



Benign liver tumours

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Benigne levertumoren

- No disclosures

leerdoelen

- Kennis over voorkomen van benigne levertumoren, met name hemangiomen, FNH en adenomen
- Kennis over diagnostiek van deze tumoren
- Kennis over beleid bij deze tumoren
- Kennis over behandelingsmogelijkheden van deze tumoren

EASL Clinical Practice Guidelines on the management of benign liver tumours[☆]

European Association for the Study of the Liver (EASL)*

Clinical Practice Guideline Panel: Massimo Colombo (Chairman), Jan Ijzermans, Alejandro Forner, Valerie Paradis, Helen Reeves, Valerie Vilgrain, Jessica Zucman-Rossi

Introduction

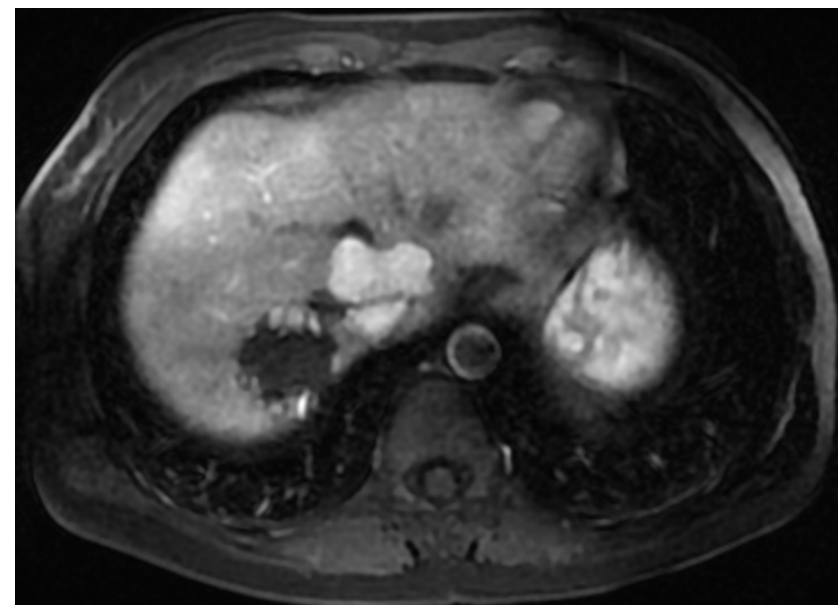
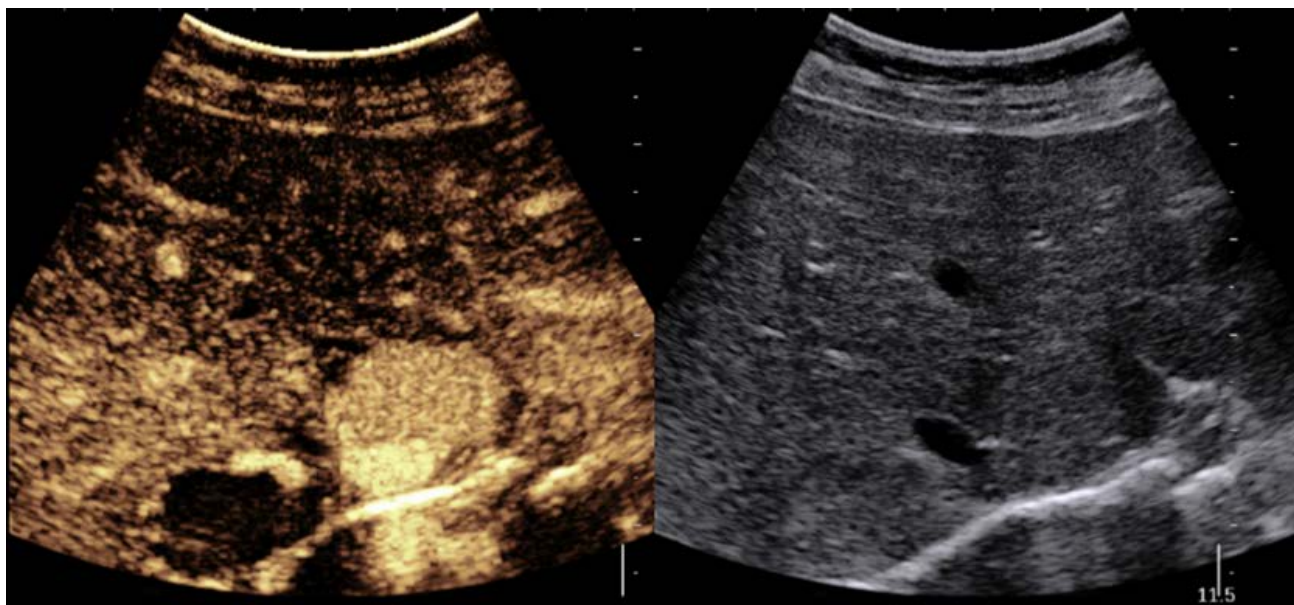
- A heterogenous group of lesions ^[1]
- Often incidental findings
- Some are of greater clinical significance than others
- Aim – a contemporary aid for the practical diagnosis and management of the three common benign tumours:
 - Haemangioma common (4-5%)
 - Focal nodular hyperplasia (FNH) less common (~0.04%)
 - Hepatocellular adenoma (HCA) relatively rare (~0.004%)

Basic management of a 'liver nodule'

- History
 - associated symptoms? fever? foreign travel? Medication? Risk factors for chronic liver disease?
- Examination & baseline investigations
 - Risk factor for or evidence of chronic liver disease?
 - BMI, type 2 diabetes? hypertension?
- Contrast enhanced Imaging
 - CEUS, CT, MRI

The benign liver tumour multidisciplinary team

The team should be one with expertise in the management of benign liver lesions and should include a hepatologist, a hepatobiliary surgeon, diagnostic and interventional radiologists and a pathologist. Each member of the team must hold specific and relevant training, expertise and experience relevant to the management of benign liver lesions. The team should be one with the skills required not only to appropriately manage these patients, but also manage the rare but known complications of diagnostic or therapeutic interventions.

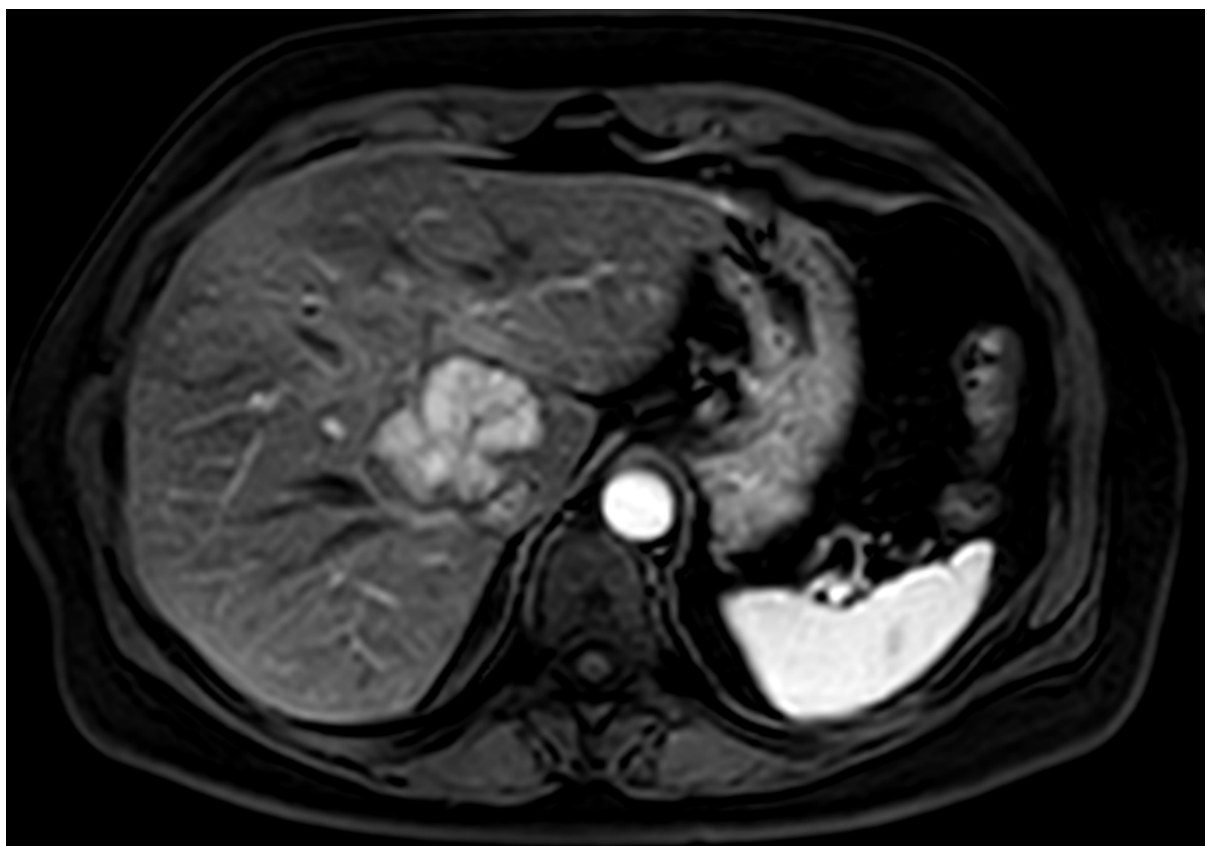


Hepatic hemangioma

- Vascular more than epithelial lesions
- First peripheral, second phase central enhancement
- Mostly asymptomatic, even if large
- If very large and thrombopenia consider.....
- Most cases have a solitary lesion <4 cm
- Rarely of any clinical significance
- DD calcified hemangiomas and HCC

