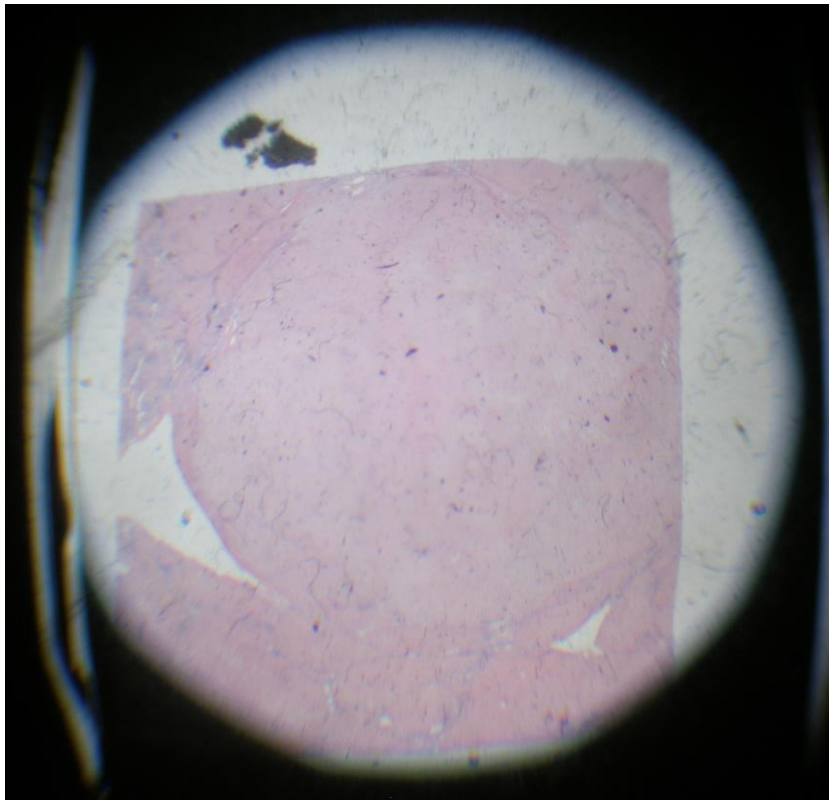
Steatohepatitic hepatocellular carcinoma and TACE

Annual Liver Update Meeting, 22/11/18

Tim Kendall
Senior Clinical Fellow in Pathology, University of Edinburgh
Honorary Consultant Histopathologist, NHS Lothian

Clinical features

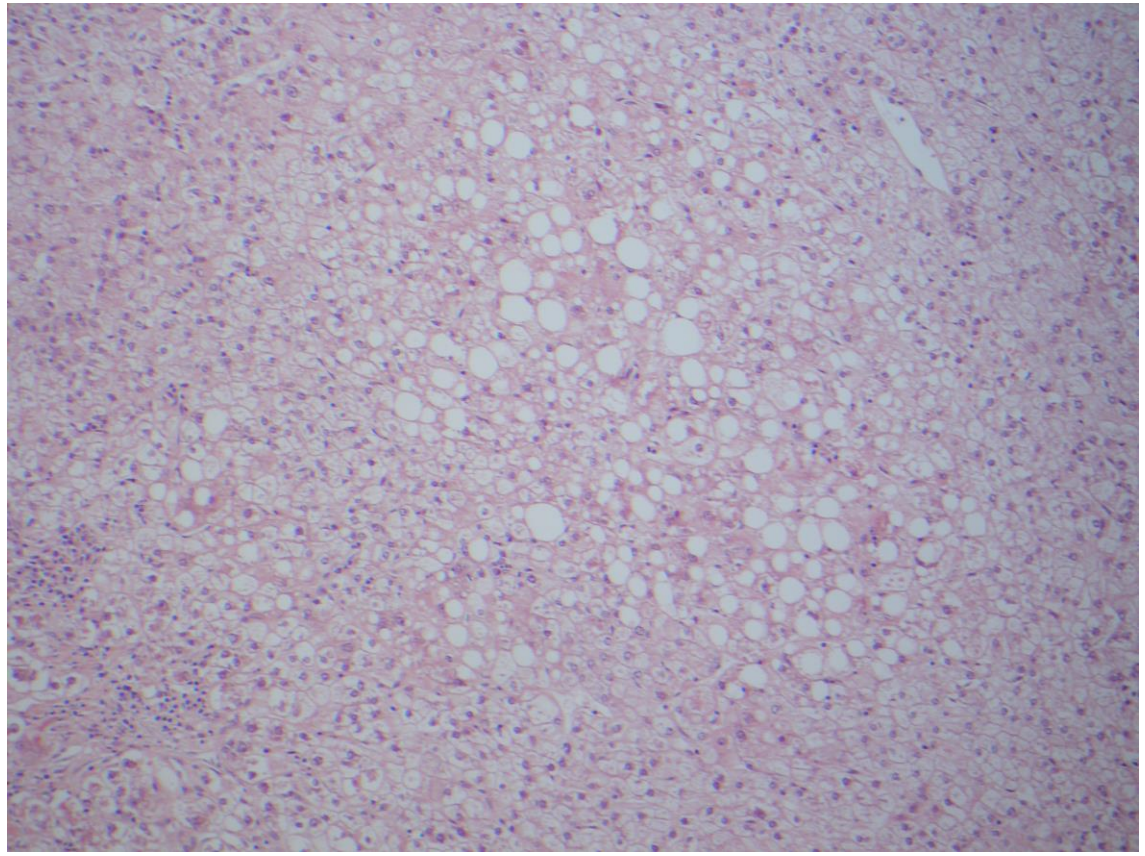
- SH-HCC described in chronic HCV explants (Am J Surg Pathol 2010;34:1630–1636)
- Represents ~13% of HCCs (Human Pathology (2012) 43, 737–746)
- Non-lesional liver usually shows NAFLD/NASH
- Commonest in NAFLD and ALD, found in all other aetiologies (NB HCV) (Hepatology Research 2018; 48: 947–955)
- Associated with diabetes, obesity, dyslipidaemia



Histological features

SH-HCCs show:

