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**ASSESSMENT OF NEW TELEMEDICINE INSTRUMENTS  
BUILT FOR DIAGNOSIS AND PATIENT'S MONITORING**

Ph. D. Thesis Abstract

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**Key words:** *telemedicine, IT instruments, artificial intelligence, questionnaire*

## **I. STATE OF KNOWLEDGE**

The term telemedicine is not very specific. In 1997, the World Health Organization defined telemedicine as “the delivery of health care services, where distance is a critical factor, by all health care professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and evaluation, and for the continuing education of health care providers, all in the interests of advancing the health of individuals and their communities”.

The first telemedicine census was conducted in 2012 and found out that almost half of the hospitals in the United States had similar programs. These desires to expand medicine are necessary to keep pace with developments and requirements, but also to offer major benefits by lowering costs, patient-centered medicine with multiple interactions, providing quality medical services through access to medical services provided by certain experts at the right time.

The use of telemedicine also offers many challenging parts, because before it becomes a common practice, certain barriers must be overcome. Most uses so far focus on a limited number of patients and so we do not know how it will translate into the daily use, how all patients will view this type of development and the associated costs. It is not yet clear what ways to quantify telemedicine can be used.

### **1.1 Approach in inflammatory bowel disease**

Inflammatory bowel disease is a group of chronic diseases that include Crohn's disease (CD) and ulcerative colitis (UC), which affects about 3.1 million Americans. The incidence of IBD is increasing globally, being frequently diagnosed at an early age.

In the 21<sup>st</sup> century, technology has evolved considerably, and this has led to the desire to integrate new technologies into our medical practice. Thus, there has been an increase in interest in telemedicine and remote monitoring of patients with chronic diseases. Telemedicine has been defined by the American Telemedicine Association as a "technological system for health management". Telemedicine includes several forms, including remote patient monitoring, telehealth,

teleconsultations and mobile applications. A study on the use of telemedicine in IBD demonstrated the safe and effective delivery of care, high patient acceptance, improved levels of patient education, adherence and quality of life.

## **1.2 Artificial intelligence**

Artificial intelligence (AI), along with its Machine Learning (ML) and Deep Learning (DL) subdisciplines, emerge as key technologies in healthcare, with great potential to change lives and improve the situation of patients in many fields of medicine. Healthcare projects, especially AI projects, have attracted greater investment than in any other sector of the global economy. In 2018, it is estimated that \$ 2.1 billion has been invested in AI-based products, and the growth is expected to reach \$ 36.1 billion by 2025.

The innovation opportunities offered by AI have been widely discussed in the medical literature. Backed by the ability to learn remarkably large volumes of medical data, an AI system can help clinicians by interpreting diagnosis, prognosis, and therapeutic data from very large patient populations, providing real-time guidance on the risks, options, and outcomes of care, but also provides up-to-date medical information from medical journals, manuals and clinical practices to support proper patient care [39]. By combining access to such vast knowledge, an AI system can help reduce diagnostic and therapeutic errors that are inevitable in conventional, everyday human practice.

Given the widespread application of AI, methods based on computational pathology, it is worth considering the status of art in deep learning and the potential evolution of technology in the future. Although many of these are developed and proven in areas other than pathology, the field progresses and through continuous improvement will increase the ability to be used in computational pathology.

Current interpretation of histopathology images includes the detection of tumor patterns, Gleason gradation and a combination of notations in a Gleason score, which is essential in determining the clinical outcome. The higher the degree of Gleason and the more prominent the biopsy pattern, the more aggressive the cancer, the more likely it is that the disease has metastasized. Gleason grading is not only

time consuming, but is also prone to erroneous variation. Cellular and tissue imaging have long been proposed as a quantitative tool in assessing the degree of prostate cancer. However, this has been limited by the technology and accuracy of imaging algorithms. More recently, several research teams have proposed the use of AI-based technologies for the automatic analysis of prostate cancer as a means of accurately detecting prostate cancer patterns in tissue sections and also to objectively assess disease.

