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The Role of Computer Aided Diagnosis (CAD) in Medical Imaging

Seung Won Shin[1], Kwang Gi Kim[1]
[1]Biomedical Engineering Branch, Division of Convergence Technology, National Cancer Center, Goyang, Korea

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Corresponding Author
Kwang Gi Kim, PhD
Biomedical Engineering Branch,
Division of Convergence Technology,
National Cancer Center, 323
Ilsan-ro, Ilsandong-gu, Goyang-si,
Gyeonggi-do 410-769, Korea.
Tel: +82-31-920-2241
Fax: +82-31-920-2242
E-mail: kimkg@ncc.re.kr

Objectives: We introduce the various methods of image analysis used for CAD. In addition, we provide a guide for the clinician through examples which use the CAD. **Methods:** Medical images consist of individual pixel elements, to which discrete brightness or color values are assigned. Various methods have been utilized for the analysis of these images. We introduce the five methods: shape analysis, texture analysis, parametric mapping analysis, classification methods and segmentation methods. **Results:** Various image analysis techniques used in the CAD are quantified by analyzing the various features of the lesion shown in the image. It is used as a process for deriving the best diagnosis for the disease through the comparison of the existing data. It proposes an example of a CAD system being studied using a variety of image analysis techniques. **Conclusion:** Nowadays, medical imaging has improved to show the functional state of the inner body. Furthermore, accelerated advances in computer-based technology have widely enlarged efficiency of saving, transmission and analysis. Improvement of CAD will expand the utilization range of CAD in 2D and 3D medical imaging. Also, we expect that CAD system will evolve the automatic diagnosis support system.

Keywords: Diagnosis, Computer-Assisted, Diagnostic Imaging, Image Processing, Computer-Assisted

Introduction

Medical imaging is important to non-invasively provide the information necessary to indicate the exact disease diagnosis by imaging inside the body. Today, in the process of disease diagnosis in hospitals, medical imaging plays an important role, and acquisition of medical images for diagnosis of disease has been established as a common process. Accordingly, medical imaging technologies are evolving for more precise and faster diagnosis from day to day.

With the development of medical imaging technologies, necessity of computer aided diagnosis (CAD) tools is increasing day by day, because the number of medical images that need analysis by radiologists is rapidly increasing. Currently, the CAD tool is established as an important part of the diagnostic process of radiologists using medical imaging. Hence, CAD has become more active area of research in the medical imaging field [1-3].

The basic concept of CAD is to provide information on the basis of a quantitative diagnostic analysis of the medical image using computers. This concept can improve the accuracy and consistency of lesion diagnosis and reduced image-reading time. Therefore, 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 the radiologist's decision. CAD is defined as detection and/or diagnosis made by a radiologist/physician who takes into account the computer output as a second opinion. CAD is often categorized into two major groups: computer-aided detection (CADe) and computer-aided diagnosis (CADx). CADe focuses on a detection task, in other words, detection (or localization) of lesions in medical images. CADx focuses on a diagnosis (characterization) task, for example, distinction between benign and malignant lesions, and classification among different lesion types [1-3]. Figure 1 shows the steps of medical image analysis.

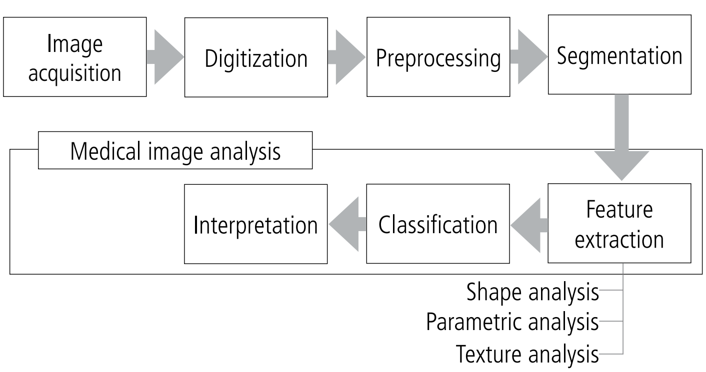


Figure 1. Steps of medical image analysis.

Early attempts to build a CAD system were initiated in the early 1950s. Ledley and Lusted described their early symbolic logic and probability theory that facilitated diagnoses similar to those speculated by physicians' complex reasoning in 1959 [5]. Although early attempts at computerized analysis of medical images were made in the 1960s, serious and systematic investigation on CAD at the University of Chicago began in the 1980s with a fundamental change in the concept for utilization of the computer output from automated computer diagnosis to computer-aided diagnosis. 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 [1-4]. CAD products that are currently commercially available are breast radiation imaging (Mammography) CAD, breast magnetic resonance imaging (Breast MRI) CAD, thoracic radiographic images (Chest radiography) CAD, CAD for liver surgery planning and CAD for lung, colon and cardiac image analysis, etc.