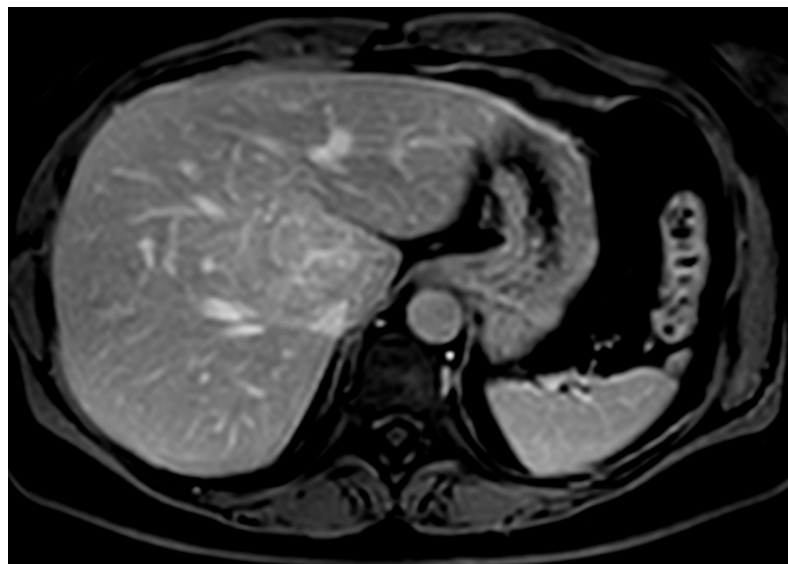
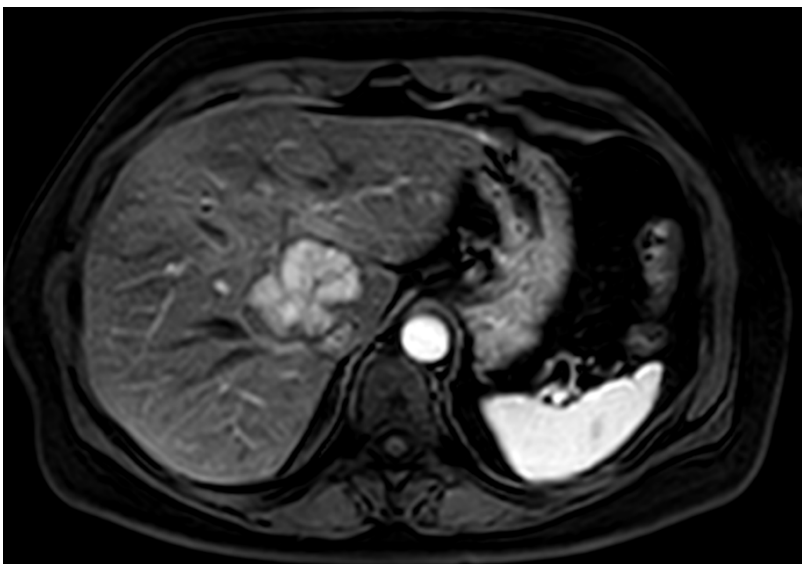
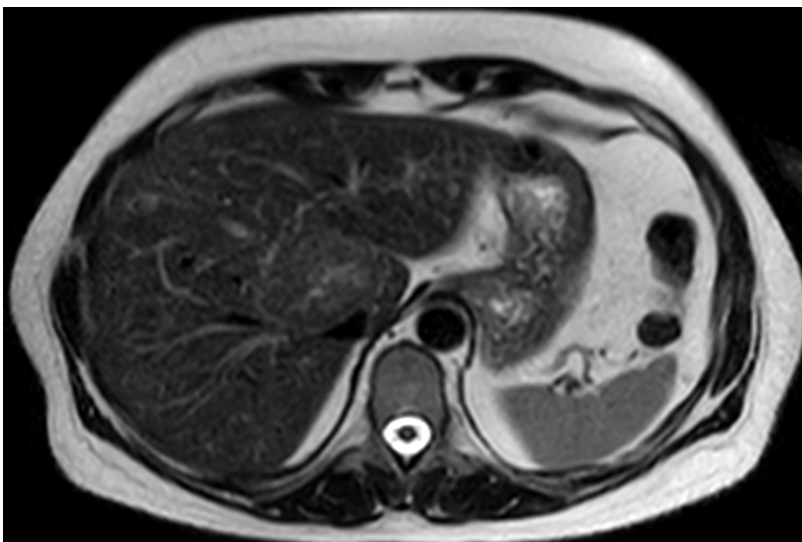
Hepatic haemangioma -recommendations

- Due to its benign course, imaging follow-up is not required for typical haemangioma (**evidence level II-2, grade of recommendation 1**)
- Pregnancy and oral contraceptives are not contraindicated (**evidence level III; grade of recommendation 2**)
- Conservative management is appropriate for typical cases (**evidence level II-2, grade of recommendation 1**)
- In the presence of Kasabach-Merrit syndrome, growing or lesions symptomatic by compression - refer to benign liver tumour MDT (**evidence level III, grade of recommendation 1**)



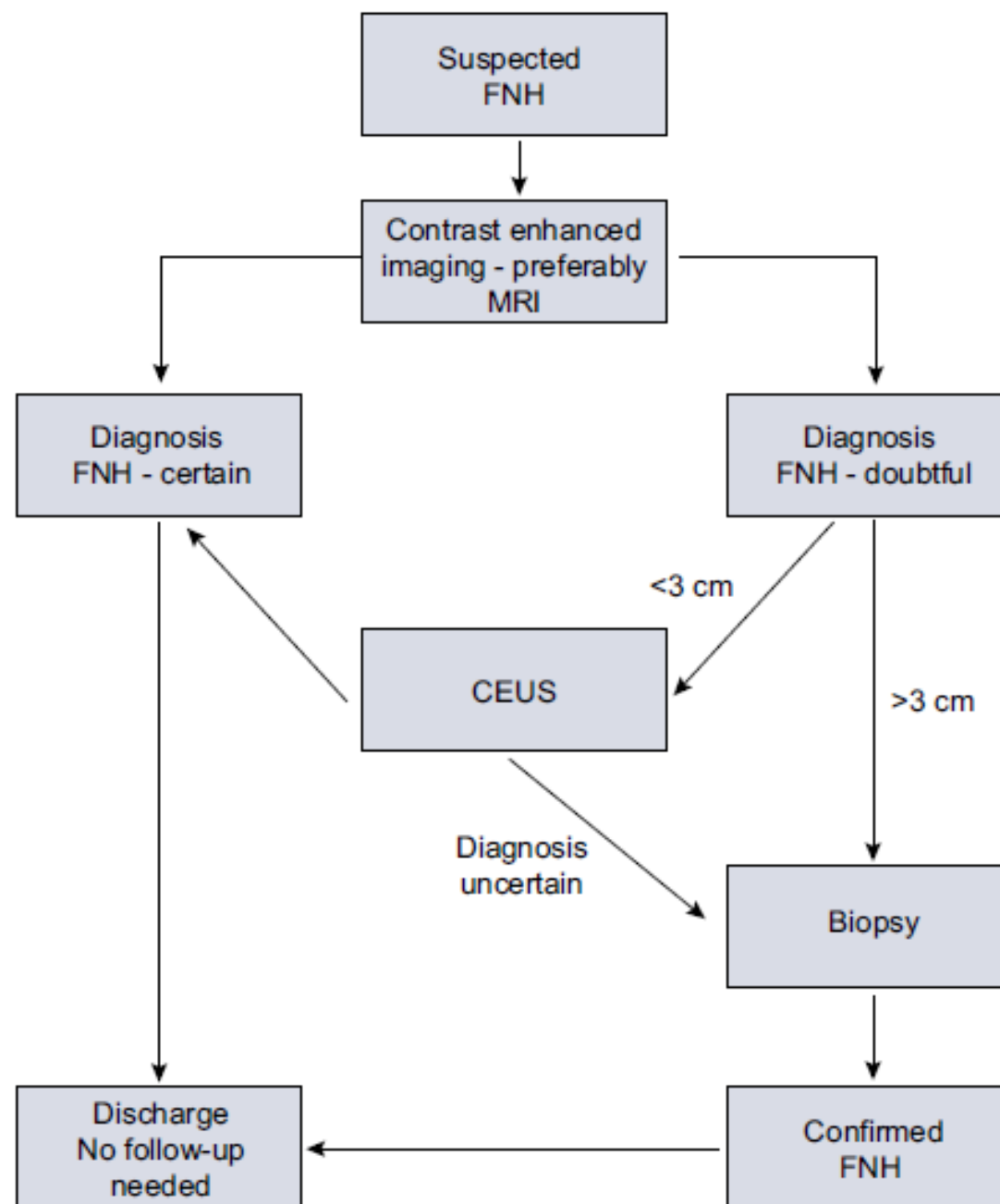
FNH

- Hyperplastic hepatocellular lesions, result from an arterial malformation
- No mutations, upregulation ECM genes (*TGF β* , Wnt targets eg. *GLUL*)
- Rarely clinically relevant, may be symptomatic in S2/3 or 6



FNH

- CEUS, CT, or MRI can diagnose FNH with nearly 100% specificity when typical imaging features are seen in combination (**evidence level II-2, grade of recommendation 1**)
- MRI has the highest diagnostic performance overall. The highest diagnostic accuracy by CEUS is achieved in FNH less than 3 cm (**evidence level II-2, grade of recommendation 1**)

