UNIVERSITY OF MEDICINE AND PHARMACY OF CRAIOVA
PHD SCHOOL

PhD THESIS
DIAGNOSTIC ROLE OF WIRELESS CAPSULE ENDOSCOPY IN CORRELATION WITH SOFTWARE APPLICATIONS IN THE PATHOLOGY OF THE SMALL BOWEL

-ABSTRACT-

Scientific coordinator:
Prof. Univ. Dr. VERE CRISTIN CONSTANTIN

PhD student:
CONSTANTINESCU ADRIANA FLORENTINA

CRAIOVA
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INTRODUCTION

The small intestine is the longest segment of the digestive tract, being difficult to investigate due to its anatomical features and localization. Several exploration methods have been used to examine the small intestine, but these are either too invasive or do not provide sufficient information to establish the correct diagnosis.

Wireless capsule endoscopy is the most widely used method of investigation of the small intestine with a higher diagnostic accuracy than other techniques for assessing its pathology. The rich information content offered by this examination technique is both an asset through the complete exploration of the intestinal mucosa and a disadvantage through the relatively long time of about 2-4 hours required by the examiner to visualize and analyze all the images captured by the videocapsule. Another disadvantage may be represented by the size of a lesion, which may be very small compared to the bowel region present in that image, or may be incompletely captured, thus being difficult to detect and analyze. The small number of successive frames in which a lesion can be seen is also a disadvantage, the lesion being omitted by the examining physician, especially if the images are continuous, such as in a film, and not frame by frame.

Computer-assisted diagnostic software could counteract these drawbacks by optimizing analysis time, by automatically segmenting the images recorded by the capsule and by identifying potential lesions present within these images.

Key words: small bowel pathology, wireless capsule endoscopy, software applications.

PART I – PRIOR KNOWLEDGE

The small intestine is the longest segment of the digestive tract, being comprised between the pylorus and the ileocecal valve.

Due to the anatomical features, the small intestine is relatively difficult to investigate from the imaging point of view. The main imaging exploration techniques of the small intestine are radiographs, computed tomography (CT), ultrasound, nuclear magnetic resonance (MRI), enteroscopy. Wireless capsule endoscopy (WCE) is another modern method of examination of the small bowel, being non-invasive and one of the main exploration techniques for this segment of the digestive tract.

Diverticulitis, Crohn's disease, celiac disease, intestinal tuberculosis, benign or malignant tumors and obscure gastrointestinal bleeding are the major pathological diseases of the small intestine.

The first endoscopic videocapsule, called Pillcam M2A, was launched in 2001 in Yokneam, Israel by Given Imaging. In that period, first clinical trials on human subjects were also carried out. The capsule endoscopy system consists of a small device comprising a recording sensor, a lens system, a radio antenna and an integrated circuit, a recording device that stores the images acquired by the endoscopic capsule through the electrodes attached to the patient abdomen, as well a computerized interface that uses a software application to play back the recorded frames. The investigation with wireless capsule endoscopy requires patient informal consent and a previous bowel preparation to improve the clarity of recorded images and, implicitly, the precision of the diagnosis.

The endoscopic videocapsule has a wide field of clinical indications, the diagnostic evaluation of obscure gastrointestinal bleeding being the most important of these.

The absolute contraindication of endoscopic capsule administration is the digestive stenosis, which could cause the capsule obstruction at a certain segment of the gastrointestinal tract, but this can be prevented by using the capsule patency.

Wireless capsule endoscopy is a modern method of examination of the small intestine, which has the advantages of being minimally invasive, painless for the patient, without requiring sedation, unlike the upper and lower digestive endoscopy, which cause a significant degree of discomfort to the patients during their deployment. One of the main disadvantages of this investigation is the long time necessary for the visualization and the analysis of all WCE frames.

