

SUPPLEMENTARY DATA

Table s1: NASH CRN and Metavir scoring systems

Table s1a: Metavir scoring system (Hepatology 1994;20:15-20)

F stage	Liver fibrosis pattern
0	No fibrosis
1	Portal fibrosis without septa
2	Portal fibrosis and few septa
3	Numerous septa without cirrhosis
4	Cirrhosis

Table s1b: NASH CRN scoring system (Hepatology 2005;41:1313-1321)

F stage	Liver fibrosis pattern
0	No fibrosis
1	Perisinusoidal or portal/periportal fibrosis
2	Perisinusoidal and portal/periportal fibrosis
3	Bridging fibrosis (i.e., with septa)
4	Cirrhosis

Table s1c: Correspondence between the NASH CRN and the Metavir systems

Metavir	NASH CRN	Present study	
F0	F0 or F1 (isolated perisinusoidal fibrosis)	No/mild fibrosis	
F1	F1 (isolated periportal fibrosis) or F2		
F2	F3	Septal fibrosis	Advanced fibrosis
F3	F3		
F4	F4	Cirrhosis	

Table s2: Comparison between paired M and XL probe results as a function of the liver fibrosis level

	All	No/mild fibrosis	Septal fibrosis	Cirrhosis
Patients (n)	382	219	110	53
M probe (kPa)	9.5 (6.7 – 14.6)	7.6 (5.7 – 10.5)	11.8 (8.7 – 14.8)	23.5 (15.5 – 33.0)
XL probe (kPa)	7.9 (5.6 – 11.7)	6.1 (4.9 – 8.5)	9.0 (7.1 – 11.7)	19.1 (12.4 – 26.9)
p	<0.001	<0.001	<0.001	<0.001

Results are expressed as median with first and third quartiles.

Table s3: Characteristics of patients matched according to age, sex, liver fibrosis on liver biopsy, and serum transaminases in the SCD (skin-liver capsule distance) <25mm and SCD ≥25mm groups

	Skin-liver capsule distance			p
	All (n=230)	<25 mm (n=115)	≥25 mm (n=115)	
Age (years)	56.6 ± 11.8	56.7 ± 12.0	56.4 ± 11.6	0.944
Male sex (%)	53.9	53.9	53.9	1.000
BMI (kg/m ²)	31.9 ± 6.1	28.5 ± 4.1	35.3 ± 5.8	<0.001
Diabetes (%)	50.9	40.0	61.7	0.001
Cause of chronic liver disease (%):				<0.001
- NAFLD	81.7	71.3	92.2	
- Virus	5.2	9.6	0.9	
- Alcohol	7.0	9.6	4.3	
- Others	6.1	9.6	2.6	
Biopsy length (mm)	26 ± 9	26 ± 9	26 ± 10	0.768
Advanced fibrosis	44.3	44.3	44.3	1.000
Cirrhosis	11.3	11.3	11.3	1.000
AST (IU/l)	41 (31 – 60)	40 (33 – 60)	42 (30 – 60)	0.890
ALT (IU/l)	55 (38 – 79)	53 (37 – 80)	57 (39 – 79)	0.960
GGT (IU/l)	75 (44 – 148)	80 (43 – 151)	70 (44 – 147)	0.903
Bilirubin (μmol/l)	11 (8 – 15)	11 (9 – 16)	10 (8 – 13)	0.113
Albumin (g/l)	42.0 ± 3.6	41.8 ± 4.2	42.1 ± 2.9	0.716
Platelets (G/l)	215 ± 66	213 ± 71	216 ± 60	0.314
Prothrombin time (%)	96 ± 17	97 ± 16	96 ± 17	0.715
FibroScan M probe:				
- Result (kPa)	10.1 (7.2 – 14.7)	8.8 (6.0 – 12.0)	11.9 (8.7 – 16.3)	<0.001
- IQR/M	0.18 (0.12 – 0.24)	0.16 (0.11 – 0.24)	0.20 (0.12 – 0.25)	0.221
FibroScan XL probe:				
- Result (kPa)	8.0 (5.9 – 12.1)	6.9 (5.1 – 10.9)	9.1 (6.7 – 12.8)	<0.001
- IQR/M	0.16 (0.11 – 0.23)	0.17 (0.12 – 0.23)	0.16 (0.11 – 0.23)	0.489

