

HCC: i Limiti della Diagnosi Radiologica

Pier Paolo Mainenti

IBB-CNR NAPOLI

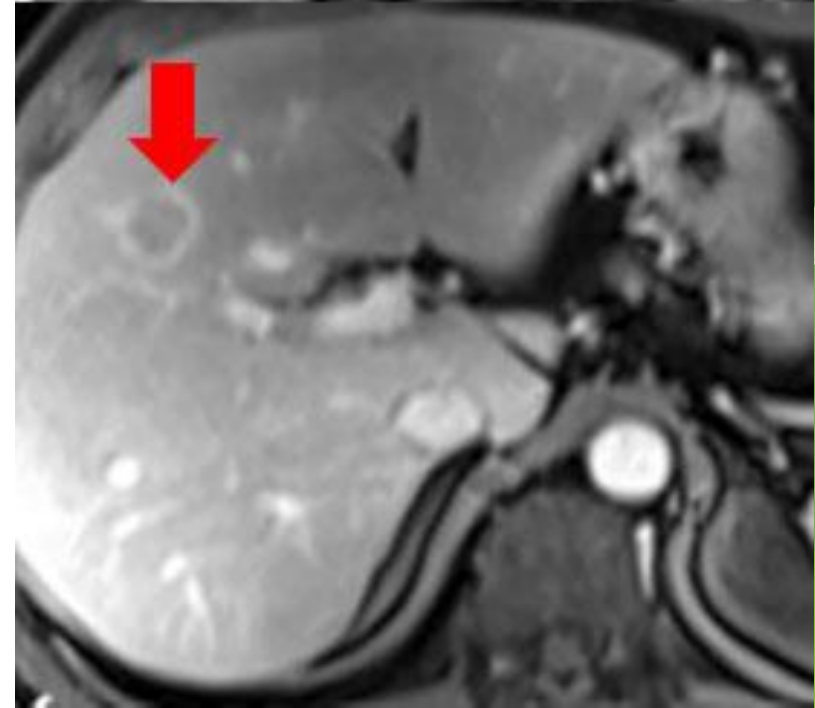
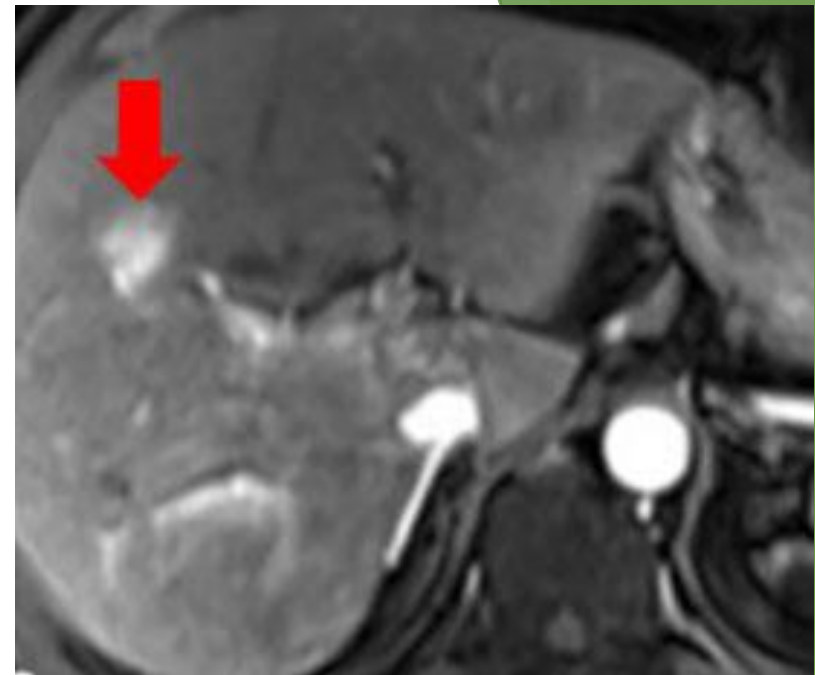
**L'EPATOLOGIA
NEL III MILLENNIO:
TRA BISOGNI DEL PAZIENTE
E SOSTENIBILITÀ DEL SISTEMA**

**NAPOLI
26 - 27
NOVEMBRE
2021**



CERTEZZE

- **In pazienti ad alto rischio per HCC, un nodulo epatico può essere definito come HCC se:**
 - **> 10 mm**
 - **ipervascolare in fase arteriosa**
 - **ipovascolare con pseudocapsula in fase portale/equilibrio**



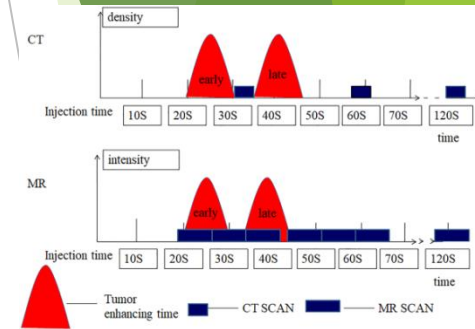
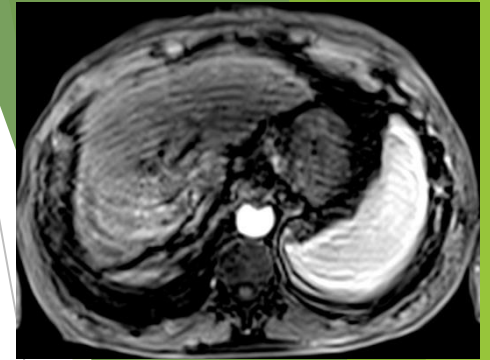
PROBLEMATICHE

Tecniche

- **Limiti di acquisizione:**
 - *artefatti da respiro (TC e RM) e da troncamento (RM)*
 - *inadeguata sincronizzazione del tempo di scansione arterioso della TC/RM con la fase arteriosa effettiva della lesione*
- **Limiti intrinseci della metodica :**
 - *Limitata risoluzione di contrasto e monoparametricità (TC)*
 - *Limitata risoluzione spaziale (RM)*

Diagnosi differenziale

- **HCC con pattern atipico** (*40% degli HCC Lee Br J Radiol 2012*)
→ *ipovascolare, a bersaglio, metamorfosi adiposo, scar centrale, infiltrativa, a crescita intraduttale*
- **Simulatori di HCC**
- **Noduli indeterminati**



Hepatocellular carcinoma detection in liver cirrhosis: diagnostic performance of contrast-enhanced CT vs. MRI with extracellular contrast vs. gadoxetic acid

Seeman, European Radiology 2019

Limiti intrinseci della metodica

Table 3 Per-lesion sensitivity for each modality for HCC detection stratified by lesion size with 95% confidence intervals

	Size 1–1.9 cm				Size ≥ 2 cm			
	Reader 1	Reader 2	Reader 3	Pooled Reader Data	Reader 1	Reader 2	Reader 3	Pooled Reader Data
CT				34.4% (27.7–41.6%)				93.1% (87.6–96.6%)
EC-MRI				64.6% (54.4–74.0%)				91.5% (84.8–95.8%)
Dynamic EOB-MRI				57.3% (51.5–63.0%)				83.9% (78.9–88.2%)
Full EOB-MRI				67.3% (61.7–72.6%)				87.7% (83.1–91.5%)
<i>p</i> (CT vs. EC-MRI)				0.012				0.529
<i>p</i> (CT vs. Dynamic EOB-MRI)				0.001				0.491
<i>p</i> (CT vs. Full EOB-MRI)				0.003				0.987
<i>p</i> (EC-MRI vs. Dynamic EOB-MRI)				0.900				0.919
<i>p</i> (EC-MRI vs. Full EOB-MRI)				0.249				0.528
<i>p</i> (Dynamic EOB-MRI vs. Full EOB-MRI)				0.002				0.268

Specificità n.s.