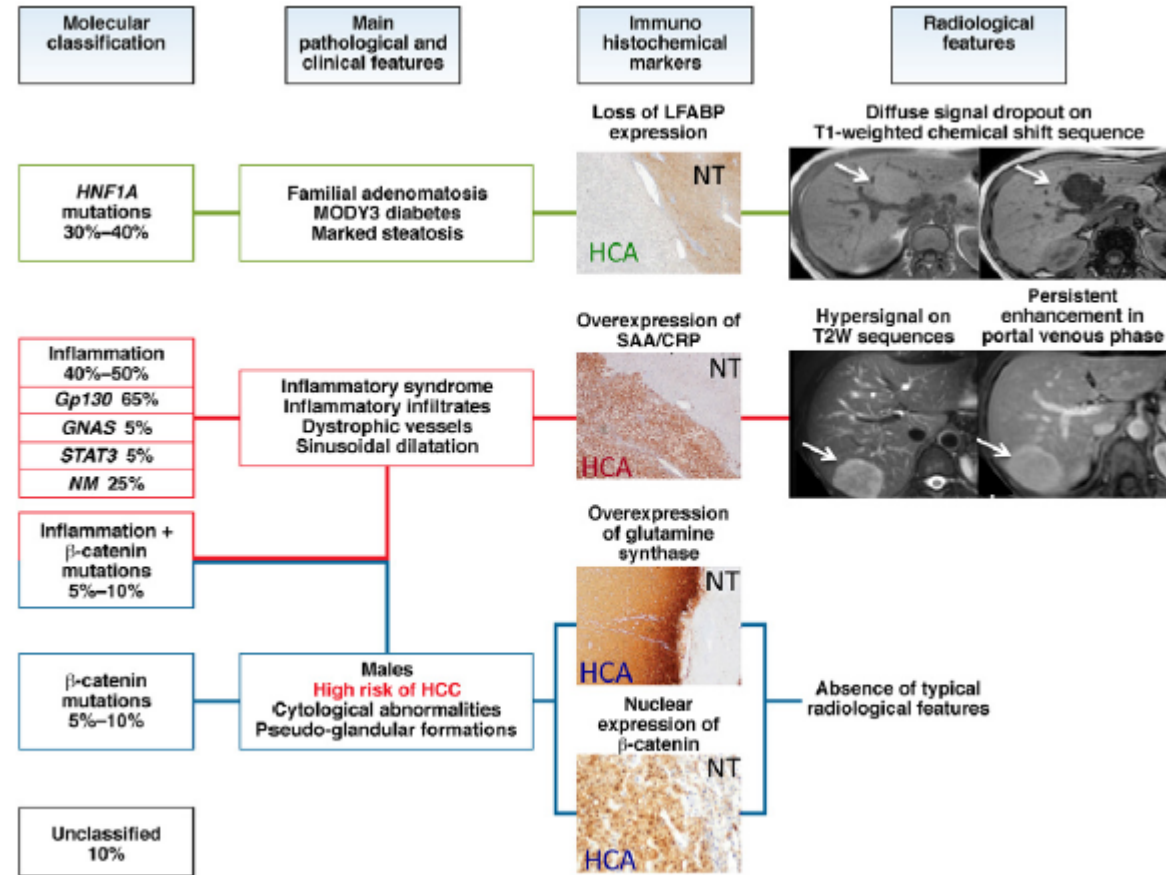


Hepatocellular adenoma (HCA)

- Not as common as haemangioma or FNH
- May also follow a benign course, however may
 - Rupture
 - Undergo malignant transformation
- Therefore there is a need to recognize these lesions and to follow them more closely
- Pathologically - benign hepatocellular proliferation, with molecular subgroups – with different patterns of imaging & behavior – recently described

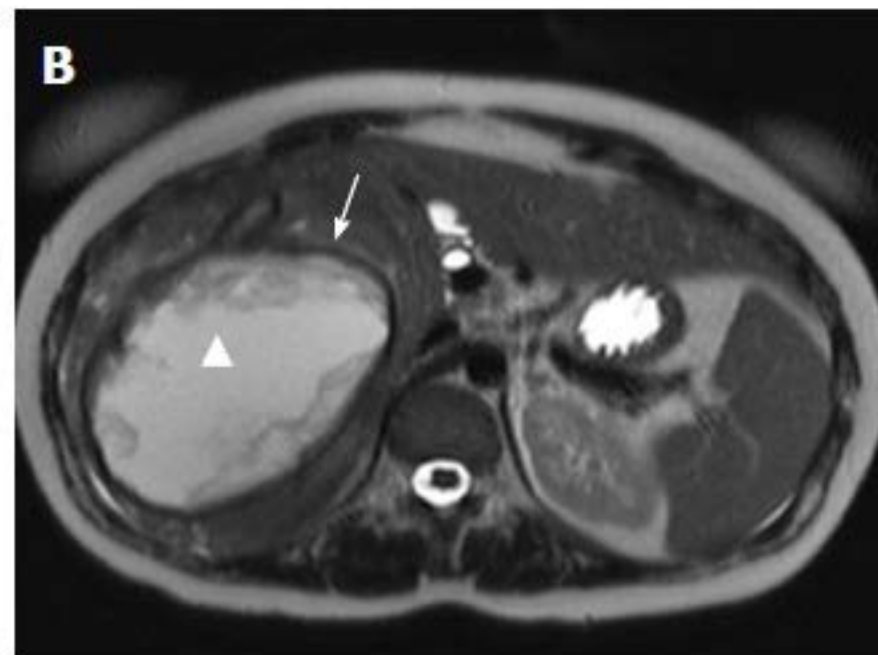
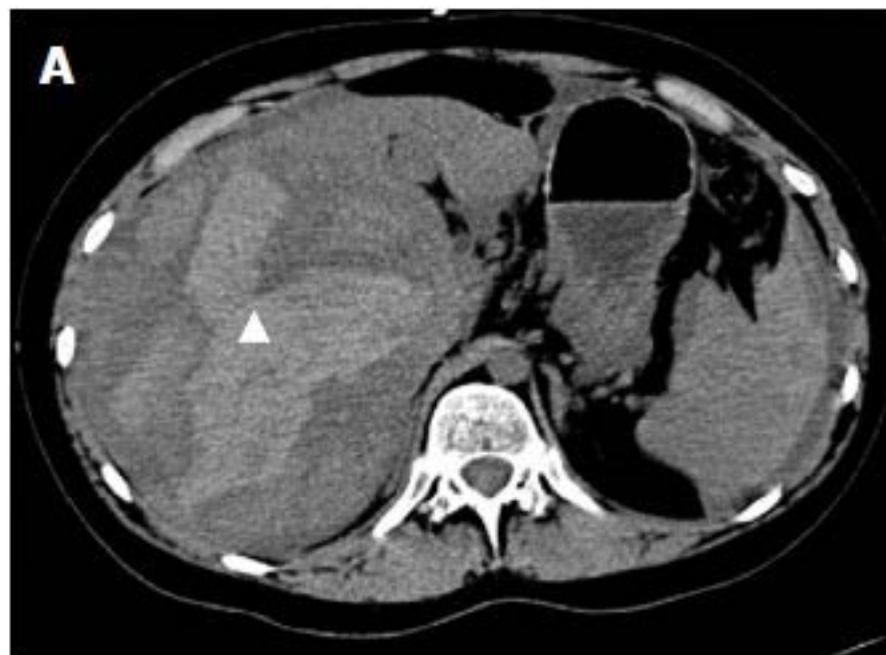
HCA – key features based on molecular subtype

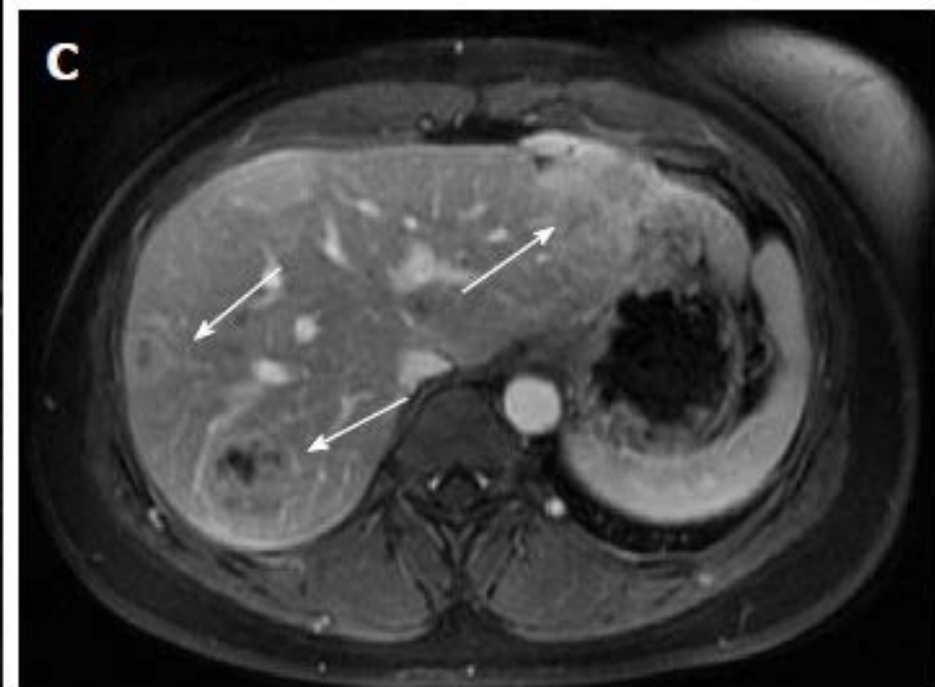
Genetic alterations	Pathology	IHC	Typical features	
			Clinical	MRI**
<i>HNF1-A</i> mutations (30-40%)	Extensive steatosis	LFABP -ve	Adenomatosis, MODY3	Diffuse and homogenous signal dropout on opposed-phase T1
Inflammatory <i>Gp130</i> (65%), <i>GNAS</i> (5%), <i>STAT3</i> (5%), <i>FRK</i> (10%), <i>JAK1</i> (2%)	Inflammatory infiltration Clusters of vessels Sinusoidal dilatation	LFABP +ve SAA (± CRP) +ve	Obesity Alcohol consumption	Strong hyperintense on T2 and persistent enhancement on delayed phase using extracellular MR contrast agents
β-catenin mutations* exon 3 (5-10%)	Cell atypias Pseudoglandular formations Cholestasis	LFABP +ve GS +ve (diffuse) β-catenin nuclear +ve	Male Androgens use increased risk of HCC	No specific feature. Often heterogeneous on T1 and T2. No signal dropout on opposed-phase T1
β-catenin mutations exons 7-8 (5-10%)	No typical features or inflammatory phenotype	GS +ve (faint and patchy) β-catenin nuclear -ve		No specific Feature
Unclassified (5-10%)	None	LFABP +ve SAA/CRP -ve β-catenin nuclear -ve		No specific Feature



