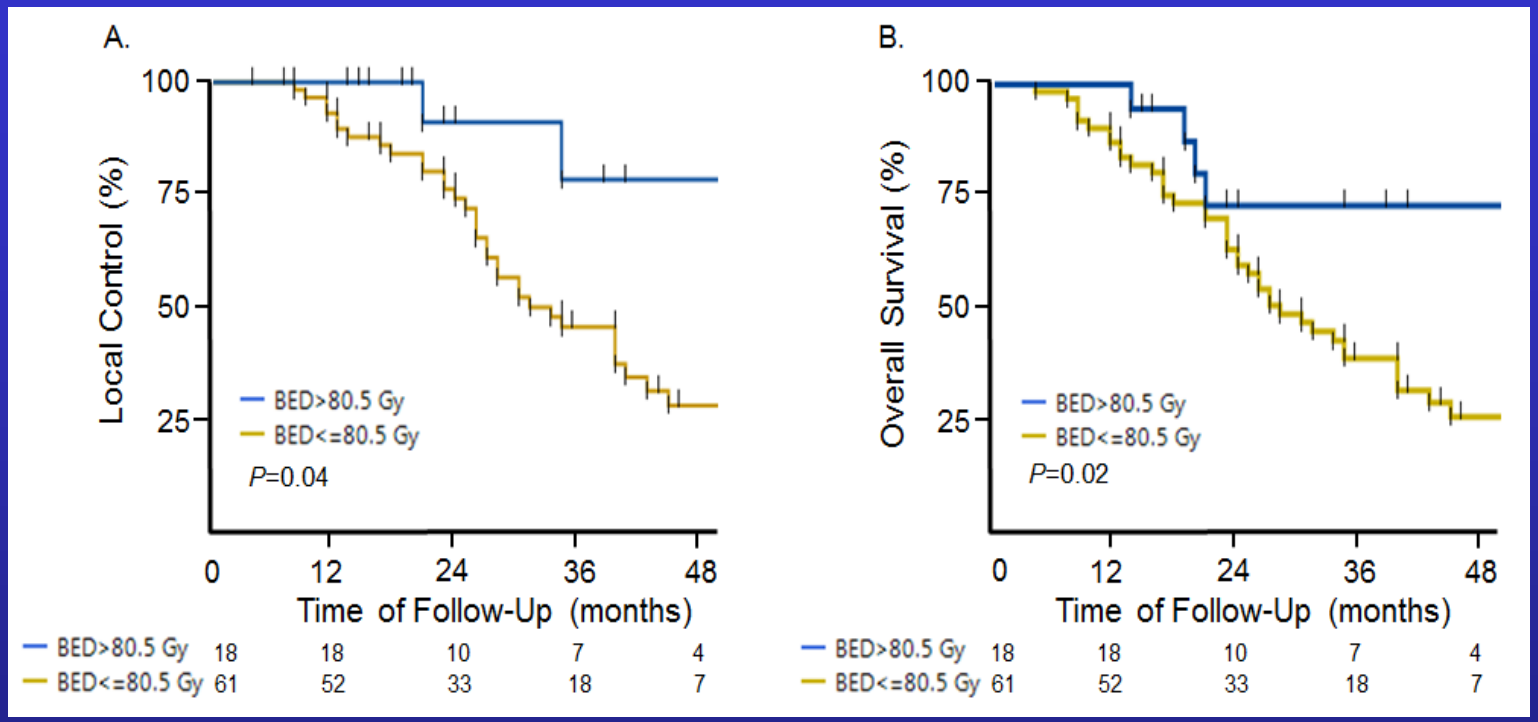
Dose Response for Intrahepatic CholangioCa
MDACC, 2002-2014



MVA: Dose only sign factor for LC (p=0.004) and OS (p=0.006)

Tao and Crane, JCO, 2015

Effect of radiation dose - BED of >80.5 Gy or less



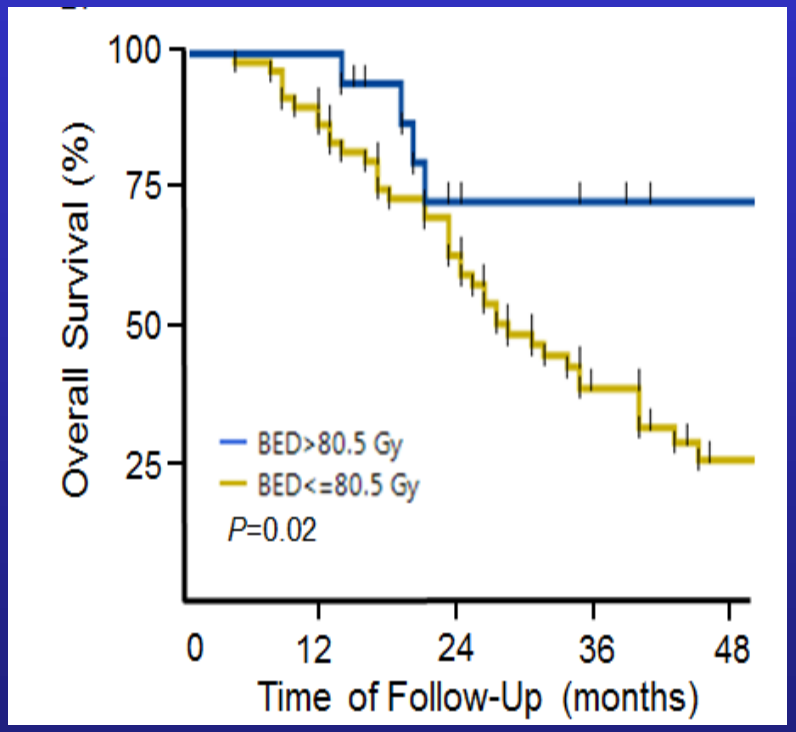
local control overall survival

75Gy in 25 fx	95.5 BED
67.5Gy in 15 fx	97.9 BED

Tao and Crane JCO, 2015

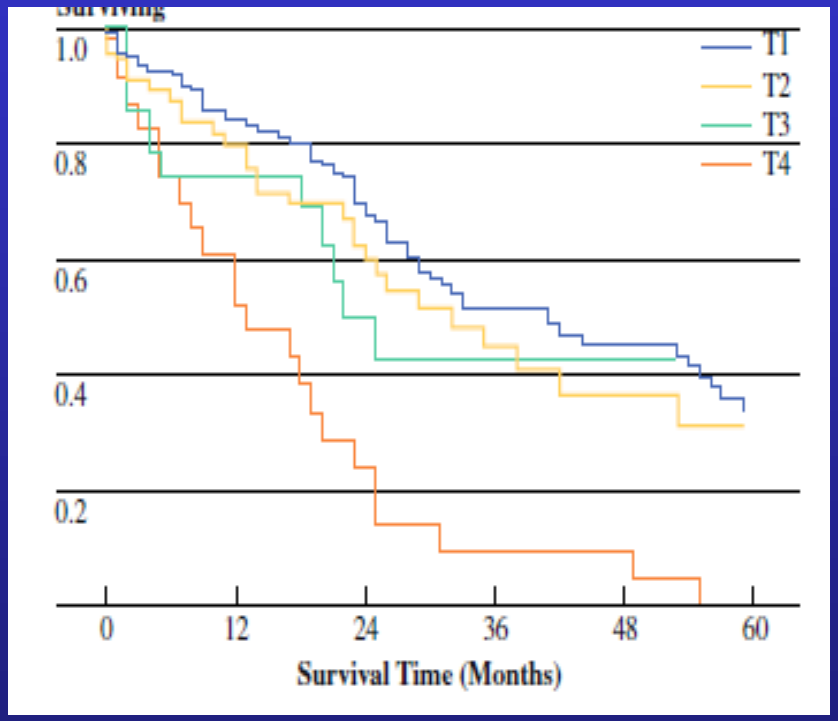
Intrahepatic CCa
(XRT - compared to Surgery)

