

Non-invasive diagnosis of cirrhosis in clinical practice in hepatitis C

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Introduction

- Cirrhosis diagnosis is clinically important.
- However, the accuracy of non-invasive diagnostic means has historically been evaluated according to a binary diagnosis (cirrhosis present or absent), even though it would be more exact to consider diagnosis probability as a function of test results.
- Also, the use of a test meant originally for significant fibrosis represents a second limit.
- Our aim was thus to evaluate a cirrhosis-specific test in clinical practice.

Methods

- 1710 patients with hepatitis C and liver biopsy, providing Metavir fibrosis (F) stage, were included:
- 1013 in a test population including blood tests,
- 596 in a cross-sectional validating study including blood tests and Fibroscan,
- 101 in follow-up for 2 years (with two liver biopsies) including blood tests.

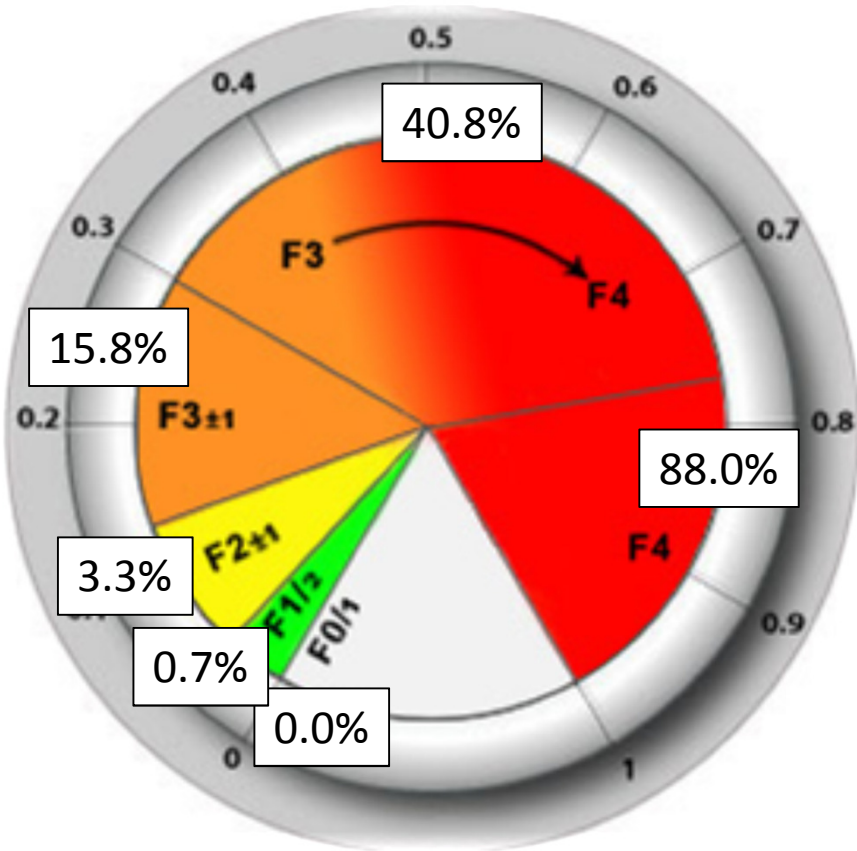
Results: Test population

- We first developed a blood test called CirrhoMeter with an AUROC of 0.911 for cirrhosis.
- The correct classification rate for cirrhosis diagnosis was 81.7% (85.2% in cirrhosis) vs 75.1% ($p < 10^{-3}$) using an equivalent test targeted for significant fibrosis.
- We then constructed a detailed classification including 6 fibrosis classes.
- The probabilities for cirrhosis were: F0/1: 0%, F1/2: 0.7%, F2±1: 3.3%, F3±1: 15.8%, F3/4: 40.8%, F4: 88.0% (**figure 1**).
- The correct classification rate was 87.6% (93.0% in patients with cirrhosis).
- Other results are presented in **figures 2 and 3**.