In order to provide more detailed and accurate information through CAD, it is important that effective image analysis techniques be used for the main diagnostic procedures. Also, various methods need to be applied for the verification of accuracy and effectiveness as an auxiliary diagnostic tool. Therefore, studies on the development of the CAD system in a variety of medical images have been conducted recently.

1. Methods for CAD

Today, the medical devices in hospitals are mostly digital, and medical images consist of individual pixel elements, to which discrete brightness or color values are assigned. They can be processed effectively, evaluated objectively, and made available at many sites at the same time by using appropriate networks and protocols. Generally, we should consider three aspects in medical image analysis. First, biological structures are subject to both inter- and intra- individual alterability. Thus, universal formulation of a priori knowledge is not as effective as specific case treatments. Second, interesting biological structures often cannot be separated conveniently from others because the diagnostically-relevant object is represented by the entire image. Finally, reliability and robustness of algorithms is necessary. These mean that images, which cannot be processed correctly, must be automatically classified as such and rejected and withdrawn from further processing [6-7].

1.1 Shape analysis

The shape of an object refers to its profile and physical structures. These characteristics can be represented by boundary, region, moment, and structural representations. These can be used to match shapes, to recognize objects, and to make measurements of shapes. Shape descriptor features are calculated from an object's contour: in other words, circularity, aspect ratio, discontinuity, angle irregularity, length irregularity, complexity, right-angleness, sharpness, and directedness. Those are translation, rotation and scale invariant shape descriptors [8-10]. All contour-based data representations usually result in substantial data compression compared to image matrix. Figure 2 shows an example of shape descriptors. Where, a radial function R (Θ) shows the distance R between an interior point and the contour points, as a function of the polar angle Θ, Ri represents a distance between the i-th boundary point and the centroid of the object.

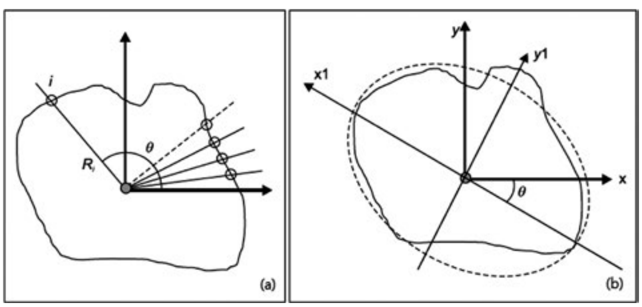


Figure 2. Examples of shape descriptor, (a) contour-based radiation function, (b) moment-based orientation.

Many shape features also can be conveniently represented in terms of moments, such as perimeter, area, radial function, bending energy, roundness, and symmetry. Moment-based features are used for recognition of small sets of distinct objects or for pre-classification before more precise comparison in order to reduce number of candidates. In selecting descriptors, there are certain desirable qualities: 1) uniqueness that there is one and only one set of descriptors for a given two-dimensional shape, 2) calculation independency that a descriptor independent from others can be discarded without additional calculation of the others (especially a descriptor which does not affect to others may be eliminated painlessly), 3) rotation invariance that the orientation of an object does not affect the value of the descriptor, and 4) scale invariance that the outline will not affect the outcome (for example, a large circle and a small one have the same shape).

Shape descriptors are important in several contexts. For example, the shape and the size of tumors in mammograms are essential to classify them as benign or malignant. As is well-known, tumors with irregular shape are usually malignant and tumors with regular shape are usually benign [11, 12].

1.2 Texture analysis

Some diseases, such as interstitial fibrosis, affect the lungs in such a manner that the changes of effect in the X-ray images are texture changes as opposed to clearly delineated lesions. In such applications, texture analysis methods are ideally suited for these images.

Image texture refers to the spatial relationship of pixel values in an image region. Texture also determines the local spectral or frequency content in an image. Here, changes in local texture should cause changes in the local spatial frequency [13]. Based on these definitions, there are ongoing studies into various mathematical methods of quantifying image texture, including statistical, Fourier, and wavelet-based methods. Texture analysis is a three-layer process [14]. The first layer identifies the texture primitives, of which texture patterns are composed. The second layer extracts certain properties from the identified texture primitives. Depending on the types of primitives, the properties can be pixel or geometric. The third layer builds the spatial and/or statistical distribution of the primitives in terms of their attributes.

