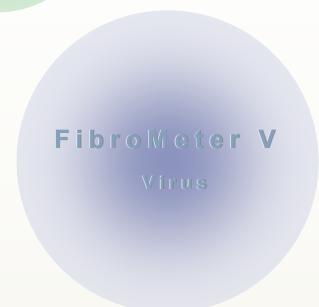
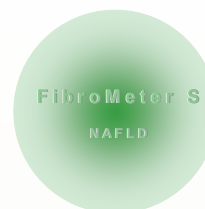
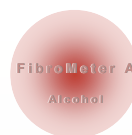


FibroMeters

CirrhoMeter



Practical use

Available tests

	Cause		
	Virus B or C*	Alcohol	Metabolic steatosis
Test :			
Fibrosis score	FibroMeter ^{3G} V	FibroMeter A	FibroMeter S
Cirrhosis score	CirrhoMeter ^{3G} V	-	-
Area of fibrosis (%)	-	AreaMeter A	AreaMeter S
Activity score	InflaMeter	-	-

* with or without HIV co-infection

Indications

FibroMeters are indicated¹ in the initial evaluation of every patient with a chronic liver disease due to one of the 3 main causes, especially by age ≥ 40 years.

If different etiologies are present or suspected, the following FibroMeter choice is suggested:

- Virus + other : FibroMeter^{3G} V.
- Alcohol + NAFLD : FibroMeter S.

Restrictions for use

FibroMeters have been validated in chronic viral hepatitis (B, C, HIV co-infection), chronic alcoholic liver diseases and NAFLD (metabolic steatosis).

FibroMeter have not been validated in other clinical settings:

- Children.
- Acute hepatitis.
- Associated or other cause of chronic liver disease.
- Pregnancy.
- Associated dysfunction of other organ than the liver, especially renal insufficiency. However, the expert system takes into account renal insufficiency in FibroMeter for viral hepatitis.
- Patients under treatment for their liver disease.
- Acute or chronic non-liver conditions inducing an inflammatory syndrome such as arthritis... However, the expert system can take into account these additional changes in biomarkers in FibroMeter for viral hepatitis.

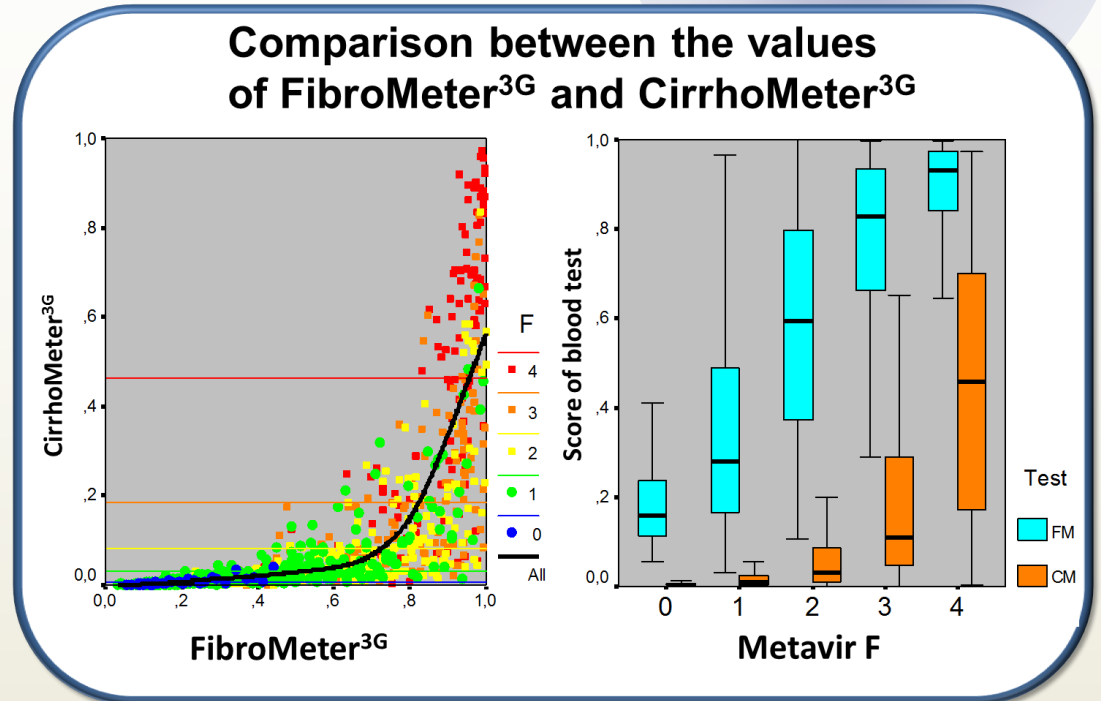
(1) FibroMeter V is included in French (HAS, 2009) and European (EASL, 2011) guidelines for hepatitis C and FibroMeter S is quoted by European experts (EASL) for NAFLD