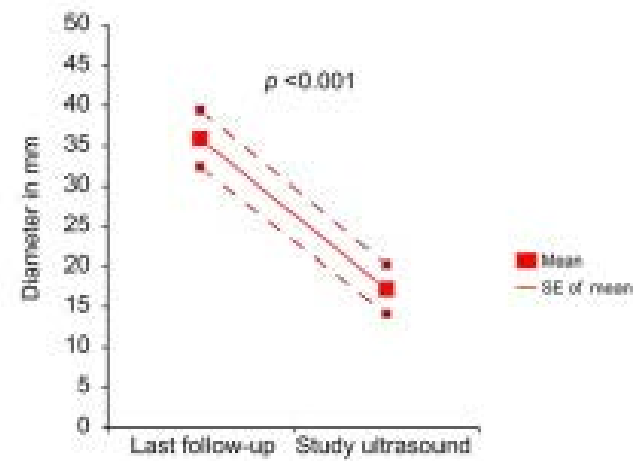
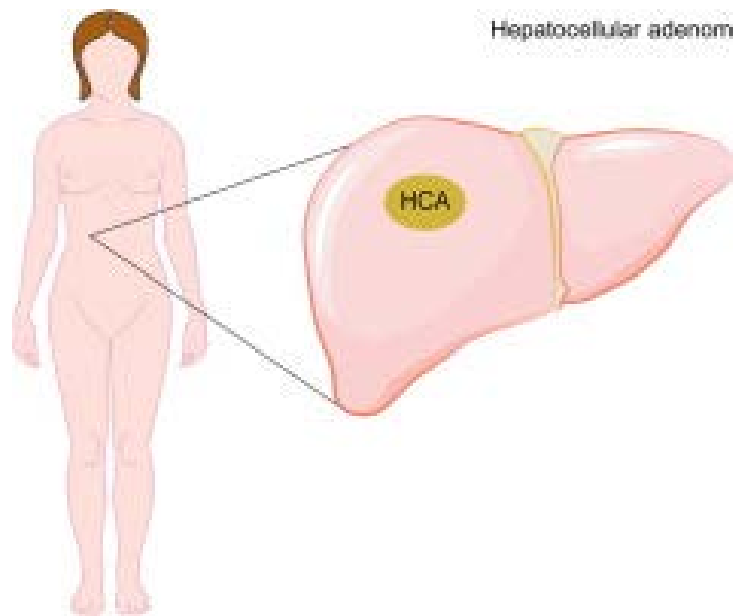
Size of the HA and bleeding

Series	Patients with hemorrhaged HCA	Size of smallest HCA (cm)	Percentage < 5 cm of total (%)
Reddy et al.[55]	3 of 25	4	-
Hung et al.[56]	4 of 25	4,2	-
Toso et al.[57]	10 of 25	1,7	-
Cho et al.[43]	12 of 41	1	8.3 (1/12)%
Bioulac-Sage et al.[9]	23 of 128	<5	-
Dokmak et al.[21, 58]	26 of 122	<5	11.5 (3/26)%
Edmondson et al. [58]	10 of 42	>5	0 %
Leese et al. [59]	2 of 24	5	0 %
Ault et al. [60]	4 of 12	6	0 %
Closset et al. [61]	7 of 16	7	0 %
Deneve et al. [62]	31 of 124	>5	0 %
Chung et al. [63]	-	5	0 %





Hepatocellular adenoma in post-menopausal women



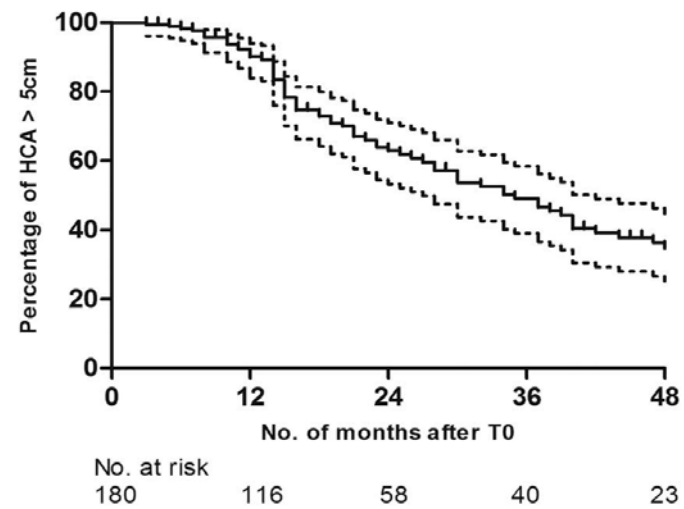
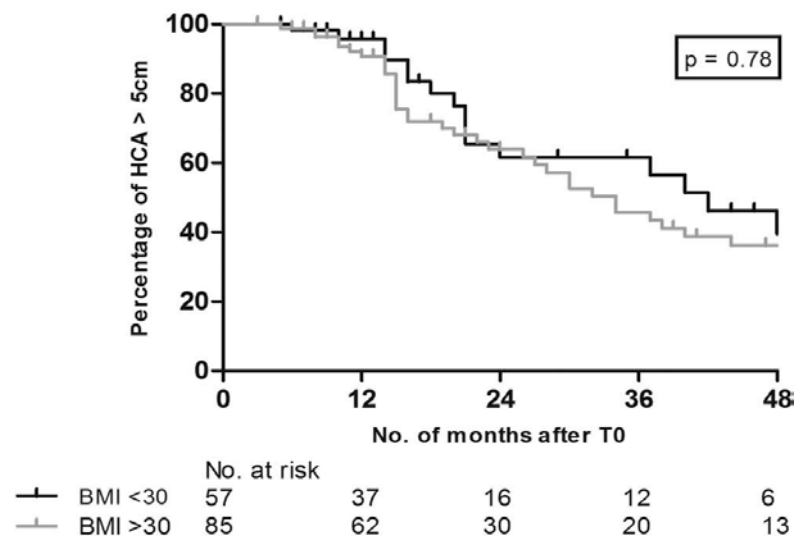
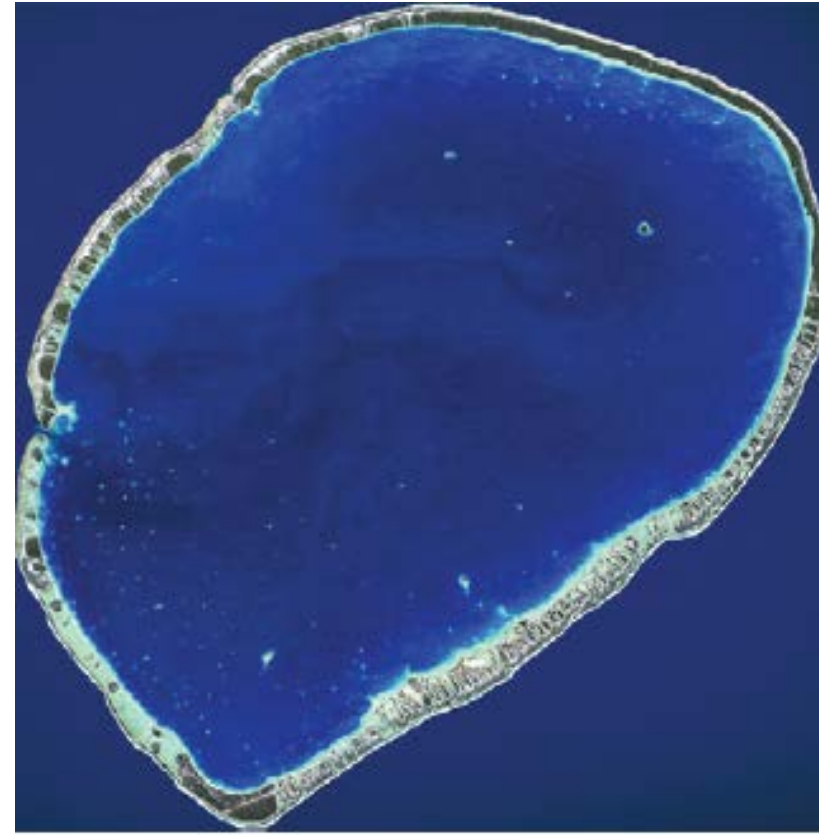
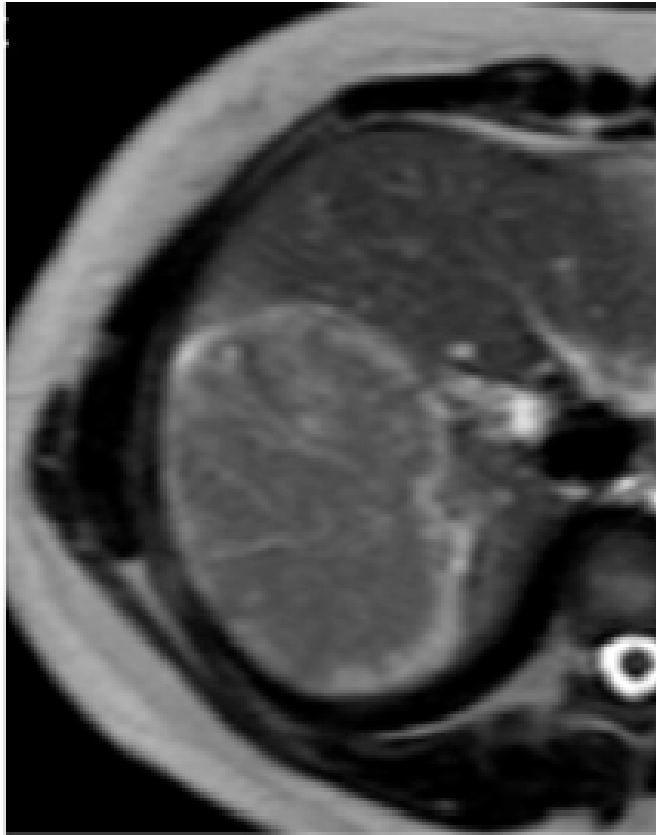
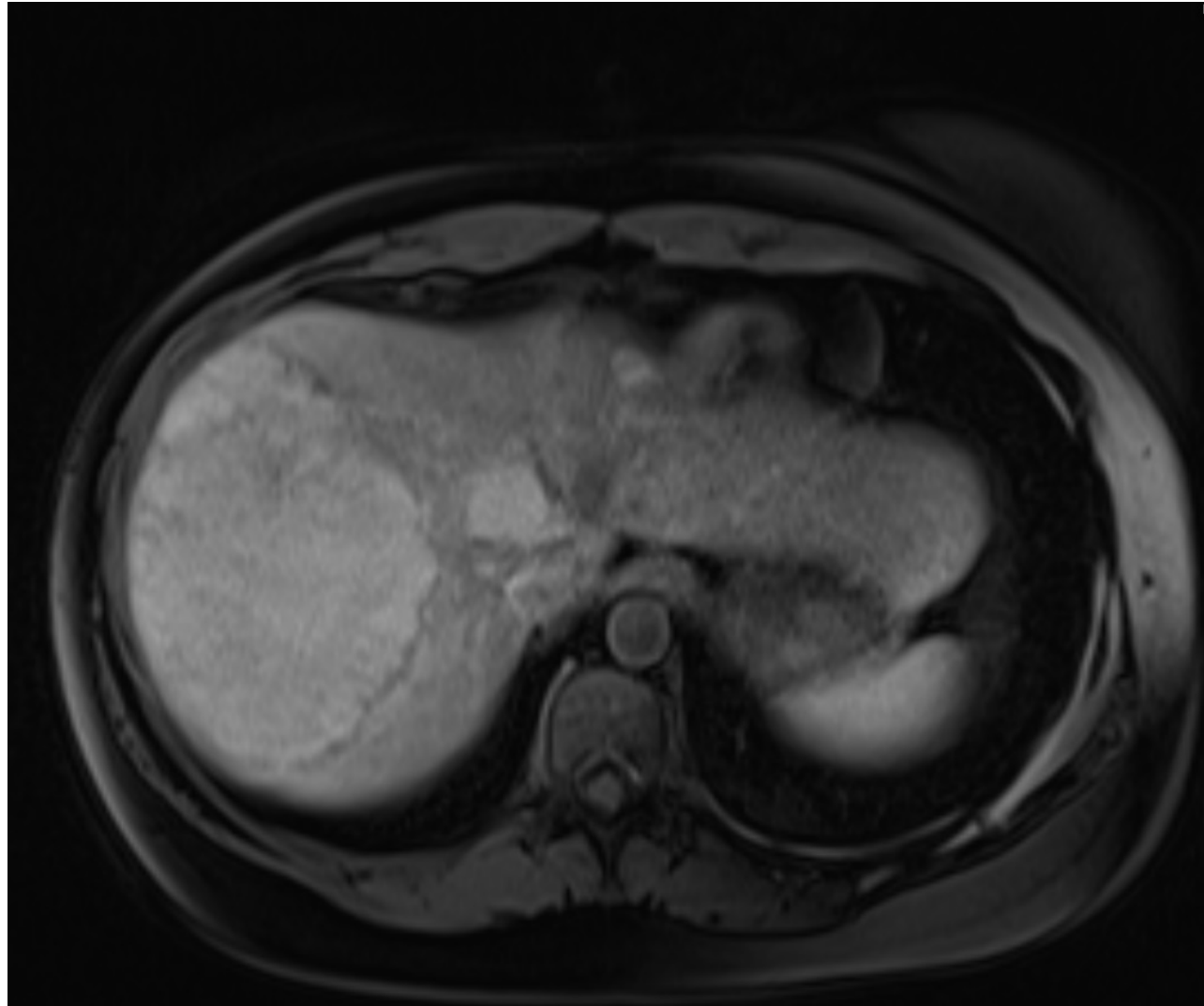
A**B**