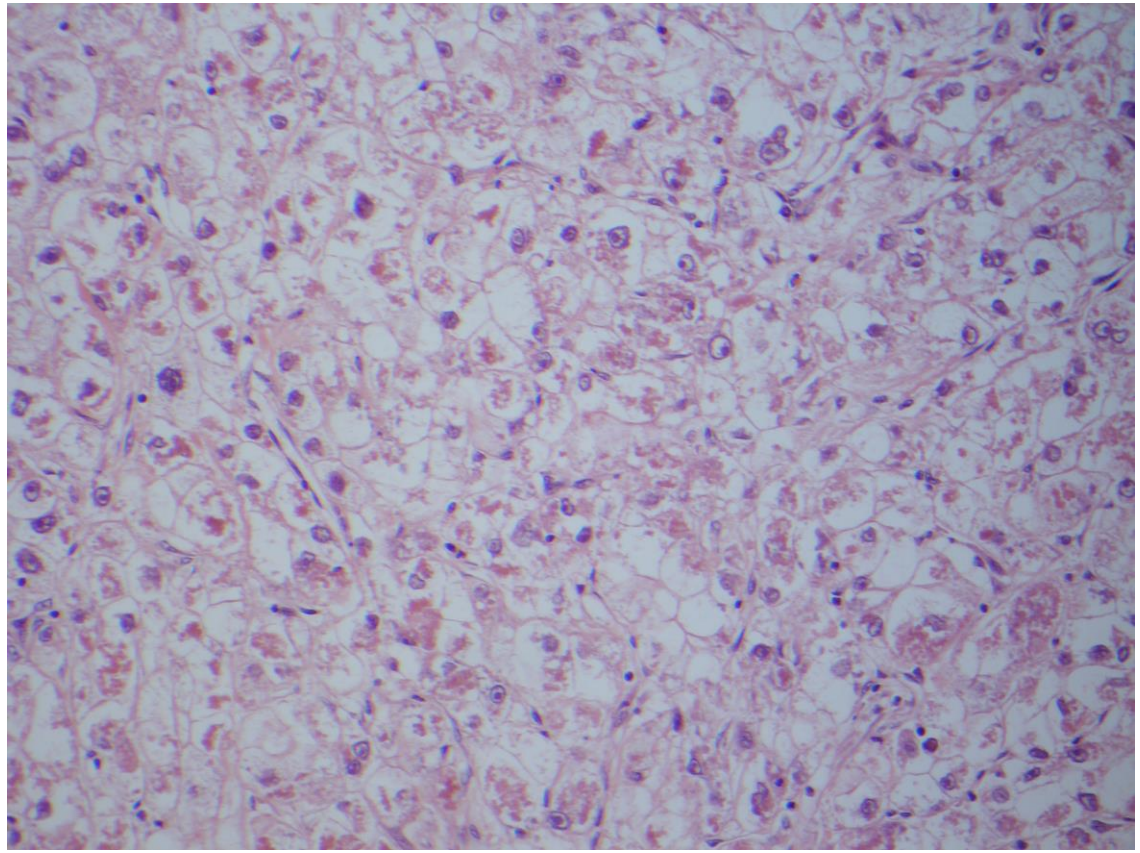
- Lesional cell large droplet steatosis
- Lesional cell ballooning
- Lesional cell Mallory-Denk bodies
- Intralesional fibrosis
- Intralesional inflammation



Histological features

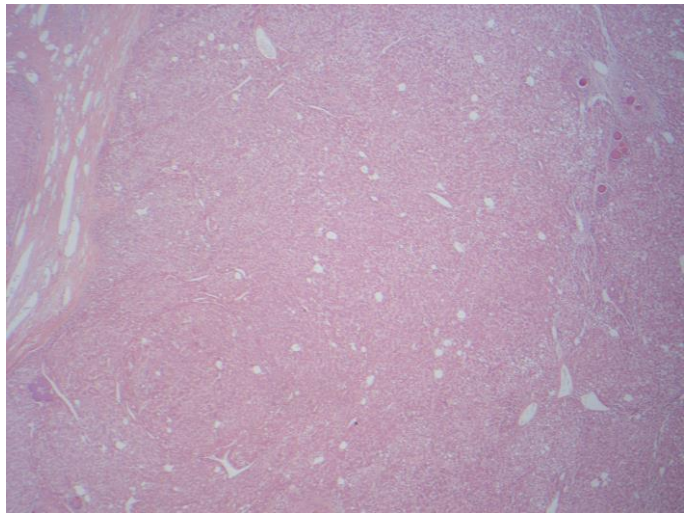
SH-HCCs show:

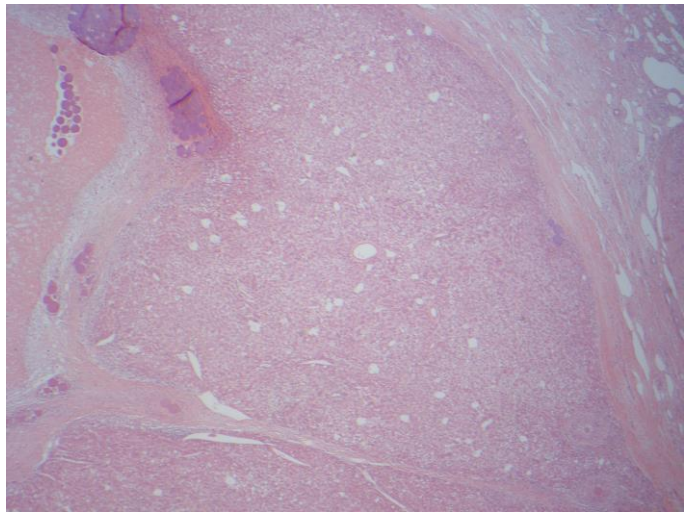
- Lesional cell large droplet steatosis
- Lesional cell ballooning
- Lesional cell Mallory-Denk bodies
- Intralesional fibrosis
- Intralesional inflammation



