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Computer Aided Detection on Mammography

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***Abstract*—**A typical definition of the Computer Aided Diagnosis (CAD), found in literature, can be: A diagnosis made by a radiologist using the output of a computerized scheme for automated image analysis as a diagnostic aid. Often it is possible to find the expression Computer Aided Detection (CAD or CADe): this definition emphasizes the intent of CAD to support rather than substitute the human observer in the analysis of radiographic images. In this article we will illustrate the application of CAD systems and the aim of these definitions.

Commercially available CAD systems use computerized algorithms for identifying suspicious regions of interest. In this paper are described the general CAD systems as an expert system constituted of the following components: segmentation / detection, feature extraction, and classification / decision making.

As example, in this work is shown the realization of a Computer-Aided Detection system that is able to assist the radiologist in identifying types of mammary tumor lesions. Furthermore this prototype of station uses a GRID configuration to work on a large distributed database of digitized mammographic images.

***Keywords*—**Computer Aided Detection, Computer Aided Diagnosis, mammography, GRID.

I. Introduction

COMPUTER technology has had a tremendous impact on medical imaging. The *interpretation* of medical images, however, is still almost exclusively the work of humans. In the next decades, the use of computers in image interpretation is expected to increase vastly. The idea of using computer help in the analysis of radiographic images is not new [1]. Already in 1964, Meyers et al. [2] proposed a system to automatically determine the cardio-thoracic ratio on chest radiographs.

In 1967, Winsberg et al. [3] developed a system for automated analysis of mammograms based on bilateral comparison; something which they recognized might especially be useful in screening mammography with routine viewing of a large number of mostly normal examinations. In 1975 Tasto et al. [4] described an algorithm for detection of microcalcifications on mammograms, which were based on identification of gray value in a mammographic image.

Despite those early reports on CAD in radiology, it was not before the late 1980's that improved digitization techniques and sufficient computer power started to make clinical CAD applications feasible. Currently, a large number of institutions around the world are actively engaged in research on CAD.

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For a summary of the current developments, the reader is referred to recent review articles [5-14]. Furthermore the US Food and Drug Administration (FDA) approved the first CAD system as an aid to the radiologist in screening mammography in June 1998. As 2001, only 130 CAD units were in clinical operation in the United States, many in academic centers. Now, more than 1600 units are being used in active clinical practice, and many new vendors have entered the CAD arena [15].

In Italy, starting form the 1999 a collaboration among italian physicists and radiologists, has built a large distributed database of digitized mammographic images[9-14]. This collaboration, now named MAGIC-5 (Medical Application on Grid Infrastructure Connection), has developed a CAD system which, installed in an integrated station, can also be used for digitization, as archive and to perform statistical analysis. Furthermore this kind of station can also represent a very good system for mammographic educational programs. CAD stations have been implemented and are currently on clinical trial in several italian hospitals and research centers. With a GRID configuration it would be possible for the clinicians tele- and co-working in new and innovative groupings ('virtual organisations') and, using the whole database, by the tools several analysis can be performed. Furthermore the system allows to be abreast of the CAD technical progressing into several hospital locations always with remote working by GRID connection.

The conceptual boundary between Computer Aided Diagnosis and Computer Aided Detection can be somewhat ambiguous. Regarding nomenclature, CAD stands for computer-aided detection. In its present form, CAD should be used only for detection and never for diagnosis or reassurance. Regrettably, the erroneous term computer-aided diagnosis has been written into the lay and radiologic literature [15].

The computer scheme acts as a "second reader", pointing out to the radiologists, abnormalities which otherwise might have been missed. The final diagnosis is made by the radiologist [1].

While the human observer is capable of analyzing even a complex visual scene within a fraction of a second image analysis belongs to the most difficult tasks for a computer. The detection of abnormalities on a radiographic image by the human observer is often accomplished subconsciously without a complete definition of the rule.

The performance of a human observer may be influenced by a variety of circumstances including distraction, fatigue, as well as emotional stress.

Although a specific radiologist may detect a radiographic abnormality in the majority of cases, he may miss the same abnormality under different circumstances. There is hope that this lack of consistency of the human observer may be

overcome by using CAD schemes as a reminder or "second opinion".

The typical situation, where CAD schemes will be most helpful, are large volume examinations with a low incidence of disease (e. g. screening mammography) [1]. Other possible applications to improve radiological diagnosis are:

- Screening, where we have large volume examination with a low incidence of disease (up to 30% of lesions may be missed by the human observer) and the computer task is the automatic lesion detection and characterization;
- Follow-up examinations, where we have to do lesion extraction and quantification because the manual measurements of lesion size may be inaccurate and to much time consuming.
- Functional imaging, where we need a creation of parameter images to visualize functional information (a large number of individual images may be difficult to extract for the human observer).

