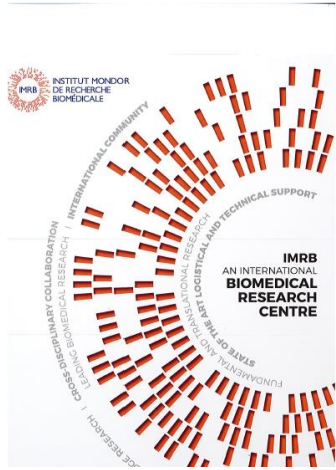
JFHOD 2017 PARIS
Thématique Le vieillissement
Invité LE QUÉBEC
23/26 MARS

Imagerie de l'imagerie de diffusion et utilisation de produits de contraste hépatobiliaires dans l'imagerie du foie



Alain LUCIANI, Frédéric PIGNEUR

Université Paris Est Créteil, Faculté de Médecine
AP-HP, CHU Henri Mondor, Creteil France

- **OBJECTIFS PEDAGOGIQUES**

- ❑ **Connaître les principales indications de l'imagerie de diffusion dans l'étude du foie**

- ❑ **Connaître l'apport des produits de contraste hépato biliaires dans l'étude des lésions du foie**

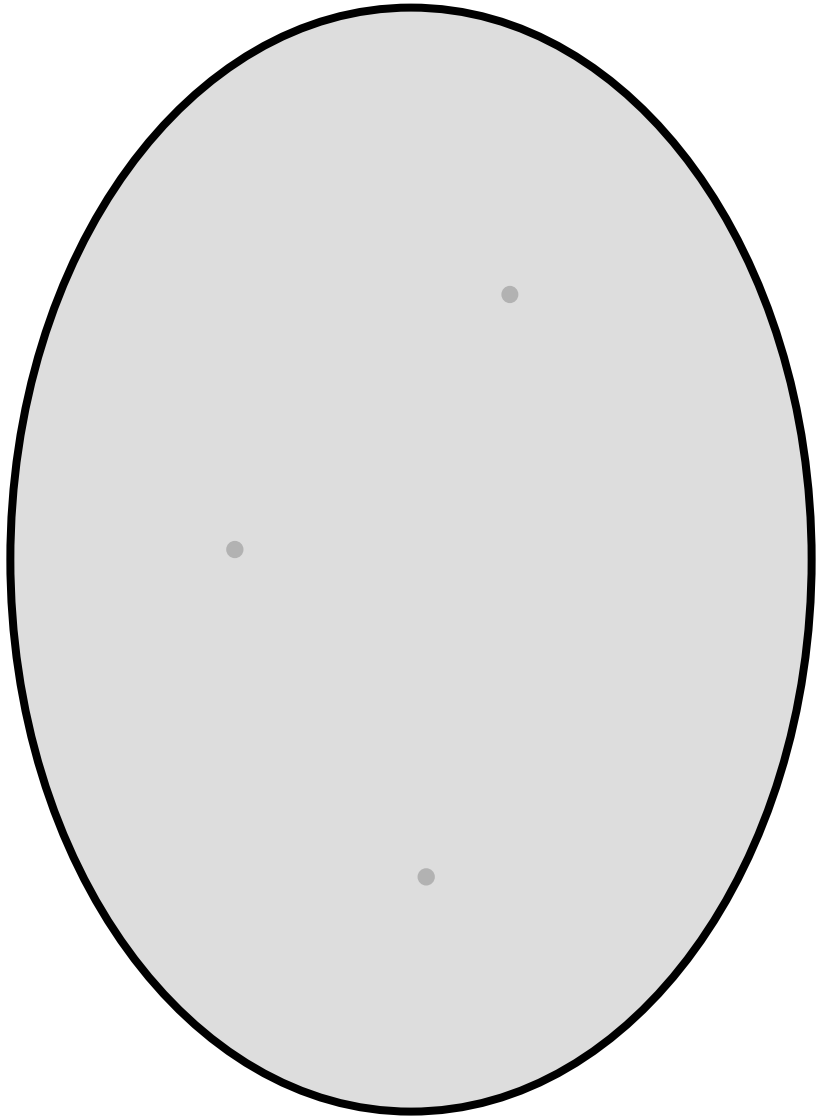
LIENS D'INTÉRÊT

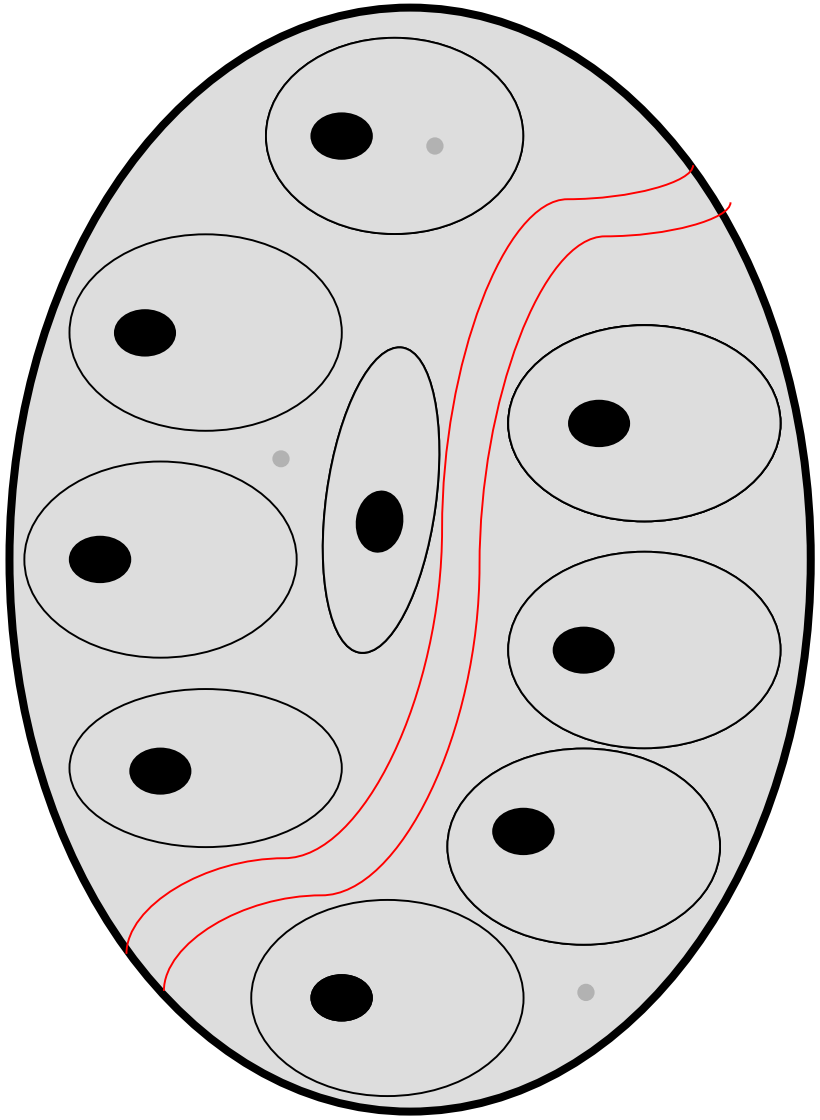
- Auteur :**Partenariat recherche GE Medical System France**
- Auteur :**Partenariat recherche Siemens Healthineers**
- Auteur :**Partenariat recherche Bracco France**

Imagerie de diffusion : Rappels

- Mise en évidence des mouvements microscopiques des protons H

- Applications de **gradients de déphasage** dans la séquence IRM, pondérée T2 :
  - Ce qui est **immobile** se rephase → **Signal** → **Diffusion Restreinte**
  - Ce qui est **mobile** ne se rephase pas → **Chute de signal** → **Pas de restriction**





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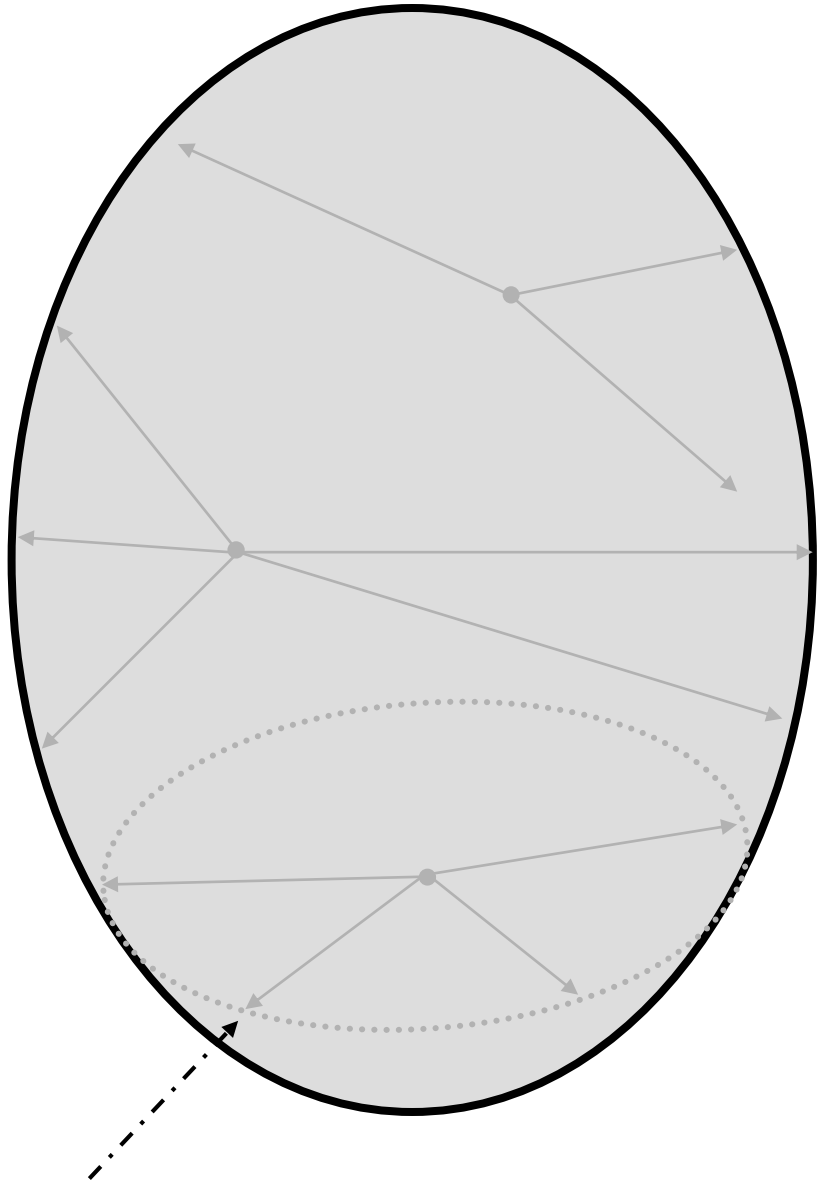
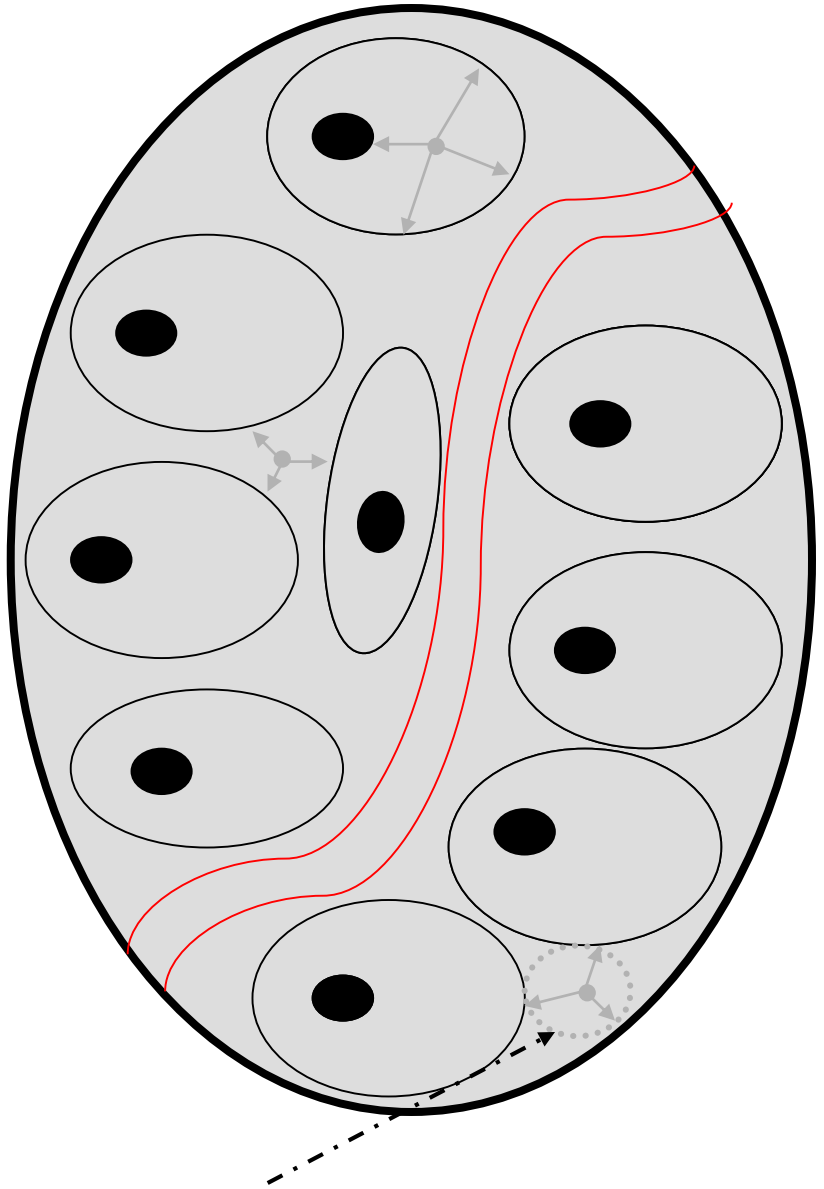
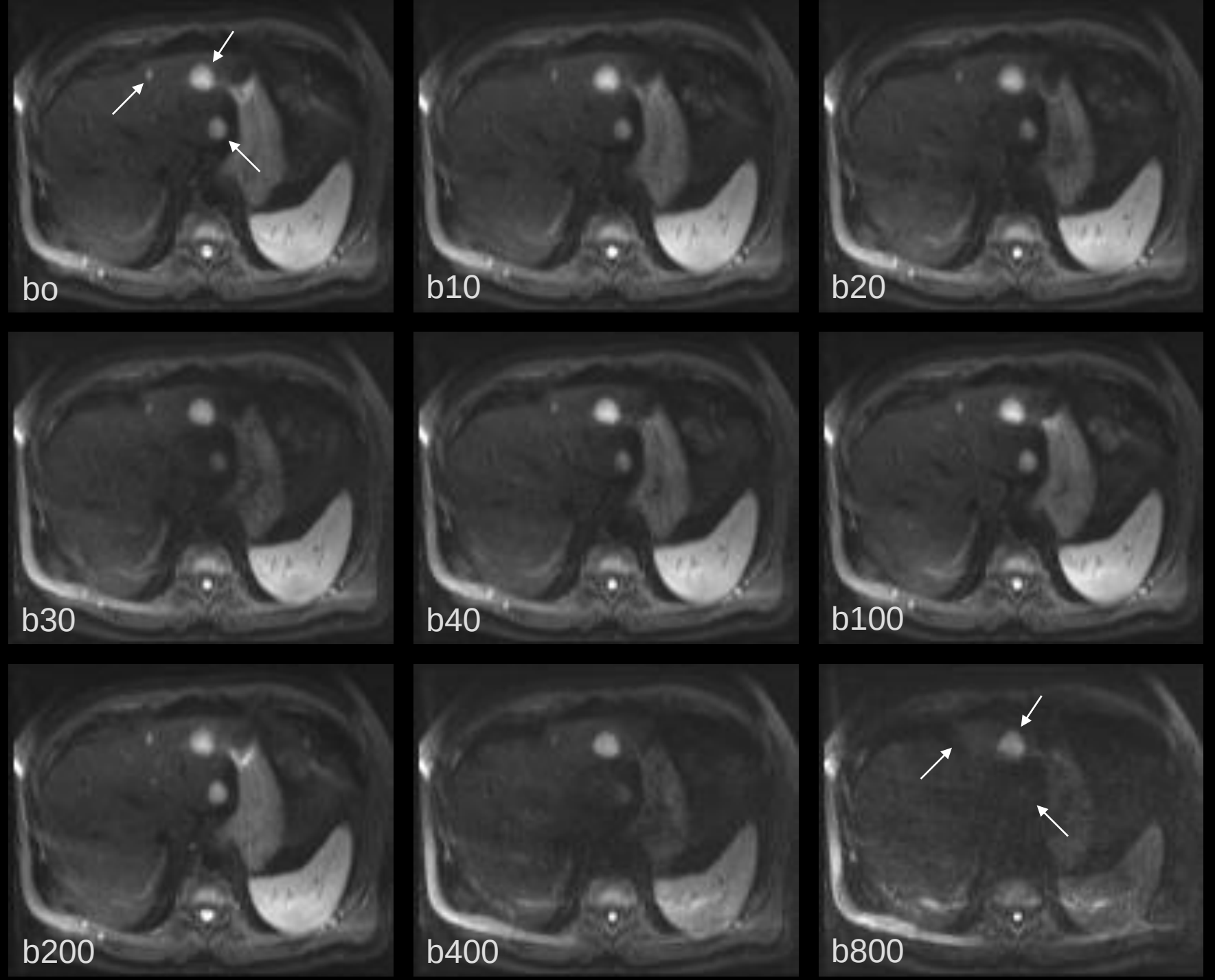
Absence de restriction de la diffusion