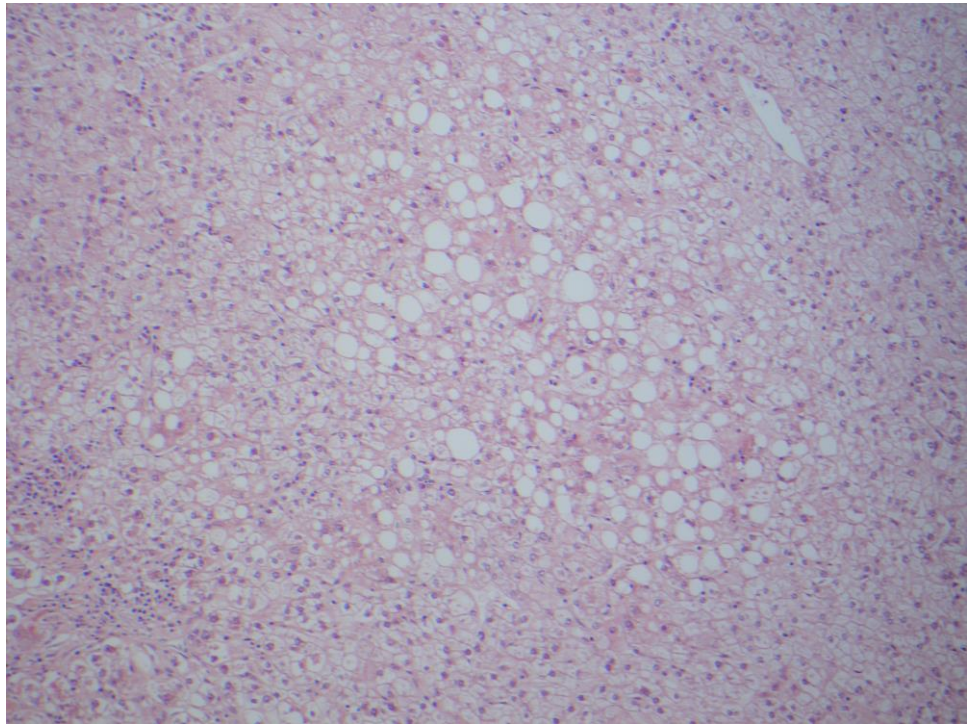
Diagnostic formal criteria

"HCCs designated as SH-HCC type showed the combination of features described in steatohepatitis including large droplet steatosis, ballooning of malignant hepatocytes, MDBs, fibrosis, and inflammation…. HCCs included as SH-HCC type showed steatohepatitic features in > 5% of the tumor area. " (Am J Surg Pathol 2010;34:1630–1636)

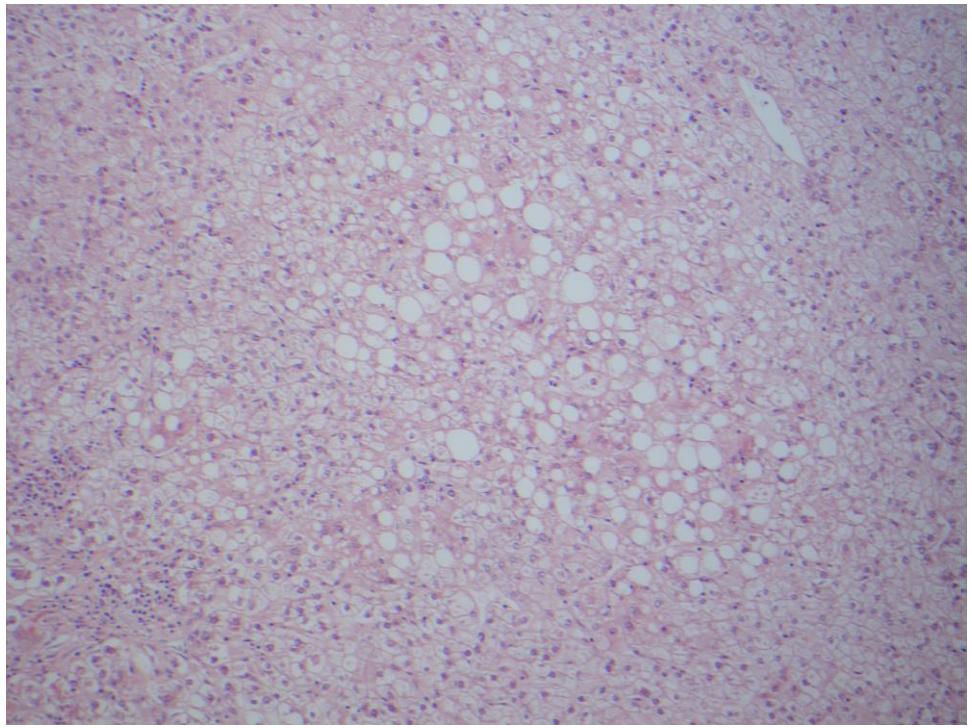




“at least 3 (usually all) SH features mentioned above (no specific minimal amount of each feature was required for diagnosis) were present, with a “steatohepatitic” phenotype involving at least 50% of the tumor on representative sections. ” (Human Pathology (2012) 43, 737–746)