Texture analysis has a long history, and a wide variety of methods has been studied and proposed in the past [15-17]. The gray level co-occurrence matrix (GLCM) is recognized as the most representative algorithm in spatial texture related research [18, 19]. In short, a GLCM is constructed by systematically considering the relationship between pixel pairs and tabulating the frequency of various gray level combinations within an image or within a region of interest. In a similar manner, run-length features can be computed to evaluate the coarseness of a texture in a predetermined direction. A gray-level run consists of a set of consecutive collinear pixels in a given direction.

A wavelet transform provides improved flexibility over Fourier transform, with trading some degree of spatial-frequency resolution for the ability to localize this frequency content in time. The wavelet transform may be intuitively understood by imagining a window of constant area but fluid dimensions, its width (time) narrowing with increasing length (spatial frequency), and vice versa, by making it equally suitable for identifying fine texture (short bursts of high spatial frequency) and coarse texture (slow waves of low-frequency content) [20-22]. For example, the wavelet energy features reflect the distribution of energy along the frequency axis over scale and orientation, and have proven to be very effective for texture characterization. Because most relevant texture information is removed by iterative low-pass filtering, the energy of the low-resolution image is generally not considered a texture feature. The wavelet entropy can be interpreted as a measure of uncertainty, variability, and complexity. Entropy reaches its maximum in a completely random state and its minimum in a state of certainty. As a result, a homogeneous region produces zero entropy.

Characterization of micro-calcifications (MCs) on mammograms is a great example of texture analysis. A variety of computer-extracted features and classification schemes have been used to automatically discriminate between benign and malignant clusters. This approach is based on extracting image features from regions of interest and estimating the probability of malignancy for a given MC cluster [23, 24].

1.3 Parametric mapping analysis

Parametric mapping analysis is generally used to identify functionally specialized responses and is the most prevalent approach to characterizing functional anatomy and disease-related changes. It entails the construction of spatially-extended statistical processes to test hypotheses about regionally specific effects. Resultant parametric maps are image descriptors with voxel values that are, under the null hypothesis, distributed according to a known probability density function.

Dynamic perfusion imaging utilizes the imaging evaluation of bio-distribution of the contrast medium infusion acting as a tracer. The contrast medium following infusion is distributed into the body tissue in relation to local micro-vascularization and on the diffusion across the endothelial membrane into the interstitial space [25]. The imaging depicts the distribution of the contrast medium by measuring variations in the vessels and in the tissue enhancement over time. The elaborated images are represented by parametric color maps. The perfusion studies, both with CT and/or MRI, considered by recent studies, can be used for preoperative grading of the gliomas, in particular for the differential diagnosis of low and high-grade astrocitomas because these techniques can provide complementary information about tumor hemodynamics not available with conventional CT or MR.

Elastography is a non-invasive method in which stiffness or strain images of soft tissue are used to detect or classify tumors [26]. A tumor or a suspicious cancerous growth is normally 5 to 28 times stiffer than the background of normal soft tissue. When a mechanical compression or vibration is applied, the tumor deforms less than the surrounding tissue. In other words, the strain in the tumor is less than the surrounding tissue. While sonograms convey information related to the local acoustic backscatter energy from tissue components, elastograms relate to its local strain. Some research has been conducted using magnetic resonance elastography and CT. However, ultrasonography still has the advantages of being cheaper, faster and more portable over other techniques.

1.4 Classification methods

Classification is a step used for detecting or analyzing patterns of interest contained within images, and is performed by experimenting with many different types of classifiers (classification model), comparing their performance and choosing the best.

In quantitative analysis, not only feature selection is important, classifier selection and training are very important. A number of classifiers have been used, including the nearest neighborhood, neural networks, Fisher discriminant analysis, fuzzy-based methods, learning vector quantization, etc. [27-29].

Linear discriminant analysis is a statistical technique to classify a set of observations into predefined classes. The model is built based on a set of observations (or training set) for which the classes are known. Based on it, the technique constructs a set of a linear functions of the predictors, known as discriminant functions. This technique can be used to determine the variables discriminating between two or more naturally occurring groups.

Artificial neural networks (ANNs) work, as do linear discriminants, by mapping a generally multi-dimensional observation to a scalar decision variable. Unlike linear discriminants, however, ANNs typically use a non-linear mapping function. In its simplest form, a neural network is a set of connected nodes roughly resembling the human neuron system. ANNs are automated classifiers that have been extensively applied to the field of medical imaging over the past 20 years with much success.