## **II. SELF CONTRIBUTIONS**

### **WORKING HYPOTHESIS AND GENERAL OBJECTIVES**

This thesis aims to provide an alternative to the current status of telemedicine in Romania through a multidisciplinary approach in order to identify certain particle situations that will facilitate the use of such techniques in the future. The objectification of certain situations, adapted and individualized to patients and their conditions confirms the implementation of alternative approaches and successfully achieves the combination between current available technologies and medicine.

The paper addresses three different aspects of telemedicine and tries to provide an overview of its use in current practice. The three studies conducted in the doctoral program combine different particular technological situations, whether we are talking about creating a monitoring platform, using artificial intelligence technologies for rapid diagnosis and even personal interpretation of patients and their satisfaction in remote consultations.

- **Optimization of targeted therapy in patients with inflammatory bowel disease by remote monitoring**
- **The use of neural networks in the diagnosis of prostate cancer**
- **Assessing patient satisfaction by using telemedicine as a method of interaction**

## **2.1 Optimization of targeted therapy in patients with inflammatory bowel disease by remote monitoring**

### 2.1.1 Aim

Under the auspices of RCCC (Romanian Club of Crohn's and Colitis) we proposed the development of a new software for collecting medical data of patients with IBD, according to STRIDE recommendations, in order to have continuous access to their evolutionary history and all therapeutic aspects. The major objective was to create a platform that allows remote monitoring of patients with IBD, an important aspect for the attending physician with a positive clinical, economic and evolutionary impact for the patient with IBD.

### 2.1.2 Materials and methods

Because this platform is addressed to all doctors in Romania, one of the objectives was to create a dedicated field for each doctor, by creating an interface for individual connection. Thus, each doctor had access only to the patients he monitors. Therefore, the design of this platform was based on a client-server architecture, with the client being represented by the attending physician and the server, represented by the back-end system.

#### *Software*

It was an open-source based on a Qt 5.3 platform (Qt Company Ltd, Finland, 2014.). The user interface was easily created and the design could be achieved both in terms of security and connectivity. The “hypertext preprocessor - PHP” language was used to allow connectivity on several platforms, being the one also used for websites. It includes components in which databases interact and provide protection against certain cyber attacks, such as SQL - structured query language which is a technique used to exploit a server's data.

### 2.1.3 Results and discussions

***IT tool for the implementation of targeted treatment in medical practice***

The complexity of IBD has led to the need for a complete management in which the clinical, psycho-social, environmental and even economic components have very important roles. One possible solution is to develop and implement a technological tool for collecting, aggregating and calculating all available medical data for patients with IBD, in order to obtain an overview and clear them over time.

Thus, this IT tool was designed in order to fill the technological gap in IBD management in Romania being represented by an online platform implemented under the directives of RCCC (Romanian Club of Crohn's and Colitis).

The aim was to create a new monitoring method by creating a new environment, including clinical and non-clinical elements. Remote communication has facilitated the implementation of these methods much easier and thus the generation of statistical data can influence the decision of the attending physician regarding the therapeutic approach over time. Being a chronic disease with unpredictable evolution that can be influenced by various events, the supervision of patients who cannot benefit from the conditions of presentation at a routine examination, can be overcome by close doctor-patient communication in order to provide targeted treatment.

## **2.2 The use of neural networks in the diagnosis of prostate cancer**

### **2.2.1. Aim**

Our goal was to develop a learning algorithm capable of recognizing histological images with high accuracy according to the GGS score. The involvement of telemedicine through pathological digital analysis of GGS and the use of computerized medical diagnostic (CAD) systems can provide an alternative for rapid and remote diagnosis.

### **2.2.2 Materials and methods**

For the histopathological study of brain lesions, brain fragments were collected from the injured and perilesional areas which were fixed in 10% neutral formalin solution and included with paraffin, according to the usual histological procedure.