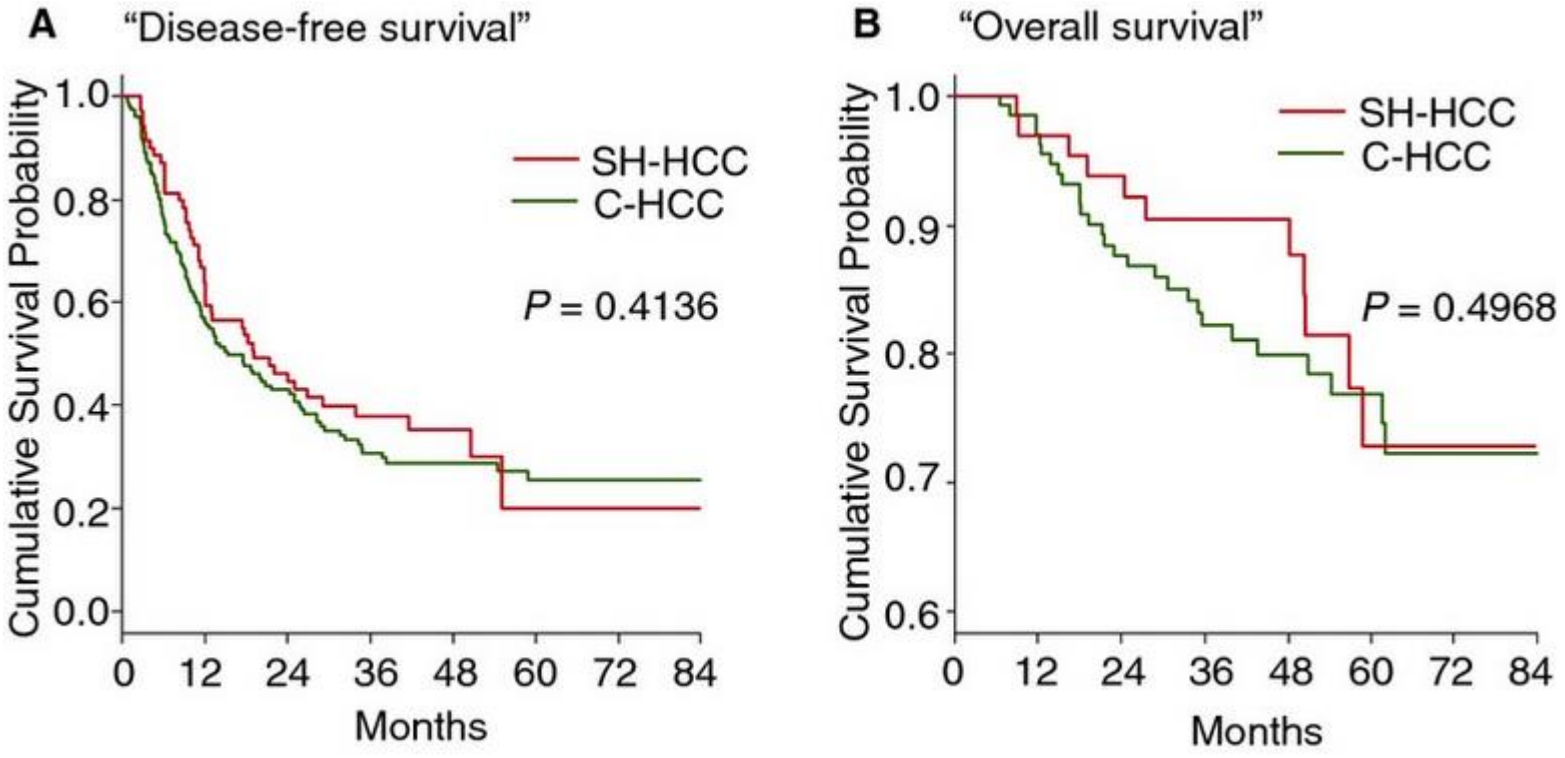


"The diagnosis of SH-HCC was made if the tumor fulfilled the following five criteria in >50% of cancerous tissue, with (i)–(iii) being essential: (i) cancer cell steatosis (>50% of cancer cells); (ii) intracancerous inflammatory infiltrates; (iii) cancer cell ballooning; (iv) Mallory bodies within cancer cells; and (v) pericancerous cellular fibrosis." (Hepatology Research 2018; 48: 947–955)

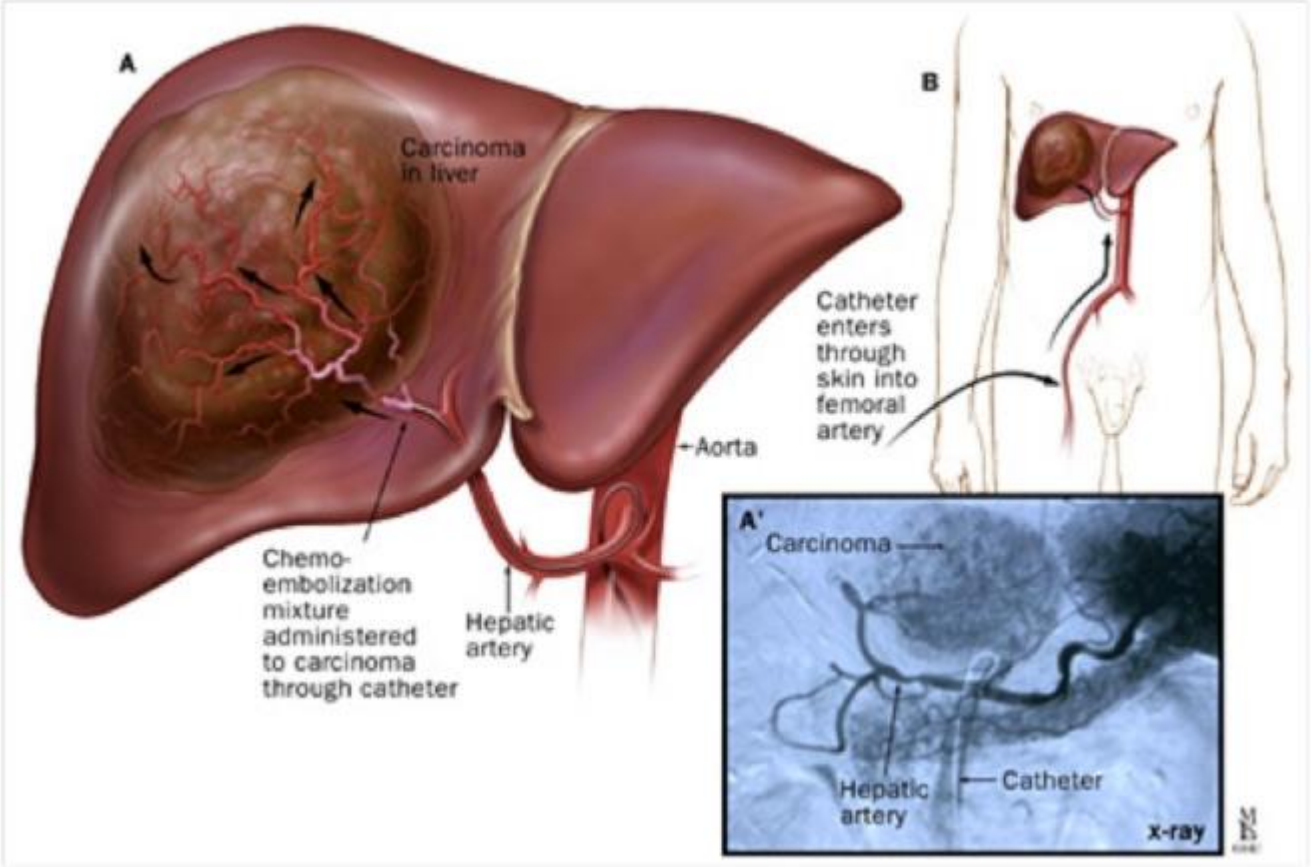


Consequence

- We can't agree when to classify as SH-HCC
- It probably doesn't matter (Histopathology, 64, 951–962)