In recent years the support vector machine (SVM) has started to be widely used as a very successful classifier [30].

SVM attempts to separate points belonging to two given sets in multi-dimensional space by a nonlinear surface, often only implicitly defined by a kernel function. An important advantage of the SVM is that it is based on the principle of structural risk minimization. Thus SVMs aim at minimizing a bounding on the generalization error.

Generally, classifiers require a supervised training technique. Image samples are divided into two sub sets. One is used to determine the discriminant function (training) and the other to test the derived function (testing). Since there is a limited amount of available data in training, it is very important to test with enough extra data.

1.5 Segmentation methods

Image segmentation is a fundamental, yet still challenging, problem in computer vision and image processing. In particular, it is an essential process for many applications such as object recognition, target tracking, content-based image retrieval, medical image processing, etc. Generally speaking, the goal of image segmentation is to partition an image into a certain number of pieces which have coherent features (color, texture, etc.) and in the meanwhile to group the meaningful pieces together for the convenience of perceiving [31].

Many promising methods have been proposed for image segmentation, such as the region merging-based methods [32, 33], the graph-based methods [34-36], and the active contour model (ACM)-based methods [37-48], etc. ACM for segmentation aims to drive the curves to reach the boundaries of the interested objects. The driven forces are mainly from the image data, including edge-based [39, 40] or region-based forces [41-48]. The edge-based ACM often utilizes the local image gradient information to build some stopping functions in order to drive the contour to stop at the object boundary, while the region-based ACM aims to drive the curve to evolve through some region-based descriptors [46, 47].

The edge-based ACM methods are applicable to images with intensity inhomogeneity but, in general, they are sensitive to the initialization of the level set function. Moreover, they easily suffer from serious boundary leakage for images with weak boundaries [44]. Many region-based ACMs are based on the global region information; they assume that the image intensity is homogeneous [41], and thus are not suitable for segmenting images with intensity inhomogeneity.

2. Examples of CAD

Thus, various image analysis techniques used in the CAD are quantified by analyzing the various features of the lesion shown in the image. It is used as a process for deriving the best diagnosis for the disease through the comparison of the existing data. It proposes an example of a CAD system being studied using a variety of image analysis techniques.

2.1 Analysis of bone age using CAD

Bone age is a value indicating how well the bone grows to suit its age. It is determined by measuring when the object stopped growing and its physical maturity. If the bone age is smaller than the actual age, it physically is young because growth stops late. On the other hand, if the bone age is larger than the actual age, it physically is old because growth stops early. Also, final adult height can be estimated with consideration of the current height and bone age [48]. The bone age analysis method estimates bone age by applying the method of matching between the reference image and the measured image: reference image is the most common image for the age (standard image) and the measured image is the input image (original image). A number of selected lines (line profile) in the measurement image and the reference image are drawn in the process and compared with each movement to find the best image. Figure 3 is an example of CAD software for analysis of bone age which was developed at the National Cancer Center Korea. This figure shows process of bone age measurement, method of contour line selection and prototype of CAD software.

2.2 Rib fracture detection using CAD

Rib fracture is the most common diseases found in complex emergency room trauma patients, up to 40%, and it is an important disease directly related to organ damage. Chest radiography is the most commonly-used imaging tool to detect rib fractures, because of its economic and clinical benefits. However, it is difficult to read the exact rib fracture in many images because this image is utilized in the diagnosis of various diseases. A previous investigation reported that plain radiography alone might miss up to 50% of the rib fractures [50]. In earlier studies on computer-aided bone fracture detection, an automatic fracture detection method was proposed for long bone radiographs [51]. Recently, a vertebral crack detection method on plain radiographs using region splitting by means of