Quantitative variables are expressed as mean ± standard deviation or median with first and third quartiles. BMI: body mass index; NAFLD: non-alcoholic fatty liver disease; IQR/M: interquartile range/median ratio

Table s4: Diagnostic accuracy of M and XL probes used according to the manufacturer recommendation in the 230 matched patients in the SCD <25mm and SCD ≥25mm groups

Target	Cut-off	Probe	SCD	AUROC	DA	Se	Spe	NPV	PPV	-LR	+LR	OR
Advanced Fibrosis	7.3 kPa ^a	M probe	<25 mm	0.812 ± 0.039	73.9	88.2	62.5	87.0	65.2	0.19	2.4	12.5
		XL probe	≥25 mm	0.755 ± 0.045	68.7	92.2	50.0	88.9	59.5	0.16	1.8	11.8
		p	-	0.338	0.466	0.741	0.212	-	-	-	-	-
Cirrhosis	15.0 kPa ^a	M probe	<25 mm	0.906 ± 0.040	88.7	69.2	91.2	95.9	50.0	0.34	7.8	23.3
		XL probe	≥25 mm	0.855 ± 0.046	82.6	61.5	85.3	94.6	34.8	0.45	4.2	9.3
		p	-	0.403	0.259	1.000	0.277	-	-	-	-	-

^a Diagnostic cut-offs from the Tsochatzis et al meta-analysis (12)

SCD: skin-liver capsule distance; DA: diagnostic accuracy (rate of well-classified patients, %); Se: sensitivity (%); Spe: specificity (%); NPV: negative predictive value (%); PPV: positive predictive value (%); -LR: negative likelihood ratio; +LR: positive likelihood ratio; OR: odds ratio

Table s5: Diagnostic accuracy of liver stiffness measurement (LSM) obtained by choosing the probe according to the skin-liver capsule distance as measured by ultrasonography (LSM_{SCD}: M probe if SCD <25mm, XL probe if SCD ≥25mm) or according to the study algorithm (LSM_{ALGO})

Target	Cut-off	LSM	AUROC	DA	Se	Spe	NPV	PPV	-LR	+LR	OR
Advanced Fibrosis	7.3 kPa ^a	LSM _{SCD}	0.815 ± 0.029	70.6	88.4	58.4	88.0	59.4	0.20	2.1	10.7
		LSM _{ALGO}	0.832 ± 0.028	71.6	88.4	60.0	88.2	60.3	0.19	2.2	11.4
		p	0.025	0.625	1.000	0.625	-	-	-	-	-
Cirrhosis	15.0 kPa ^a	LSM _{SCD}	0.902 ± 0.025	86.3	81.3	86.7	98.3	33.3	0.22	6.1	28.2
		LSM _{ALGO}	0.909 ± 0.024	86.7	81.3	87.2	98.3	34.2	0.22	6.3	29.5
		p	0.135	1.000	1.000	1.000	-	-	-	-	-

^a Diagnostic cut-offs from the Tsochatzis et al meta-analysis (12)

SCD: skin-liver capsule distance; DA: diagnostic accuracy (rate of well-classified patients, %); Se: sensitivity (%); Spe: specificity (%); NPV: negative predictive value (%); PPV: positive predictive value (%); -LR: negative likelihood ratio; +LR: positive likelihood ratio; OR: odds ratio

Figure s1: Automated Probe Selection tool included in the FibroScan device

The latest versions of the FibroScan device include the Automatic Probe Selection tool that automatically measures the skin-liver capsule distance and indicates which probe to use for LSM. In practice, the indication “M” or “XL” appears highlighted on the FibroScan screen when the probe is applied on the skin.