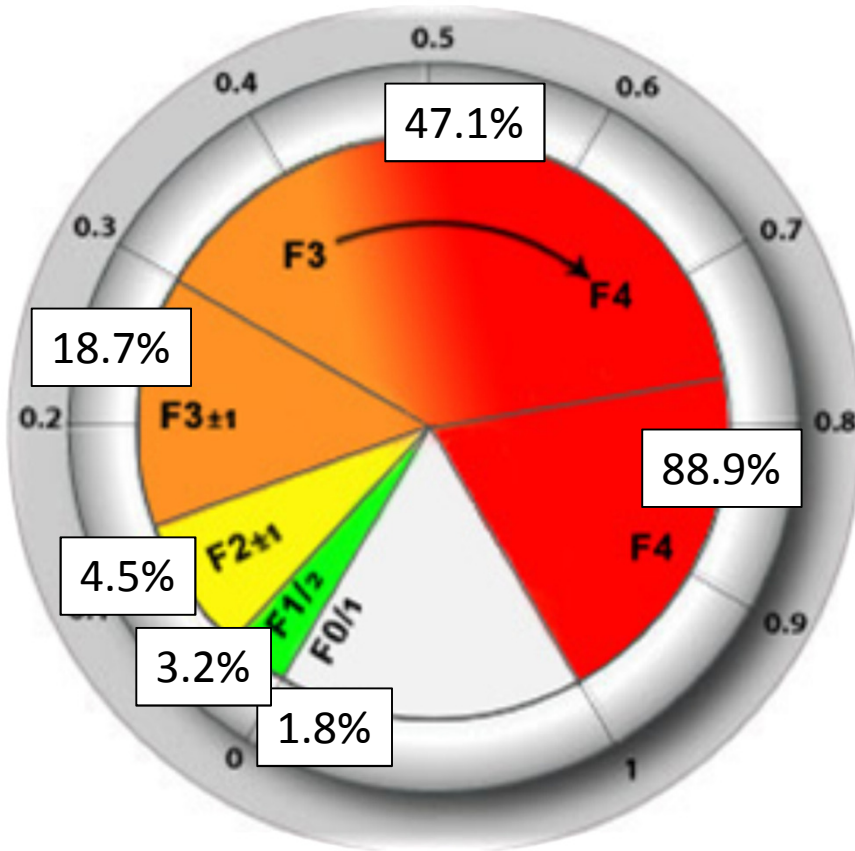
Results: Validating populations

- ***Cross-sectional study:***
- The probabilities for cirrhosis were: F0/1: 1.8%, F1/2: 3.2%, F2±1: 4.5%, F3±1: 18.7%, F3/4: 47.1%, F4: 88.9% (**figure 1**).
- The correct classification rate was 83.2% (85.4% in patients with cirrhosis).
- Other results are presented in **figures 2, 3 and 4**.
- ***Longitudinal study:***
- CirrhoMeter was the most sensitive ($p < 0.001$ between % changes) of 5 blood tests for detecting fibrosis progression (0.25 ± 0.29 at baseline vs 0.31 ± 0.32 at 2 years, $p = 0.003$) (**figure 5**).
- CirrhoMeter was also reproducible ($r_{ic} = 0.815$).
- The % change in CirrhoMeter was significantly ($p = 0.039$) higher (median: 32.3%) than that of area of fibrosis (median: 19.9%), which was the histological characteristic having the most significant change but poorly reproducible ($r_{ic} = 0.439$).