Targets of tests

FibroMeter: this test is designed for the diagnosis of significant fibrosis (Metavir fibrosis stage ≥ 2). FibroMeter^{3G} means a FibroMeter of third generation (2010).

CirrhoMeter: this test is designed for the diagnosis of cirrhosis (Metavir fibrosis stage = 4). The CirrhoMeter has a test range mostly devoted to severe fibrosis (figure 1). Consequently, this test is more interesting in F3 and F4 stages where its diagnosis is more precise than that of FibroMeter.

Figure 1:
On the left: the black curve indicates the regression line and the horizontal lines indicate the mean of CirrhoMeter^{3G} as a function of Metavir fibrosis (F) stages.
On the right, the figure shows that CirrhoMeter^{3G} (CM) is more adapted to F3 and 4 stages than FibroMeter^{3G} (FM).



InflaMeter: this test is designed for the diagnosis of significant activity (Metavir necrotico-inflammatory activity grade ≥ 2).

Result interpretation

General comments

The accuracy and predictive values are provided by data bases of patients with liver biopsy interpreted by two senior expert pathologists. The accuracy cannot reach 100% since liver biopsy is presently the best but not the gold standard. In addition, in clinical practice, it has been shown that the performance of FibroMeter was superior to that of a first line pathologist. The figures are provided by several data bases: 1056 patients with HCV hepatitis, 235 patients with NAFLD and 241 patients with chronic alcoholic liver diseases. A test cannot reach 100% accuracy and its result has to be interpreted in the light of the full clinical context and with other examinations.

Score value

Fibrosis score: the score from 0 to 1 means the probability to have a significant fibrosis (Metavir fibrosis stage ≥ 2). For example, a FibroMeter at 0.16 means that the patient has a 16% probability of having significant fibrosis.

Cirrhosis score: the score from 0 to 1 expresses the probability to have cirrhosis (Metavir fibrosis stage = 4).

InflaMeter: the score from 0 to 1 expresses the probability to have a significant activity (Metavir activity grade ≥ 2).

