



The PanNASH initiative

PanNASH initiative is supported by

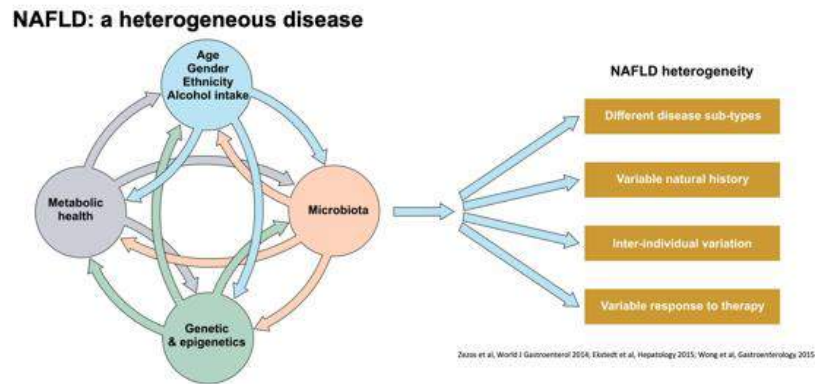
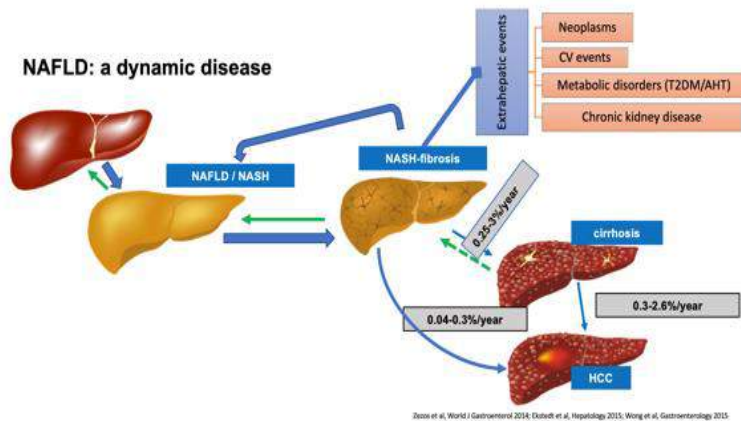


Imaging biomarkers in NAFLD: Could they avoid liver biopsy?

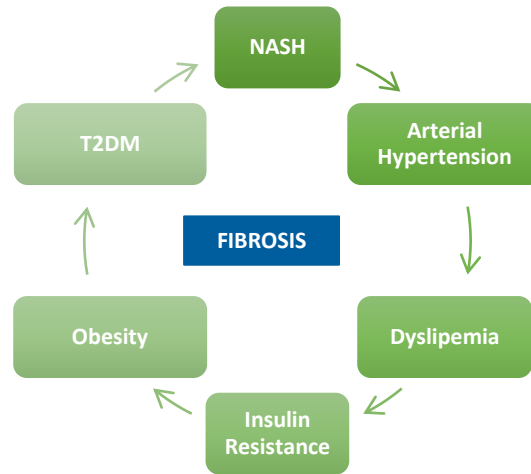
Prof. Manuel Romero-Gómez

UCM Digestive Diseases and Ciberehd, Virgen del Rocío University Hospital, SeLiver Group,
IBIS University of Seville
Sevilla, Spain



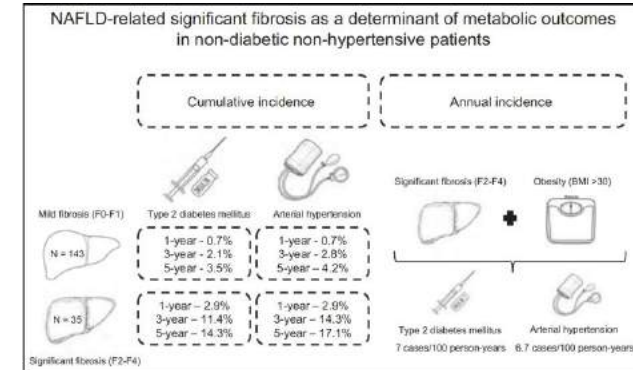


"EVERYTHING STARTS FROM A DOT."
WASSILY KANDINSKY

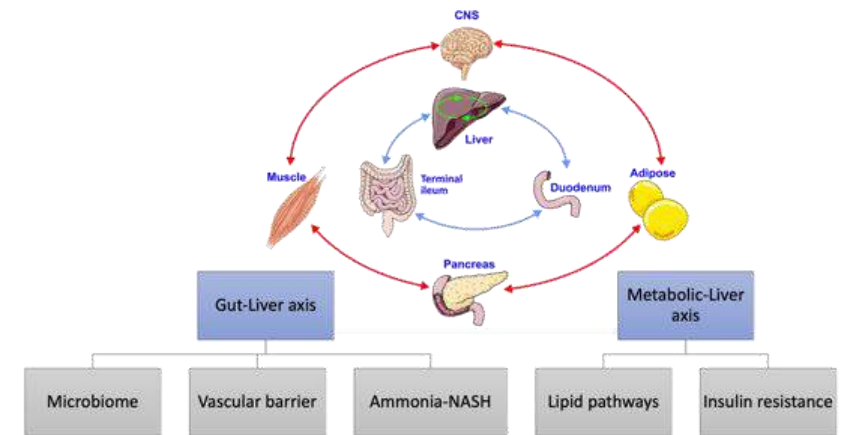


A frame in the movie: "MAFLD"

NAFLD -- FIBROSIS >> HTA >> T2DM



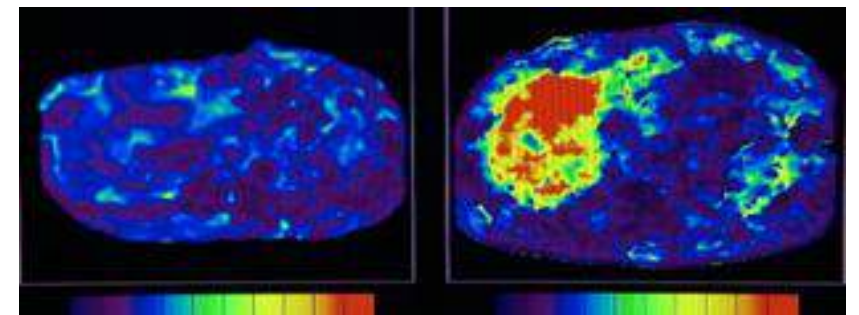
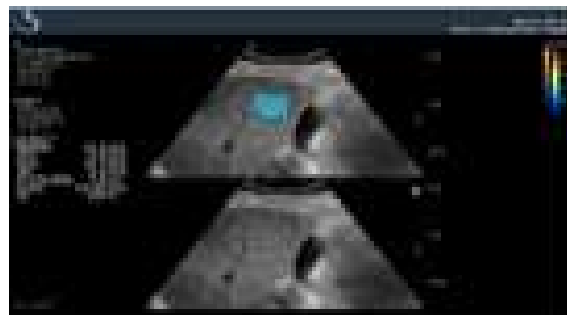
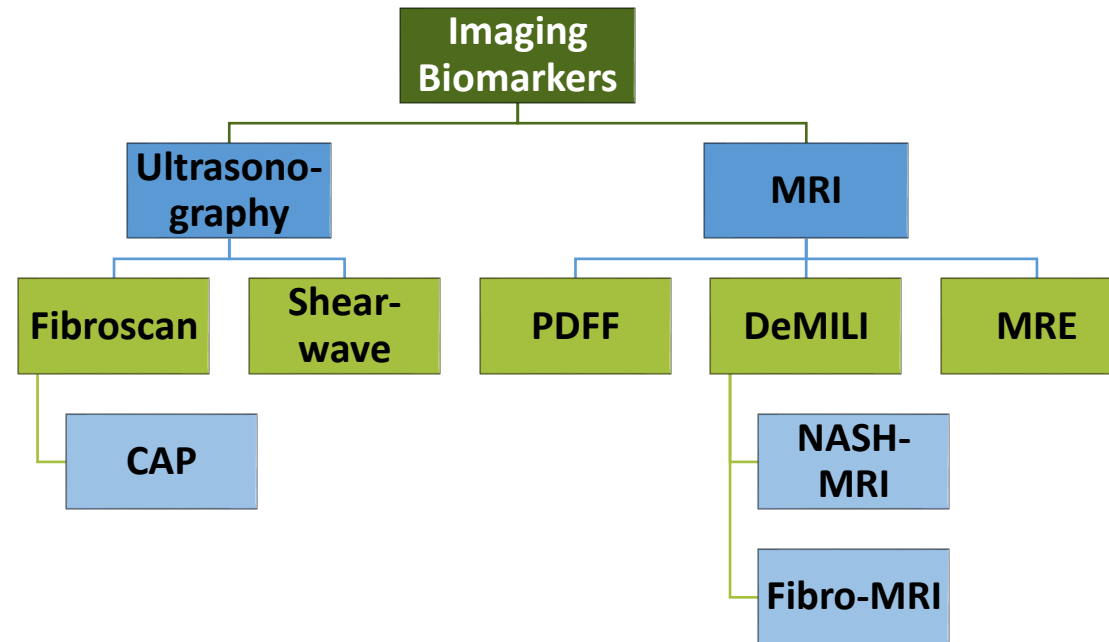
NAFLD: A MULTIAxis DISEASE