Figure 1: Classification in Metavir fibrosis stages by CirrhoMeter



Test population
 Well classified :
 all: 87.6%, F4: 93.0%



Validation population
 Well classified :
 all: 83.2%, F4: 85.4%

Figure 2: Distribution of histological F4 as a function of test classification (evaluation of positive predictive value for cirrhosis)

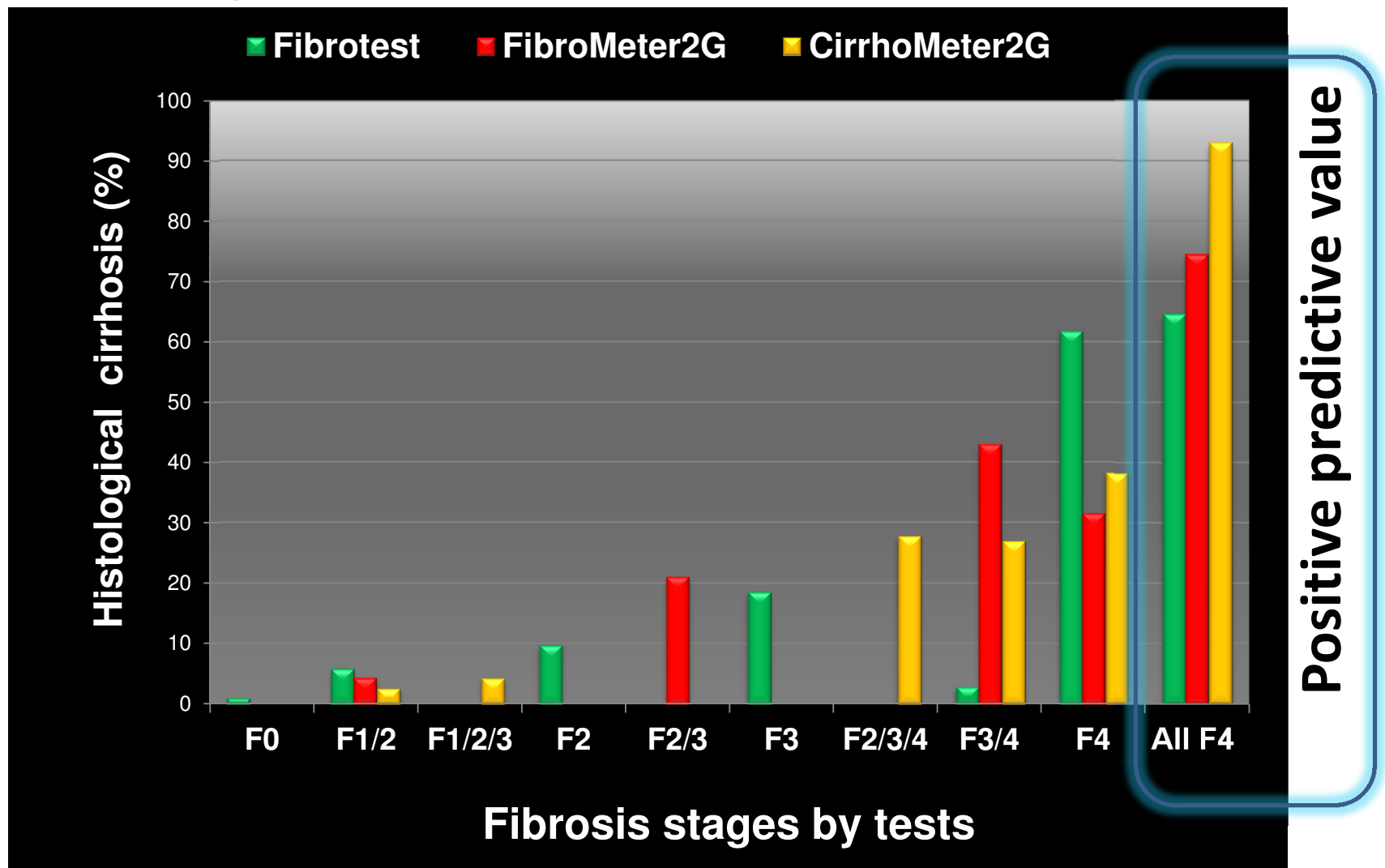


Figure 3: Distribution of F4 diagnosed by test classification as a function of Metavir F stage (sensitivity evaluation)