Table 1. Immunohistochemical and MRI signs used for differentiating the HCA subtypes				
	HNF1A-mutated HCA	β -catenin-mutated HCA	Inflammatory HCA ^a	Unclassified HCA
Immunohistochemical staining				
Glutamine synthetase ^b	-	+/-	+/-	-
β -catenin	-	+	+/-	-
C-reactive protein	-	-	+	-
Serum amyloid A	-	-	+	-
LFABP	-	+	+	+
Typical MRI findings ^c	Diffuse homogenous lesional steatosis	Faint scar	Atoll sign and strong, diffuse, hyperintense signal on T2-weighting	

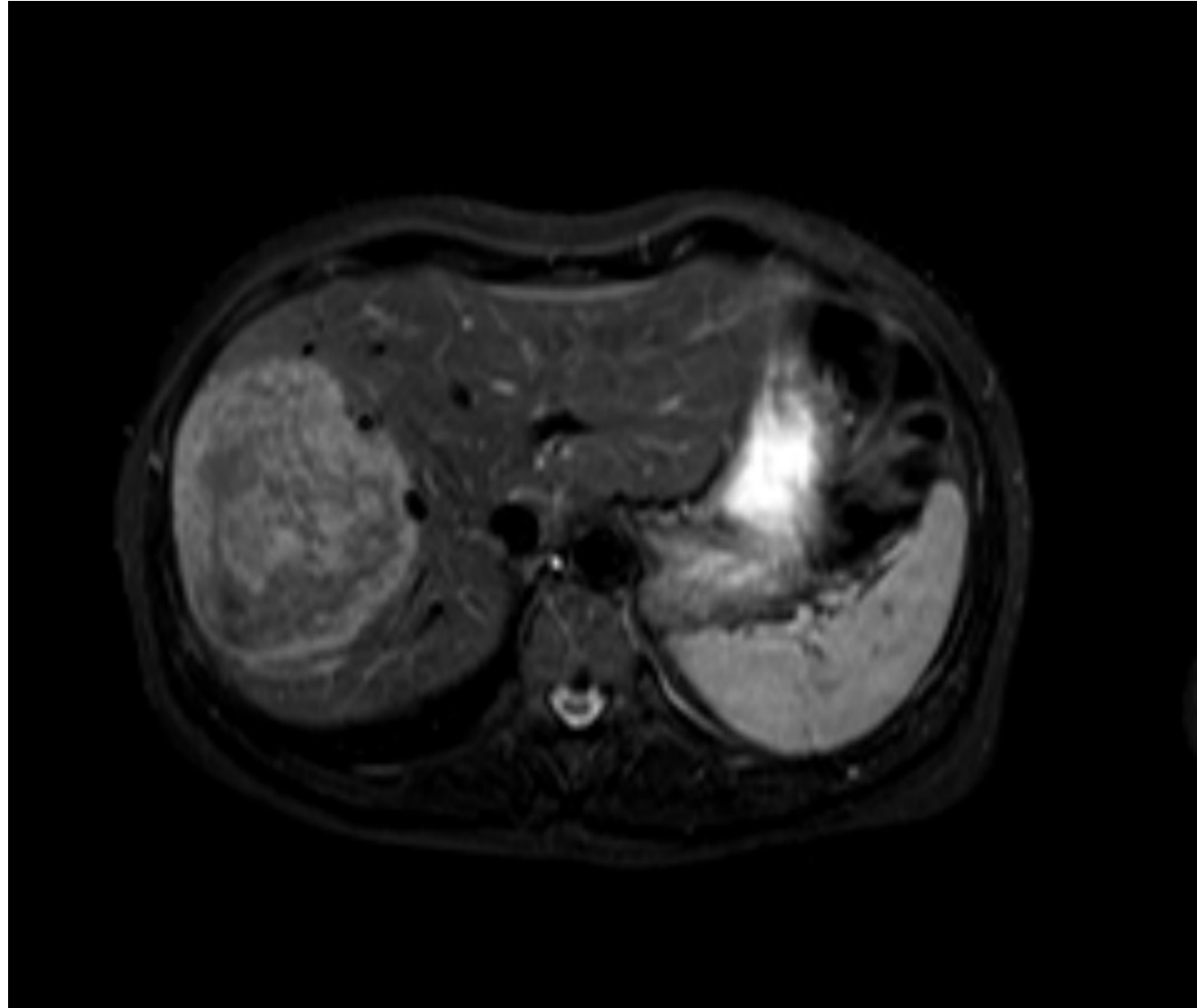


Hepatocellular Adenomas: Correlation of MR Imaging Findings with Pathologic Subtype Classification
Van Aalten et al. Gastrointestinal Imaging 2011