- Accumulation of iron and fat in hepatocytes contributes to chronic liver inflammation, a key driver for fibrosis progression.
- There is a need for new biomarkers that allow the detection and quantification of liver diseases supported on the measurement of fat, iron, fibrosis, inflammation.
- Current Gold Standard: Liver biopsy: Histology vs. Clinical outcomes:
 1. Liver-related: Cirrhosis >> HCC >> decompensation >> OLT
 2. Extrahepatic: CV events >> Extrahepatic neoplasms
 3. Survival

Imaging biomarkers



Liver ultrasonography



Clinical Practice Guidelines



EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease*

European Association for the Study of the Liver (EASL)*, European Association for the Study of Diabetes (EASD) and European Association for the Study of Obesity (EASO)

Recommendations

- US is the preferred first-line diagnostic procedure for imaging of NAFLD, as it provides additional diagnostic information (**A1**)

Clinical value of liver ultrasound for the diagnosis of non-alcoholic fatty liver disease in overweight and obese patients.

Brill F et al. *Liver Int.* 2015;35:2139-2146

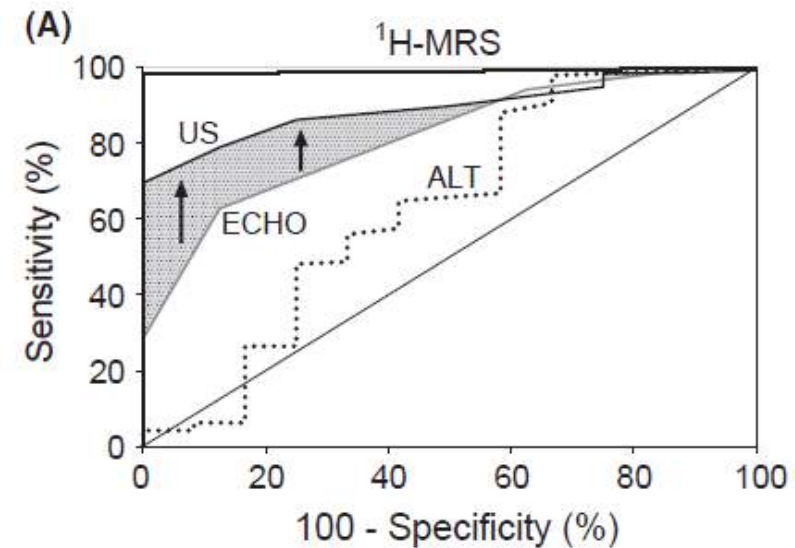
Parenchymal echogenicity	Far gain attenuation	GB wall blurring	Portal vein blurring	Hepatic vein blurring
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Threshold for steatosis detection: 12.5%

Ultrasonography limitations:

- Not able to segregate steatohepatitis from steatosis.
- Liver hyper-ecogenicity do not correlate with hepatic injury
- Brilliant liver requires differential diagnosis
- Steatosis detected by ultrasonography when higher than **12.5%**

N=146



AUROC
0,96
0,89
0,82

Shear-wave elastography



Individual patient data meta-analysis CAP detecting steatosis



N=2735

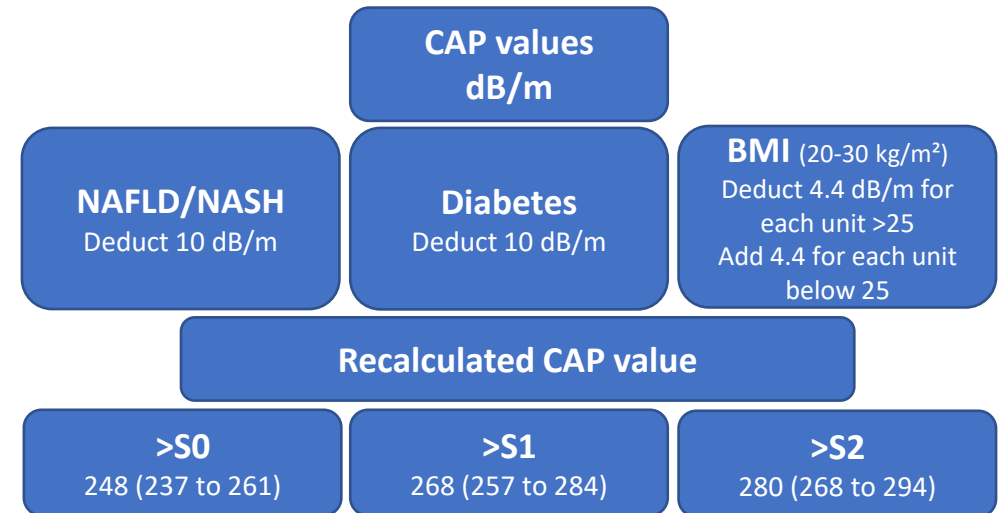
NAFLD (n=537); HepC (n=997); HepB (n=1003); Others (n=198)

F0: 304 (11%); F1: 970 (36%); F2: 725 (27%); F3:334 (12%); F4: 350 (13%)



Transient Elastography CAP (dB/m)

Etiology – Diabetes – BMI



	AUROC
S0 vs. S1-S3	0.82 (0.81-0.84)
S0-S1 vs. S2-S3	0.87 (0.85-0.88)
S0-S1-S2 vs. S3	0.88 (0.86-0.91)



