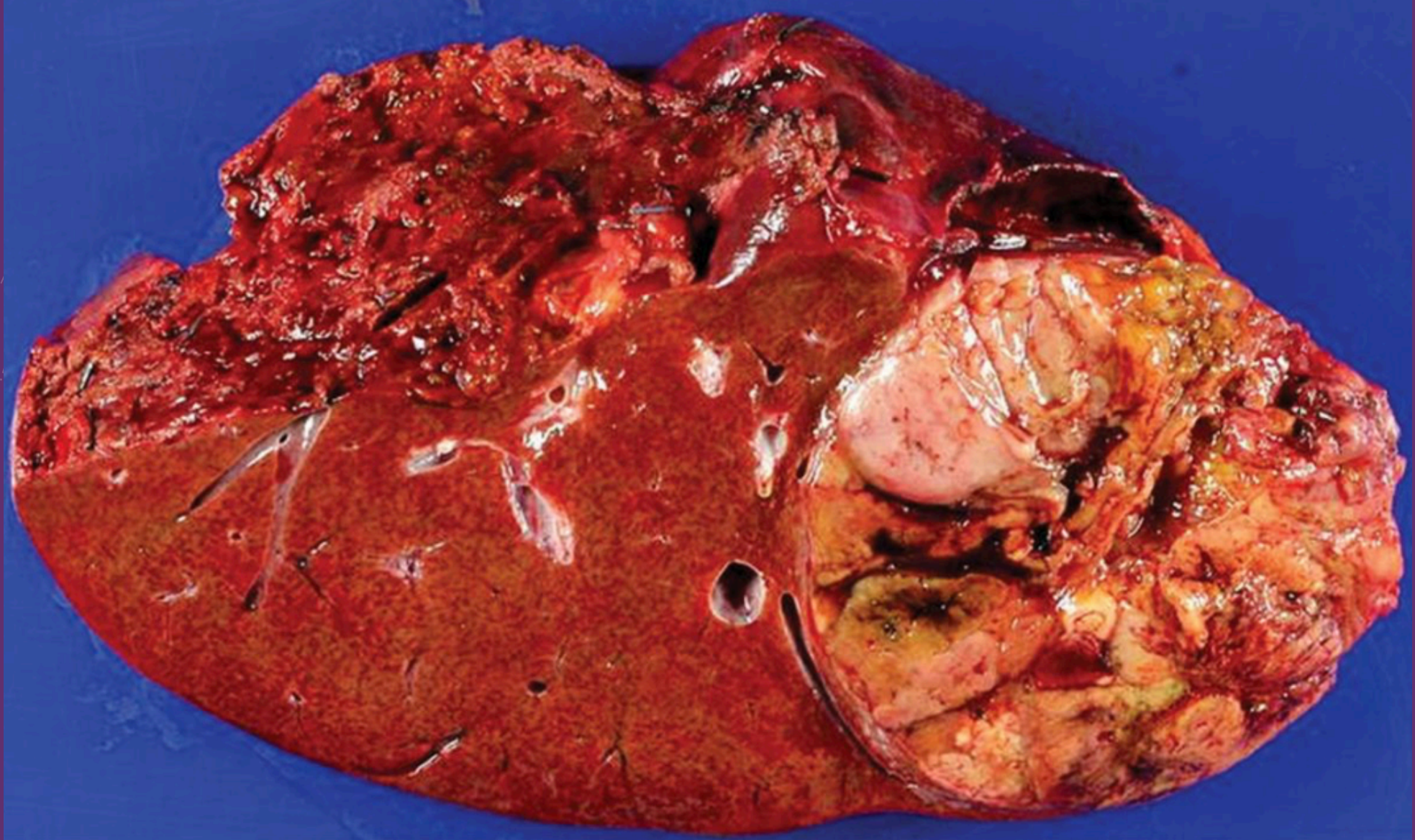


Hepatocellular Carcinoma

Jeffrey A. Kahn, MD

Keck School of Medicine of USC



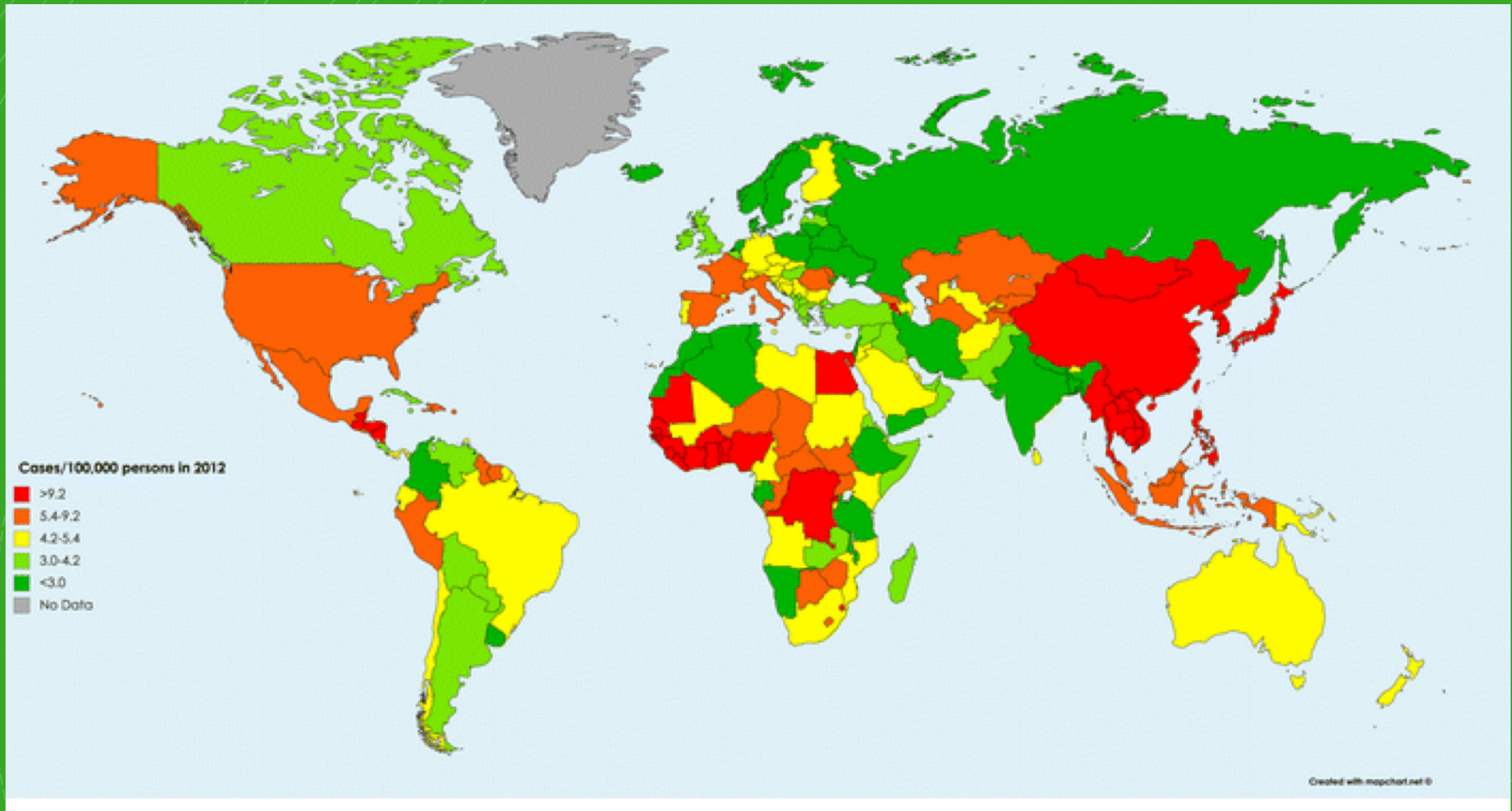
Questions

- What are the classic contrast imaging findings of HCC?
- Does a normal AFP exclude HCC?
- Requirements for a MELD exception for HCC

Background

- Hepatocellular carcinoma is the 5th most common cancer worldwide
- 3rd leading cause of cancer-related mortality worldwide
- Fastest rising cause of cancer deaths worldwide
- Preventable in many cases

HCC WORLD MAP



Tang, A., Hallouch, O., Chernyak, V. et al. Abdom Radiol (2018) 43: 13. <https://doi.org/10.1007/s00261-017-1209->

TABLE 1. PATIENTS AT THE HIGHEST RISK FOR HCC

Population Group	Threshold Incidence for Efficacy of Surveillance (>0.25 LYG; % per year)	Incidence of HCC
Surveillance benefit		
Asian male hepatitis B carriers over age 40	0.2	0.4%-0.6% per year
Asian female hepatitis B carriers over age 50	0.2	0.3%-0.6% per year
Hepatitis B carrier with family history of HCC	0.2	Incidence higher than without family history
African and/or North American blacks with hepatitis B	0.2	HCC occurs at a younger age
Hepatitis B carriers with cirrhosis	0.2-1.5	3%-8% per year
Hepatitis C cirrhosis	1.5	3%-5% per year
Stage 4 PBC	1.5	3%-5% per year
Genetic hemochromatosis and cirrhosis	1.5	Unknown, but probably >1.5% per year
Alpha-1 antitrypsin deficiency and cirrhosis	1.5	Unknown, but probably >1.5% per year
Other cirrhosis	1.5	Unknown
Surveillance benefit uncertain		
Hepatitis B carriers younger than 40 (males) or 50 (females)	0.2	<0.2% per year
Hepatitis C and stage 3 fibrosis	1.5	<1.5% per year
NAFLD without cirrhosis	1.5	<1.5% per year

Abbreviation: LYG, life-years gained.

Screening and Surveillance

Usual Strategy

- All patients with cirrhosis should undergo screening
 - Also, patients with a large amount of scarring or cirrhosis should be considered for screening
 - Patients with chronic hepatitis B even without fibrosis should also be considered based upon age and other risk factors for cancer development
 - Standard screening is an ultrasound and a blood test called alfafetoprotein every 6 months
 - An abnormal ultrasound might prompt a CT scan or MRI
- Standard screening is an ultrasound of the liver and a blood test called alfafetoprotein every 6 months

SURVEILLANCE TESTING

1A. The AASLD recommends surveillance of adults with cirrhosis because it improves overall survival (OS).

Quality/Certainty of Evidence: Moderate

Strength of Recommendation: Strong

1B. The AASLD recommends surveillance using US, with or without AFP, every 6 months.

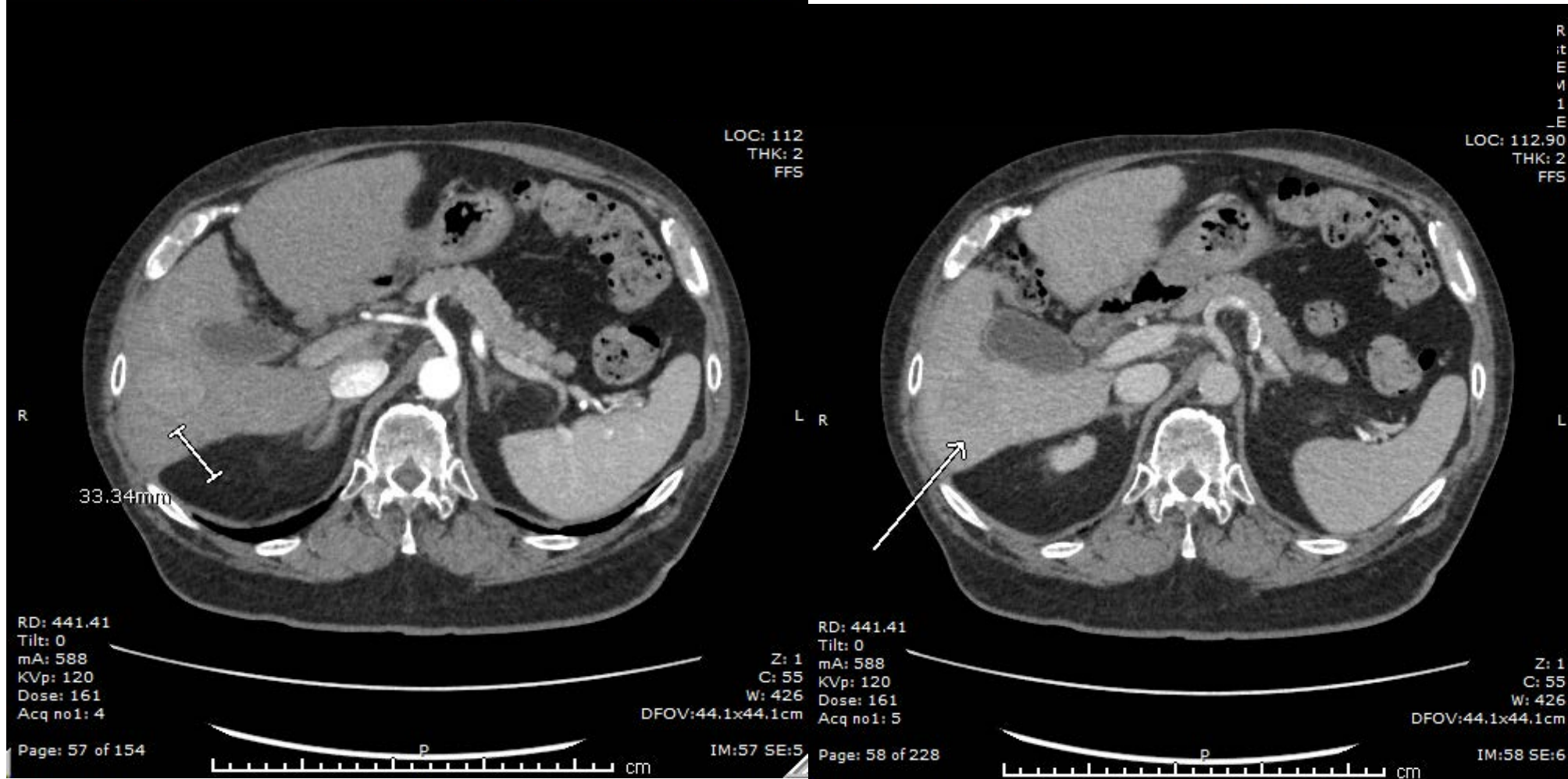
Quality/Certainty of Evidence: Low

Strength of Recommendation: Conditional

1C. The AASLD recommends not performing surveillance of patients with cirrhosis with Child's class C unless they are on the transplant waiting list, given the low anticipated survival for patients with Child's C cirrhosis.

