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The Measure of Intrahepatic Fat, Mirror of Health

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Editorial

Cardiovascular, digestive, metabolic, neoplastic and neuro-degenerative diseases are currently major causes of death; familiarity, genetics or early symptoms are used for preventive/early diagnosis and treatment [1-3]. The Metabolic Syndrome (MetS) that predisposes to all of these diseases is beckoned years in advance by fatty liver (fat, mostly triglycerides in more than 5% of total liver weight, steatosis, fatty liver disease, FLD, [1-3]). FLD which prevails in 10% to 30% of the overall population worldwide rising above 50% in the elderly; it is an indolent pathology unless it is complicated by inflammation, Steatohepatitis (SH, [1-3]). SH is a chronic liver disease which may progress rapidly to cirrhosis and hepatocellular carcinoma, but it is also a co-factor of rapid evolution of liver diseases of different etiology and non-hepatic chronic diseases [3-4]. FLD is qualitatively diagnosed by a simple non-invasive abdominal ultrasound examination, but a reliable measure of Intrahepatic Fat (IHF) is mandatory. Liver biopsy is invasive and in addition hampered by sampling errors, because it represents only a minimal part of the liver and in about 30% of cases the intrahepatic fat distribution is not homogenous [3]. Magnetic Resonance (MR) driven spectrometry and multiparametric analysis are the gold standard methods for measuring IHF and the liver fibroinflammatory lesions, however they need an expensive equipment and highly specialized operators, thus they are not feasible for general screening [5]. Recently simple non-invasive methods which use common ultrasound instruments and combine in AI algorithms multiple standardized imaging parameters proposed reliable methods for quantification of intrahepatic liver fat (IHF, [6-7]). Using these new techniques it is possible to study whether drugs and/or changes of life style or alimentary habit determine an effective reduction of IHF in every single patient in clinical practice as well as in randomized clinical trials.

In clinical practice IHF qualifies for a simple reliable mirror of general health to be used to monitor the efficacy of alimentary and preventive care particularly in the pre-symptomatic subject. Metaphorically the measure of fat in the liver reservoir serves as preventive measure as the measure of oil for life saving of any internal combustion engine (Figure 1A).

This paradigm brings back to the future the relevance of the liver analysis for the prediction of health of the single individual (Figure 1B). In ancestral cultures, Etruscan as well as Anatolian the liver of sacrificed animals was isolated, observed and subdivided into sections for haruspicy (predictive hepatoscopy) to foresee the future. The Etruscan Piacenza liver (a bronze artifact found in 1877, near the city of Piacenza, kept in the Palazzo Farnese Museum, (Figure 1B) a model of the liver used to predict the future [8]. FLD have many different etiologies and it is mandatory to stratify patients accordingly [9]; to consider all subjects with FLD as affected by the same disease is very naïve and introduces a major bias in both research and clinical practice. Unfortunately the acritical approach to consider FLD a unique disease has killed and is killing most of new therapeutic approaches (which are very specifically targeted) when experimented in inadequate clinical trials stratifying cases and controls randomly picked-up from the garbage can of a huge variety multi-etiologic diseases. Non-surprisingly after decades these studies did not bring any useful breakthrough in clinical practice. Thus the recent guidelines and expert opinions for the management of FLD patients prompt new systems medicine approaches for the study of the complex interplays between major physiology systems [1-3]. New concepts for patient stratification are mandatory to identify different clinical prototypes within the general metabolic-syndrome and/or FLD generic definitions. Using the new non-invasive techniques for IHF quantification it is possible to evaluate in clinical trials as well as in the single subject in clinical practice whether drugs and/or changes of life style or alimentary habit determine an effective reduction of IHF. In addition the rapidly growing field of molecular imaging is providing new opportunities [10]. The widespread use of reliable non-invasive IHF measurements provides new research perspectives for the non-invasive study of *in vivo* physiopathology of fatty liver and the complexity of the interplay between imaging biomarkers, blood metabolomics, genetic and epigenetic factors. Hopefully these new studies will identify the different etiologies of FLD,

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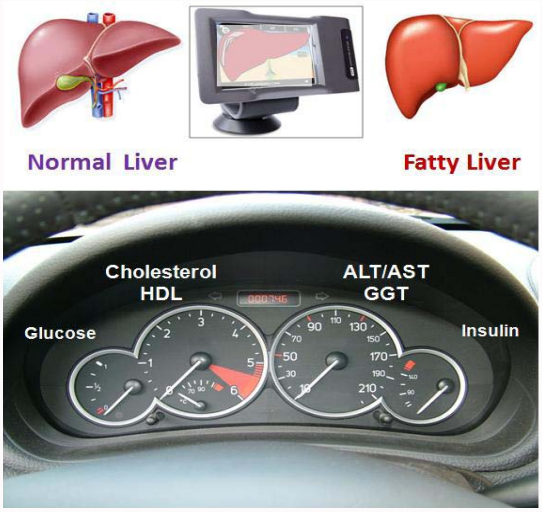

Figure 1A: Metaphorically the measure of fat in the liver reservoir serves as preventive measure as the measure of oil for life saving of any internal combustion engine.

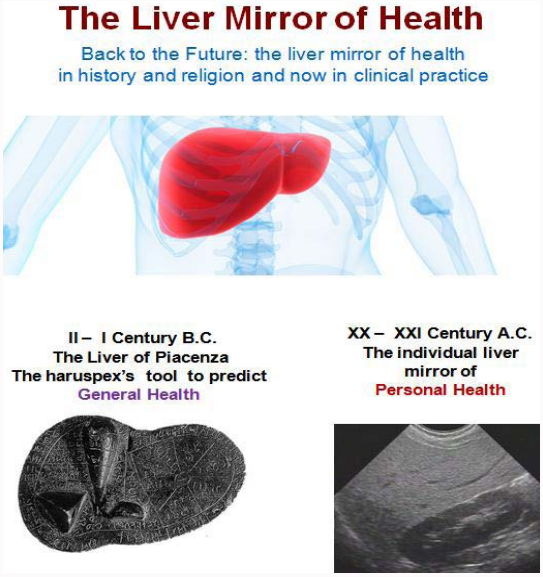

Figure 1B: The Liver Mirror of Health. Back to the Future: The liver mirror of health in history and religion and now in clinical practice.

new diagnostic and prognostic biomarkers and therapy targets for a better stratification of the patients for both prevention and outcome prediction and personalized treatment of fatty liver.

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