

Imaging features of histological subtypes of hepatocellular carcinoma: implication for LI-RADS

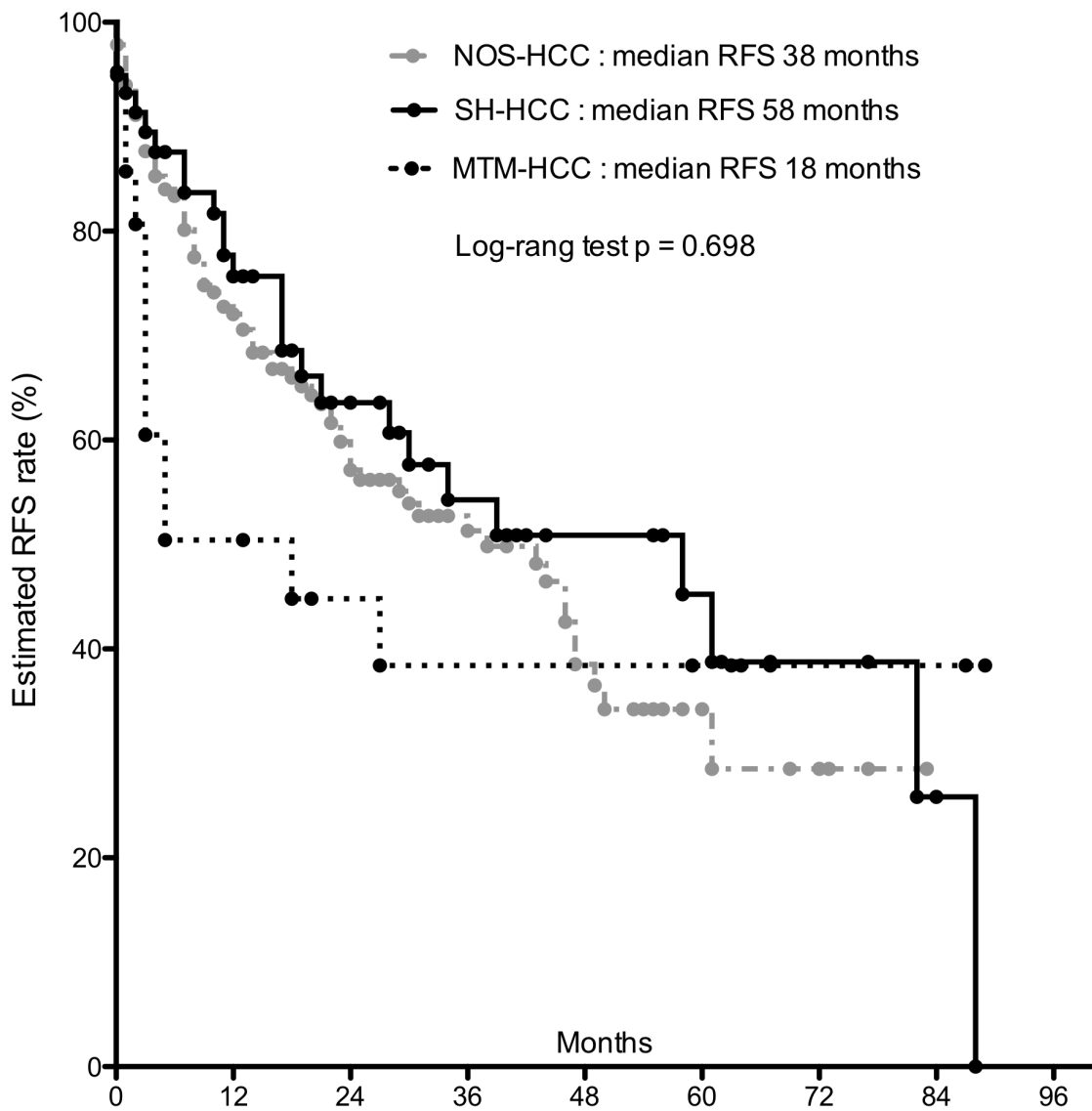
Roberto Cannella, Marco Dioguardi Burgio, Aurélie Beaufrère, Loïc Trapani, Valérie Paradis,
Christian Hobeika, Francois Cauchy, Mohamed Bouattour, Valérie Vilgrain, Riccardo
Sartoris, Maxime Ronot.

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IMAGING TECHNIQUE

CT and MRI exams were acquired with different scanners due to the retrospective design of the study. Patients were intravenously administered a weight-based dose of iodinated contrast agent for contrast-enhanced CT, with an iodine concentration of 350 g/L, injected with a power injector at a rate of 3-4 ml/s. MRI exams were acquired before and after the intravenous administration of gadolinium-based contrast agent (Gd-BOPTA, Gadobenate Dimeglumine, MultiHance, Bracco Imaging, Milan, Italy; Gd-DOTA, gadoterate meglumine, Dotarem, Guerbet, Aulnay-sous-Bois, France; or occasionally other gadolinium-based extracellular contrast agents), injected with a power injector at a rate of 2 ml/s. Post-contrast phases included at least late hepatic arterial (acquired with bolus triggering technique), portal venous (70 to 90 seconds), and delayed (180 seconds) phases. Due to the retrospective study design, diffusion-weighted imaging and dual gradient-echo sequences were missing in ten and four patients, respectively. Hepatobiliary phase (HBP) images were acquired at 2 hours after the administration of Gd-BOPTA in 68 exams.

Fig. S1. Kaplan-Meier curves for recurrence-free survival (RFS) according to hepatocellular carcinoma (HCC) main subtypes. Abbreviations: MTM-HCC=macrotrabecular massive hepatocellular carcinoma; NOS-HCC=not otherwise specified hepatocellular carcinoma; RFS=Recurrence-free survival; SH-HCC=steatohepatitic hepatocellular carcinoma.



NOS - HCC	186	103	66	37	21	8	4	1	0
SH-HCC	59	41	24	17	12	9	5	2	0
MTM-HCC	21	12	8	7	7	6	3	2	0

Fig. S2. Kaplan-Meier curves for overall survival (OS) according to hepatocellular carcinoma (HCC) main subtypes. Abbreviations: MTM-HCC=macrotrabecular massive hepatocellular carcinoma; NOS-HCC=not otherwise specified hepatocellular carcinoma; OS=overall survival; SH-HCC=steatohepatic hepatocellular carcinoma.