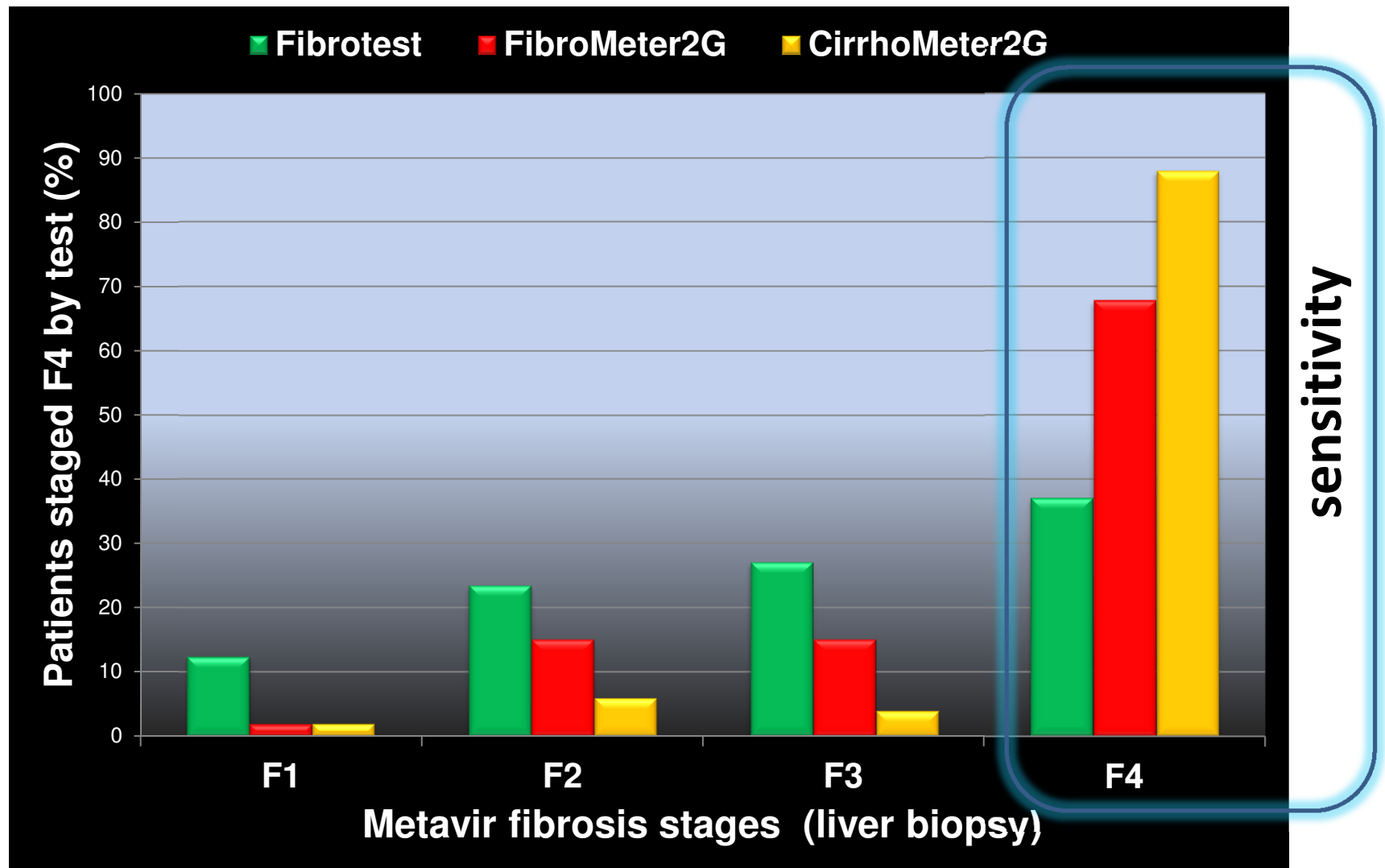