Unresectable tumors



MDACC High vs low Dose
Inoperable IHCa

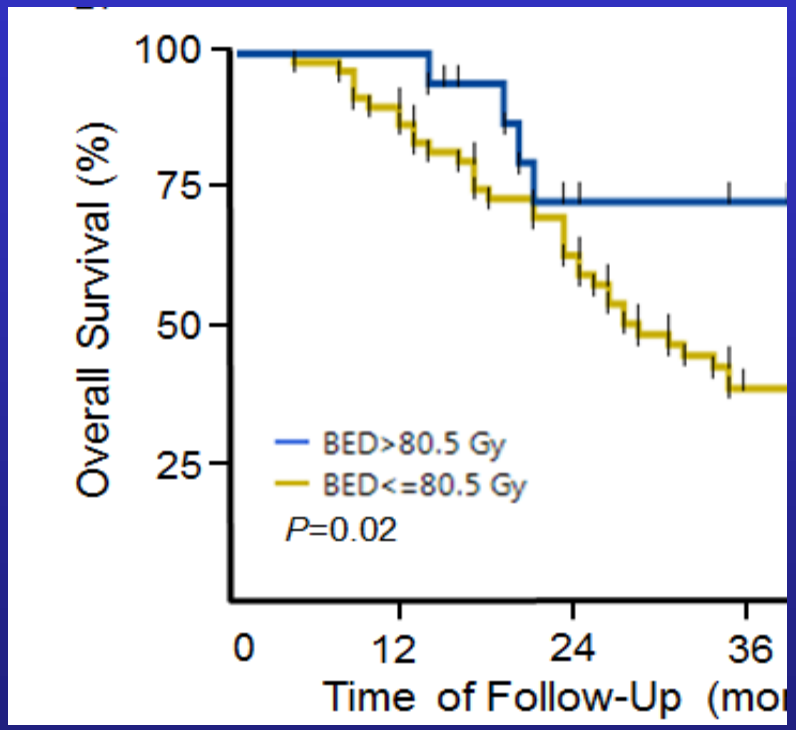
Resected tumors



Nathan, et al Ann Surg Oncol (2009)
SEER Results, Resected Tumors

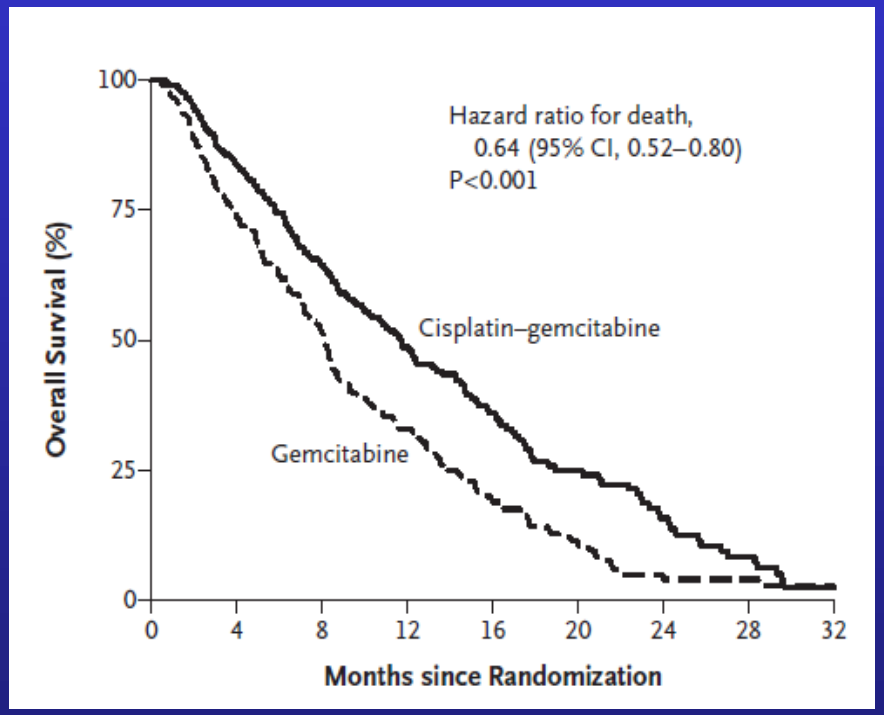
Intrahepatic CCa
(XRT - compared to Chemo)

Unresectable tumors



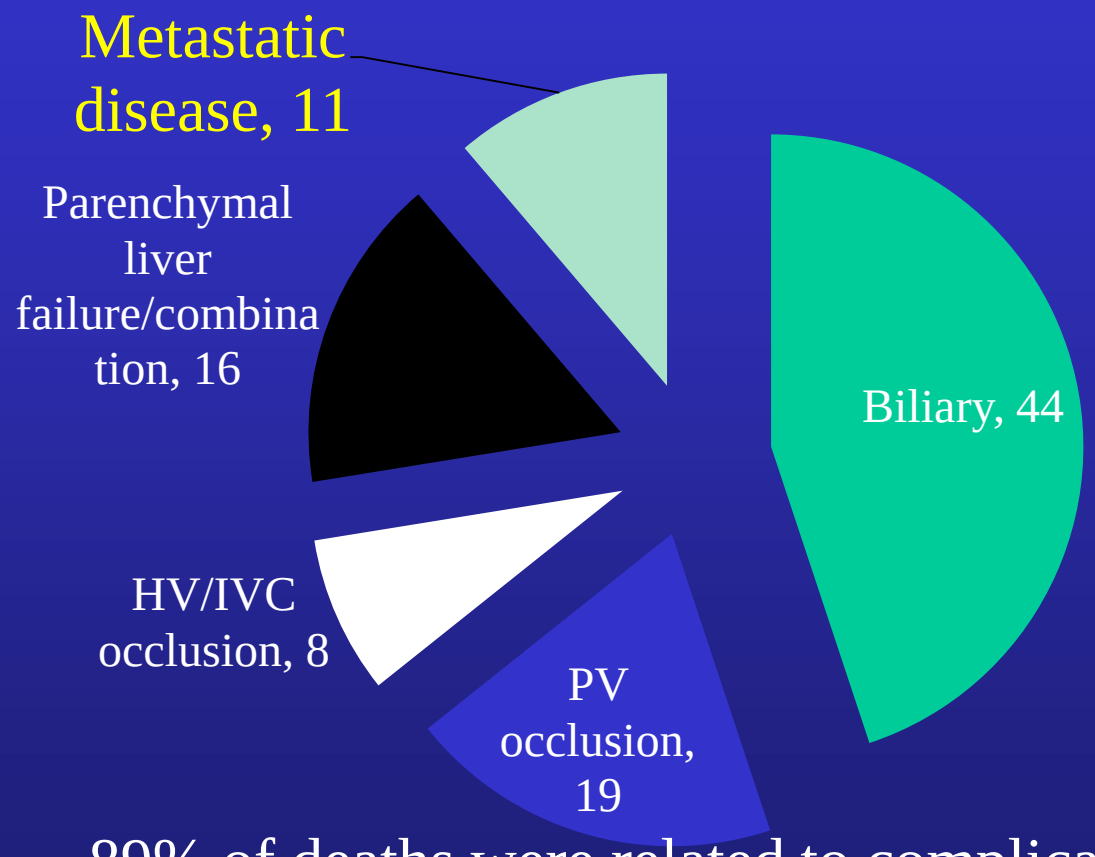
MDACC High vs low Dose
Inoperable IHCa

ABC 2: Advanced / met tumors



Valle J, et al. N Engl J Med 2010

Causes of Death – IHCCa
(inadequate XRT dose / tumor control)



89% of deaths were related to complications related to liver tumors

Tao and Crane, submitted, 2015

NRG GI001– Phase III Trial

Unresectable Cholangioca

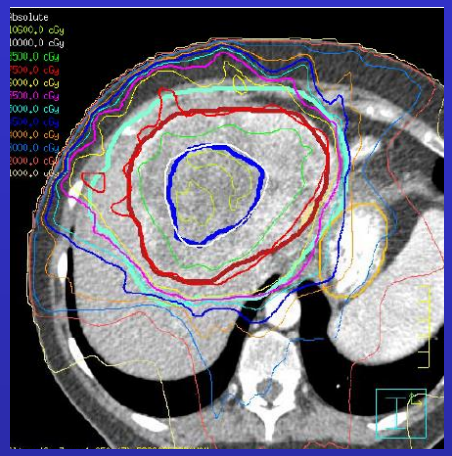
-liver confined

-no cirrhosis or CPC A

-up to 2 satellite lesions

-12 cm or less

Gem/Cis x 4



67.5 Gy / 15 fx

Re-staging AND Randomization after cycle 3 Radiation Planning during cycle 4

Gem/Cis x 4

Stratify:

-Largest tumor > 6 cm

--satellite y/n

Ted Hong, PI

Unresectable 14 cm IHC -Before XRT

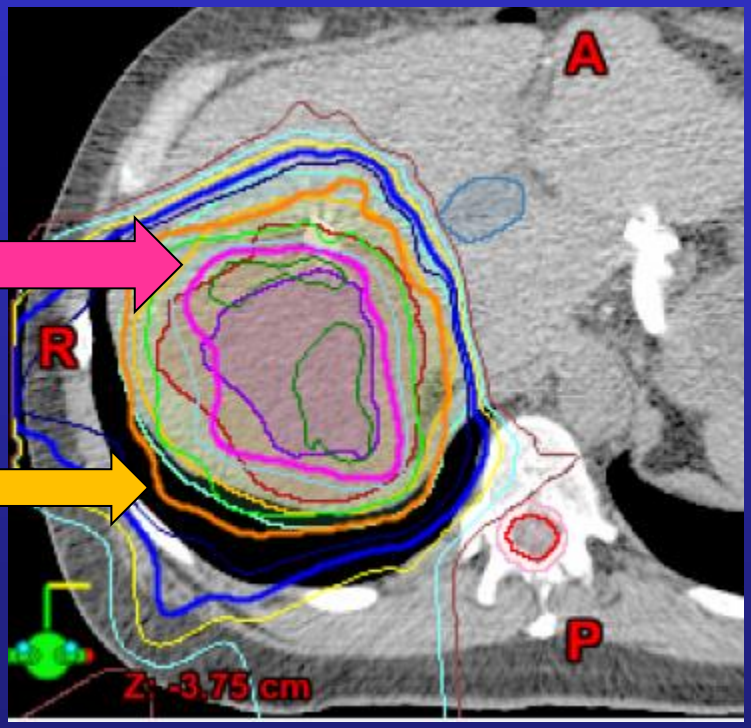
Liquefaction

3 months post therapy

Same SIB Technique with Protons

100Gy/25x

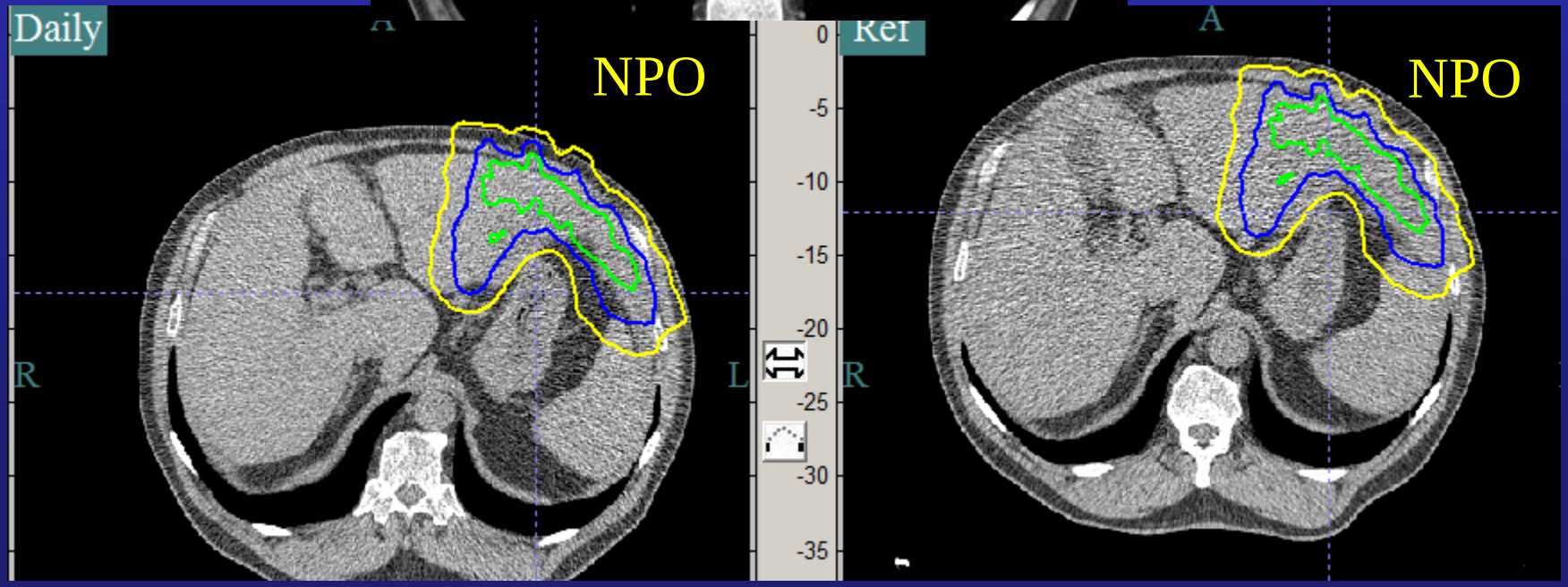
75Gy/25fx



Liquefaction

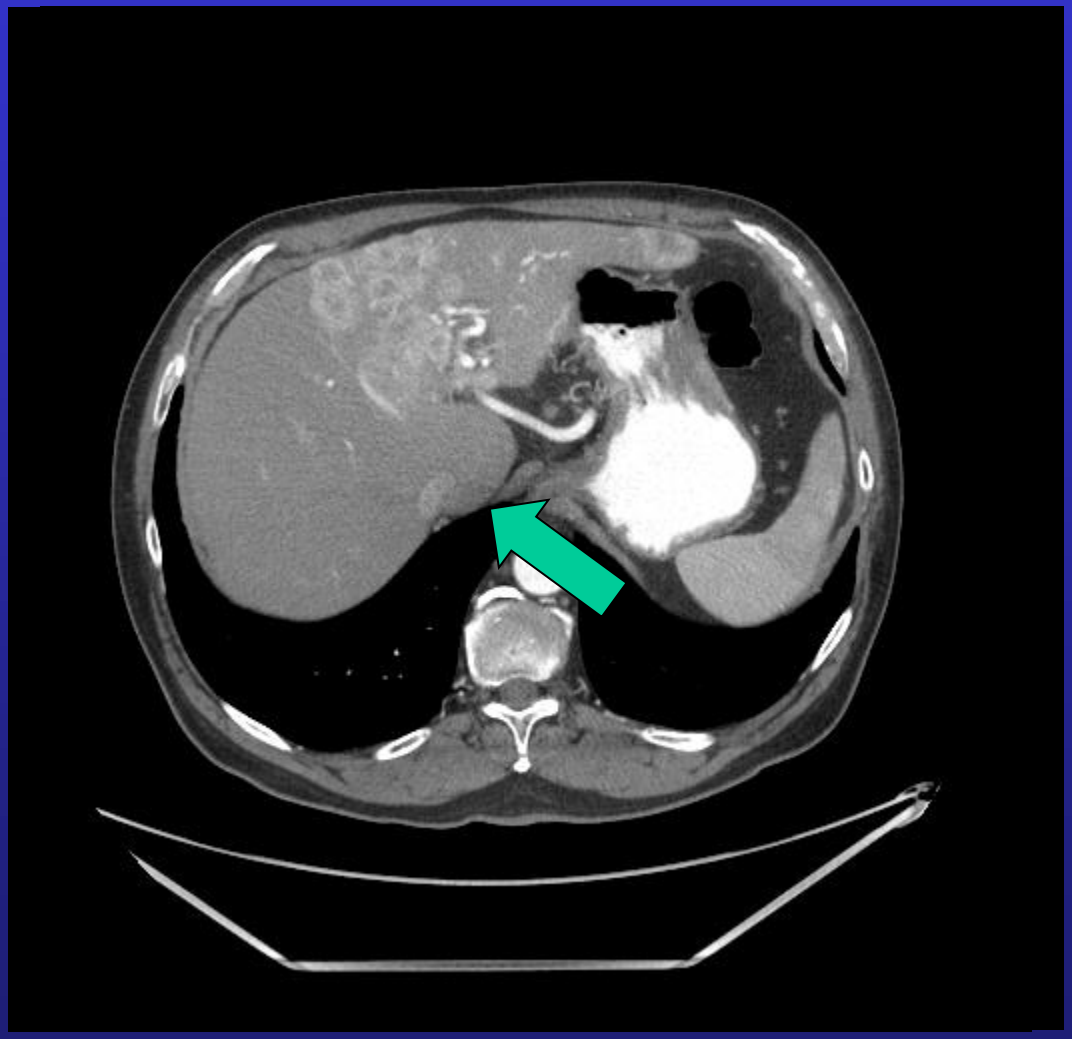
IHCA (segments 2&3) near stomach:
67.5Gy/15fx - IMRT