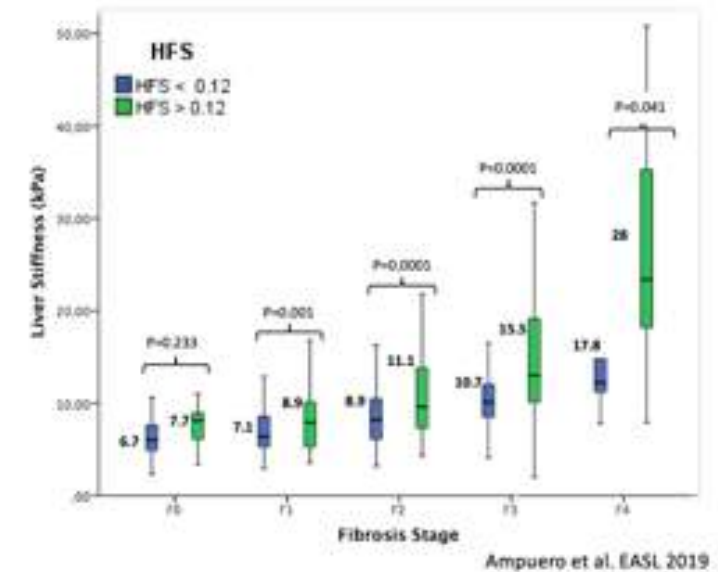
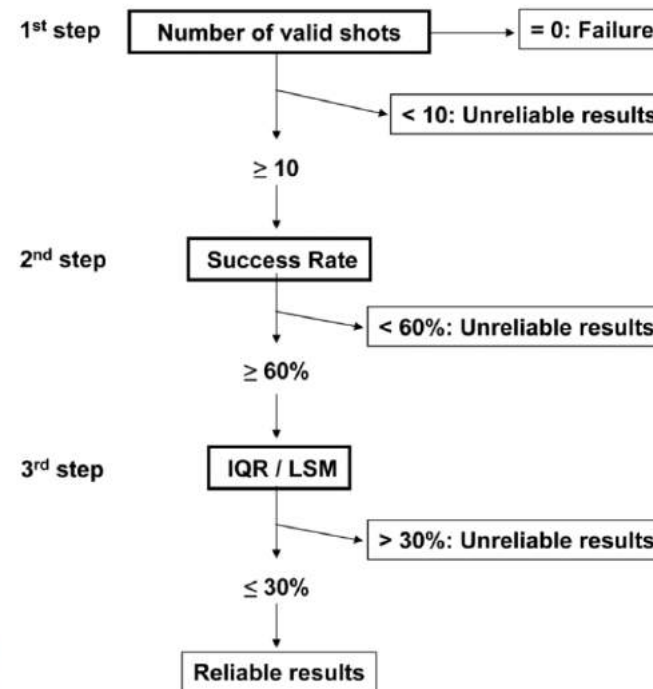
EASL-ALEH Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis

Correct interpretation of TE results in clinical practice must consider the following parameters:

- IQR/median value (<30%)
- Serum aminotransferases levels (<5 x ULN)
- BMI (use XL probe above 30 kg/m² or if skin-to-capsule distance is >25 mm)
- Absence of extra-hepatic cholestasis
- Absence of right heart failure, or other causes of congestive liver
- Absence of ongoing excessive alcohol intake

