An Introduction and Survey of Computer-aided Detection/Diagnosis (CAD)

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ABSTRACT: This paper brielyfly outlines the basic concepts of computer-aided detection/diagnosis (CAD), including some fundamental techniques used in CAD system. Commercial CAD products and several ongoing CAD projects are also described in the field of medical image processing. The data presented at the special IFCSTA 2010 session on the "state-of-the-art of CAD" are summarized in this report, with information on the topics related to the latest technological developments and applications of CAD, which include 3D torso and lung computed tomography (CT) imaging, hepetic magnetic resonance (MR) and CT imaging, torso FDG-PET (positron emission tomography) scanning, and fundus photography.

KEYWORDS: computer-aided detection/diagnosis (CAD), medical imaging, image processing and analysis

I. Introduction

With rapid technological development in the fields of medicine and computer science, an "electronic doctor" does not seem to be a far-fetched possibility. Electronic doctors will be soon or later available in our real life, and will impact the traditional diagnosis methods. The introduction of computer-aided detection/diagnosis (CAD) in the field of medicine is not a new concept. Ledley and Lusted [1] described their early symbolic logic and probability theory that facilitated diagnoses similar to those speculated by physicians' complex reasoning in 1959. Since then, there have been many improvements in the scope, methods, and capabilities CAD systems. However, many limitations of CAD systems in the fields of medicine and computer science hinder their application in clinical practice. Since the late 1980s, there has been tremendous advancement in information science and medical imaging technology, and the calculating ability of computers and quality of medical digital imaging have improved; this has facilitated the widespread use of CAD systems. Particularly, in the late 1990s, few CAD schemes were used commercially indicating the beginning of a new era of CAD.

What is CAD: CAD is a technique that can help radiologists accurately interpret images and identify potential findings to avoid incorrect interpretation or overlooking of lesions due to subjective judgment. It should be noted that the CAD system can only provide a second opinion and cannot replace radiologists; hence, the final diagnosis must be made by human beings.

What are the components of CAD - hardware and software: Images derived from computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), X-ray radiography, ultrasound imaging, fundus photography, etc., which may be in the form of 2-D or 3-D (sometimes 4D), can be analyzed using the CAD system. Not all data from these imaging modalities can be obtained in digital formats. Some radiological devices such as CT and MRI output digital images directly. In case of X-ray radiographs (films) such as mammograms they must be converted into digital images by using a digitizer. Recently, with the use of computed radiography (CR) and flat panel detector (FPD), digitizing images are not required; this will reduce the time required for intervention by humans and hence improve the efficiency of diagnosis. One important factor for the hardware in the CAD system is the diagnostic time during inspection. Both patients and doctors would obviously avoid computer-based analysis if it requires more time than that required by the usual conventional method. The CAD system requires a super computer workstation with powerful calculating capability. Nowadays, the speed of a CPU in a personal computer is over 3 GHz, which is hundred times more than that of CPUs available 10 years ago; besides, parallel computing may facilitate performing tasks that are extremely difficult, tedious, and time-consuming.

The continued development of computer technology enables realization of some hardware functions by software, because computing tasks can now be performed in a lesser time than that required previously. Some time-consuming calculations such as first Fourier transform (FFT) or artificial neural network (ANN) could be realized by using software instead of hardware. Computer algorithms involved in the CAD scheme consist of 4 major components: (1) image acquisition and data preprocessing for noise reduction and removal of artifacts; (2) image extraction and representation; (3) detection of the region of interest (ROI) by image analysis on the basis of segmentation and matching; and (4) evaluation and classification using an appropriate decision-making scheme.

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Interpretation without/with CAD: Early detection of breast cancer prolongs life expectancy and may allow patients to undergo thymectomy before metastasis occurs. Mammography is currently considered to be a major significant approach for the detection of abnormalities in the breasts; this method has reduced the breast cancer mortality rates by 30–35%. However, radiologists, especially inexperienced residents or general radiologists, cannot detect all breast cancers that are visible on mammograms. Double reading of mammograms is very helpful and may improve the performance of radiologists. Hendee et al. suggested that all mammograms should be read twice [2]. Unfortunately, increasing number of mammography examinations and worsening manpower crisis make this option impractical.