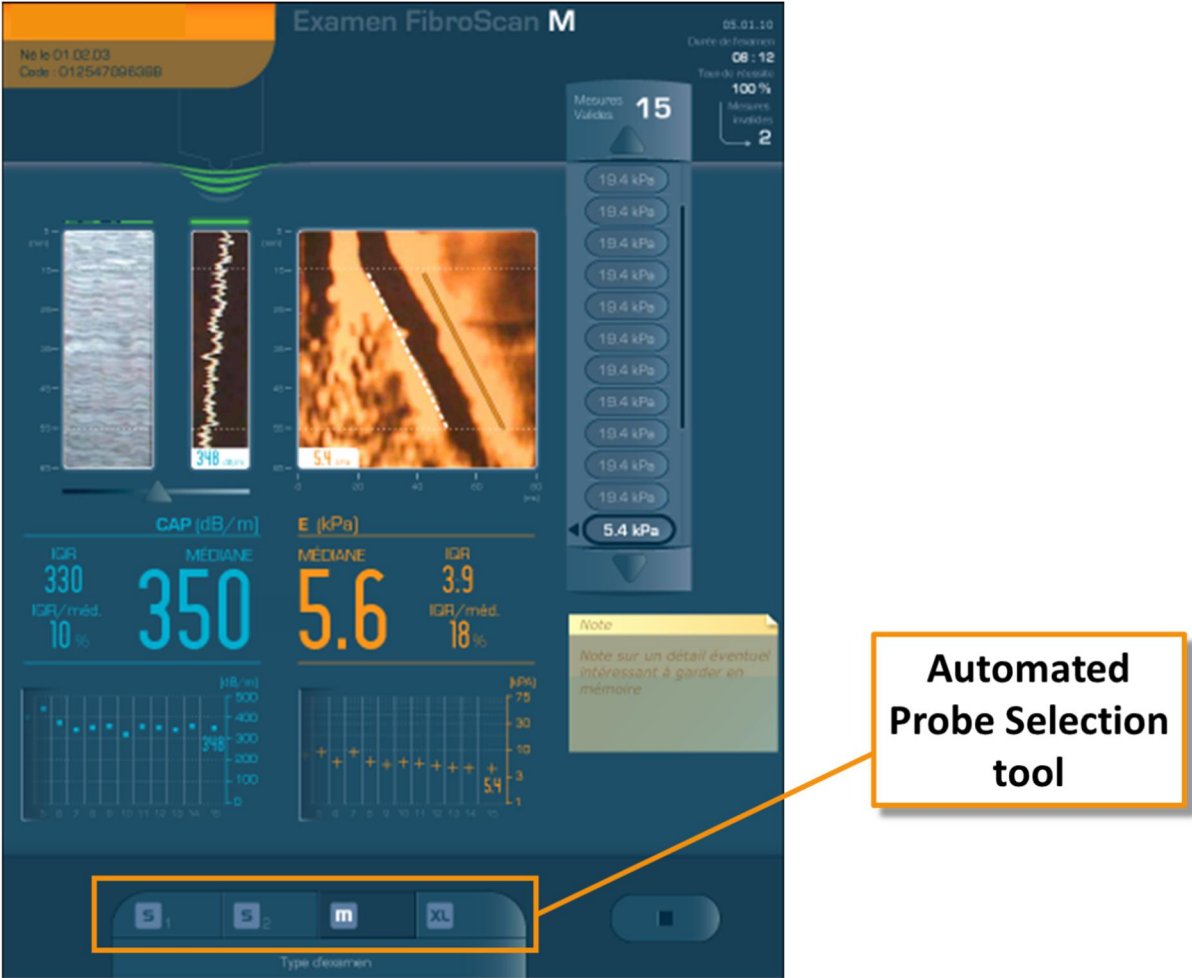


Figure s2: Sensitivity and specificity curves of the M and XL probes for the diagnosis of advanced fibrosis (Figure s2a) and the diagnosis of cirrhosis (Figure s2b)