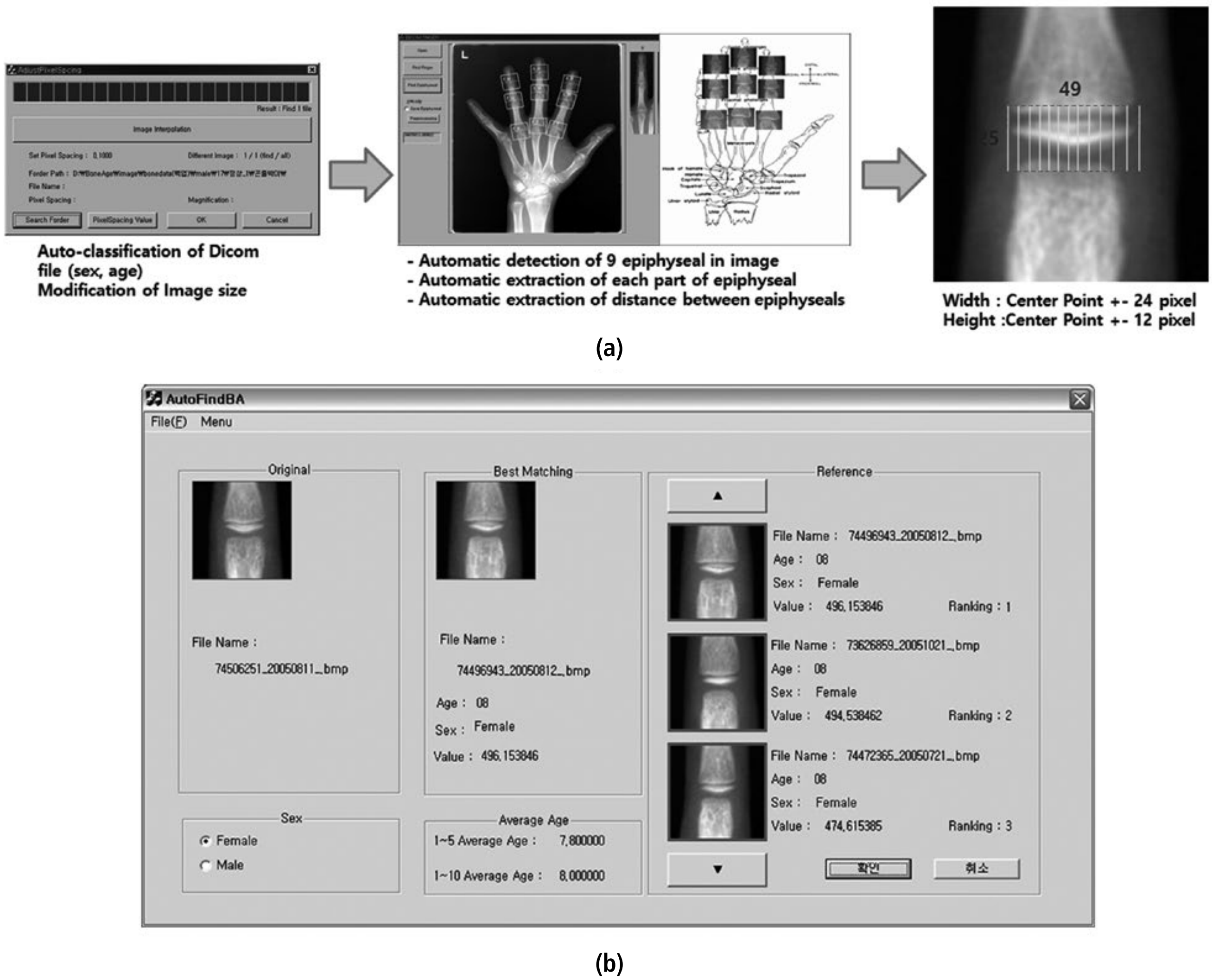
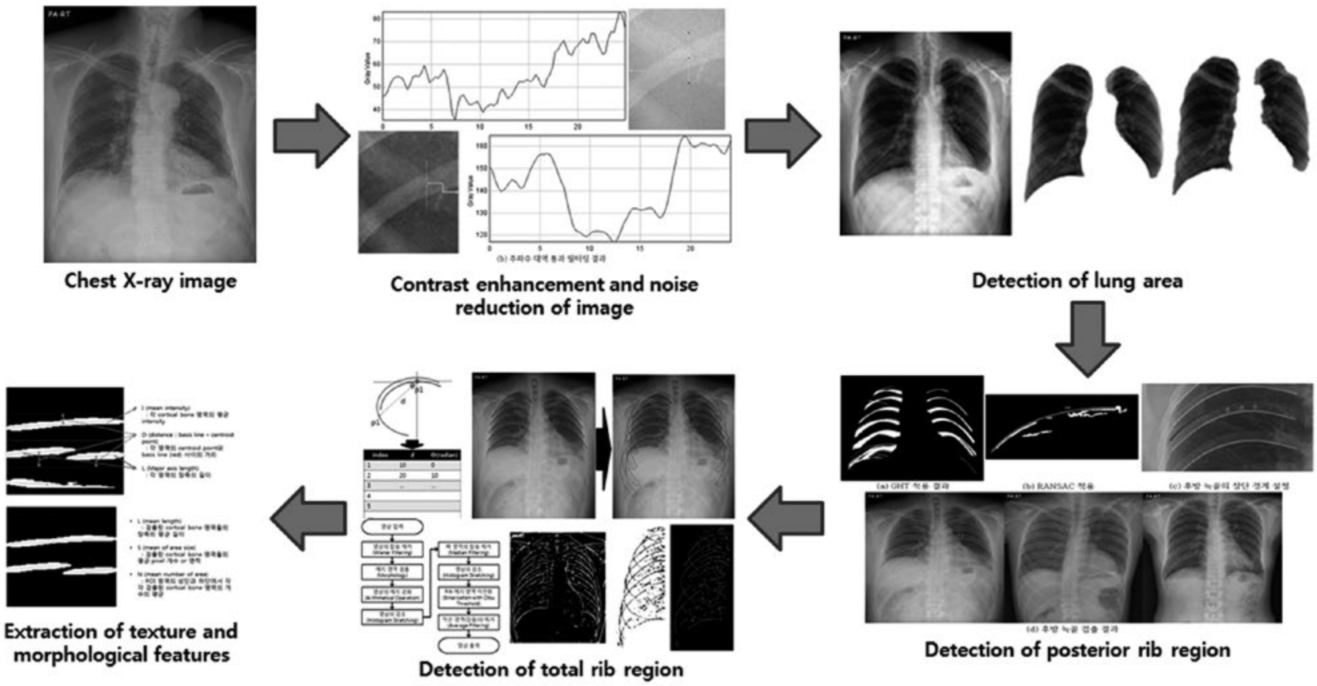