- Noncurative intervention
- Prolong survival by slowing tumour progression
- Intra-arterial infusion of cytotoxic followed by embolisation



Guidelines – AASLD/EASL

- Downstaging if outwith Milan criteria
- 'bridging' to OLT in Milan (OPTN) T2
- Cirrhosis/HCC (T2/T3, no vasc involvement), not surgical candidate
- Stage BCLC B HCC

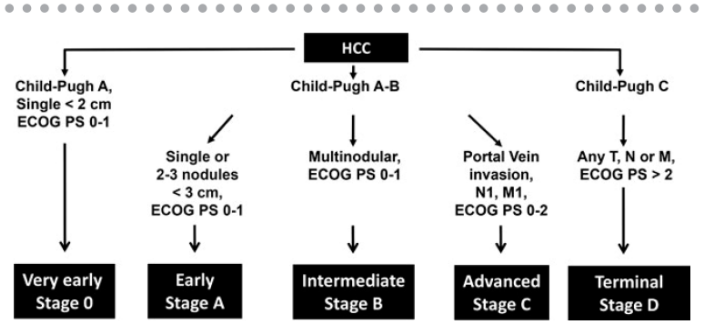
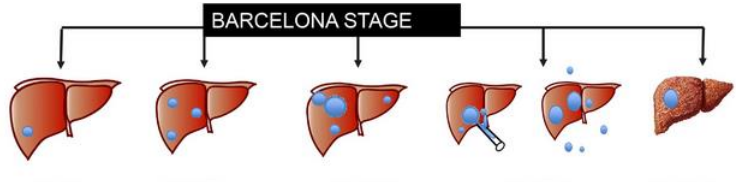


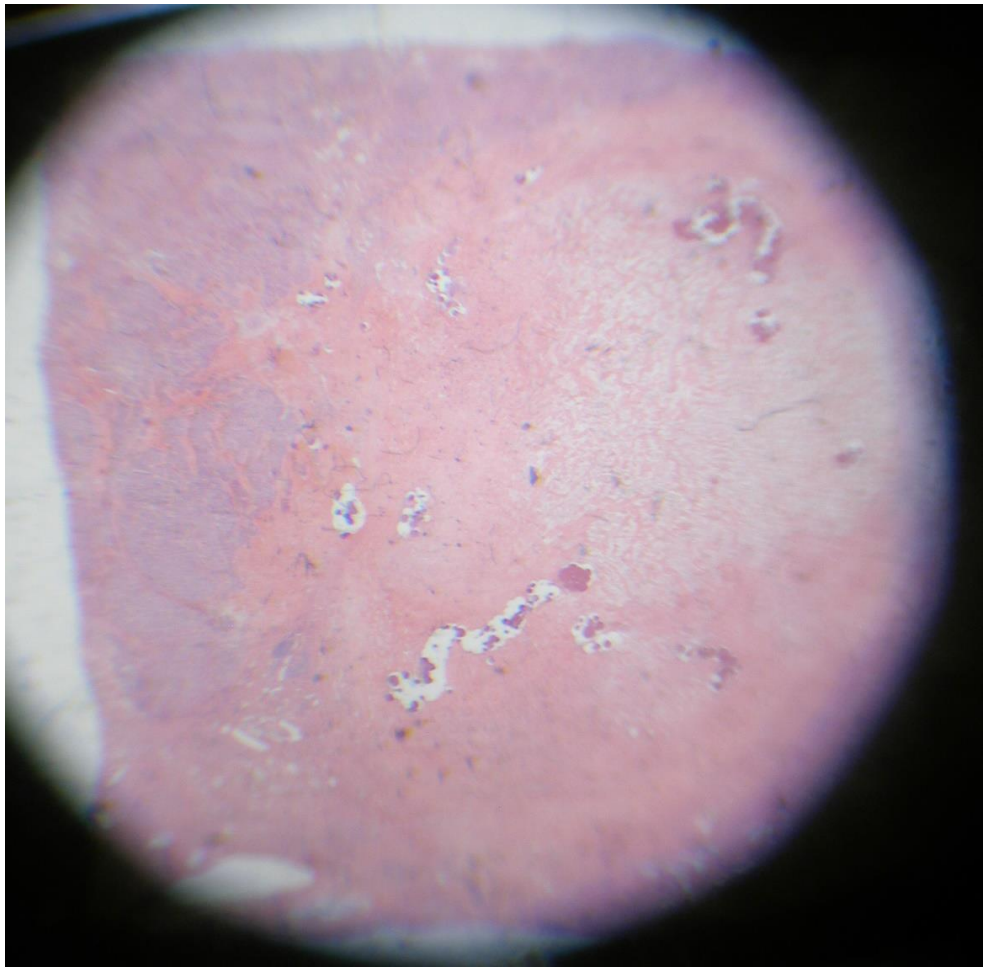
FIG. 2. BCLC HCC staging system. Abbreviations: N, nodal metastasis; M, extrahepatic metastasis.

