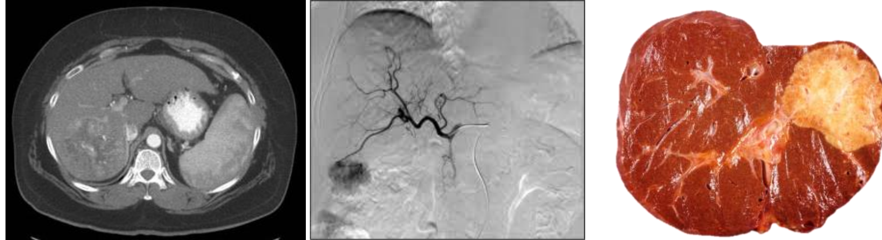
The state of play in: HCC screening, management and treatment outcomes



Dr Avik Majumdar MBBS (Hons) MPHTM PhD FRACP
AW Morrow Gastroenterology and Liver Centre
Australian National Liver Transplant Unit
Royal Prince Alfred Hospital

Disclosures

- Research grants - Gilead Sciences
- Speaker's bureau - Gilead Sciences

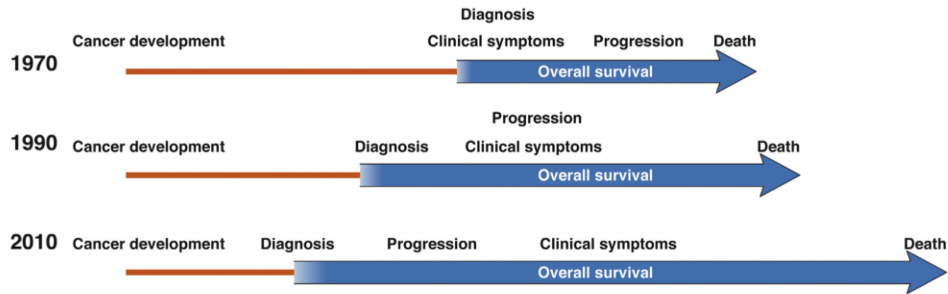
The Current Paradigm

1. Screening and Surveillance
2. Diagnosis
3. Staging
4. Treatment

Multi-Disciplinary Team
- HCC Coordinator and Nurses
- Radiologists
- Hepatologist
- Surgeons
- Medical Oncologist
- Radiation Oncologist
- Palliative Care

Individualised approach

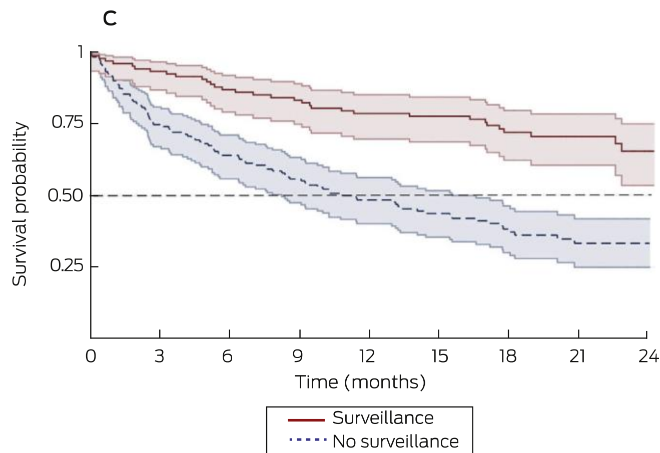
Screening



Bruix et al. Gastroenterology 2016

Surveillance improves survival of patients with hepatocellular carcinoma: a prospective population-based study

Thai P Hong[1], Paul J Gow[2], Michael Fink[3,4], Anouk Dev[5], Stuart K Roberts[2], Amanda Nicoll[6], John S Lubel[6], Ian Kronborg[7], Niranjan Arachchi[7], Marno Ryan[1], William W Kemp[8], Virginia Knight[5], Vijaya Sundararajan[3], Paul Desmond[1], Alexander JV Thompson[1], Sally J Bell[1]



Hong et al. MJA 2018

Who to screen?

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 an		
Hepatitis I		
Hepatitis C		
Stage 4 PE		
Genetic he		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.

Screen all patients with cirrhosis and most with HBV

Marrerro et al. Hepatology 2018

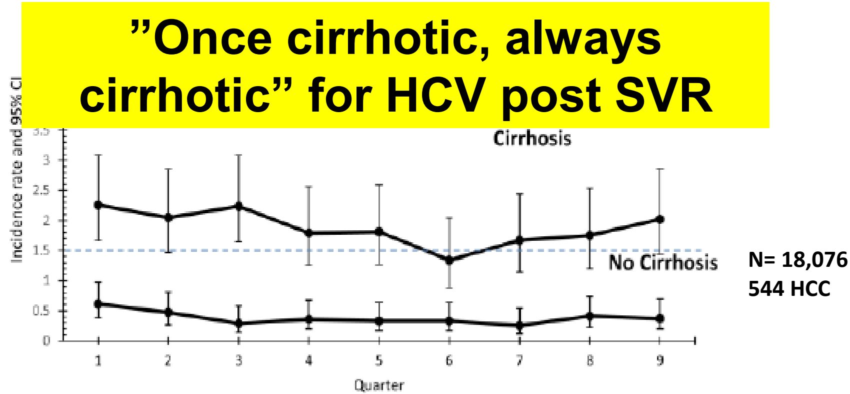
PAGE-B

Age (years)	Gender	Platelets (/mm³)
16-29: 0	Female: 0	≥200,000: 0
30-39: 2	Male: 6	100,000-199,999: 6
40-49: 4		<100,000: 9
50-59: 6		
60-69: 8		
≥70: 10		

