PhD Thesis Title: 'Algorithm Development Methodology for MRI, US Image Processing, and Analysis for Hepatic Diseases'

Author: Ilias Gatos
Email: gatose1981@gmail.com
Institution: Faculty of Medicine, School of Health Sciences, University of Patras, Patras, Greece
Supervisor: Prof. George C. Kagadis
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ABSTRACT:

The liver is an important organ of the human body which performs basic functions related to digestion, metabolism, immunity, and nutrients storage in the body. Liver disease can lead to liver failure. If untreated, leads to death. Therefore, an accurate diagnosis for targeted therapy of liver diseases is greatly important. Generally, there are two types of liver diseases, focal and diffuse. Focal liver disease (or Focal Liver Lesions (FLLs)) are considered abnormal liver tissue that is concentrated in a small area, such as a tumor or cyst. They are further classified as benign or malignant. The latter usually results in death. Therefore, the precise characterization of an FLL as malignant is of great importance. The Diffuse Liver Disease (or Chronic Liver Disease (CLD)) is distributed almost uniformly throughout the liver tissue. It causes constant and recurring inflammation of the liver tissue that is replaced by connective tissue (fibrosis), leading progressively to cirrhosis. Cirrhosis is the final stage of the disease. This leads to liver failure or hepatocellular carcinoma (HCC), a malignant FLL, and eventually death.

The consequences of the development of liver disease make early detection and an accurate diagnosis very important in order to combat the disease. Presently, a liver biopsy is considered the 'Gold Standard' for accurately diagnosing the diseases. Although, the liver biopsy is invasive, it has the potential for complications for the patient and is costly. Therefore, non-invasive approaches, mainly in the medical imaging field, have been developed and evolved over the last few years to provide a valid alternative to liver biopsy.

The aim of this thesis was to study and develop novel image processes and image analysis algorithms for Ultrasound, and Magnetic Resonance Imaging (MRI) for the different diagnoses of liver disease. They can be useful additions to the software of the respective imaging medical equipment. Through these algorithms, the diagnostic performance of Radiologists in hepatic diseases can be significantly improved.

During this thesis, four novel medical image processes and analysis algorithms were developed. Their performance surpassed those of the respective approaches of the literature.

In detail, the 1st algorithm evaluates FLLs by using image processing and analysis methods in contrast enhanced ultrasound videos. As a first step, a rough estimation of FLL's position and borders are initially set by calculating Continuous Wavelet Transform (CWT) coefficients (Maxima and Zero Crossings) on each frame of the Contrast Enhanced US (CEUS) video. This border estimation is then set as initialization step to a Markov Random Field segmentation algorithm, which gives the final accurate FLL border delineation. Through this process, the FLL is tracked by the algorithm through all video frames and its borders are extracted accurately independent of the FLL's position, shape or inner intensity change. For each frame of the video that the FLL's borders are extracted, mean intensity values in the FLL and a small Region of Interest (ROI) outside and near the FLL are calculated and a Time-Intensity Curve (TIC) is extracted. Then, the TIC features are extracted and are fed to a Support Vector Machine (SVM) classifier to determine if the final FLL is benign or malignant.

The 2nd and 3rd algorithms evaluate the CLD through processing and analyzing the Ultrasound Shear Wave Elastography (SWE) images. These algorithms extract the colored region with stiffness values from the B-Mode Grayscale values of the SWE image automatically and proceed to an inverse color (RGB) to stiffness conversion, converting the color map to a stiffness map. Then, they analyze all the region of stiffness values (2nd algorithm) and sub-regions of it (3rd algorithm) and extract textural features that are a subset of significant one. Next, it is fed to an SVM classifier to differentiate between healthy subjects and patients with CLD.

Finally, the 4th algorithm performs a differential diagnosis on the FLLs through processing and analyzing the MRIs. Through CWT Multiscale Analysis and FCM segmentation algorithm, the FLL's borders are extracted accurately. Then, the textural and morphological features are extracted. As a subset, the most significant ones are fed to a Probabilistic Neural Network (PNN) classifier for the FLL differentiation to Benign, HCC and Metastasis.

As a conclusion, the algorithms developed during this thesis have successfully confronted the clinical issues related to liver disease diagnosis through imaging. When equipped, they can improve the diagnostic accuracy of a medical imaging machine.

References to author publications that relate specifically to the dissertation:

1. **Gatos, I.**, Tsantis, S., Spiliopoulos, S., Skouroliakou, A., Theotokas, I., Zoumpoulis, P., Hazle, J. D. and Kagadis, G. C. (2015), A new automated quantification algorithm for the detection and evaluation of focal liver lesions with contrast-enhanced ultrasound. Med. Phys., 42: 3948–3959. doi:10.1118/1.4921753
2. **Gatos, I.**, Tsantis, S., Spiliopoulos, S., Karnabatidis, D., Theotokas, I., Zoumpoulis, P., Loupas, T., Hazle, J. D. and Kagadis, G. C. (2016), A new computer aided diagnosis system for evaluation of chronic liver disease with ultrasound shear wave elastography imaging. Med. Phys., 43: 1428–1436. doi:10.1118/1.4942383
3. **Gatos, I.**, Tsantis, S., Karamesini, M., Spiliopoulos, S., Karnabatidis, D., Hazle, J. D. and Kagadis, G. C. (2017), Focal liver lesions segmentation and classification in nonenhanced T2-weighted MRI. Med. Phys., 44: 3695–3705. doi:10.1002/mp.12291
4. **Gatos I.**, Tsantis S., Spiliopoulos S., Karnabatidis D., Theotokas I., Zoumpoulis P., Loupas T., Hazle J. D., Kagadis G. C. (2017), A Machine-Learning Algorithm Toward Color Analysis for Chronic Liver Disease Classification, Employing Ultrasound Shear Wave Elastography. Ultrasound Med. Biol., 43(9):1797-1810. doi:10.1016/j.ultrasmedbio.2017.05.002.