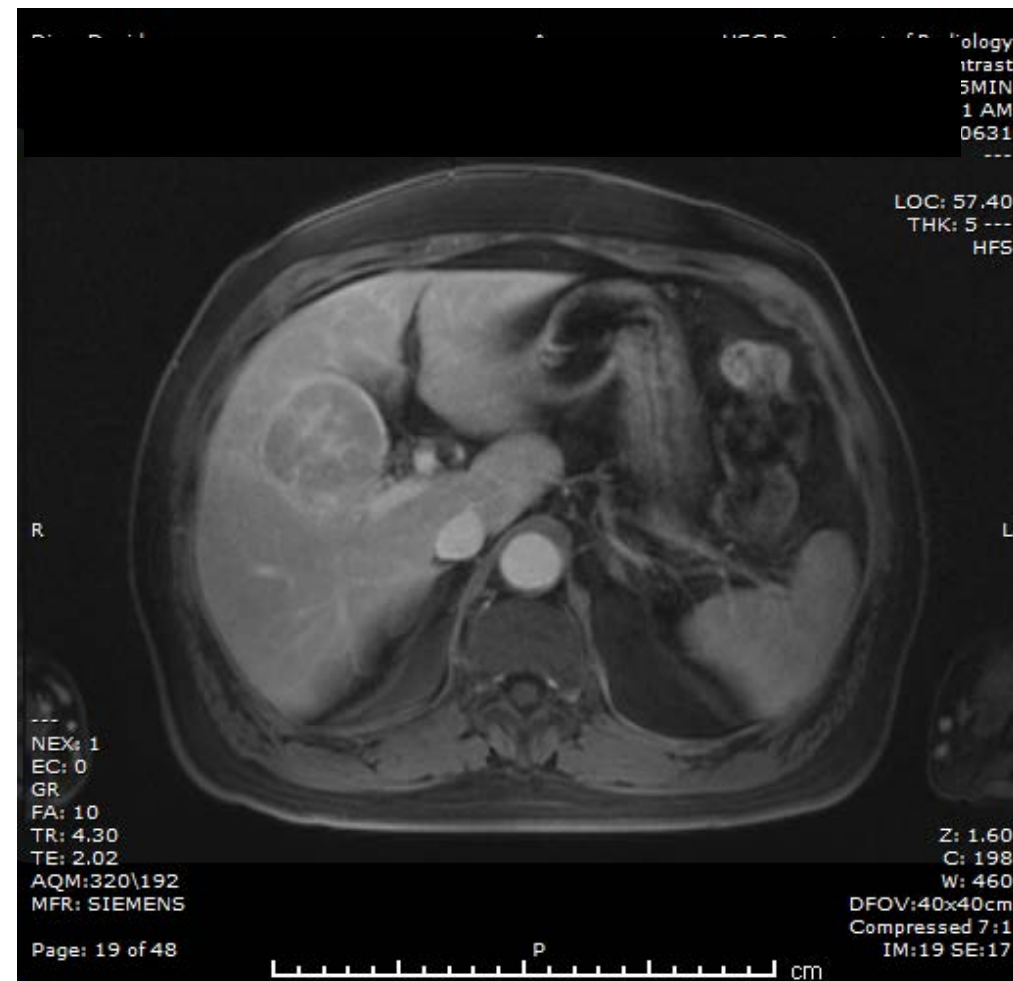
Diagnosis

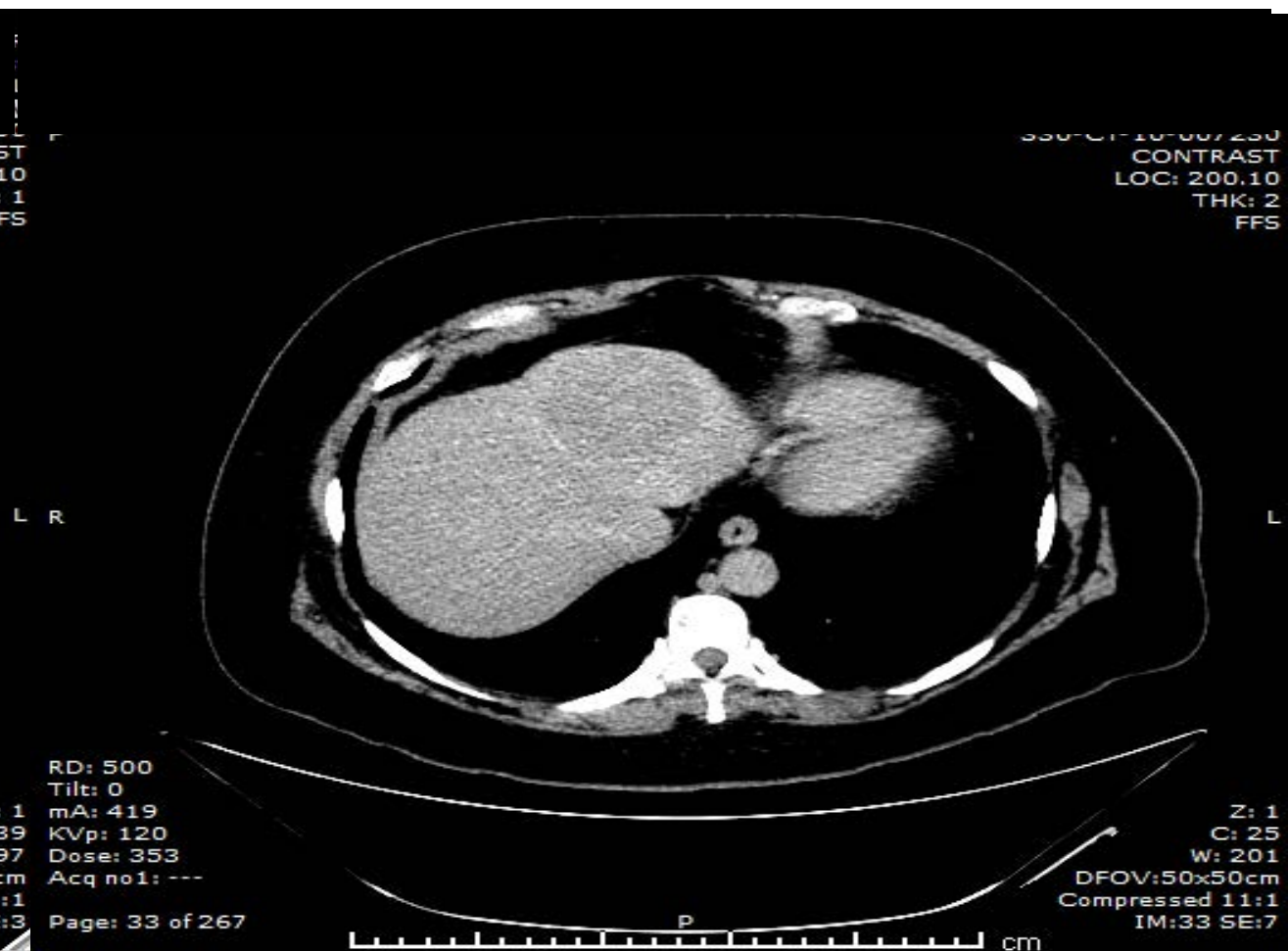
- A typical appearance on a contrast enhanced CT scan or MRI in an at-risk patient is diagnostic
- Often the alfafetoprotein blood test is often elevated
- Sometimes a biopsy is required



Arterial enhancement

Washout





A

USC/NORRIS CANCER
CT Abdomen and Pelvis w + w/o Contrast
ARTERIAL
11/30/2016 11:09:04 AM
330-CT-16-013073
CONTRAST
LOC: 284.10
THK: 2
FFS



RD: 500
Tilt: 0
mA: 267
KVp: 120
Dose: 199
Acq no1: ---

Page: 59 of 145

cm

Z: 1
C: 100
W: 300
DFOV: 50x50cm
Compressed 11:1
IM: 59 SE: 3

A

USC/NORRIS CANCER
CT Abdomen and Pelvis w + w/o Contrast
VENOUS
11/30/2016 11:09:44 AM
330-CT-16-013073
CONTRAST
LOC: 279.10
THK: 2
FFS

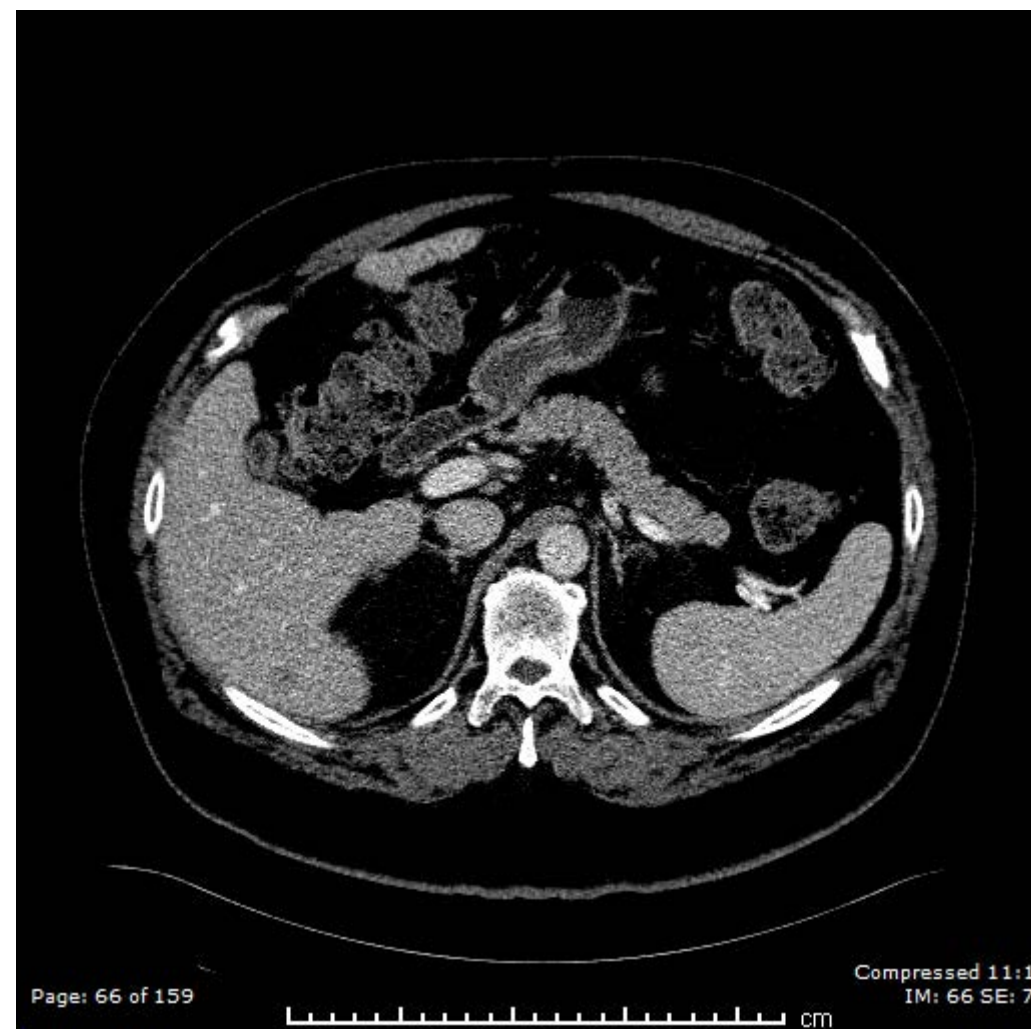
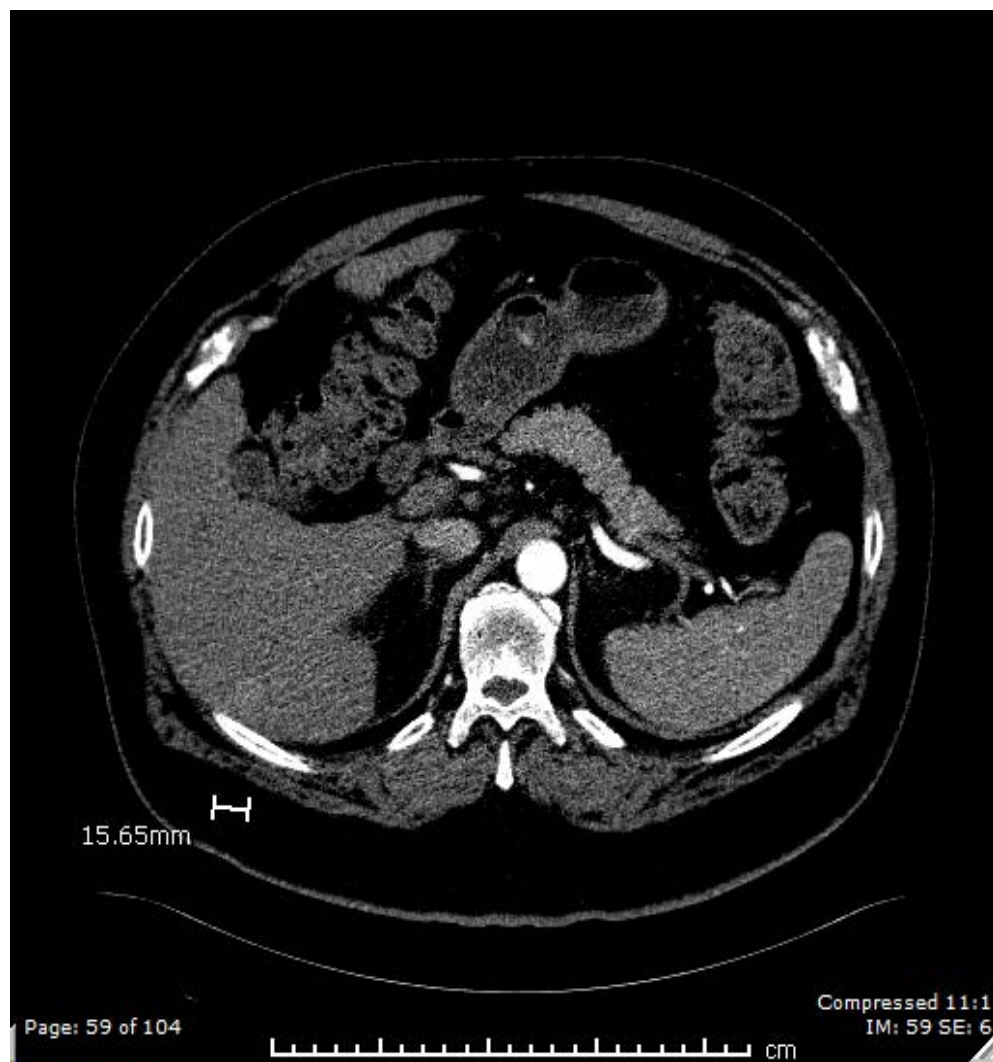