Restriction de la diffusion



CHU Henri Mondor, Faculte Medecine, Universite Paris Est Creteil, AP-HP, Creteil, France; imagerie.medicale@aphp.fr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b10
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Rôle aujourd'hui des séquences de diffusion dans l'étude du foie

- **Intégration systématique** dans l'étude du foie en IRM
- Accord de consensus international sur **« l'utilisation de ces séquences tant pour la détection que la caractérisation des lésions hépatiques »**

Eur Radiol (2016) 26:921–931
DOI 10.1007/s00330-015-3900-3

CONTRAST MEDIA

ESGAR consensus statement on liver MR imaging and clinical use of liver-specific contrast agents

E. Neri[1] · M. A. Bali[2] · A. Ba-Ssalamah[3] · P. Boraschi[1] · G. Brancatelli[4] · F. Caseiro Alves[5] · L. Grazioli[6] · T. Helmberger[7] · J. M. Lee[8] · R. Manfredi[9] · L. Martì-Bonmatì[10] · C. Matos[2] · E. M. Merkle[11] · B. Op De Beeck[12] · W. Schima[13] · S. Skehan[14] · V. Vilgrain[15] · C. Zech[16] · C. Bartolozzi[1]

Rôle aujourd'hui des séquences de diffusion dans l'étude du foie

Applications cliniques

- Détection des lésions II
- Caractérisation de certaines lésions focales

Recherche Clinique

- Evaluation de la réponse tumorale
- Evaluation fonctionnelle de la perfusion tumorale

WIP

- Substitution de certains examens avec injection de produits de contraste

Schmid-Tannwald et al. JMRI 2013; 37:35-47

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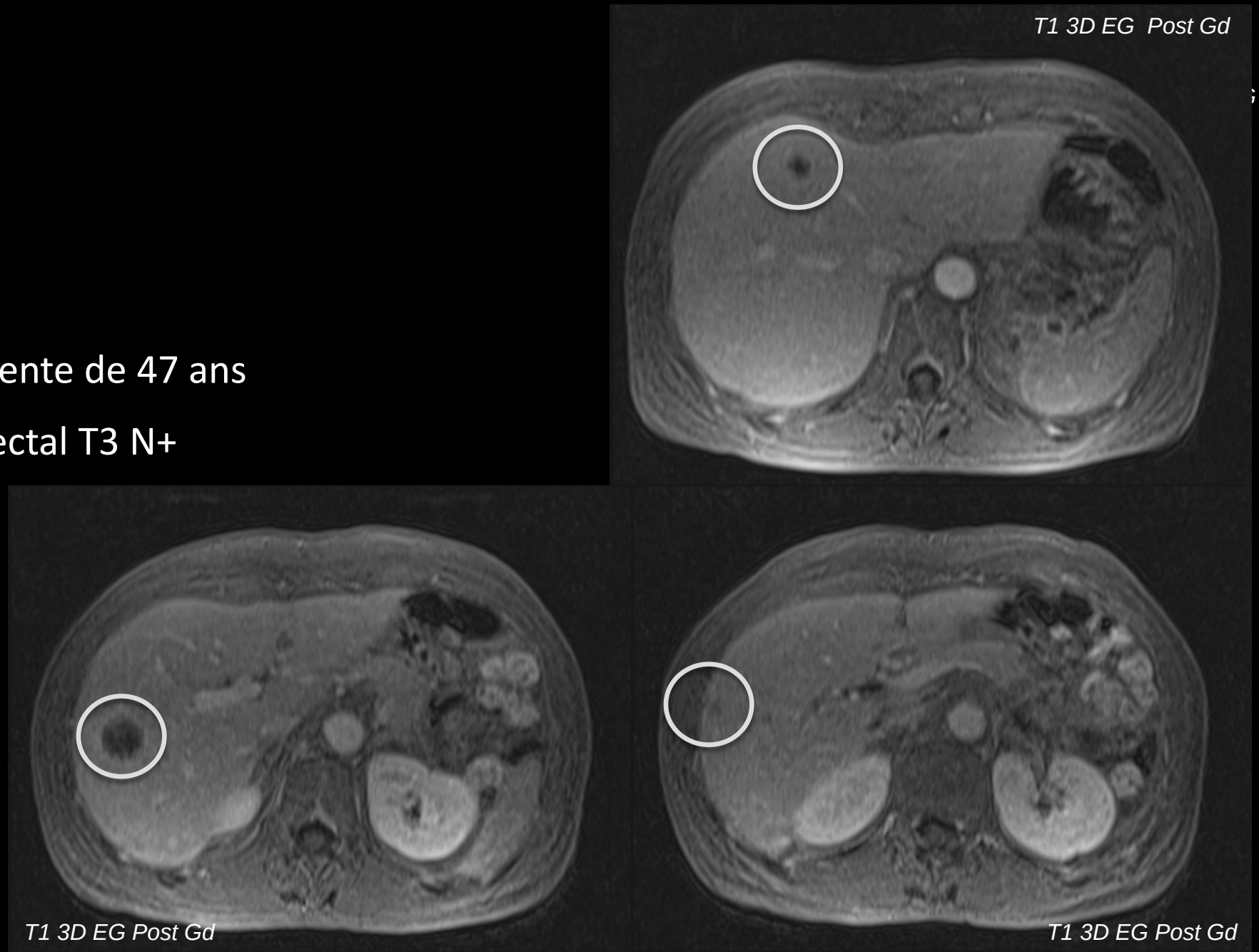
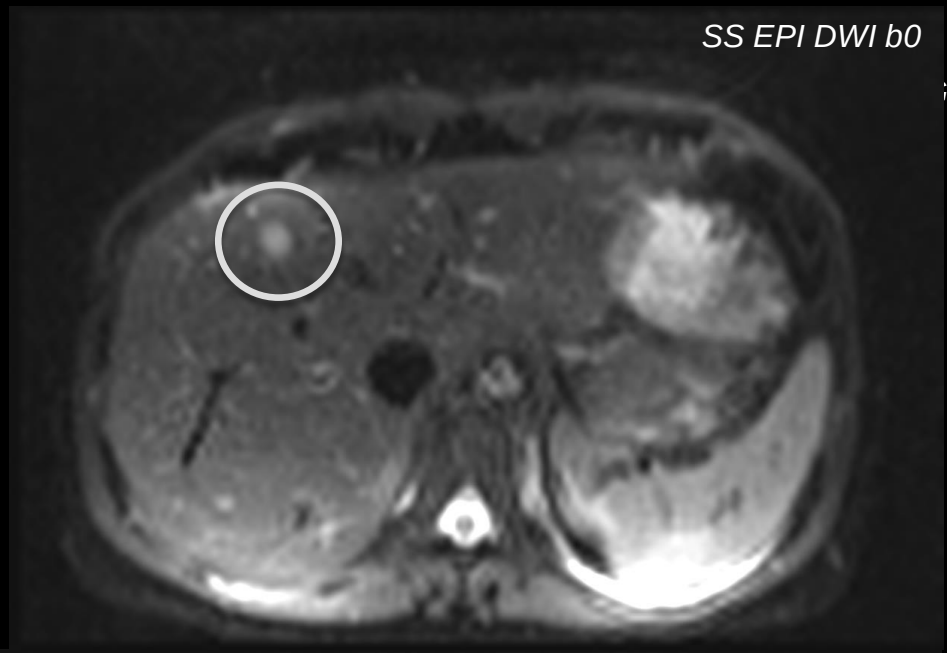
Patiente de 47 ans

K Rectal T3 N+



SS EPI DWI b100



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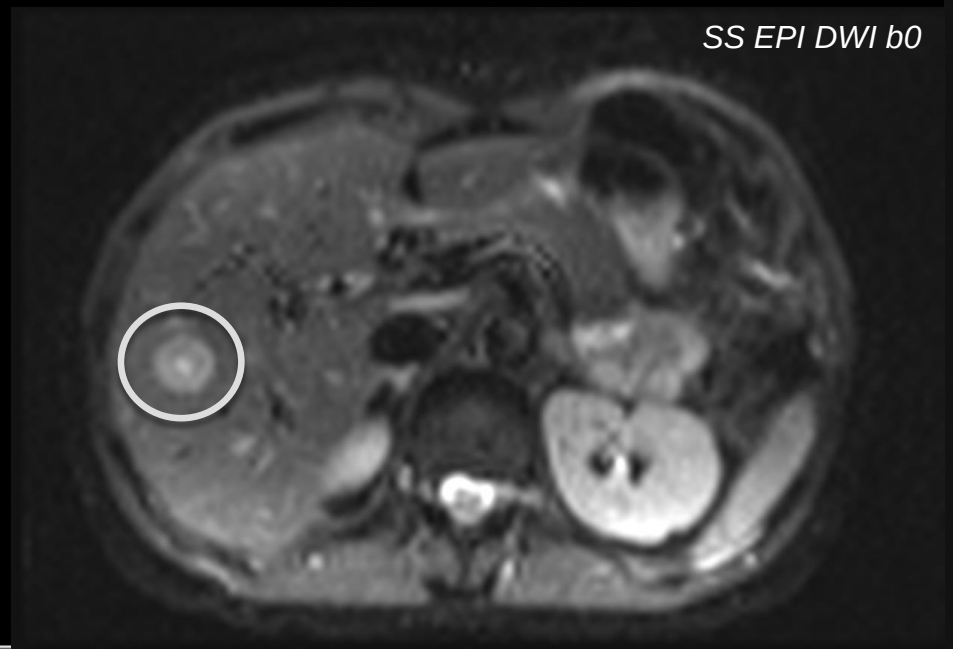