II. CAD Unit

In general a CAD unit consists of 3 main parts [15]: the scanner, the software, and the viewer. The scanner is used to scan and digitize the mammogram, similar to a desktop scanner used to digitally save photographs. Some mammograms are already captured digitally, in which case this step does not apply. The software includes sophisticated computer programs that analyze the film or image and prompt the radiologist to review areas that may suggest a lesion. An example is the CAD unit of the MAGIC-5 project [10],[14] where a pc, a CCD linear scanner (with a 85 μm pitch and 4096 grey levels), and a high resolution screen are used. The Graphical Users Interface (GUI), by means of a facility tool for image visualisation and elaboration, provides the support for medical diagnosis. The CAD system, in addition to the utility for the new patient acquisition, is also immediately usable in digital mammography, since it is compatible with the standard DICOM (Digital Imaging and Communications in Medicine) format. The portable version (with notebook) and the GUI are shown in Fig. 1.

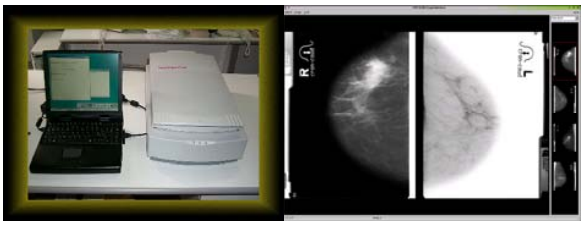

Fig. 1 A portable CAD unit of the MAGIC-5 project and the graphical users interface

As the leader in CAD technology, R2 Technology has introduced the ImageChecker DM [16] for early detection of breast cancer with CAD for both film-based and digital mammography. The ImageChecker uses algorithms of pattern recognition in order to find the abnormal areas and neural nets to classify abnormalities in benign and malignant regions. Radiologists have different reading approaches and preferences with CAD markings. R2's new algorithm provides two different operating point for the CAD algorithm: CAD Sensitivity or Marker rate: the first has higher mass sensitivity with a slight increase in false marker rate; the second provides lower false marker rate with slightly less sensitivity. In Fig. 2 the system is shown.

Fig. 2 The ImageChecker DM system is designed to integrate with new or existing mammography

In general the software of the CAD is an expert system for decision making. A complete CAD scheme is shown in Fig. 3.

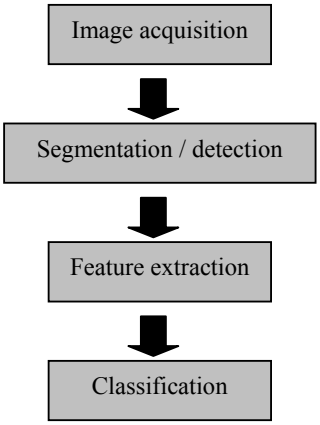

Fig. 3 A complete standard CAD scheme

The image can be a digital image or an analogical radiographic film digitized by a CCD linear scanner. The aim of the segmentation / detection of the image is to reduce the data amount to process by searching for Regions Of Interest (ROIs) that include a lesion with high probability. The traditional goal of the feature extractor is to characterize an object to be recognized by measurements whose values are very similar for objects in the same category, and very different for an object in different categories. This leads to the idea of seeking distinguishing features that are invariant

irrelevant transformation of the input (e.g. features that describe properties such as shape, color and texture are invariant translation, rotation and scaling) [17]-[18]. The conceptual boundary between feature extraction and proper classification can be somewhat arbitrary. In literature [17]-[18] many statistical methods of supervised classification are available. Often the neural networks represents a good classification system used in commercial CAD.

III. CAD Evaluation

In clinical practice the problem is to determine the efficiency of a diagnostic system detecting the presence of pathology.

There are four possible cases of classification:

- TP: true positive (correct), suspicious abnormality is in fact a mass;
- TN: true negative (correct), no abnormalities are indicated in the mammogram of a healthy person;
- FP: false positive (incorrect), in the mammogram of a healthy person regions are evidenced that are not pathological;
- FN: false negative (incorrect), a lesion in a mammogram that is not identified.

The most serious situations are the two incorrectly classified cases which delay diagnosis and compromise disease treatment, the health of the patient, and require ulterior invasive examinations to exclude the disease in the case of a false positive.