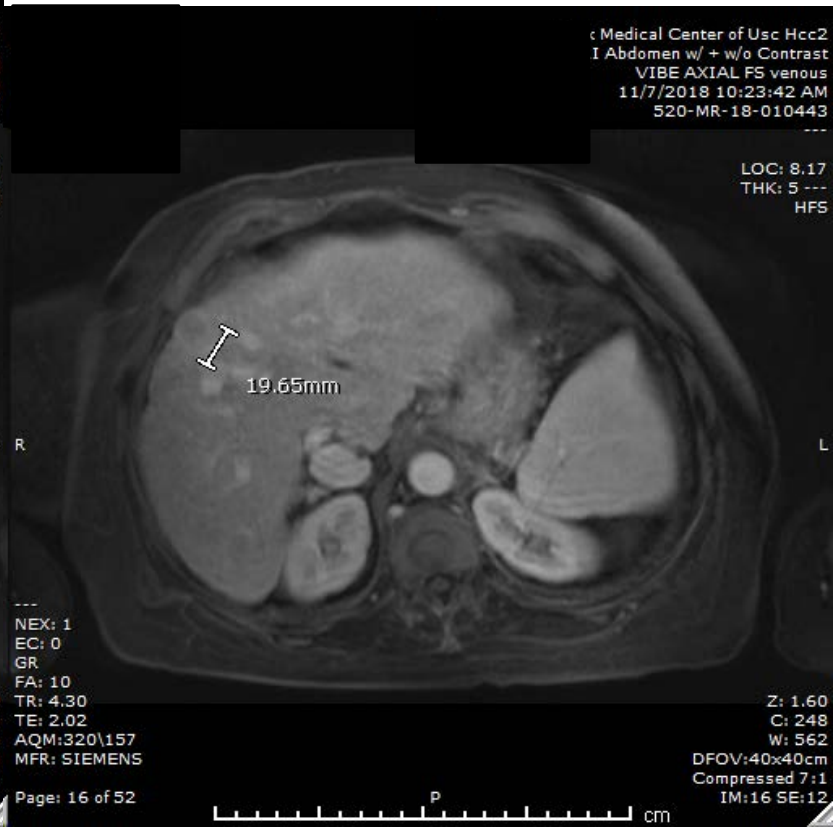
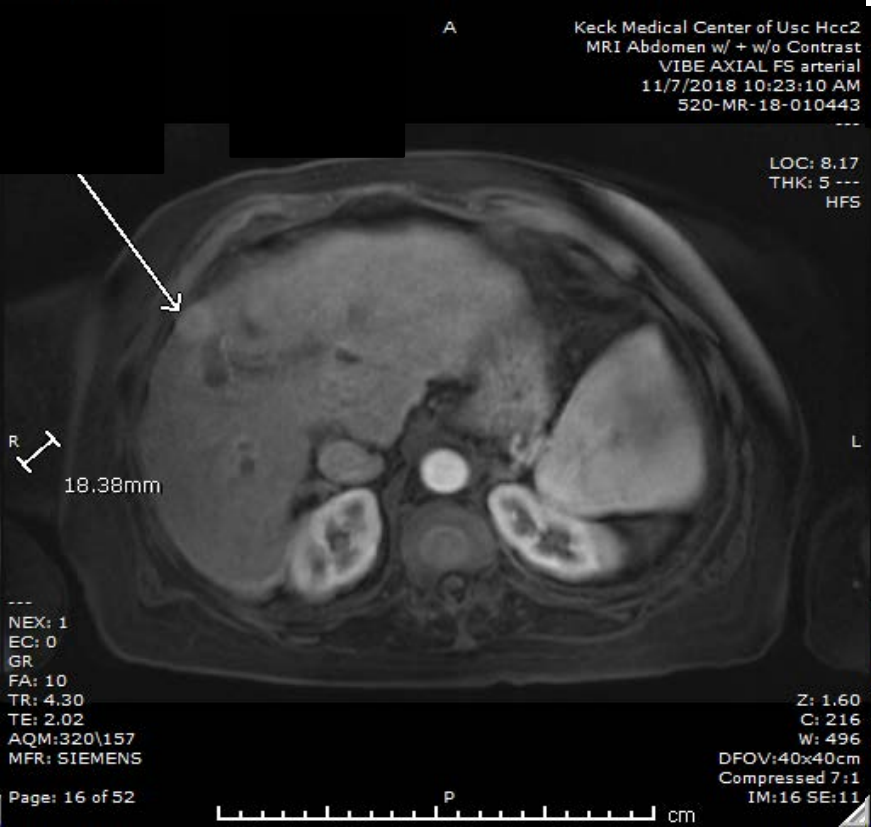
RD: 500
Tilt: 0
mA: 238
KVp: 120
Dose: 200
Acq no1: ---

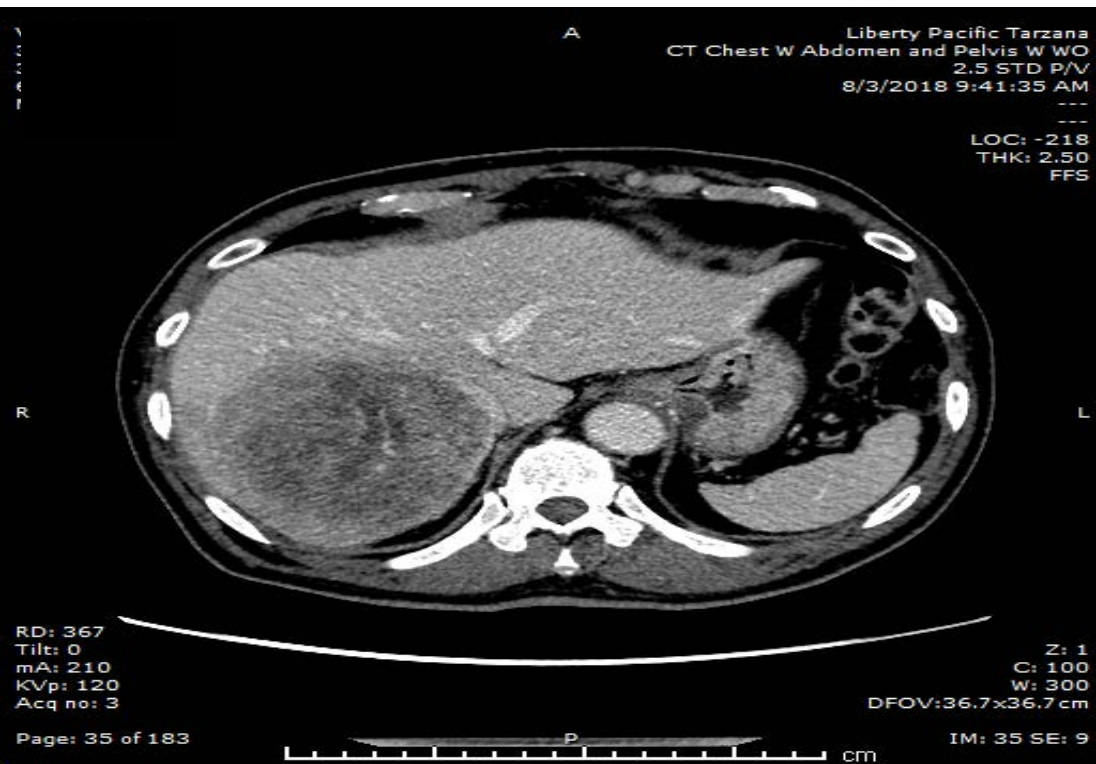
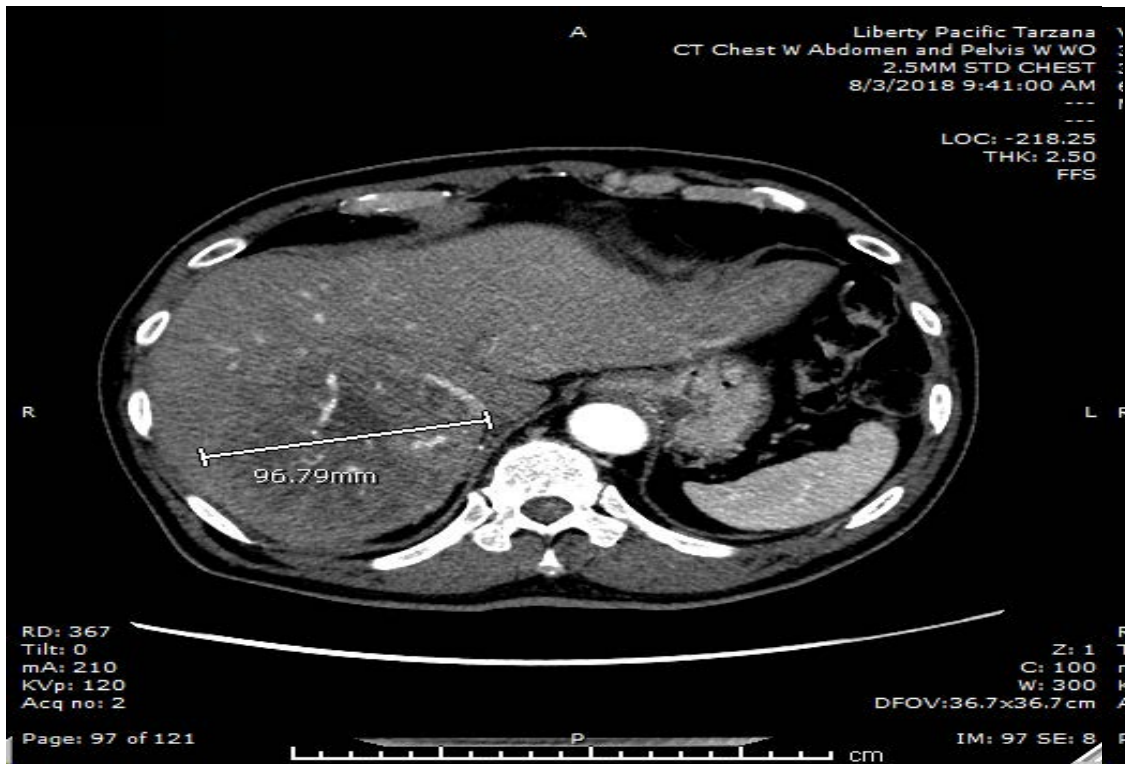
Page: 56 of 250

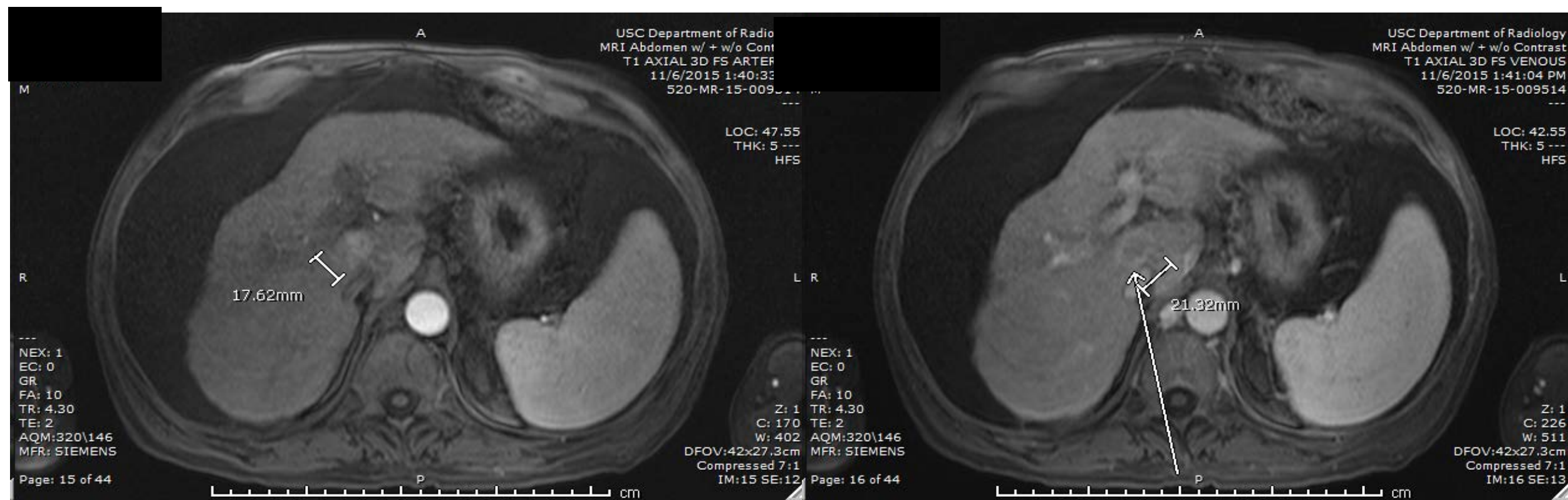
cm

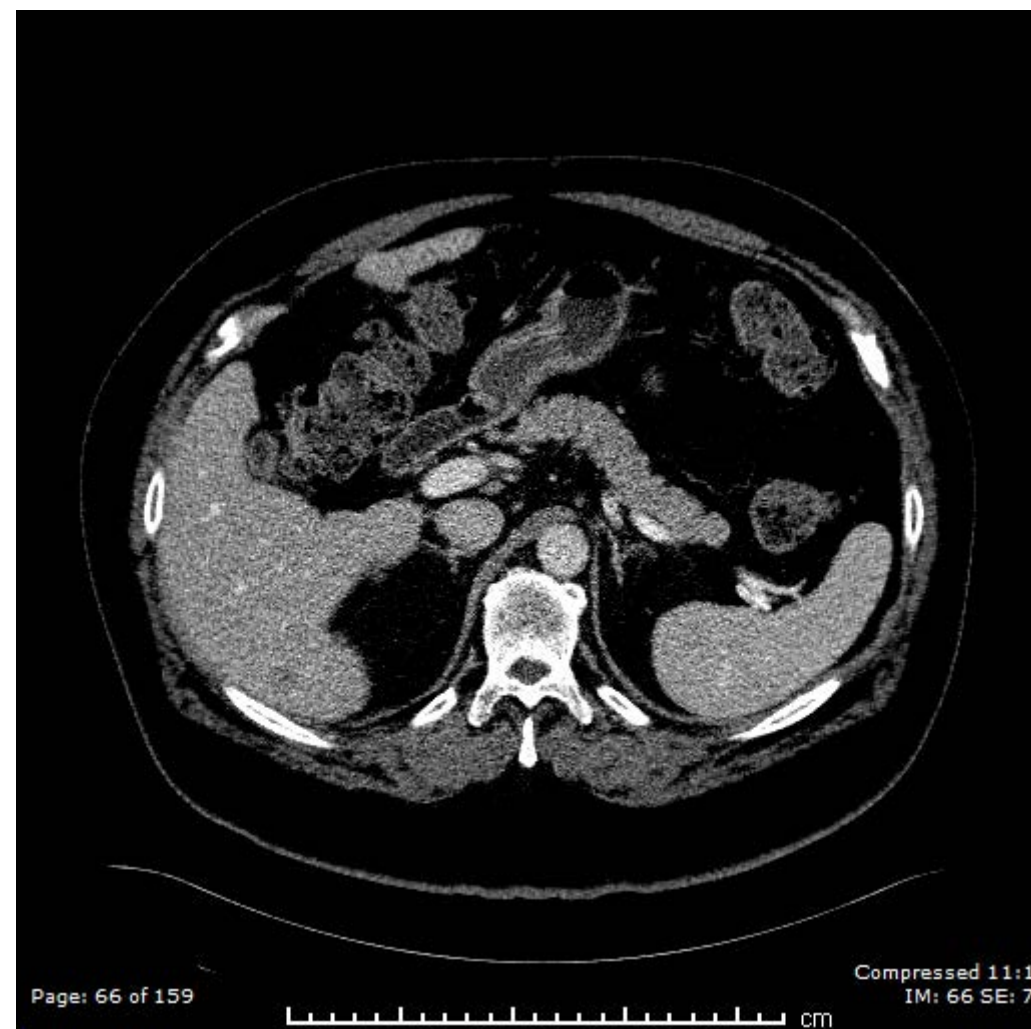
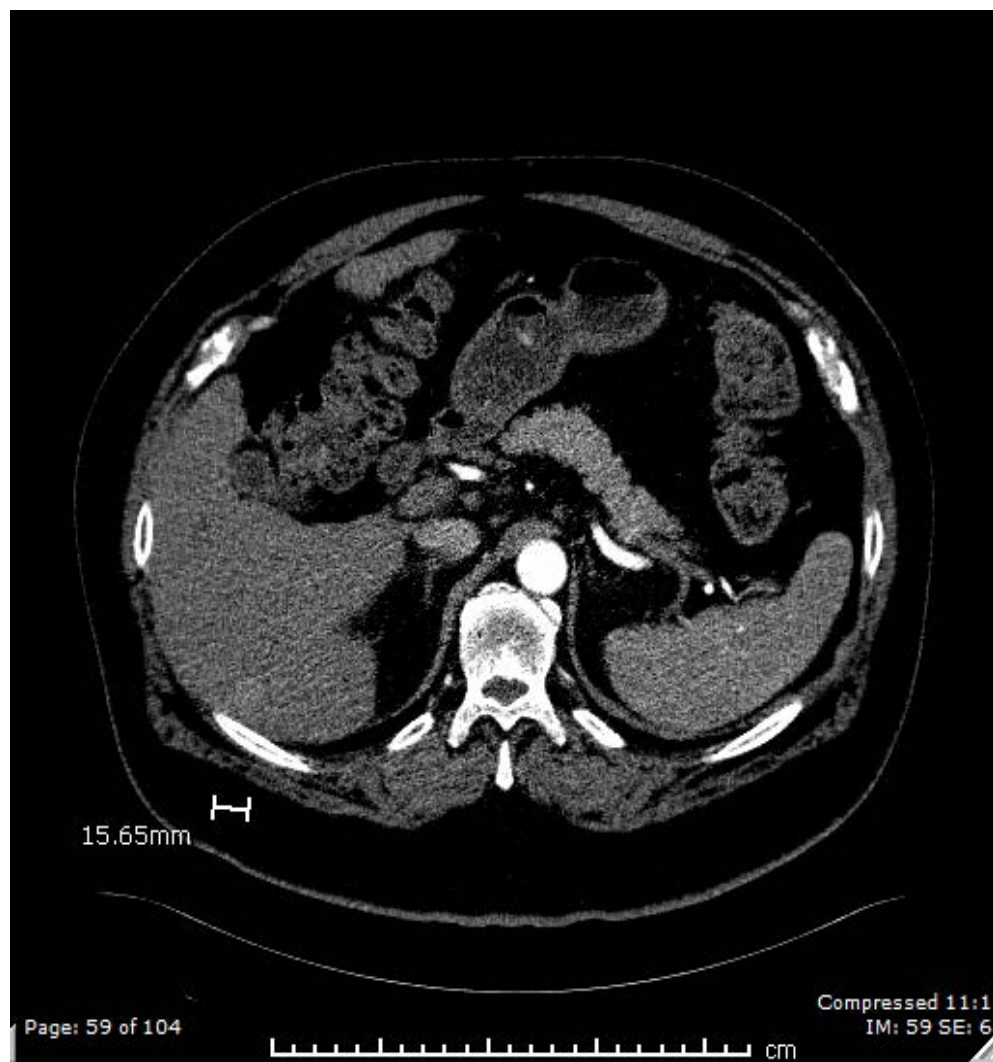
Z: 1
C: 55
W: 426
DFOV: 50x50cm
Compressed 11:1
IM: 56 SE: 5