Alternatively, a CAD system may be used as a second reader to assist radiologists in detecting and diagnosing lesions. Combining the advantages of "empirical human" and "explicit machine" can improve the diagnostic accuracy, especially in the cases of inexperienced doctors.

Commercial CAD products: ImageChecker™, a CAD system for mammography produced by R2 Technology, is the first CAD system that was approved by the American Food and Drug Administration (FDA) in 1998, followed by iCAD SecondLook™, a product manufactured by its rival company. CADstream™ (Confirma) is the CAD system for analyzing breast MRI results. Other kinds of CAD systems such as RapidScreen™, which analyzes digital chest radiograms for the detection of early-stage lung cancer; Medicsight for CAD analysis of lung, colon, and heart results; and MeVis, CAD system for planning liver surgery, received FDA approval (510 (k) clearance) in 2005, and so on.

Effects of CAD: As an example, CAD was used in 12,860 women undergoing screening with mammography, and the number of cancers detected by CAD was found to be 20% higher than that detected by the conventional method [3]. Moreover, CAD can be used to reduce variability in the interpretation of results by radiologists. Computer-aided analysis helped reduce the variation in the interpretation of results by radiologists by 46%, and two-thirds of substantial disagreements in cases in which 2 radiologists recommended biopsy and routine screening in the same patient were eliminated [4,5].

II. SOME TOPIC-RELATED CAD PROJECTS

Many CAD projects have been undertaken worldwide; however, here, we mainly describe the projects undertaken in Japan and China, some of which are involved in the CAD presentation session at IFCSTA 2010 (also see Chap. IV in this paper):

1. *Intelligent Assistance in Diagnosis of Multi-dimensional Medical Images, Japan (2003 October to 2007 March)*

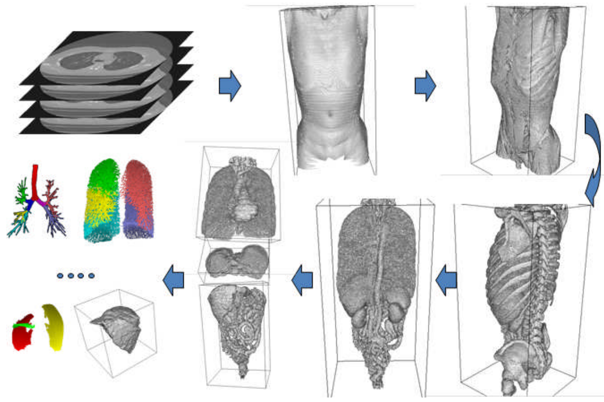

Figure 1 An automated anatomical structure recognition system developed by Fujita Laboratory at the Gifu University is a part of the Intelligent Assistance in Diagnosis of Multi-dimensional Medical Images project.

This project was funded by a Grant-in-Aid for Scientific Research on Priority Areas, MEXT, Japan, and consisted of the following 9 major parts: (1) Simultaneous segmentation of multiple organs in multi-dimensional medical images; (2) Computational modeling of organs; (3) Intelligent CAD based on anatomical classification; (4) Intelligent CAD based on localized pathological morphology; (5) Intelligent CAD based on normal structure recognition of the human body (**Fig.1**) [6–9]; (6) Intelligent CAD based on quantitative analysis of spatiotemporal change in medical image sequencing; (7) Development of a navigation-based diagnosis system as an intelligent CAD system; (8) Integration of multi-modal medical images for computer-aided diagnosis; and (9) Evaluation of signal, noise, and exposure in medical imaging for CAD.