The objective of the reliability studies of diagnostic tests is to gain information on all the four possible cases of classification. It is fundamental to have an accepted reference or protocol of disease definition, the "gold standard". With mammogram examinations, the gold standard or protocol is usually an evaluation of mammography images analyzed by an expert radiologist and confirmed with histological examination (in the pathology case) or from follow-ups for et least three years in the case of a negative report.

The performance criteria [17]-[18] of a radiologist or a diagnostic system is generally appraised by two indices: sensitivity and specificity. The sensitivity of a recognized test is the fraction of positively diagnosed cases over the total of afflicted cases, which can be expressed by:

$$sensitivity = \frac{true \quad positives}{true \quad positives + false \quad negatives}$$

A test with a high value of sensitivity must have a minimal number of false negatives and is therefore useful in order to characterize the disease.

The specificity of a test is the fraction of healthy cases over the total of un-afflicted cases, which can be expressed by:

$$specificity = \frac{true \quad negatives}{true \quad negatives + false \quad positives}$$

A test with a high value of specificity must have a minimal number of false positives and is therefore useful to exclude the disease.

Using sensitivity and specificity, the results obtained with the analysis are described in terms of the Receiver Operating Characteristic curve(ROC) which is defined [17]-[18] as the probability of correct detection with the probability of false alert to varying decision threshold.

A ROC curve depends on the density of conditioned probabilities of the observations given by the hypotheses. Therefore, it does not depend on costs or probability of the classes. Given the probabilistic means a curve is within quadrant (0,1) and passes trough points (0,0) and (1,1). It is not possible irregular courses of the curve, in how it is the intentional areas that express the probabilities which vary with continuity and cannot be two points on the same slope. The ROC also shows the true positive fraction (sensitivity), as a function of the false positive fraction (FPF = 1-specificity) obtained varying the threshold level of the ROI selection procedure. In this way, the ROC curve produced allows the radiologist to detect massive lesions with predictable performance, so that he can set the desired true-positives fraction value and know the corresponding false-positives fraction value. ROC curves always start from point (sensitivity = 0, specificity = 1) that it is equivalent to assert that all samples will not encounter complications (only negative cases) and end in point (sensitivity = 1, specificity = 0) which is equivalent to assert that all samples are positives (threshold on the left). The optimal point is that one up on the left (sensitivity = 1, specificity = 1) for which the rule of decision (diagnostic test) does not fail (no FP and FN). Therefore, the more the ROC curve is arched towards that point, the better the decisional test. The area over the ROC curve represents the error connected with the use of the same test. The overall performance is evaluated in terms of the area under the ROC curve and the relative errors [19]-[20].

CAD is not 100% sensitive. Occasionally, CAD fails [15] to detect an area that the radiologist thinks may be a cancer. For this reason, CAD is not a diagnostic tool. The erroneous term computer-aided diagnosis has been applied to CAD. In its current form, CAD should never be used for diagnosis but only for detection. However, this does not mean that CAD cannot be used on a diagnostic mammogram. A mammogram is considered to be diagnostic when it depicts a particular finding (e.g. a recall finding from a screening image, a palpable mass). The radiologist does not need the help of CAD to evaluate the area of concern, but the remainder of the bilateral mammogram is effectively a screening study. It easy to become entirely focus on an area of a mammogram and forget the rest of the study or simply give it a cursory review. In summary, if CAD can help with a screening mammogram, it can also help on the screening part of a diagnostic mammogram. Once the questionable spot is detected, the

radiologist analyzes, diagnoses and makes the final determination as to whether an area deserves recall for further evaluation. If a density, mass, area of architectural distortion, or calcium is worrisome, the patient should be recalled regardless of whether CAD marked the finding. A finding that merits recall should never be ignored because CAD did not mark it. It is deprecated to use the CAD for reassurance.

CAD marks areas [15] that the radiologist may dismiss, and some of these findings may later be confirmed to be cancer. The computer algorithm may be able to detect findings that the human eye still cannot perceive on the screening mammogram, which is unfortunate; however, this limitation must be accepted for now. Radiologists simply must do their best with the tools available to them. If the human eye cannot see an actionable finding, it does not matter whether CAD detects it. Technology will improve over time, and CAD algorithms will improve in their ability to detect masses and to prompt radiologist regarding a finding. Years of data collection and experience are necessary to learn about CAD and how it can be developed to best fit the everyday needs of breast radiologists.

IV. CAD Systems

In the research, CAD systems [1] are studies for:

• Lung Cancer – Currently, radiologist can fail to detect lung nodules in up to 30% of actually positive cases. If a computerized scheme could alert the radiologist to locations of suspected nodules, then potentially the number of missed nodules could be reduced. Furthermore the evaluation of diffuse interstitial disease is one of the most difficult problems in diagnostic radiology. A thoracic CT scan generates about 240 section images for radiologists to interpret.