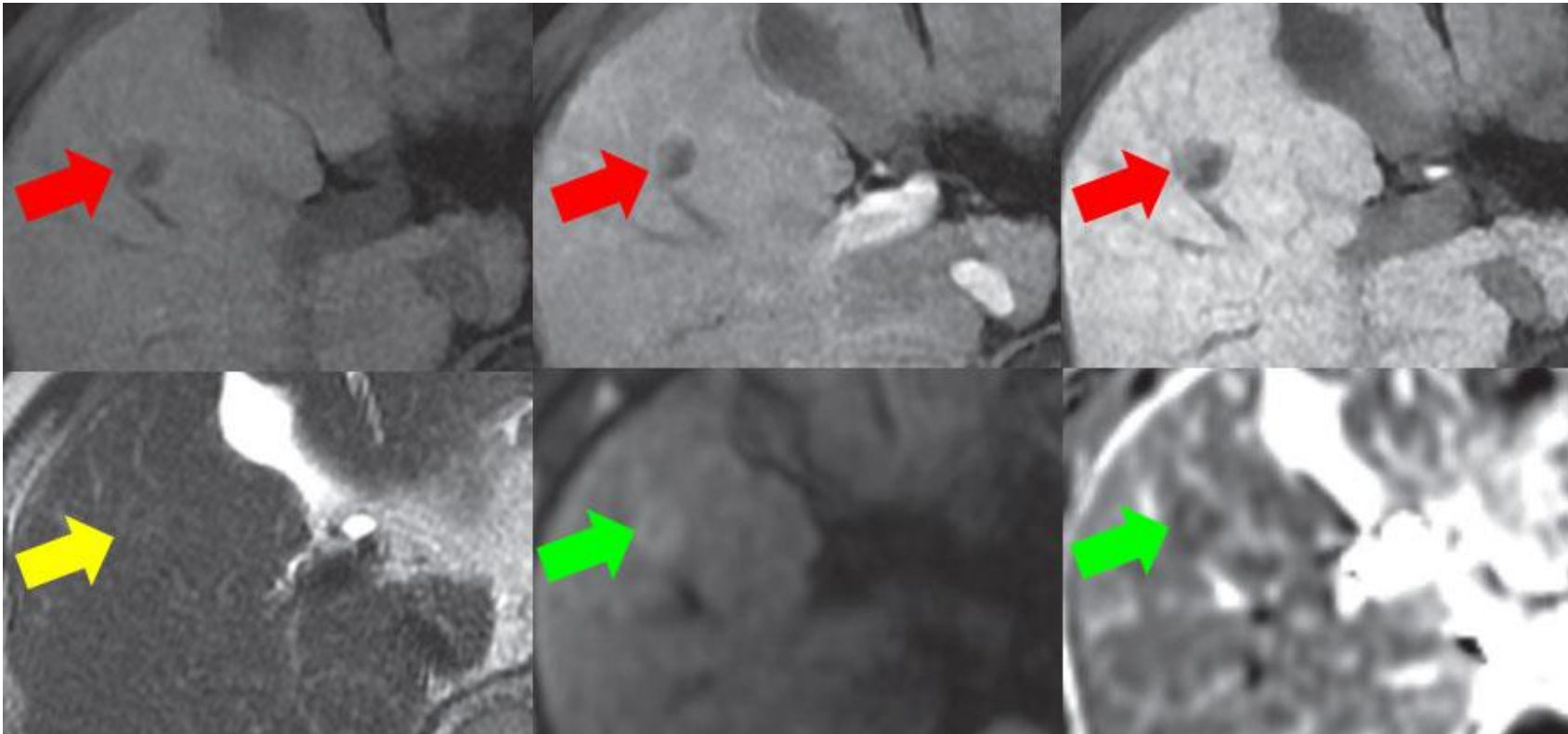
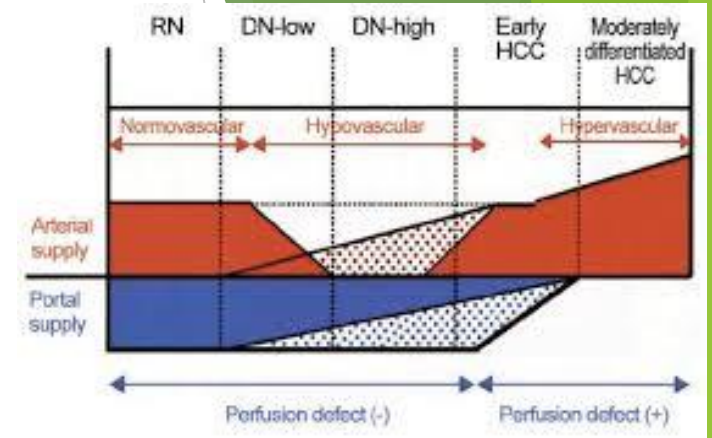
Specificità n.s.

- 277 pazienti con cirrosi epatica sottoposti a trapianto epatico
- TC con mdc o RM con mdc (extra-cellulare o ad escrezione epato-biliare) 90 giorni prima del trapianto
- Classificazione dei noduli secondo i criteri LI-RADS
- 265 HCC in 177 pazienti