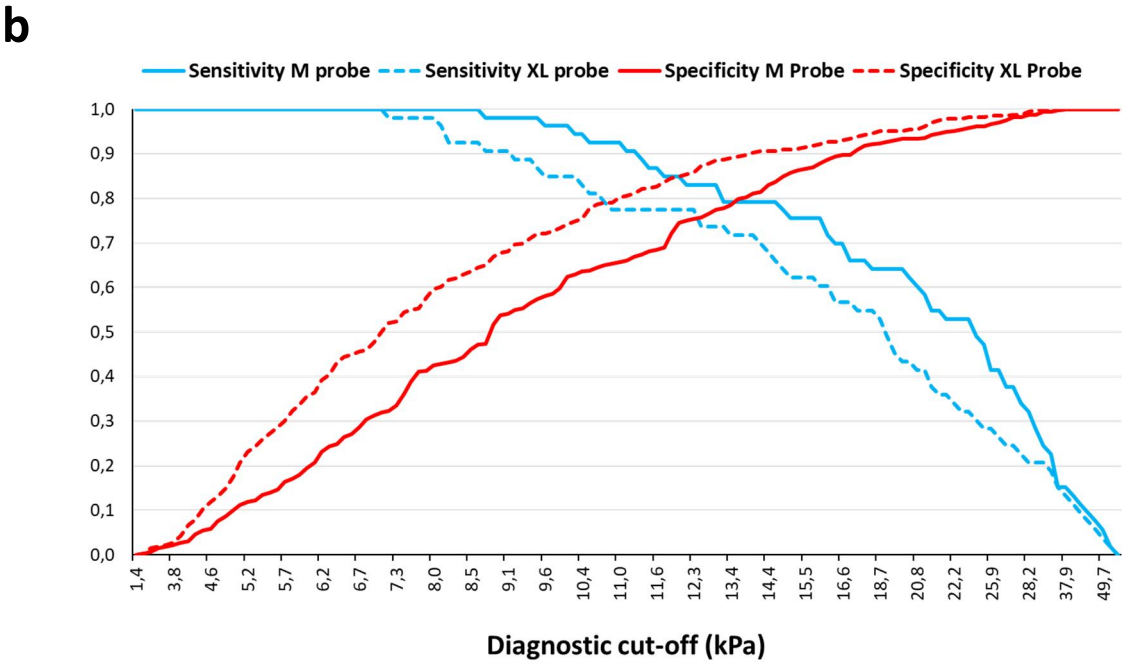
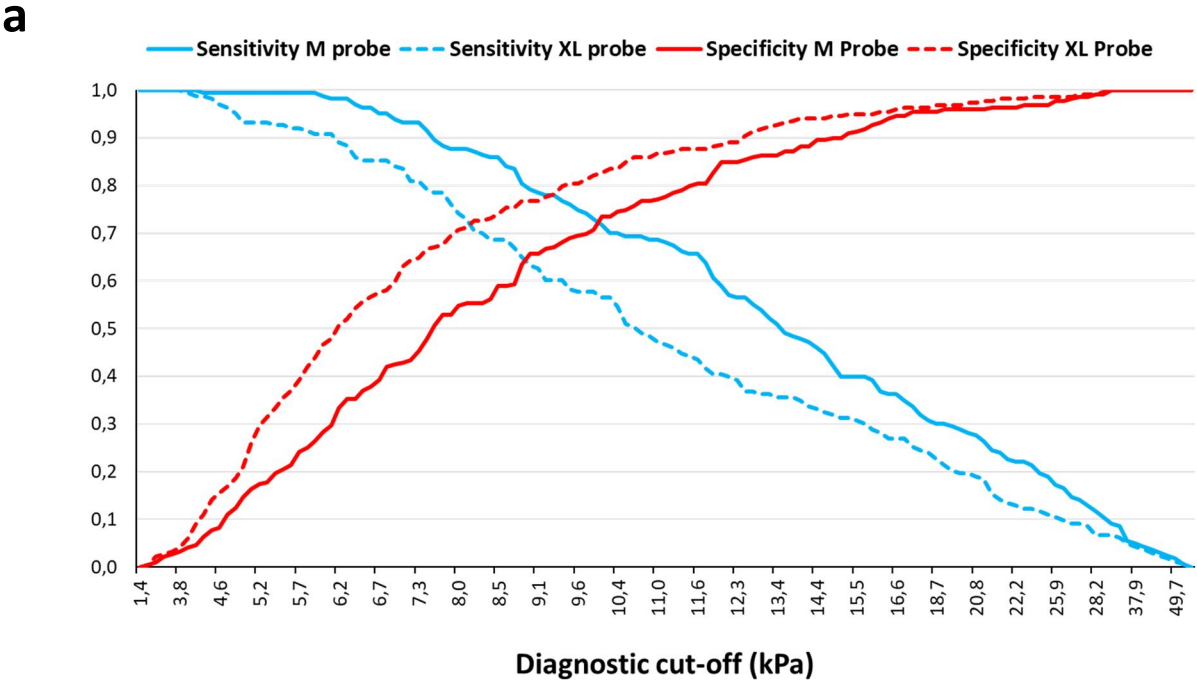


Figure s3: Skin-liver capsule distance as a function of the number of valid shots associated with a M probe recommendation by the Automated Probe Selection tool. Results were obtained using the M probe in patients with BMI <32 kg/m².

