Intelligent Information Medical Systems

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Abstract

This paper covers briefly the work carried out by the Lab of Medical Informatics of the University of Cyprus in the last 12 years, in the development of the following intelligent information medical systems: i. Ultrasound Imaging: An Integrated System for the Assessment of the Risk of Stroke, ii. Endoscopy Imaging: A CAD System for the Assessment of Gynaecological Cancer, iii. Microscopy Imaging: Breast Cancer Biopsy image Analysis Support System (BASS) and Electron Microscopy (EM) Muscle Imaging System, and iv. m-Health e-Emergency Systems. It is anticipated that these innovative information technology solutions in computational intelligence, medical imaging, and e-health will contribute towards the offering of a better service to the citizen.

Keywords: intelligent systems, medical imaging, ultrasound, endoscopy, microscopy, emergency systems, e-health

1. Introduction

This paper describes briefly the main activities of the research work carried out by the Lab of Medical Informatics of the University of Cyprus in the last 12 years, in the context of the development of innovative computational intelligence based medical systems in medical imaging and e-emergency.

For the medical imaging analysis systems developed, these incorporated all the steps from image acquisition and preprocessing, to clustering, feature extraction, classification and decision making. This work covers the development of integrated systems in medical imaging for the processing and analysis of ultrasound images of the carotid, endoscopy images in gyanaecological cancer of the endometrium, and breast cancer biopsies. A modular neural network mutli feature/multi classifier diagnostic system including image normalisation, despeckle filtering, plaque segmentation, texture and morphological feature extraction, and neural network classification has been developed for differentiating between asymptomatic and symptomatic plaques in ultrasound imaging of the carotid for the assessment of the risk of stroke. The image normalization and feature extraction modules of this system are in pilot use in several centres in North America and Europe. Furthermore, a standardised protocol for the analysis of endoscopy images in gynaecological cancer has been proposed enabling the differentiation between

normal and abnormal endometrium, cervix, and ovary tissue. Given that there is no standardised methodology for the interpretation of endoscopy images in gynaecology; our proposed standardised protocol is at presently discussed for consideration by the European Society for Gynaecological Endosopy (ESGE) and the European Academy of Gynaecological Cancer (EAGC). Also, a modular neural network architecture has been proposed for computing automatically the histopathological score in breast cancer biopsies immunohistochemically stained.

Research work on e-Health systems, focuses in mobile health systems in emergency telematics, including the wireless transmission of biosignals and video based on error resilient techniques included in recent video standards like H.264/AVC (MPEG4-Part 10). A new system is currently under development to be installed in the Pafos General Hospital connecting the ambulance services, and the rural health centres.

The structure of the paper is as follows. In sections 2, 3, and 4, systems developed in ultrasound imaging, endoscopy imaging, and microscopy imaging are briefly described respectively. Section 5 covers the development of e-health systems in e-emergency, whereas section 6 covers the concluding remarks and future work.

2. Ultrasound Imaging: An Integrated System for the Assessment of the Risk of Stroke

Stroke is the third leading cause of death in the Western World and the major cause of disability in adults. There are indications that the morphology of atherosclerotic carotid plaques obtained by high resolution ultrasound imaging has prognostic implications. The objective of this work was to develop an integrated system which will facilitate the automated characterisation of carotid plaques for the identification of individuals with asymptomatic carotid stenosis at risk of stroke. The system is based on the following componenets: (i) despeckle filtering and normalisation, (ii) segmentation, (iii) texture feature extraction, and (iv) neural network classification.

2.1 Despeckle Filtering

For despeckle filtering, a comparative evaluation of despeckle filtering based on texture analysis, image quality evaluation metrics, and visual evaluation by medical experts, in the assessment of 440 (220 asymptomatic and 220 symptomatic) ultrasound images of the carotid artery bifurcation was carried out. A total of 10 despeckle filters were evaluated based on local statistics, median filtering, pixel homogeneity, geometric filtering, homomorphic filtering, anisotropic diffusion, non-linear coherence diffusion and wavelet filtering. The results of this study suggest that the first order statistics filter gave the best performance, followed by the geometric filter, and the homogeneous mask area filter. These filters improved the class separation between the asymptomatic

and the symptomatic classes based on the statistics of the extracted texture features, gave only a marginal improvement in the classification success rate, and improved the visual assessment carried out by the two experts [Loizou et. Al. (2005), (2006)].