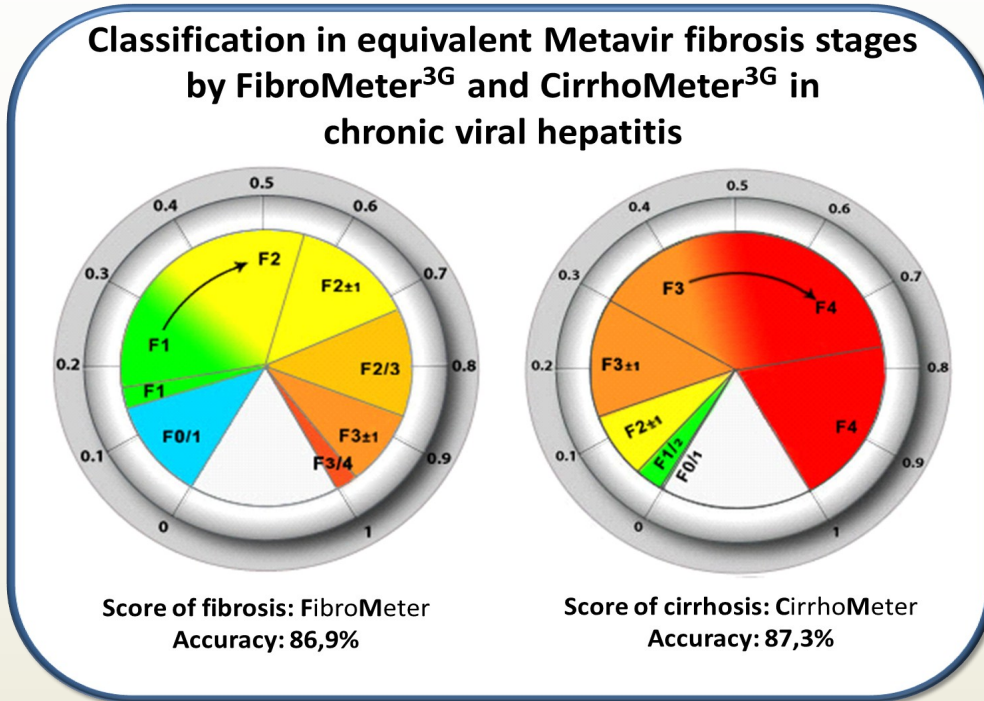
However, it is possible to refine the diagnosis of fibrosis stage or activity grade:

Fibrosis stage diagnosis

Fibrosis stage classification

The classification or meter indicates the most probable fibrosis stage(s) in a defined range values of FibroMeter and CirrhoMeter.

This and the overall accuracy are presented in the following figure:



Interpretation of classes with several fibrosis stages

Within a fibrosis class, the fibrosis stage probability increases with the FibroMeter value, e.g. a FibroMeter at 0.75 is in favor of F2 and a FibroMeter at 0.85 is in favor of F3. The size of the font indicates the most probable stages: e.g. F2 in the class F2±1 and F4 in the class F3/4.

The interpretation is the same for the CirrhoMeter: the most probable fibrosis stage is F0 in the class F0/1, F1 in the class F1/2, F2 in the class F2±1...

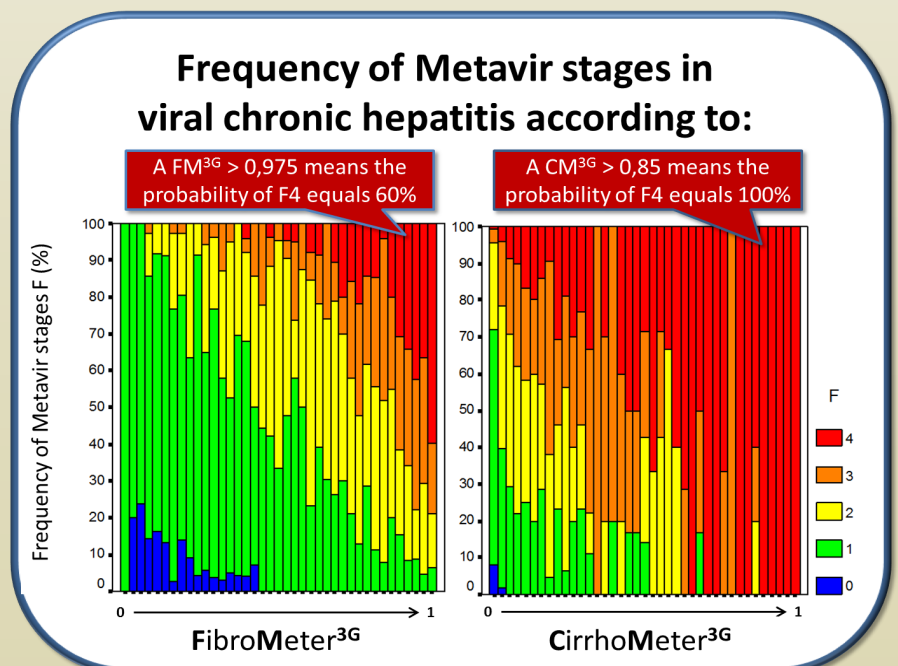
Interpretation of fibrosis stage between FibroMeter and CirrhoMeter

As stated before, CirrhoMeter is more performing in F3 and F4 stages so its diagnosis is dominant in these stages,

e.g. in a patient with a FibroMeter at F3±1 and CirrhoMeter at F4, F4 is the most probable fibrosis stage.