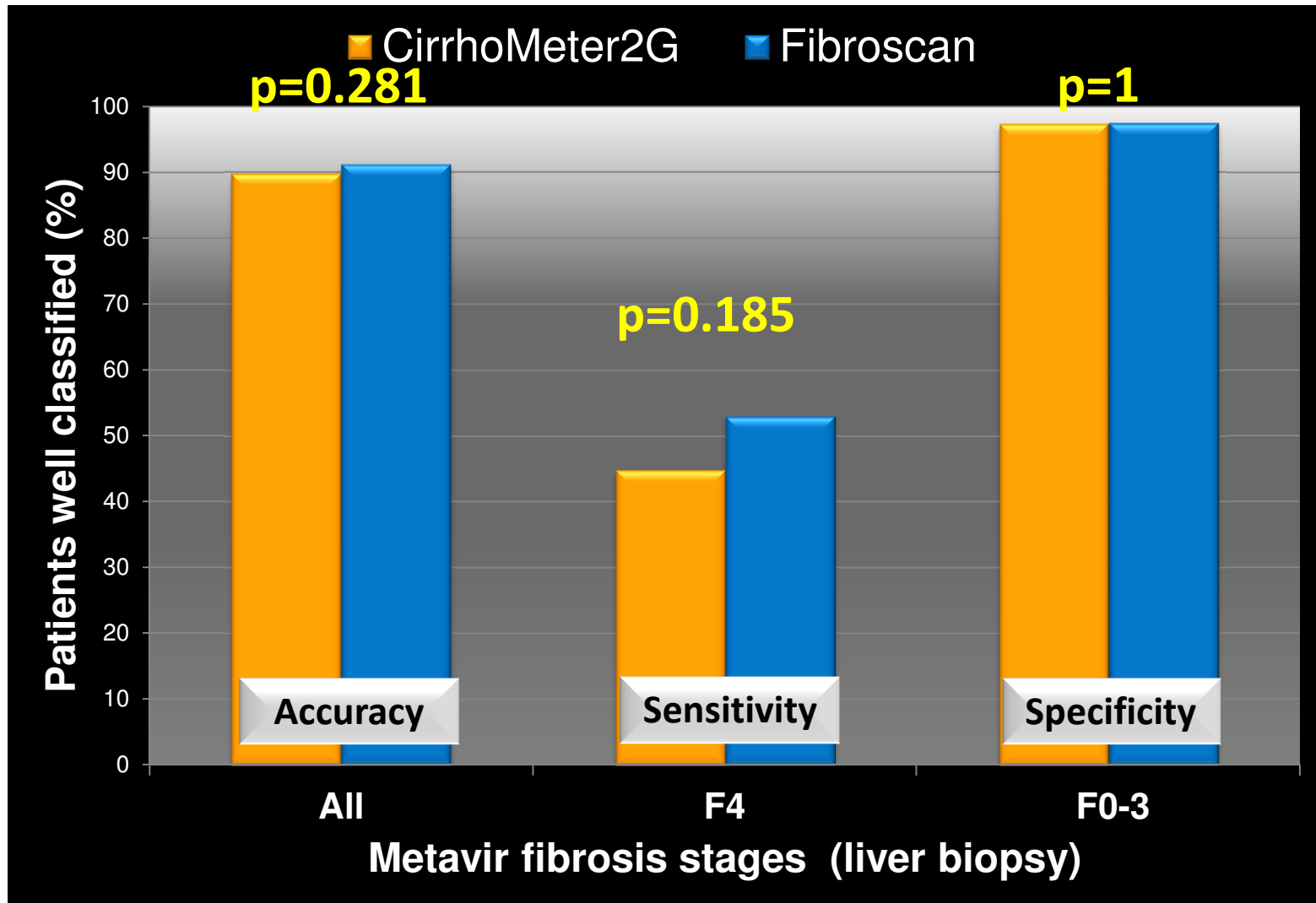


