Telemmedicine Network for Ultrasound Screening of HCC

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Abstract — Neoplastic diseases are widely recognized as extremely disabling, requiring in advanced stages a large amount of medical, technical, and financial support and, eventually, leading to death. This is why it is recommended to early diagnose them, gaining time for proper care and/or cure. Hepatocellular carcinoma (HCC) is one of these neoplastic diseases, meeting the requirements to become the target of a close surveillance: it is a frequent condition; it has a high rate of mortality; it affects a very well defined at risk population (chronic liver diseases patients). This population can be closely followed-up using a sensitive and easily accepted method (ultrasonography – US). Under these circumstances, the improvement of the screening and surveillance system for the patients at risk for HCC is needed, so the early diagnosis is increased, as well as the chance for an efficient and curative therapeutic intervention. A possible choice would be a telemedicine network for the US screening of a large number of chronic liver disease patients (especially liver cirrhosis) for the early detection of HCC.

Keywords: telemedicine, hepatocellular carcinoma (HCC), ultrasound screening, web based application, image analysis.

1. INTRODUCTION

Nowadays, the hepatocellular carcinoma (HCC) is recognized as the fifth cancer worldwide, in terms of both incidence and mortality rate [1]. The incidence of HCC has a great geographical variability, which is related mostly to different risk factors incidence in general population [1]. Any agent that produces liver suffering and leads to cirrhosis is considerate to be a risk factor for HCC. The most important ones are hepatitis B virus (HBV), hepatitis C virus (HCV) and alcohol. The screening means testing of a large number of individuals designed to identify those with a particular genetic trait, characteristic, or biological condition [2]. This has been proven to be the most efficient method in diagnosis of cancers, as well as cost-effective. The criteria that define an efficient screening program are: (1) high incidence and high mortality disease; (2) high sensitivity and specificity of the screening test; (3) easily accepted by the target population; (4) efficient curative treatment offered.

HCC meets the requirements to become the target of surveillance and a sensitive tool – ultrasonography (US) is easily acceptable, can screen the population and effective treatment options are available [1]. US is preferred for the HCC screening mainly because is an available, repeatable, non invasive, non irradiating and relatively low cost imaging technique. Used for screening in conjunction with AFP determination, US may early diagnose HCC in cirrhotic patients.

A telemedicine-supported process that will monitor this disease into the northwestern part of Romania is both practical and advantageous. The objective of this paper is to describe the development and implementation of a Web application that allows efficient communication between general practitioners and ultrasound specialists, in order to support a telescreening programme for patients with HCC.

The screening process is performed according to the following steps: the patients are presenting to the general practitioner and undergo a specific medical consultation comprising, inter alia, ultrasound examination. The ultrasound images, acquired according to a specific protocol, are sent together with the other medical data regarding HCC screening to an expert diagnosis center. At this level, the specialists analyze the images and the additional information and establish the existence of cancerous formations. Based on the specialist evaluation, transposed into an electronic form, the system establishes a new date for the patients to present themselves to the GP, in order to undergo a new examination. The term for the new examination date appears to the GP when he/she accesses the patient’s records. The application provides dedicated functionality for each user group already identified: GP’s specialists, database administrators.
2. Defining the requirements for the HCC tele-screening system

Developing the telemedicine network in order to monitor the HCC patients, involves several steps:
1. Identifying and including general practitioners GPs in the project, selecting them taking into account the equipment available, the physician’s expertise in US, the epidemiological status (as far as the interest pathology is concerned) in the area.
2. Training the GP with no US competence for the capture of significant US images, through an intensive training course. The required equipment in the GP offices will consist in a not sophisticated, but good resolution ultrasound device and a secure Internet connection. The GP will therefore be able to use ultrasound in order to evaluate the liver, bile ducts and gall bladder, portal and hepatic veins, spleen, pancreas and kidneys, as well as the possible existence of ascites, and will then transmit the images to the expert center. The US investigation of patients of risk for developing HCC will be performed monthly, in order to follow the tumor growth rate in the expert center, to offer general recommendations of US screening. The identification of focal liver lesions will impose the thorough study of their placement and relationships, size and structure, compared to the neighbouring parenchyma.
3. The automatic selection analysis and classification of images has to be performed in the expert center, as well as the creation and administration of the database. Furthermore, during the preparation stage, the expert center will store normal and pathological US images of the liver in large supply and representing a wide variety of liver diseases, in order to provide the system with sufficient and good-quality models, allowing it to operate the automatic triage. In addition, a prospective randomized study will be run, attempting to evaluate the diagnostic value of US in HCC occurring in cirrhotic patients vs. US plus one or two biological tests (US vs. US+AFP vs. US+AFP+DCP – descarboxiprothrombyne).

3. Description of the examination protocol in US screening of HCC

The aim of US examination in HCC screening is to characterize the hepatic parenchyma both regarding the base disease (mainly, the hepatic cirrhosis – aiming to follow aspects as echogenity, homogeneity, capsular contour), as well as nodule presence. Furthermore, the portal trunk and its branches are followed for observing the presence of portal hypertension syndrome (dimensions, obstruction) or tumor invasion. The US images should be of acceptable quality in order to detect nodules with diameter between 2 and 3 cm, when we can speak about early HCC, increasing the chances for favourable response to treatment. This is why the liver examination should offer information about all eight segments of the liver from two plans and about the portal venous system. In order to don’t miss valuable information from the US examination in real time, we included in the screening protocol two cine-loop sequences, one for each liver lobe. In order to ease the communication during the project, we proposed a coding system of the US sections that will be detailed further on. Description of the examination procedure is presented together with an image of the transducer on the patient’s abdomen and the corresponding US section.