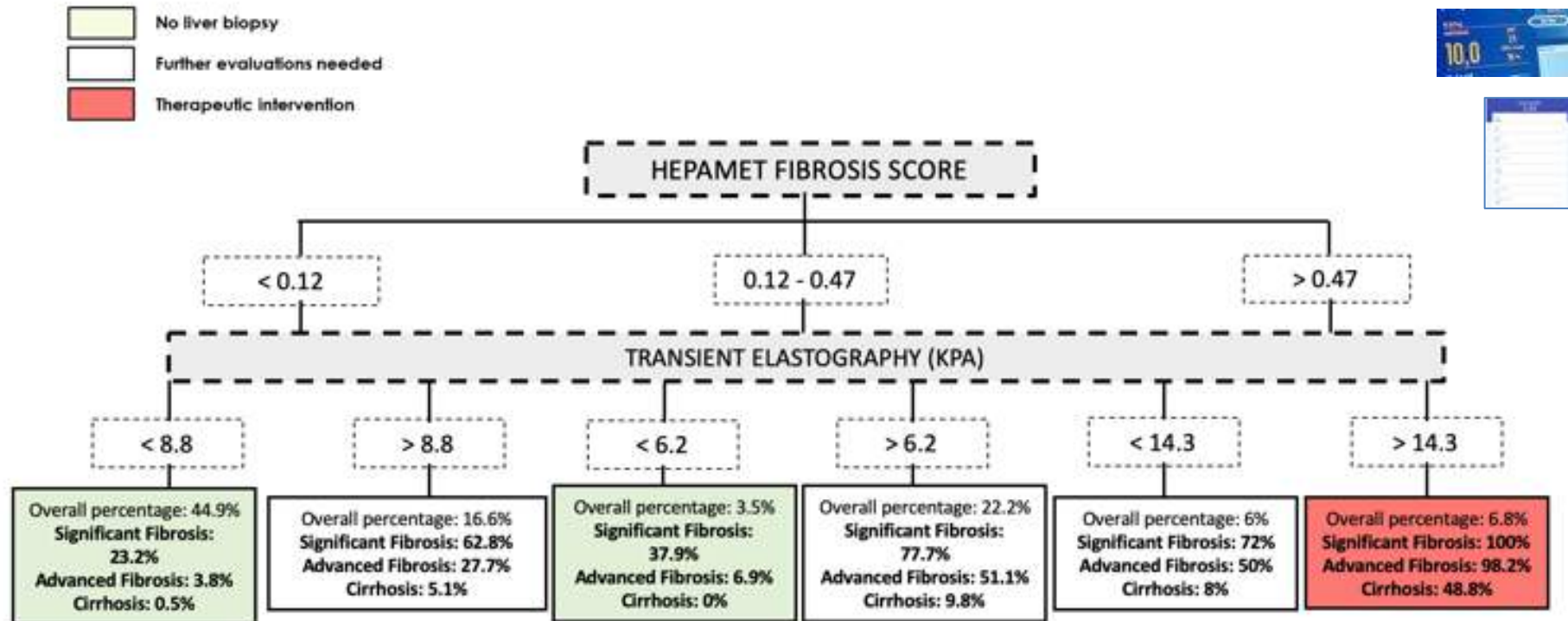


J Hepatol 2015



Ampuero et al, EASL 2019

Interpretation of kPa according to metabolic derangement of the liver

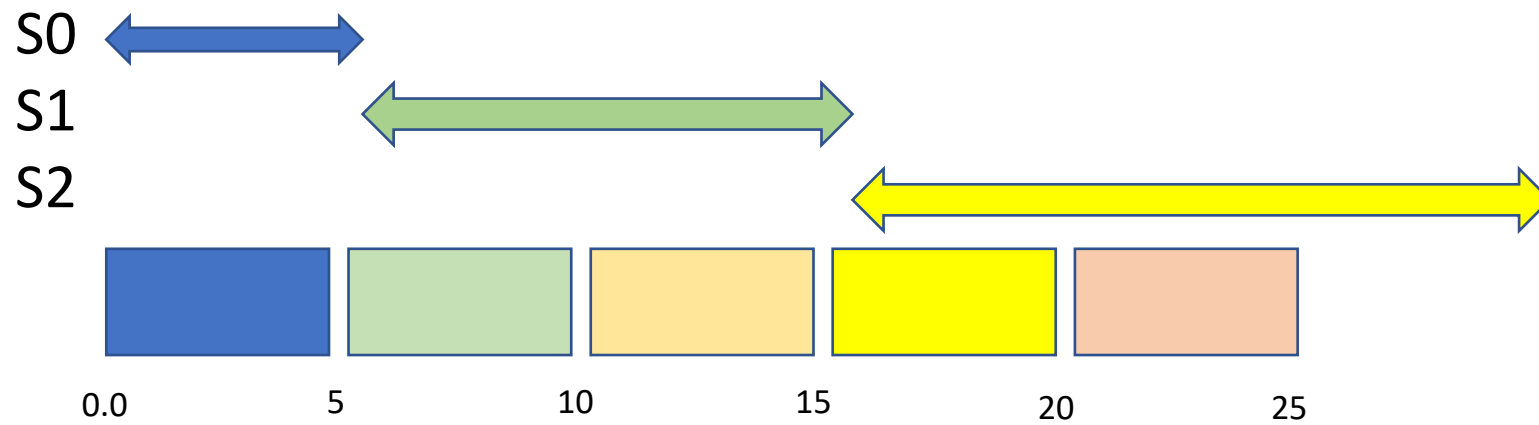
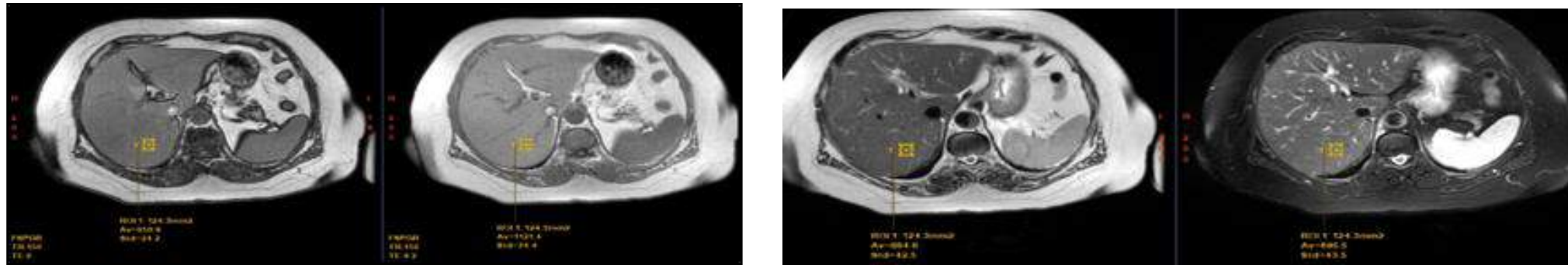


No Liver Biopsy required	44.9% + 3.5% + 6.8%	55.2%
MR studies	16.6% + 22.2% + 6%	44.8%

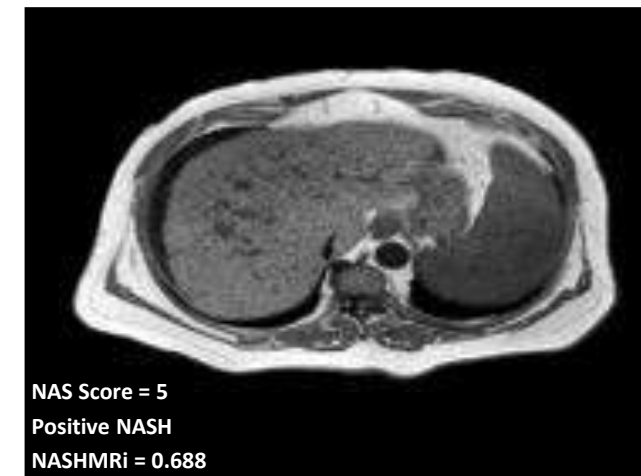
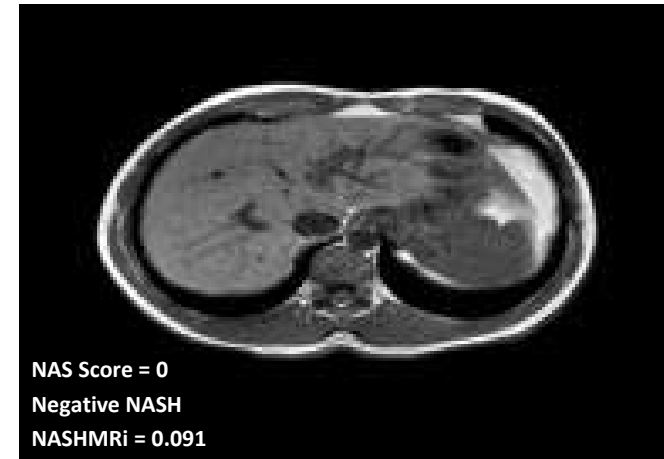
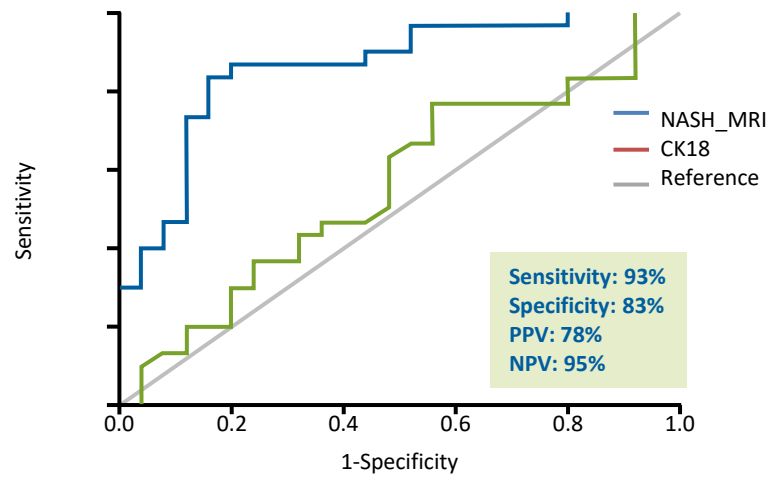
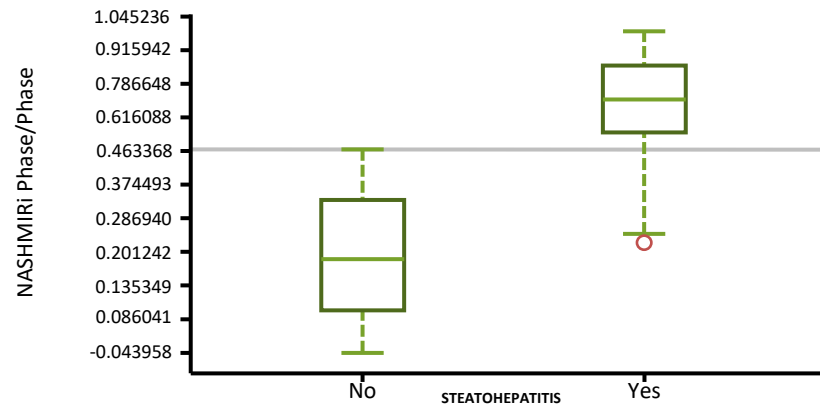
Magnetic Resonance on the diagnosis of MAFLD