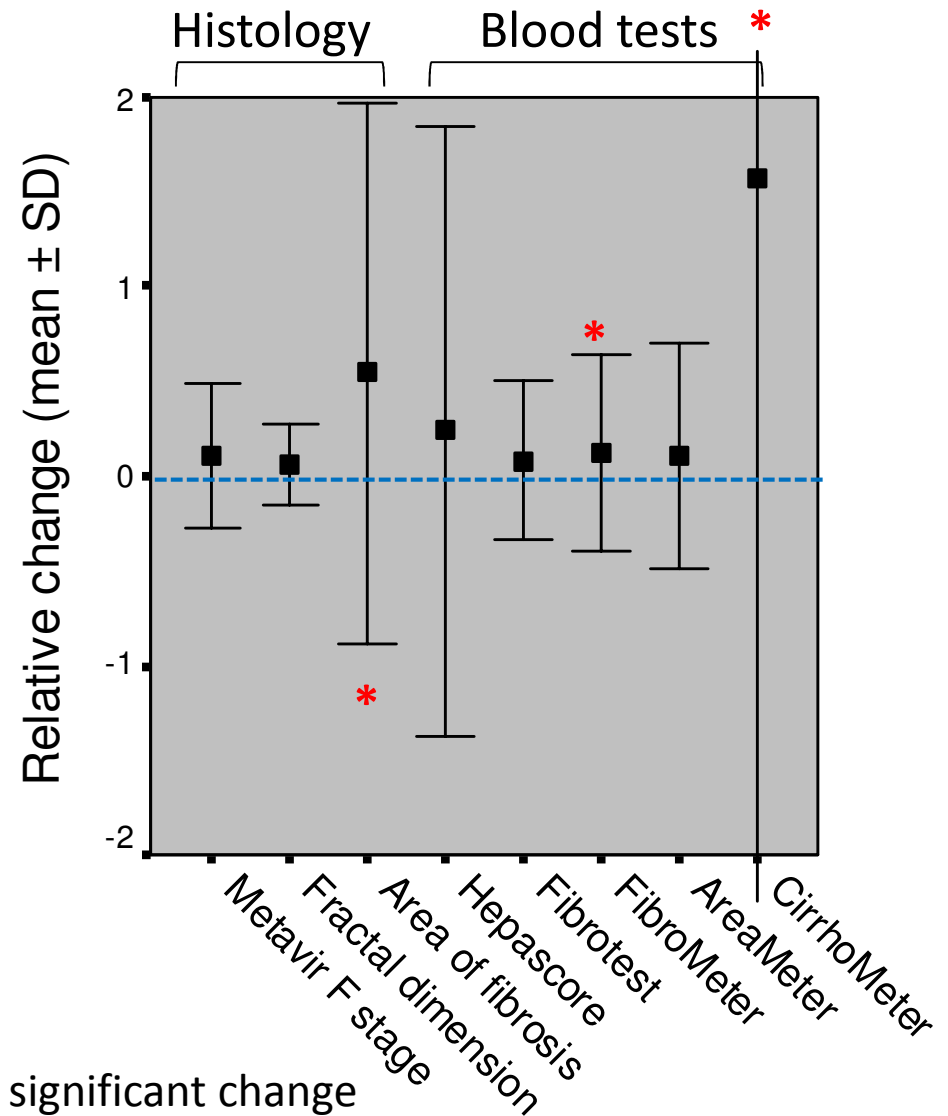
Figure 4: Binary diagnosis of cirrhosis: CirrhoMeter^{2G} vs Fibroscan



a posteriori accuracy cut-offs

Figure 5: Comparison of liver morphometry and blood tests to assess fibrosis progression

- Among histological characteristics, the relative change (%) in area of fibrosis was significantly higher than other measures.
- CirrhoMeter was the only blood test with a change significantly higher than that of area of fibrosis ($p=0.039$).



Conclusion

- For the diagnosis of cirrhosis, a specific test like CirrhoMeter is more appropriate than a standard fibrosis test.
- A specific test offers the advantages of a high correct classification rate and excellent dynamic sensitivity and reproducibility.
- Its detailed classification (6 classes) also offers precise diagnostic probability. Thus, the CirrhoMeter test, with its specific classification, offers a more exact diagnostic method adapted to clinical practice.