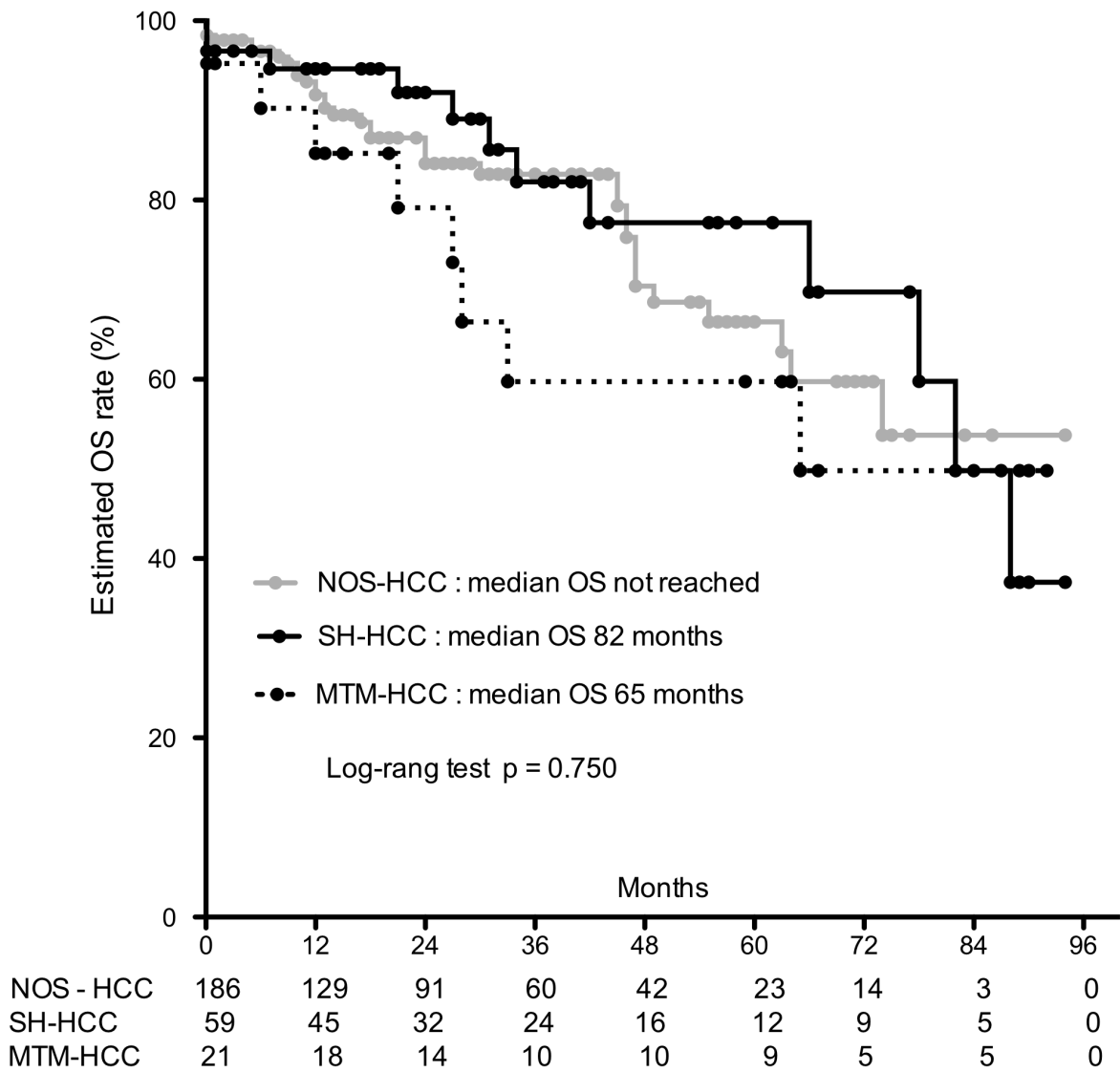


Table S1: Clinical and laboratory and histopathological characteristics of the patients with other hepatocellular carcinoma (HCC) subtypes.

Characteristics	All	Clear Cell HCC	Lymphocyte-rich HCC	Scirrhou HCC	Fibrolamellar HCC
<i>Clinical and laboratory features</i>					
Patients	12	5	4	2	1
Age (years)	62.5	60.0	68.5	70.5	43.0
Sex					
Men	8 (66.7)	3 (60.0)	4 (100)	1 (50.0)	0 (0)
Women	4 (33.3)	2 (40.0)	0 (0)	1 (50.0)	1 (100)
Age men (years)	64.0	36.0	68.5	78.0	NA
Age women (years)	61.5	65.0	NA	63.0	43.0
Chronic liver disease*					
Hepatitis C	1 (8.3)	0 (0)	1 (25.0)	0 (0)	0 (0)
Hepatitis B	4 (33.3)	2 (40.0)	1 (25.0)	1 (50.0)	0 (0)
Alcohol abuse	2 (16.7)	1 (20.0)	0 (0)	1 (50.0)	0 (0)
NAFLD	5 (41.7)	3 (60.0)	2 (50.0)	0 (0)	0 (0)
Vascular liver disease	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Others	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
No risk	1 (8.3)	0 (0)	0 (0)	0 (0)	1 (100)
Cirrhosis	3 (25.0)	1 (20.0)	1 (25.0)	1 (50.0)	0 (0)
LI-RADS high risk status	7 (58.3)	3 (60.0)	2 (50.0)	2 (100)	0 (0)
AST (IU/L)	46.0	42.0	41.5	182.5	44.0
ALT (IU/L)	44.5	28.0	45.5	120.0	50.0
Albumin (g/L)	35.0	35.0	38.0	32.5	25.0
Creatinine (μmol/L)	87.5	93.0	82.5	63.5	78.0
Total bilirubin (mg/L)	8.0	8.0	9.0	27.0	6.0
Platelet count (x10³/μL)	228	272	175	131	266
α-fetoprotein (ng/mL)	193.0	647.0	7.0	NA	NA
RFS (months)	19.5	4.0	46.5	58.5	2.0
Overall survival (months)	39.5	37.0	46.5	58.5	15.0
<i>Histopathological features</i>					
HCC	13	5	4	2	2
Edmonson-Steiner grade					
I-II	3 (23.1)	4 (40.0)	1 (25.0)	0 (0)	0 (0)
III-IV	10 (76.9)	3 (60.0)	3 (75.0)	2 (100)	2 (100)
Macrovascular invasion	1 (7.7)	1 (20.0)	0 (0)	0 (0)	0 (0)
Microvascular invasion	8 (61.5)	4 (80.0)	1 (25.0)	2 (100)	1 (50.0)
Satellite nodules	5 (38.5)	3 (60.0)	0 (0)	0 (0)	2 (100)
Macroscopic capsule	8 (61.5)	3 (60.0)	3 (75.0)	0 (0)	2 (100)

Microscopic capsule	8 (61.5)	3 (60.0)	3 (75.0)	0 (0)	2 (100)
Hepatic steatosis					
None	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mild	3 (23.1)	1 (20.0)	2 (50.0)	0 (0)	0 (0)
Moderate	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hepatic fibrosis stage					
F0	7 (7.7)	1 (20.0)	0 (0)	0 (0)	0 (0)
F1	3 (23.1)	0 (0)	1 (25.0)	0 (0)	2 (100)
F2	3 (23.1)	2 (40.0)	1 (25.0)	0 (0)	0 (0)
F3	3 (23.1)	1 (20.0)	1 (25.0)	1 (50.0)	0 (0)
F4	3 (23.1)	1 (20.0)	1 (25.0)	1 (50.0)	0 (0)

Note.—Continuous variables are expressed as medians, categorical variables are expressed as numbers and percentages in parenthesis.

*More than one etiology could be present in each patient.

Abbreviations: ALT=alanine transaminase, AST=aspartate transaminase; HCC=hepatocellular carcinoma; NAFLD=nonalcoholic fatty liver disease; RFS=Recurrence-free survival.

Table S2: Differences in LI-RADS-defined ancillary features favoring malignancy, not HCC in particular and favoring HCC in particular, in non-otherwise specified (NOS), steatohepatitic (SH), and macrotrabecular-massive (MTM) hepatocellular carcinoma (HCC) subtypes in the entire cohort with contrast-enhanced CT ($n=253$).