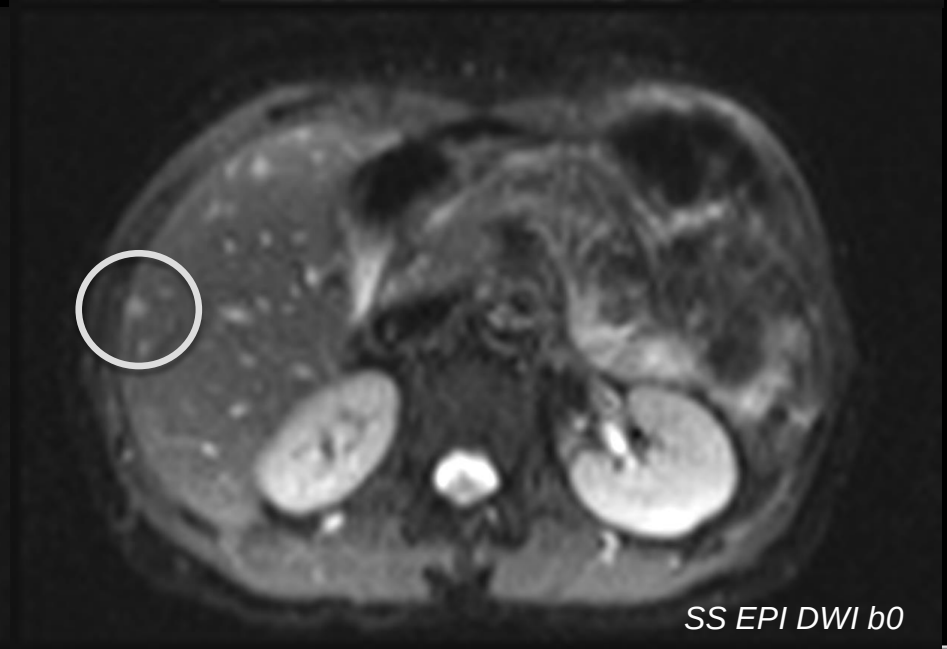

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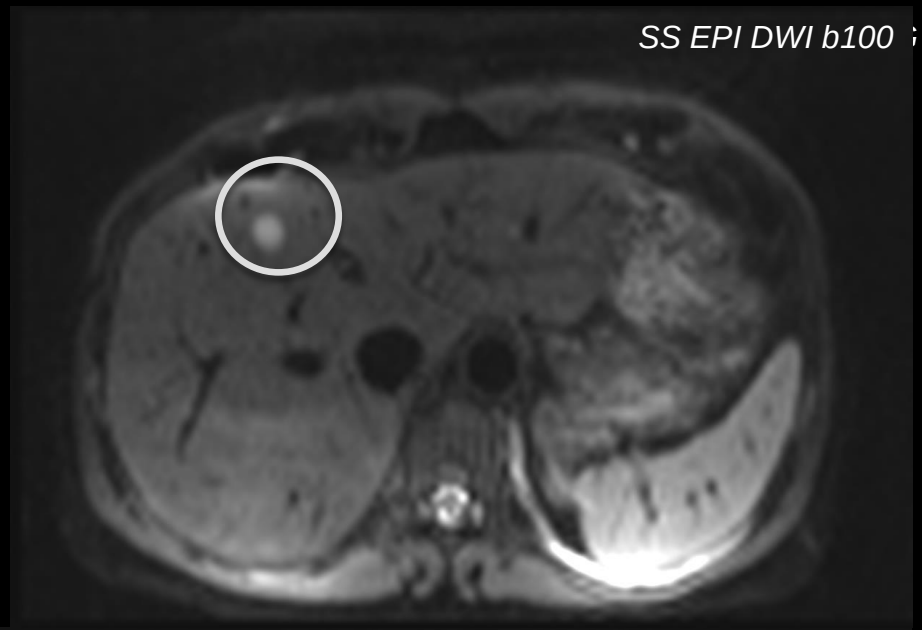
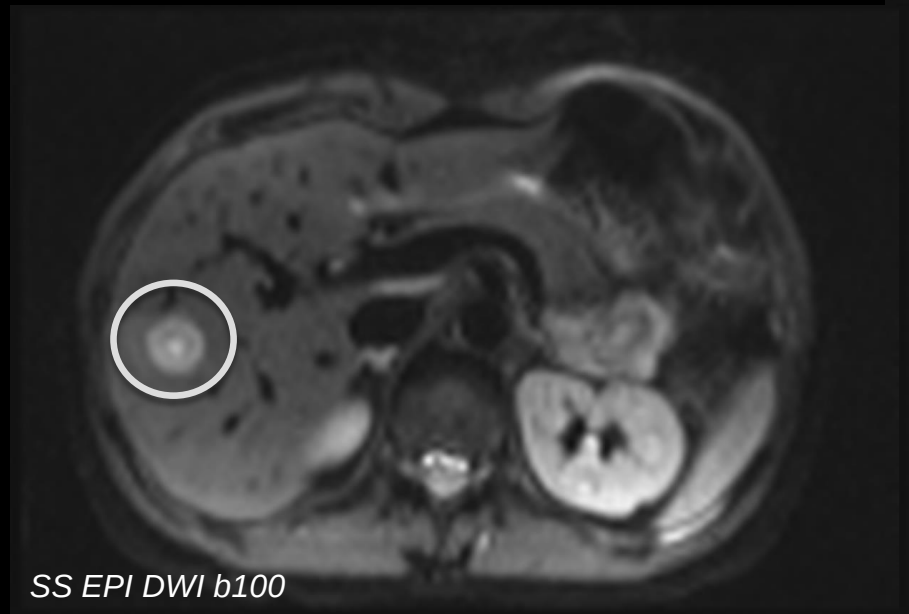
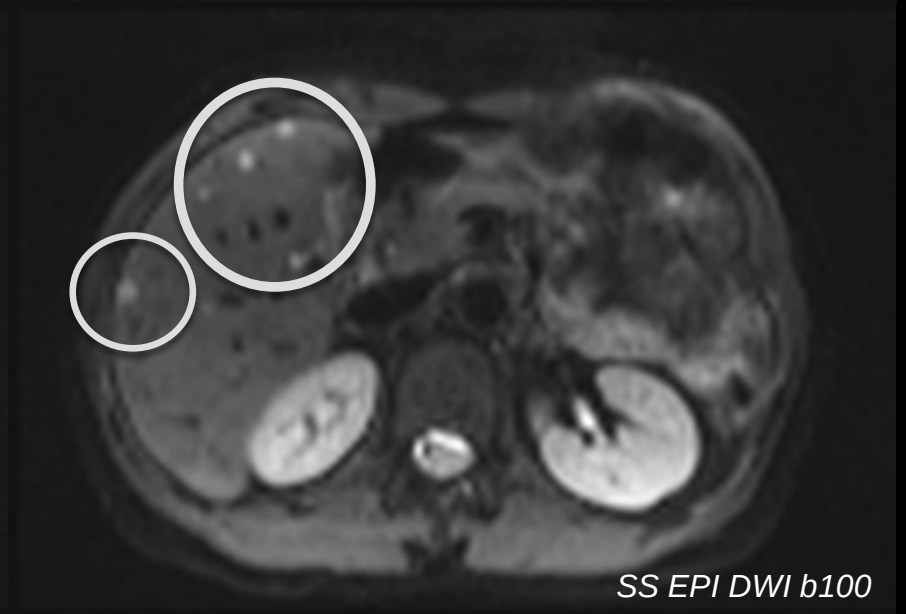






ORIGINAL ARTICLE

Selection for hepatic resection of colorectal liver metastases: expert consensus statement

Reid B. Adams[1], Thomas A. Aloia[2], Evelyne Loyer[3], Timothy M. Pawlik[4], Bachir Taouli[5] & Jean-Nicolas Vauthey[2]

[1]Division of General Surgery, University of Virginia School of Medicine, Charlottesville, VA, Departments of [2]Surgical Oncology and [3]Diagnostic Radiology, The University of Texas MD Anderson Cancer Center, Houston, TX, [4]Department of Surgery, Johns Hopkins University, Baltimore, MD, and [5]Department of Radiology, Mount Sinai Medical Center, New York, NY, USA

IRM avec diffusion recommandée en première intention

- ***Lésion < 1cm***
- ***Stéatose hépatique ou après chimiothérapie***

TEP / TEP-TDM utiles pour M+ extra hépatique mais insuffisant pour lésions < 1cms ou lésions intra-thoraciques

HPB (Oxford). 2013 Feb;15(2):91-103.

IRM et détection lésionnelle – Lésions I

- 52 patients
- Corrélations avec explants hépatiques
- Imagerie DWI seule, séquences dynamiques seules ou combinaison des deux
- 72 CHC chez 33 patients
- **Amélioration des performances surtout pour lecteur experimenté**

Table 3. Diagnostic Sensitivity for HCC Detection Stratified by Lesion Size in 52 Patients with 72 HCCs

Modality*	Lesion Size		
	≤1 cm	1-2 cm	>2 cm
DW-set, mean (95% CI)	25.8 (9.0-54.9)	42.0 (27.3-58.3)	89.3 (72.4-97.0)
CE-set, mean (95% CI)	31.8 (21.4-44.4)	74.0 (60.9-83.9)	96.4 (83.0-99.8)
All-set, mean (95% CI)	37.9 (19.8-60.1)	76.0 (61.5-87.2)	100.0 (89.3-100.0)
P (DW-set versus CE-set)†	0.44	**0.001**	0.43
P (CE-set versus All-set)†	0.46	0.81	0.78
95% CI (DW-set versus CE-set)‡	−7.8 to 17.7	16.4 to 35.9	−8.7 to 14.1
95% CI (CE-set versus All-set)‡	−7.8 to 17.9	−10.4 to 13.1	−3.4 to 3.6

Abbreviation: CI, confidence interval.
*DW-set includes unenhanced T1WI, T2WI, and DWI. CE-set includes unenhanced T1WI, T2WI, and CET1WI. All-set includes all sequences.
†Generalized estimating equation analysis. Significant *P* values appear in boldface type.
‡CIs for the difference between sensitivity of DW-set versus CE-set, and CE-set versus All-set (using pooled data from two observers).

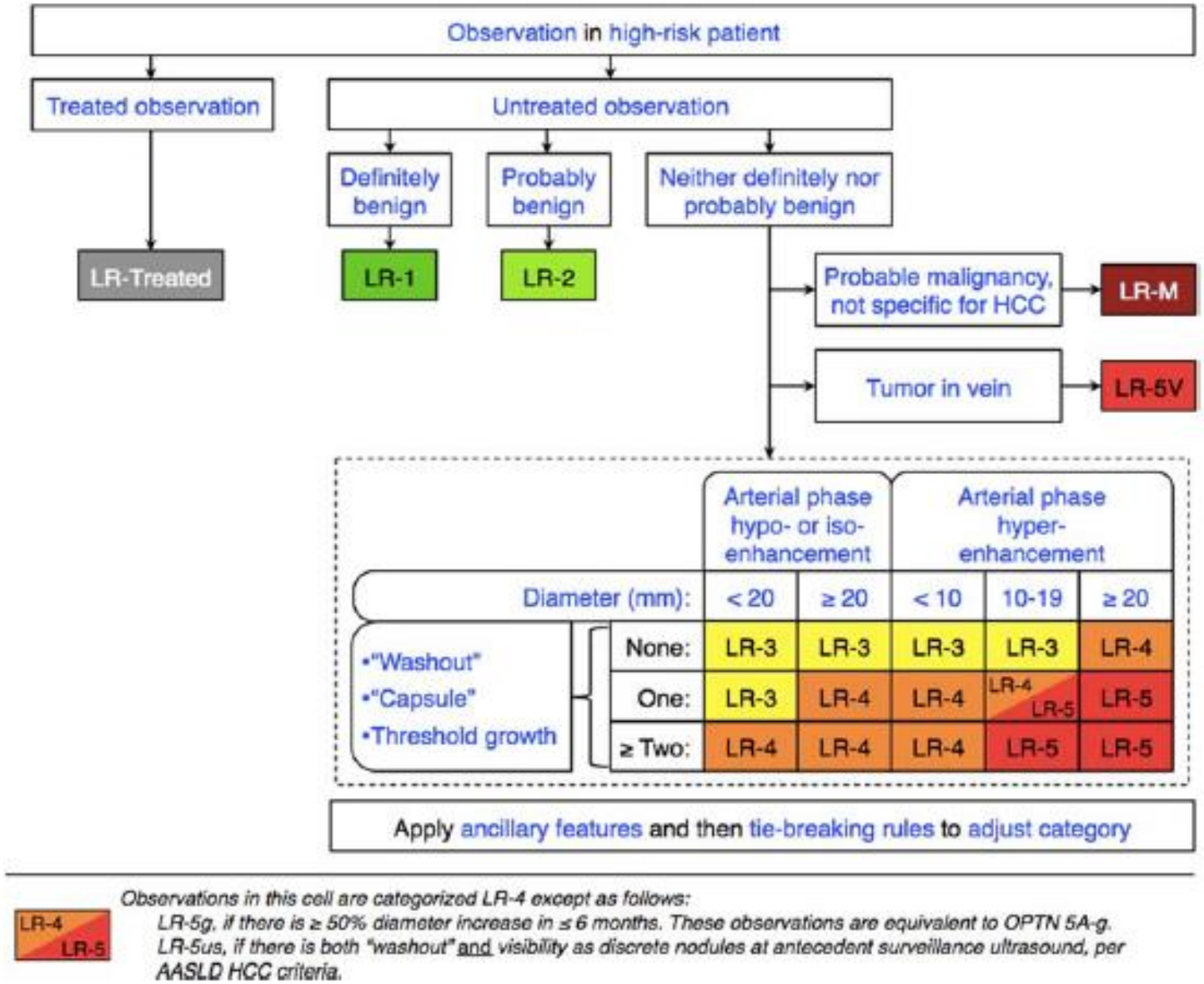
Hepatocellular Carcinoma: Detection With Diffusion-Weighted Versus Contrast-Enhanced Magnetic Resonance Imaging in Pretransplant Patients