HCC con pattern atipico all'imaging

Ipoavascolare

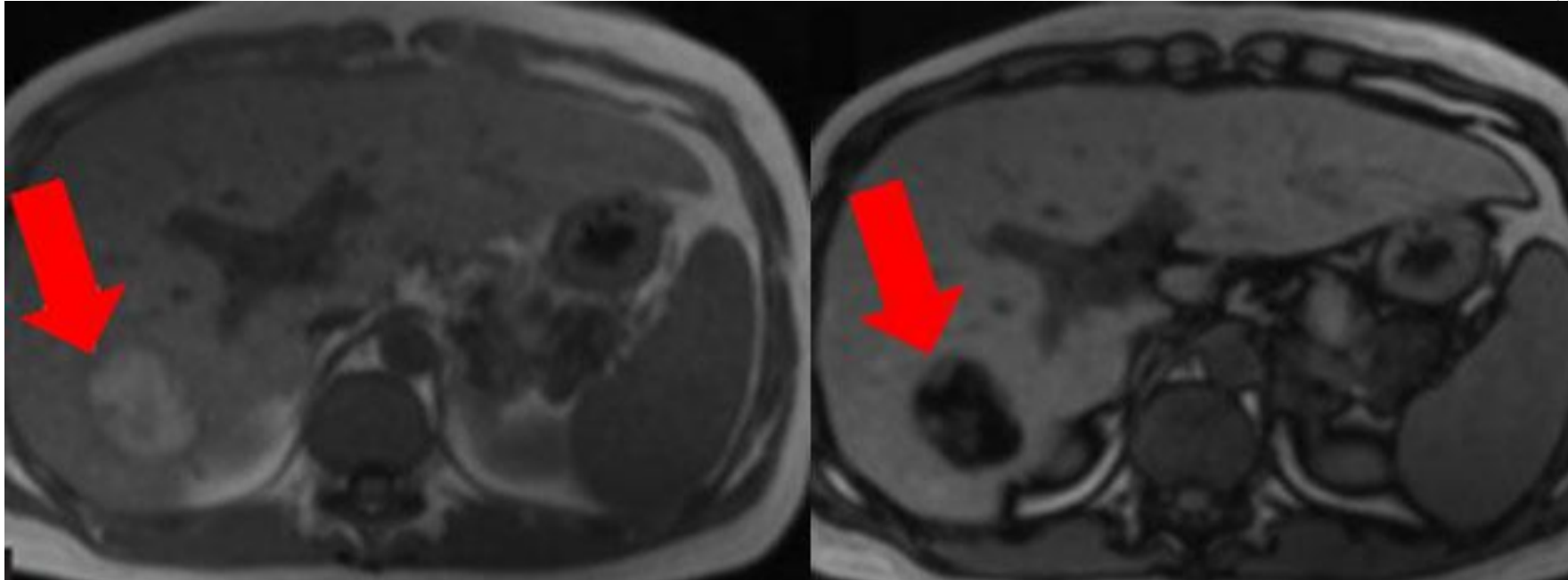
- *prevalente decremento della vascolarizzazione portale rispetto alla insufficiente neovascolarizzazione arteriosa*
- *d.d. con nodulo displasico*



Nodulo con metamorfosi adiposa

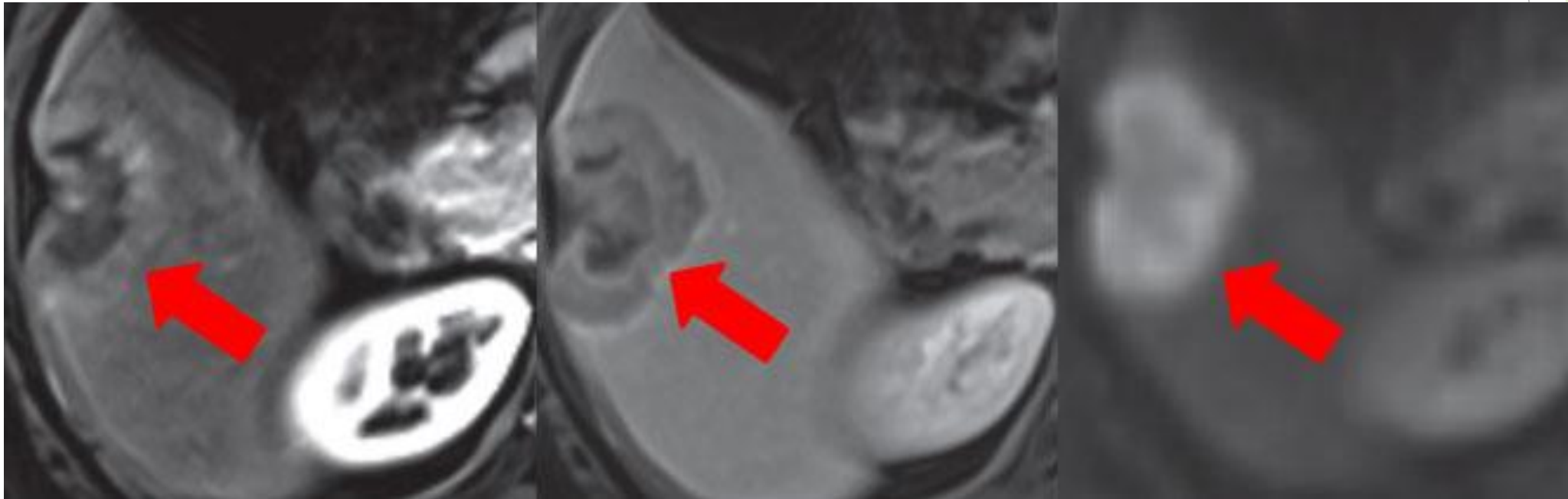
HCC con pattern atipico all'imaging

- *si osserva nell'early HCC: la riduzione dell'apporto portale in assenza di una completa neo-arterializzazione promuove la metamorfosi adiposa come risposta all'ipossia*
- *la metamorfosi adiposa si risolve con la progressione dell'HCC*
- *d.d.: adenoma steatosico, nodulo displasico, lipoma, angiomiolipoma, metastasi*



Aspetto a bersaglio

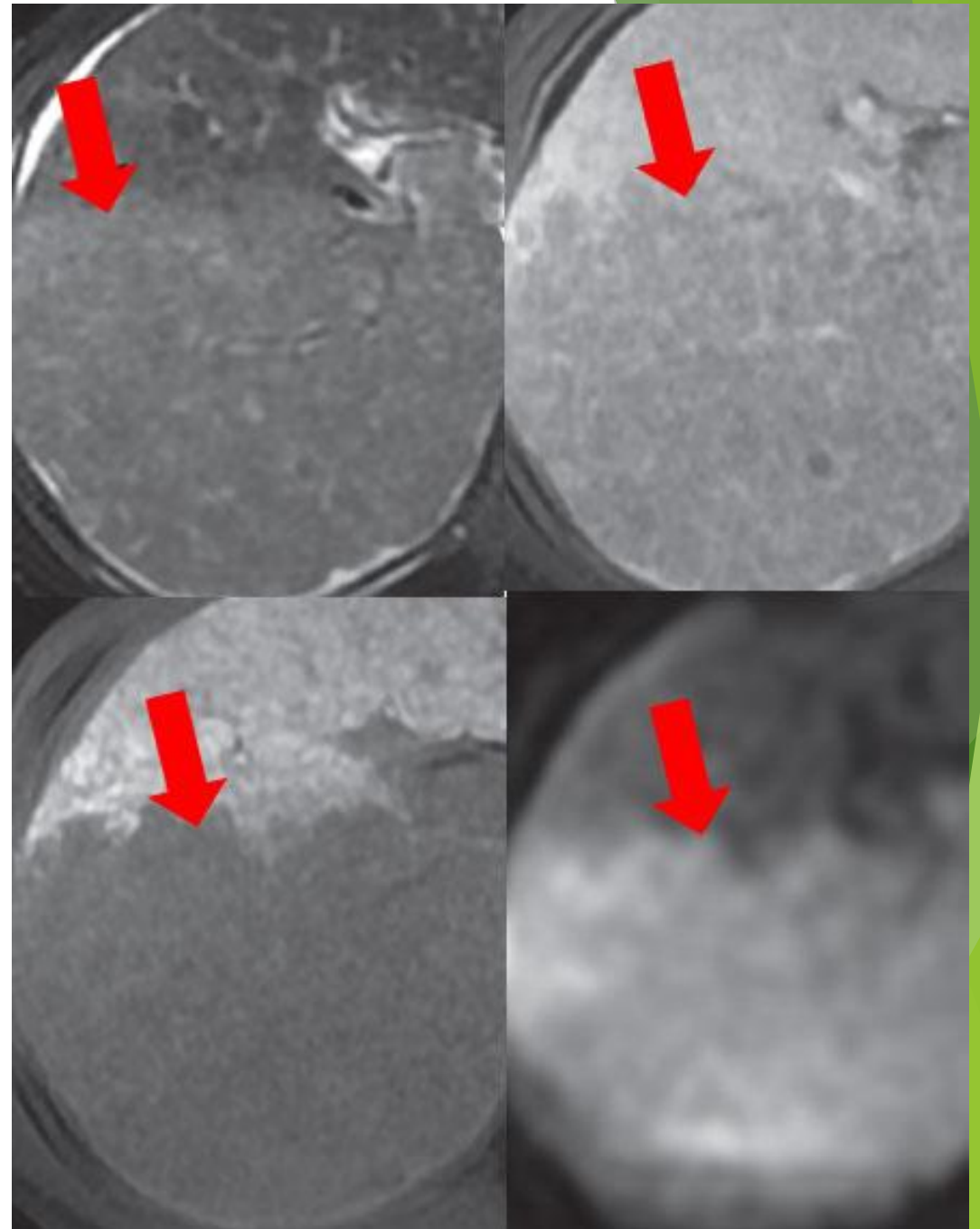
- *forme scarsamente differenziate, scirroso, sarcomatoidi o large HCC ≥ 5 cm*
- *ipercellulare in periferia e fibrosi/ischemia/necrosi centrali*
- *d.d. con ICC*