Ancillary Features	NOS-HCC ($n=175$)	SH-HCC ($n=58$)	MTM-HCC ($n=20$)	P value	R1 vs R2 N agreement (%) k value (95% CI)	R1 vs R3 N agreement (%) k value (95% CI)	R2 vs R3 N agreement (%) k value (95% CI)
Favoring malignancy, not HCC in particular							
Subthreshold growth							
Reader 1	40 (22.9)	13 (22.4)	4 (20.0)	0.959	199 (78.7)	202 (79.8)	192 (75.9)
Reader 2	29 (16.6)	14 (24.1)	4 (20.0)	0.432	0.34 (0.21, 0.48)	0.48 (0.36, 0.60)	0.35 (0.23, 0.48)
Reader 3	47 (26.9)	23 (39.7)	6 (30.0)	0.183			
Corona enhancement							
Reader 1	6 (3.4)	2 (3.4)	0 (0)	0.701	236 (93.3)	240 (94.9)	239 (94.5)
Reader 2	10 (5.7)	3 (5.2)	0 (0)	0.548	0.15 (-0.07, 0.38)	0.10 (-0.13, 0.34)	0.27 (0.008, 0.54)
Reader 3	5 (2.9)	1 (1.7)	1 (5.0)	0.737			
Fat sparing in solid mass							
Reader 1	2 (1.1)	3 (5.2)	0 (0)	0.129	246 (97.2)	246 (97.2)	247 (97.6)
Reader 2	1 (0.6)	5 (8.6)	0 (0)	0.002	0.35 (-0.01, 0.71)	0.20 (-0.15, 0.57)	0.38 (0.00, 0.77)
Reader 3	1 (0.6)	3 (5.2)	0 (0)	0.043			
Favoring malignancy, HCC in particular							
Nonenhancing "capsule"							
Reader 1	1 (0.6)	0 (0)	1 (5.0)	0.079	248 (98.0)	249 (98.4)	246 (97.2)

Reader 2	5 (2.9)	0 (0)	0 (0)	0.321	0.27 (-0.16, 0.71)	-0.007 (-0.01, -	-0.01 (-0.02,
Reader 3	2 (1.1)	0 (0)	0 (0)	0.638		0.0001)	0.0002)
Nodule-in-nodule architecture							
Reader 1	0 (0)	0 (0)	0 (0)	1.000	239 (92.9)	247 (97.6)	237 (93.7)
Reader 2	14 (8.0)	3 (5.2)	1 (5.0)	0.714	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.30 (0.06, 0.55)
Reader 3	5 (2.9)	1 (1.7)	0 (0)	0.681			
Mosaic architecture							
Reader 1	34 (19.4)	13 (22.4)	4 (20.0)	0.886	177 (70.0)	214 (84.6)	196 (80.2)
Reader 2	83 (47.4)	25 (43.1)	11 (55.5)	0.644	0.37 (0.28, 0.47)	0.59 (0.47, 0.70)	0.53 (0.44, 0.63)
Reader 3	53 (30.3)	14 (24.1)	7 (35.0)	0.565			
Fat in mass, more than adjacent liver							
Reader 1	22 (12.6)	19 (32.8)	0 (0)	< 0.001	205 (81.1)	224 (88.5)	196 (77.5)
Reader 2	39 (23.3)	19 (32.8)	3 (15.0)	0.166	0.41 (0.28, 0.55)	0.54 (0.40, 0.69)	0.27 (0.133, 0.41)
Reader 3	14 (8.0)	19 (32.8)	1 (5.0)	< 0.001			
Blood products in mass							
Reader 1	10 (5.7)	1 (1.7)	1 (5.0)	0.463	213 (84.2)	241 (95.3)	215 (85.0)
Reader 2	35 (20.0)	9 (15.5)	2 (10.0)	0.457	0.25 (0.10, 0.40)	0.43 (0.16, 0.69)	0.27 (0.12, 0.42)
Reader 3	7 (4.0)	3 (3.4)	1 (5.0)	0.952			

Note.- Categorical variables are expressed as numbers and percentages in parenthesis. Differences between HCC subtypes were assessed using the Pearson χ^2 test. Inter-reader agreement was assessed using the Cohen's kappa (k) test. Statistically significant values ($P < 0.05$) are highlighted in bold.

Abbreviations: CI=confidence interval; HCC=hepatocellular carcinoma; MTM-HCC=macrotrabecular massive hepatocellular carcinoma; NOS-HCC=not otherwise specified hepatocellular carcinoma; SH-HCC=steatohepatitic hepatocellular carcinoma.

Table S3: Differences in LI-RADS-defined TIV, LR-M features, and major features in non-otherwise specified (NOS), steatohepatic (SH), and macrotrabecular-massive (MTM) hepatocellular carcinoma (HCC) subtypes in high-risk patients with contrast-enhanced CT ($n=134$).

Features	NOS-HCC ($n=88$)	SH-HCC ($n=30$)	MTM-HCC ($n=16$)	P value	R1 vs R2 N agreement (%) <i>k</i> value (95% CI)	R1 vs R3 N agreement (%) <i>k</i> value (95% CI)	R2 vs R3 N agreement (%) <i>k</i> value (95% CI)
TIV							
Reader 1	4 (4.5)	0 (0)	3 (18.8)	0.022	124 (92.6)	129 (96.2)	123 (91.8)
Reader 2	10 (11.4)	1 (3.3)	4 (25.0)	0.085	0.51 (0.25, 0.76)	0.52 (0.16, 0.89)	0.39 (0.11, 0.66)
Reader 3	2 (2.3)	0 (0)	2 (12.5)	0.048			
LR-M features							
At least one LR-M feature							
Reader 1	36 (40.9)	4 (13.3)	10 (62.5)	0.002	111 (82.9)	119 (88.8)	116 (86.6)
Reader 2	30 (34.1)	4 (13.3)	7 (43.8)	0.049	0.61 (0.48, 0.75)	0.74 (0.63, 0.86)	0.67 (0.53, 0.81)
Reader 3	25 (28.4)	4 (13.3)	8 (50.0)	0.029			
At least one targetoid features							
Reader 1	10 (11.4)	0 (0)	3 (18.8)	0.082	122 (91.0)	125 (93.3)	123 (91.8)
Reader 2	2 (2.3)	1 (3.3)	0 (0)	0.479	0.22 (-0.0, 0.49)	0.62 (0.40, 0.85)	0.32 (0.04, 0.61)
Reader 3	10 (11.4)	1 (3.3)	3 (18.8)	0.237			
Rim APHE							
Reader 1	6 (6.8)	0 (0)	2 (12.5)	0.199	127 (94.8)	129 (96.3)	124 (92.5)
Reader 2	2 (2.3)	1 (3.3)	0 (0)	0.767	0.34 (-0.02, 0.70)	0.74 (0.52, 0.95)	0.35 (0.05, 0.64)
Reader 3	9 (10.2)	1 (3.3)	3 (18.8)	0.233			
Peripheral “washout”							
Reader 1	1 (1.1)	0 (0)	0 (0)	0.768	133 (99.3)	131 (97.7)	130 (97.0)

Reader 2	0 (0)	0 (0)	0 (0)	1.000	0.00 (0.00, 0.00)	0.39 (-0.14, 0.93)	0.00 (0.00, 0.00)
Reader 3	3 (3.4)	0 (0)	1 (6.2)	0.457			
Delayed central enhancement							
Reader 1	3 (3.4)	0 (0)	1 (6.2)	0.457	130 (97.0)	128 (95.5)	132 (98.5)
Reader 2	0 (0)	0 (0)	0 (0)	1.000	0.00 (0.00, 0.00)	-0.02 (-0.04, -	0.00 (0.00, 0.00)
Reader 3	1 (1.1)	0 (0)	1 (6.2)	0.244		0.0003)	
Infiltrative appearance							
Reader 1	10 (11.4)	0 (0)	4 (25.0)	0.027	127 (94.9)	124 (92.5)	125 (93.3)
Reader 2	9 (10.2)	1 (3.3)	1 (6.2)	0.472	0.69 (0.47, 0.90)	0.46 (0.19, 0.74)	0.43 (0.13, 0.74)
Reader 3	5 (5.7)	0 (0)	1 (6.2)	0.402			
Necrosis or severe ischemia							
Reader 1	20 (22.7)	4 (13.3)	7 (43.8)	0.065	117 (87.3)	122 (91.0)	119 (88.8)
Reader 2	19 (21.6)	3 (10.0)	6 (37.5)	0.089	0.63 (0.47, 0.69)	0.73 (0.59, 0.87)	0.65 (0.49, 0.81)
Reader 3	16 (18.2)	4 (13.3)	7 (43.8)	0.037			
Major features							
Size (mm)							
Reader 1	36.5 (21.0, 56.7)	31.5 (15.0, 38.0)	86.5 (33.2, 141.2)	0.003	0.98 (0.97, 0.98)*	0.98 (0.97, 0.98)*	0.98 (0.97, 0.98)*
Reader 2	43.0 (25.0, 62.5)	33.5 (21.2, 50.2)	100.0 (36.2, 138.0)	0.006			
Reader 3	36.0 (19.2, 57.2)	32.0 (19.2, 47.2)	93.0 (34.2, 142.0)	0.014			
Nonrim APHE							
Reader 1	75 (85.2)	27 (90.0)	12 (75.0)	0.396	122 (91.0)	125 (93.3)	115 (85.9)
Reader 2	83 (94.3)	26 (86.7)	15 (93.8)	0.380	0.55 (0.33, 0.77)	0.77 (0.64, 0.91)	0.45 (0.26, 0.64)
Reader 3	70 (79.5)	24 (80.0)	11 (68.8)	0.609			
Nonperipheral "washout"							
Reader 1	79 (89.8)	25 (83.3)	16 (100)	0.211	122 (91.0)	116 (86.6)	112 (83.6)