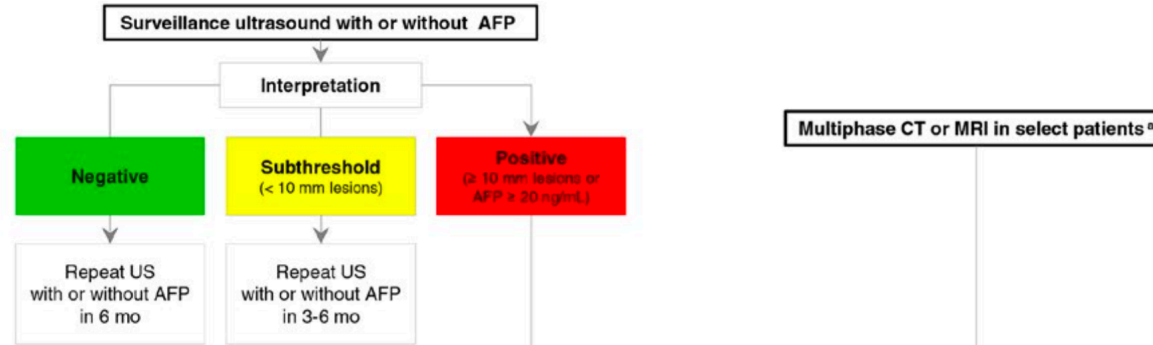




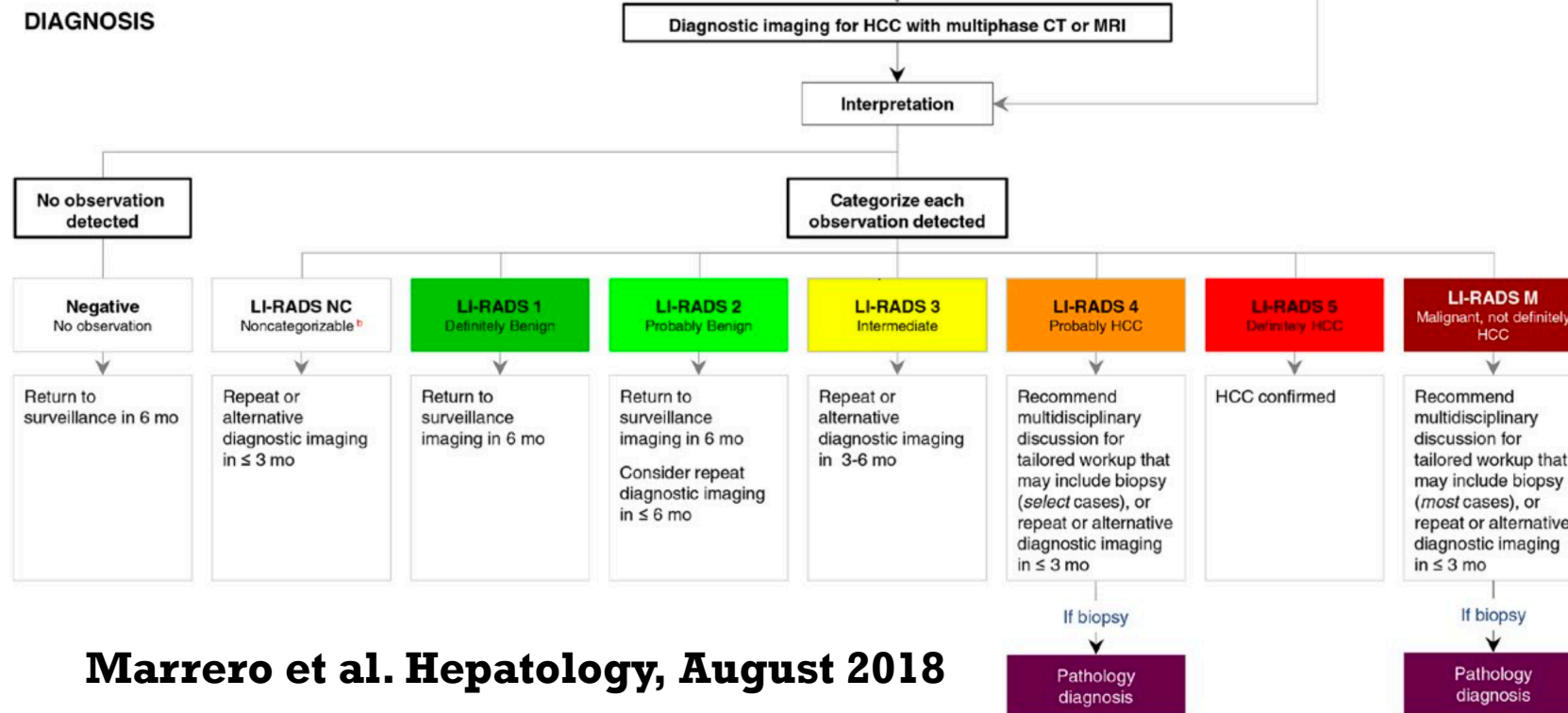


OPTN 5a

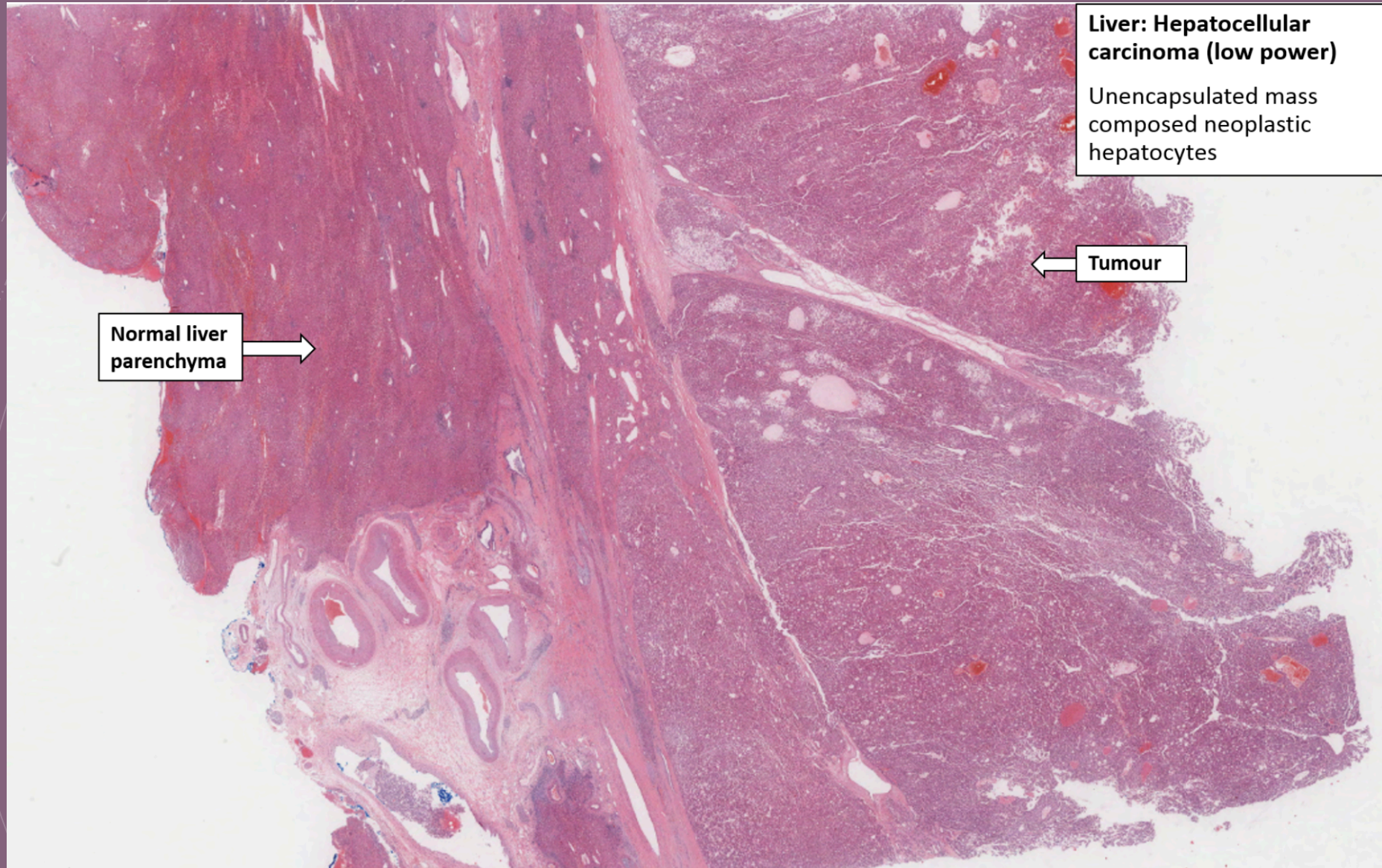
SURVEILLANCE

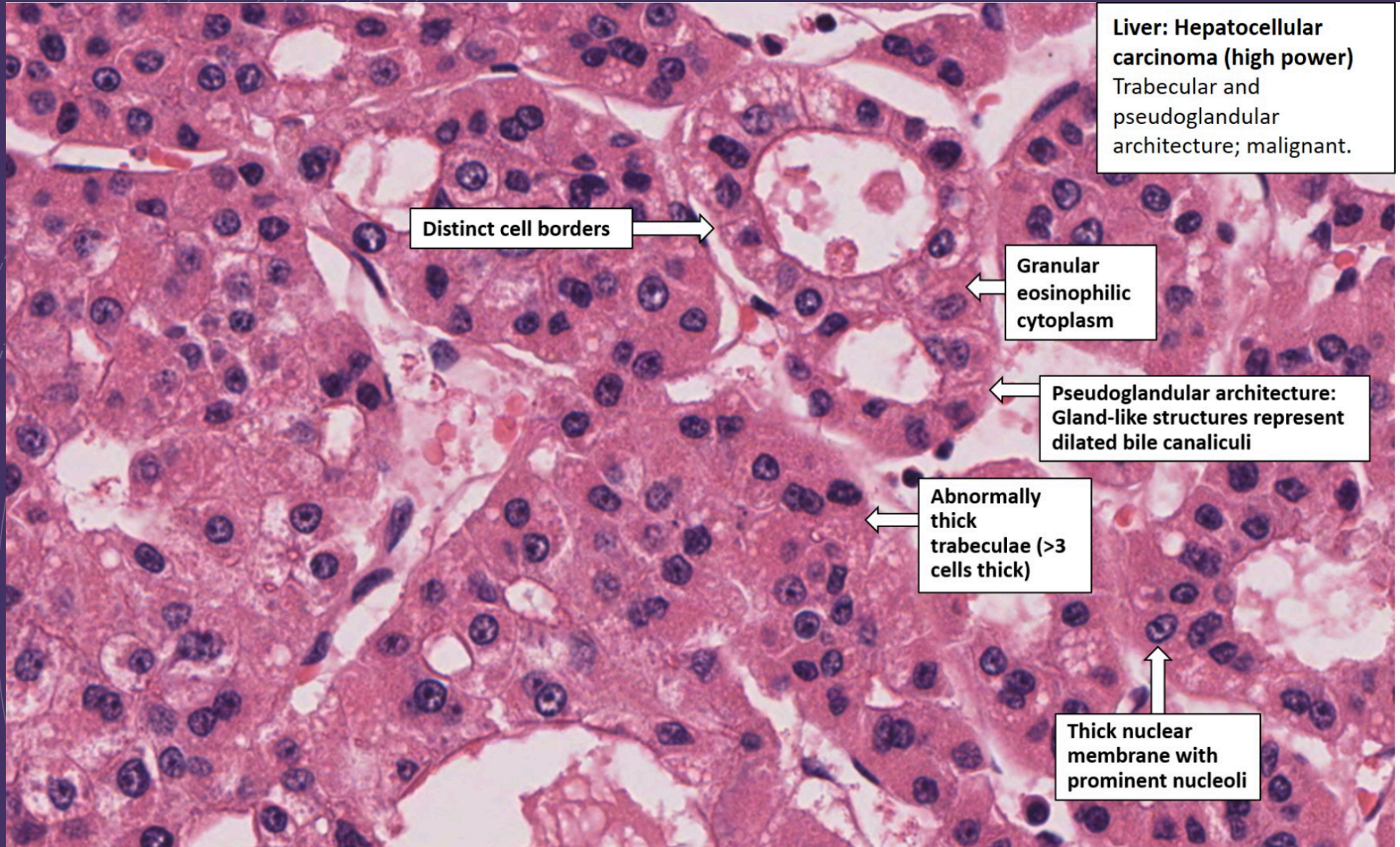


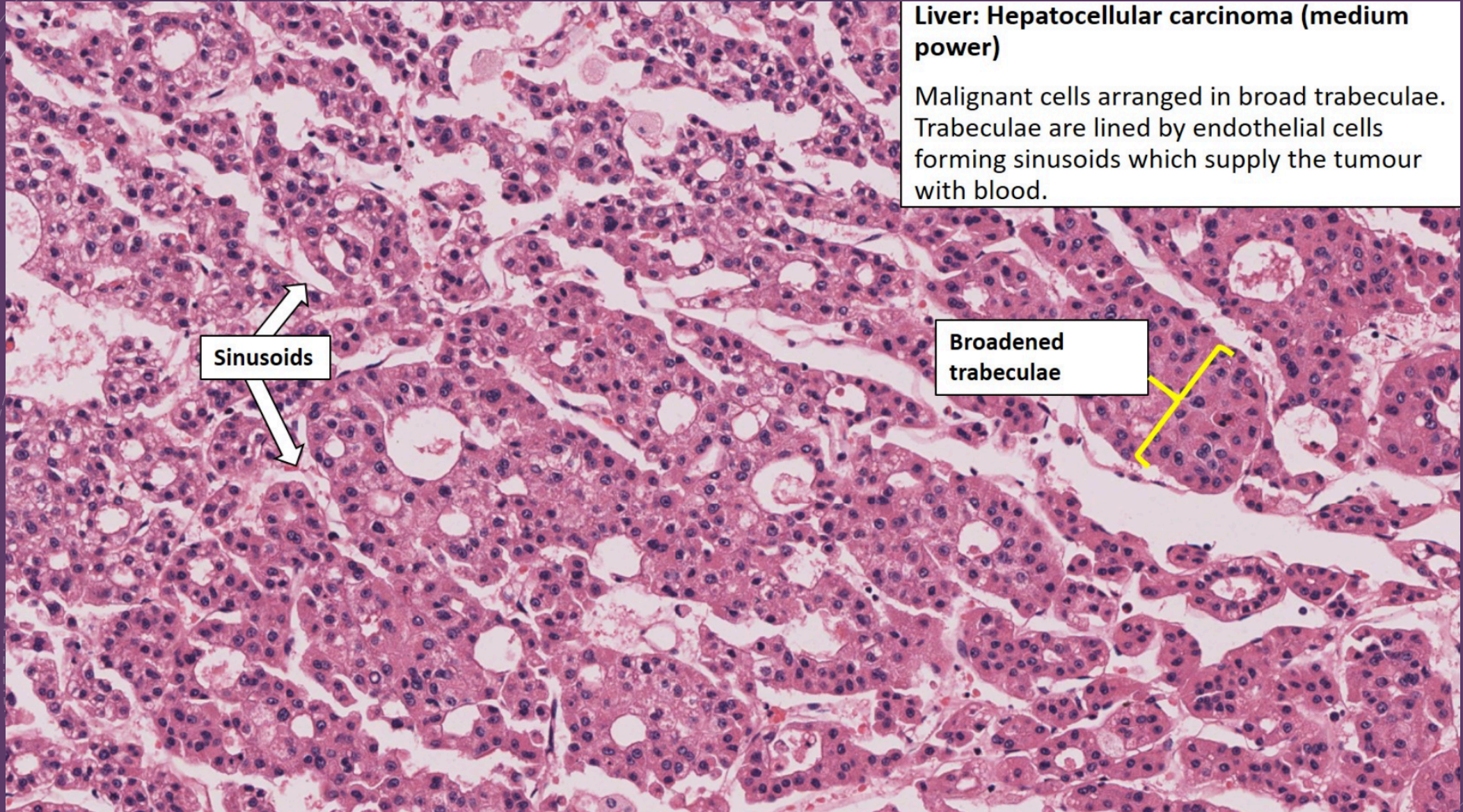
DIAGNOSIS



Marrero et al. Hepatology, August 2018



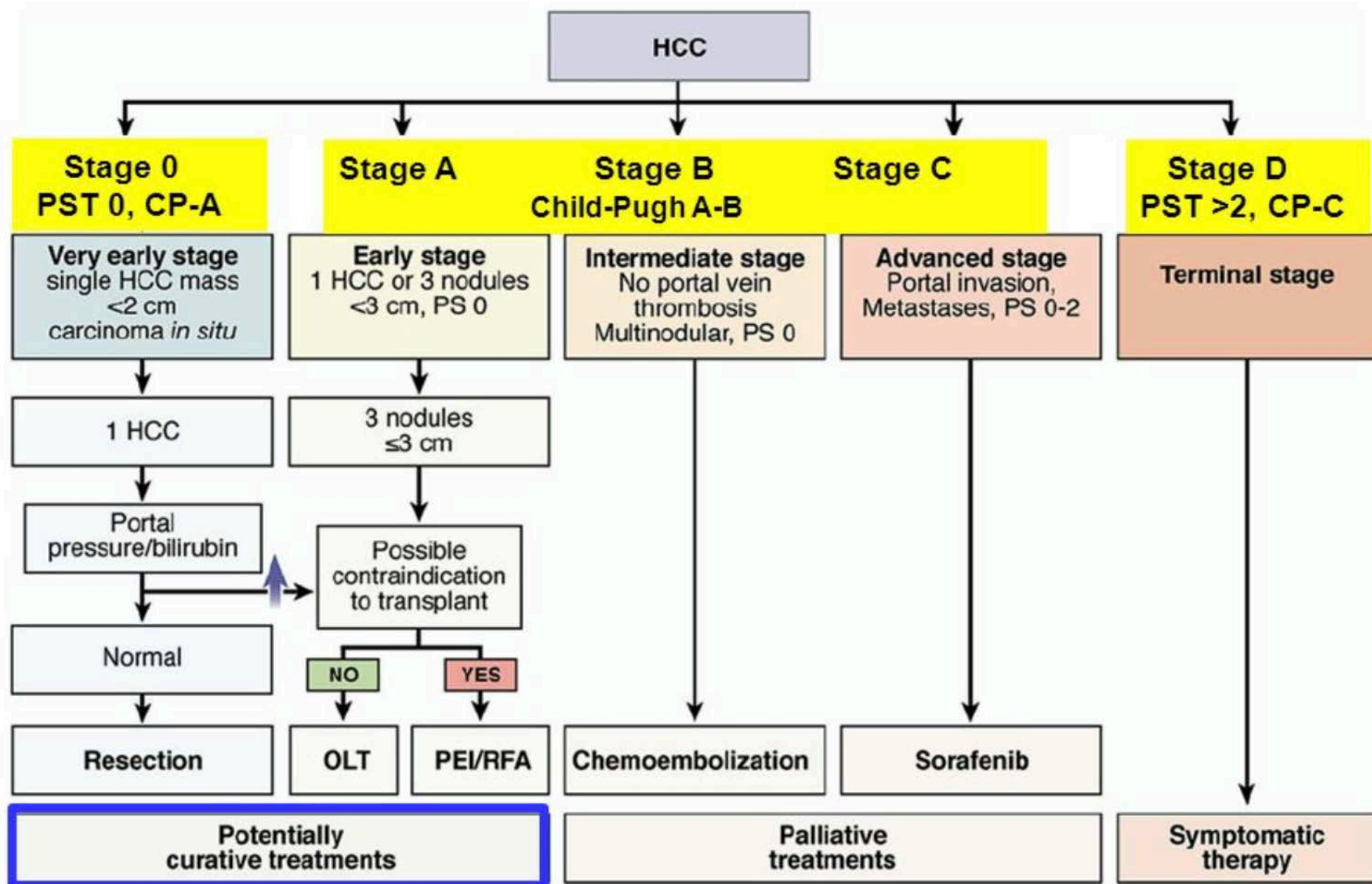




Treatment Decisions

- Functional status
- Liver function/portal hypertension
- Extent of tumor
- Eligibility for liver transplantation

BCLC staging of HCC



ECOG PERFORMANCE STATUS	KARNOFSKY PERFORMANCE STATUS
0—Fully active, able to carry on all pre-disease performance without restriction	100—Normal, no complaints; no evidence of disease 90—Able to carry on normal activity; minor signs or symptoms of disease
1—Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work	80—Normal activity with effort, some signs or symptoms of disease 70—Cares for self but unable to carry on normal activity or to do active work
2—Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours	60—Requires occasional assistance but is able to care for most of personal needs 50—Requires considerable assistance and frequent medical care