Mi-Suk Park,[1]* Sooah Kim,[1] Jignesh Patel,[1] Cristina H. Hajdu,[2] Richard K. G. Do,[1] Lorenzo Mannelli,[1] James S. Babb,[1] and Bachir Taouli[1]

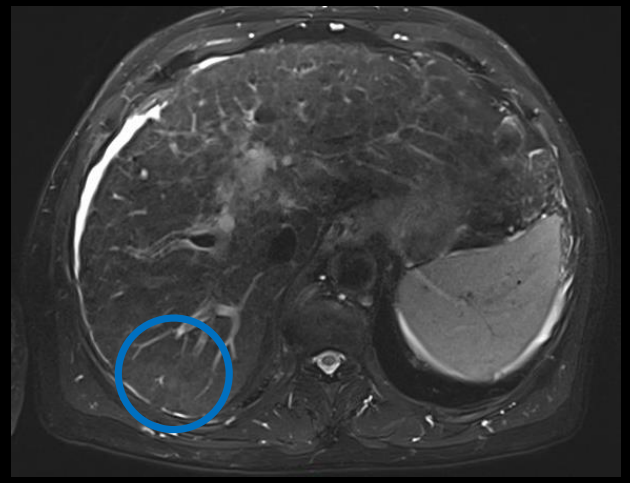
Park et al. HEPATOLOGY 2012;56:140-148

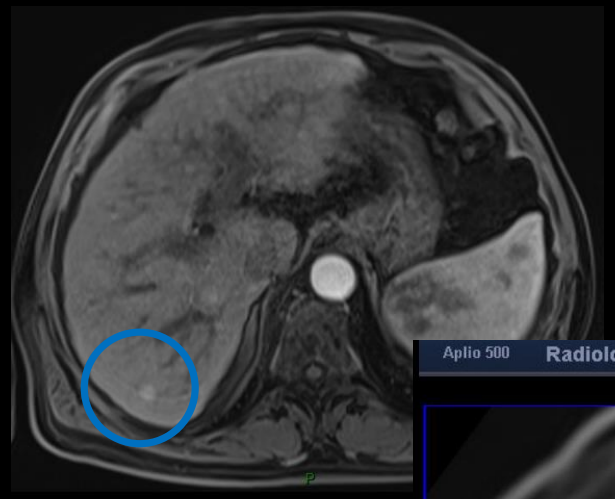
IRM et caractérisation lésionnelle – Lésions I

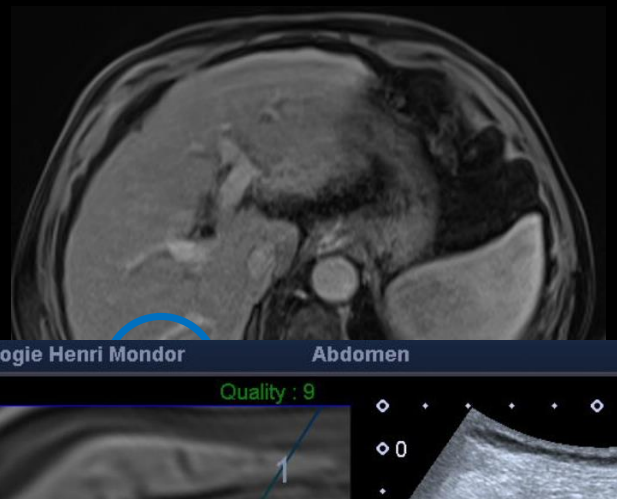
- Une intégration progressive dans les **algorithmes de caractérisation des lésions primitives malignes**
- **Hypersignal en diffusion : critère ancillaire permettant de passer de catégorie LR-3 à LR-4**

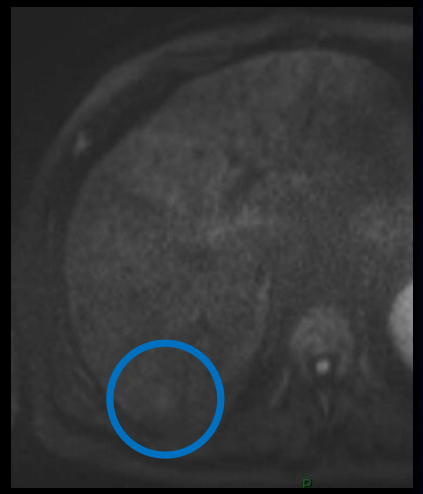


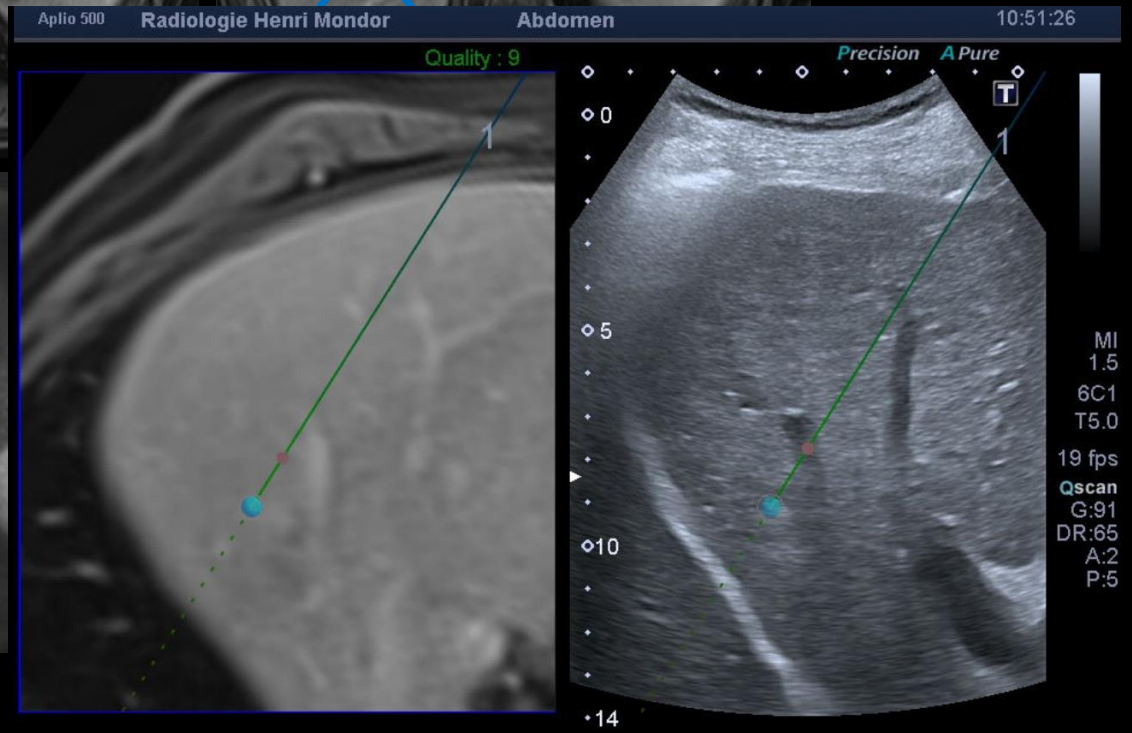
LiRADS – v2014











- 68 ans
- Cirrhose et NASH
- Nodule de 8mm
  Hypervasculaire sans WO
  Foie droit
- Signal élevé en diffusion

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Des limites

- **D'abord Instrumentales**
  - Système IRM
  - Choix des paramètres de séquences et variation du signal
  - Modélisation de l'extraction des paramètres de diffusion
  - Expliquent en grande partie la variabilité des paramètres quantitatifs de la diffusion

Koh et al. Eur Radiol 2009;19:2728–2738
Kakite et al. Magn Reson Imaging 2015; 41:149–156

- **Applications cliniques ?**
  - Oui pour étude **qualitative / Détection**

Parikh et al. Radiology 2008; 246: 812-822

  - Variabilité encore forte pour outil quantitatif / biomarqueur
  - Pas d'utilisation quantitative pour distinguer les lésions tumorales hépatiques solides

Diffusion-Weighted Imaging Outside the Brain: Consensus Statement From an ISMRM-Sponsored Workshop

Bachir Taouli, MD,[1]* Ambros J. Beer, MD,[2] Thomas Chenevert, PhD,[3] David Collins, BA,[4] Constance Lehman, MD, PhD,[5] Celso Matos, MD,[6] Anwar R. Padhani, MD,[7] Andrew B. Rosenkrantz, MD,[8] Amita Shukla-Dave, PhD,[9] Eric Sigmund, PhD,[10] Lawrence Tanenbaum, MD,[11] Harriet Thoeny, MD,[12] Isabelle Thomassin-Naggara, MD, PhD,[13] Sebastiano Barbieri, PhD,[12] Idoia Corcuera-Solano, MD,[1] Matthew Orton, PhD,[4] Savannah C. Partridge, PhD,[14] and Dow-Mu Koh, MD[15]

The significant advances in magnetic resonance imaging (MRI) hardware and software, sequence design, and postprocessing methods have made diffusion-weighted imaging (DWI) an important part of body MRI protocols and have fueled extensive research on quantitative diffusion outside the brain, particularly in the oncologic setting. In this review, we summarize the most up-to-date information on DWI acquisition and clinical applications outside the brain, as discussed in an ISMRM-sponsored symposium held in April 2015. We first introduce recent advances in acquisition, processing, and quality control; then review scientific evidence in major organ systems; and finally describe future directions.
J. MAGN. RESON. IMAGING 2016;44:521–540.

Produits de contraste hépatospécifiques

Gd-BOPTA

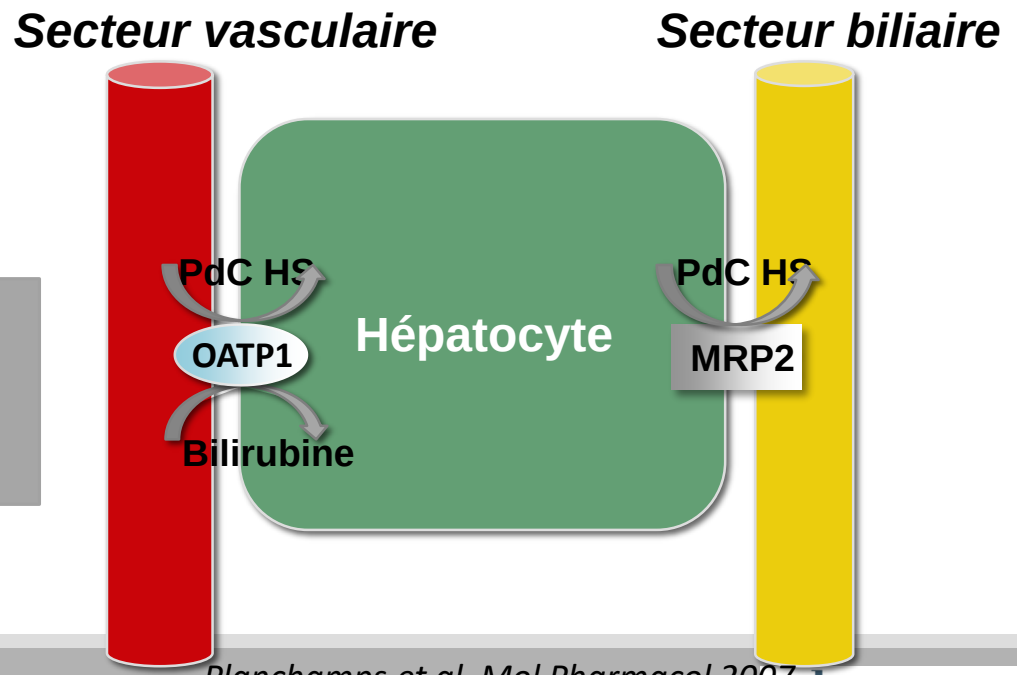
- gadobenate dimeglumine, Multihance®, Bracco Imaging, Milan, Italie

Gd-EOB-DTPA

- acide gadoxetique, Primovist®/Eovist®, Bayer-Schering Pharma, Berlin, Allemagne

- Distribution extracellulaire
- Captation par les hépatocytes fonctionnels via OATP1B3
- Excrétion dans la bile via MRP2

⇒ Acquisition d'images
⇒ à la phase dynamique
⇒ à la phase hépatobiliaire



OATP1 = Organic Anion Transporting Polypeptide 1
MRP2 = Multridrug Resistance associated Protein 2