For the immunohistochemical study, we used the following antibodies: anti-CD68 (clone KP1, 1/100 dilution, Dako) to highlight the macrophage reaction, including brain microglia; anti-glial fibrillated acid protein (GFAP) (clone ab7260, 1/150 dilution, Abcam) to highlight the microglia reaction.

Two study algorithms were developed using data transfer from AlexNet and GoogleNet networks. AlexNet is a convolutional neural network that has been tested on more than one million images in the ImageNet database available for free at <http://www.image-net.org>. GoogleNet is a convolutional neural network with 22 levels, also tested on ImageNet. The network also classifies images into 1000 categories of elements such as AlexNet.

### 2.2.3 Results and discussions

This study included 439 images obtained from 83 patients who were diagnosed with prostate cancer following a total prostate resection between January 2013 and December 2015 at the Cluj-Napoca Municipal Clinical Hospital, Romania. All presumptive diagnoses resulted from a combination of clinical and imaging data and were confirmed by anatomopathological examination. It was found that of the 29 deaths caused by head injuries, 20 (68.96%) were the result of car accidents.

The differences between the accuracies resulting from multiple tests of the stochastic algorithm require a calculation of the standard deviation (SD) of the ACC obtained. The model is suitable if the deviation value is low.

Before performing different statistical tests it is necessary to verify the distribution of the sample data. If the data do not show a normal distribution, the results may change due to the existence of extreme values. The Kolmogorov-Smirnov and Shapiro-Wilk W tests were used in this study.

After 100 tests for ACC, the value of the standard deviation was  $61.17 + 7$  and  $60.90 + 7.4$  for AlexNet and GoogleNet, respectively.

The algorithm resulting from the AlexNet network was introduced in a standalone application (Microsoft Windows) capable of recognizing new sets of

images, transferring information from different networks and classifying new images.

Digitized microscopic images of prostate cancer, classified as Gleason 2 and 5 models, were used in this study. This study demonstrated the feasibility of DL in terms of medical classification regardless of network architecture, using AlexNet or GoogleNet, which produced comparable results.

An increased risk of progression was demonstrated regardless of the stage and margins of resection in the case of the Gleason 4 + 3 score ( $P < 0.0001$ ). It is also considered that the risk of progression at 5 years for the Gleason 3 + 4 score was 15% and for 4 + 3 tumors 40%. There is a high classification error rate between model 3 and model 4. Therefore, AlexNet mislabeled five images as model 3, although they corresponded to model 4 and eight images as model 4, although they belonged to model 3. GoogleNet framed incorrectly nine images of model 4 as model 3, and ten images of model 3 as model 4. This represents 25% of the total classification errors of AlexNet and GoogleNet networks. These errors are primarily due to the fact that the classification system was tested using subjectively labeled images by pathologists and secondly due to a problem of the GGS system with high inter-observer variability between these categories.

### **2.3 Assessing patient satisfaction by using telemedicine as a method of interaction**

#### 2.3.1 Aim

The aim of this study was the use of telemedicine as a method of communication and monitoring of NAFLD for a limited period in order to monitor the level of patient satisfaction and implicitly following the indications of the attending physician.

#### 2.3.2 Materials and methods

The study was retrospective, being carried out for a period of 1 year within the Clinical Emergency County Hospital of Craiova, starting with 01.01.2016. During this interval, the data obtained by selecting the hospitalization files by emergency or by transfer from the other hospitals in Dolj County in the first 12 hours after the injury, the discharge sheets and the statements of the patients diagnosed with CBT were analyzed.

Patients aged 20 to 70 years with diffuse hepatic steatosis initially assessed by ultrasound or computed tomography were included.

We used MRI spectroscopy as a reference method for the diagnosis of NAFLD, a technique validated internationally and which can thus replace liver biopsy puncture.