Stomach/Tumor interface

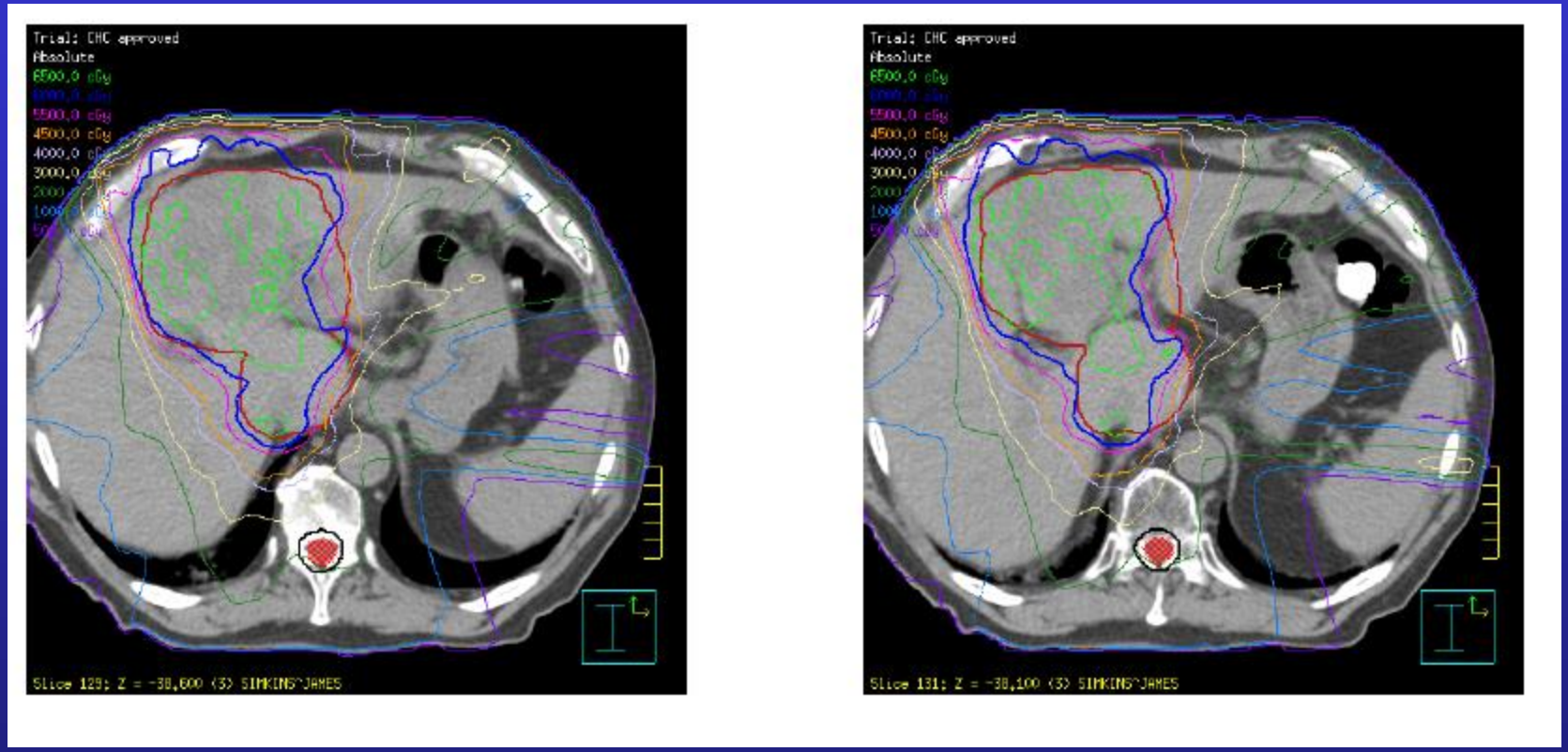


9 months later…

Satellitosis –segments 4a & 4b



Here's what we did:
60Gy in 15fx IMRT



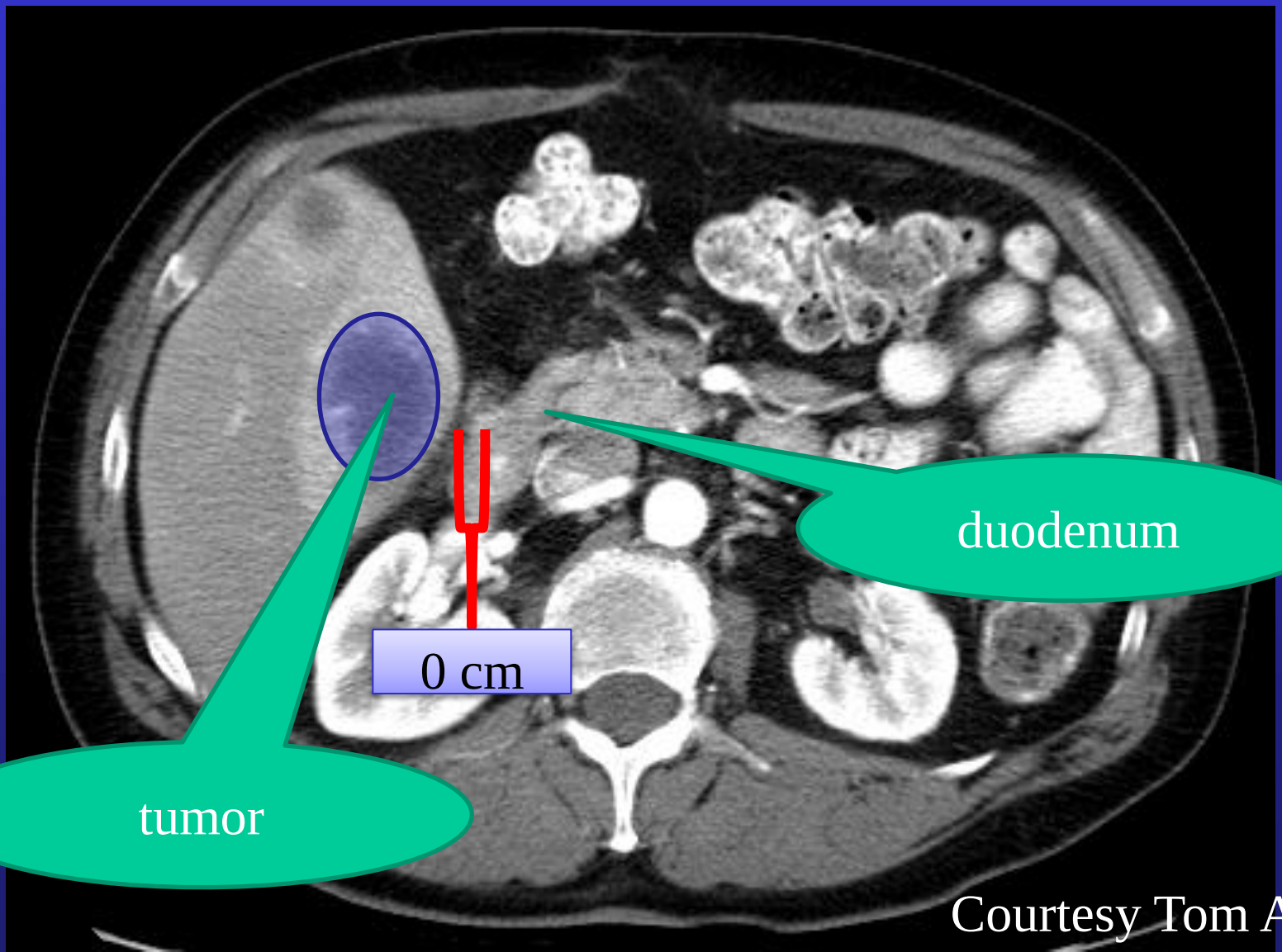
Challenges: stomach and liver dose

Laparoscopic/open Alloderm Placement

Yoon, et al, PRO, 9/2013