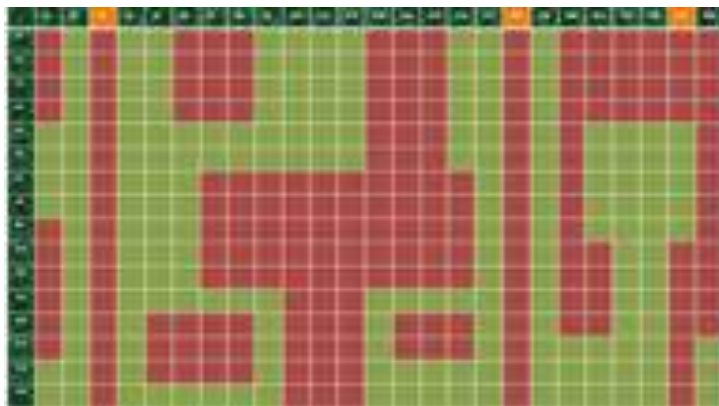
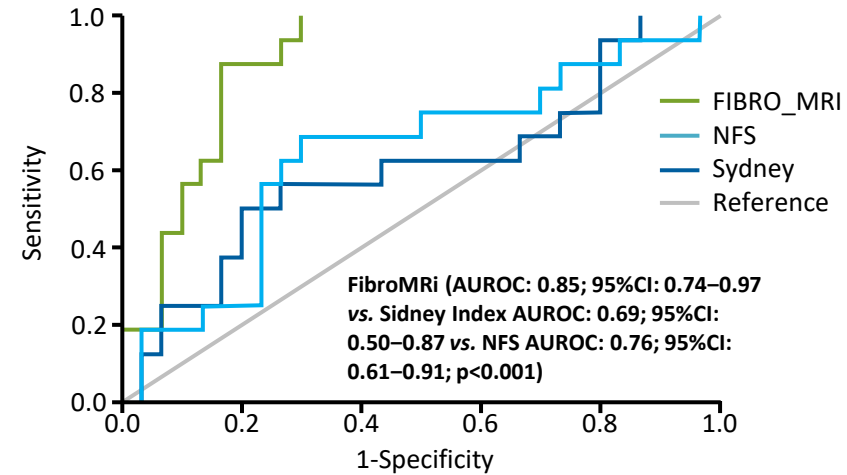
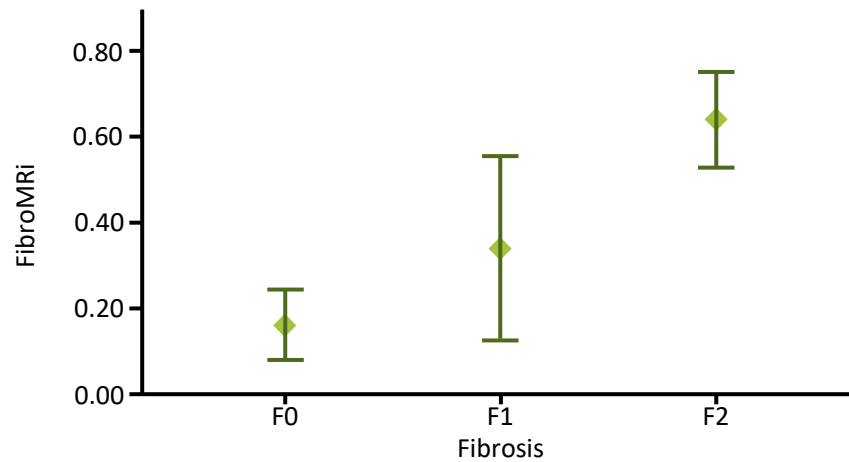
PDFF a gold estándar for Fat Infiltration



DeMILI: NASHMRI

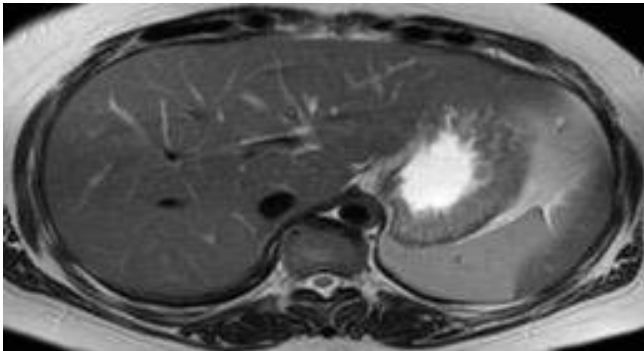


FibroMRI & significant fibrosis

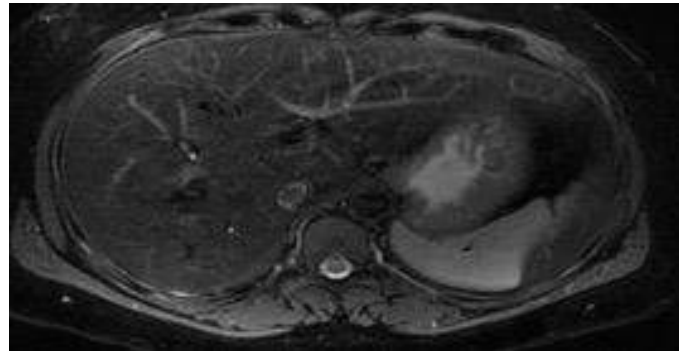


PROTOCOL	ESTIMATOR	NAME
SSFSE-T2	E3	Harmonic mean
DYNAMIC	E57	Second order contrast
FAST-STIR	E73	Weighted mean curvature
SSFSE-T2	E22	Pearson's asymmetry coefficient
DYNAMIC	E6	Mode
DYNAMIC	E31	Column's mean of multi-oriented co-occurrence matrix
DYNAMIC	E75	Maximum of main curvatures

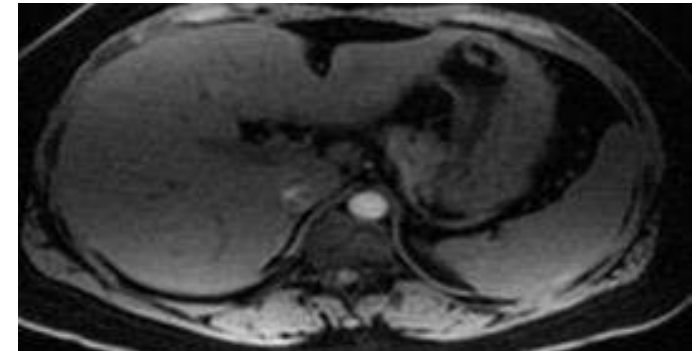
NASH-MRI the only one imaging biomarker to detect steatohepatitis