	PAGE-B risk score >10	
	Derivation cohort (N = 1264)	Validation cohort (N = 484)
Sensitivity	100%	100%
Specificity	41.2%	19.6%
Positive predictive value	9.8%	10.3%
Negative predictive value	100%	100%

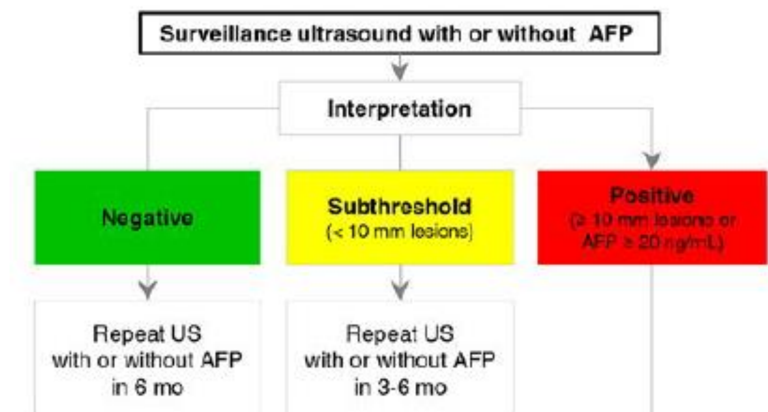
Papatheoridis et al. J Hepatol 2016

Consensus recommendations	Grade
HCV qualitative PCR should be performed 12 weeks after cessation of DAA therapy.	A1
People with cirrhosis should continue in long-term variceal and HCC surveillance programs.	A1
People with no cirrhosis who achieve SVR and normal liver function test results should be medically managed as individuals who have never had HCV infection.	B1
People with persistently abnormal liver function test results after SVR should undergo further assessment and monitoring for alternative causes of liver disease.	A1



Kanwal et al. Hepatology 2019 *In Press*

How to screen?



Marrerro et al. Hepatology 2018

Ultrasound +/- AFP?

- US sensitivity 58-89%, specificity >90%

Bolondi et al. J Hepatol 2003

- Addition of AFP previously reported increase detection of cases by 6-8%

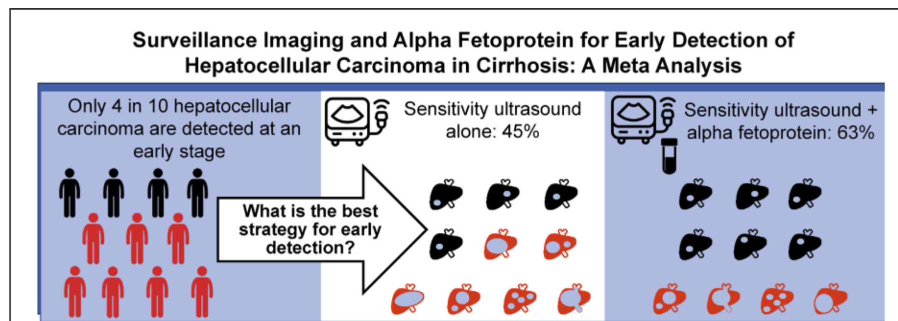
Biselli et al. Br J Cancer 2015

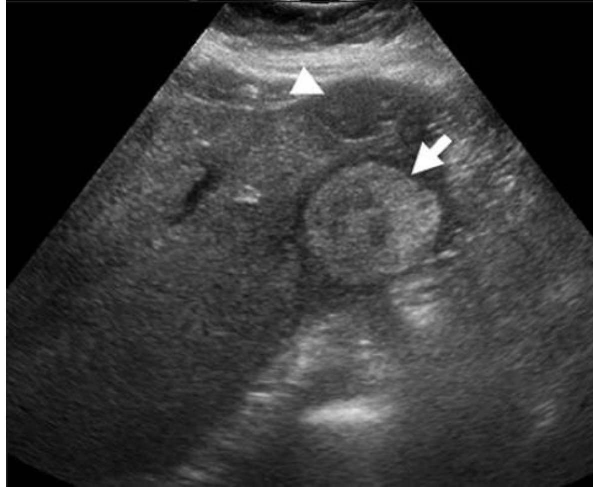
- However…

Surveillance Imaging and Alpha Fetoprotein for Early Detection of Hepatocellular Carcinoma in Patients With Cirrhosis: A Meta-analysis