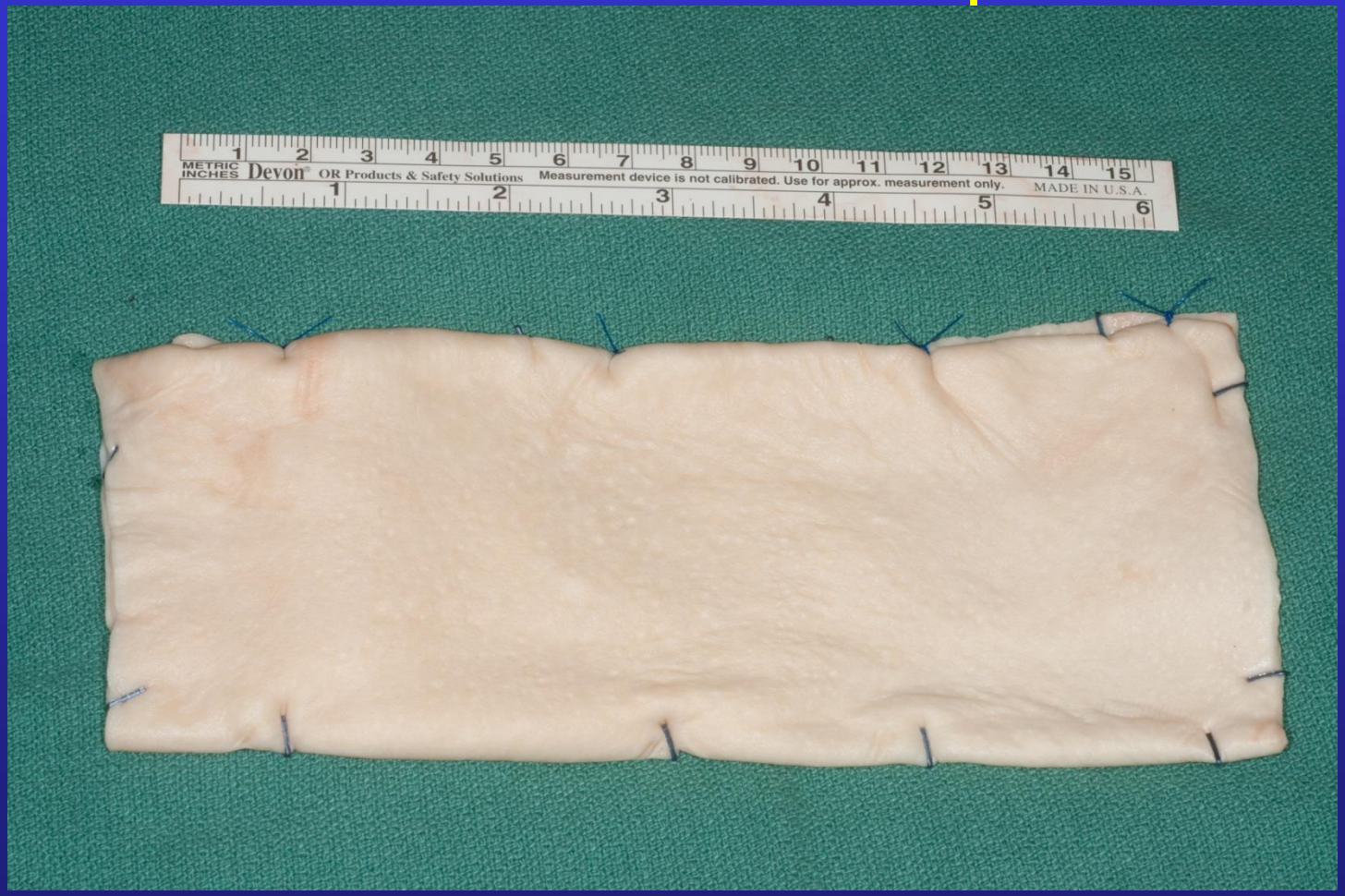
Sometimes the bowel is too close

Colon, duodenum, stomach are dose limiting



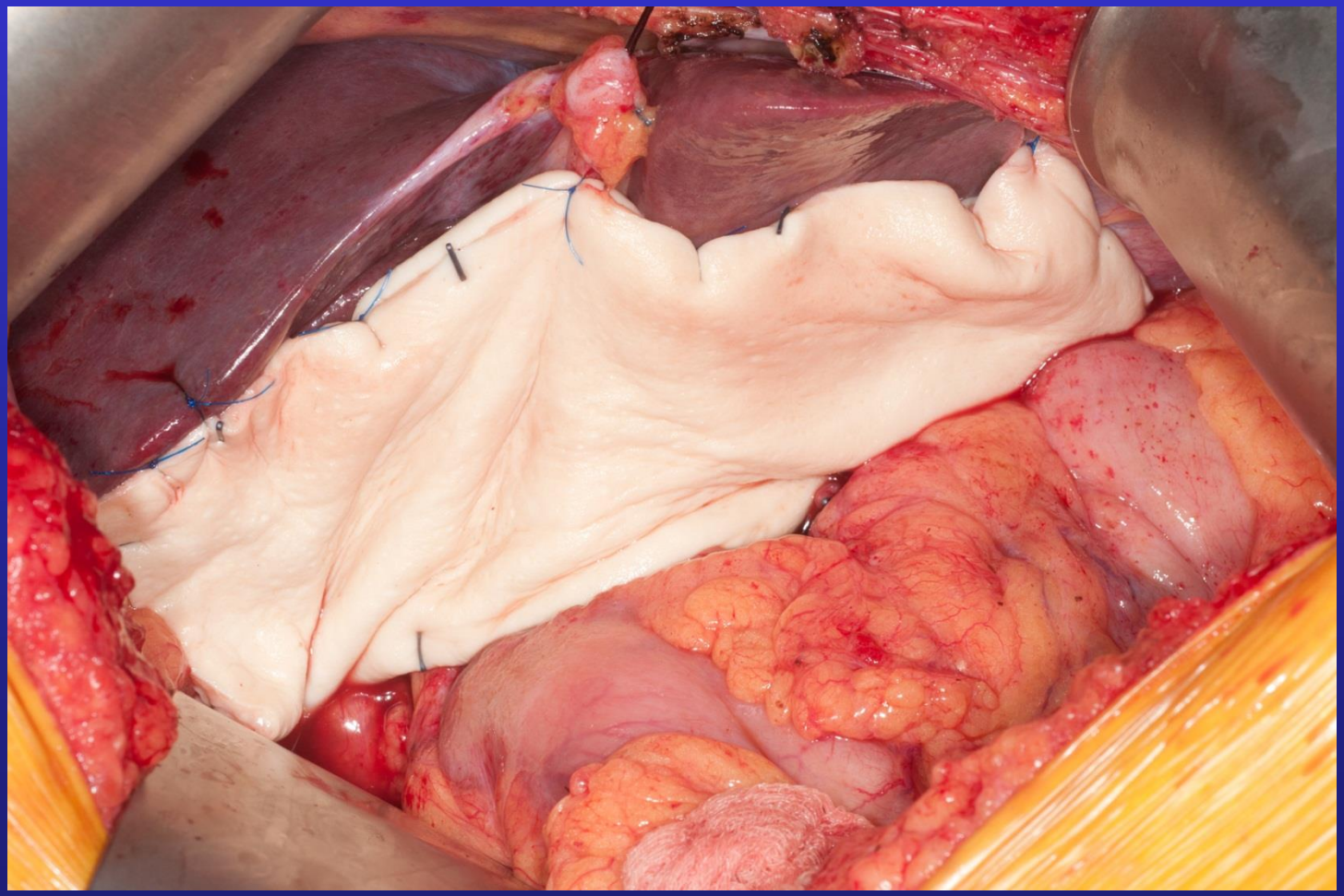
Courtesy Tom Aloia

AlloDerm® Envelope

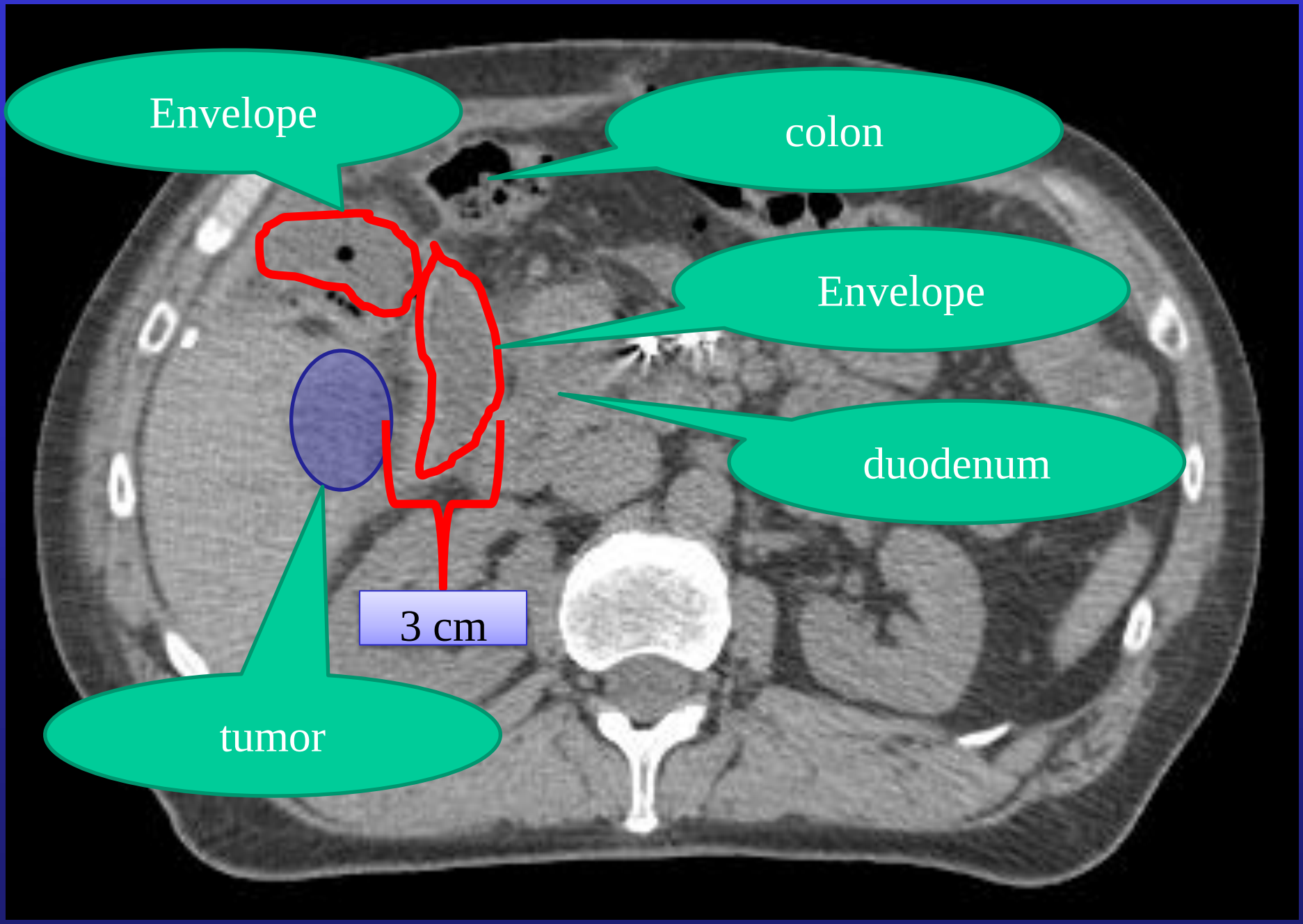


Courtesy Tom Aloia

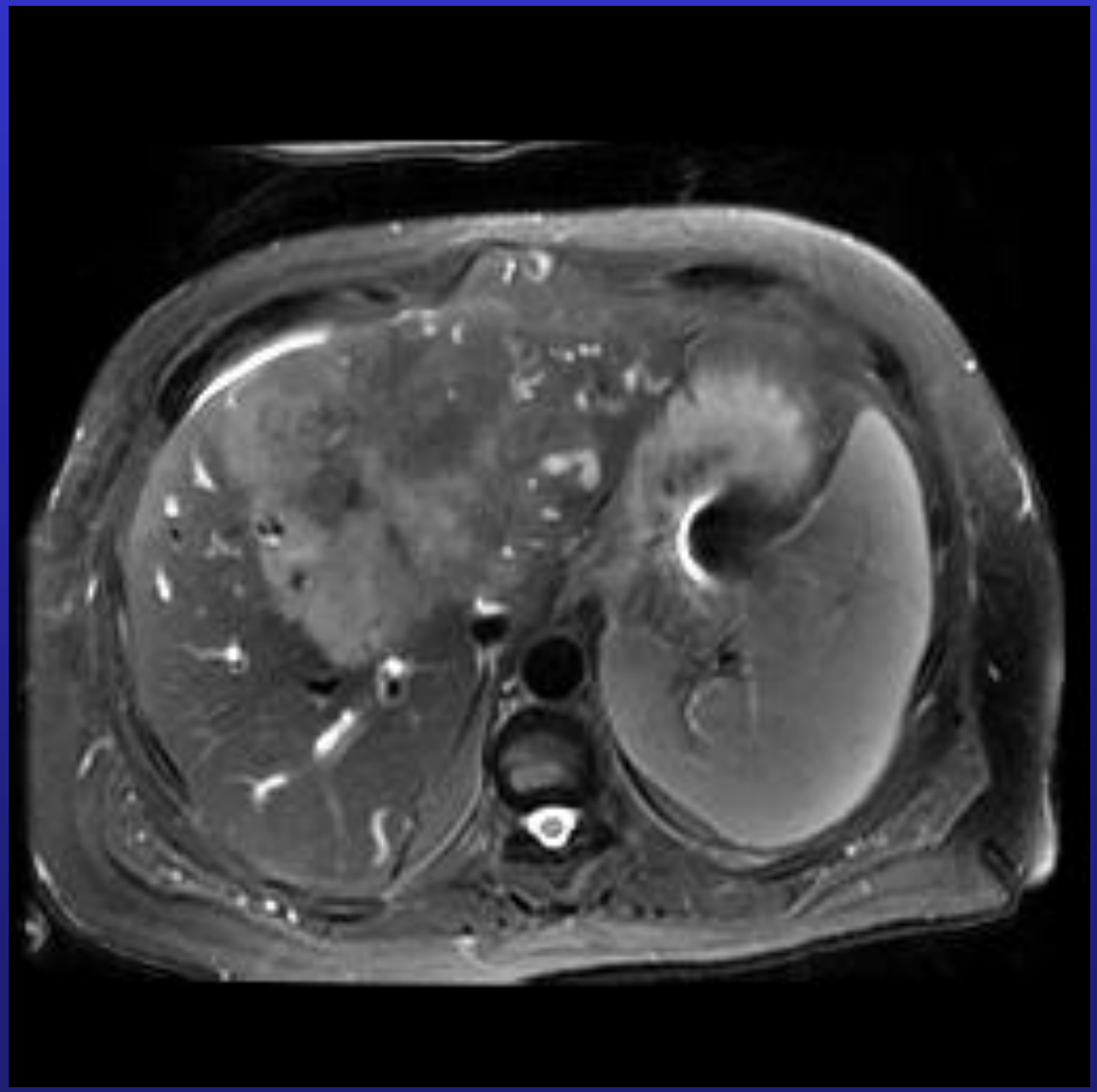
Open AlloDerm® Spacer Placement