3—Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours	40—Disabled; requires special care and assistance 30—Severely disabled; hospitalization is indicated although death not imminent
4—Completely disabled; cannot carry on any selfcare; totally confined to bed or chair	20—Very ill; hospitalization and active supportive care necessary 10—Moribund
5—Dead	0—Dead

*Karnofsky D, Burchenal J, The clinical evaluation of chemotherapeutic agents in cancer. In: MacLeod C, ed. Evaluation of Chemotherapeutic Agents. New York, NY: Columbia University Press; 1949:191–205.

**Zubrod C, et al. Appraisal of methods for the study of chemotherapy in man: Comparative therapeutic trial of nitrogen mustard and thiophosphoramidate. *Journal of Chronic Diseases*; 1960:11:7-33.

Treatment

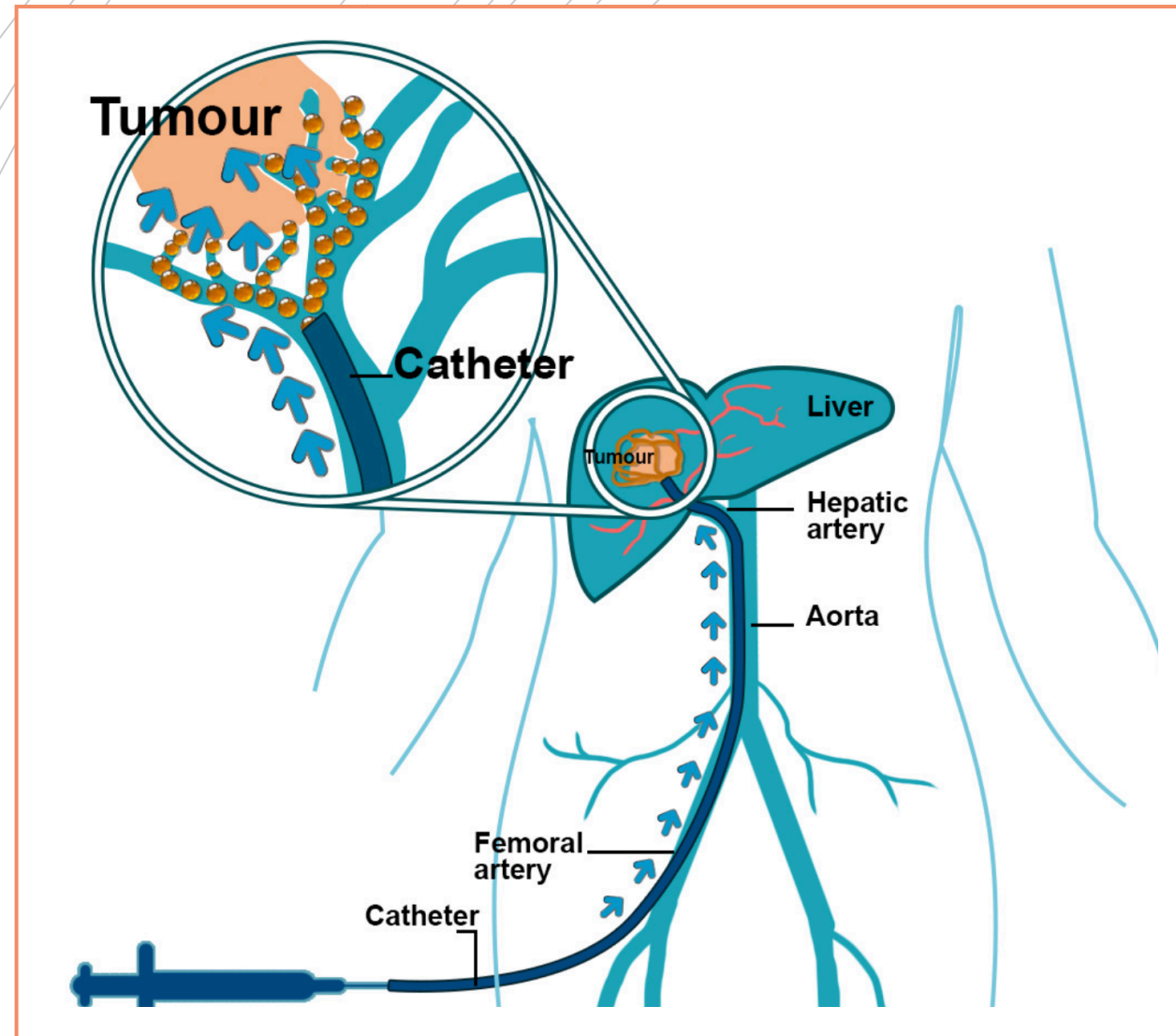
- Resection of the tumor
 - Candidacy depends on
 - Characteristics of the patient (severity of liver disease)
 - Location of the tumor
 - Involvement of blood vessels or spread outside of the liver
 - Whether multiple parts of the liver are involved
- Liver transplantation

The background of the slide features several thin, curved lines in a light gray color, some solid and some dashed, creating a sense of motion or a stylized globe. A large red speech bubble is positioned on the left side, containing the main title.