Reader 2	80 (90.9)	27 (90.0)	15 (93.8)	0.911	0.48 (0.24, 0.73)	0.47 (0.28, 0.67)	0.34 (0.13, 0.54)
Reader 3	69 (78.4)	25 (83.3)	14 (87.5)	0.621			
Enhancing “capsule”							
Reader 1	33 (37.5)	16 (53.3)	5 (31.2)	0.229	95 (70.9)	107 (79.9)	102 (76.1)
Reader 2	46 (52.3)	16 (53.3)	11 (68.8)	0.472	0.42 (0.28, 0.57)	0.58 (0.53, 0.72)	0.53 (0.39, 0.66)
Reader 3	32 (36.4)	15 (50.0)	6 (37.5)	0.412			
Threshold growth							
Reader 1	4 (4.5)	2 (6.7)	2 (12.5)	0.459	127 (94.7)	126 (94.0)	127 (94.7)
Reader 2	4 (4.5)	0 (0)	1 (6.2)	0.448	0.43 (0.09, 0.78)	0.30 (-0.04, 0.65)	0.19 (-0.17, 0.56)
Reader 3	3 (3.4)	1 (3.3)	0 (0)	0.756			

Note.- Categorical variables are expressed as numbers and percentages in parenthesis. Continuous variable (size) is reported as median and interquartile range (25th to 75th percentile) in parenthesis. Differences between HCC subtypes were assessed using the Pearson χ^2 test for categorical variables. Inter-reader agreement was assessed using the Cohen’s kappa (*k*) test for categorical variables and using the intraclass correlation coefficient con continuous variable (size). Statistically significant values ($P < 0.05$) are highlighted in bold.

*Agreement assessed with intraclass correlation coefficient.

Abbreviations: APHE=arterial phase hyperenhancement; CI=confidence interval; MTM-HCC=macrotrabecular massive hepatocellular carcinoma; NOS-HCC=not otherwise specified hepatocellular carcinoma; SH-HCC=steatohepatic hepatocellular carcinoma; TIV=tumor-in-vein.

Table S4: Differences in LI-RADS-defined ancillary features favoring malignancy, not HCC in particular and favoring HCC in particular, in non-otherwise specified (NOS), steatohepatitic (SH), and macrotrabecular-massive (MTM) hepatocellular carcinoma (HCC) subtypes in high-risk patients with contrast-enhanced CT ($n=134$).

Ancillary features	NOS-HCC ($n=88$)	SH-HCC ($n=30$)	MTM-HCC ($n=16$)	P value	R1 vs R2 N agreement (%) k value (95% CI)	R1 vs R3 N agreement (%) k value (95% CI)	R2 vs R3 N agreement (%) k value (95% CI)
Favoring malignancy, not HCC in particular							
Subthreshold growth							
Reader 1	17 (19.3)	5 (16.7)	3 (18.8)	0.949	106 (79.1)	107 (79.9)	109 (81.3)
Reader 2	12 (13.6)	10 (33.3)	3 (18.8)	0.057	0.31 (0.11, 0.51)	0.43 (0.25, 0.60)	0.47 (0.30, 0.64)
Reader 3	21 (23.9)	10 (33.3)	5 (31.2)	0.549			
Corona enhancement							
Reader 1	2 (2.3)	0 (0)	0 (0)	0.588	125 (93.3)	127 (94.8)	126 (94.0)
Reader 2	5 (5.7)	2 (6.7)	0 (0)	0.593	-0.02 (-0.05, -	-0.02 (-0.04, -	0.30 (-0.05, 0.65)
Reader 3	3 (3.4)	1 (3.3)	1 (6.2)	0.852	0.002)	0.0006)	
Fat sparing in solid mass							
Reader 1	2 (2.3)	0 (0)	0 (0)	0.588	129 (96.3)	130 (97.0)	131 (97.7)
Reader 2	1 (1.1)	2 (6.7)	0 (0)	0.170	-0.01 (-0.03, -	-0.01 (-0.03, -	0.38 (-0.16, 0.93)
Reader 3	1 (1.1)	1 (3.3)	0 (0)	0.604	0.0009)	0.0003)	
Favoring malignancy, HCC in particular							
Nonenhancing "capsule"							
Reader 1	0 (0)	0 (0)	1 (6.2)	0.024	131 (97.8)	131 (97.8)	130 (97.0)

Reader 2	2 (2.3)	0 (0)	0 (0)	0.588	-0.01 (-0.02,	-0.01 (-0.02,	-0.01 (-0.02,
Reader 3	2 (2.3)	0 (0)	0 (0)	0.588	0.003)	0.003)	-0.0003)
Nodule-in-nodule architecture							
Reader 1	0 (0)	0 (0)	0 (0)	1.000	123 (91.8)	130 (97.0)	125 (93.2)
Reader 2	8 (9.1)	2 (6.7)	1 (6.2)	0.875	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.37 (0.05, 0.68)
Reader 3	4 (4.5)	0 (0)	0 (0)	0.340			
Mosaic architecture							
Reader 1	8 (9.1)	4 (13.3)	3 (18.8)	0.485	97 (72.4)	120 (89.6)	105 (78.4)
Reader 2	32 (36.4)	8 (26.7)	8 (50.0)	0.286	0.29 (0.14, 0.43)	0.57 (0.37, 0.77)	0.46 (0.31, 0.61)
Reader 3	14 (15.9)	4 (13.3)	5 (31.2)	0.267			
Fat in mass, more than adjacent liver							
Reader 1	8 (9.1)	9 (30.0)	0 (0)	0.003	113 (84.3)	119 (88.8)	106 (79.1)
Reader 2	19 (21.6)	9 (30.0)	2 (12.5)	0.380	0.46 (0.27, 0.65)	0.45 (0.22, 0.68)	0.25 (0.06, 0.45)
Reader 3	5 (5.7)	8 (26.7)	1 (6.2)	0.004			
Blood products in mass							
Reader 1	3 (3.4)	0 (0)	0 (0)	0.488	118 (88.0)	128 (95.5)	122 (91.1)
Reader 2	10 (11.4)	4 (13.3)	1 (6.2)	0.766	0.07 (-0.11, 0.27)	0.22 (-0.17, 0.63)	0.36 (0.09, 0.63)
Reader 3	2 (2.3)	2 (6.7)	1 (6.2)	0.467			

Note.- Categorical variables are expressed as numbers and percentages in parenthesis. Differences between HCC subtypes were assessed using the Pearson χ^2 test for categorical variables. Inter-reader agreement was assessed using the Cohen's kappa (k). Statistically significant values ($P < 0.05$) are highlighted in bold.