HCC con pattern atipico all'imaging

Infiltrativo

- *Aspetto diffusamente infiltrativo, a margini non definiti, frequente trombosi infiltrativa neoplastica della vena porta.*
- *L'infiltrazione dei rami portalì modifica il tipico pattern vascolare dell'HCC.*
- *d.d. con ICC*



Simulatori di HCC all'imaging in pazienti ad alto rischio

(epatite cronica HBV – HCV, malattia epatica alcolica, cirrosi)

Benigne

Angioma

Adenoma

Angiomiolipoma

Pseudolesioni infiammatorie

Pseudolesioni ipervascolari

Noduli FNH-like

Maligne

Colangiocarcinoma intraepatico (ICC)

Forme combinate HCC-ICC

Hepatoblastoma

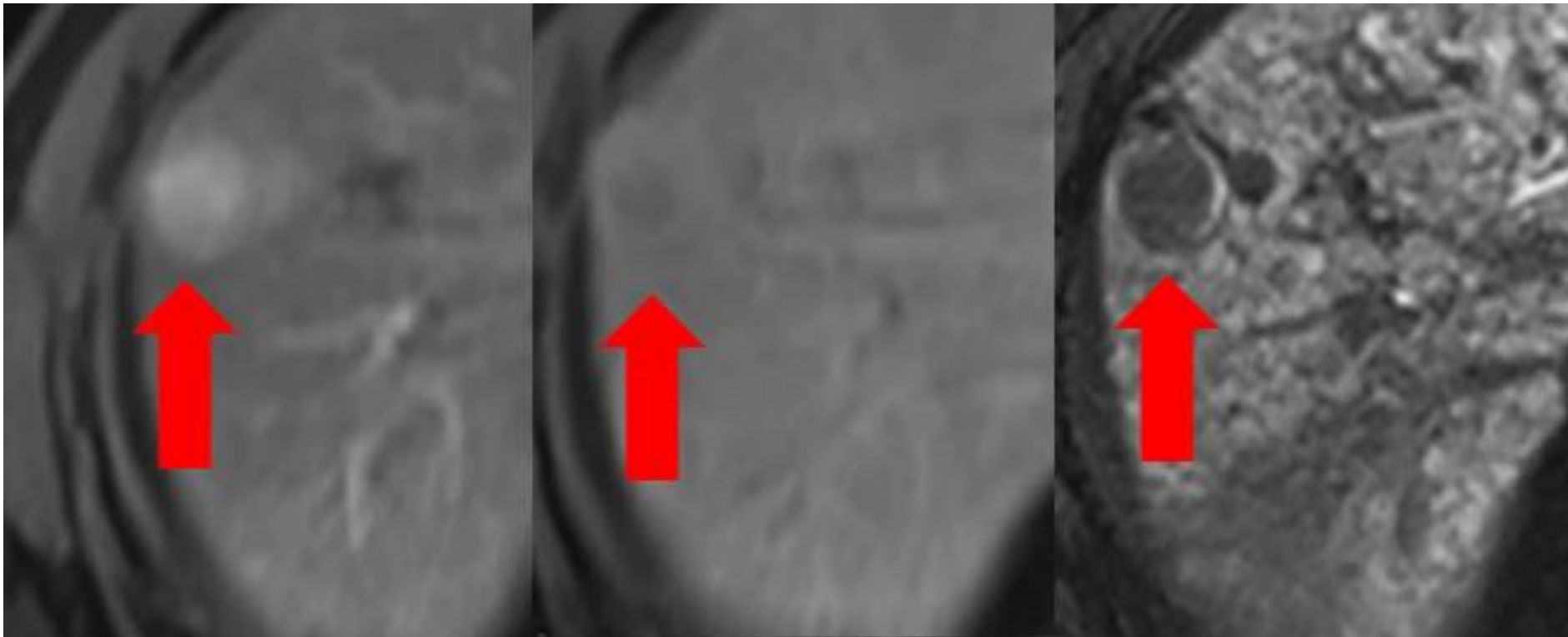
Plasmocitoma

Metastasi

Small ICC mass forming

- *< 3 cm*
- *Sono ipercellulari e non presentano componente fibrotica*
- *Possono presentare enhancement arterioso omogeneo e wash out tardivo.*