2. *Computational Anatomy, Japan (2009 September to 2014 March)*

This project—named "Computational Anatomy for Computer-aided diagnosis and Therapy: Frontiers of Medical Image Sciences," funded by a Grant-in-Aid for Scientific Research on Innovative Areas, MEXT, Japan—aims to establish a new discipline "Computational Anatomy," which provides a mathematical framework to understand human anatomy [10]. The challenges of this project are the following: (1) development of theories for the representation of anatomical models that cover inter-individual variability in organic shape, topology, and construction through statistical analysis of population data; (2) investigation of methodologies for precise and robust retrieval of anatomical information from medical images, virtually equivalent to real human body dissection; and (3) development of innovative technologies assisting medical diagnosis and interventions based on computational anatomy. The outcomes are expected to contribute to advanced medicine, basic biomedical research, medical education, and information science.

3. *Knowledge Cluster Initiative, Japan (2004 March to 2009 March)*

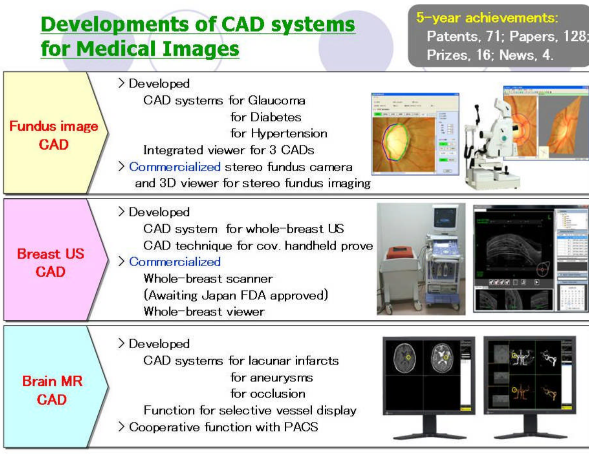

Figure 2 Summary of the developed CAD systems for the 3 different areas of medical imaging by the Gifu/Ogaki Cluster project in Japan.

This project, named "A Knowledge Cluster Initiative Project for Robotics Advanced Medical Cluster in Gifu & Ogaki Area," was supported by the Ministry of Education, Culture, Sports, Science and Technology, Japan, under a Grant-In-Aid for Scientific Research. Eighteen "knowledge clusters" were established in Japan under the "Knowledge Cluster Initiative." The aim of the project was to promote industrial, academic, and government cooperation in regional areas, and to conduct innovative and technological research with a focus on the needs of the industry. The Fujita Laboratory at Gifu University was a part of this big project and was involved in the development of the state-of-the-art medical imaging equipments and CAD systems [11] (**Fig.2**) for analysis of brain MR images [12,13], retinal fundus images [14–16] (**Fig. 3**), and breast ultrasonograms [17–19].

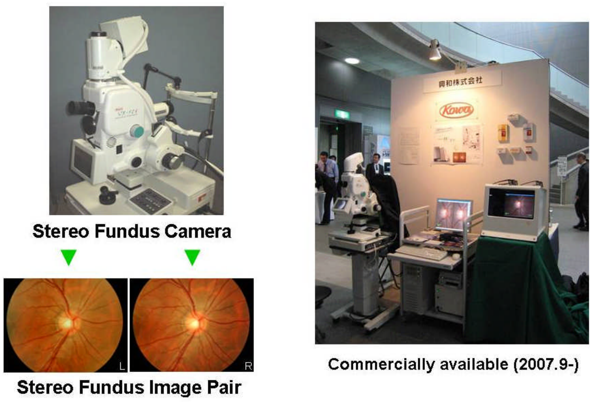

Figure 3 Commercially available stereo fundus digital camera developed by the cluster project in Japan, which can be useful especially for the early detection of glaucoma and other eye diseases. Quantitative depth analysis of the optic disc is possible using this camera system (Kowa Company, Japan). The development of this product was also supported partly by the Ministry of Economy, Trade and Industry (2006 June to 2008 March).