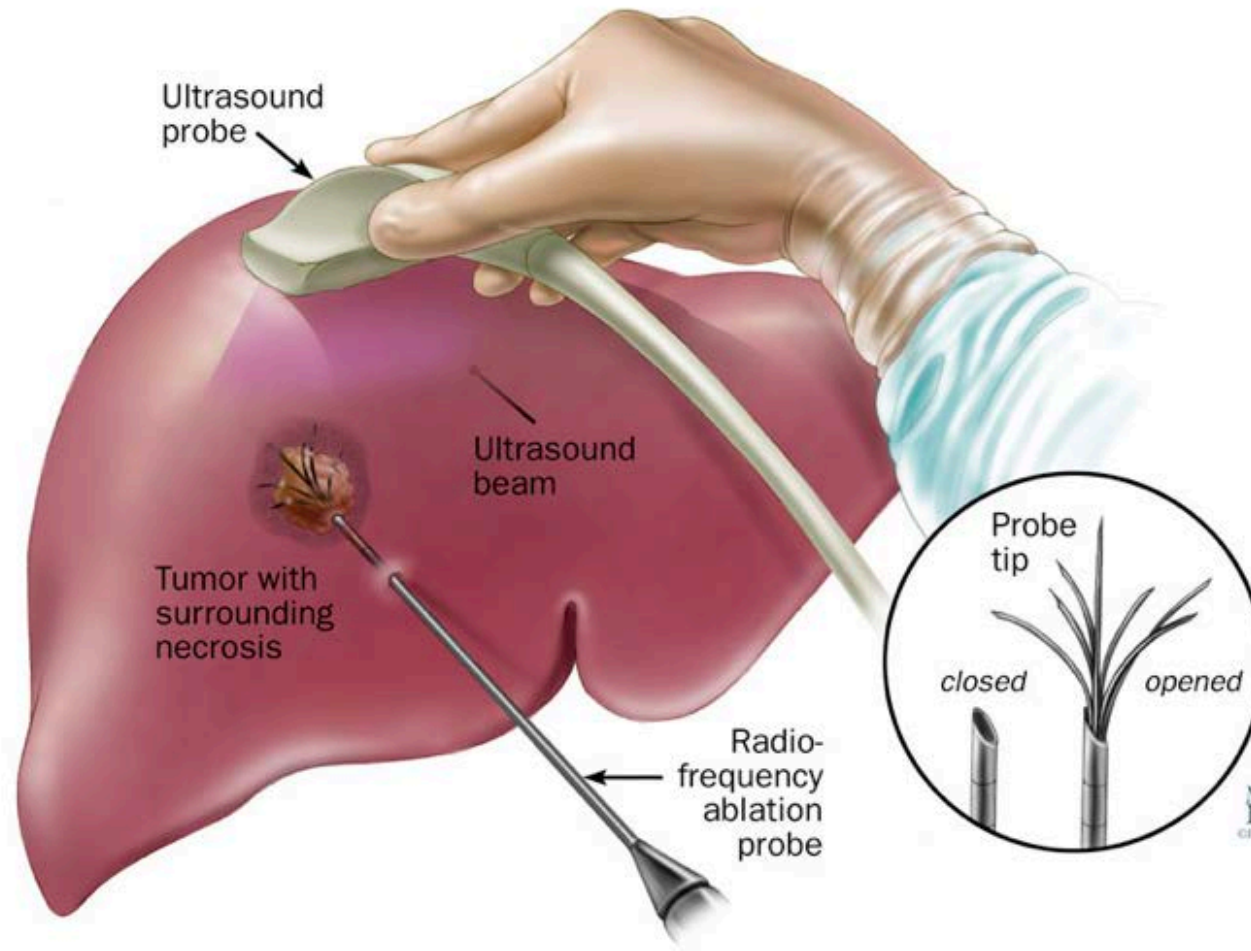
Loco-ablative and locoregional therapies

- TACE
- RFA/MWA
- Y-90
- SBRT

TACE





<http://deliver.iut-auvergne.com>



*Radiofrequency ablation (RFA) in liver cancer
(hepatocellular carcinoma)*

<https://southfloridasurgicaloncology.com/liver-tumor-ablation/>

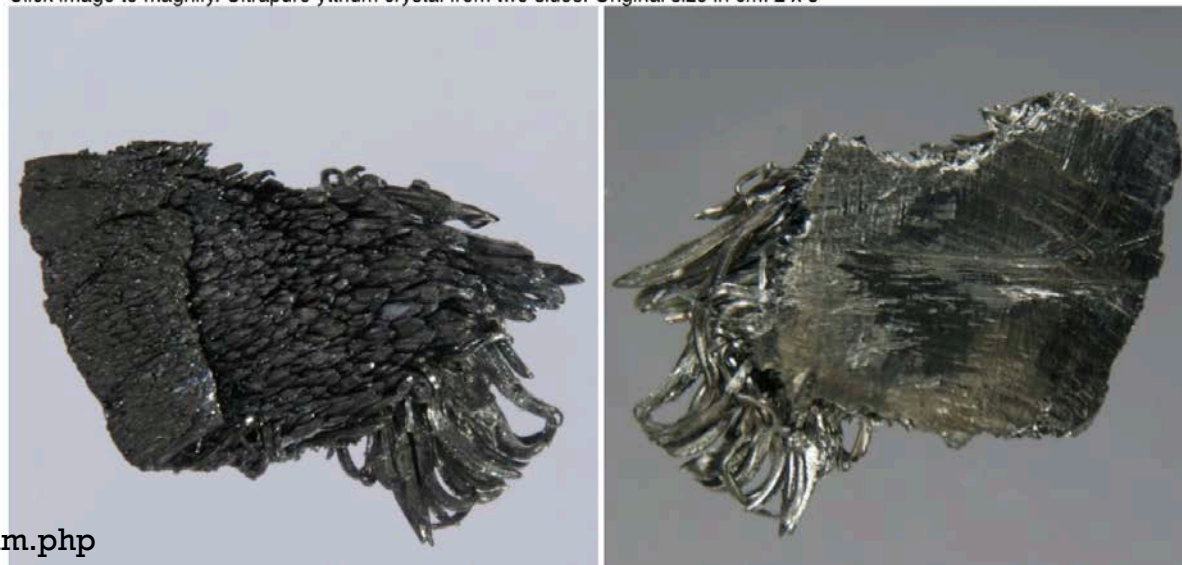
1 H .	2 He .																						
3 Li ...	4 Be ...																	5 B ...	6 C ...	7 N .	8 O .	9 F .	10 Ne .
11 Na ...	12 Mg ...																	13 Al ...	14 Si ...	15 P ...	16 S ...	17 Cl .	18 Ar .
19 K ...	20 Ca ...	21 Sc ...	22 Ti ...	23 V ...	24 Cr ...	25 Mn ...	26 Fe ...	27 Co ...	28 Ni ...	29 Cu ...	30 Zn ...	31 Ga ...	32 Ge ...	33 As ...	34 Se ...	35 Br ..	36 Kr .						
37 Rb ...	38 Sr ...	39 Y ...	40 Zr ...	41 Nb ...	42 Mo ...	43 Tc ...	44 Ru ...	45 Rh ...	46 Pd ...	47 Ag ...	48 Cd ...	49 In ...	50 Sn ...	51 Sb ...	52 Te ...	53 I ...	54 Xe .						
55 Cs ...	56 Ba ...	57-71 La-Lu ...	72 Hf ...	73 Ta ...	74 W ...	75 Re ...	76 Os ...	77 Ir ...	78 Pt ...	79 Au ...	80 Hg ..	81 Tl ...	82 Pb ...	83 Bi ...	84 Po ...	85 At ...	86 Rn .						
87 Fr ...	88 Ra ...	89-103 Ac-Lr ...	104 Rf ...	105 Db ...	106 Sg ...	107 Bh ...	108 Hs ...	109 Mt ...	110 Ds ...	111 Rg ...	112 Cn ...	113 Nh ...	114 Fl ...	115 Mc ...	116 Lv ...	117 Ts ...	118 Og ...						
Home Random All , All2 , Mosaic Concentration game Knowledge Element properties Records, Archives		57 La ...	58 Ce ...	59 Pr ...	60 Nd ...	61 Pm ...	62 Sm ...	63 Eu ...	64 Gd ...	65 Tb ...	66 Dy ...	67 Ho ...	68 Er ...	69 Tm ...	70 Yb ...	71 Lu ...							
		89 Ac ...	90 Th ...	91 Pa ...	92 U ...	93 Np ...	94 Pu ...	95 Am ...	96 Cm ...	97 Bk ...	98 Cf ...	99 Es ...	100 Fm ...	101 Md ...	102 No ...	103 Lr ...							
Particle Zoo  AdChoices		earth rod					virtual earth					yttrium metal					Advertisement						

↑ ← 39 → ↓

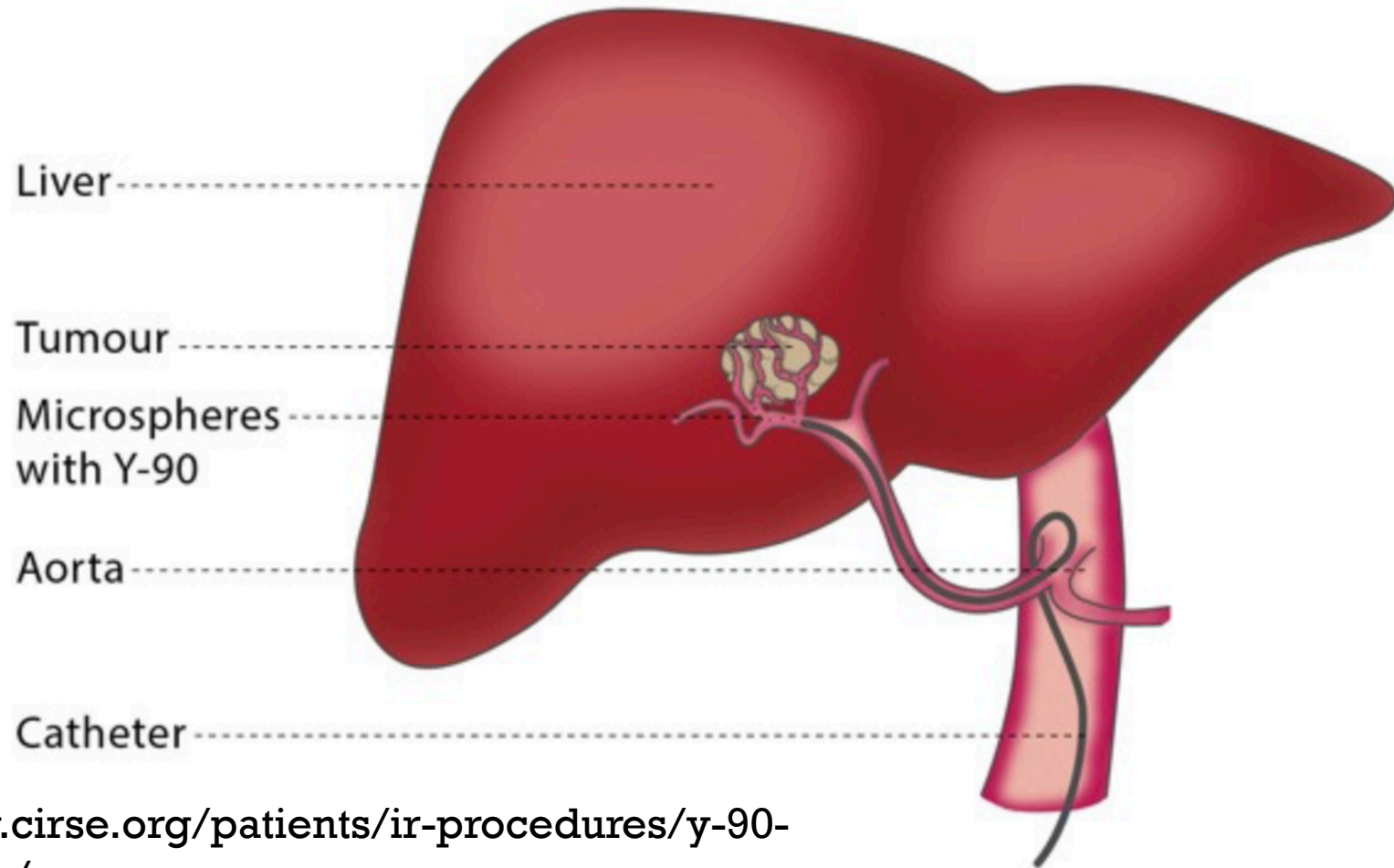
39 Y Yttrium

Transition metal, mass: 88.906 u, 1 stable isotope (89), abundance rank (earth/space): 32/42

Click image to magnify. Ultrapure yttrium crystal from two sides. Original size in cm: 2 x 3



Y-90 embolisation



<https://www.cirse.org/patients/ir-procedures/y-90-embolisation/>

The background features a series of concentric circles in light gray, some solid and some dashed, creating a ripple effect. A large, solid red speech bubble is centered on the page, pointing downwards. The text "Liver Transplantation" is written in white inside the bubble.