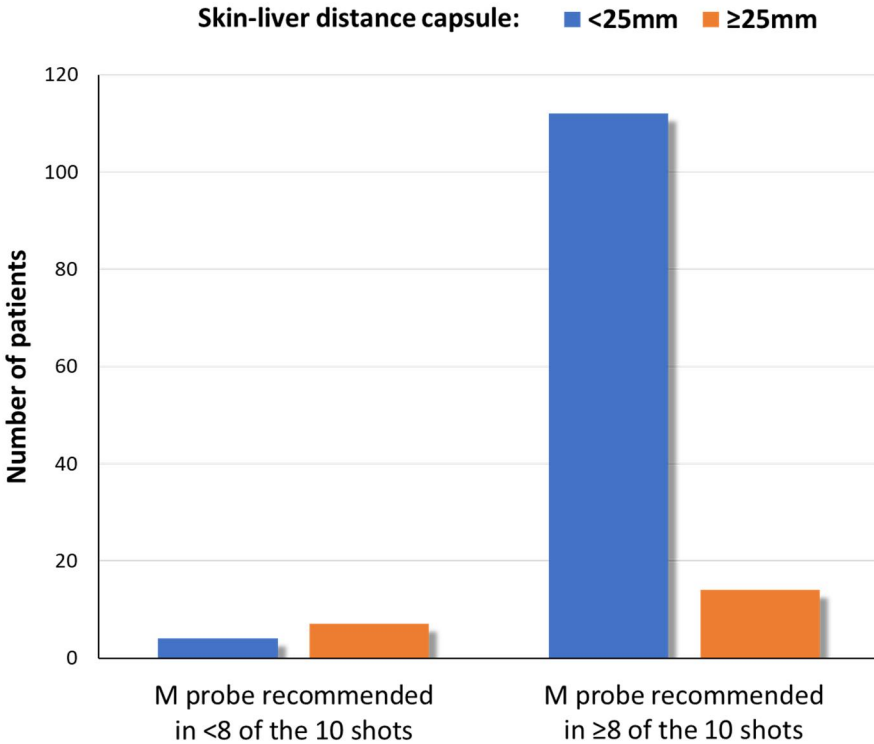
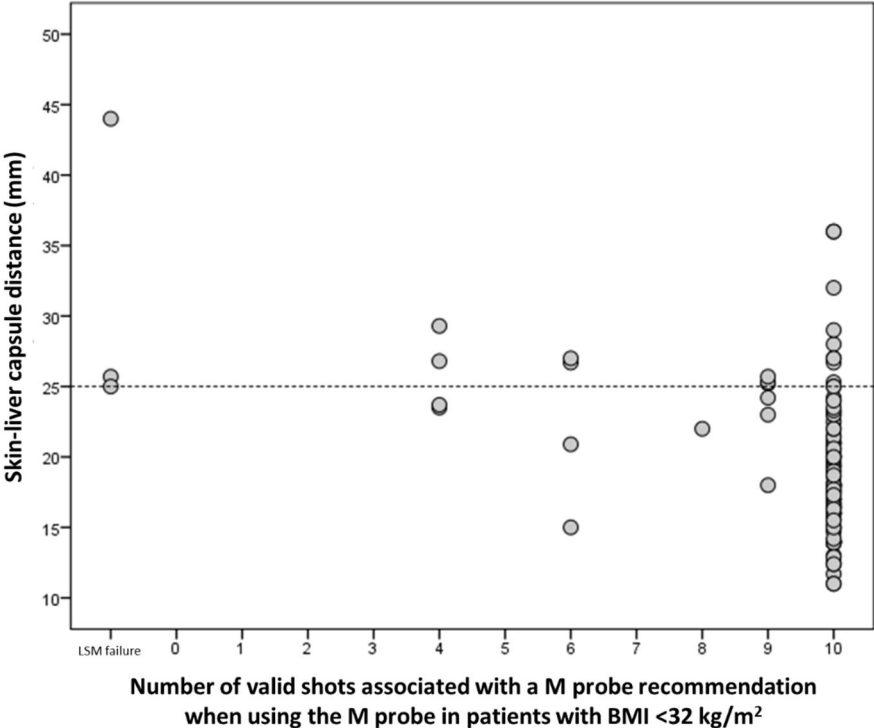


Figure s4: Skin-liver capsule distance as a function of the number of valid shots associated with a XL probe recommendation by the Automated Probe Selection tool. Results were obtained using the XL probe in patients with BMI $\geq 32 \text{ kg/m}^2$.