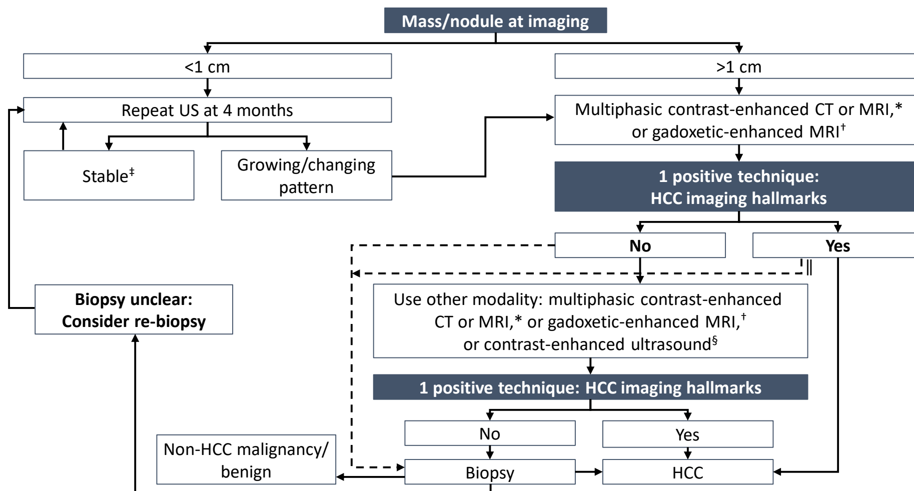
Kristina Tzartzeva,[1,*] **Joseph Obi**,[1,*] Nicole E. Rich,[1] Neehar D. Parikh,[2] Jorge A. Marrero,[1] Adam Yopp,[3] Akbar K. Waljee,[2,4] and Amit G. Singal[1,5]

Gastroenterology 2018;154:1706–1718



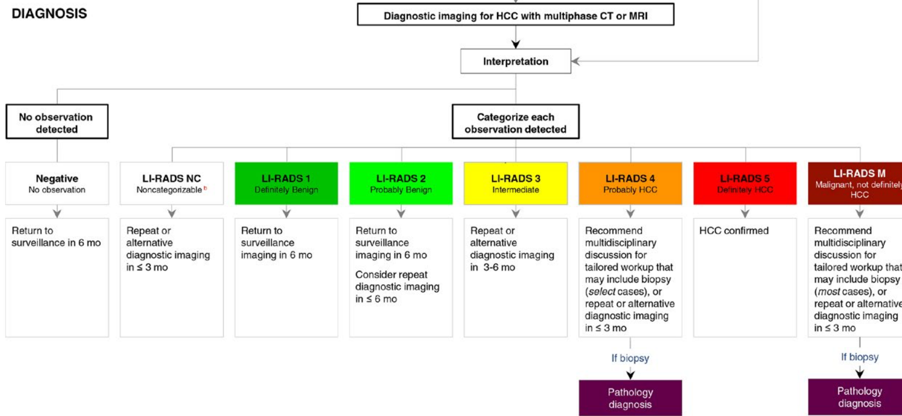


HCC Diagnosis

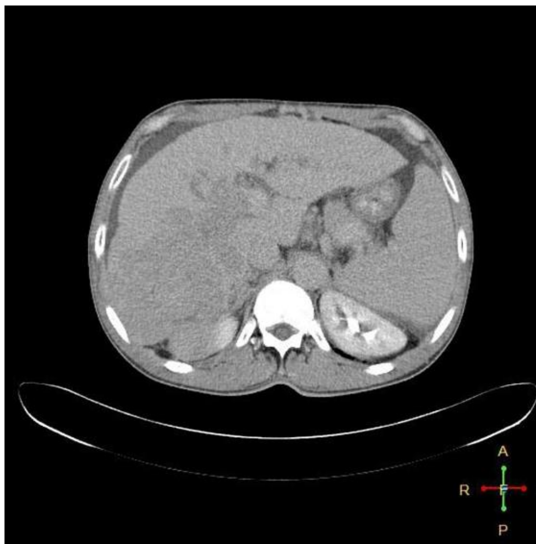


EASL CPG 2018

LI-RADS



Marrerro et al. Hepatology 2018



Quad-phase helical CT

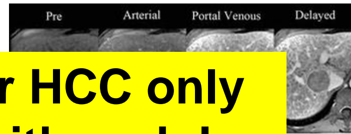
- Non-contrast
- Arterial
- Portal venous
- Delayed

1. **Arterial enhancement**
2. **Washout on portal venous or delayed phase**

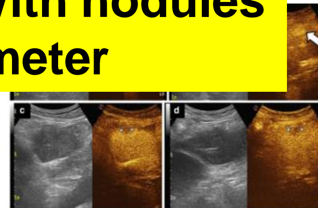
Case courtesy of Dr Heba Mohamed, Radiopaedia.org, rID: 47965