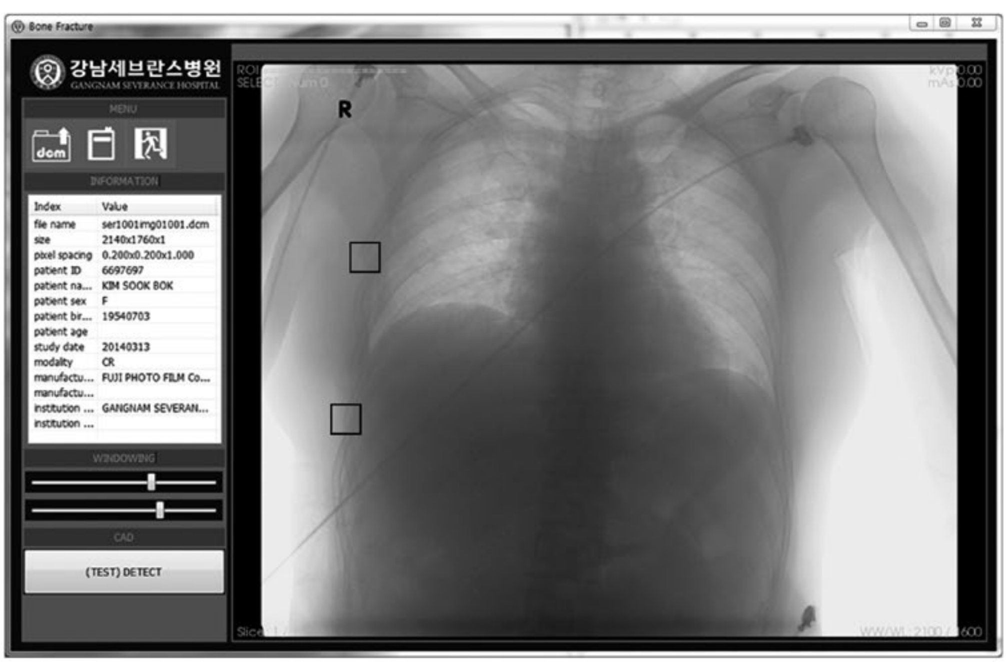
Figure 3. An example of CAD for analysis of bone age, (a) method of bone age measurement, (b) CAD software prototype of bone age measurement.

a fuzzy index measure was proposed. However, these methods are difficult to apply to rib fracture detection because ribs have different characteristics from the other bone structures seen in chest radiographs. Therefore, the development of an effective method for detecting rib fractures is necessary.