Abbreviations: CI=confidence interval; HCC=hepatocellular carcinoma; MTM-HCC=macrotrabecular massive hepatocellular carcinoma; NOS-HCC=not otherwise specified hepatocellular carcinoma; SH-HCC=steatohepatitic hepatocellular carcinoma.

Table S5: Differences in LI-RADS-defined ancillary features favoring malignancy, not HCC in particular and favoring HCC in particular, in non-otherwise specified (NOS), steatohepatic (SH), and macrotrabecular-massive (MTM) hepatocellular carcinoma (HCC) subtypes in the entire cohort with contrast-enhanced MRI ($n=227$).

Ancillary features	NOS-HCC ($n=165$)	SH-HCC ($n=48$)	MTM-HCC ($n=14$)	P value	R1 vs R2 N agreement (%) k value (95% CI)	R1 vs R3 N agreement (%) k value (95% CI)	R2 vs R3 N agreement (%) k value (95% CI)
Favoring malignancy, not HCC in particular							
Subthreshold growth							
Reader 1	35 (21.2)	8 (16.7)	4 (28.6)	0.597	168 (74.0)	179 (78.9)	180 (79.3)
Reader 2	21 (12.7)	11 (22.9)	2 (14.3)	0.219	0.18 (-0.02, 0.26)	0.31 (0.16, 0.46)	0.36 (0.21, 0.51)
Reader 3	33 (20.0)	13 (27.1)	3 (21.4)	0.576			
Corona enhancement							
Reader 1	7 (4.2)	1 (2.1)	0 (0)	0.590	216 (95.1)	215 (94.7)	218 (96.0)
Reader 2	7 (4.2)	2 (4.2)	0 (0)	0.735	0.31 (0.02, 0.62)	0.16 (-0.13, 0.37)	0.38 (0.06, 0.70)
Reader 3	4 (2.4)	2 (4.2)	0 (0)	0.562			
Fat sparing in solid mass*							
Reader 1	15 (9.3)	11 (22.9)	1 (7.1)	0.034	203 (91.0)	211 (94.6)	209 (93.7)
Reader 2	18 (11.2)	8 (16.7)	1 (7.1)	0.499	0.59 (0.41, 0.75)	0.68 (0.52, 0.85)	0.63 (0.42, 0.80)
Reader 3	10 (6.2)	5 (10.4)	0 (0)	0.347			
Restricted diffusion [†]							
Reader 1	127 (80.9)	38 (82.6)	13 (92.9)	0.532	175 (80.7)	187 (86.2)	183 (84.3)
Reader 2	140 (89.2)	44 (95.7)	14 (100)	0.191	0.17 (0.02, 0.33)	0.49 (0.33, 0.64)	0.23 (0.05, 0.41)
Reader 3	134 (85.4)	38 (82.6)	14 (100)	0.258			

Mild-moderate T2 hyperintensity							
Reader 1	144 (87.3)	39 (81.2)	14 (100)	0.178	198 (87.2)	202 (89.0)	205 (90.3)
Reader 2	157 (95.2)	43 (89.6)	14 (100)	0.219	0.27 (0.08, 0.45)	0.46 (0.29, 0.64)	0.34 (0.13, 0.55)
Reader 3	149 (90.3)	41 (85.4)	14 (100)	0.265			
Iron sparing in solid mass*							
Reader 1	3 (1.9)	1 (2.1)	0 (0)	0.868	207 (97.3)	220 (98.6)	218 (97.7)
Reader 2	6 (3.7)	0 (0)	0 (0)	0.305	0.38 (-0.001,	0.66 (0.29, 1.00)	0.53 (0.17, 0.89)
Reader 3	5 (3.1)	0 (0)	0 (0)	0.374	0.77)		
Hepatobiliary phase hypointensity							
Reader 1 (adequate, n=59)	39 (90.7)	11 (91.7)	4 (100)	0.815	34 (87.2)	37 (94.9)	34 (87.2)
Reader 2 (adequate, n=53)	32 (84.2)	9 (90.0)	4 (80.0)	0.849	0.38 (-0.04, 0.80)†	0.48 (-0.12, 1.00)†	0.25 (-0.15, 0.65)†
Reader 3 (adequate, n=55)	40 (95.2)	9 (100)	4 (100)	0.725			
Favoring malignancy, HCC in particular							
Nonenhancing "capsule"							
Reader 1	2 (1.2)	1 (2.1)	0 (0)	0.812	224 (98.6)	220 (96.9)	219 (96.5)
Reader 2	1 (0.6)	1 (2.1)	0 (0)	0.588	0.39 (-0.15, 0.94)	0.20 (-0.15, 0.57)	-0.01 (-0.02,
Reader 3	5 (3.0)	1 (2.1)	0 (0)	0.765			0.008)
Nodule-in-nodule architecture							
Reader 1	1 (0.6)	0 (0)	0 (0)	0.828	211 (93.0)	215 (94.7)	215 (94.7)
Reader 2	11 (6.7)	4 (8.3)	0 (0)	0.543	-0.008 (-0.02,	0.13 (-0.10, 0.37)	0.54 (0.31, 0.57)
Reader 3	10 (6.1)	3 (6.2)	0 (0)	0.635	0.007)		
Mosaic architecture							
Reader 1	41 (24.8)	8 (16.7)	2 (14.3)	0.367	161 (70.9)	201 (88.5)	175 (77.1)
Reader 2	82 (49.7)	21 (43.8)	8 (57.1)	0.627	0.41 (0.31, 0.51)	0.70 (0.59, 0.80)	0.53 (0.43, 0.63)

Reader 3	50 (30.3)	11 (22.9)	4 (28.6)	0.609			
Fat in mass, more than adjacent liver*							
Reader 1	38 (23.6)	26 (54.2)	2 (14.3)	< 0.001	175 (78.5)	186 (83.4)	182 (84.7)
Reader 2	51 (31.5)	28 (58.3)	7 (50.0)	0.002	0.52 (0.41, 0.64)	0.60 (0.48, 0.71)	0.59 (0.48, 0.70)
Reader 3	35 (21.7)	26 (54.2)	4 (28.6)	< 0.001			
Blood products in mass							
Reader 1	36 (21.8)	5 (10.4)	2 (14.3)	0.168	193 (85.1)	204 (89.9)	192 (84.6)
Reader 2	48 (29.1)	11 (22.9)	4 (28.6)	0.701	0.58 (0.46, 0.70)	0.63 (0.54, 0.79)	0.57 (0.45, 0.69)
Reader 3	33 (20.0)	8 (16.7)	3 (21.4)	0.859			

Note.- Categorical variables are expressed as numbers and percentages in parenthesis. Differences between categorical variables were assessed using the Pearson χ^2 test. Inter-reader agreement was assessed using the Cohen's kappa (k) test. Statistically significant values ($P < 0.05$) are highlighted in bold.

*Features assessed in 223/227 observations due to the lack of in-phase and out-of-phase sequences in 4 observations.

†Feature assessed in 217/227 observations due to the lack of diffusion weighted imaging in 10 observations.

‡Agreement assessed only in observations considered with adequate hepatobiliary phase for all readers.

Abbreviations: CI=confidence interval; HCC=hepatocellular carcinoma; MTM-HCC=macrotrabecular massive hepatocellular carcinoma; NOS-HCC=not otherwise specified hepatocellular carcinoma; SH-HCC=steatohepatitic hepatocellular carcinoma.

Table S6: Differences in LI-RADS-defined TIV, LR-M features, and major features in non-otherwise specified (NOS), steatohepatic (SH), and macrotrabecular-massive (MTM) hepatocellular carcinoma (HCC) subtypes in high-risk patients with contrast-enhanced MRI (n=120).