Diagnostic Modalities

- MRI with contrast



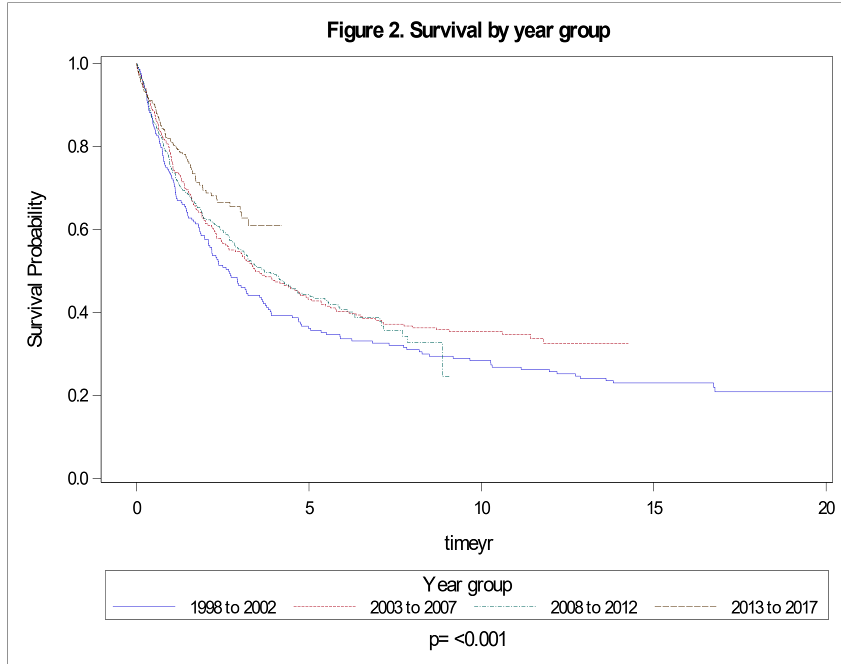
Imaging criteria for HCC only apply in cirrhosis with nodules >1cm in diameter