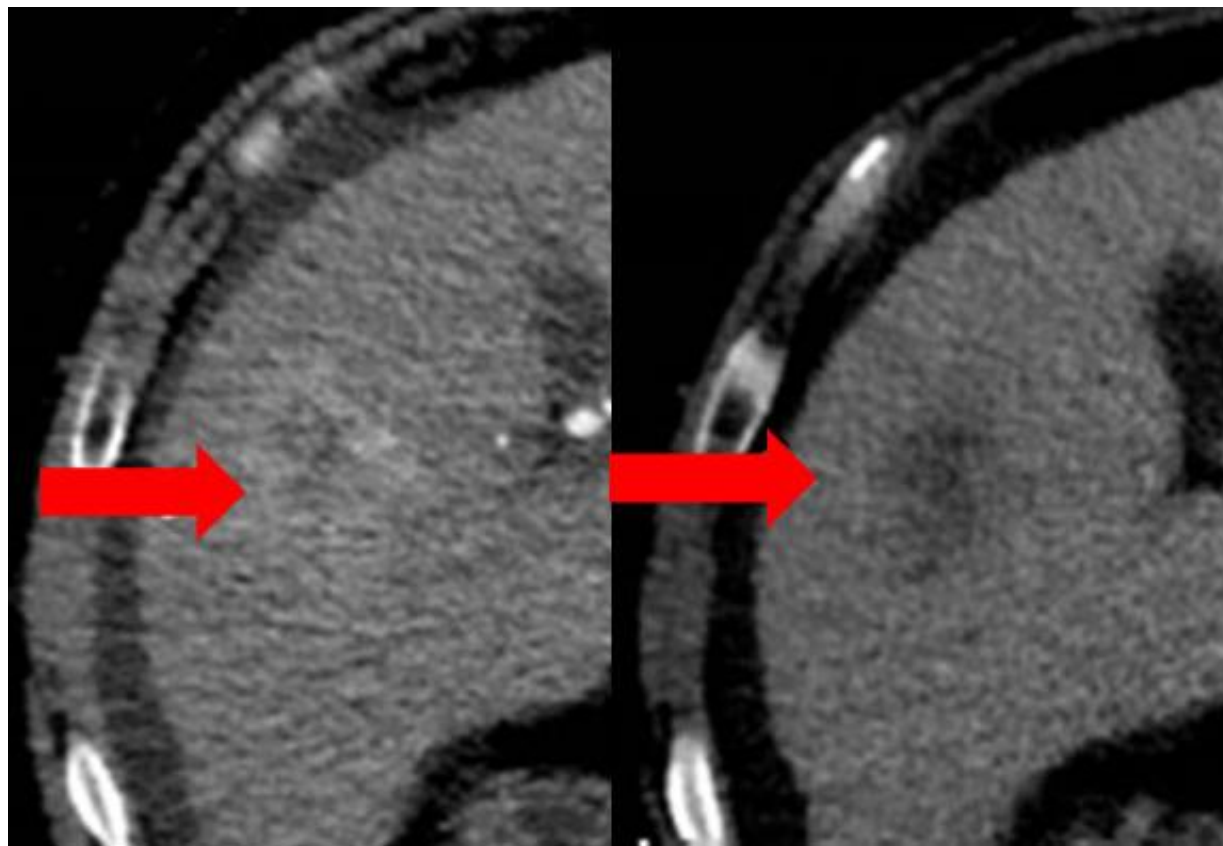
Simulatori di HCC all'imaging



Forme miste ICC-HCC

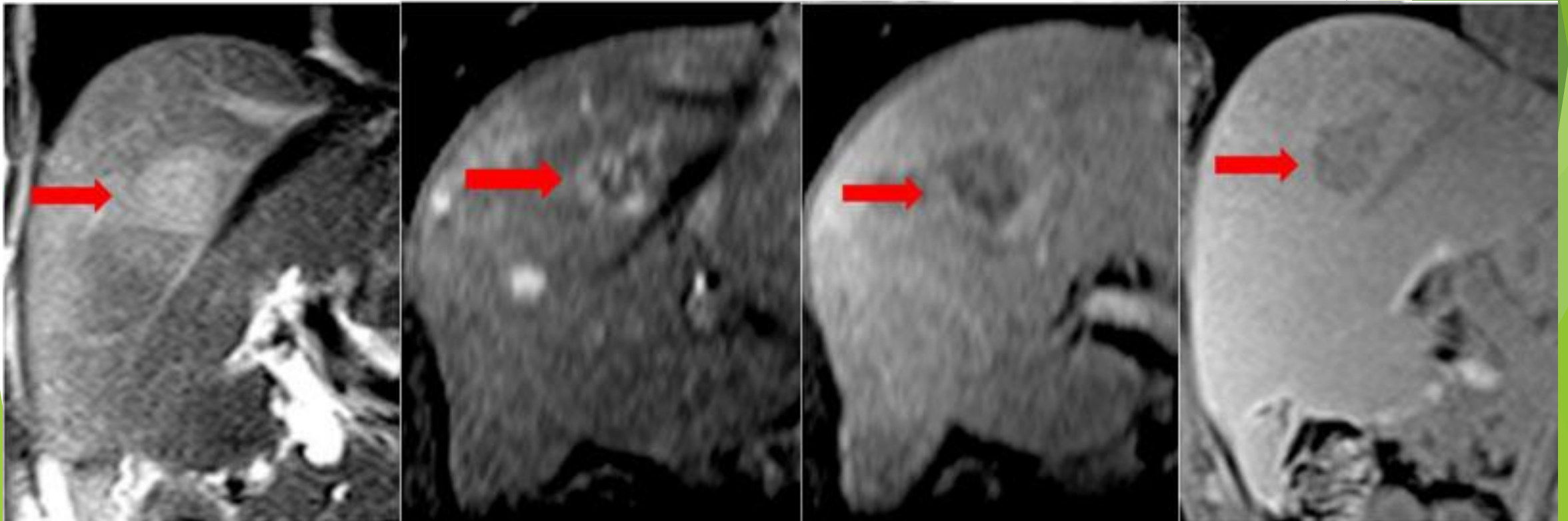
Simulatori di HCC all'imaging

- *caratteristiche di imaging: miste con aspetto a carta geografica o prevalente HCC o prevalente ICC*
- *markers (alfafetoproteina e CA19-9) possono contribuire alla diagnosi*