Fibrosis stage probability

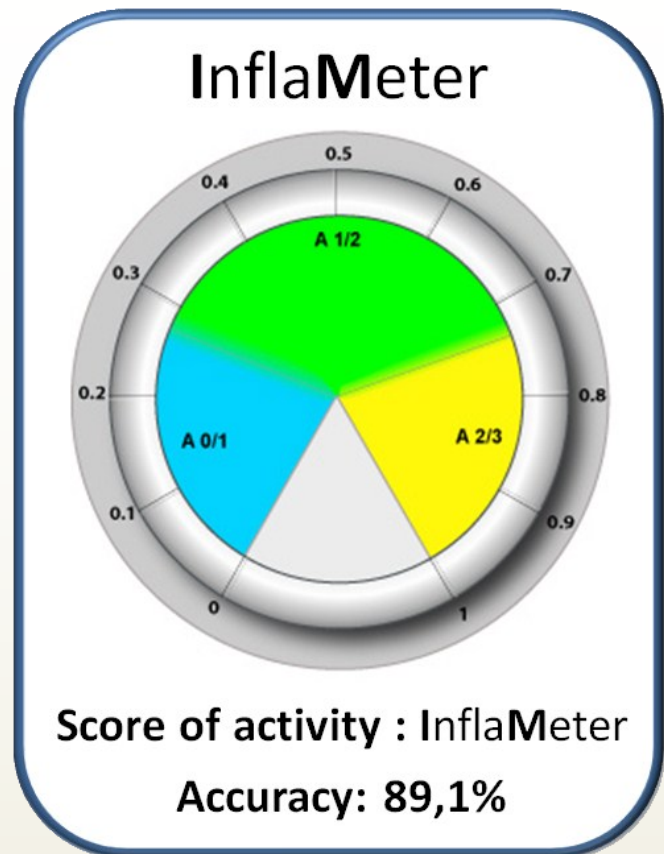
It is possible to obtain the exact probability for fibrosis stages in chronic viral hepatitis according to the following plots:



However, the same explanation for the most probable stage has to be considered as stated in the previous paragraph.

Activity grade diagnosis

The meter provides the most probable fibrosis grades in a defined range values. The overall accuracy is presented in the following figure:



Expert system

This system has several targets:

- It is aimed at detecting discordant values of markers responsible for false positive or false negative, e.g. isolated decrease in prothrombin index due to anti-vitamin K.
- If necessary, this system corrects the putative false result by using a formula without this discrepant marker.
- It provides the exclusion or affirmation diagnosis for different diagnostic targets (fibrosis, significant fibrosis, severe fibrosis, cirrhosis) in individual patients when the thresholds of 100% negative or positive predictive values are reached.

Presently, this system is only available in FibroMeter and CirrhoMeter for chronic viral hepatitis.

Follow-up

FibroMeter has excellent dynamic reproducibility and sensitivity allowing the following suggestions for follow-up:

Frequency of monitoring of a chronic hepatopathy:

Cause	Cause and fibrosis stage				
	Untreated or ongoing		Treated		
Fibrosis (Metavir F)	F ≤ 1	F ≥ 2	F ≤ 1	F ≥ 2	F4 (cirrhosis)
FibroMeter F	2 years	Yearly	On demand	Yearly	Yearly
CirrhoMeter or AreaMeter	-	-	-	-	1 to 2 years



BioLiveScale

Faculty of Medicine, rue Haute de Reculée
49045 ANGERS Cedex / FRANCE
Tél. : +33 2.41.36.07.19 / Fax : +33 2.41.36.18.94.
www.biols.com / contact@biols.com