Liver Transplantation

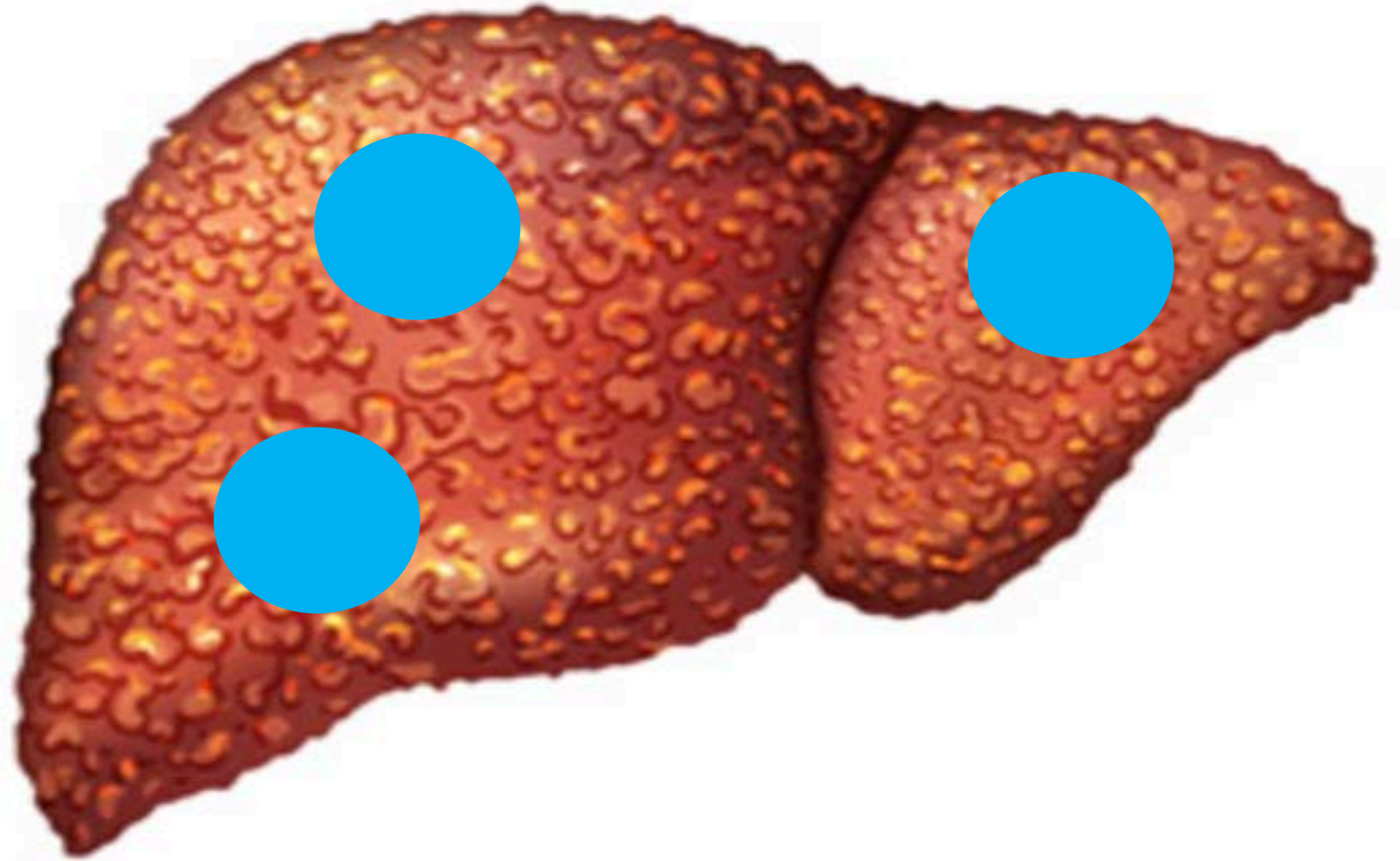
Transplant Considerations

- Time on the waitlist
- AFP
 - >500 bad biology
- Stage

Transplant Criteria

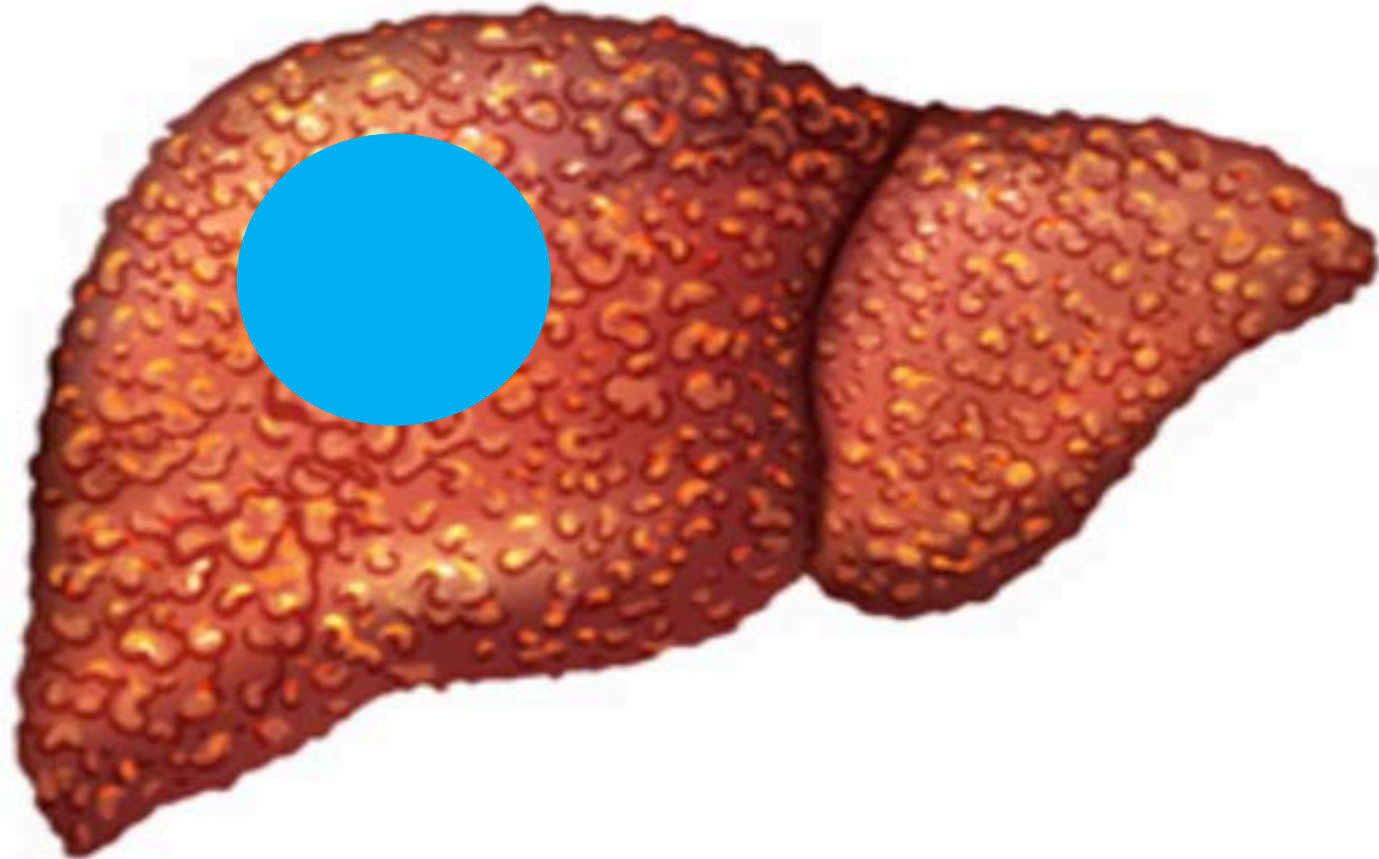
- Milan
 - Given transplant priority
- UCSF
 - No priority but reasonable outcomes if transplanted
- UCSF Downstaging

Milan Criteria



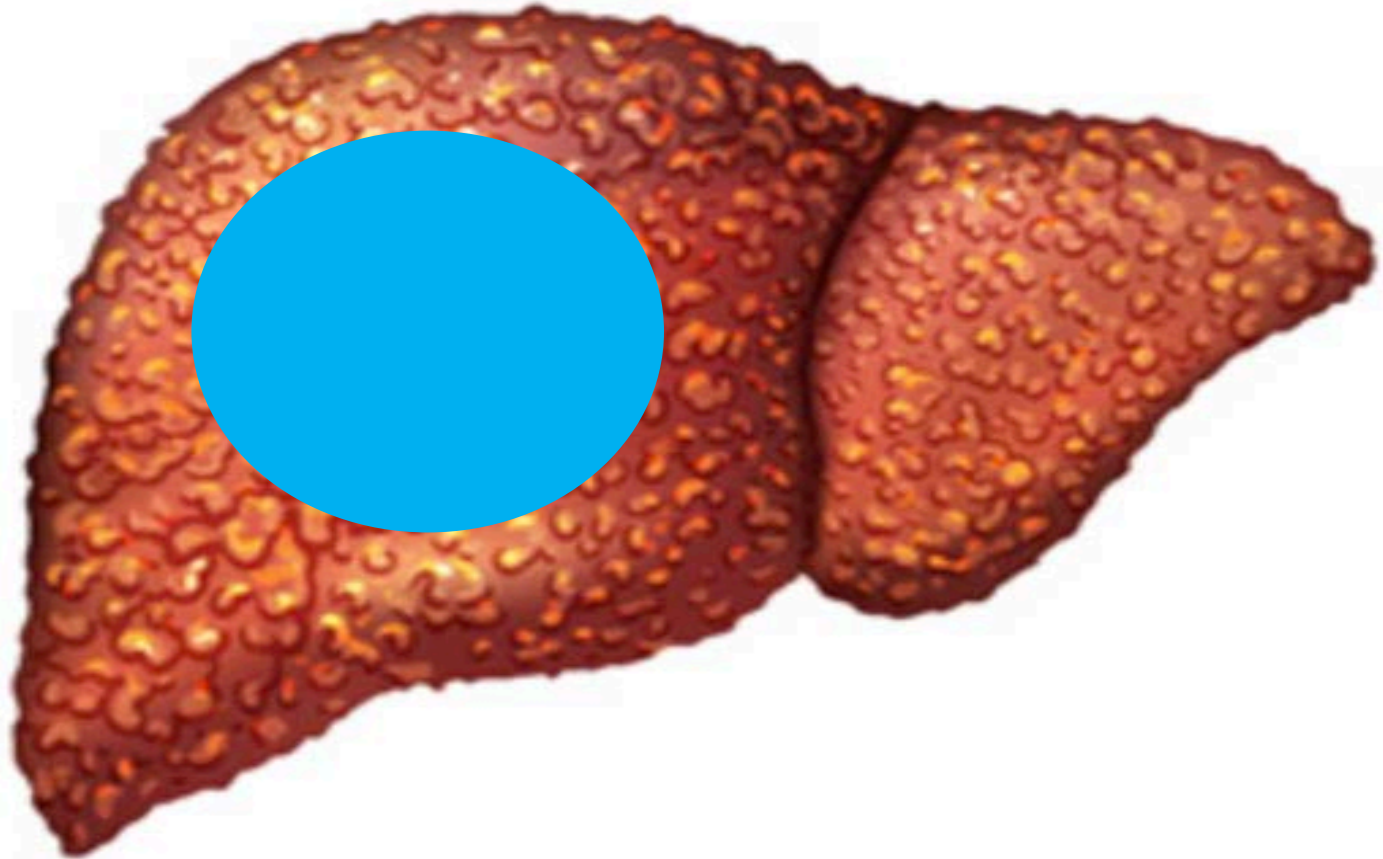
Up to three lesions none over 3 cm

OR



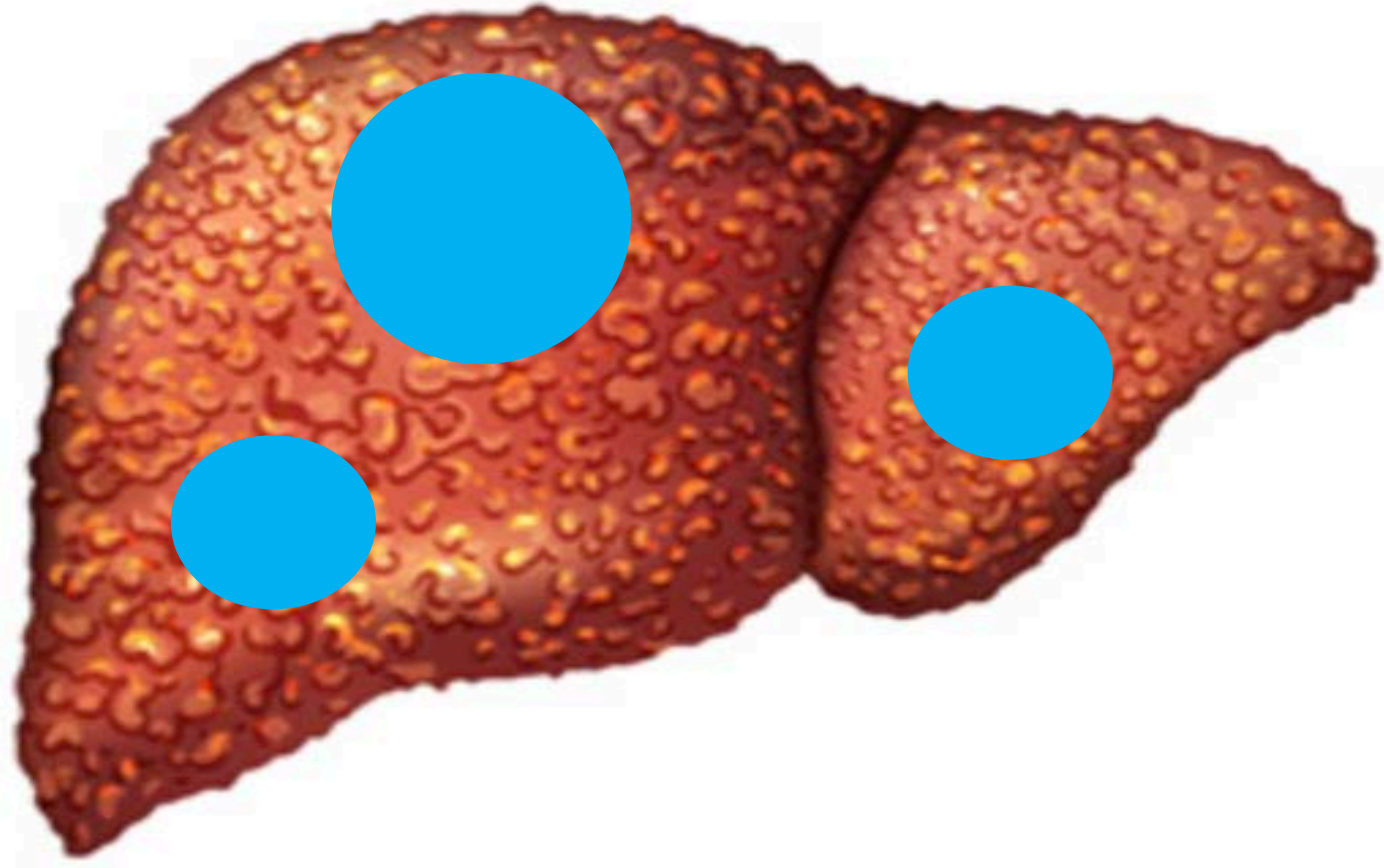
One lesion up to 5 cm

UCSF Criteria



1 lesion up to 6.5 cm

Or



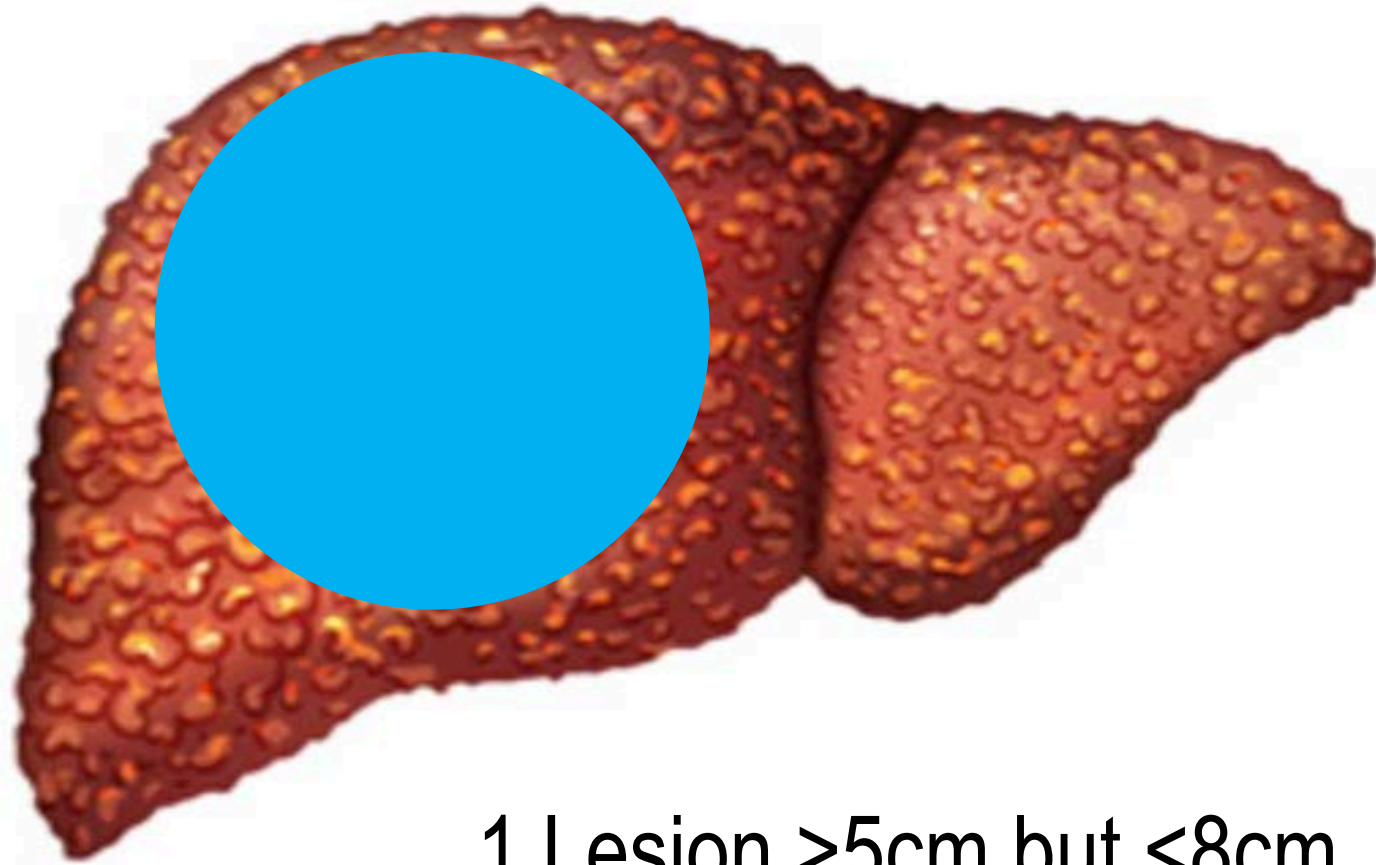
Up to 3 lesions, none >4.5 cm, aggregate diameter up to 8 cm