The difficulties encountered in fully visualizing and analyzing WCE films have led to the development of software applications for the automated analysis of the WCE frames and also to provide support in the identification and classification of the intestinal lesions, in particular to the young doctors with a reduced experience. Software applications used in correlation with videocapsule endoscopy may contribute to the reduction of the amount of information, artifacts detection, identification and classification of the intestinal lesions and, implicitly, can reduce the time needed for the examiner for the interpretation of the WCE frames.

PART II – PERSONAL CONTRIBUTIONS

1. Aim and objectives of the research

The purpose of this study, by using capsule endoscopy in correlation with software applications, is to analyze the reduction of the necessary time to the examiner for the interpretation of the recorded images by indicating the frames with potential lesions and classifying them with a certain probability and also to provide support in diagnosis.

The major objectives of such a software application whose aim is to automatic detect the small bowel lesions from a video recorded by the endoscopic capsule are represented by:

- the ability to capture as input a WCE video and subsequently provide as output a set of images illustrating a single lesion of the examined segment from one or more perspectives associated with a possible classification;
- the complete and rapid analysis of the entire set of frames provided by the endoscopic capsule through comparisons of certain parameters;
- the inclusion of several imaging processing techniques to highlight certain features implemented as individual modules with well-defined functions;
- the possibility of integration with other software applications specific to other examinations techniques, thus aggregating the results of several investigations performed to the same patient, so that the accuracy of the final diagnosis to be greater.

2. Lot and methods

2.1. Lot

The study included 75 patients within the Gastroenterology department and within the first Internal Medicine department of the Emergency Clinical County Hospital of Craiova.

The patients were included in the study group after a rigorous selection based on a previously established study protocol. The study has been conducted after obtaining the approval of the Ethics Committee of the University of Medicine and Pharmacy of Craiova in accordance with the Helsinki Declaration. All patients included in the study expressed their informed consent

by signing the consent information and acceptance forms, regarding the endoscopic capsule administration and the use of the anonymous results.

2.2. Methodology and research algorithm

Prior to endoscopic capsule administration, all patients were investigated biologically and by using conventional endoscopic techniques, respectively, by the upper and lower digestive endoscopy, but these investigations were inconclusive.

The preparation for the capsule endoscopy administration was similar with the one for the inferior digestive endoscopy, assuming a time of at least 12 hours of fasting and administration of macrogol solution with 12-16 hours before capsule ingestion, for improving the quality of the recorded images. At the end of the investigation, the recording device was taken and connected to the work station for downloading the recorded images.

After the images were downloaded on the computer, the study was divided into 2 phases. WCE videos have been fully viewed for all patients included in the study group, both in proprietary and exported formats, by the examiners, with the EndoSoftware.

The first phase of the study consisted of manual analysis of the entire set of frames in order to detect potential lesions of the small intestine. At the end, the examiners physicians noted all the frames with intestinal lesions for their subsequent comparison with those detected by the software application. The automatic lesion detection system was developed within the Research Center of Gastroenterology and Hepatology in Craiova, Romania, based on an artificial neural network (ANN) for the identification of intestinal lesions and on the local binary pattern operator (LBP) for the detection of angiodisplasias.

The second phase, realized with the software application, involved the pre-processing of the original frames from the analysis set, before being subjected to the classification algorithm. At the end of the two phases, the frames identified with intestinal lesions by the examiners physicians were compared with those detected by the software application in terms of the specificity, sensitivity, positive predictive value (PPV), and negative predictive value (NPV).

Given that the predominant pathology of the patients included in the study group was represented by the intestinal polyps and by the angiodysplasia, we conducted two studies in order to highlight the diagnostic contribution of the endoscopic videocapsule in correlation with the software application in identifying these lesions, preceded by a study to highlight the optimization of the necessary time to the examiner to analyze WCE videos.

2.3. Statistical analysis of the data

The statistical analysis of clinical research data was performed using the Microsoft (MS) Excel program for the descriptive statistics and with GraphPad Prism 6.0 (GraphPad Software Inc., LaJolla, CA) for the analysis of the images sets with intestinal polyps and with angiodysplasia from the last two studies performed.