Features	NOS-HCC (n=85)	SH-HCC (n=25)	MTM-HCC (n=10)	P value	R1 vs R2 N agreement (%) k value (95% CI)	R1 vs R3 N agreement (%) k value (95% CI)	R2 vs R3 N agreement (%) k value (95% CI)
TIV							
Reader 1	2 (2.4)	0 (0)	1 (10.0)	0.228	114 (95.0)	118 (98.4)	114 (95.0)
Reader 2	6 (7.1)	0 (0)	3 (30.0)	0.009	0.48 (0.13, 0.82)	0.65 (0.21, 1.00)	0.48 (0.13, 0.82)
Reader 3	2 (2.4)	0 (0)	1 (10.0)	0.228			
LR-M features							
At least one LR-M feature							
Reader 1	26 (30.6)	4 (16.0)	5 (50.0)	0.118	96 (80.0)	102 (85.0)	96 (83.4)
Reader 2	28 (32.9)	4 (16.0)	3 (30.0)	0.261	0.51 (0.34, 0.68)	0.62 (0.46, 0.68)	0.58 (0.42, 0.74)
Reader 3	20 (23.5)	6 (24.0)	5 (50.0)	0.189			
At least one targetoid features							
Reader 1	9 (10.6)	1 (4.0)	2 (20.0)	0.342	108 (90.0)	107 (89.2)	107 (89.2)
Reader 2	10 (11.8)	2 (8.0)	0 (0)	0.469	0.44 (0.18, 0.80)	0.45 (0.21, 0.70)	0.45 (0.21, 0.70)
Reader 3	10 (11.8)	3 (12.0)	2 (20.0)	0.755			
Rim APHE							
Reader 1	6 (7.1)	1 (4.0)	2 (20.0)	0.257	111 (92.5)	112 (93.3)	109 (90.8)
Reader 2	5 (5.9)	1 (4.0)	0 (0)	0.698	0.36 (0.03, 0.68)	0.56 (0.26, 0.83)	0.30 (0.007, 0.60)
Reader 3	8 (9.4)	1 (4.0)	2 (20.0)	0.330			
Peripheral “washout”							
Reader 1	0 (0)	0 (0)	0 (0)	1.000	120 (100)	119 (99.2)	119 (99.2)

Reader 2	0 (0)	0 (0)	0 (0)	1.000	NA**	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Reader 3	1 (1.2)	0 (0)	0 (0)	0.813			
Delayed central enhancement							
Reader 1	5 (5.9)	0 (0)	0 (0)	0.342	115 (95.8)	116 (96.7)	115 (95.8)
Reader 2	4 (4.7)	0 (0)	0 (0)	0.427	0.42 (0.008, 0.83)	0.48 (0.05, 0.91)	0.26 (-0.18, 0.71)
Reader 3	2 (2.4)	1 (4.0)	0 (0)	0.781			
Targetoid restriction*							
Reader 1	0 (0)	0 (0)	0 (0)	1.000	115 (100)	113 (98.3)	113 (98.3)
Reader 2	0 (0)	0 (0)	0 (0)	1.000	NA**	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Reader 3	0 (0)	2 (8.3)	0 (0)	0.021			
Targetoid appearance on HBP							
Reader 1 (adequate, n=31)	0 (0)	0 (0)	0 (0)	1.000	19 (100) [†]	19 (100) [†]	19 (100) [†]
Reader 2 (adequate, n=27)	1 (5.9)	0 (0)	0 (0)	0.737	NA**	NA**	NA**
Reader 3 (adequate, n=27)	0 (0)	0 (0)	0 (0)	1.000			
Infiltrative appearance							
Reader 1	7 (8.2)	0 (0)	2 (20.0)	0.114	114 (95.0)	113 (94.2)	117 (97.5)
Reader 2	6 (7.1)	0 (0)	1 (10.0)	0.350	0.59 (0.30, 0.89)	0.43 (0.09, 0.77)	0.71 (0.41, 1.00)
Reader 3	4 (4.7)	0 (0)	0 (0)	0.427			
Marked restricted diffusion*							
Reader 1	3 (3.7)	0 (0)	2 (20.0)	0.29	108 (93.9)	109 (94.7)	108 (93.9)
Reader 2	4 (4.9)	0 (0)	2 (20.0)	0.056	0.33 (-0.04, 0.70)	0.37 (-0.02, 0.67)	0.33 (-0.04, 0.70)
Reader 3	3 (3.7)	0 (0)	2 (20.0)	0.029			
Necrosis or severe ischemia							
Reader 1	13 (15.3)	4 (16.0)	2 (20.0)	0.928	106 (88.3)	111 (92.5)	111 (92.5)
Reader 2	10 (11.8)	3 (12.0)	2 (20.0)	0.755	0.52 (0.30, 0.54)	0.66 (0.47, 0.86)	0.62 (0.40, 0.84)

Reader 3	7 (8.2)	3 (12.0)	2 (20.0)	0.469			
Major features							
Size (mm)							
Reader 1	33.0 (21.5, 50.0)	25.0 (16.0, 36.0)	45.0 (26.0, 100.5)	0.071	0.98 (0.97, 0.98) [‡]	0.97 (0.96, 0.98) [‡]	0.97 (0.96, 0.98) [‡]
Reader 2	43.0 (25.0, 59.5)	30.0 (18.0, 42.0)	48.0 (34.0, 130.0)	0.048			
Reader 3	36.0 (21.5, 52.0)	25.0 (17.0, 41.0)	48.0 (23.7, 124.7)	0.092			
Nonrim APHE							
Reader 1	72 (84.7)	24 (96.0)	8 (80.0)	0.279	109 (90.8)	108 (90.0)	99 (82.5)
Reader 2	77 (90.6)	24 (96.0)	10 (100)	0.427	0.51 (0.26, 0.76)	0.64 (0.46, 0.82)	0.28 (0.07, 0.49)
Reader 3	67 (78.8)	22 (80.0)	7 (70.0)	0.428			
Nonperipheral “washout”							
Reader 1	76 (89.4)	19 (76.0)	10 (100)	0.940	109 (90.9)	102 (85.0)	97 (84.2)
Reader 2	77 (90.6)	21 (84.0)	10 (100)	0.342	0.54 (0.30, 0.78)	0.46 (0.26, 0.67)	0.40 (0.19, 0.61)
Reader 3	66 (77.6)	20 (80.0)	9 (90.0)	0.657			
Enhancing “capsule”							
Reader 1	58 (68.2)	17 (68.0)	7 (70.0)	0.993	95 (79.1)	99 (82.5)	92 (76.7)
Reader 2	55 (64.7)	15 (60.0)	7 (70.0)	0.841	0.53 (0.37, 0.69)	0.58 (0.44, 0.74)	0.46 (0.29, 0.63)
Reader 3	63 (74.1)	16 (64.0)	8 (80.0)	0.522			
Threshold growth							
Reader 1	0 (0)	0 (0)	0 (0)	1.000	118 (98.3)	117 (97.5)	117 (97.5)
Reader 2	1 (1.2)	0 (0)	1 (10.0)	0.091	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.38 (-0.16, 0.93)
Reader 3	1 (1.2)	0 (0)	2 (20.0)	0.001			

Note.- Categorical variables are expressed as numbers and percentages in parenthesis. Continuous variable (size) is reported as median and interquartile range (25th to 75th percentile) in parenthesis. Differences between HCC subtypes were assessed using the Pearson χ^2 test for categorical variables. Inter-reader agreement was assessed using the Cohen’s kappa (*k*) test for categorical variables and intraclass correlation coefficient of continuous variable (size). Statistically significant values ($P < 0.05$) are highlighted in bold.

