Liver i-Biopsy™ and the Corresponding Intelligent Fibrosis Scoring Systems: i-Metavir F and i-Ishak F

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Abstract. An important goal of modern medicine is to replace invasive, painful procedures with non-invasive techniques for diagnosis. We investigated the possibility of a knowledge discovery in data approach, based on computational intelligence tools, to integrate information from various data sources - imaging data, clinical and laboratory data, to predict with acceptable accuracy the results of the biopsy. The resulted intelligent systems, tested on 700 patients with chronic hepatitis C, based on C5.0 decision trees and boosting, predict with 100% accuracy the fibrosis stage results of the liver biopsy, according to two largely accepted fibrosis scoring systems, Metavir and Ishak, with and without liver stiffness (FibroScan®). We also introduced the concepts of intelligent virtual biopsy or i-Biopsy™ and that of i-scores. To our best knowledge i-Biopsy™ outperformed all similar systems published in the literature and offer a realistic opportunity to replace liver biopsy in many important medical contexts.

1 Introduction

An important goal of modern medicine is to replace invasive procedures with non-invasive techniques for diagnosis. Non-invasive techniques do not penetrate mechanically, nor break the skin or a body cavity, i.e., they don’t require an incision into the body or the removal of biological tissue. An important invasive procedure is biopsy and the main non-invasive techniques are diagnostic images and diagnostic signals. Usually, the information content of the non-invasive imaging techniques is lower than the that of the invasive techniques. As a consequence, the accuracy of the diagnostic based on these non-invasive techniques alone is lower.

The main question addressed in our studies is: can we extract and integrate information from various (non-invasive) data sources, e.g. imaging data, clinical and laboratory data, to reach an acceptable 95%-100% diagnostic accuracy? For any usual or traditional medical approach, the answer to this important question is NO. This is because our brain is very skilled in dealing with images, but the
information content of the medical images does not seem to be enough for a diagnostic, and is less skilled in dealing simultaneously with many variables, and this seems to be the solution to the problem.

A knowledge discovery in data or data mining approach, based on computational intelligence tools, could be the foundation for a positive answer to the above important medical question. The extraction and integration of information from various data sources is indeed possible, and the diagnostic accuracy of the resulted intelligent systems could even reach 100%.

To illustrate this thesis, we present an overview of some of our recent investigations, and also some new results, on building intelligent systems capable to predict the results of liver biopsy \cite{1}, \cite{2}. We used several non-invasive approaches - routine laboratory tests and basic ultrasonographic features - with and without liver stiffness measurement by transient elastography (FibroScan\textsuperscript{R}), to build intelligent systems for staging liver fibrosis in chronic hepatitis C. The fact that we reached similar results for prostate biopsy (manuscript in preparation) corroborate our believe that this approach can become a standard one.

2 Biomedical Background

The hepatitis C virus is one of the most important causes of chronic liver disease. It accounts for about 15% of acute viral hepatitis, 60% to 70% of chronic hepatitis, and up to 50% of cirrhosis, end-stage liver disease, and liver cancer. An estimated 150-200 million people worldwide are infected with hepatitis C.

Liver fibrosis can accompany almost any chronic liver disease arising as a result of wound repair. It is the net result of the balance between fibrinogenesis - production of extracellular matrix - and fibrolysis - degradation of extracellular matrix (see \cite{3} for a recent review of liver fibrosis). Progressive fibrosis of the hepatic parenchyma leads to cirrhosis, nodule formation, altered hepatic function and risk of liver-related morbidity and mortality. Evaluating the degree of fibrosis is valuable for the following medical reasons \cite{4}:

1. The actual stage of fibrosis will indicate the likelihood of response to treatment; advanced stages generally have an inferior response rate.
2. If fibrosis progression is slow, treatment with antiviral therapy may be less urgent.
3. The approximate time to the development of cirrhosis, the end-stage liver disease, can be estimated.

Liver biopsy is the gold standard for grading the severity of disease and staging the degree of fibrosis and permanent architectural damage. Liver biopsy is invasive and usually painful; complications severe enough to require hospitalization can occur in approximately 4% of patients \cite{5}. In a review of over 68,000 patients recovering from liver biopsy, 96% experienced adverse symptoms during the first 24 hours of recovery. Hemorrhage was the most common symptom, but infections also occurred. Side effects of the biopsies included pain, tenderness, internal bleeding, pneumothorax, and rarely, death \cite{6}.