Courtesy Tom Aloia


Envelope
colon
Envelope
duodenum
3 cm
tumor

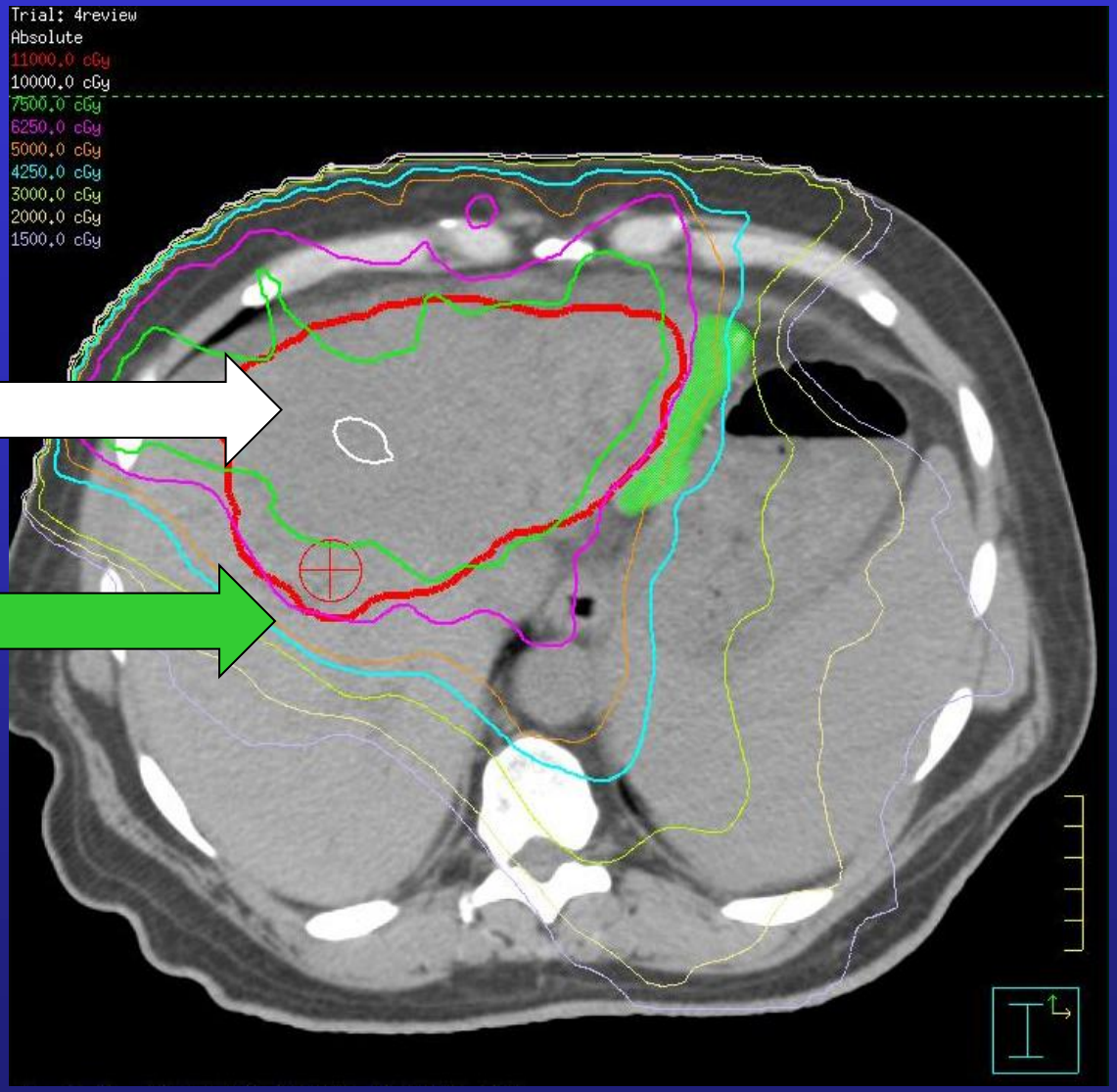
Unresectable Intrahepatic Cholangio near Stomach



IMRT after Alloderm Placement

100Gy/25x

75Gy/25fx



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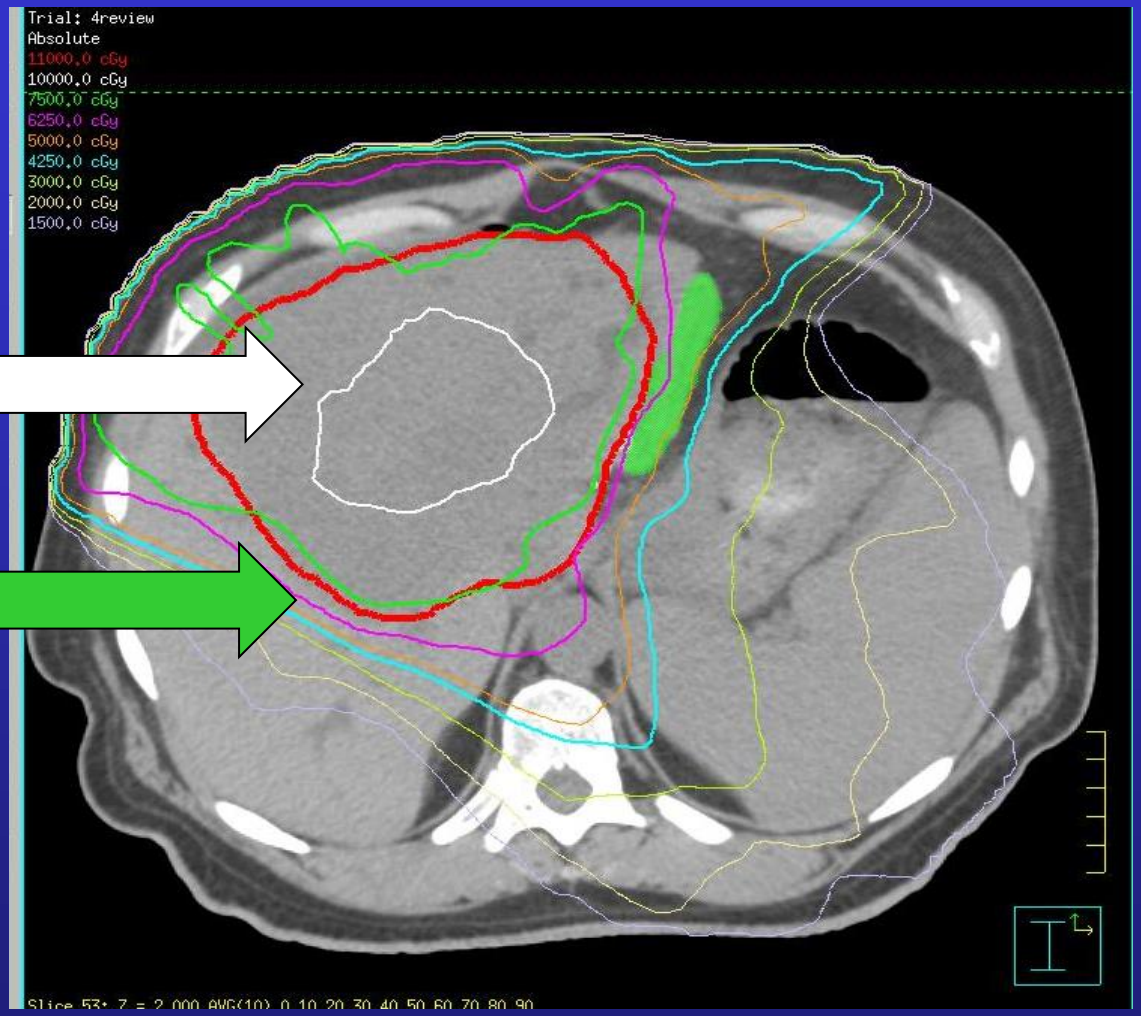