Plasmocitoma

- Può insorgere dopo terapie loco-regionali termo-ablative

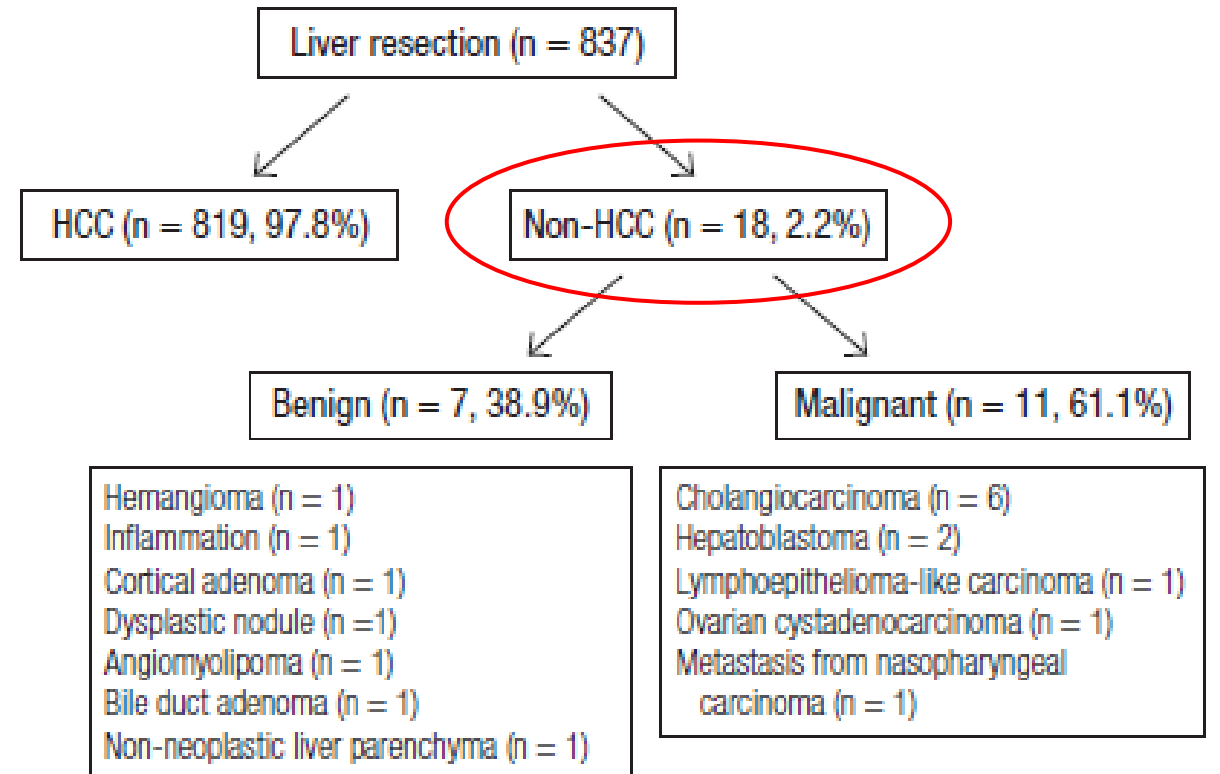


False Positive Diagnosis of Hepatocellular Carcinoma in Liver Resection Patients

Lee, J Korean Med Sci 2017

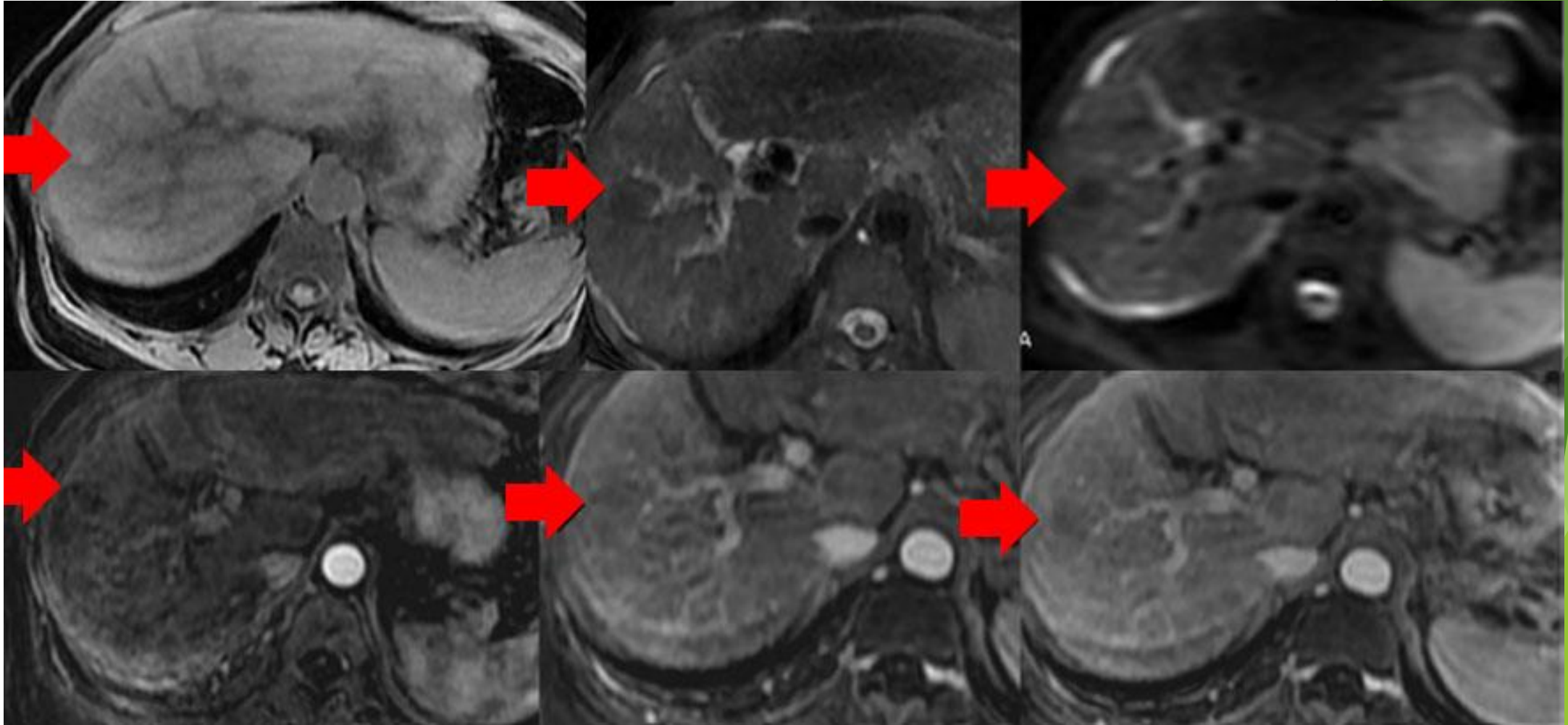
- **837 lesioni sospette per HCC alla TC/RM sottoposte a resezione chirurgica in pazienti ad alto rischio***

* epatite cronica HBV – HCV, malattia epatica su base alcolica, cirrosi

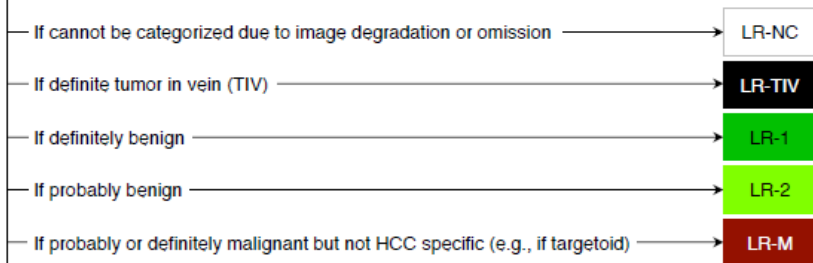


- **Lesioni < 1 cm: 0**
- **Lesioni < 2 cm: 3 (16,7%)**
- **Lesioni 2-5 cm: 10 (55,6%)**
- **Lesioni > 5 cm: 5 (27,7%)**

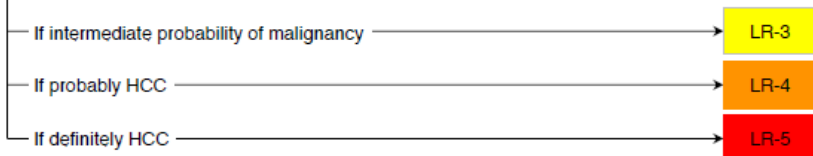
- **Lesioni non classificabili né come benigne né come maligne meritevoli di follow up strumentale**



Untreated observation without pathologic proof in patient at high risk for HCC



Otherwise, use CT/MRI diagnostic table below



		Diameter:	Arterial phase hypo- or iso-enhancement		Arterial phase hyper-enhancement		
			< 20 mm	≥ 20 mm	< 10 mm	10-19 mm	≥ 20 mm
• "Washout"	None:	LR-3	LR-3	LR-3	LR-3	LR-4	
		One:	LR-3	LR-4	LR-4	LR-4	LR-5
		≥Two	LR-4	LR-4	LR-4	LR-5	LR-5