2.2 Segmentation

Ultrasound measurements of the human carotid artery walls are conventionally obtained by manually tracing interfaces between tissue layers. A snakes based segmentation technique for detecting the intima-media layer and measuring the intima media thickness (IMT) of the far wall of the common carotid artery (CCA) in longitudinal ultrasound images, after normalization, speckle reduction, and normalization and speckle reduction was developed. The proposed technique utilizes an improved snake initialization method, and an improved validation of the segmentation method. We have tested and clinically validated the segmentation technique on 100 longitudinal ultrasound images of the carotid artery based on manual measurements by two vascular experts, and a set of different evaluation criteria based on statistical measures and univariate statistical analysis. The results showed that there was no significant difference between all the snakes segmentation measurements and the manual measurements [Loizou et. Al. (2007)].

Furthermore, a system was developed for the segmentation of atherosclerotic plaque in ultrasound imaging of the carotid artery. The following snakes segmentation methods were investigated: the Williams & Shah, Balloon, Lai & Chin, and the gradient vector flow (GVF) snake. The performance of the four different plaque snakes segmentation methods was tested on 80 longitudinal ultrasound images of the carotid artery using receiver operating characteristic (ROC) analysis and the manual delineations of an expert. All four methods performed very satisfactorily and similarly in all measures evaluated with no significant differences between them; however the Lai & Chin snakes segmentation method gave slightly better results [Loizou et. Al. (2007)].

2.3 Multi-Feature Texture Analysis and Classification Using Modular Neural Networks

The following different texture feature sets and shape parameters were extracted from the segmented plaque images: First Order Statistics (FOS), Spatial Gray Level Dependence Matrices (SGLDM), Gray Level Difference Statistics (GLDS), Neighborhood Gray Tone Difference Matrix (NGTDM), Statistical Feature Matrix (SFM), Laws Texture Energy Measures (TEM), Fractal Dimension Texture Analysis (FDTA), and Fourier Power Spectrum (FPS), and Shape Parameters. In addition multilevel binary and gray scale morphological features were extracted. The plaques were classified into two types: symptomatic because of ipsilateral hemispheric symptoms, or asymptomatic because they were not connected with ipsilateral

hemispheric events. A total of 274 (137 symptomatic and 137 asymptomatic) ultrasound images of carotid plaques were analysed, with the statistics of all features extracted for the two classes indicating a high degree of overlap. For the classification a modular neural network composed of self-organizing map (SOM), Probabilistic Neural Network (PNN) and Support Vector Machine (SVM) classifiers, and combining techniques based on a confidence measure were used. Combining the classification results of the different classifiers inputted with the texture and morphological feature sets, improved the classification rate obtained by the individual feature sets reaching an average diagnostic yield of 76%. The results in this work show that it is possible to identify a group of patients at risk of stroke based on texture features extracted from ultrasound images of carotid plaques. This group of patients will benefit from a carotid endarterectomy whereas other patients will be spared from an unnecessary operation [Christodoulou et. Al. (2003), (2005)], [Kyriakou et. Al. (2005)].

3. Endoscopy Imaging: A CAD System for the Assessment of Gynaecological Cancer

Within the female population, gynaecological cancer accounts for the second highest mortality rate. Early diagnosis and treatment of gynaecological cancer are essential for better quality and longer life. The development of minimally invasive surgery based on hysteroscopy, transabdominal/transvaginal laparoscopy operations have already demonstrated the advantages of endoscopic techniques. Research work is carried out, towards the development of a CAD system to facilitate the standardised differentiation between normal and abnormal tissue in endoscopy imaging.