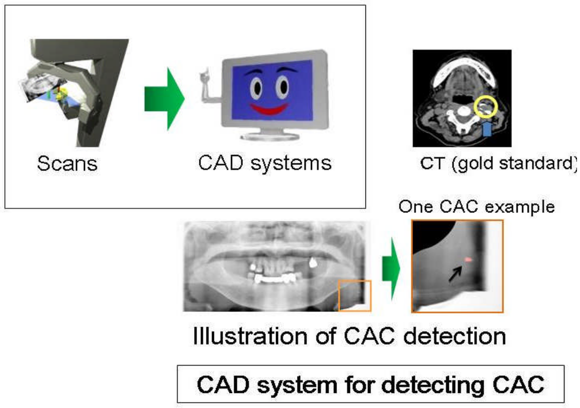

Figure 4 CAD for dental panoramic radiography developing under the City Area Program in Japan: Carotid artery calcifications (CACs) are one of the indices for predicting the progress of arteriosclerosis. Dentists may recommend patients to visit specialists for the treatment of this possible hidden disease.

4. City Area Program, Japan (2009 June to 2012 March)

The City Area Program is one of the policies of the Ministry of Education, Culture, Sports, Science and Technology, Japan, for promoting science and technology in local regions. It aims to foster and develop industries that focus on regional characteristics by promoting regional cooperation among industries (private companies), academia (universities, etc.), and government (public research and experiment institutions, etc.). The ongoing project of this program in southern Gifu area (Development Stage) is named "Development of Advanced Medical Equipment Using Manufacturing Technologies and Information Technologies" [20], and a study on the "development of an assisting system for image diagnosis in the field of dentistry" is ongoing. All dental clinics in Japan have X-ray devices, and digital systems are widely used in recent years. Therefore, the aim of this CAD study is to develop a CAD system for automatically detecting abnormalities on dental X-ray images. Odontopathies, as well as various abnormalities related to systemic illness (e.g., osteoporosis, carotid artery calcifications (**Fig.4**), and maxillary sinusitis), are visualized on dental X-ray images [21].

5. CAD project by the National Natural Science Foundation of China (NSFC), China (2008–2011)

The National Natural Science Foundations of China (No. 60863014) entitled "Study of computer-aided diagnosis/ detection and information management and analysis system on liver disease" was started in 2008. The purpose of this research is to establish a CAD and surgery system for aiding decision-making with regard to the diagnosis of liver cancer or supporting radiologists and surgeons in planning liver resections or living donor transplantations by using multiphase CT/MRI images. CAD use in clinical practice is expected to reduce mortality caused by liver cancer in Asian countries.

III. TECHNIQUES USED IN CAD

CAD has now become one of the important research topics, especially in radiology, medical physics, and medical engineering. Many reported achievements indicate the brilliant future of CAD, especially because the commercial CAD products for the analysis of mammograms and lung images (radiography and CT) have been approved by the US FDA. Although CAD offers various advantages, one should note that only few radiologists are involved in the research of CAD. Nonetheless, such research requires a developer to have some knowledge on interpreting radiological images. One option is that more radiologists can be made to join or share a part of this study. In order to make doctors or beginners understand the principle of CAD systems and to evaluate its performance, we have introduced some fundamental techniques that are widely used in the development of the CAD scheme. Although the mentioned methods, especially for image processing, are relatively old and basic, they provide reliable performance. Many exciting new theoretical areas are generally built on the principles of the traditional methods rather than by replacing them.

A. A typical flowchart of CAD

A desired CAD scheme may allow the detection of the location of abnormalities and allow the differentiation of disease categories. A typical flowchart of a CAD scheme is shown in **Fig.5**. The research object can be any kind of medical digital (or digitized) images. The purpose of the preprocessing step is to unify the original images into a standard condition so that a computer algorithm can be developed such that it can be applicable to a wide range of input images with different qualities. The typical methods include extracting ROI region, smoothing or reducing noise, diminishing image size, etc. Detecting abnormalities as true positives (TPs) may allow physicians to identify the locations of lesions, which can be determined on the basis of thresholding techniques, edge detection, or by using many other intelligent algorithms such as ANN, fuzzy, etc. However, the detection step always yields many false positives (FPs) that may mislead the diagnosis result and unnecessarily necessitate biopsy. Eliminating FPs while maintaining the TP rate constant becomes an important component during programming; this is generally realized by calculating the parameters of candidates detected, for example, size, shape, intensity, circularity, etc. Finally, for a complete CAD scheme, classification of lesions into benign or malignant is expected. Pattern recognition methods are useful for this step. Pattern recognition methods are useful in this step.