Planchamps et al. Mol Pharmacol 2007
Pastor et al. Radiology 2010

Gd-BOPTA et Gd-EOB-DTPA : comparaison

	Gd-BOPTA	Gd-EOB-DTPA
Noms	Gadobenate dimeglumine Multihance® Bracco Imaging	Acide gadoxetique Primovist®/Eovist® Bayer HealthCare
AMM en France	Oui	Non
Captation	Transporteurs OATP1	Transporteurs OATP1
Excrétion	3-5% biliaire 95-97% rénale	50% biliaire 50% rénale
Dose	0,05 mmol/kg 0,1 ml/kg	0,025 mmol/kg 0,1 ml/kg
Délai phase hépatobiliaire	60 -120 minutes	15 - 20 minutes

Rohrer et al. Invest Radiol 2005
Frydrychowicz et al. J Magn Reson Imaging 2012
Thomsen et al. Eur Radiol 2013

Runge et al. J Comput Assist Tomogr 1998
Dahlqvist et al. Eur Radiol 2012

Questions: Recommandations – Consensus sur PdC HBP

Eur Radiol (2016) 26:674–682
DOI 10.1007/s00330-015-3873-2

MAGNETIC RESONANCE

Consensus report from the 7th International Forum for Liver Magnetic Resonance Imaging

Elmar M. Merkle[1] · Christoph J. Zech[1] · Carlo Bartolozzi[2] · Mustafa R. Bashir[3] · Ahmed Ba-Ssalamah[4] · Alexander Huppertz[5] · Jeong Min Lee[6] · Jens Ricke[7] · Michiie Sakamoto[8] · Claude B. Sirlin[9] · Sheng-Long Ye[10] · Mengsu Zeng[11]

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MAGNETIC RESONANCE

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- **Lésions Malignes secondaires**
  - IRM avec injection de Gd-EOB DTPA combinée à l'IRM de diffusion est la modalité d'imagerie la plus performante pour le staging pré-opératoire des lésions secondaires hépatiques (54/66, 81,8% d'accord)

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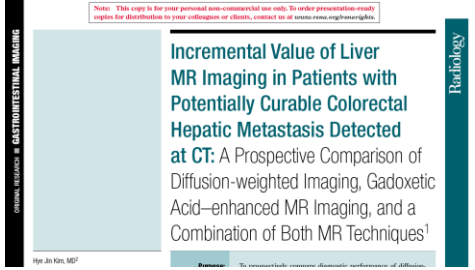
Key role of liver MRI – With DWI and/or HBP contrast agent



- 47 / 51 Patients M+ confirmed ; total 104 Lesions
  - 77 Pathology
  - 27 Lesions : Follow-up in 7 patients, mean FU 3 months