3.1 A Standardised Protocol for Capturing Endoscopic Images

A standardized protocol in endoscopic imaging is proposed in order to eliminate significant texture feature differences due to variations in (i) the distance from the tissue, (ii) difference in viewing angles, and (iii) color correction. All images were captured at clinically optimum illumination and focus using 720x576 pixels and 24 bits color for: (i) a variety of testing targets from a color palette with a known color distribution, (ii) different viewing angles, and (iii) two different distances from a calf endometrial and from a chicken cavity. For the viewing conditions proposed in the standardized protocol, results indicate that there is no significant difference in texture features between the panoramic and close up views and between angles. For a calibrated target image, gamma correction provided an acquired image that was a significantly better approximation to the original target image. In turn, this implies that the texture features extracted from the corrected images provided for better approximations to the original images. This study provides a standardized protocol that should be followed in Computer Aided Diagnosis (CAD) systems in the assessment of gynaecological cancer of the endometrium for avoiding any significant texture feature

differences that may arise due to variability in the viewing conditions or the lack of color correction [Neophytou et. Al. (2004), (2007)].

3.2 Texture-Based Classification

The objective of this study was to classify hysteroscopy images of the endometrium based on texture analysis for the early detection of gynaecological cancer. A total of 418 Regions of Interest (ROIs) were extracted (209 normal and 209 abnormal) from 40 subjects. Images were gamma corrected and were converted to gray scale. The following texture features were extracted: (i) Statistical Features (SF), (ii) Spatial Gray Level Dependence Matrices (SGLDM), and (iii) Gray Level Difference Statistics (GLDS). The PNN and SVM neural network classifiers were also investigated for classifying normal and abnormal ROIs. Results show that there is significant difference between the texture features of normal and abnormal ROIs for both the gamma corrected and uncorrected images. Abnormal ROIs had lower gray scale median and homogeneity values, and higher entropy and contrast values when compared to the normal ROIs. The highest percentage of correct classifications score was 77% and was achieved for the SVM models trained with the SF and GLDS features. Concluding, texture features provide useful information differentiating between normal and abnormal ROIs of the endometrium [Neophytou et. Al. (2006), (2007)].

4 Microscopy Imaging: Breast Cancer Biopsy image Analysis Support System (BASS) and Electron Microscopy (EM) Muscle Imaging System

4.1 A Modular Neural Network System for the Analysis of Nuclei in Histopathological Sections

The evaluation of immunocytochemically stained histopathological sections presents a complex problem due to many variations that are inherent in the methodology. In this study a modular neural network based approach to the detection and classification of breast cancer nuclei named Biopsy Analysis Support System (BASS), was designed. The system is based on a modular architecture where the detection and classification stages are independent. The system uses two different methods for the detection of nuclei: the one approach is based on a feed forward neural network (FNN) which uses a block-based singular value decomposition (SVD) of the image to signal the likelihood of occurrence of nuclei. The other approach consists of a combination of a receptive field filter and a squashing function (RFS), adapting to local image statistics to decide on the presence of nuclei at any particular image location. The classification module of the system is based on a radial basis function neural network. A total of 57 images captured from 41 biopsy slides containing over

8300 nuclei were individually and independently marked by two experts. A five scale grading system, known as diagnostic index, was used to classify the nuclei staining intensities. The experts' mutual detection sensitivity (SS) and positive predictive value (PPV) were found to be 79% and 77% respectively. The overall joint performance of the FNN and RFS modules were 55% for SS and 82% for PPV. The classification module correctly classified 76% of all nuclei in an independent validation set containing 25 images**.** This study shows that the BASS system simulates the detection and grading strategies of human experts and it will enable the formulation of more efficient standardization criteria, which will in turn improve the assessment accuracy of histopathological sections [Schnorrenberg et. Al. (1996), (1997), (2000)].

4.2 AM-FM Texture Segmentation in Electron Microscopic Muscle Imaging

Beyond the fixed-scale limitations of Wavelet techniques, Amplitude Modulation - Frequency Modulation (AM-FM) models allow continuous-scale analysis of texture images. In AM-FM representations, variations in the frequency content are modelled by an instantaneous frequency vector field which can dramatically change from pixel to pixel. Variations in contranst in the image are modeled as ampltitude modulation. The new AM-FM models provide a powerful new technique for non-stationary texture analysis. This work investigated the application of an AM-FM image representation in segmenting electron micrographs of skeletal muscle for the recognition of: (i) normal sarcomere ultrastructural pattern, and (ii) abnormal regions that occur in sarcomeres in various myopathies. A total of 26 electron micrographs from different myopathies were used for this study. It is shown that the AM-FM image representation can identify normal repetitive structures and sarcomeres, with a good degree of accuracy. This system can also detect abnormalities in sarcomeres which alter the normal regular pattern, as seen in muscle pathology, with a recognition accuracy of 75 to 84% as compared to a human expert [Pattichis et. Al. (2000)].