*Features assessed in 115/120 observations due to the lack of diffusion weighted imaging in 5 observations.

**Not available since both readers never reported the feature.

†Agreement assessed only in observations considered with adequate HBP for all readers.

‡Agreement assessed with intraclass correlation coefficient.

Abbreviations: APHE=arterial phase hyperenhancement; CI=confidence interval; HBP=hepatobiliary phase; HCC=hepatocellular carcinoma; MTM-HCC=macrotrabecular massive hepatocellular carcinoma; NOS-HCC=not otherwise specified hepatocellular carcinoma; SH-HCC=steatohepatitic hepatocellular carcinoma; TIV=tumor-in-vein.

Table S7: Differences in LI-RADS-defined ancillary features favoring malignancy, not HCC in particular and favoring HCC in particular in non-otherwise specified (NOS), steatohepatic (SH), and macrotrabecular-massive (MTM) hepatocellular carcinoma (HCC) subtypes in high-risk patients with contrast-enhanced MRI ($n=120$).

Ancillary features	NOS-HCC ($n=85$)	SH-HCC ($n=25$)	MTM-HCC ($n=10$)	P value	R1 vs R2 N agreement (%) k value (95% CI)	R1 vs R3 N agreement (%) k value (95% CI)	R2 vs R3 N agreement (%) k value (95% CI)
Favoring malignancy, not HCC in particular							
Subthreshold growth							
Reader 1	16 (18.8)	2 (8.0)	3 (30.0)	0.253	93 (77.5)	93 (77.5)	98 (81.7)
Reader 2	10 (11.8)	5 (20.0)	1 (10.0)	0.538	0.14 (-0.06, 0.34)	0.26 (0.05, 0.47)	0.34 (0.13, 0.55)
Reader 3	17 (20.0)	5 (20.0)	2 (20.0)	1.000			
Corona enhancement							
Reader 1	3 (3.5)	0 (0)	0 (0)	0.531	114 (95.0)	115 (95.8)	115 (95.8)
Reader 2	4 (4.7)	1 (4.0)	0 (0)	0.779	0.26 (-0.17, 0.62)	0.26 (-0.18, 0.71)	0.42 (0.008, 0.83)
Reader 3	4 (4.7)	0 (0)	0 (0)	0.427			
Fat sparing in solid mass*							
Reader 1	10 (11.9)	5 (20.0)	0 (0)	0.257	111 (93.3)	113 (95.0)	115 (96.7)
Reader 2	8 (9.5)	4 (16.0)	1 (10.0)	0.657	0.67 (0.46, 0.88)	0.74 (0.51, 0.93)	0.80 (0.61, 0.98)
Reader 3	7 (8.3)	2 (8.0)	0 (0)	0.639			
Restricted diffusion [†]							
Reader 1	60 (71.4)	19 (79.2)	10 (100)	0.176	90 (78.2)	100 (86.9)	97 (84.3)
Reader 2	74 (91.4)	22 (91.7)	10 (100)	0.627	0.19 (-0.004,	0.58 (0.40, 0.73)	0.28 (0.04, 0.51)
Reader 3	67 (82.7)	19 (79.2)	10 (100)	0.311	0.38)		

Mild-moderate T2 hyperintensity							
Reader 1	68 (80.0)	18 (72.0)	10 (100)	0.174	99 (82.5)	104 (86.7)	109 (90.8)
Reader 2	80 (94.1)	21 (84.0)	10 (100)	0.155	0.28 (0.07, 0.49)	0.50 (0.30, 0.51)	0.47 (0.21, 0.73)
Reader 3	77 (90.6)	19 (76.0)	10 (100)	0.066			
Iron sparing in solid mass*							
Reader 1	0 (0)	0 (0)	0 (0)	1.000	117 (98.3)	117 (98.3)	117 (98.3)
Reader 2	2 (2.4)	0 (0)	0 (0)	0.844	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.49 (-0.16, 1.00)
Reader 3	2 (2.4)	0 (0)	0 (0)	0.655			
Hepatobiliary phase hypointensity							
Reader 1 (adequate, n=31)	19 (95.0)	7 (100)	4 (100)	0.753	17 (89.5)	19 (100) [‡]	17 (89.5)
Reader 2 (adequate, n=27)	15 (88.2)	4 (80.0)	4 (80.0)	0.830	0.00 (0.00, 0.00) [‡]	NA**	0.00 (0.00, 0.00) [‡]
Reader 3 (adequate, n=27)	17 (94.4)	5 (100)	4 (100)	0.771			
Favoring malignancy, HCC in particular							
Nonenhancing "capsule"							
Reader 1	1 (1.2)	0 (0)	0 (0)	0.813	118 (98.3)	117 (97.5)	115 (95.8)
Reader 2	1 (1.2)	0 (0)	0 (0)	0.813	-0.008 (-0.02, 0.003)	0.39 (-0.14, 0.93)	-0.01 (-0.03, 0.007)
Reader 3	3 (3.5)	1 (4.0)	0 (0)	0.823			
Nodule-in-nodule architecture							
Reader 1	0 (0)	0 (0)	0 (0)	1.000	109 (90.8)	111 (92.5)	114 (95.0)
Reader 2	8 (9.4)	3 (12.0)	0 (0)	0.534	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.67 (0.42, 0.91)
Reader 3	6 (7.1)	3 (12.0)	0 (0)	0.457			
Mosaic architecture							
Reader 1	11 (12.9)	2 (8.0)	2 (20.0)	0.609	89 (74.2)	112 (93.3)	93 (77.5)
Reader 2	32 (37.6)	9 (36.0)	5 (50.0)	0.722	0.37 (0.22, 0.52)	0.72 (0.54, 0.90)	0.46 (0.31, 0.61)

Reader 3	13 (15.3)	3 (12.0)	3 (30.0)	0.407			
Fat in mass, more than adjacent liver*							
Reader 1	17 (20.2)	12 (48.0)	1 (10.0)	0.010	94 (79.0)	101 (84.8)	100 (84.0)
Reader 2	11 (25.9)	13 (52.0)	4 (40.0)	0.043	0.49 (0.32, 0.66)	0.59 (0.43, 0.76)	0.61 (0.46, 0.76)
Reader 3	35 (21.7)	26 (54.2)	4 (40.0)	0.013			
Blood products in mass							
Reader 1	11 (12.9)	3 (12.0)	2 (20.0)	0.805	106 (88.3)	115 (95.8)	105 (87.5=
Reader 2	18 (21.2)	4 (16.0)	2 (20.0)	0.851	0.58 (0.39, 0.77)	0.81 (0.65, 0.97)	0.54 (0.34, 0.74)
Reader 3	11 (12.9)	3 (12.0)	1 (10.0)	0.962			

Note.- Categorical variables are expressed as numbers and percentages in parenthesis. Differences between categorical variables were assessed using the Pearson χ^2 test. Inter-reader agreement was assessed using the Cohen's kappa (k) test. Statistically significant values ($P < 0.05$) are highlighted in bold.

*Features assessed in 119/120 observations due to the lack of in-phase and out-of-phase sequences in 4 observations.

†Feature assessed in 115/120 observations due to the lack of diffusion weighted imaging in 5 observations.

‡Agreement assessed only in observations considered with adequate hepatobiliary phase for all readers.

**Agreement not assessed because it was a constant.

Abbreviations: CI=confidence interval; HCC=hepatocellular carcinoma; MTM-HCC=macrotrabecular massive hepatocellular carcinoma; NOS-HCC=not otherwise specified hepatocellular carcinoma; SH-HCC=steatohepatitic hepatocellular carcinoma.