  - CT 64 slices; collimation 0,6mm
  - MRI
    - DWI 1.5 T (50, 300, 600, 900 sec/mm2)
    - Gd EOB DTPA DCE+ HBP10' and 20' after IV
- Kim et al. Radiology 2015; 274:712-722

Sensitivities for the Detection of Hepatic Metastases

	Reader 1		Reader 2		Pooled Data	
Lesion Group and Imaging Modality	Sensitivity (%)	95% Confidence Interval	Sensitivity (%)	95% Confidence Interval	Sensitivity (%)	95% Confidence Interval
All metastases						
CT	87 (90/104)	79, 92	84 (87/104)	75, 90	85	80, 89
DW MR imaging	88 (92/104)	81, 93	88 (92/104)	81, 93	88	83, 92
Gadoxetic acid MR imaging	98 (102/104)*	93, 100	92 (96/104)	85, 96	95*	91, 97
Combined MR imaging	99 (103/104)*	93, 100	97 (101/104)*	92, 99	98†	95, 99
Metastases ≤ 1.0 cm in diameter						
CT	57 (16/28)	39, 74	43 (12/28)	26, 61	50	37, 63
DW MR imaging	75 (21/28)	56, 88	82 (23/28)	64, 93	79*	66, 87
Gadoxetic acid MR imaging	93 (26/28)*	76, 99	79 (22/28)*	60, 90	86*	74, 93
Combined MR imaging	96 (27/28)*	81,100	93 (26/28)*	76, 99	95†	85, 99

Note.—Numbers in parentheses are the numbers of lesions, which were used for calculating the percentages. Percentages were rounded.

* The sensitivity is significantly higher than that of CT ($P \leq .003$).

† The sensitivity is significantly higher than that of CT ($P < .001$). The sensitivity is significantly higher than that of DW MR imaging for both all metastases and metastases of 1 cm or smaller in diameter ($P \leq .003$).

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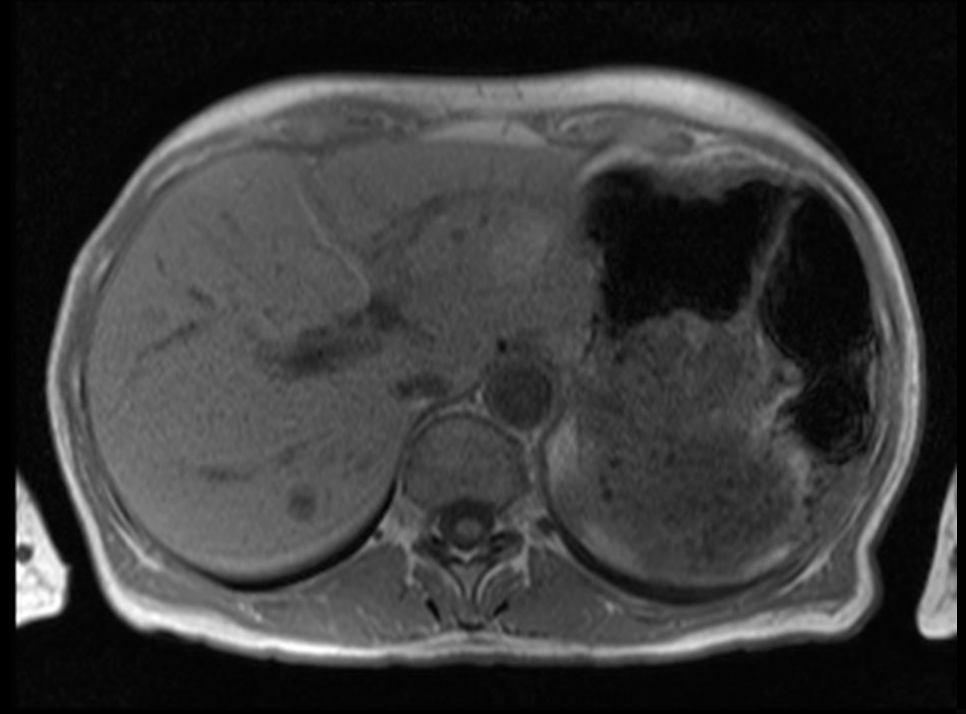
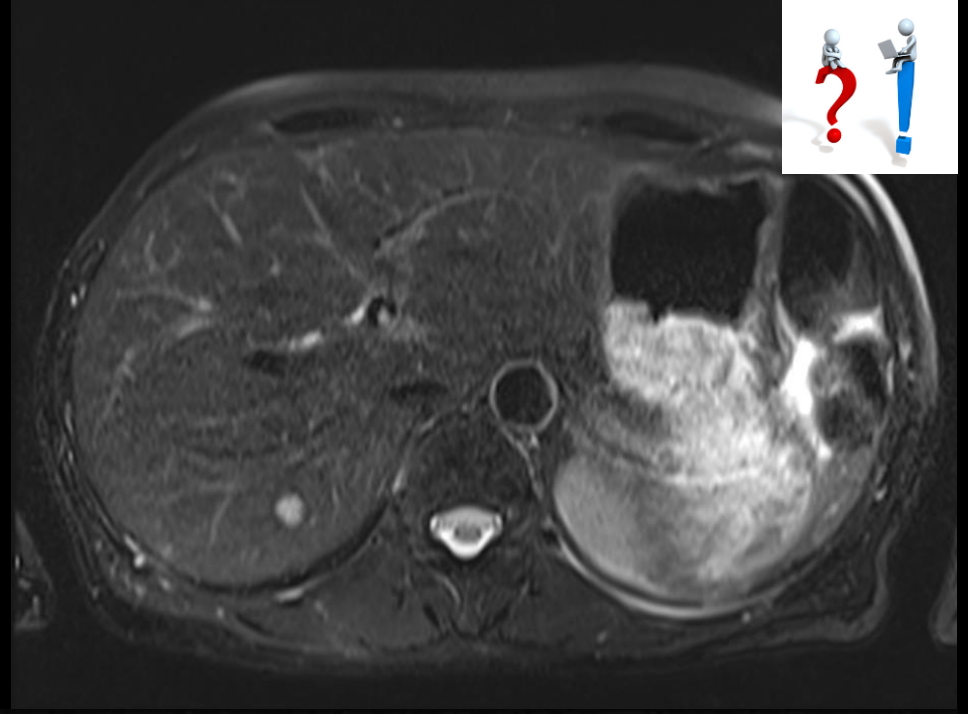
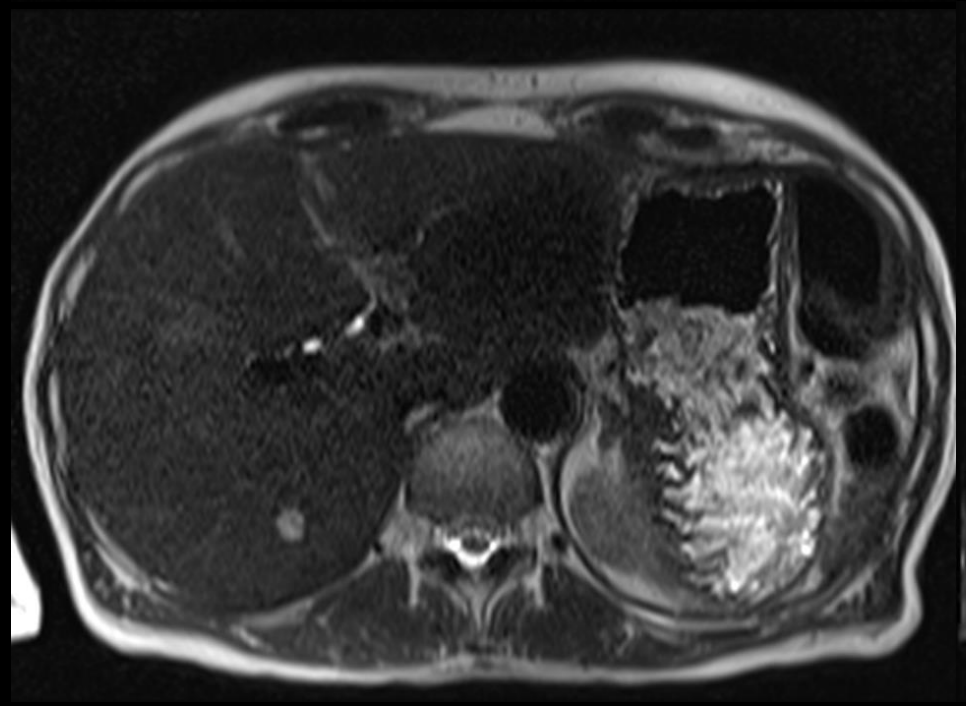
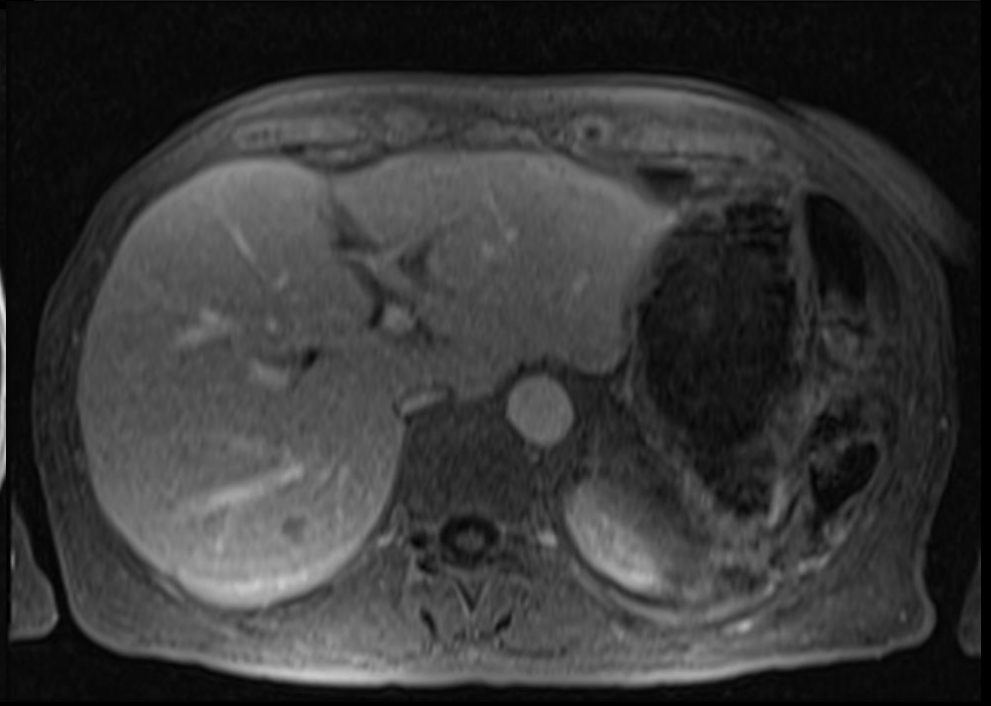
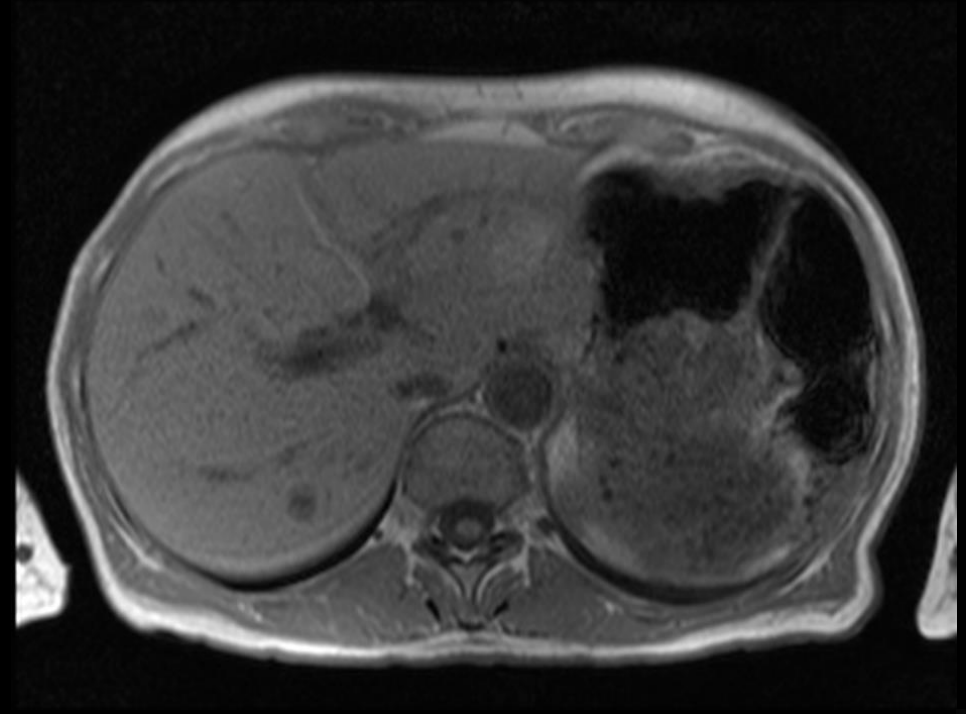
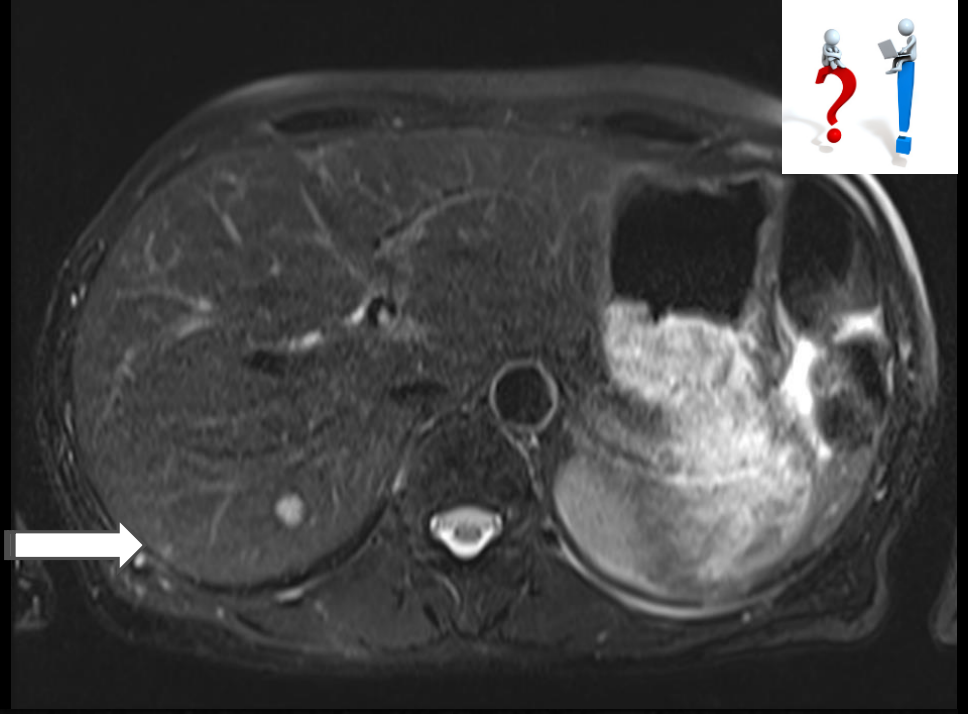
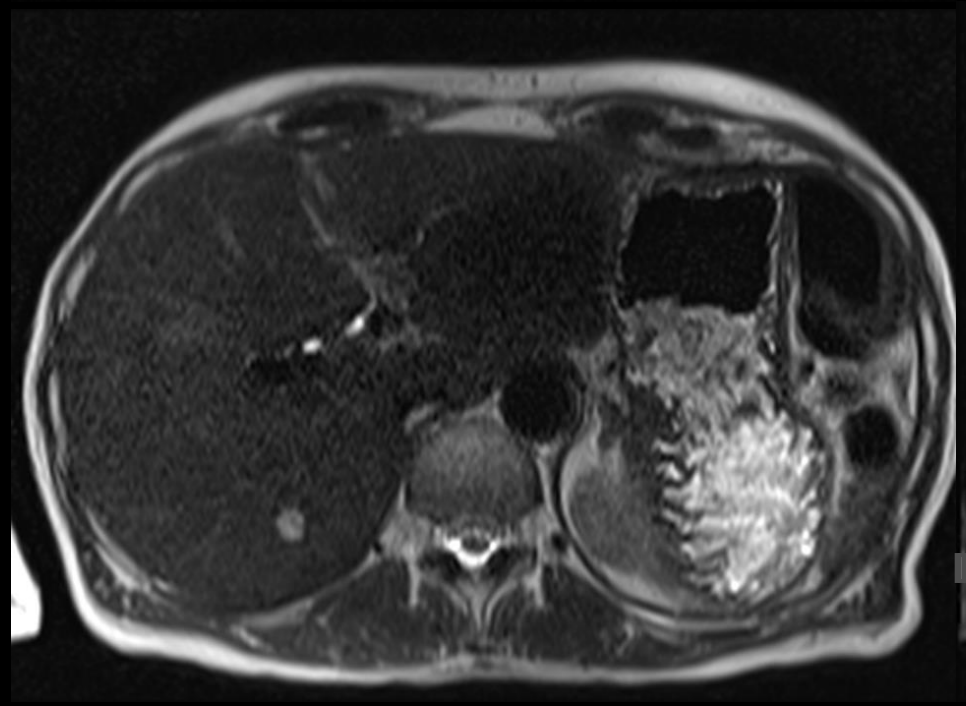
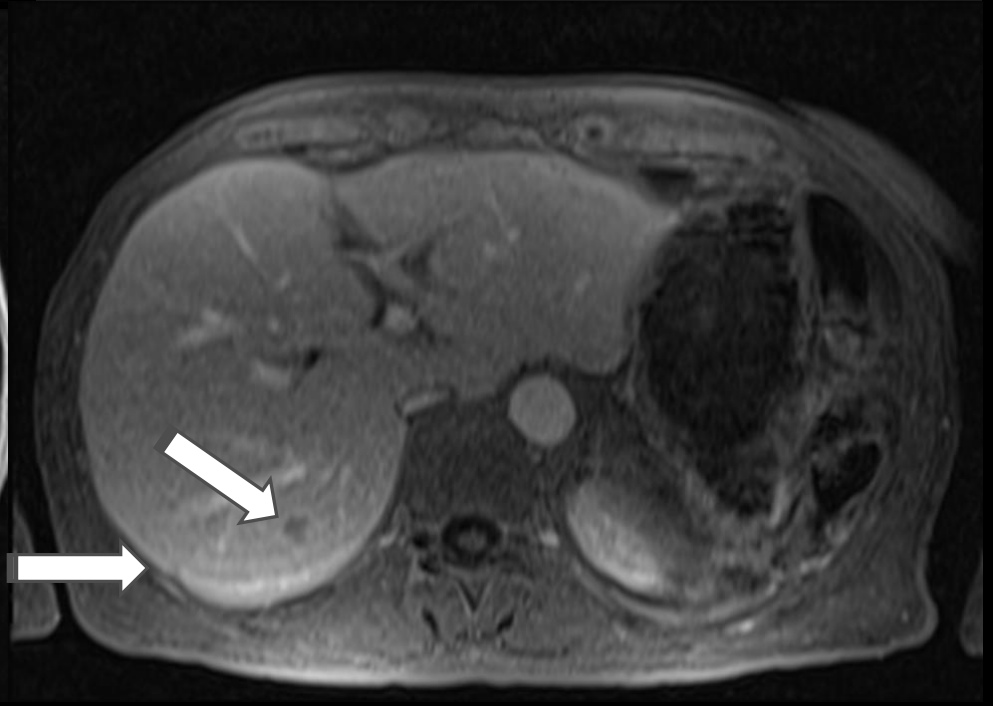