SSFE-T2 BH



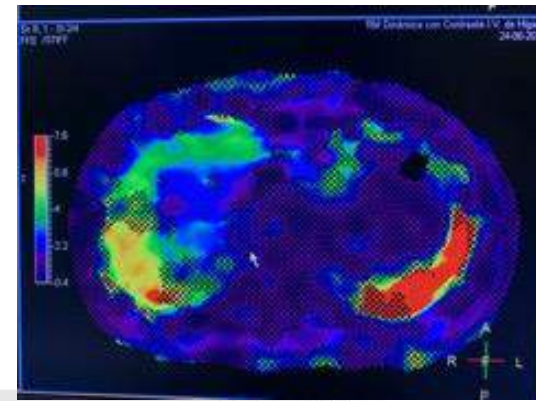
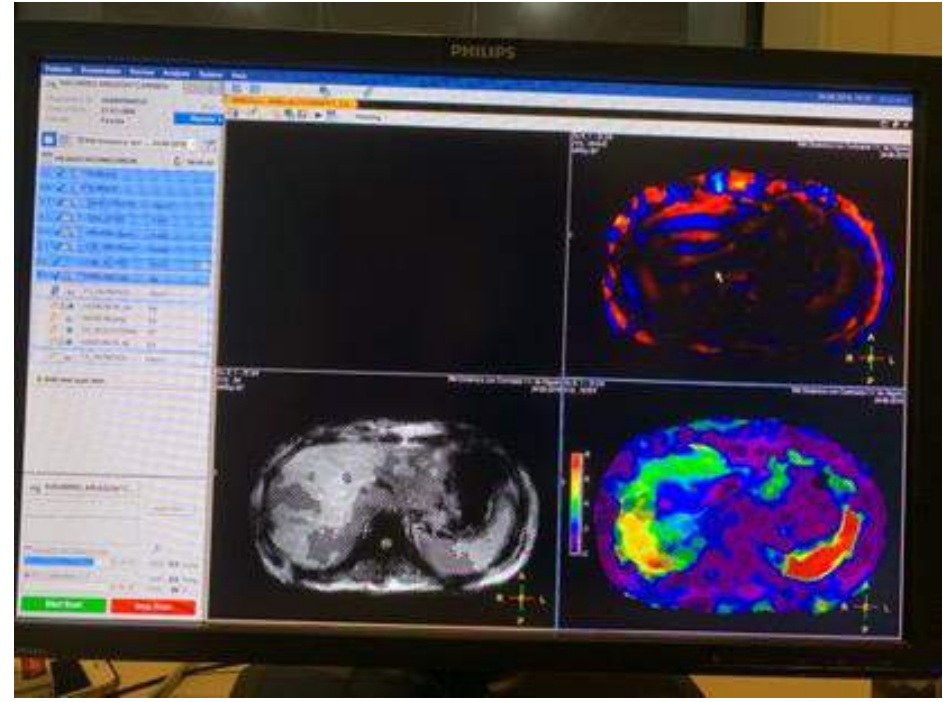
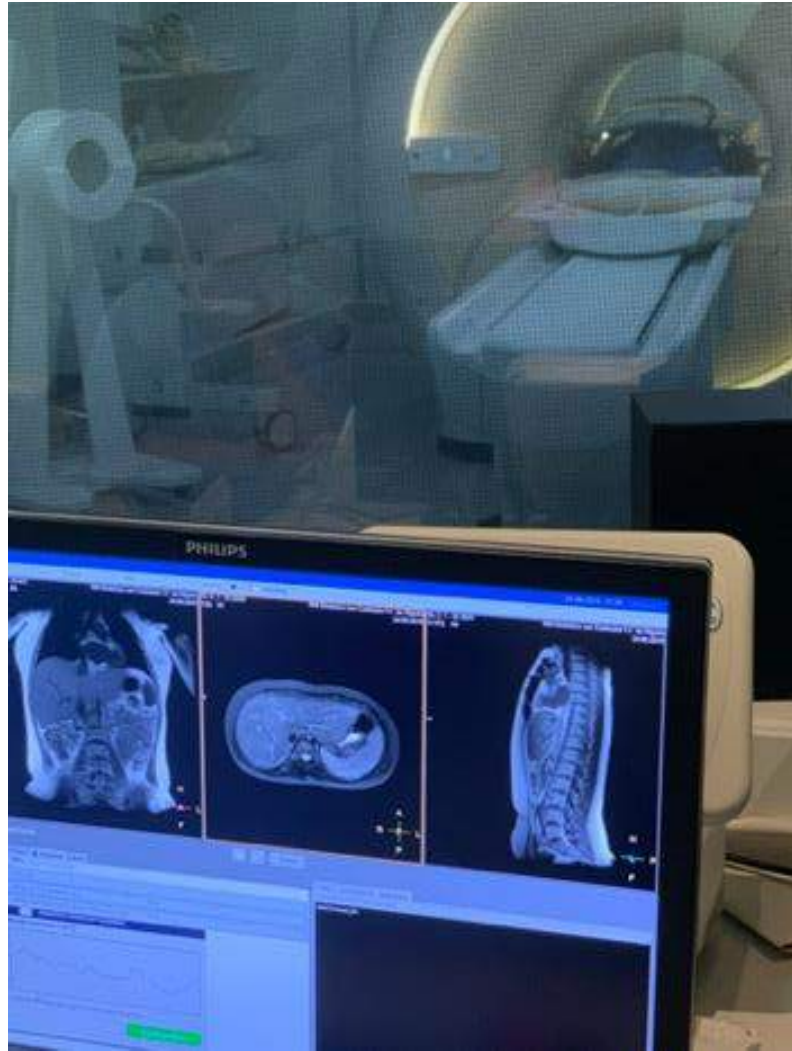
FAST-STIR



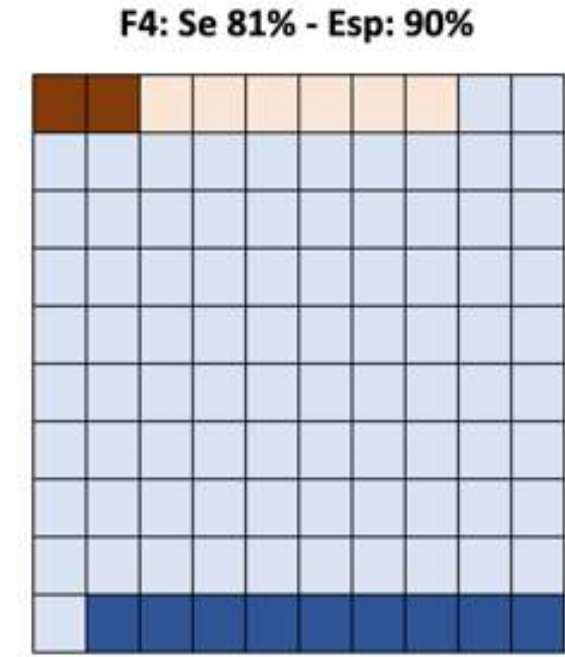
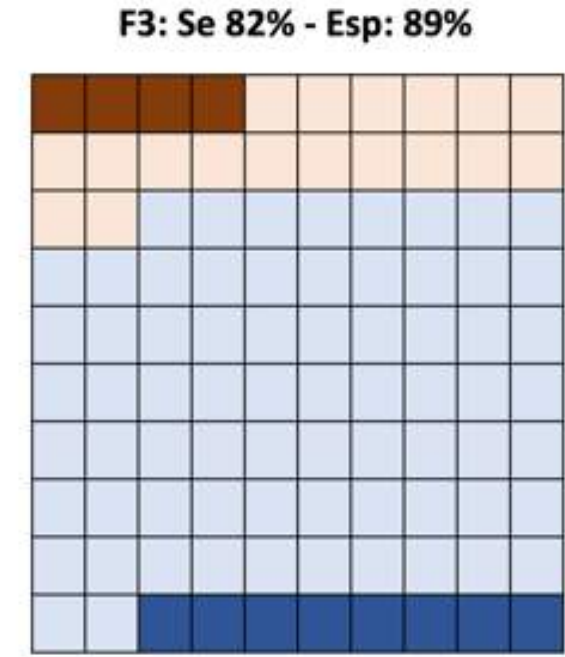
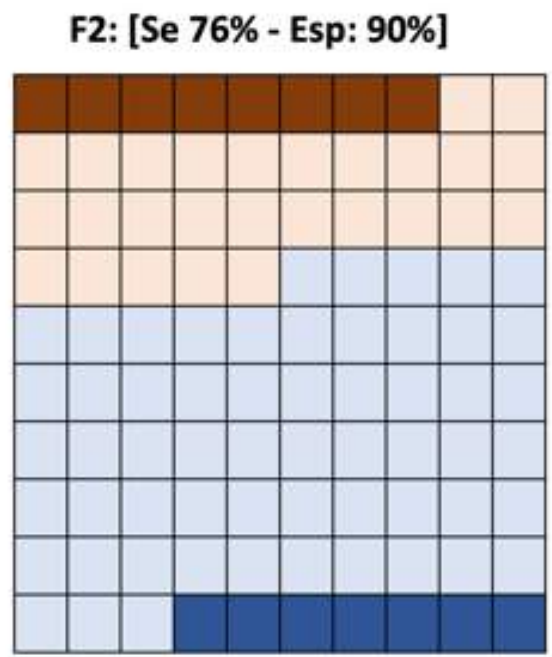
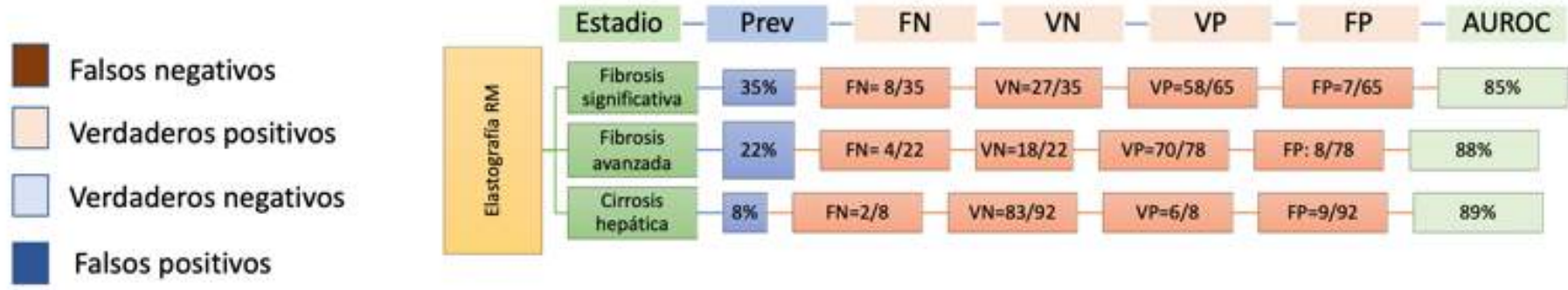
2D-FFE-T1