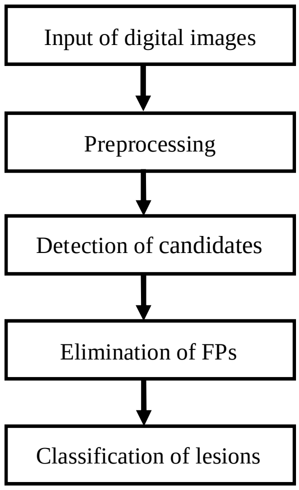

Figure 5 A typical flowchart of a CAD scheme

B. Fundamental techniques

There are many fundamental technologies for image processing, such as gray-level-based, shape-based, and machine-learning-based methods. Histogram analysis, binarization, edge detection, template matching are some of the gray-level-based techniques, which access pixels located at the designed area or parameters. These methods are often applied to the images with fine contrast. Atlas and active shape models are shape-based techniques that are used in the images without fine contrast but have a regular-shaped target. ANN, genetic algorithm (GA), and ensemble learning based methods are machine-learning-based methods that can be trained with samples and detecting unknown data by learned knowledge.

C. Evaluation method for CAD

There are many features that can be used as the criterion for evaluating CAD performance. We first list some common terms used for such evaluation: sensitivity and specificity, TP and FP (number of TPs and FPs), TPF (TP fraction or sensitivity), FPF (FP fraction or 1 - specificity), FP/image (number of FPs per image), TNF (true-negative fraction), FNF (false-negative fraction), PPV (positive predictive value), NPV (negative predictive value), ROC, FROC (free-response receiver operating characteristic), A_Z (area under the ROC curve), and recall rate (ratio of recalled cases for future follow-up in a screening practice divided by the total number of cases).

Sensitivity and Specificity

The quality of a diagnostic test can be characterized by its sensitivity and specificity. Sensitivity describes the number of abnormal cases correctly identified as positive divided by the total number of abnormal cases. Specificity is normal cases correctly identified as negative divided by the total number of normal cases.

ROC Curve

Because sensitivity and specificity change depending on different thresholds, an ROC curve can be drawn to describe the complete relationship between them. Two different patterns can be obtained by drawing a discriminable line on a 2D future space, and one can note that increasing TPs always make additional numbers of FP.

IV. STATE-OF-THE-ART CAD TOPICS

In this chapter, all the presentations that appeared on the special CAD session during IFCSTA 2010 are summarized; these presentations cover the new topics of CAD for the analysis of different imaging modalities for different parts of the human body. Details on these topics can be found in the proceedings.

A. 3D Torso CT Images

This section describes a new approach to automatically identify the location of a target solid organ in 3D CT scans. Specifically, the goal is to detect a 3D rectangle on the target organ such that this rectangle binds the organ region tightly and accurately. The proposed approach combines the ensemble learning and majority voting techniques to achieve a robust detection by requiring a small number of CT scans for training. A database, including 3,329 torso CT scans, is used in this experiment. Among the scan database, those for the heart and the left/right kidneys are manually labeled from nearly 100 3D CT scans as training samples, and the proposed approach is employed to localize those organs in other CT scans. Experimental results show that the detection rates are 99% for the heart and 85%–87% for the right and left kidneys, with a computation time of less than 15 seconds per CT scan on a general PC.

B. Thoracic CT Images

Thoracic CT is a computed tomography scan of the chest and upper abdomen. Many CAD algorithms have been developed using thoracic CT images. There are 2 targets in the development of CAD algorithms for pulmonary diseases. One is CAD for localized pulmonary diseases. In this target, CAD-mediated detection of pulmonary nodules is important, and many algorithms have been reported for this. The other is CAD for diffuse lung diseases. This target includes many kinds of diseases and variety of texture patterns. For the CAD for diffuse lung diseases, considering morphological and functional viewpoints is important. However, the number of published schemes for this algorithm is smaller than those for localized pulmonary diseases. In this study, therefore, the CAD algorithms have been investigated using thoracic CT images, especially for diffuse lung diseases. By using the developed CAD algorithms, radiologists will be expected to be able to obtain objective and quantitative information about diffuse lung diseases and use this information as a second opinion. Moreover, the CAD algorithms are expected to contribute to clarifying the diagnostic logic and improving the diagnostic accuracy for diffuse lung diseases for which imaging diagnosis is difficult.