3.Results

3.1. Medical results

The individual characteristics of the patients included in the study group were centralized according to gender, age, background, WCE clinical indications, symptomatology, identified intestinal lesions after the endoscopic capsule ingestion and according to the number of frames recorded.

3.2. Diagnostic role of wireless capsule endoscopy in correlation with software applications in optimizing analysis time of the WCE images

For each of the 75 patients included in the study group, we registered the analysis time both for the examiners (considered as the average time of the 4 physicians) and for the software application; the value of the time was expressed in minutes to facilitate subsequent statistical operations.

In doctors' case, it was obtained an average time of 218 minutes, equivalent to 3 hours and 38 minutes, with a minimum of 137 minutes and a maximum of 270 minutes. In case of software application, it was obtained an average time of 103 minutes, equivalent to 1 hour and 43 minutes, with a minimum of 76 minutes and a maximum of 145 minutes.

According to the data for each patient included in the study group, the software application brought in average an improvement of 52.75% of the analysis time, as compared with the time obtained by doctors.

Subsequently, we also performed the statistical analysis of the recorded data, resulting the fact that there is no correlation between the doctors' time and the software application' time for the same video ($P > 0.05$), although the imaging analysis is very similar.

We also did not determine any correlation between the time obtained by doctors or the application and the number of frames composing the WCE video ($P > 0.05$), which is explained strictly through the relevance of the imaging content of the videos.

3.3. Diagnostic role of wireless capsule endoscopy in correlation with software applications in identifying intestinal polyps

This study was performed on a smaller group of eight patients who presented polyps in the small intestine. Of patients with polyps, two patients had duodenal polyps, while jejunal and ileal polyps were identified in two and respectively six patients. Two of the patients from this smaller group were identified with more polyps, one of them had duodenal and ileal polyps and the other, jejunal and ileal. All polyps identified had normal surface area.

After the examiners' manual analysis of all the images recorded, we obtained the following results: sensitivity 94.79%, 93.68% specificity, 89.22% positive predictive value and 97.02% predictive negative value. After automatic analysis of all the images from the test set, the contour detection phase showed an accuracy of 97.68% in detecting and approximating pixels. Concerning the final classification, the automatic lesion detection system obtained almost similar results compared to human interpretation: 93.75% sensitivity, 91.38% specificity, 85.71% PPV and 96.36% NPV.

The system correctly detected 30 lesions as being polyps, only two polyps being omitted. At the same time, five intestinal folds partially present in some images were defined as polyps, based on their elliptical contours similar to polyps.

The differences between the automated lesion detection system and the classification of the polyps from the small bowel by examiners were not statistically significant from the point of view of specificity and sensitivity, as the value of P was greater than 0.05.

3.4. Diagnostic role of wireless capsule endoscopy in correlation with software applications in identifying angiodysplasia

This research study was conducted on a smaller group of 24 patients diagnosed with angiodysplasia in the small intestine after the administration of capsule endoscopy.

The sensitivity and specificity obtained by the examiners in the detection of the angiodysplasias were 97.33% and 98.84% respectively, and the positive and negative predictive

values were 98.42% and 98.02%, respectively. For software application, sensitivity was 94.67%, specificity 97.00%, positive predictive value 95.95%, and negative predictive value 96.04%.

The system correctly detected 142 lesions as angiodysplasias, only 8 lesions being omitted. At the same time, 6 normal areas were defined as lesions, based on their similar color to angiodysplasia.

4.Discussions

Several research studies in the literature have compared WCE with other methods of investigation of the small intestine, illustrating a higher efficacy of videocapsule compared to these.

Wireless capsule endoscopy, as any other investigation, besides advantages also has some disadvantages. Some of these are represented by the impossibility of taking biopsy and performing therapeutic maneuvers, as well as by the long time necessary to the examiner for the visualization and the analysis of the WCE videos.