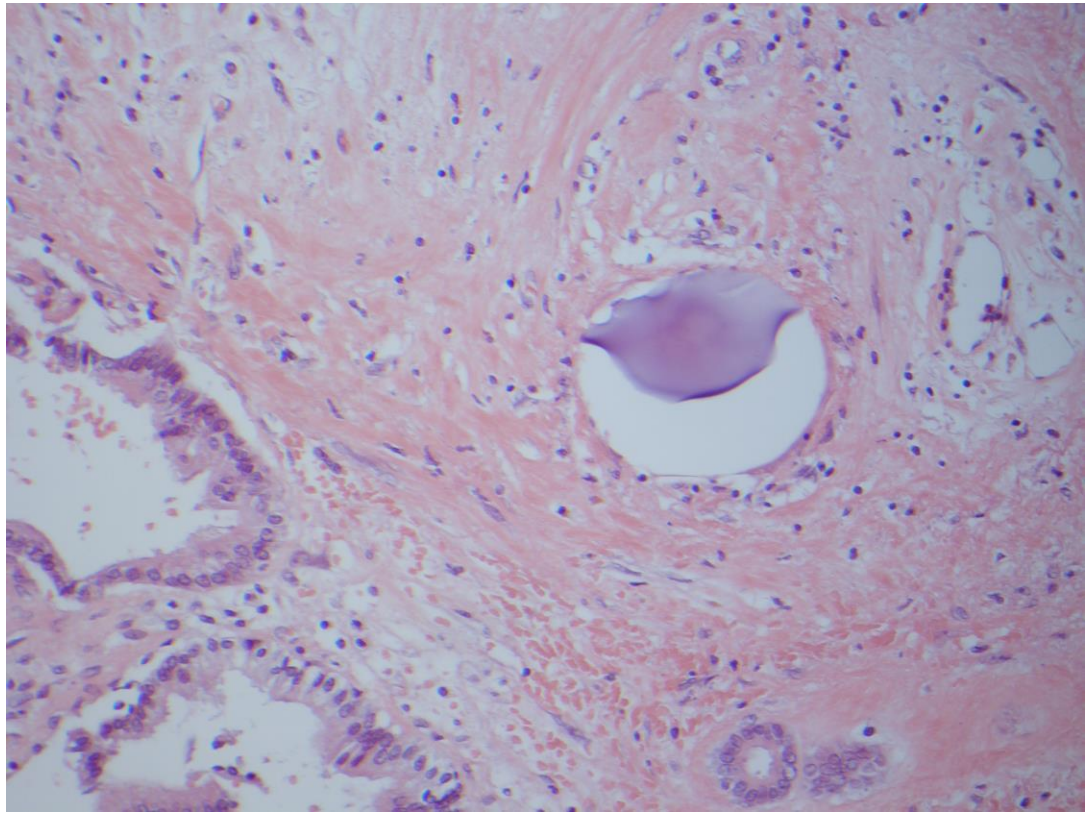


Level of Evidence					
1	Resection		TACE	Sorafenib (1L) Lenvatinib (1L) Regorafenib (2L) Cabozantinib (2L)	
2	RFA MWA	Resection OLT RFA MWA TARE TACE SBRT	TARE Downsize OLT	Nivolumab (2L)	OLT BSC
3				TARE	