+/- CT arterioportography
- Targeted liver Biopsy
  Risk of Seeding 2.7%

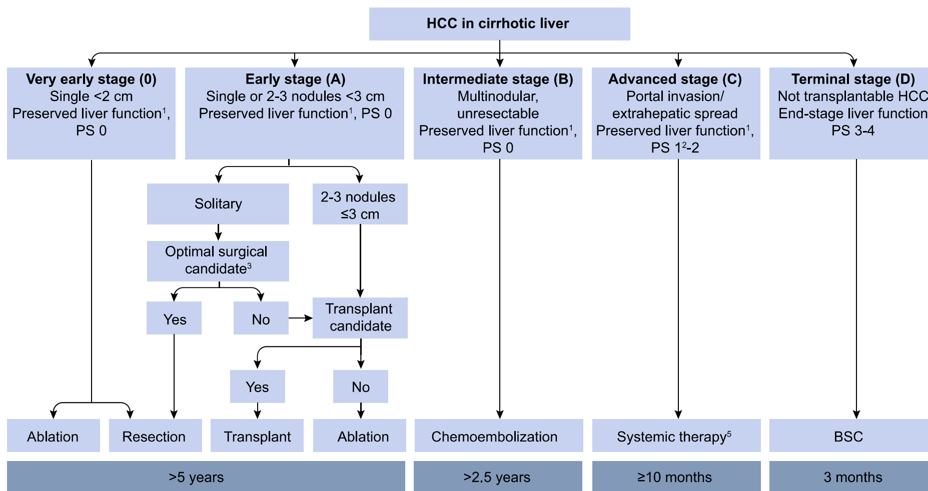
Silva et al. Gut. 2008;57(11):1592

Management and Treatment Outcomes

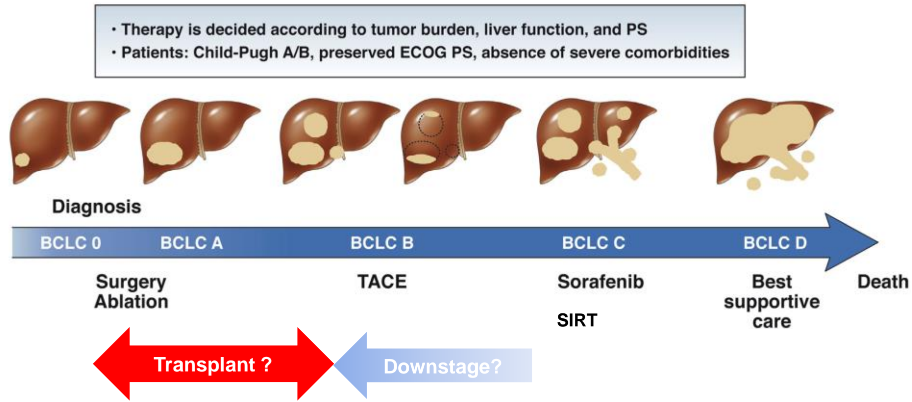


Stoklasa et al. Unpublished data

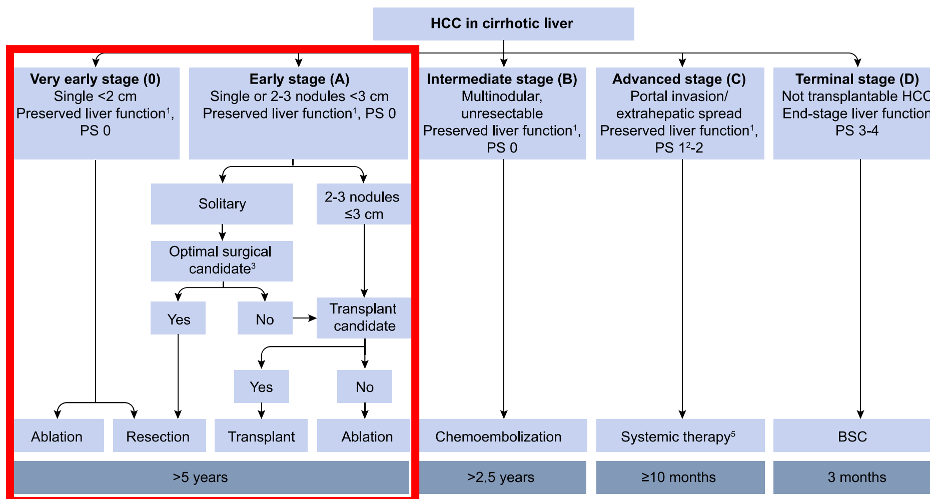
BCLC Classification

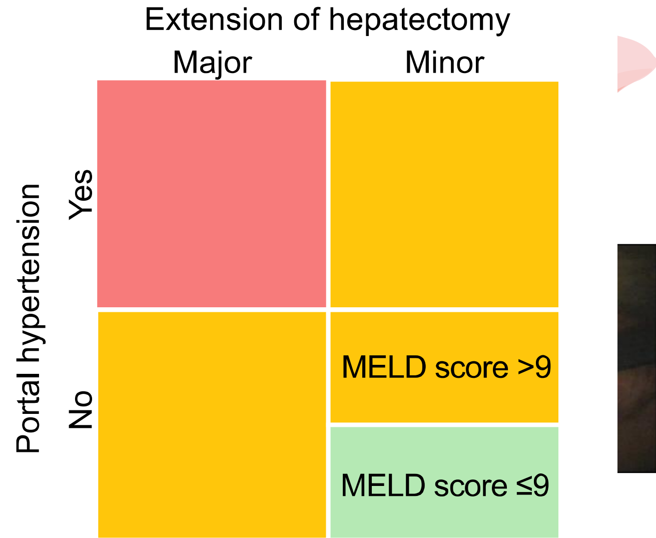


EASL CPG 2018



Early Stage (BCLC 0/A)





EASL CPG 2018

Percutaneous Ablation

Radiofrequency ablation
Monopolar RFA
Active energy deposition: few mm
Multibipolar No touch RFA
Heat diffusion
Electrode
Thermal diffusion
HCC
Ablation margins (target: >5 mm)

Microwave ablation
Active energy deposition: ~1 cm
Heat diffusion

Cryoablation
Ice ball: ~1–3 cm
Argon gaz
Cold diffusion

Irreversible electroporation
Cell membrane

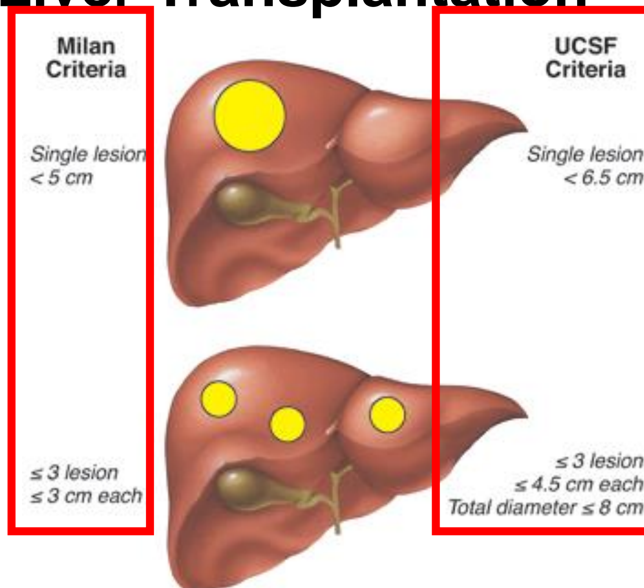
	Radiofrequency ablation	Microwave ablation	Cryoablation	Irreversible electroporation
Advantages	• Well-evaluated treatment (reference) • Multibipolar mode: increases volume and predictability (margin) of ablation zone	• Higher and faster temperature picks reached than with RFA (less sensitive to heat sink effect than monopolar RFA)	• Easy monitoring with imaging of ice ball progression	• Limited risk of thermal injury to neighbouring critical structures • Unsensitive to heat sink effect • Advantage of multibipolar mode (no touch technique, predictability of margins)
Limitations	• Thermal injury of adjacent structure • Heat sink effect (near major vessels) • Multibipolar mode is less sensitive to heat sink effect	• No reliable endpoint to set the amount of energy deposition	• Cryoshock with first device • Limited clinical data available with new devices	• Only preliminary clinical data • General anaesthesia using curare and major analgesic drugs is mandatory

Nault J-C, et al. J Hepatol 2018;68:783–97
EASL CPG HCC. J Hepatol 2018; doi: 10.1016/j.jhep.2018.03.019