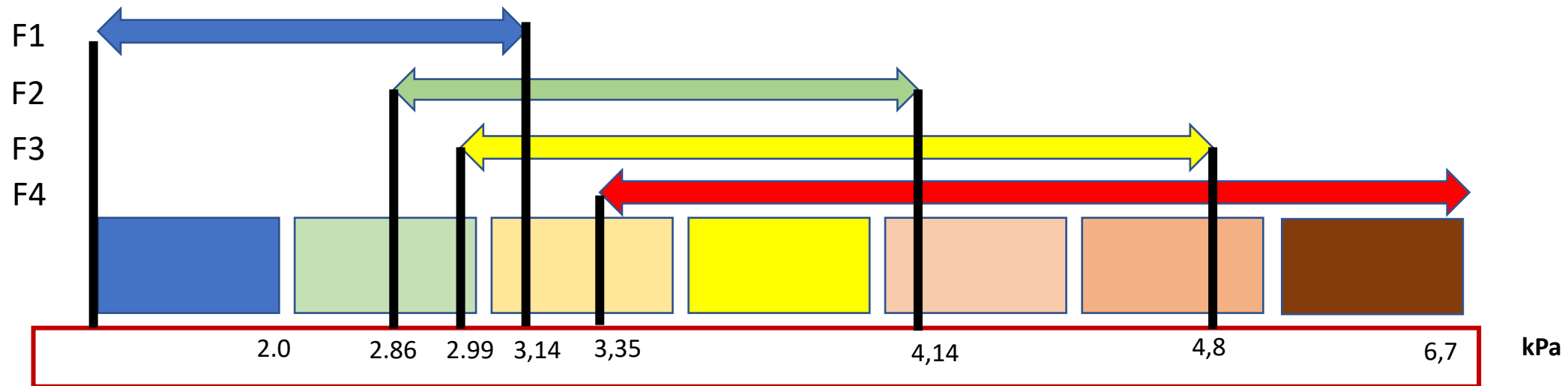
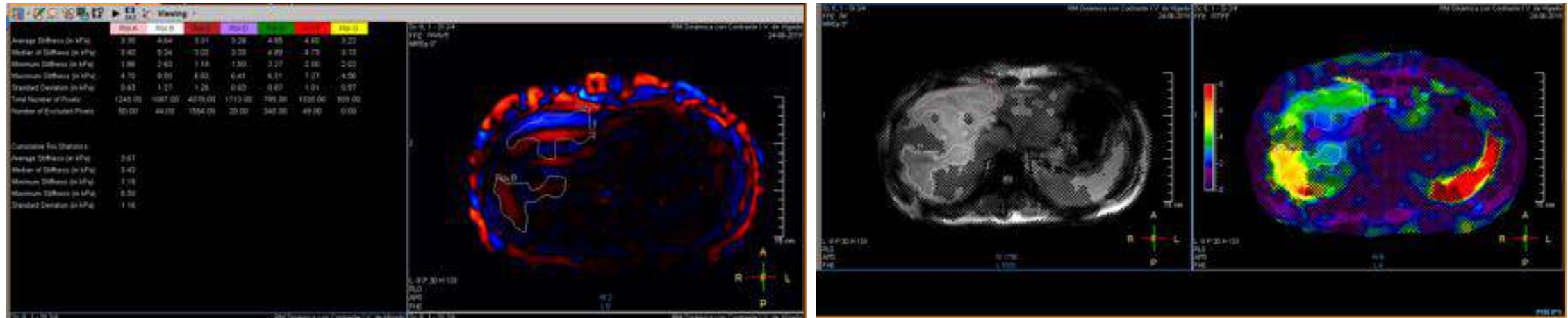
DeMRI



Diagnostic accuracy of elastography, and magnetic resonance imaging in patients with NAFLD: a systematic review and meta-analysis



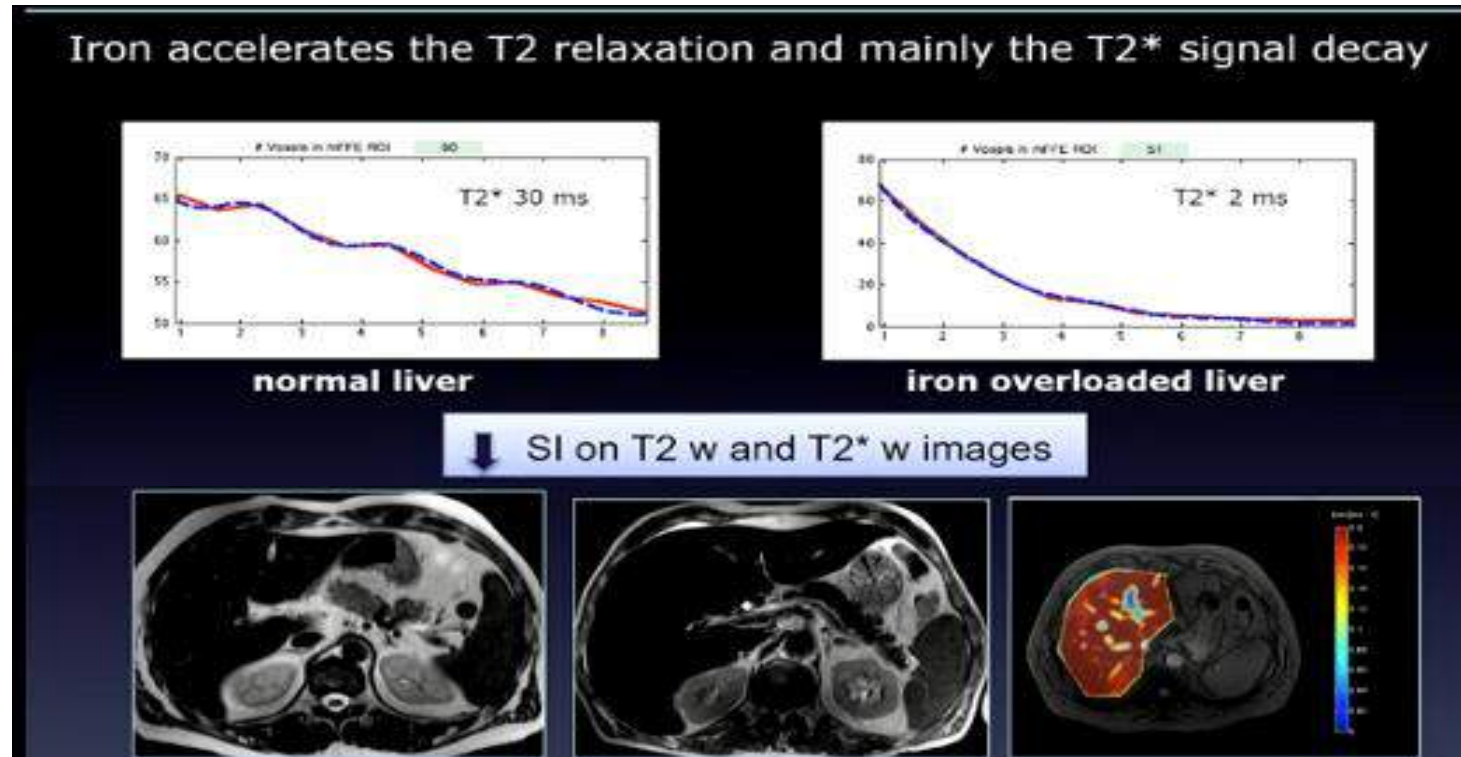
Magnetic Resonance Elastography to detect liver fibrosis in MAFLD