We proposed the development of a questionnaire to assess the level of satisfaction of patients with NAFLD monitored within the Research Center in Gastroenterology and Hepatology, especially from the perspective of teleconferencing monitoring.

The questionnaire was based on 15 items that were based on interpersonal communication, care, medical approach and medical knowledge. Then we aimed to scale the items with a score from 1 to 5 with 1 representing the lowest value and 5 the highest.

### 2.3.3 Discussions and conclusions

The 15 items included in the questionnaire were arranged in 3 groups according to the initial premise. Group I the level of quality of the medical act, the similarity with the face-to-face meeting, the perception of the interaction.

The internal consistency of the questionnaire was 0.92, which indicates an important correlation between 15 items used. For new tests or questionnaires performed, an internal consistency above 0.7 is considered important for validation.

The intra-class correlation coefficient was used to determine the degree of correspondence between the obtained values, being considered a more rigorous approach than the internal consistency. The value obtained was 0.41 which is considered appropriate for the situation, because telemedicine is a relatively new approach in medical research. In the early stages of a research, a low reliability coefficient is considered appropriate.

The three selected components or factors explained 68% of the variation in patient satisfaction. The rotating matrix factor revealed that all elements on a single factor were greater than 0.3, which is accepted as being within the standard level for assigning a particular single-factor element. Elements 5, 7, 8, 10, 11, 13, 14 and 15

were loaded on factor I. Elements 1, 2, 3, 4 and 9 loaded on factor II. Element 6 loaded on factor III. Factor I, called "Quality of Care Provided," contained elements related to the provision of health care, accessibility, reliability, and care. Factor II was called "The resemblance to a consultation in reality. Factor III extracted elements involving telemedicine communication and was called "Perception of interaction".

The Pearson correlation coefficient was calculated to determine the relationship between the level of satisfaction and the biological constants, especially AST as well as adherence. The results showed that there was a positive correlation between the questionnaire and adherence ( $r = 0.51$ ,  $p < 0.05$ ). Telemedicine can stimulate patients to support the indicated regimen and lifestyle, a fact suggested by the two sessions. This can encourage the interaction between the patient and the doctor, and consequently will increase compliance, even if the interaction is done remotely.

### **3. Conclusions**

- Telemedicine is a major option for current medicine, both through the challenges of society, but also to maintain continuous progress;
- The concept of telemedicine offers advantages both to patients by avoiding travel to the medical unit or by contact with certain experts in the field, but also to medical staff or by communicating with other medical staff and developing knowledge, monitoring and treating patients, and by managing a diagnosis or complex treatment;
- Based on the experience of using the software and the good results obtained later, we could claim that this IT application is a valuable tool for the clinician, providing him with a quantity of essential medical data covering STRIDE recommendations, in minimum time, without effort, in a friendly virtual environment. It has also been shown that the use of software for a T2T approach has had a positive impact on the clinical and economic outcomes centered on the patient with IBD. Objectives such as better adherence and adherence to treatment, patient involvement in therapeutic management and increased quality of life are easy to achieve with an IT solution that provides all the data needed to reach the window of therapeutic opportunity;

- Due to an accuracy of  $61.17 \pm 7$  in the case of the AlexNet network and  $60.90 \pm 7.4$  for GoogleNet and a small data set of 439 cases distributed asymmetrically in 4 GGS classes, the result seems to be promising;
- The questionnaire in this paper was developed to assess patient satisfaction with telemedicine care;
- The three major factors identified in the study were correlated with one of the most significant predictors of patient satisfaction in telemedicine, namely the ability to meet patients' needs;
- The Pearson correlation coefficient was calculated to determine the relationship between the level of satisfaction and the biological constants, especially AST as well as adherence. The results showed that there was a positive correlation between the questionnaire and adherence ( $r = 0.51, p < 0.05$ );
- The questionnaire is a preliminary process and a tool for measuring patient satisfaction through telemedicine.

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