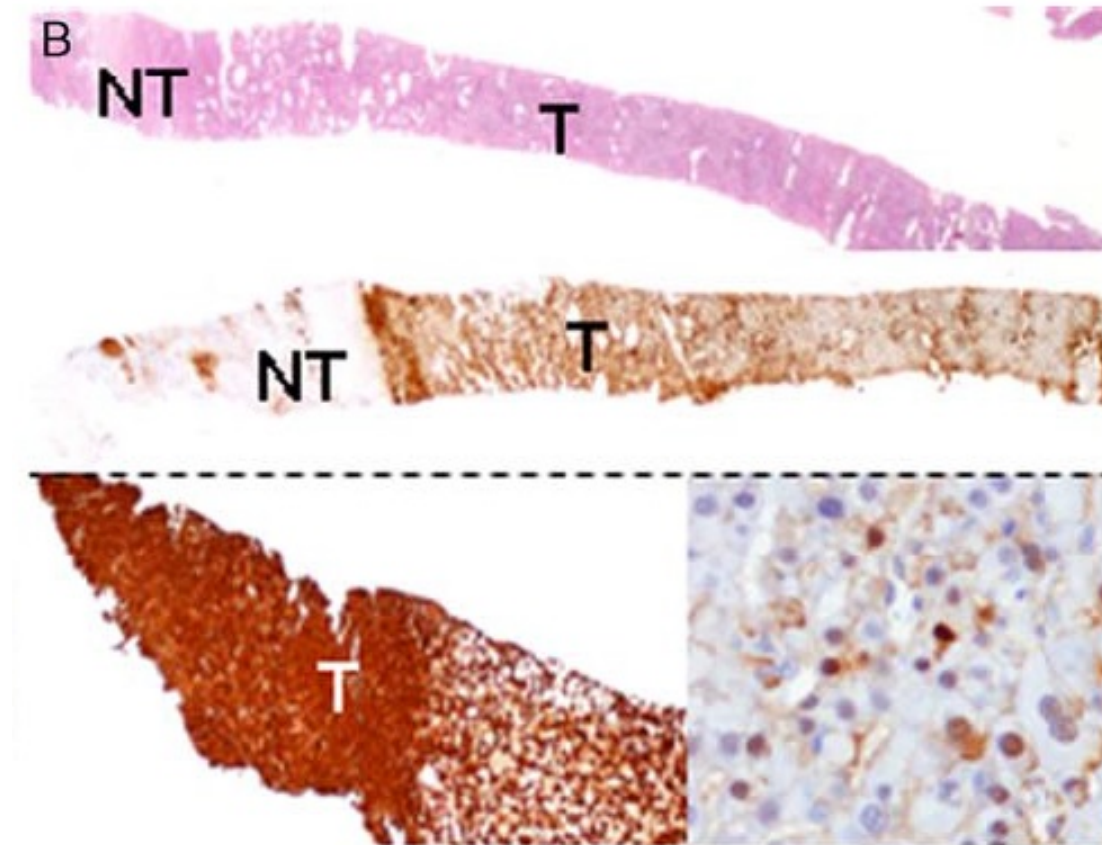
Liver adenoma with heterogeneity



Liver adenoma with bleeding

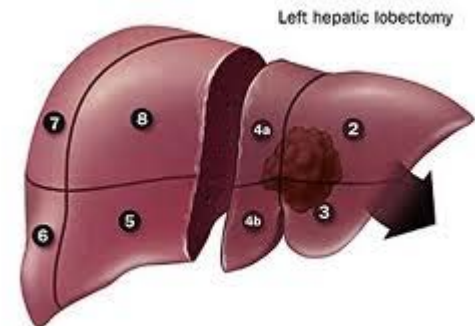
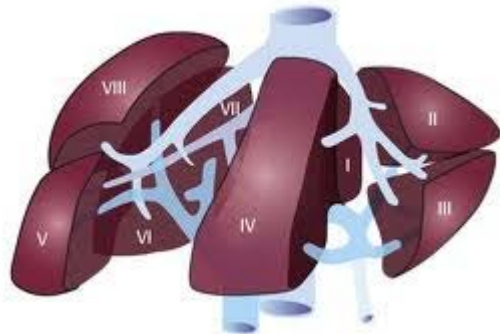
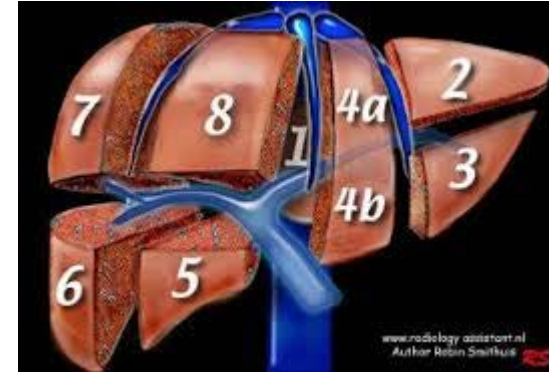
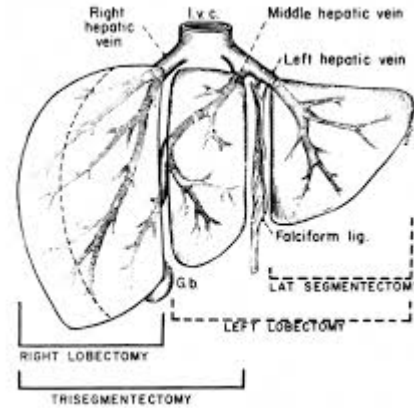
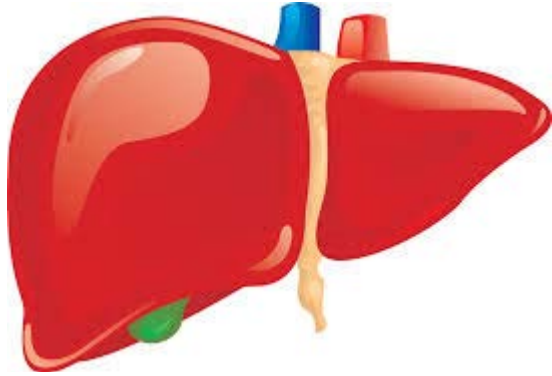


Beta-cat positive staining

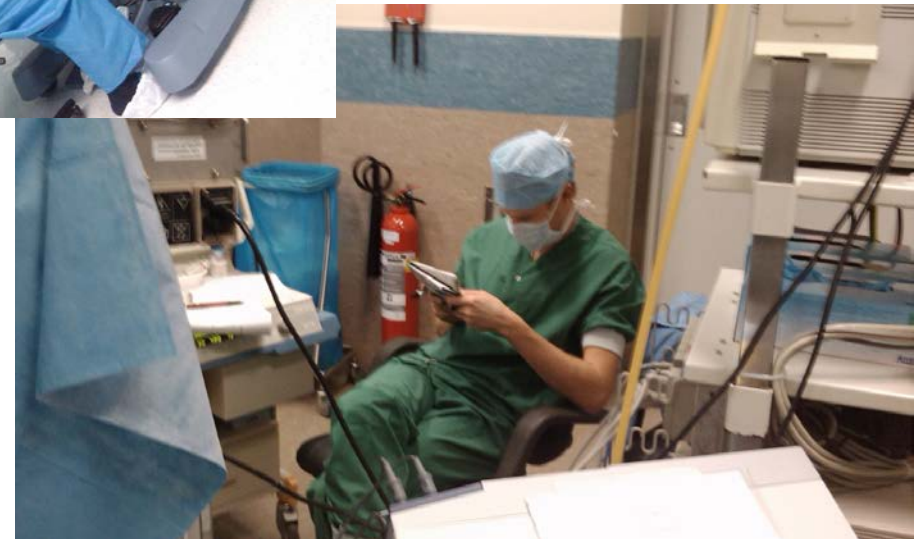


Bioulac-Sage, P., et al. (2012). "Immunohistochemical markers on needle biopsies are helpful for the diagnosis of focal nodular hyperplasia and hepatocellular adenoma subtypes." *Am J Surg Pathol* **36**(11): 1691-1699.