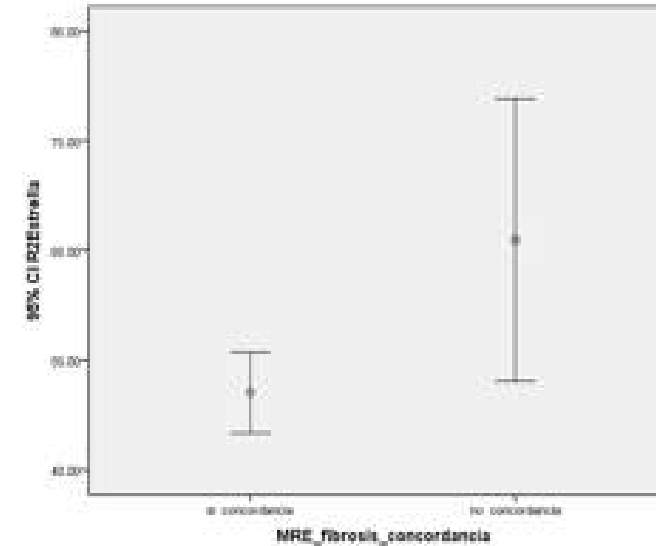
Prevalence of liver iron overload in general population



Elevated Liver Iron Concentration (> 1.8 mg/g)
(444/9108; **4,87%**)

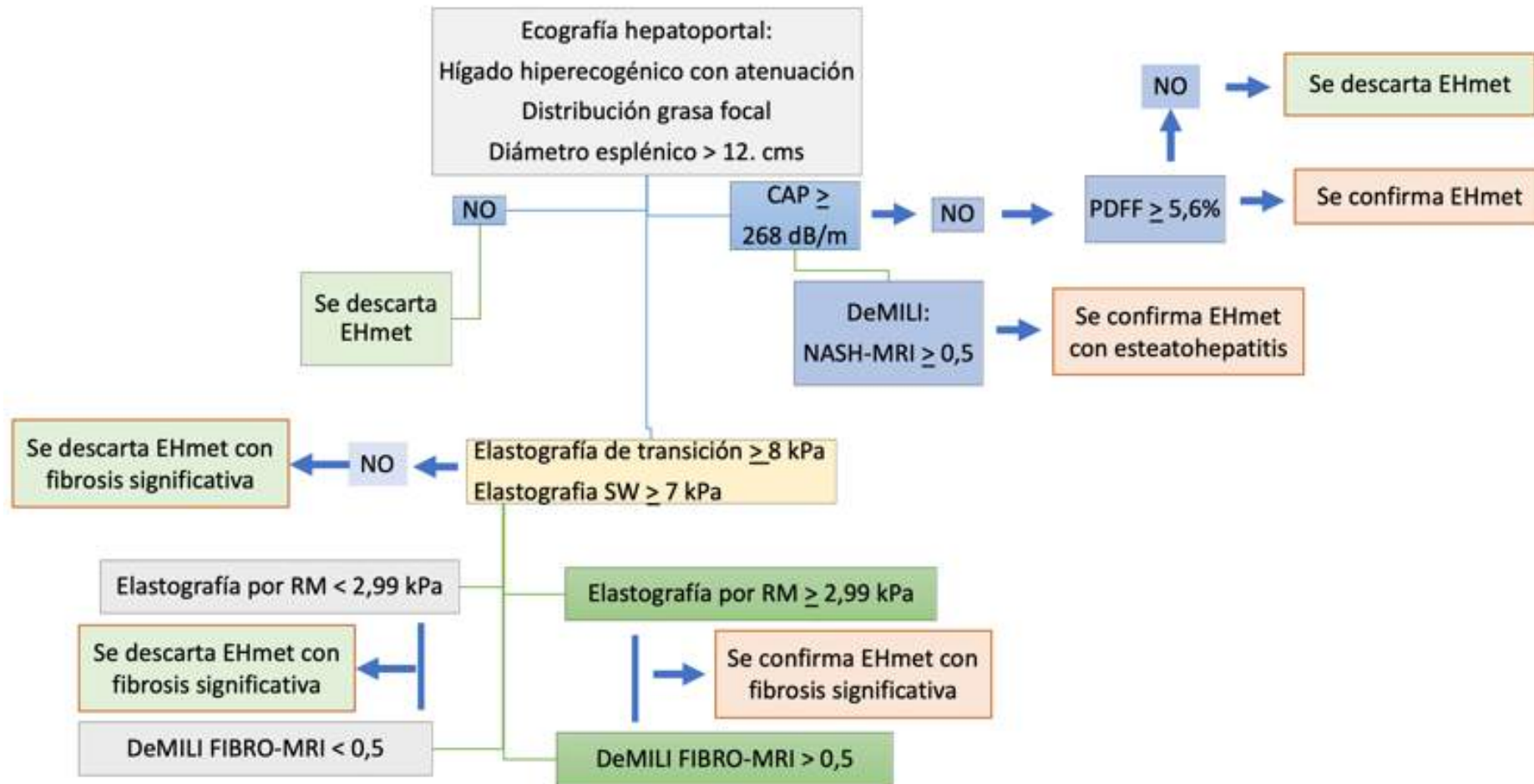


Análisis de factores que afectan la seguridad diagnóstica de la elastografía por resonancia magnética (ERM) en pacientes con MAFLD



	β	S.E	Wals	P value	OR	OR 95% C.I.	
R2*	0.306	0.150	4.139	0.042	1.358	1.011	1.823
IMC	0.054	0.199	0.074	0.786	1.056	0.714	1.560
grosor del panículo adiposo	-0.398	0.237	2.831	0.092	0.672	0.423	1.068
Diametro de bazo esteatohepatitis	0.268	0.389	0.475	0.491	1.307	0.610	2.799
Ferritina	0.777	1.720	0.204	0.652	2.174	0.075	63.300
TG	-0.011	0.007	2.761	0.097	0.989	0.977	1.002
	0.005	0.006	0.855	0.355	1.005	0.994	1.016

Algoritmo diagnóstico de enfermedad hepática metabólica basado en biomarcadores de imagen



Take home messages



- Imaging biomarkers (transient elastography and shear-wave) plus MRI techniques allow assessment of liver damage in NAFLD with high diagnostic accuracy:
 1. Transient Elastography should add metabolic status of the liver to the interpretation of stiffness.
 2. MR Elastography correctly classify across fibrosis stages
 3. Proton-Density Fat Fraction accurately quantify fat accumulation in the liver
 4. DeMILI showed the best diagnostic accuracy for NASH

“tunnel of MRI-based NASH & Fibrosis diagnosis”

PDFF >> MRI (LMS + DeMILI) >> MRE