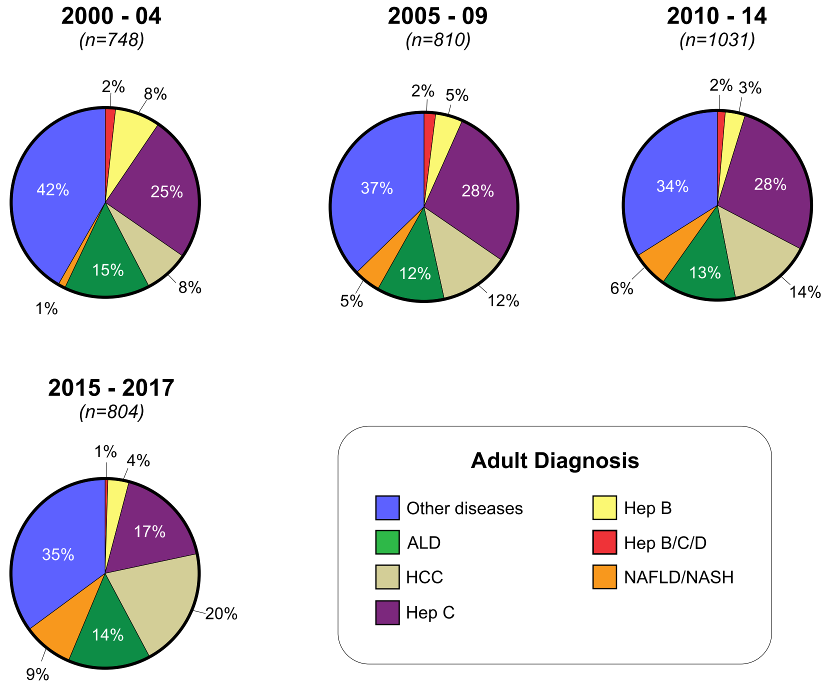
- **In surgical candidates:**
  - No evidence of difference between surgery and RFA in terms of mortality
  - Surgery has lower recurrence, but more adverse events
- **Non-surgical candidates:**
  - RFA/MWA is superior to Ethanol ablation and Acetic acid ablation in terms of mortality, without increasing adverse events
- **Overall quality of evidence was low/very low**