IMRT after Alloderm Placement

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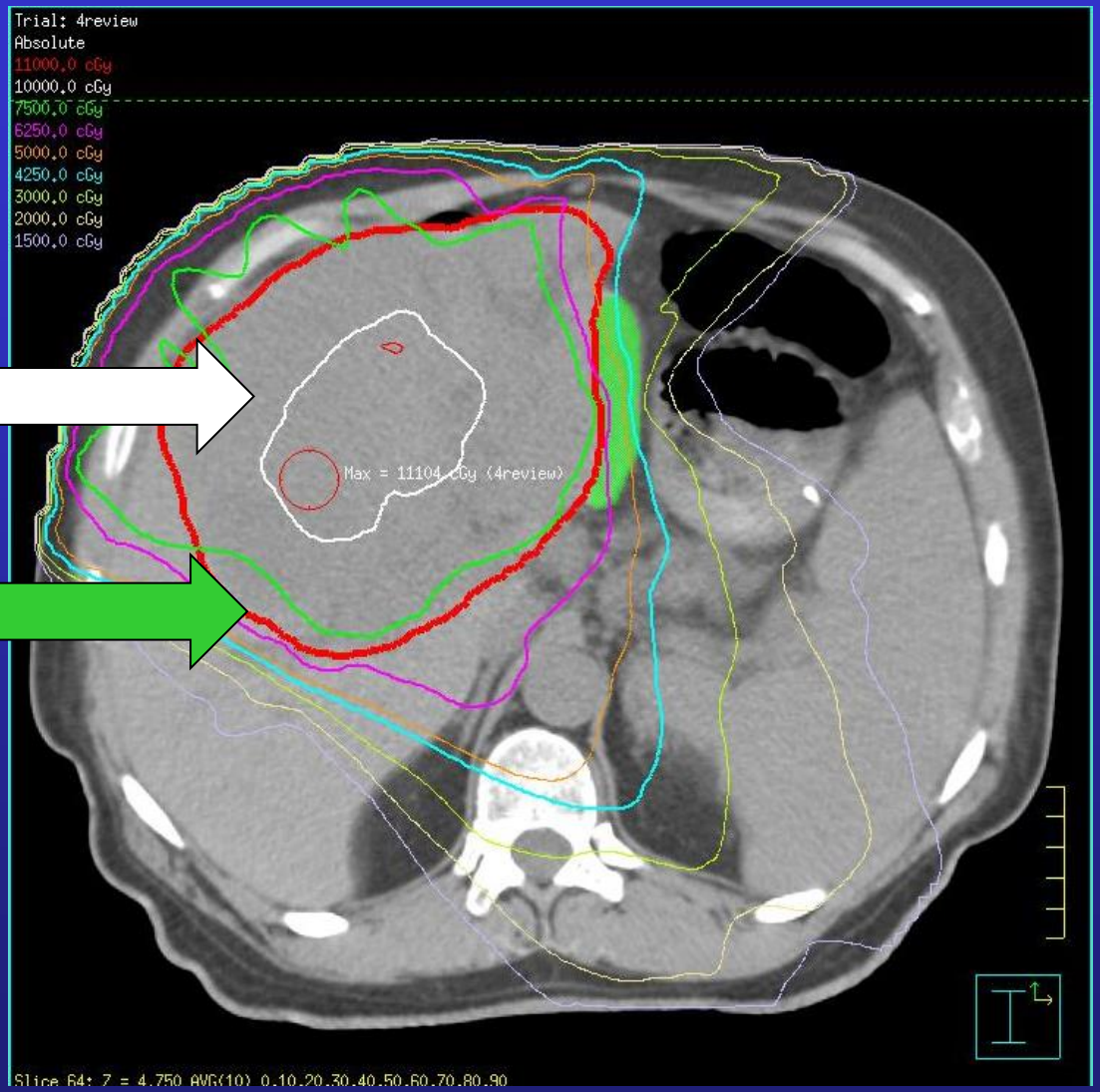
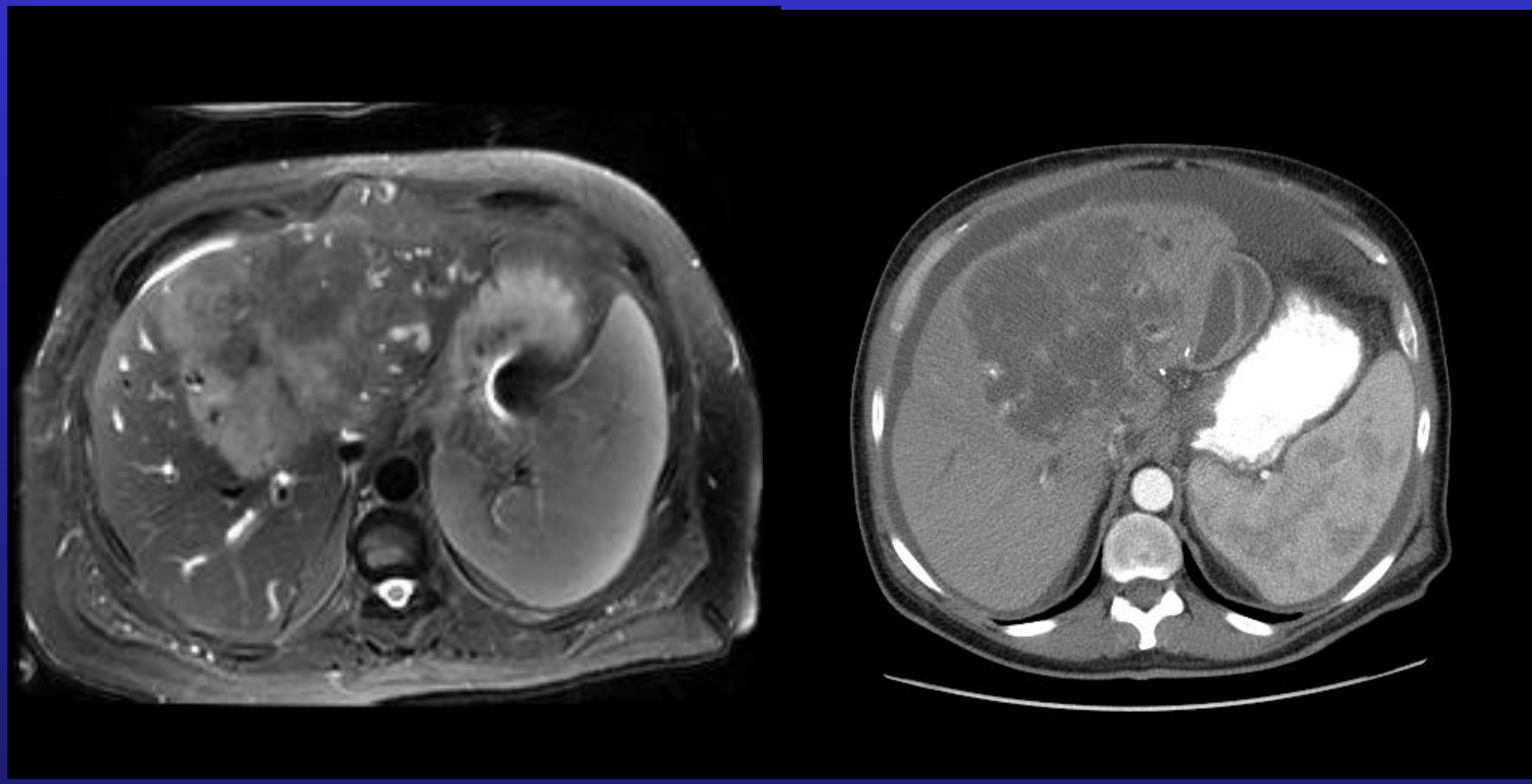