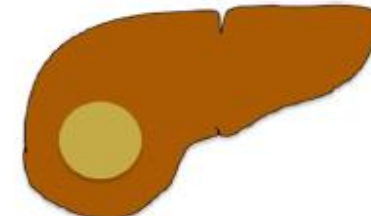
Observations in this cell are categorized based on one additional major feature:

- LR-4 – if enhancing "capsule"
- LR-5 – if nonperipheral "washout" OR threshold growth

Arterial Phase

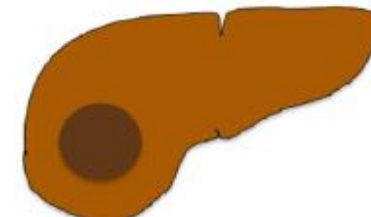
Hyperenhancement

- Non-rim-like enhancement in arterial phase unequivocally greater than enhancement of liver



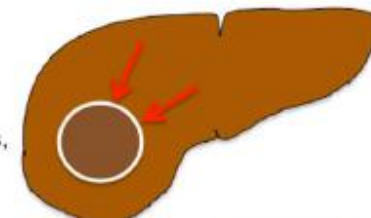
„Wash-out“

- Non-peripheral reduction in enhancement in whole or part of lesion (i.e., hypointensity/hypoattenuation in comparison to parenchyma)



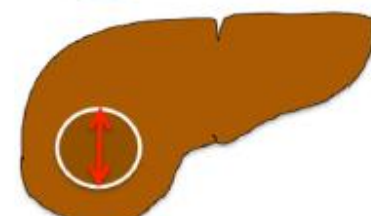
Capsule

- Smooth, uniform border around most of or entire lesion
- Visible as enhancing rim on portal venous, delayed and/or transitional phase



Size of mass:

- Largest outer-to-outer dimension
- Include capsule, if present



Threshold growth

- Size increase by a minimum of 5 mm AND:
 - ≥ 50% increase in ≤ 6 months OR



Liver Imaging Reporting and Data System (LI-RADS) v2018
 cirrosi , epatite cronica HBV , HCC progresso o in atto,
 potenziale inclusione epatite cronica HCV)

La classificazione LI-RADS è stato disegnata per ottenere un'elevata specificità piuttosto che un'elevata sensibilità nella diagnosi di HCC.

Table 1: Ancillary Features in LI-RADS Version 2018

Ancillary features favoring malignancy in general

- US visibility as discrete nodule
- Subthreshold growth
- Corona enhancement
- Fat sparing in solid mass
- Restricted diffusion
- Mild-moderate T2 hyperintensity
- Iron sparing in solid mass
- Transitional phase hypointensity
- Hepatobiliary phase (HBP) hypointensity

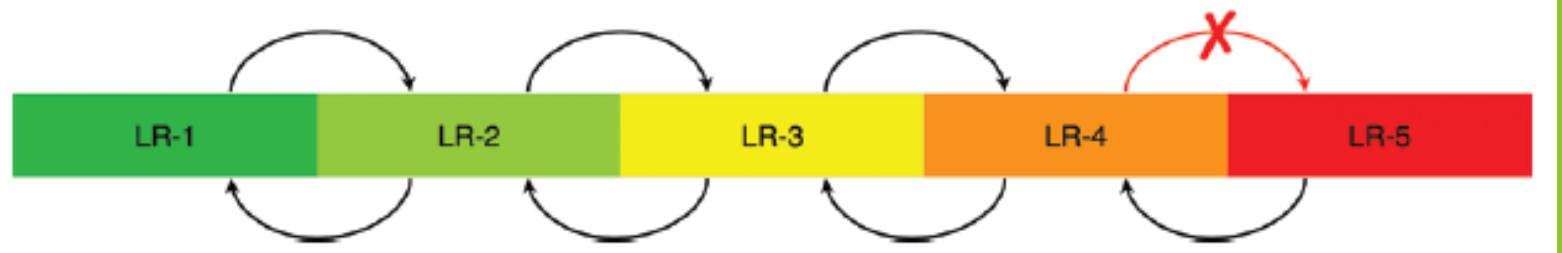
Ancillary features favoring HCC in particular

- Nonenhancing “capsule”
- Mosaic architecture
- Nodule-in-nodule architecture
- Fat in mass, more than in adjacent liver
- Blood products in mass

Ancillary features favoring benignity

- Size stability for ≥ 2 y
- Size reduction
- Parallels blood pool enhancement
- Undistorted vessels
- Iron in mass, more than in liver
- Marked T2 hyperintensity
- HBP isointensity

those favoring HCC (8). Their use is optional, and they may be used to up- or downgrade a category by one, but they cannot be used to upgrade to LR-5. An-



LR-3: LESIONE INDETERMINATE IN PAZIENTI AD ALTO RISCHIO

		Diameter:	Arterial phase hypo- or iso-enhancement		Arterial phase hyper-enhancement		
			< 20 mm	≥ 20 mm	< 10 mm	10-19 mm	≥ 20 mm
<ul style="list-style-type: none"> • "Washout" • "Capsule" • Threshold growth 	}	None:	LR-3	LR-3	LR-3	LR-3	
		One:	LR-3				
		≥Two					

LR-3:
Intermediate probability of malignancy

“Non rim” ipervascolarizzazione arteriosa

- < 20 mm in assenza di criteri maggiori addizionali

Ipo- o iso-vascolarizzazione arteriosa

- < 20 mm con al massimo 1 criterio maggiore addizionale
- ≥ 20 mm in assenza di criteri maggiori addizionali

META-ANALISI

Van der Pool, Gastroenterology 2019

- 17 studi
- 2760 pazienti
- 3556 lesioni
- 2482 HCC

Hepatocellular Carcinoma and Overall Malignancy per LI-RADS Category

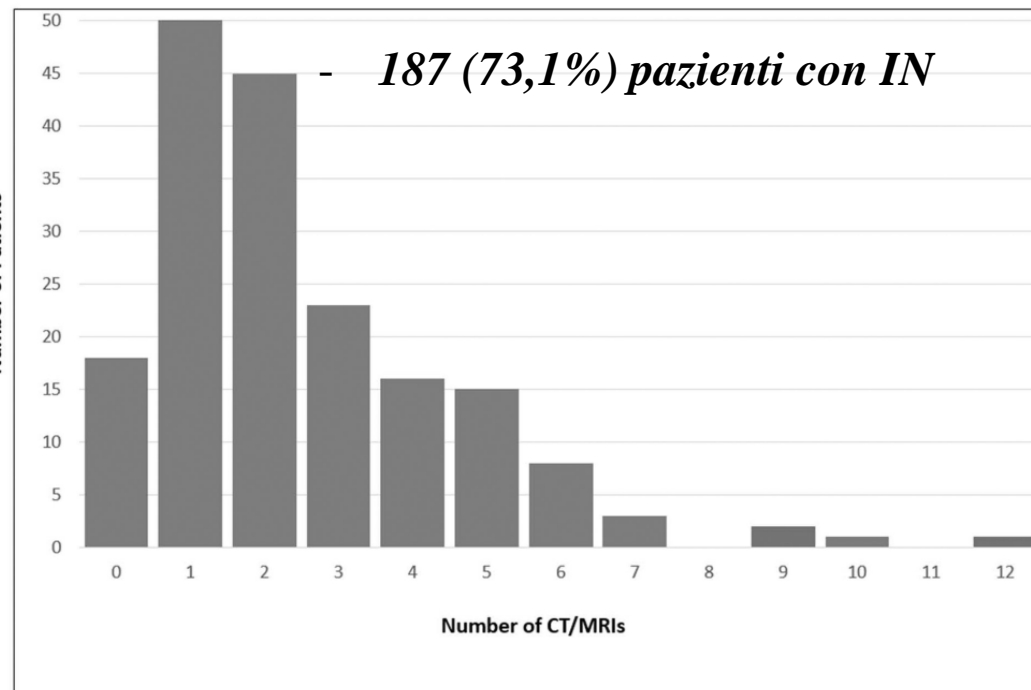
LI-RADS Category	HCC (%)	Overall Malignancy (%)
LR-1	0	0
LR-2	13 (8, 22)	14 (9, 21)
LR-3	38 (31, 45)	40 (31, 50)
LR-4	74 (67, 80)	80 (75, 85)
LR-5	94 (92, 96)	97 (95, 99)
LR-M	36 (26, 48)	93 (87, 97)