Table S8: Differences in LI-RADS-defined TIV, LR-M features, major features, and ancillary features favoring malignancy in other hepatocellular carcinoma (HCC) subtypes in the entire cohort with contrast-enhanced CT ($n=9$) or MRI ($n=10$).

	CT ($n=9$)	MRI ($n=10$)
TIV		
Reader 1	1 (11.1)	1 (10.0)
Reader 2	1 (11.1)	1 (10.0)
Reader 3	1 (11.1)	1 (10.0)
LR-M features		
At least one LR-M feature		
Reader 1	7 (77.8)	6 (60.0)
Reader 2	6 (66.7)	5 (50.0)
Reader 3	6 (66.7)	6 (60.0)
At least one targetoid feature		
Reader 1	2 (22.2)	2 (20.0)
Reader 2	1 (11.1)	1 (10.0)
Reader 3	1 (11.1)	1 (10.0)
Rim APHE		
Reader 1	2 (22.2)	1 (10.0)
Reader 2	1 (11.1)	1 (10.0)
Reader 3	1 (11.1)	1 (10.0)
Peripheral “washout”		
Reader 1	0 (0)	0 (0)
Reader 2	0 (0)	0 (0)
Reader 3	0 (0)	0 (0)
Delayed central enhancement		
Reader 1	1 (11.1)	1 (10.0)
Reader 2	1 (11.1)	1 (10.0)
Reader 3	1 (11.1)	1 (10.0)
Targetoid restriction		
Reader 1	-	2 (20.0)
Reader 2	-	1 (10.0)
Reader 3	-	1 (10.0)
Targetoid appearance on HBP		
Reader 1 (adequate, $n=3$)	-	1 (33.3)
Reader 2 (adequate, $n=3$)	-	0 (0)

Reader 3 (adequate, n=3)	-	0 (0)
Infiltrative appearance		
Reader 1	1 (11.1)	1 (10.0)
Reader 2	1 (11.1)	1 (10.0)
Reader 3	1 (11.1)	1 (10.0)
Marked restricted diffusion		
Reader 1	-	0 (0)
Reader 2	-	0 (0)
Reader 3	-	2 (20.0)
Necrosis or severe ischemia		
Reader 1	4 (44.4)	3 (30.0)
Reader 2	4 (44.4)	3 (30.0)
Reader 3	4 (44.4)	3 (30.0)
Major features		
Size (mm)		
Reader 1	61.0 (31.5, 112.0)	31.5 (24.5, 98.5)
Reader 2	70.0 (33.5, 120.5)	37.5 (32.0, 119.5)
Reader 3	45.0 (32.5, 114.0)	31.0 (27.5, 107.2)
Nonrim APHE		
Reader 1	6 (66.7)	8 (80.0)
Reader 2	8 (88.9)	9 (90.0)
Reader 3	7 (77.8)	8 (80.0)
Nonperipheral "washout"		
Reader 1	8 (88.9)	8 (80.0)
Reader 2	9 (100)	9 (90.0)
Reader 3	8 (88.9)	8 (80.0)
Enhancing "capsule"		
Reader 1	5 (55.6)	7 (70.0)
Reader 2	7 (77.8)	7 (70.0)
Reader 3	6 (66.7)	7 (70.0)
Threshold growth		
Reader 1	0 (0)	0 (0)
Reader 2	0 (0)	0 (0)
Reader 3	1 (11.1)	1 (10.0)
Ancillary features favoring malignancy, not HCC in particular		
Subthreshold growth		
Reader 1	4 (44.4)	3 (30.0)

Reader 2	0 (0)	0 (0)
Reader 3	3 (33.3)	2 (20.0)
Corona enhancement		
Reader 1	0 (0)	0 (0)
Reader 2	1 (11.1)	1 (10.0)
Reader 3	2 (22.2)	2 (20.0)
Fat sparing in solid mass		
Reader 1	0 (0)	0 (0)
Reader 2	0 (0)	0 (0)
Reader 3	0 (0)	0 (0)
Restricted diffusion		
Reader 1	-	9 (90.0)
Reader 2	-	10 (100)
Reader 3	-	9 (90.0)
Mild-moderate T2 hyperintensity		
Reader 1	-	10 (100)
Reader 2	-	10 (100)
Reader 3	-	10 (100)
Iron sparing in solid mass		
Reader 1	-	0 (0)
Reader 2	-	0 (0)
Reader 3	-	0 (0)
Hepatobiliary phase hypointensity		
Reader 1 (adequate, n=3)	-	3 (100)
Reader 2 (adequate, n=3)	-	3 (100)
Reader 3 (adequate, n=3)	-	3 (100)
Ancillary features favoring malignancy, HCC in particular		
Nonenhancing "capsule"		
Reader 1	0 (0)	0 (0)
Reader 2	0 (0)	0 (0)
Reader 3	0 (0)	0 (0)
Nodule-in-nodule architecture		
Reader 1	0 (0)	0 (0)
Reader 2	0 (0)	0 (0)
Reader 3	0 (0)	0 (0)
Mosaic architecture		
Reader 1	3 (33.3)	3 (30.0)

Reader 2	6 (66.7)	5 (50.0)
Reader 3	3 (33.3)	3 (30.0)
Fat in mass, more than adjacent liver		
Reader 1	0 (0)	0 (0)
Reader 2	1 (11.1)	4 (40.0)
Reader 3	0 (0)	0 (0)
Blood products in mass		
Reader 1	1 (11.1)	2 (20.0)
Reader 2	2 (22.2)	3 (30.0)
Reader 3	0 (0)	2 (20.0)

Note.- Categorical variables are expressed as numbers and percentages in parenthesis. Continuous variable (size) is reported as median and interquartile range (25th to 75th percentile) in parenthesis.

Abbreviations: APHE=arterial phase hyperenhancement; HBP=hepatobiliary phase; HCC=hepatocellular carcinoma.

Table S9: LI-RADS categories using major features only and after final adjustment for ancillary features in other hepatocellular carcinoma (HCC) subtypes high-risk patients with contrast-enhanced CT ($n=3$) or MRI ($n=7$).

	CT ($n=3$)	MRI ($n=7$)
LI-RADS categories with major features only		
Reader 1		
LR-3	0 (0)	0 (0)
LR-4	0 (0)	2 (28.6)
LR-5	1 (33.3)	3 (42.9)
LR-M	1 (33.3)	1 (14.3)
LR-TIV	1 (33.3)	1 (14.3)
Reader 2		
LR-3	0 (0)	0 (0)
LR-4	0 (0)	1 (14.3)
LR-5	1 (33.3)	4 (57.1)
LR-M	1 (33.3)	1 (14.3)
LR-TIV	1 (33.3)	1 (13.3)
Reader 3		
LR-3	0 (0)	0 (0)
LR-4	0 (0)	1 (14.3)
LR-5	1 (33.3)	3 (42.9)
LR-M	1 (33.3)	2 (28.6)
LR-TIV	1 (33.3)	1 (13.3)
LI-RADS categories with major and ancillary features		
Reader 1		
LR-3	0 (0)	0 (0)
LR-4	0 (0)	2 (28.6)
LR-5	1 (33.3)	3 (42.9)
LR-M	1 (33.3)	1 (14.3)
LR-TIV	1 (33.3)	1 (14.3)
Reader 2		
LR-3	0 (0)	0 (0)
LR-4	0 (0)	1 (14.3)
LR-5	1 (33.3)	4 (57.1)
LR-M	1 (33.3)	1 (14.3)
LR-TIV	1 (33.3)	1 (14.3)

Reader 3		
LR-3	0 (0)	0 (0)
LR-4	0 (0)	1 (14.3)
LR-5	1 (33.3)	3 (42.9)
LR-M	1 (33.3)	2 (28.6)
LR-TIV	1 (33.3)	1 (13.3)

Abbreviation: TIV=tumor-in-vein.