5. m-Health e-Emergency Systems

The provision of effective emergency telemedicine and home monitoring services are the major fields of interest discussed in this study. Ambulances, Rural Health Centers (RHC) or other remote health location such as ships navigating in wide seas are common examples of possible emergency sites, while critical care telemetry and telemedicine home follow-ups are important issues of telemonitoring. In order to support the above different growing application fields we developed a combined real-time and store and forward facility that consists of a base unit and a telemedicine (mobile) unit. This integrated system can be used when handling emergency cases in ambulances, RHC or ships by using a mobile telemedicine unit at the emergency site and a base unit at the hospital-expert's site. The system allows the transmission of vital

biosignals (3, or 12 lead ECG, SPO2, NIBP, IBP, Temp) and still images of the patient. The transmission is performed through GSM, GPRS, or UMTS mobile networks, through satellite links or through Plain Old Telephony Systems (POTS) where available. Using this device a specialist doctor can telematically "move" to the patient's site and instruct unspecialized personnel when handling an emergency or telemonitoring case. The performance of the system has been technically tested over several telecommunication means; in addition the system has been clinically validated in three different countries using a standardized medical protocol [Kyriakou et. Al. (2003), (2007)], [Pattichis et. Al. (2002)].

6. Concluding Remarks and Future work

A brief outline of the work carried out by the Lab of Medical Informatics of the University of Cyprus in the last 12 years, in the context of the development of innovative computational intelligence based medical systems in medical imaging and e-emergency was presented. This work will be continued in the corresponding future research directions that are briefly outlined below:

Ultrasound Imaging: This work will focus on the computation of motion trajectories in ultrasound videos of atherosclerotic plaques. Preliminary results indicate that motion trajectories follow the cardiac cycles, forcing motions from different parts of the plaque and arterial walls to appear in phase. Based on the periodicity of the motion, we found that a Fourier series, using a small number of harmonics, can approximate the periodic motion due to the cardiac motion cycle. Furthermore, plaque motion exhibited larger deviations and more abrupt changes than arterial wall motion [Murillo et. Al. (2006)].

Endoscopy Imaging: Research work will be expanded to investigate the automated segmentation of hysteroscopy imaging of the endometrium, cervix, and ovary, and the subsequent texture analysis and differentiation between normal and abnormal tissue. Furthermore, a 3D reconstruction of the endometrium volume with ROI annotation will be investigated. This will allow the gynaecologist to navigate through the reconstructed organ and investigate further the tissue geometry and texture.

Microscopy Imaging: A new biopsy image analysis support system based on active contours, formulated using the level set method, is being developed that will be applied to estimate the intensity of steroid receptors in cell nuclei, in sections from breast cancer biopsies, that have been labeled immunohistochemically. Steroid receptors provide important prognostic information which is necessary for managing breast cancer patients and for tailoring individual treatment. These findings will be

combined with clinical and pathological data in order to define more accurate models for predicting survival rates.

m-Health e-Emergency Systems: Growing demand for mobile and wireless e-Health e-Emergency applications supporting video streaming, has led into exploring different ways of providing satisfactory quality content to the expert physician. Given the error prone nature of these environments, the presence of these errors must be somehow concealed. Towards this direction, our effort will be focused on exploring numerous error resilience techniques developed over the past few years as these are standardised into video coding standards such as H.264/AVC-MPEG-4 part 10. Video coding standards incorporate a plethora of encoder-based error resilience techniques and decoder-based error concealment ones. In these systems, the availability of a back communication channel between the encoder and the decoder can help tackling error control more effectively as the codec can adapt to channel conditions. These technologies will be evaluated for the provision of QoS in the transmission of ultrasound video as well as video of the patient in emergency scenery [Kyriakou et. Al. (2007)], [Pattichis et. Al. (2006)], [Rodriquez et. Al. (2006)].

Concluding, it is anticipated that this research will continue the development of innovative information technology solutions in computational intelligence, medical imaging, and e-Health for the benefit of the citizen.

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