THE UNIVERSITY of EDINBURGH
Centre for Inflammation Research

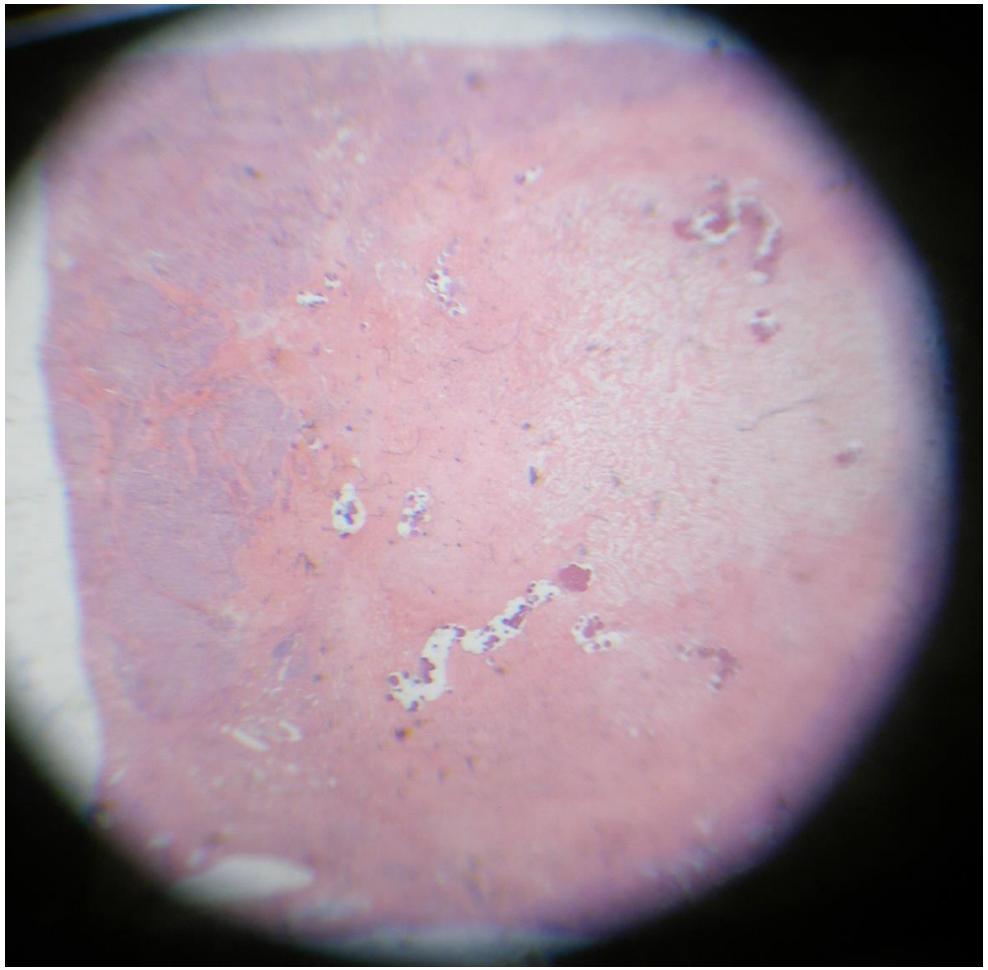
Histological appearance

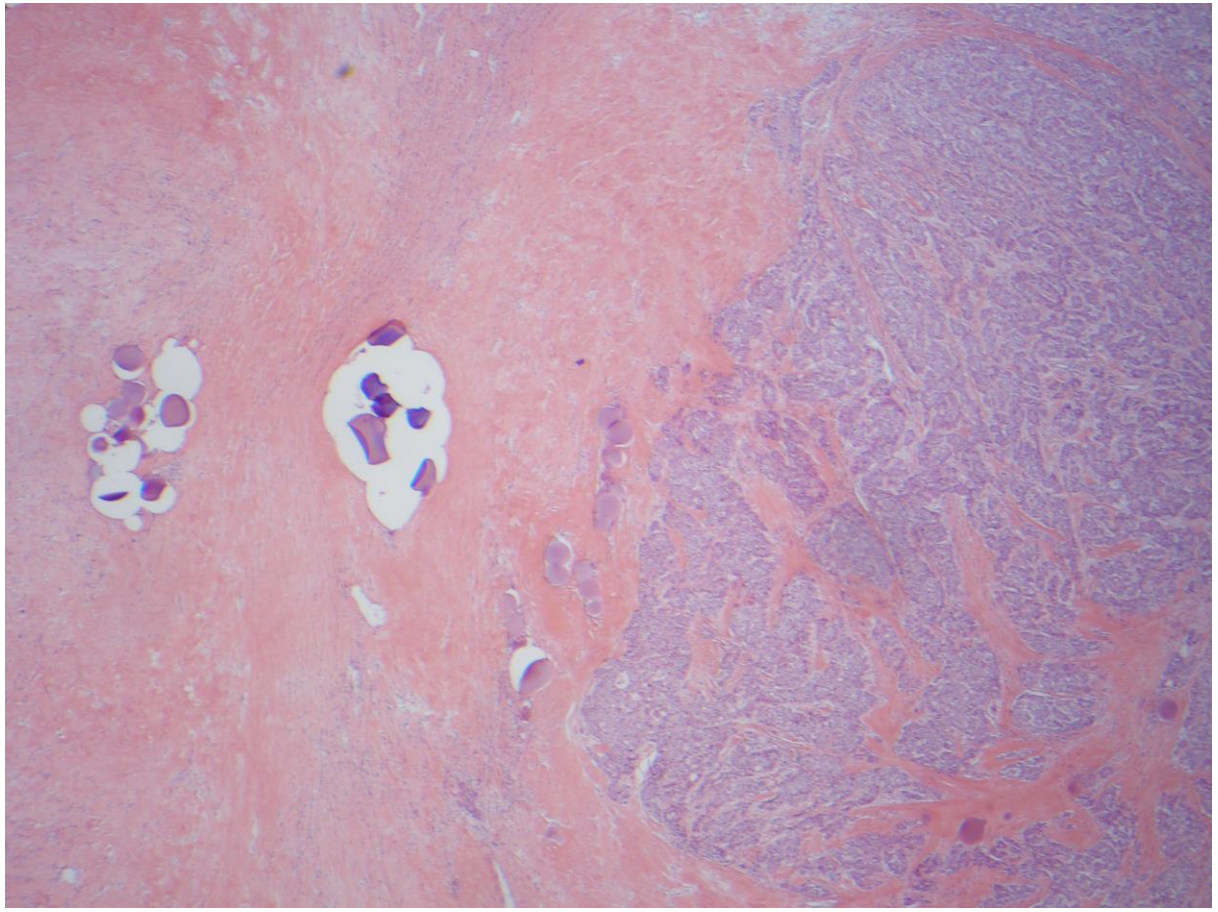




THE UNIVERSITY of EDINBURGH
Centre for Inflammation Research

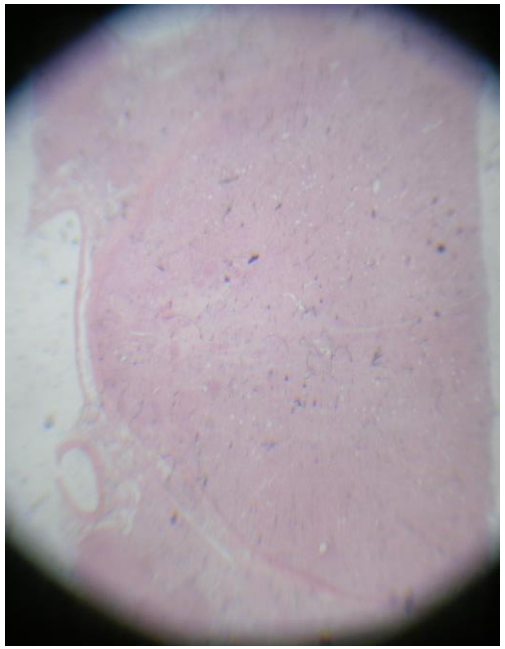
Histological response

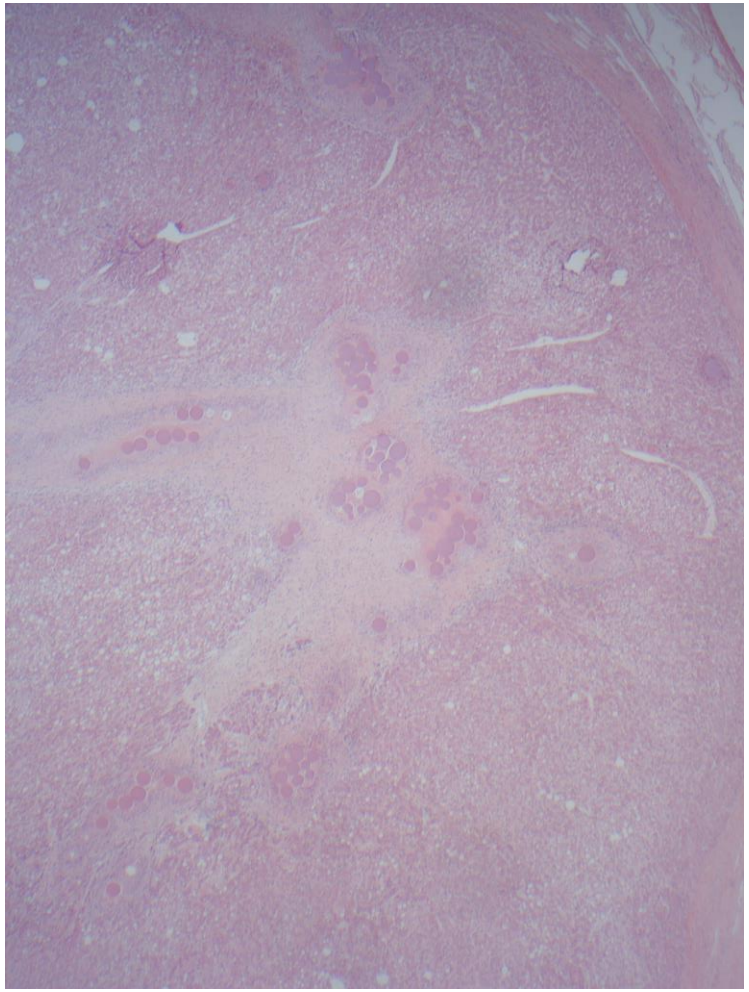


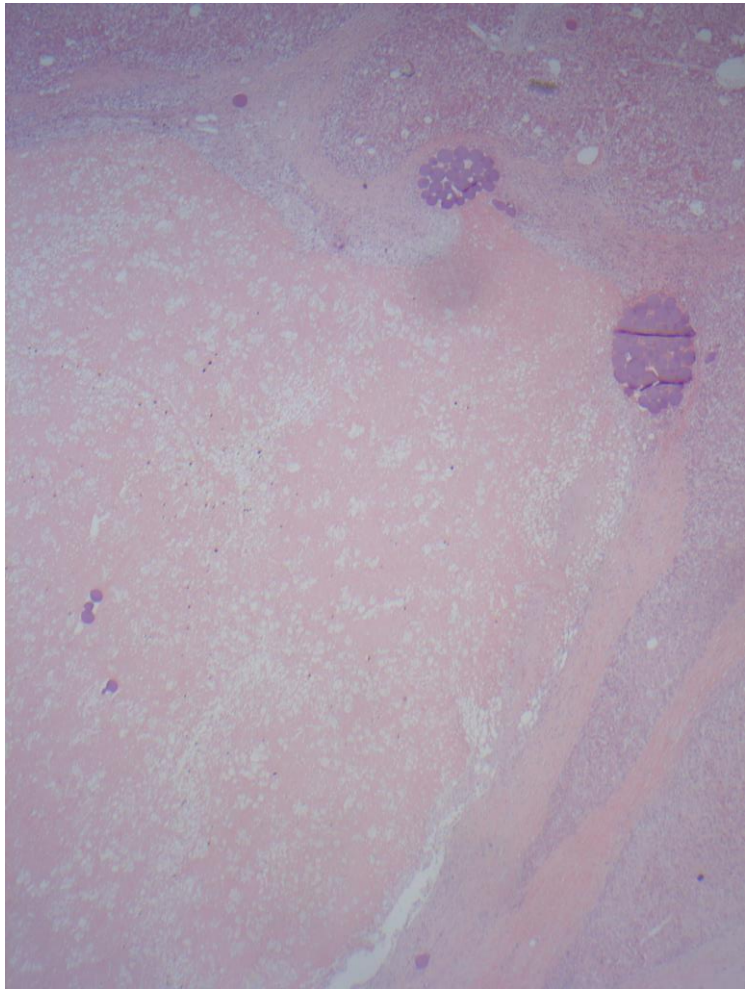


THE UNIVERSITY of EDINBURGH
Centre for Inflammation Research

Histological response







Treatment response

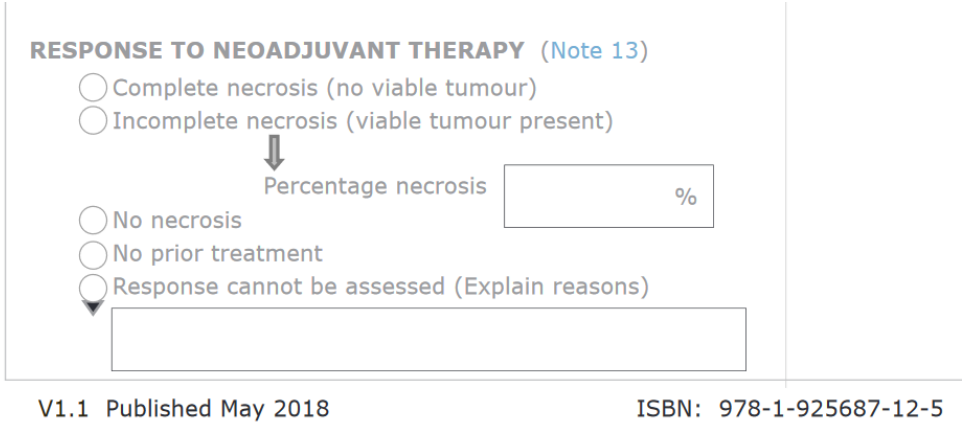
- Partial response in 15-55% of patients
- Response is variably defined
- ? Benefit – intermediate HCC survival increased from 16 to 20 months vs. Cochrane review

"Contrary to current clinical practice, we conclude that there is [an] absence of evidence of TACE or TAE having a beneficial effect on survival in participants with unresectable HCC. Methods of tumour response evaluation and reporting of adverse events varied considerably and did not allow meta-analysis of data."
(Cochrane Database Syst. Rev. 2011, March 16)

- **To reference this dataset please use the following citation:** Burt A, Alves V, Bedossa P, Clouston A, Guido M, Hübscher S, Kakar S, Ng I, Nyun Park Y, Reeves H, Wyatt J, Yeh M, Ellis D. (2017). *Intrahepatic Cholangiocarcinoma, Perihilar Cholangiocarcinoma and Hepatocellular Carcinoma Histopathology Reporting Guide, 1st Edition*. International Collaboration on Cancer Reporting; Sydney, Australia. ISBN: 978-1-925687-12-5

- "..limited data to determine the significance of pathologic quantification of tumour necrosis after locoregional therapy. ..figures such as 50% and 90% necrosis have been used…insufficient evidence to make definite recommendations about cut off values for necrosis that correlate with outcome."
- "extent of necrosis can provide valuable feedback to the clinical team to correlate it with the down-staging observed on imaging."

- "..no definite guidelines on how to assess the extent of necrosis and the pathological analysis in most studies has not been performed in a systematic manner. "
- "Microscopic examination of the entire tumour should be done when feasible."
- "overall extent of necrosis should be estimated based on a combination of gross and microscopic findings…extent of necrosis should be reported in up to 5 of the largest tumour nodules." Liver Transpl 16(3):262-278


RESPONSE TO NEOADJUVANT THERAPY (Note 13)
Complete necrosis (no viable tumour)
Incomplete necrosis (viable tumour present)
Percentage necrosis
%
No necrosis
No prior treatment
Response cannot be assessed (Explain reasons)
V1.1 Published May 2018
ISBN: 978-1-925687-12-5