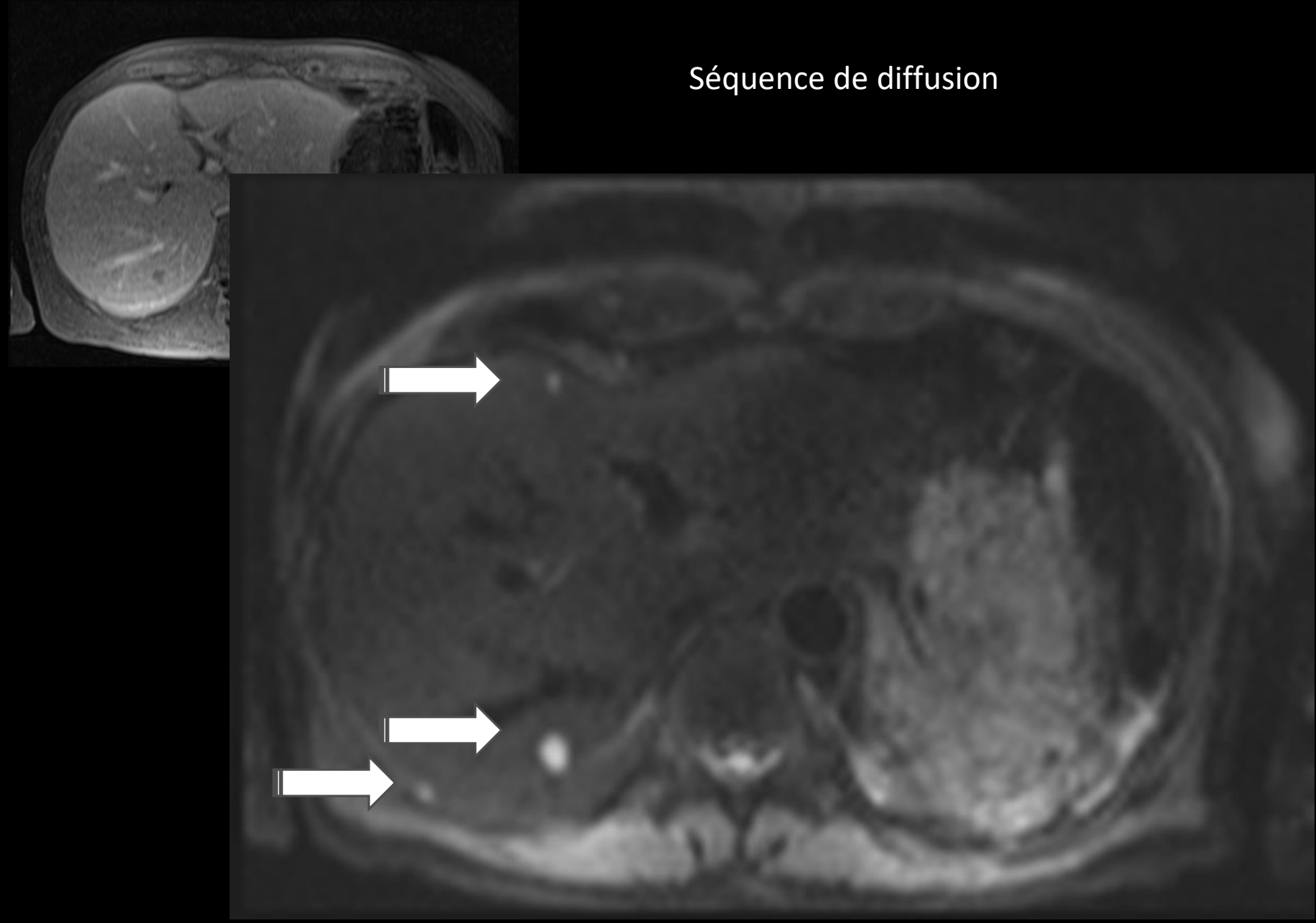


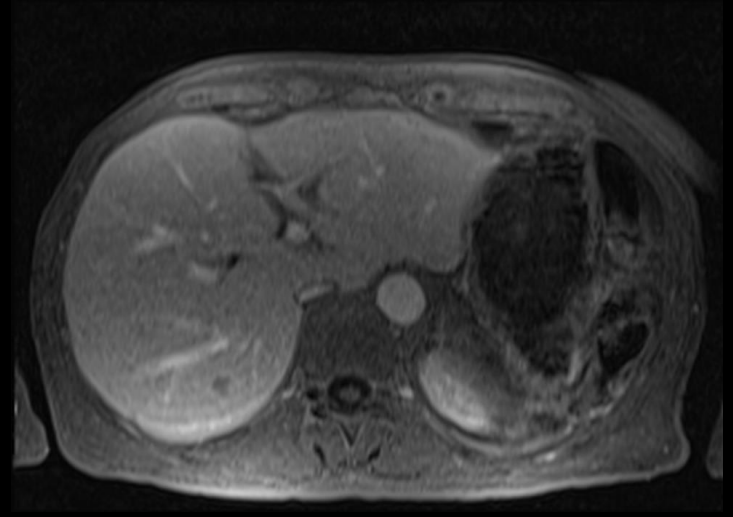


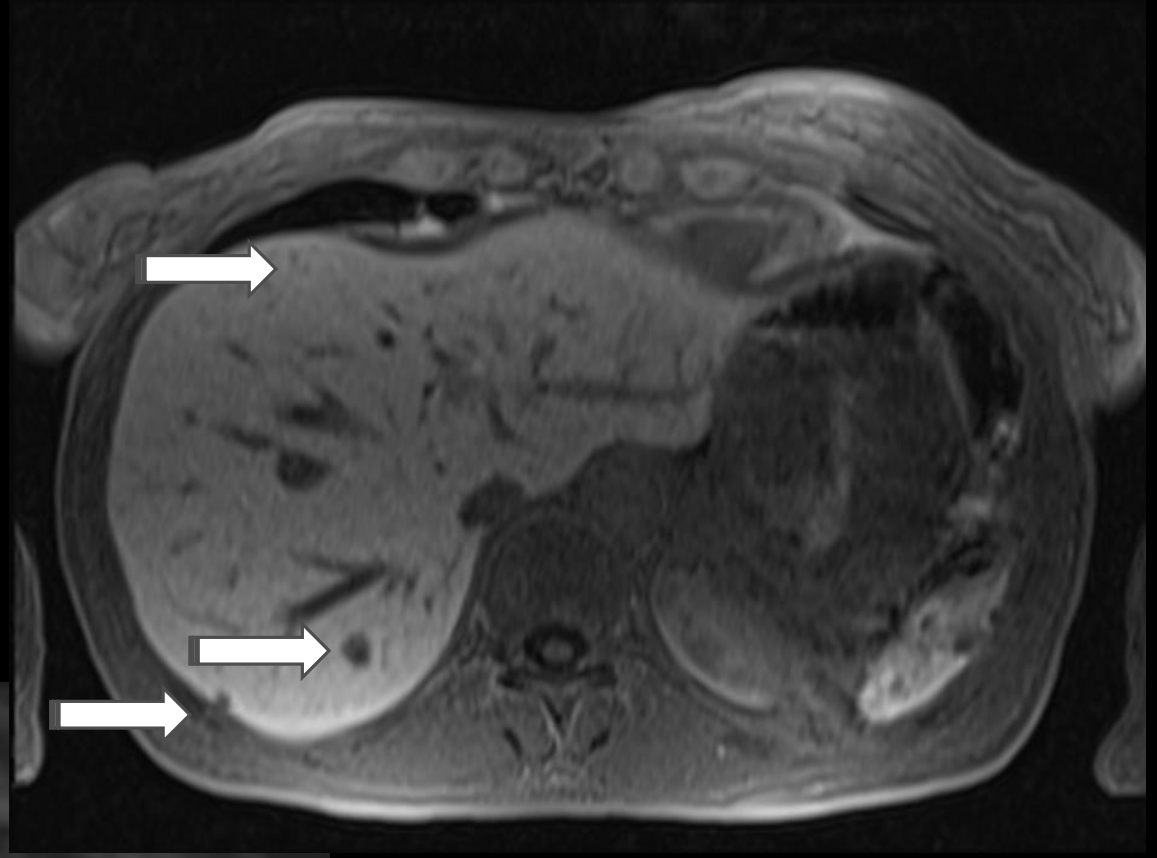


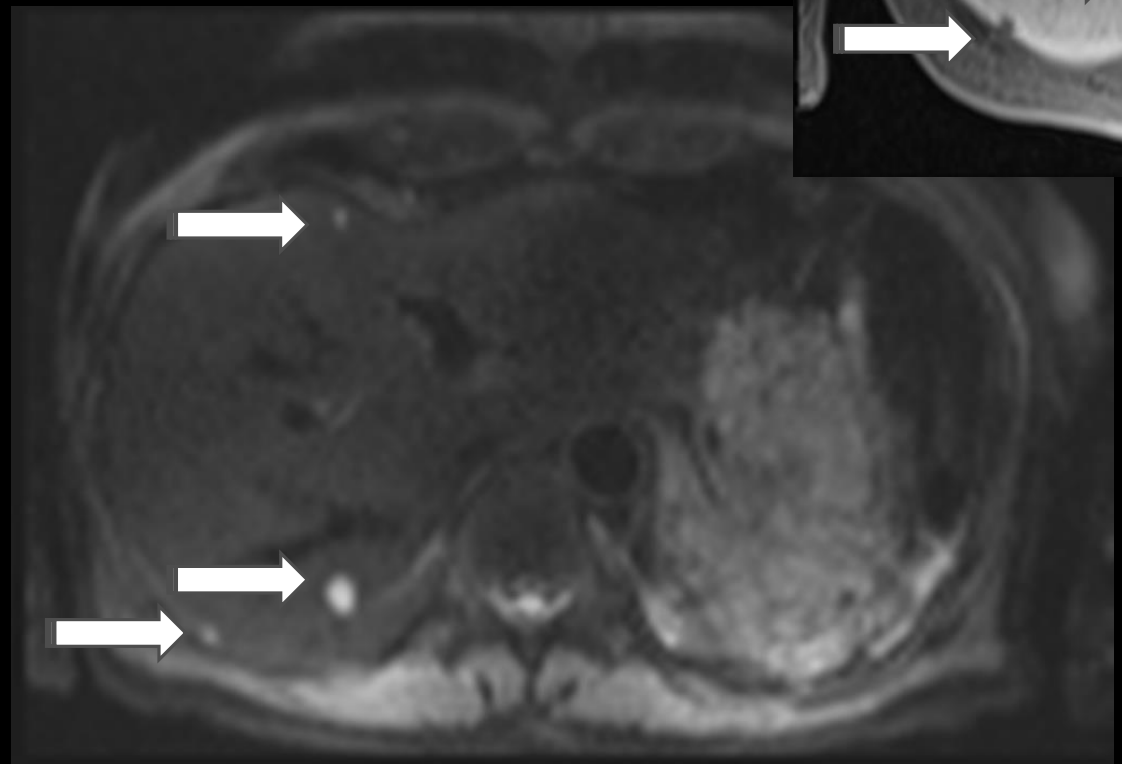


Séquence de diffusion









Phase hépatobiliaire

Eur Radiol (2016) 26:674–682
DOI 10.1007/s00330-015-3873-2

MAGNETIC RESONANCE

Consensus report from the 7th International Forum for Liver Magnetic Resonance Imaging

Elmar M. Merkle[1] · Christoph J. Zech[1] · Carlo Bartolozzi[2] · Mustafa R. Bashir[3] · Ahmed Ba-Ssalamah[4] · Alexander Huppertz[5] · Jeong Min Lee[6] · Jens Ricke[7] · Michiie Sakamoto[8] · Claude B. Sirlin[9] · Sheng-Long Ye[10] · Mengsu Zeng[11]

Lésions bénignes hépatocytaires : HNF vs Adénomes hépatocellulaires: Faut il les utiliser ?

- La phase hépatobiliaire de l'IRM peut aider à la différentiation HNF/Adénomes
- Des recherches doivent être poursuives pour savoir si l'IRM après injection de Gd-EOB DTPA pourrait permettre un sous-typage des adénomes hépatocellulaires (71/73, 97,3% d'accord)

CHU Henri Mondor, Faculte Medecine, Universite Paris Est Creteil, AP-HP, Creteil, France; imagerie.medicale@aphp.fr

Produits de contraste hépatobiliaires Lésions bénignes du foie

Suh et al. Eur Radiol 2015; 25(4): 950-960

10 études – 8 retrospectives 2 Prospectives

165 FNH and 87 HCA

Eur Radiol
DOI 10.1007/s00330-014-3499-9

HEPATOBILIARY-PANCREAS

The diagnostic value of Gd-EOB-DTPA-MRI for the diagnosis of focal nodular hyperplasia: a systematic review and meta-analysis

Chong Hyun Suh · Kyung Won Kim · Gene Young Kim · Yong Moon Shin · Pyo Nyun Kim · Seong Ho Park

Received: 3 April 2014 / Revised: 5 November 2014 / Accepted: 12 November 2014

Produits de contraste hépatobiliaires Lésions bénignes du foie

Suh et al. Eur Radiol

Table 2 Summary of the meta-analytic pooled proportions for the imaging findings

Imaging Findings	No. of Studies	No. of Cases	Summary Estimate			*p* value† for Reporting Bias	Trim-and-Fill Estimate	
			Pooled Proportion (95 % CI)	*P* value for Heterogeneity*	I^2 %§		No. of Missing Studies	Adjusted Pooled Proportion (95 % CI)
High/iso SI on the HBP	10	381	93 % (90–97 %)	< 0.01	58.7	< 0.01	5	97 % (92-102 %)
Presence of central scar	7	287	61 % (47–74 %)	< 0.01	85.9	0.79		
Arterial enhancement	6	210	99 % (97–100 %)	0.69	0.0	0.13		
High/iso SI on the PVP or EP	6	210	97 % (95–99 %)	0.83	0.0	0.22		

**p* value by Cochran-Q method to test the heterogeneity of the pooled data. Values <0.10 indicate substantial heterogeneity

§ I^2 is the Higgin's index for heterogeneity and values greater than 50 % indicate substantial heterogeneity

† *p* values are to test publication/reporting bias using the Egger's test. *p* values less than 0.1 indicate significant bias

Abbreviations: SI = signal intensity; HBP = hepatobiliary phase; PVP = portal-venous phase; EP = equilibrium phase

Produits de contraste hépatobiliaires Lésions bénignes du foie

Suh et al. Eur Radiol

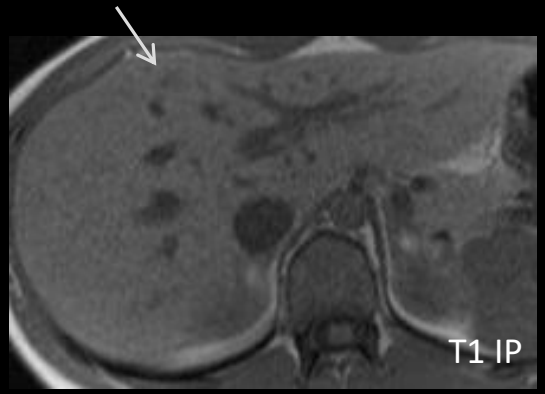
Table 3 Summary of the bivariate indices of diagnostic accuracy of high/iso SI on the HBP

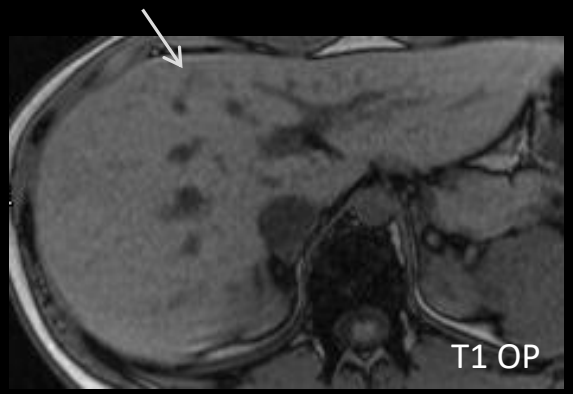
Study	*N*	True Positive	True Negative	False Positive	False Negative	Sensitivity	Specificity	Positive LR	Negative LR
Bieze M (2012)	52	27	23	1	1	96.4 %	95.8 %	23.1	0.04
Grazioli L (2012)	111	62	40	3	6	91.2 %	93.0 %	13.1	0.10
Mohajer K (2012)	40	34	6	0	0	100.0 %	100.0 %	13.8	0.02
Purysko AS (2012)	47	32	12	0	3	91.4 %	100.0 %	23.5	0.10
Summary indices (95 % CI)	250					93.9 % (89.1–97.1 %)	95.3 % (88.4–98.7 %)	15.6 (6.7–36.4 %)	0.08 (0.05–0.15 %)
P value for Heterogeneity*						0.124	0.535	0.948	0.473
I^2 %§						47.9 %	0.0 %	0.0 %	0.0 %

**p* value using the Cochran-Q method to test the heterogeneity of the pooled data. Values <0.10 indicate substantial heterogeneity

§ I^2 is the Higgin's index for heterogeneity and values greater than 50 % indicate substantial heterogeneity