Majumdar et al. Cochrane Database of Systematic Reviews 2017

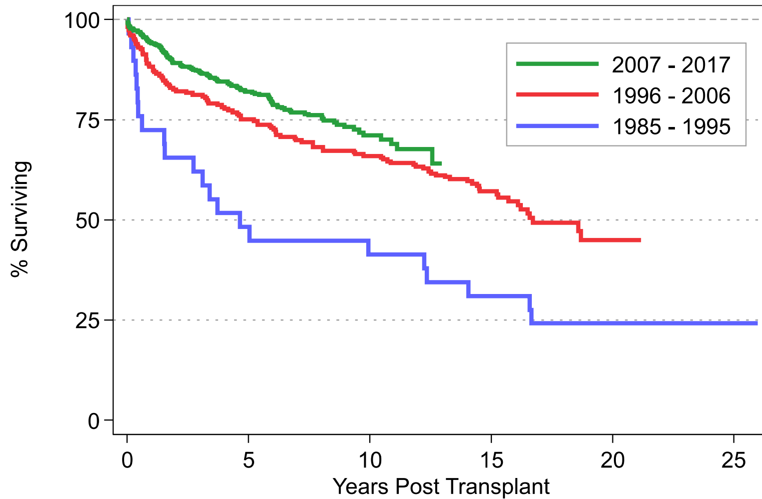
Liver Transplantation



Mazzaferro et al NEJM 1996
Yao et al Hepatology 2001



ANZLTR 29th Report 2018

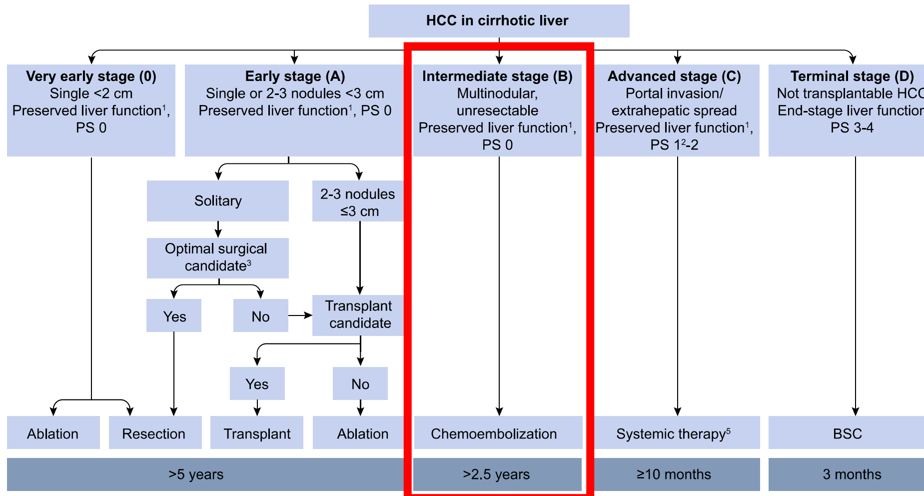


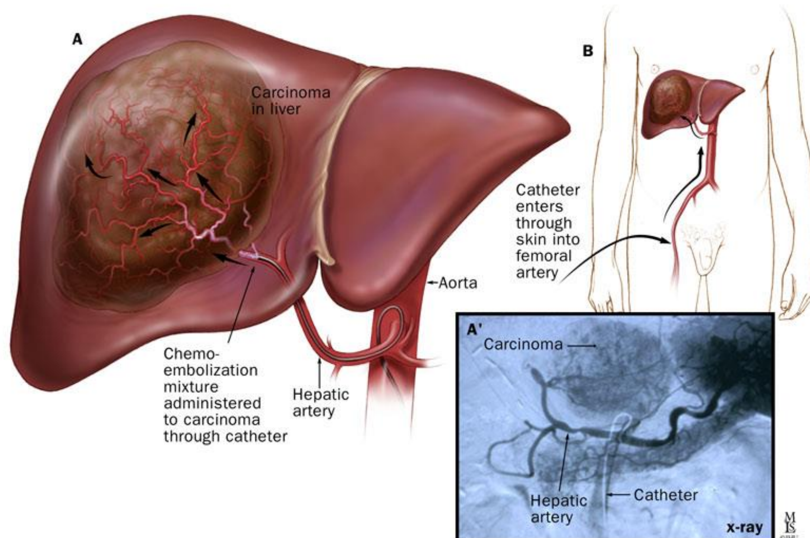
Number at risk

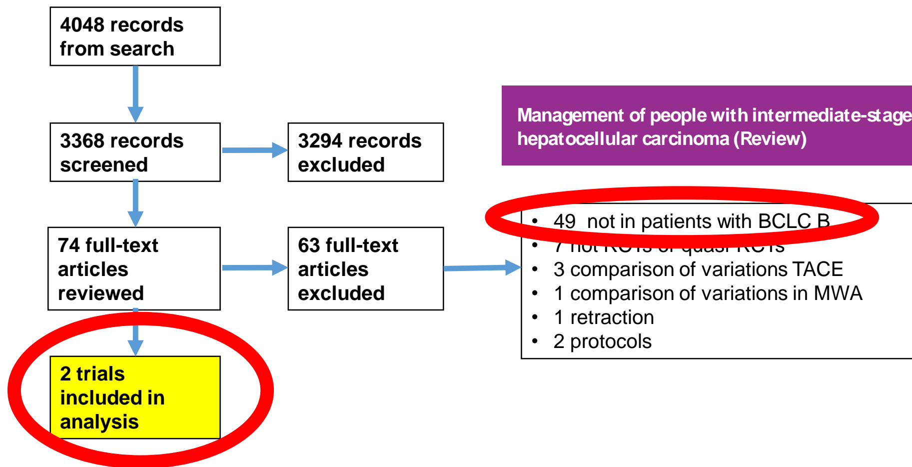
1985-1995	29	14	12	9	7	3
1996-2006	229	172	151	76	9	0
2007-2017	934	350	84	0	0	0

ANZLTR 29th Report 2018

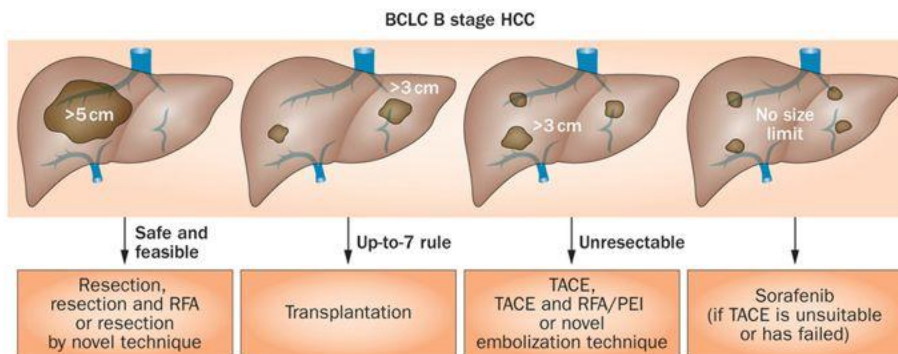
Intermediate Stage (BCLC B)