Frequency and Outcomes of Abnormal Imaging in Patients with Cirrhosis Enrolled in a Hepatocellular Carcinoma Surveillance Program

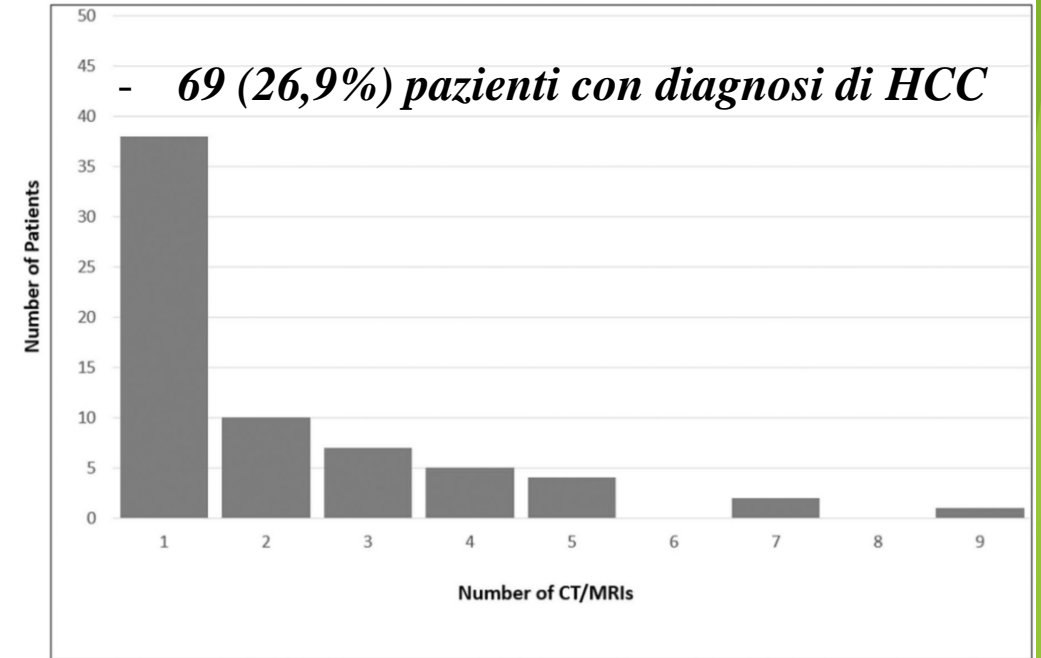
Konerman, Liver Transpl 2019

- 999 pazienti (età ≥ 18) con cirrosi sottoposti a sorveglianza ambulatoriale per HCC e con un'ecografia iniziale senza l'evidenza di noduli indeterminati (IN) o HCC
- Periodo di follow up: mediana 2,17 anni; IQR: 0,92- 3,89
- 256/999 mostravano uno o più noduli all'ecografia di follow up

CT/MRI Utilization Among Patients with Abnormal Imaging without Subsequent Diagnosis of HCC



CT/MRI Utilization Among Patients with Abnormal Imaging with Subsequent Diagnosis of HCC



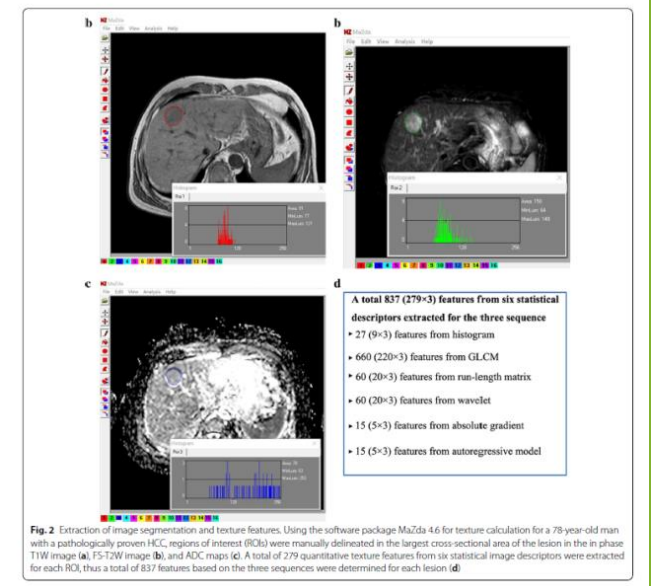
Danno fisico
(radiazioni ionizzanti, nefropatia da mdc)

Danno economico

Danno psicologico

Differentiation of small (≤ 3 cm) hepatocellular carcinomas from benign nodules in cirrhotic liver: the added additive value of MRI-based radiomics analysis to LI-RADS version 2018 algorithm

Zhong et al. *BMC Gastroenterol* (2021) 21:155



Compared with LI-RADS alone, the combined approach significantly improved the specificity (97.7% vs 81.8%, $p = 0.030$) and positive predictive value (99.1% vs 92.9%, $p = 0.031$) and afforded comparable sensitivity (97.3% vs 93.8%, $p = 0.215$) and negative predictive value (93.5% vs 83.7%, $p = 0.188$).

Table 5 Diagnostic performance of LI-RADS categories in the discrimination of HCCs from benign nodules

Diagnostic pattern	A_z (95%CI)	Sensitivity	Specificity	PPV	NPV	Accuracy
LI-RADS	0.898 (0.834–0.961)	93.8% (105/112)	81.8% (36/44)	92.9% (105/113)	83.7% (36/43)	90.4% (141/156)
Radiomics signature	0.917 (0.860–0.974)	93.8% (105/112)	86.4% (38/44)	94.6% (105/111)	84.4% (38/45)	91.7% (143/156)
Combined nomogram	0.975 (0.954–0.996)	97.3% (109/112)	97.7% (43/44)	99.1% (109/110)	93.5% (43/46)	97.4% (152/156)

LI-RADS liver imaging reporting and data system, A_z area under the receiver operating characteristic curve, PPV positive predictive value, NPV negative predictive value

Grazie per l'attenzione!!!