C. Hepetic MR and CT Images

CAD systems for qualitative and quantitative diagnosis/detection of liver disease and also for visual surgical simulation have been developed. The sensitivity and usefulness of this system have been clinically tested. The entire study is significant in terms of both radiological and surgical studies because it plays an important role in reducing mortality caused by liver cancer. Algorithms for detecting lesions will help radiologists locate cancers at an early stage; accurate liver and tumor(s) localization is very crucial in radiotherapy; and surgical simulation would reduce the risk associated with living donor liver transplantation and oncological resections. Furthermore, these studies can be easily adapted as a commercial CAD product that might have a huge potential market, especially in Asian countries.

D. Torso FDG-PET Images

An automated method to calculate the Z-scores of standard uptake values (SUVs) for the torso region on FDG-PET scans has been developed to estimate the abnormalities by using the scores of SUVs for a normal model constructed. The 3D distributions for the mean and standard deviation (SD) of SUVs are stored in each volume to score the SUVs in the corresponding pixel position within unknown scans. The modeling method is based on the statistical parametric mapping (SPM) approach using the correction technique of Euler characteristics and resel values (Resolution element). Seventy-three abnormal spots are used to estimate the effectiveness of the scoring methods. Hence, the Z-score images correctly represent that their values for normal cases are between zeros to plus/minus 2SD. Most of the Z-scores of abnormal spots associated with cancer are larger than the upper interval of the SUVs for normal organs.

E. Fundus Photographys

In order to diagnose the presence of arteriolosclerosis, physicians locate the silver-wire arteries, the copper-wire arteries, and arteriovenous crossing phenomenon on retinal fundus images. The focus of this study is to develop an automated method for detecting the arteriovenous crossing phenomenon on retinal images. The blood vessel regions are detected using a double-ring filter, and the cross sections of the arteries and veins are detected using the ring filter. The center of that ring is an interest point, and that point is determined as a cross section when there are more than 4 blood vessel segments on that ring. Two blood vessels that pass through the ring are classified as an artery and vein by using the pixel values on the red and blue component images. Finally, V2:V1 ratio is calculated for detecting the abnormalities, where V1 is the venous diameter away from the blood vessel cross section, and V2 is the venous diameter close to the blood vessel cross section.

F. Open-MR Images

Large deformations of the abdominal organs are noted when the abdominal cavity of patients undergoing laparoscopic surgeries are exposed to carbon dioxide gas. Surgeons find it difficult to detect the corresponding positions of target organs on the pre- and intraoperative images in such situations. A 3D non-rigid registration method is used to eliminate the deformation of organs in order to align the 2 images. The registration method can be divided into 2 steps. First, a global registration parameterized by a rigid transformation is performed in order to eliminate the global spatial differences. Next, the parameters of deformation are calculated in a local registration parameterized by a B-spline deformable transformation. The registration is only operated within the regions of target organs; hence, manual segmentation of organs is required as a pre-processing step. This method is evaluated on the images captured using an Open-MR scanner during laparoscopic surgeries. The registration method has been found to function well in the experiments.

V. SUMMARY

In this report, we have described the data presented at the special session of CAD/IFCSTA2010 covering the latest research and technology development in multi-disciplinary areas. CAD has now become a vital and powerful method for diagnostics. With the continual efforts of improving the accuracy of CAD schemes, we believe that it will have a major impact on diagnostic radiography in the near future and have immediate beneficial effects on the communities such as medicare, telemedicine, and multimedia information processing. These applications will not only increase the efficiency and productivity in the business environment, but also enhance health services for the public. In the future, with the rapid development of CAD technology, computer doctors may be able to diagnose almost all diseases, and automated inspection and treatment will become a major method at hospitals.

Acknowledgments

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