For the detection of rib fracture, chest radiography has been performed with contrast enhancement and noise reduction through image preprocessing, and a rib area segmentation algorithm is constructed in the process of posterior rib detection after lung area detection. Also, a new method of image enhancement and the boundary-tracking algorithm was applied for the total rib area segmentation based on the segmented posterior rib. Based on this result, various features of rib fracture are obtained and rib fracture is detected. Figure 4 is an example of CAD software for detection of rib fracture which was developed at the National Cancer Center Korea. This figure shows process of rib fracture detection in chest radiographs and a prototype of CAD software.



(a)



(b)

Figure 4. An example of CAD for rib fracture detection, (a) detection process of rib fracture in chest radiograph, (b) CAD software prototype of rib fracture detection.

2.3 CAD in ophthalmology

The patients who have eye diseases are found after a long disease progression because there are no symptoms. Therefore, early detection and treatment are important [52]. Currently, it is not based on objective or quantitative measures of the structural indicator of the optic nerve and retina in the fundus image. So it depends on the subjective judgment of the doctor. According to research conducted about the world's eminent ophthalmologists in 2010, when performing the diagnosis of glaucoma with only a fundus image, the misdiagnosis rate was 30% and misdiagnosis rate of hereditary optic nerve disease appears as high as 80%. Therefore, critical to the age-related eye disease diagnosis is an accurate assessment and interpretation of the structural features in the eye fundus image.

Thus the research of the CAD system for identifying optic atrophy and retinal nerve fiber layer (RNFL) defect in order to improve the accuracy of diagnosis for glaucoma in the eye fundus images has been actively conducted domestically and abroad. Figure 5 shows an example of the RNFL defect for glaucoma in the eye fundus image that used automatic detection CAD software through the following process: increasing the contrast of the image through pre-process and dividing the optic disk segmentation by using the brightness information, brightness, angle, location, length etc. Finally, combining these processes, the characteristic information allows for detecting a lesion of the RNFL.

Furthermore, as another example utilized in eye disease, there is a CAD software for automatic strabismus test. Strabismus is a common disease that occurs in approximately 4 per 100 infants. Strabismus test is conducted by simple inspection and can be influenced by the subjectivity of the examiner since it is difficult to find the location of eyes. Therefore, the study of improving reliable and accurate measurement of clinical measurement is being actively conducted. Figure 6 is an example of the CAD software for automatic measurement of strabismus, which was developed at the National Cancer Center Korea. The process was as follows, the cornea of the eye is divided into regions using a three-dimensional model based on the eye cornea reflection point measuring of the strabismus.

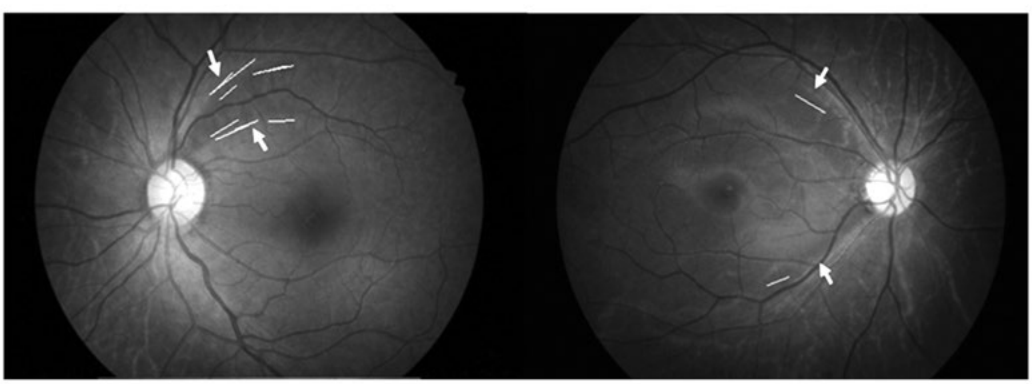


Figure 5. An example of CAD for RNFL defect.