Pre vs post XRT scan



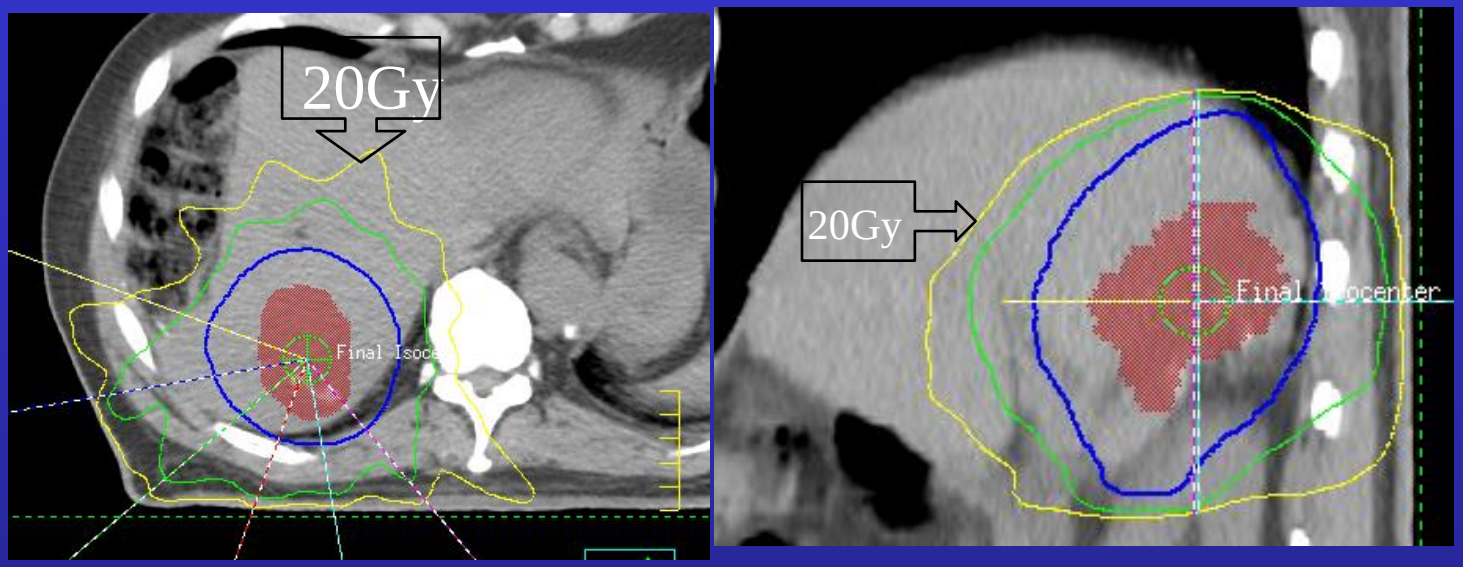
IMRT vs Protons

- IMRT- better bowel sparing
  - sharper edge (penumbra)
- Protons / Charged particles– better liver sparing
  - don’t exit, but high dose volume larger

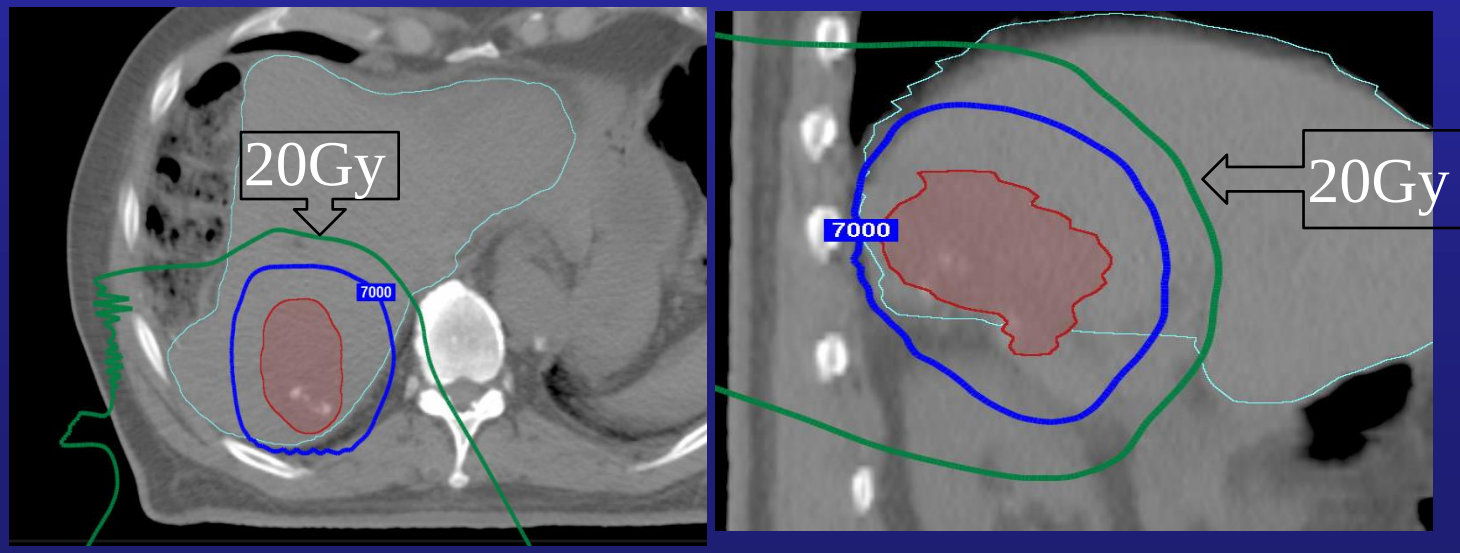
6cm Isolated Unresectable IHCCa

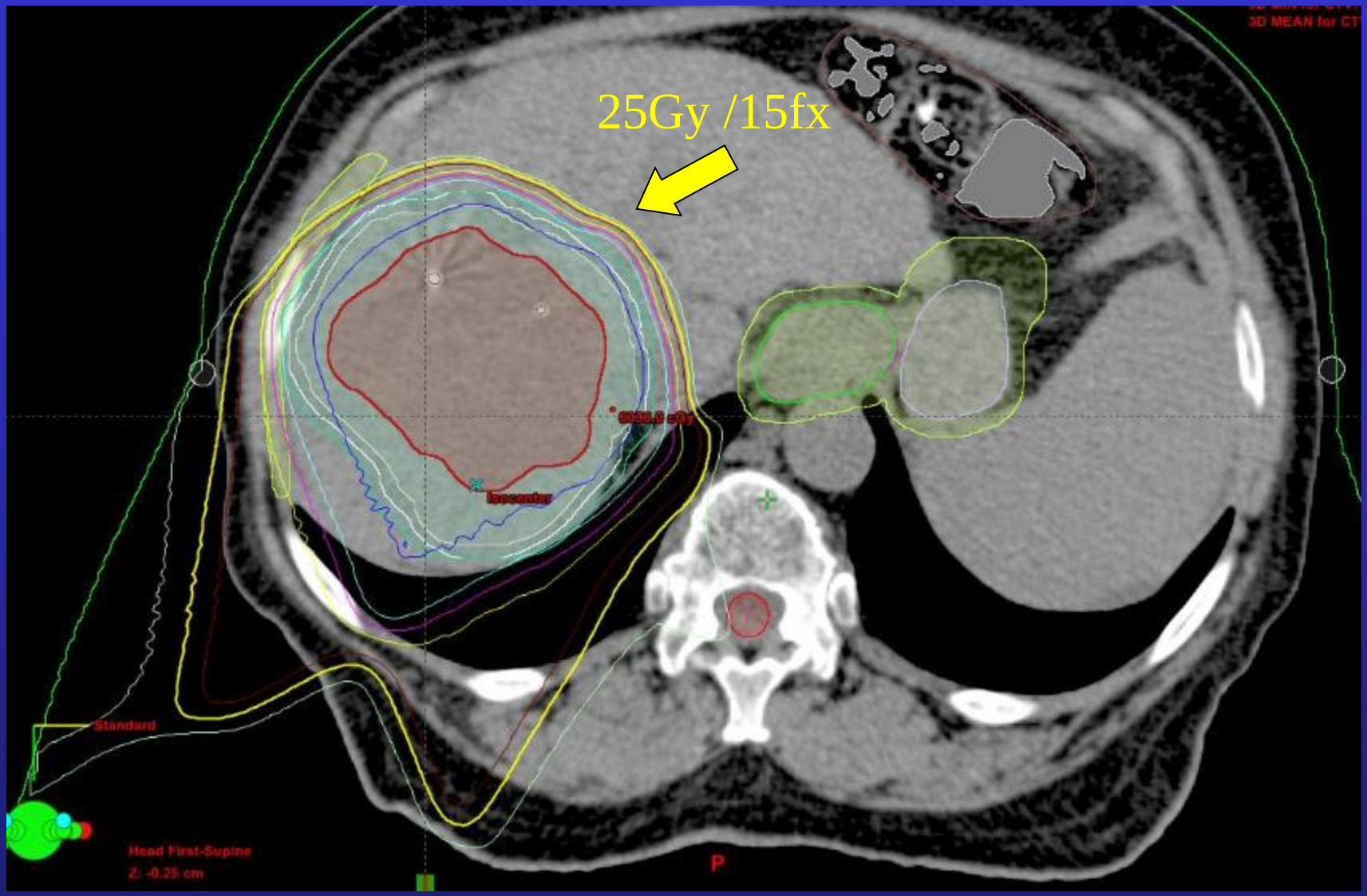
Max dose greater with Proton than IMRT

IMRT
50GGE /10 fx



Proton
70CGE / 10 fx




25Gy /15fx
3D MEAN for CT
Isocenter
Standard
Head First-Supine
Z: -0.25 cm
P

Summary
Ablative XRT for Liver Tumors

- Tumor control is dose related
  - Protons / IMRT complementary options
  - Choice based on protecting organs
- Major survival benefit (years)
- Inoperable patients: Curative treatment option
  - Comparable to surgery

Take home point
Large Liver Tumors

- Equivalent dose (BED) of 100 Gy is needed to control tumors
  - Liver, bile duct, and bowel are dose limiting
  - Possible with 15-25 treatments
  - Not possible with 5 treatments
    - Liver damage
    - Bile duct stricture
    - Bowel – bleeding