4. Description of the tele-screening information system

The tele-screening network architecture, presented in Figure 1, consists of several terminals for the acquisition and transmission of specific US images and other medical data placed at general practitioners’ (GP) office, a digital communication network, and a core, placed at a University Hospital, able to handle, store, process, analyze, and classify the images and biomedical data. The system allows bi-directional communication between general practitioners and imaging experts. The images and biomedical data are transmitted over the network and integrated into the medical database at the core level.

In order to manage all the data flow in the system, and the interaction between the different medical entities scattered along great distances, there was clearly that a Web-based application would be needed, which had to connect to the central database that stores the patients’ medical data.

During the project execution, the consortium had to take several decisions regarding the underlying technological infrastructure and the development environment. Two alternatives were considered in order to develop the Web-based applications: use J2EE open-source solution, based on Apache Web server and JSP, or the Microsoft .NET solution. We chose the Microsoft proprietary solution, because of the large set of services and features it offers, but most important, higher productivity in terms of development time.

![Figure 1. Telescreening system architecture.](image-url)
integrated security gateway, Microsoft’s Internet Security and Acceleration (ISA) Server is deployed on the Web server machine. It provides users with fast and secure remote access to applications and data. The main features of the application are:
- secure access: each user connects to the application according to its level of permissions; each physician, may it be general practitioner, or imaging specialist can only access information regarding its own patients
- standard forms: based on medical specifications, and particular data structures required for the tele-screening procedures, the user is presented with static interfaces, that allows him/her to input required information;
- automatically establish the next call for patient examination, based on calculations that take into account old values of medical parameters stored in the database, and the imaging specialist’s examination result;
- allows access to an image analysis module that automatically describes the texture of liver parenchyma and allow the discrimination of cirrhotic patients from those having normal liver or early stages chronic liver diseases.

The patient is allowed to choose this screening program as an alternative, its inclusion in the system being conditioned by its desire. Moreover, the patient involved in the tele-screening program can be excluded in certain cases: he/she is hospitalized in order to receive special treatment, or if the patient refuses to present to the next scheduled consultation. The idea is to implement both a rigorous system, but also open towards the patient desire.

5. THE IMAGE ANALYSIS MODULE

The image analyzes module implements a set of functions that allows the pre-processing of the US images in order to enhance their quality, the selection of Regions Of Interest for focusing further processing, metric measurements applied to a specific region and texture characterization of the liver parenchyma.

5.1. Image pre-processing

Since the analyzed US images came from different sources (different devices which can be calibrated differently), it is possible to have differences in terms of image intensity, contrast, noise levels. Moreover, the US devices used in the current project are portable ones and therefore the provided image quality is lower compared to standard US devices. The purpose of the pre-processing operations is to improve the quality of the images to a standardized level of intensity, and contrast.

The pre-processing functions are including: contrast and brightness enhancement, histogram equalization, gray-levels normalization and the reduction of the most common noise types (salt&pepper and gaussian) [6].

5.2. ROI selection

The ROI selection facility allows the user to delimit a specific region of interest for further processing using 3 types of selection modes:
- rectangular shape (Fig. 1.a)
- circle-sector shape (Fig. 1.b)
- free-form shape (Fig. 1.c)

Once a ROI is defined, further processing will be applied in the selected area.

![Figure 2. ROI selection modalities](image)

5.3. Metric measurements

A set of functions were implemented to allow the user the following types of measurements:
- Length computation between 2 points (Fig. 3.a)
- Angle computation between two lines (Fig. 3.b)
- Computation of the area closed in a ROI (Fig. 3.c)

All the measurement can be calibrated (proper pixel to mm conversion) by setting the length of a reference segment.

![Figure 3. Metric measurements on the image](image)

5.4. Texture descriptors

In order to define a measure for discriminating between the cirrhotic liver parenchyma from the normal one a set texture descriptors can be used:
- Texture descriptors based on the first order gray-levels statistic: energy, entropy and mean[6];
- Texture descriptors based on the Gray Levels Co-occurrence Matrix (GLCM) - second order gray-levels statistics [7]: homogeneity, entropy, energy, contrast, variance and correlation.
- Texture descriptors based on the Autocorrelation Matrix [8]: coarseness and business.
- Texture descriptors based on fractal dimension, computed using a box-counting algorithm applied on the grayscale image of the region [9];
- Texture descriptors based on edge statistics: edge contrast and edge frequency.

All the texture features are computed in the whole ROI selected, with the exception of the fractal dimension which is computed in the biggest square of size 2^n [pixels] that can be contained in the ROI.
5.5. Results

In order to test the discrimination power of the proposed texture descriptors a set of images with HCC were used. For each image two regions of interest were defined: one inside the tumor (Fig. 4.a) and one beside the tumor (on normal tissue- Fig. 4.b), placed approximately at the same depth.

- **GLCM**: homogeneity, contrast, variance and correlation;
- Fractal descriptors: fractal dimension;
- Edge statistics: edge contrast.

6. Conclusions and Future Work

This telescreening program tries to detect the hepatocarcinoma to patients presenting risk factors for this disease and which has to be monitored during months, perhaps years. In this way, it is possible to detect early the HCC and evaluate it by an expert center that will establish the optimum method to solve each case, indicating the phases that will be followed after the diagnosis.

By direct access of imaging specialist to all data relevant to the HCC evaluation, offered by the general practitioner, the circuit between medical entities is shortening.

Having electronic patient records, allows development of an optimum structured medical database that will facilitate a through analysis of the complex multimodal medical information, facilitating development of various studies in the addressed field.

Finally, the efficiency of this system is going to be determined by following the parameters that characterize the overall state of the patients at the time they were diagnosed with HCC, stadialization in accordance to some representative criteria, carry out of the curative treatment, and establishing the survival

6. References