Liver Anatomy



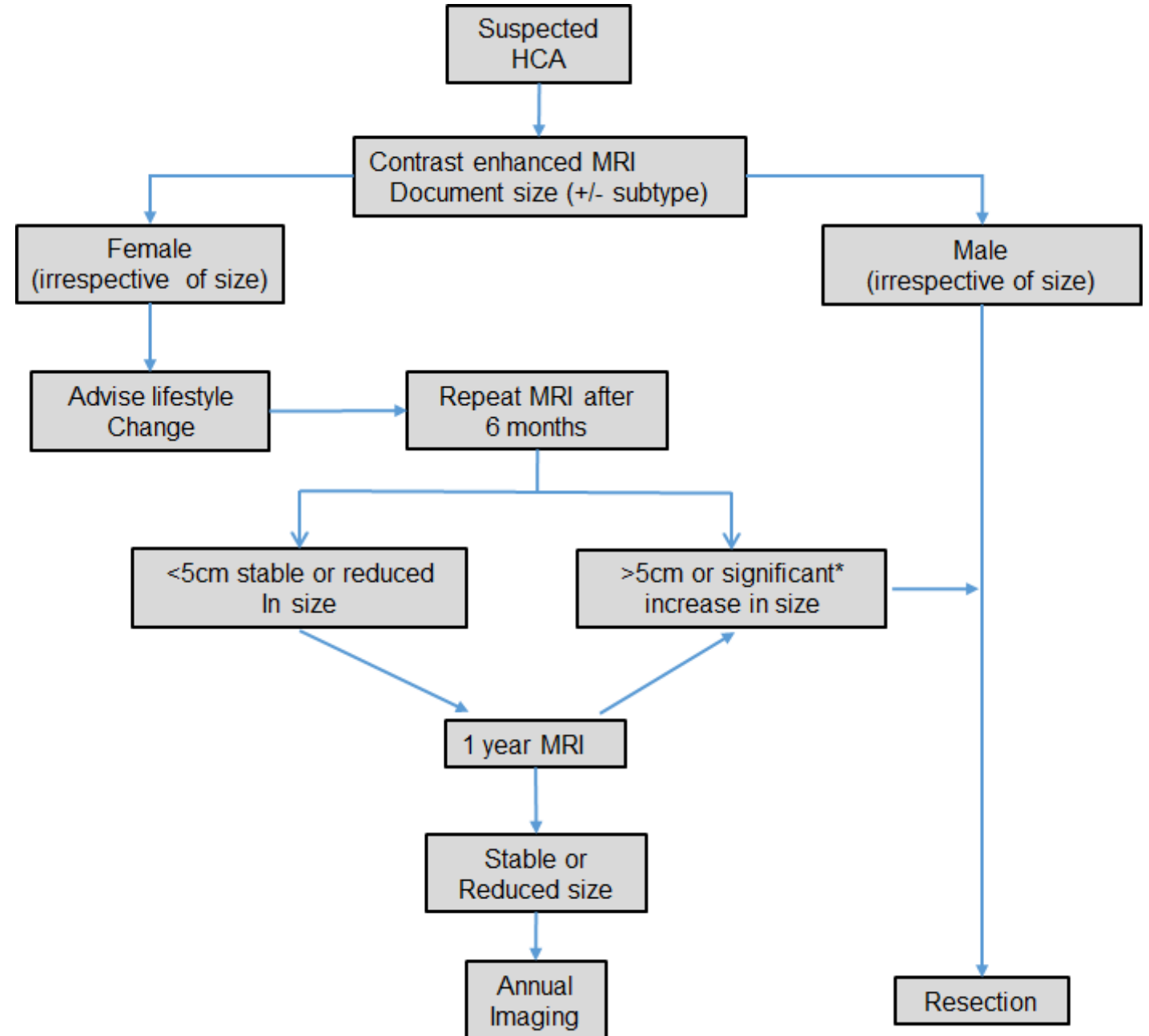
Robot - Da Vinci



Laparoscopic liver resections



HCA management algorithm



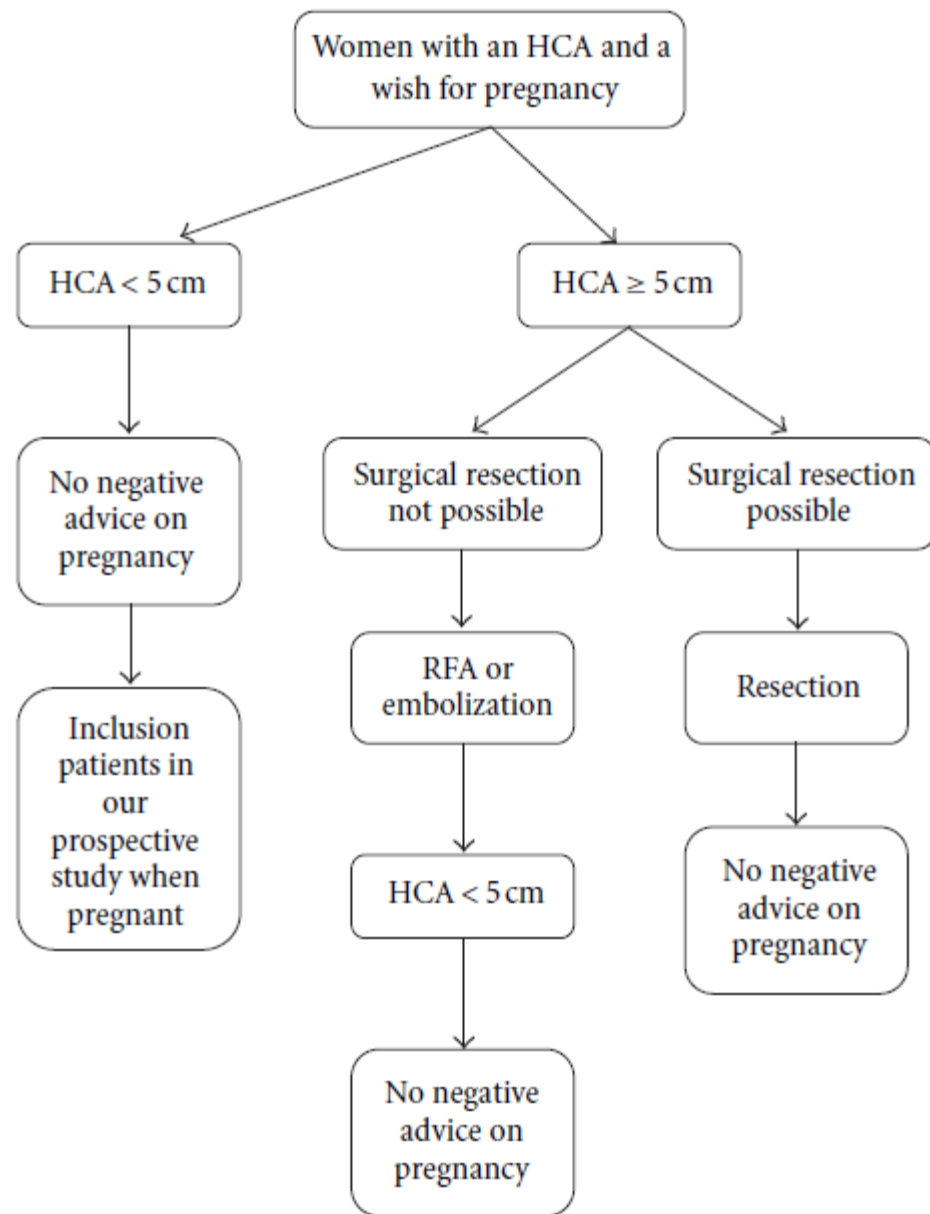


FIGURE 1: Flowchart for women with a HCA and a wish for pregnancy.

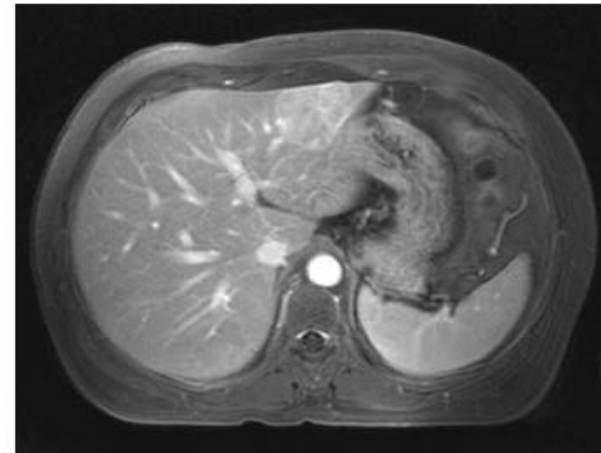
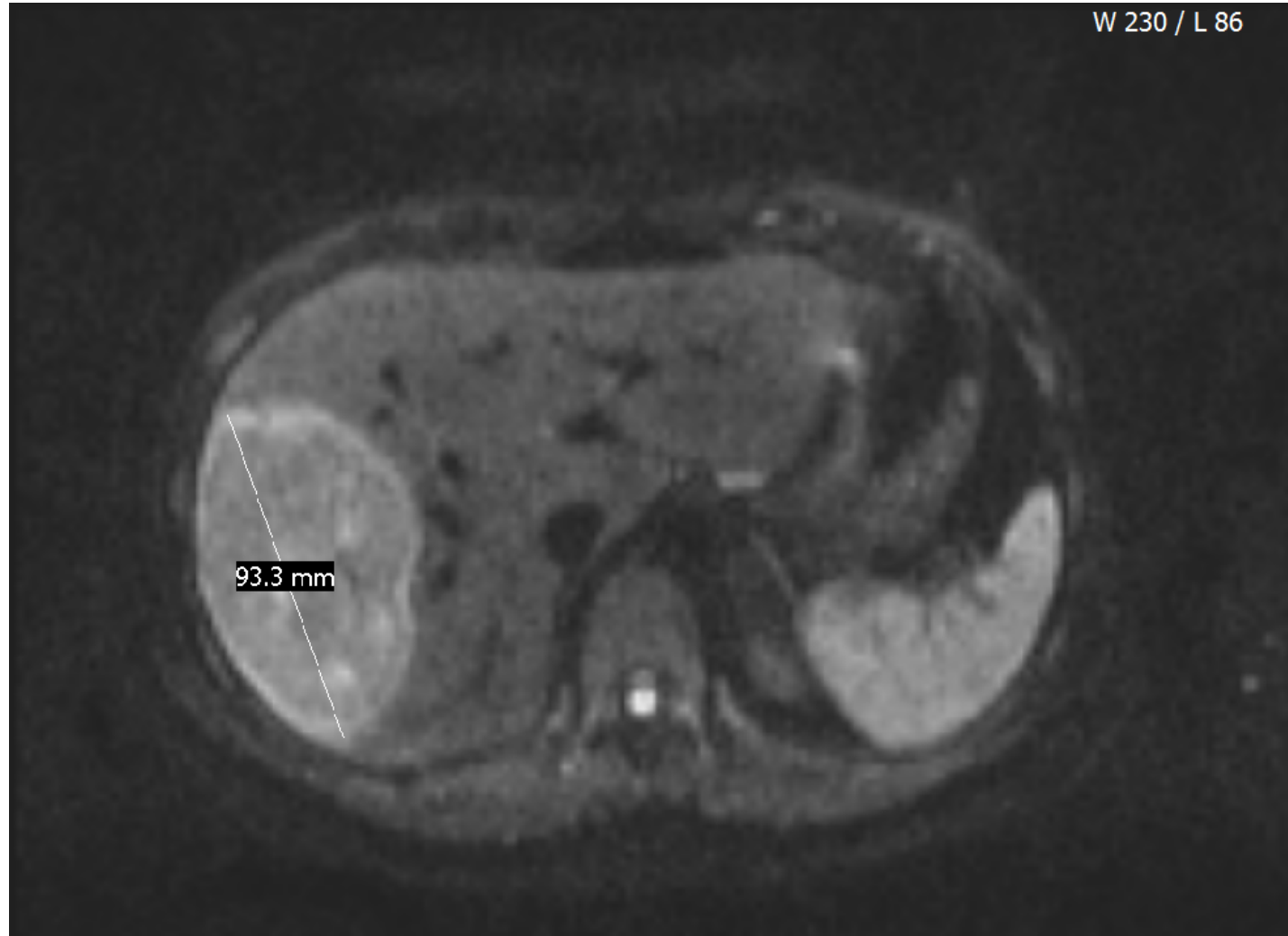


FIGURE 2: An example of a woman with a HCA of 4.2 cm in segment 2/3 in which pregnancy will not be discouraged.