Our research has been focused on optimizing the analysis time of images recorded by WCE, as well as on the diagnosis role of wireless capsule endoscopy in correlation with the software application in the identification of polyps and angiodysplasia of the small intestine.

Most software applications process color, texture and shape. These also represent the foundation of WCE images global analysis, reflecting the main elements analyzed by human physicians. Other supplementary features like rotation, relative location between two consecutive frames, partial contours detection or movement speed complete the physical features of each analyzed frame.

The most important visual feature in our research study regarding intestinal polyps detection was represented by the shape. By using certain contour detection methods, it is possible to miss polyps' margins, or to detect them only partially, with the risk of not corresponding to the real contours. Despite these drawbacks, there are methods useful in detecting the contours of intestinal polyps, with a low false negative rate.

Through this research study, we have highlighted the contribution of using a computer-assisted diagnosis system based on shape and texture for the correct classification of intestinal polyps. Our algorithm was based on the detection of optimal morphological characteristics to be converted into characteristic vectors, followed by the use of neural networks for lesions' classification.

Also, the computer aided diagnosis system has contributed in shortening the necessary time for establishing the diagnosis by at least 50%, thereby facilitating the diagnosis in a correct and earlier manner.

The third research study regarding the diagnosis role of capsule endoscopy in correlation with the software application for angiodysplasia' identification, based on the local binary pattern operator, showed that the computer aided diagnosis system may shorten the required time for the visualization and analysis the WCE videos, and, implicitly, the diagnosis time.

The comparative study of the results obtained by the physicians and the software application after the interpretation of the recorded frames with endoscopic capsule to the entire lot of patients, allowed us to identify the software applications' contribution generally made to both in terms of the time optimization of analysis and in defining a conclusive diagnosis. Also, software applications may have a didactic role in supporting less experienced physicians in the field, as well in highlighting key elements in the analysis of a video. As a potential direction for the future, I mention setting all the features of the elements present in the frames recorded by the

videocapsule, for the implementation of new modules potentially acting as a generator of new lesions.

5.Conclusions

- Iron deficiency anemia and obscure gastrointestinal bleeding were the main clinical indications of patients with WCE, being found at 58 patients and respectively, at 77% from the total number of the patients.
- The most common small bowel lesions in the patients included in the study group were represented by angiodysplasias, in 32% of patients, and by polyps, present in 10.67% of the cases.
- Four patients from the research group presented multiple lesions in the small intestine, three of whom were diagnosed with polyps and angiodysplasia, and another with angiodysplasia and diverticulum.
- The software application obtained an average improvement of the time required for the interpretation of each video of 52.75%, in comparison with the time taken by the examiners.
- There is no correlation between doctors' and application analysis times, although the imaging analysis process is relatively similar in structure and organization ($P > 0.05$).
- There is no correlation between doctors' or application analysis times and the number of frames from a WCE video, so time optimisation is not dependent on the length of the movie ($P > 0.05$).
- The analysis time for the software application is dependent on the level of accuracy in the detection of lesions; depending on availability, examiners may choose different values, obtaining a shorter or longer time.
- The automatic detection system for intestinal lesions has obtained results almost similar to the physicians' in the detection of the polyps , the sensitivity and specificity being 93.75% and 91.38% for the software application, and for the examiners 94.79% and 93, 68%.
- Both predictive positive and negative predictive values obtained by the software application in polyps detection were similar to those of the examiners, being 85.71% and 96.36% for the software application, respectively 89.22% and 97, 02% for the doctors.
- The software application detected the contour of the polyps present in the frames from the study group with an accuracy of 97.68%.
- The average reduction of the number of the non-informative frames present in each WCE video from the research study was 7.02%.
- The software application obtained similar results to those of the physicians in the identification of angiodysplasias, respectively 94.67% sensitivity and 97% specificity.
- As in the case of polyps, the software application obtained similar results to those of the examiners in the detection of angiodisplasias in terms of positive predictive value and negative predictive value, respectively 95.95% and 96.04%.

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