Abbreviations: SI = signal intensity; HBP = hepatobiliary phase


T1 IP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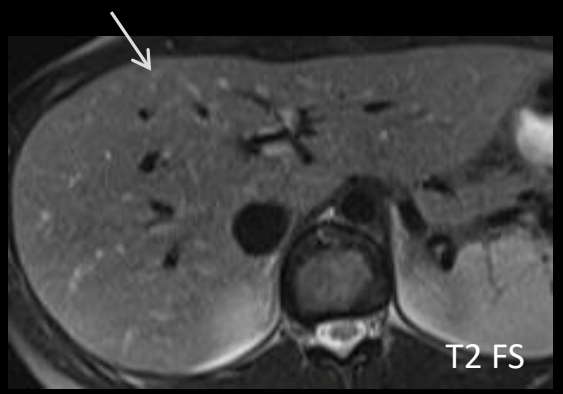
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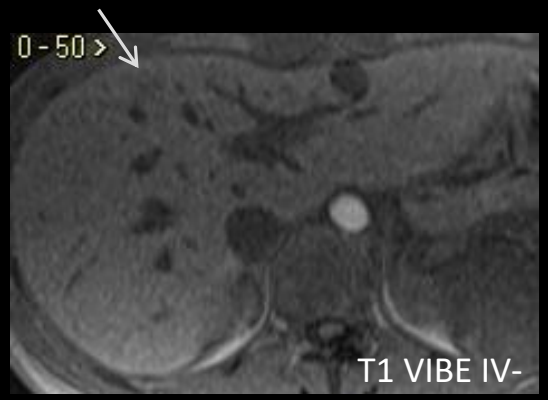
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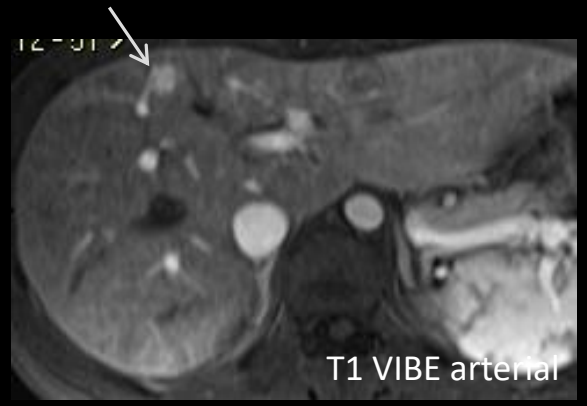
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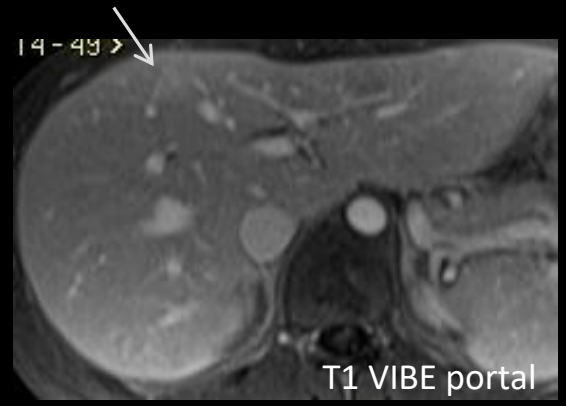
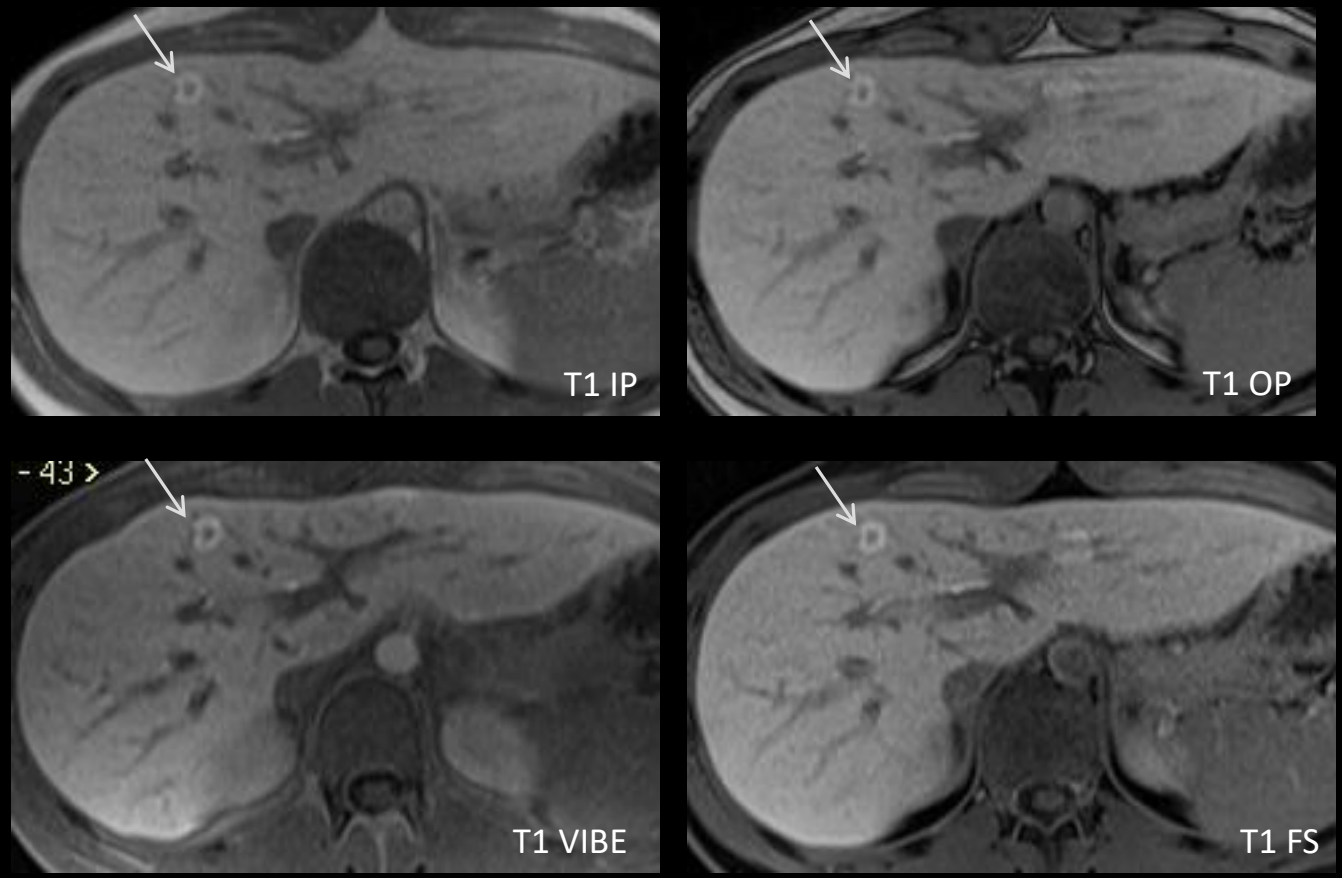

T1 VIBE portal

Capture en couronne – Phase hépatobiliaire après injection de Gd-BOPTA



HBP 60 minutes after injection of Gd-BOPTA

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MAGNETIC RESONANCE

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Lésions Dysplasiques (bas grade / haut grade) et CHC: une identification plus précoce ?

- Un nodule hypo-signal en phase hépatobiliaire est associé avec un nodule de dysplasie de haut grade ou un CHC (early); En revanche la distinction de ces deux entités n'est pas possible.
- L'utilisation de produit de contraste de type Gd-EOB DTPA peut améliorer la sensibilité de la détection des CHC.

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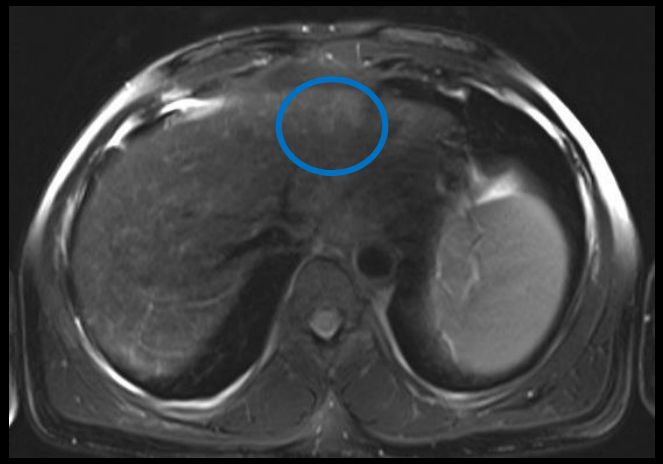
T2 FS



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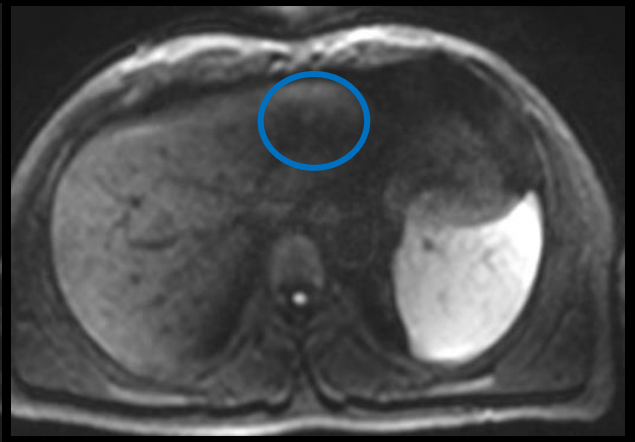
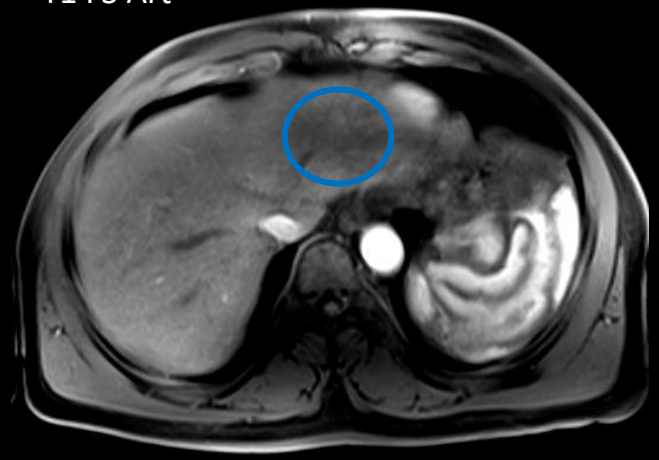


- 67 ans
- Liste d'attente Transplantation hépatique
- Nodule de 8mm Hypervasculaire hyposignal en HBP

EASL / AASLD	JSH	KLSCG
Refaire US *N'aurait jamais dû avoir IRM…*	CHC	Biopsie ou surveillance

T1 FS Art



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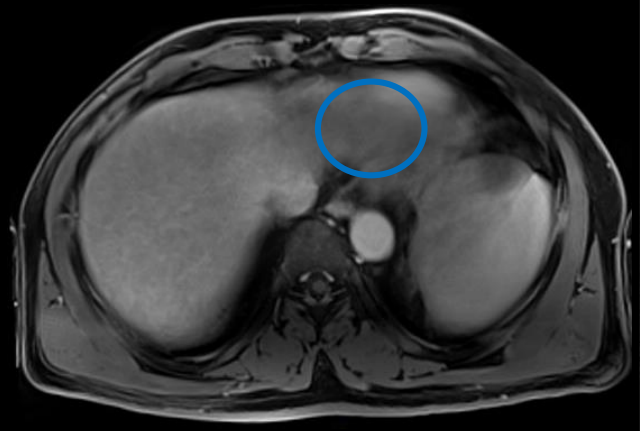
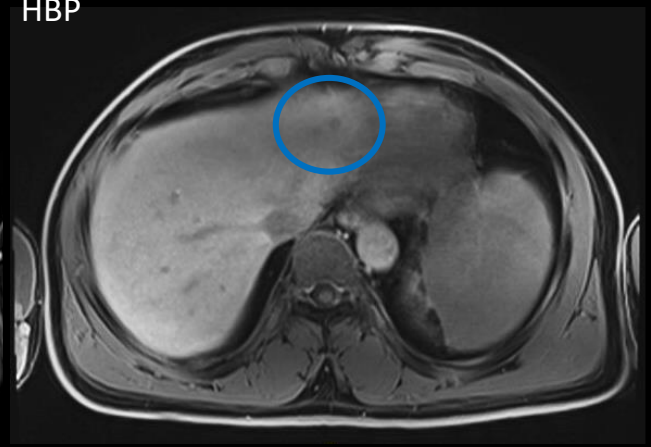


HBP



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Mais….

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Some linear agents will remain available: gadoxetic acid, a linear agent used at a low dose for liver scans, can remain on the market as it meets an important diagnostic need in patients with few alternatives. In addition, a formulation of gadopentetic acid injected directly into joints is to remain

PRAC concludes assessment of gadolinium agents used in body scans and recommends regulatory actions, including suspension for some marketing authorisations

Review finds evidence of gadolinium deposits in the brain after MRI body scans but no signs of harm

EMA's Pharmacovigilance and Risk Assessment Committee (PRAC) has recommended the suspension of the marketing authorisations for four linear gadolinium contrast agents because of evidence that small amounts of the gadolinium they contain are deposited in the brain.

Conclusion – Points Forts

- Les séquences de diffusion sont désormais **systématiquement réalisées dans l'exploration des lésions nodulaires du foie.**

- Les séquences de diffusion sont indispensables pour l'exploration de patients suspects de **lésions secondaires hépatiques**. Ces séquences seront dans les années à venir de plus en plus utilisées pour le suivi de l'efficacité des thérapies en oncologie.

- Les produits de contraste hépato-spécifiques permettent **l'optimisation de la caractérisation des lésions hépatocytaires. Ils sont utiles pour l'étude des lésions hépatocytaires bénignes et plus particulièrement pour la caractérisation formelle des HNF de petite taille**.
- Les **produits de contraste hépato-spécifiques semblent également être utiles pour la caractérisation des nodules de CHC et la détection de lésions secondaires**.
- Mais **la pharmacovigilance** est à suivre +++

Imagerie Médicale	Pathology	Surgery	Hepatology
F Pigneur	J Calderaro	D Azoulay	G Amaddeo
L Baranes	ES Zafrani	P Compagnon	C Costentin
F Legou		A Laurent	C Duvoux
M Djabbari		C Salloum	C Feray
B Zegai			C Hezode
E Herin			A Mallat
S Mulé			
R Kharrat			
M Chiaradia			
A Rahmouni			

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