Mrs XX

- A 32 year old woman with no relevant medical history presented to the Emergency Room after an accident in 2013
- Ultrasound demonstrated an incidental lesion in the liver of 9cm
- Additional imaging indicated?

MRI 2013



Mrs XX

- Additional MRI confirmed the lesion to be a hepatocellular adenoma (HCA) of 9 cm
- Management?

Mrs XX

- Lifestyle changes
- Cessation of oral contraceptives
- Reduction of body weight if indicated
- Discourage pregnancy

Mrs XX

- After cessation of OAC the HCA regressed to 4,9 cm
- Follow up indicated?
- Contra-indications for pregnancy at this size?

MRI 2015 at 24 week of gestation



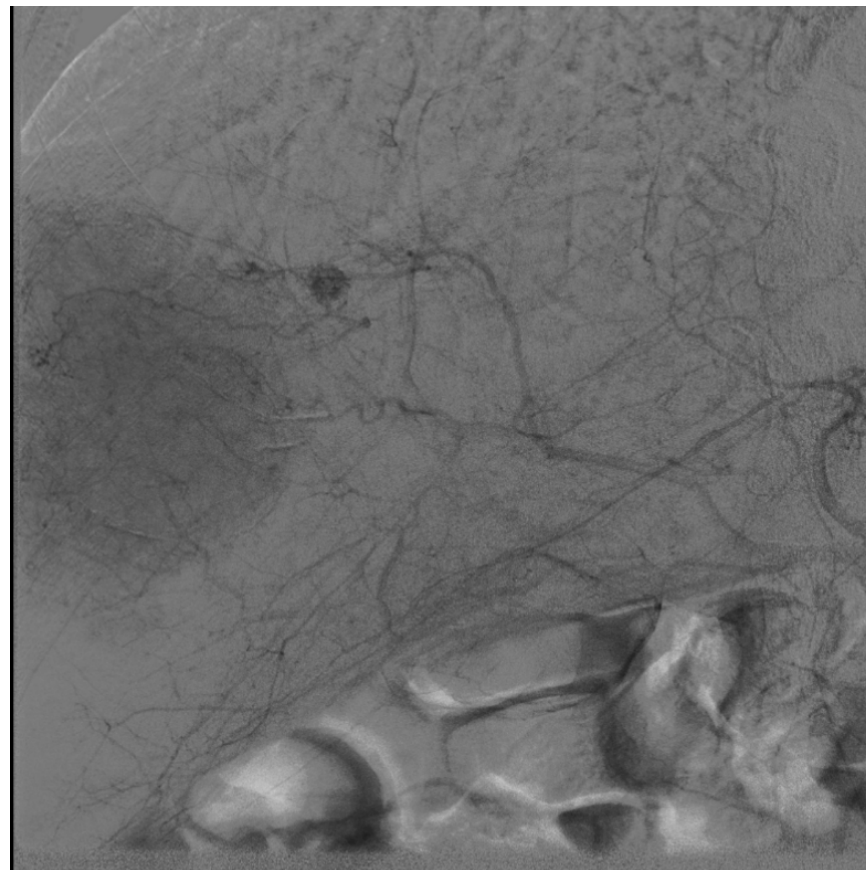
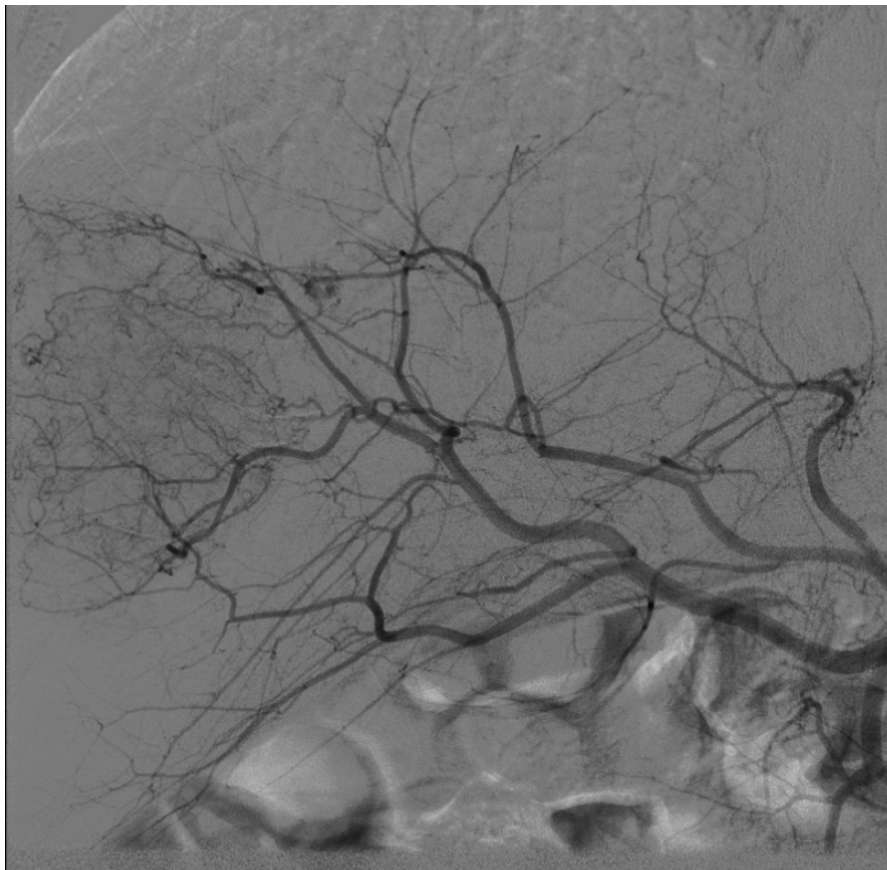
Follow-up 2015

- The patient presented again in 2015 with an unplanned pregnancy
- The patient was included in a study, implicating regular follow up
- Additional MRI
- Ultrasound showed growth of the adenoma to 7,7 cm at 28 weeks of gestation

Therapeutic considerations

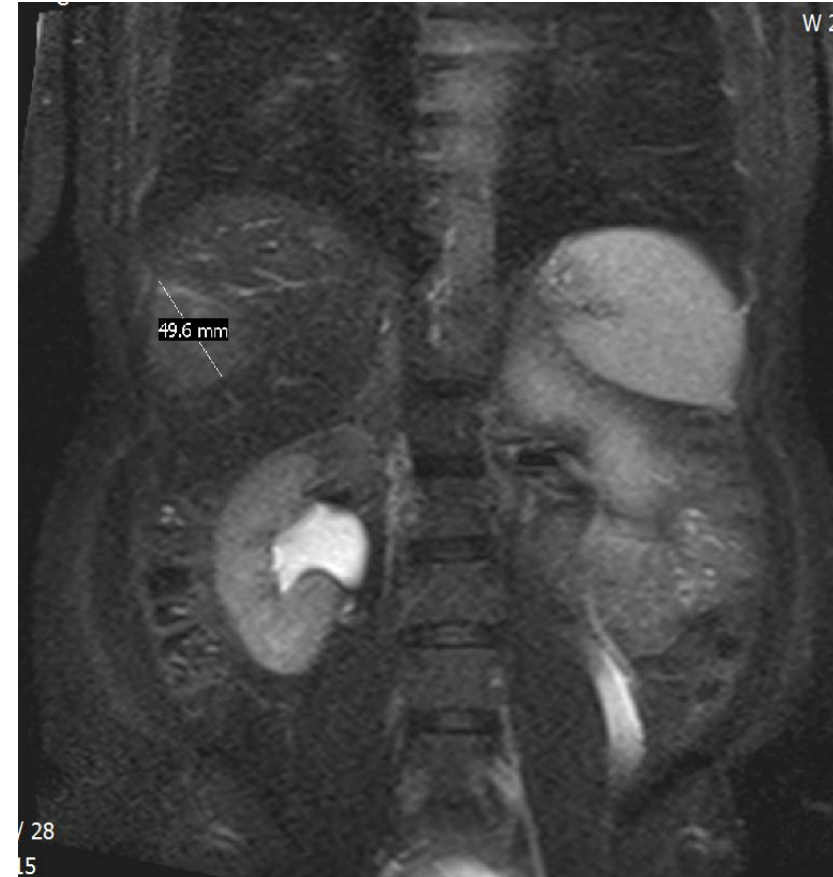
- Multidisciplinary meeting
 - Surgery ?
 - Embolization?
 - Wait and see?

Embolization 09-2015



Follow-up

- Patient was discharged without any complications
- An additional MRI one month after embolization showed further regression of the adenoma to 4,9 cm
- Pregnancy and delivery went without complications and mother and child are doing well.





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Thank you for your attention