If explant exceeded pre-OLT imaging, 1-year survival 50%

Yao F, Roberts J. Liver Transplantation 2004

UCSF Downstaging Criteria

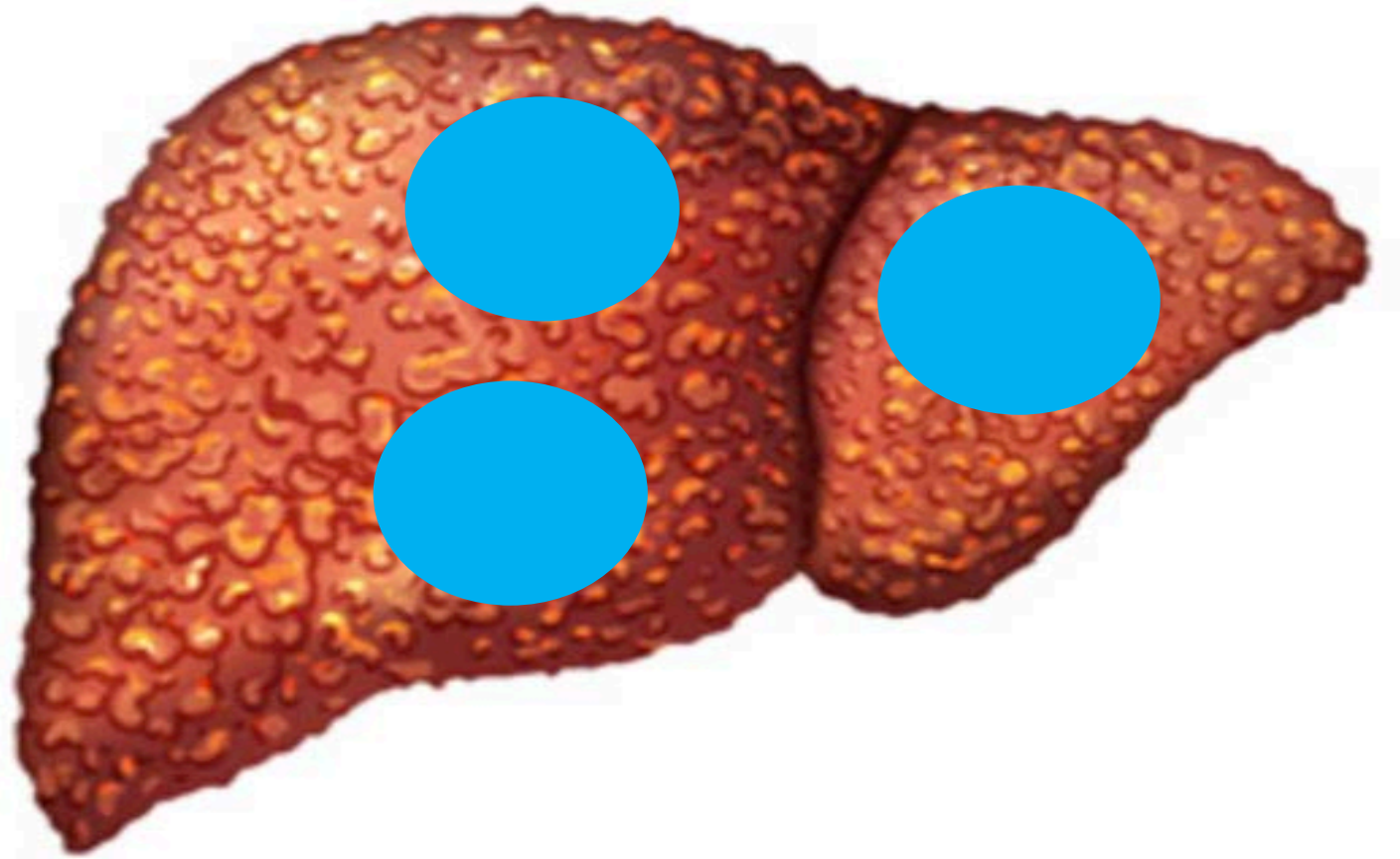
Downstage to Milan, allowing for a MELD exception



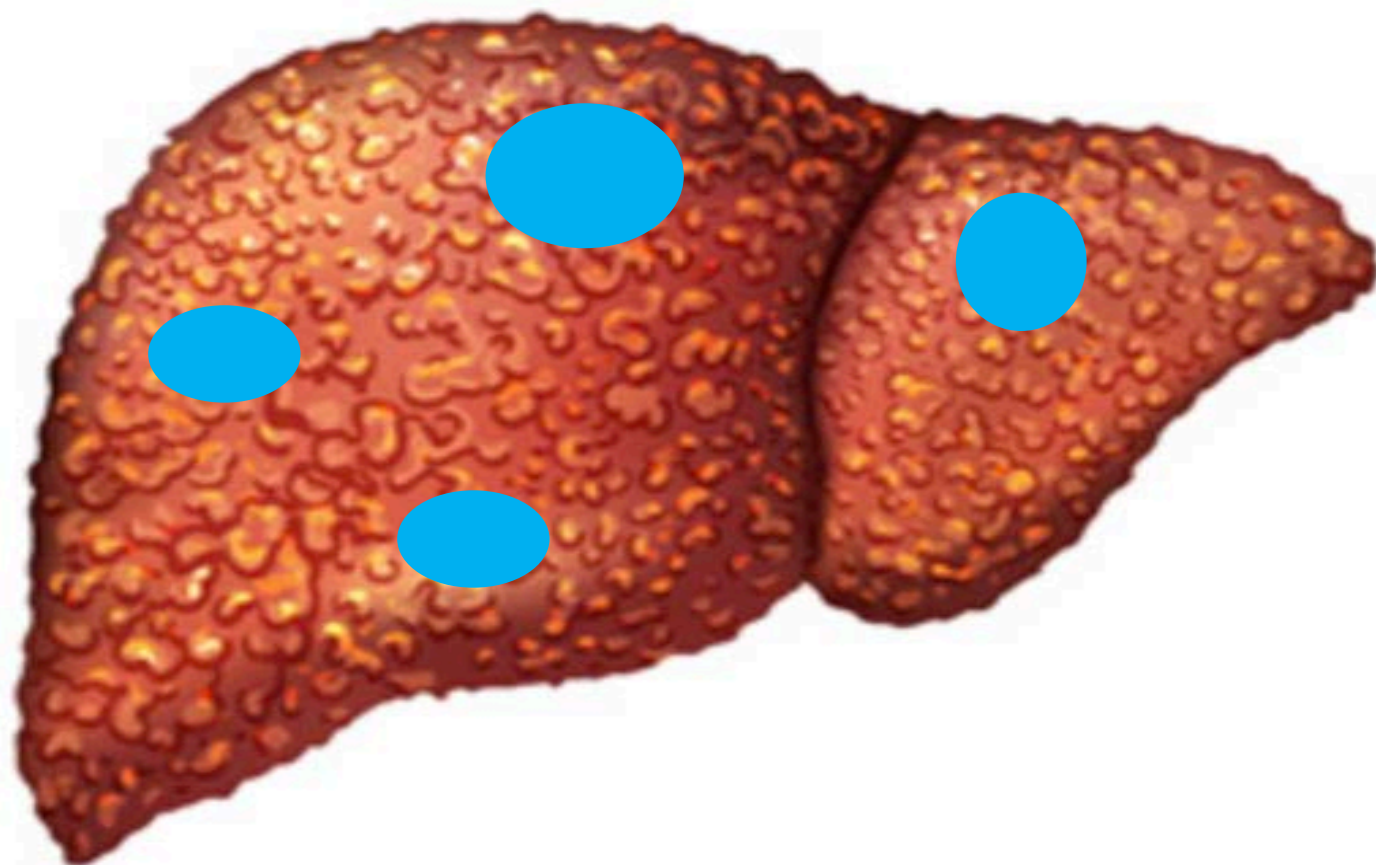
1 Lesion $>5\text{cm}$ but $\leq 8\text{cm}$

Or

2 or 3 Lesions @ least 1 $>3\text{cm}$ $\geq 5\text{cm}$, total diameter $\leq 8\text{cm}$



Or 4-5 lesions, all $\leq 3\text{cm}$, total diameter $\leq 8\text{cm}$



Maintaining Transplant Eligibility

- Scans every 3 months
- Treating lesions if they show tumor viability
- Staying within Milan criteria and keeping AFP ≤ 500

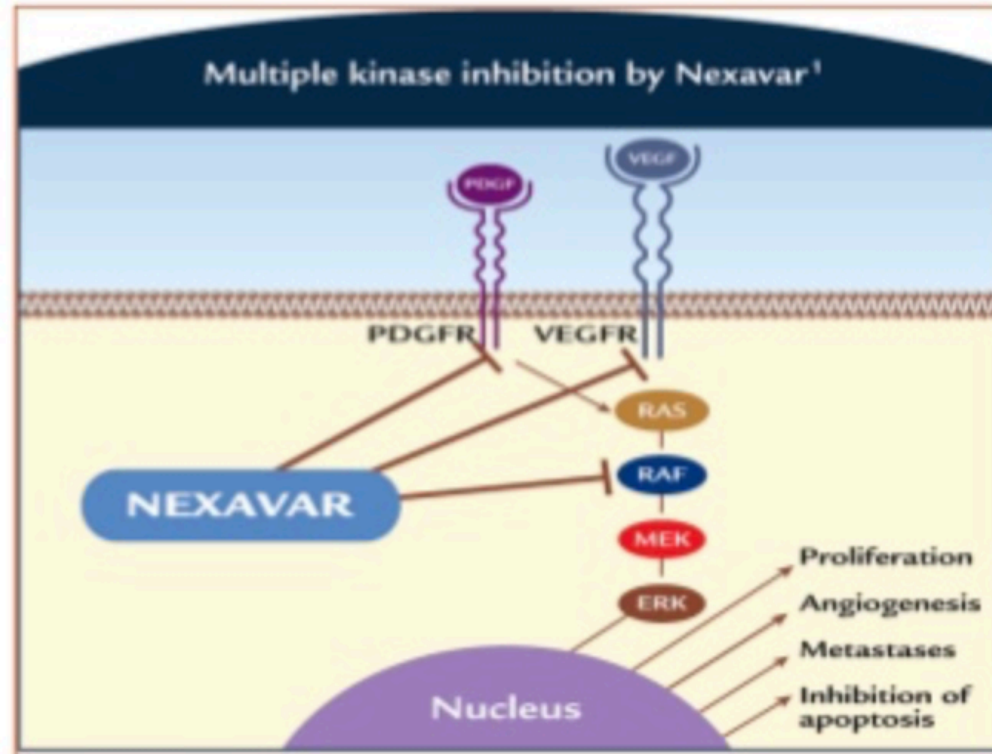
Advanced Disease

- **Systemic therapies**

- **Nexavar (sorafenib, regorafenib, lenvatinib)**
 - Oral multikinase inhibitor of the vascular endothelial growth factor receptor, the platelet-derived growth factor receptor, and Raf may be effective in hepatocellular carcinoma.
- **Parenteral: Opdivo (nivolumab)**

Sorafenib mechanism of action

oral multikinase inhibitor which suppresses tumor cell proliferation and angiogenesis,



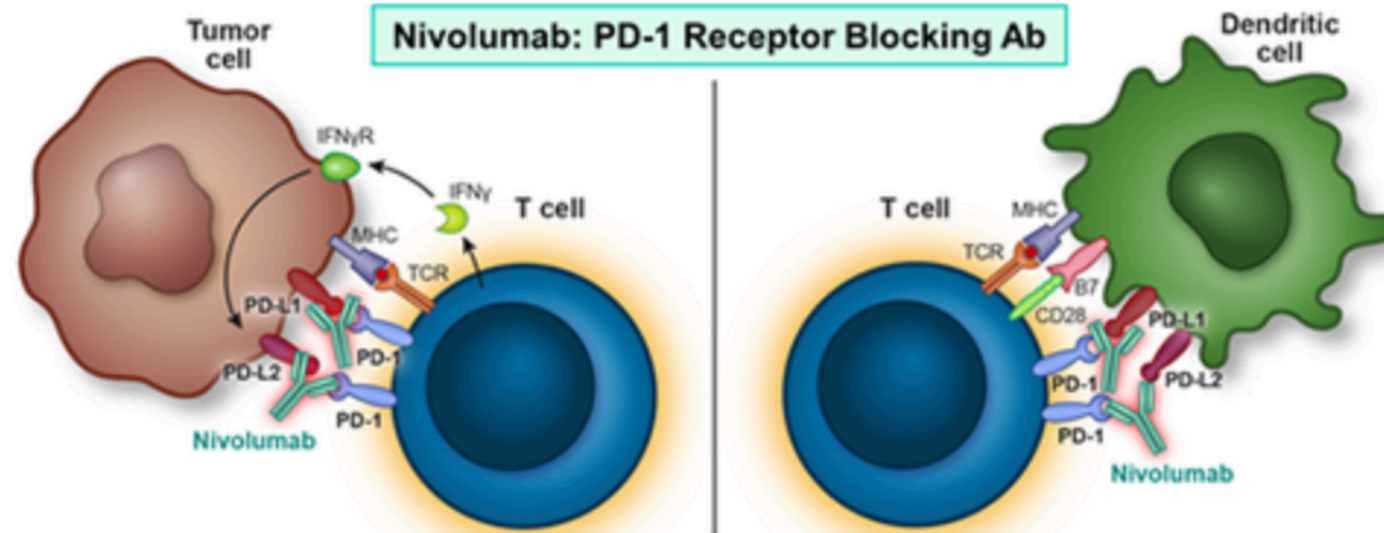
Side Effects

- diarrhea, stomach pain, loss of appetite, weight loss;
- fever, infection;
- abnormal liver function tests;
- mouth or throat pain, hoarse voice; or
- feeling weak or tired.
- vomiting, diarrhea, nausea,
- HTN
- Rash
- Hand-foot reaction

Nivolumab

Mechanism of Action

- Binding of PD-1 to its ligands PD-L1 and PD-L2 leads to downregulation of the antitumor immune response^a
- Nivolumab is a fully human IgG4 PD-1 immune checkpoint inhibitor
- Nivolumab selectively blocks the PD-1 and PD-L1/PD-L2 interaction, restoring antitumor T-cell function^{a-d}



a. Hamid O, Carvajal RD. *Exp Opin Biol Ther*. 2013;13:847-861^[34]; b. Brahmer JR, et al. *J Clin Oncol*. 2010;28:3167-3175^[41]; c. Nuriyeva RI, et al. *Immunol Rev*. 2011;241:133-144^[42]; d. Hamanishi J, et al. *Proc Natl Acad Sci USA*. 2007;104:3360-3365.^[43]

Side Effects

- Enterocolitis
- Hepatitis
- Dermatitis
- Pneumonitis
- Neuropathies
- Endocrinopathies

Questions

- What are the classic contrast imaging findings of HCC?
- Does a normal AFP exclude HCC?
- Requirements for a MELD exception for HCC