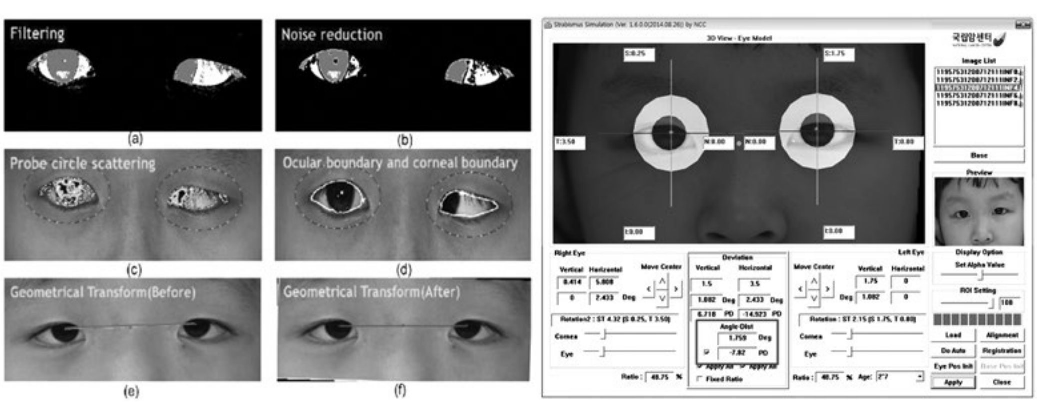


Figure 6. An example of CAD for strabismus measurement.

2.4 CAD in lung emphysema

Emphysema gradually damages the air sacs (alveoli) in the lungs, making one progressively more short of breath. Emphysema is one of several diseases known collectively as chronic obstructive pulmonary disease. Lungs' alveoli are clustered like bunches of grapes. In emphysema, the inner walls of the air sacs weaken and eventually rupture - creating one larger air space instead of many small ones. This reduces the surface area of the lungs and, in turn, the amount of oxygen that reaches the bloodstream. When one exhales, the damaged alveoli do not work properly and old air becomes trapped, leaving no room for fresh, oxygen-rich air to enter. Treatment may slow the progression of emphysema, but it cannot reverse the damage [53].

For the detection of emphysema, automatic segmentation of the lung region and air way with 3D structures is performed by using the lung CT images, and the volume of emphysema is measured quantitatively. Figure 7 is an example of CAD software for automatic detection of emphysema which was developed at the National Cancer Center Korea. This figure shows reconstruction of a 3D lung region, and the process of quantifying and measuring the location and volume of detected emphysema in the image.

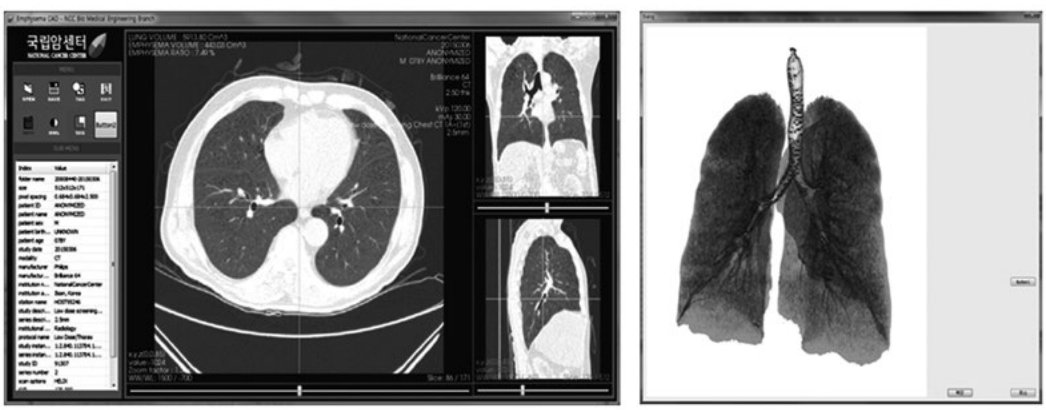


Figure 7. An example of CAD for emphysema volumetry.

Conclusion

Nowadays, medical imaging has improved to the state that positron emission tomography, functional magnetic resonance imaging and others, which show the functional state of inner body, are used for disease diagnosis in addition to existing image acquisition methods such as X-rays, CT, and MRI [54, 55]. For this reason, the use of medical imaging is increasing rapidly followed by growing necessity for CAD. Furthermore, accelerated advances in computer-based technology have widely enlarged efficiency of saving, transmission and analysis. However, use of CAD in disease diagnosis based on medical imaging is limited to minor fields. On the other hand, development of CAD could still be applied in many fields. For CAD to be used in clinical trials of various fields, it is important that interpreters be in a favorable condition to use analyzed information by computer, and already-established picture achieving and communication system (PACS) along with other 3D visualization programs in mutual contact with CAD making such process simple and quick in a single workstation. Through development of new image analysis mechanisms and improvement of the efficiency of existing imaging techniques, precise and effective results can be derived. Improvement of CAD will expand the utilization range of CAD in 2D and 3D medical imaging. Also, we expect that CAD system will evolve the automatic diagnosis support system.

Conflict of Interest

The authors state no conflict of interest.

Acknowledgements

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