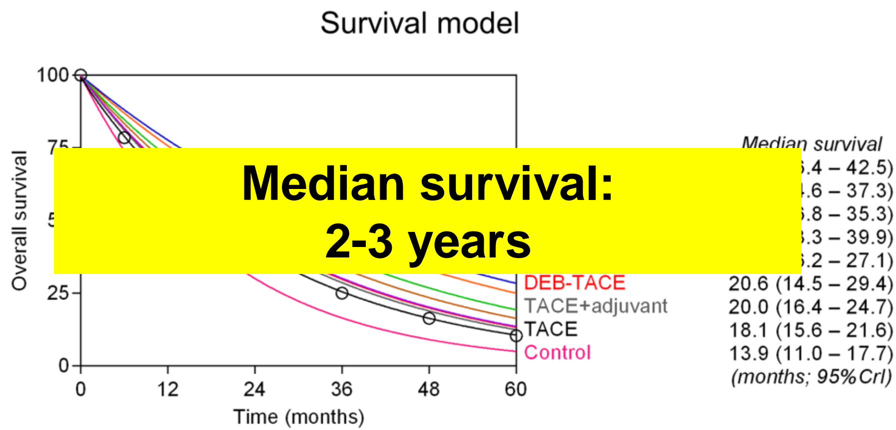




Roccarina, Majumdar et al. Cochrane Database of Systematic Reviews 2017

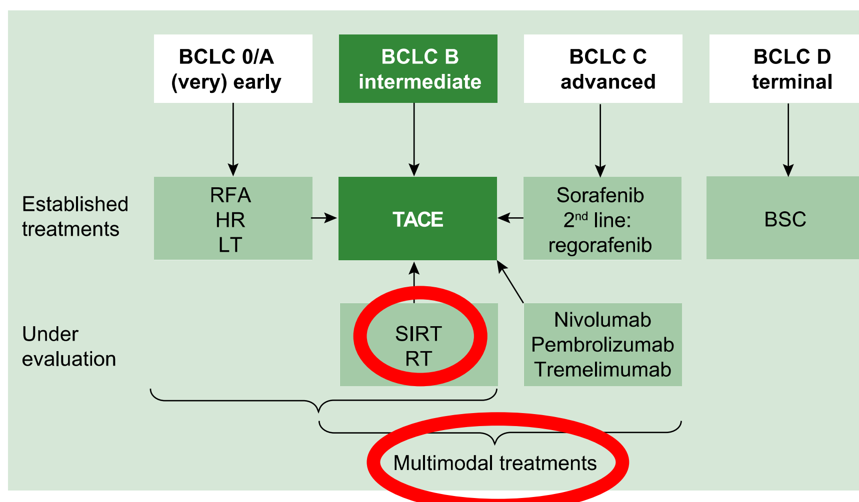


Gao et al. Nature Reviews Clin Onc 2014



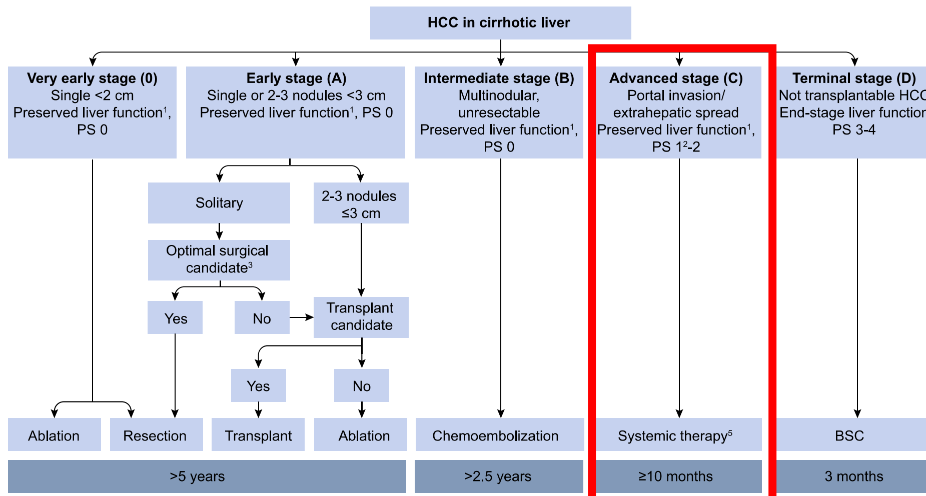
Katsanos et al Plos One. 2017

Sequential/multimodal treatment



Galle et al. J Hepatol 2017

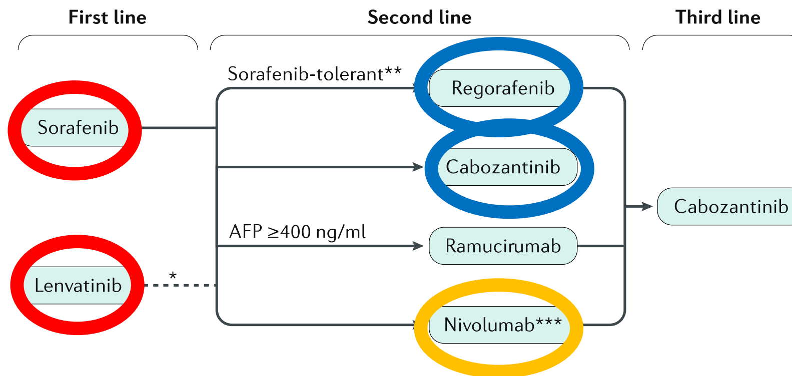
Advanced Stage (BCLC C)



Systemic Therapy in 2017

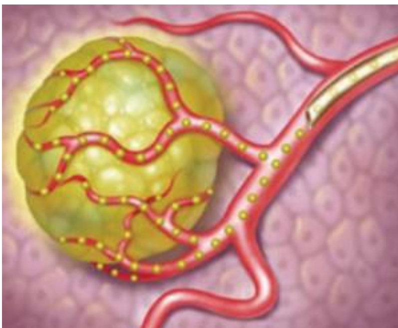
Sorafenib

Systemic Therapy in 2019

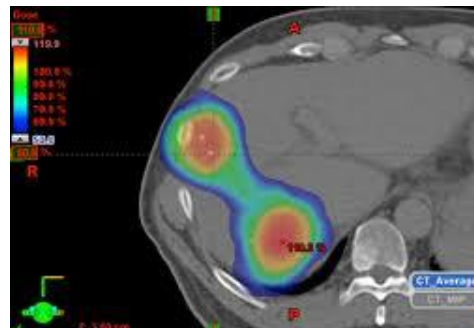


Bruix et al. Nature Gastro Hep 2019

Radiation



SIRT (Y-90)



SBRT

Treatment Summary

- **Early Stage Disease Curative Treatments**
  - Resection
  - Ablation
  - Transplant

Survival >5 years

- **Intermediate Stage Disease**
  - TACE
  - Transplant if within criteria

Survival 2-3 years

- **Advanced Stage**
  - Lenvatinib and Sorafenib are PBS-funded first line treatments
  - Palliative care referral

Survival 12-18 months

EASL CPG 2018

Conclusions

- Early detection/screening of HCC is critical to patient outcomes
- Outcomes have improved over time
- Multi-disciplinary teams should guide care
- Current guidelines are mostly comprehensive but some patients may not fit
- Rapidly moving field with several ongoing trials

Thank you!