• Chest radiography – Computerized automated analysis of heart sizes; an automated method is being developed for determining a number of parameters related to the size and shape of the heart and of the lung in chest radiographs (60 chest radiographs were generally acceptable to radiologist for the estimation of the size and area of the heart project).

• Colon Cancer – Colon cancer is the second leading case of cancer deaths for men and woman in the USA. Most colon cancers can be prevented if precursor colonic polyps are detected and removed. CT colonography (virtual colonoscopy) is being examined as a potential screening device (400-700 images).

• Breast Cancer –Such systems will be illustrated in the next sections.

V. Mammography

Breast cancer is reported as one of the first causes of women mortality [21] and an early diagnosis of breast cancer in asymptomatic women makes it possible the reduction of breast cancer mortality: in spite of a growing number of detected cancers, the death rate for this pathology decreased in the last 10 years [22], thanks also to early diagnosis, made possible by screening programs [23]. Presently, an early diagnosis is possible thanks to screening programs, which consist in a mammographic examination performed for 49-69 years old women. Mammography is widely recognized as the only imaging modality for the early detection of the abnormalities which indicate the presence of a breast cancer [24]; it is realized by screen-film modality or, more recently, by digital detectors [25]-[27]. It has been estimated that radiologists involved in screening programs fail to detect up to approximately 25% breast cancers visible on retrospective reviews and that this percentage increases if minimal signs are considered [28]-[30]. Sensitivity and specificity of this examination increase if the images are independently analyzed by two radiologists [31]. So independent double reading is now strongly recommended as it allows to reduce the rate of false negative examinations by 5-15% [32]-[33].

In mammography we have two types of problem:

- Microcalcification
- Masses or opacities

Microcalcification clusters are groups of small and brilliant objects of different shape and intensity in a very noisy background. A microcalcification is a rather small (0.1 to 1.0 mm in diameter) but very brilliant object. Some of them, either grouped in clusters or isolated, may indicate the presence of a tumour. In our database [14], the average diameter of microcalcification clusters, as indicated by our radiologists, is 2.3 cm. In Fig. 4 some microcalcification clusters are shown.

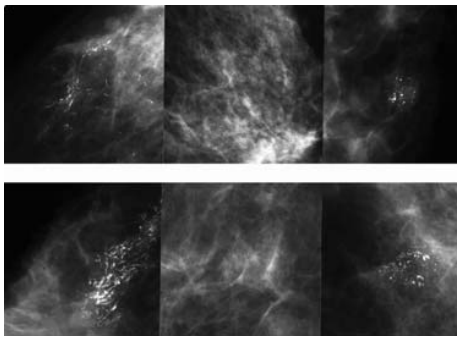

Fig. 4 Some microcalcification clusters

The mammographic masses are rather 'large objects' usually characterized by peculiar shapes. Masses can be characterized trough density, shape, and type of margin. The typical sign of an invasive breast is an irregular or speculated density. Circumscribed lesions with well-defined margins, on the other hand, are usually benign and may represent fibroadenomas, cysts or lymph nodes. In Fig. 5 some mass lesions are shown.

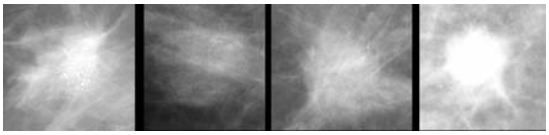

Fig. 5 Some examples of mass lesions included in the representative set extracted from the MAGIC-5 database. From left to right: speculated lesions, roundish lesions with regular, irregular, and blurred edge

VI. Mass Detection

The ROI-hunter of the Magic-5 project was described in ref. [9],[13]. Only selected ROIs are stored for the next processing steps, rather than the whole mammogram as shown in Fig. 6.

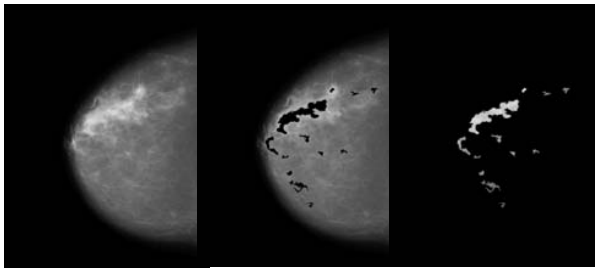

Fig. 6 The original image (left), the image without the ROI (middle) the extracted ROI (right)

Using morphological features [13] the best classifier, a Radial Basis Function (RBF) network, provides an area under the ROC curves of 0.89 ± 0.01 on the MAGIC-5 database [14]. The mass sensitivity of the overall system against the number of false positive per image (FPpI) is 0.89 with 2.9 FPpI.

It is useful to compare it respect to a commercial system. The mass sensitivity of the ImageChecker DM system [16] is 0.88 (CAD Sensitivity mode) with 2.22 FPpI.

VII. Microcalcifications

The CAD algorithm of the Magic-5 project [34] is based on wavelet transforms and artificial neural networks. Wavelets have been used in image filtering to enhance the microcalcifications with respect to the noisy patterns provided by the normal breast tissue. The features to be classified are automatically extracted by an auto-associative neural network and then analyzed by a feed-forward neural network. A straightforward scaling of the wavelet-analysis parameters allows the CAD filter to generate similar processed images despite the differences in the image acquisition procedures.

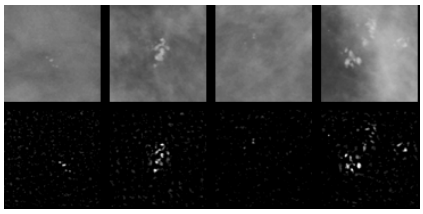

Fig. 7 Some examples of the performance of the filter on mammograms containing microcalcification clusters

The filtered images are then directly analyzed by the neural part of the system. The sensitivity values of 0.88 at a rate of 2.15 FPpI on the MAGIC-5 database [14].

The microcalcifications sensitivity of the ImageChecker DM system [16] is 0.98 with 2.22 FPpI.

VIII. Grid Connection

The database of the MAGIC-5 collaboration [14] collected in the course of these years represents a useful archive of digitized mammographic images. According to the rules established within the collaboration, it can be a valuable tool to the scientific community for different tasks such as training and testing of Neural Network based classification tools, for retrieval use and for statistics and epidemiology studies.

Like in a screening program, data are collected from geographically remote sites. The growth of the database and the distributed nature of the collaboration raise a problem, since images are generally not replicated between remote sites. The approach used to solve the problem of remote access was to use techniques developed for GRID computing. The need for acquiring and analyzing data stored in different locations requires the use of GRID Services for the management of distributed computing resources and data. GRID technologies allow remote image analysis and interactive online diagnosis, with a relevant reduction of the delays presently associated to the diagnosis in screening programs. A Virtual Organization (VO) has been deployed, so that authorized users can share data and resources and implement screening, tele-training and tele-diagnosis for mammograms. A small-scale prototype of the required GRID functionality was already implemented for the analysis of digitized mammograms as recently demonstrated at the SuperComputing 2004 Conference (Pittsburgh, nov. 2004).

As for the GRID method, it is based on a data model in which input data are not moved and their analysis is run in parallel on the nodes where they are stored and, if possible, interactively. From this point of view, the collaboration can be seen as a Virtual Organization (VO), with common services (Data and Metadata Catalogue, Job Scheduler, Information System) running on a central server and a number of distributed nodes (Clients) providing computing and storage resources. The medical application suggests these constraints:

1. some of the use cases require interactivity;
2. the network conditions do not allow the transfer of the full data sample;
3. because of privacy and data ownership, local nodes (hospitals) rarely agree on the raw data transfer to other nodes.

Integration of tools for remote disk storage access into the CAD system has been tested successfully: a prototype that makes possible to share data between the different sites of the research and to run CAD from remote sites has been built [12]. The next step would be to transfer the prototype into a clinical environment, involving radiologists collaborating in the project, to implement tele-diagnosis and tele-screening.

IX. Conclusion

In this paper a general overview of the Computer Aided Detection has been presented. The correct use of the CAD systems and the typical situation, where CAD schemes will be most helpful, are shown. A focus on mammography is made because the need for tools able to recognize the lesions at an

early stage is apparent. The CAD software for mammography has been designed in the framework of the MAGIC-5 collaboration. A comparison of it with respect to commercial CAD is made. The results on masses are comparable than those obtained with ImageChecker DM of R2 technology (leader in CAD technology). An important advantage of the CAD of MAGIC-5 is the GRID configuration. The "GRID philosophy" in mammographic CAD is *move the code rather than data* or *share the images without moving them*. So it is possible run the CAD remotely. With a GRID configuration it would be possible for the clinicians tele- and co-working in new and innovative groupings ('virtual organisations') and, using the whole database, by the CAD tools several analysis can be performed.

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