An Integrated Knowledge Base System Architecture for Histopathological Diagnosis of Breast Diseases

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Abstract— The histopathological diagnosis of breast diseases requires highly trained and experienced experts, and often strains pathologists' cognitive capabilities. Accurate and timely diagnosis of breast diseases is essential for the appropriate management of the patients.

The paper presents a knowledge base system that uses a combination of rule-based and case-based techniques to achieve the diagnosis. Rule-based systems handle problems with well-defined knowledge bases this limits the flexibility of such system. Case-based reasoning has been adopted to overcome this inherent weakness of rule-based systems by incorporating previous cases in the generation of new cases to improve the performance of the system. The result of this research shows that the system is capable of assisting pathologists in making accurate, consistent and timely diagnoses. The system also aid in eliminating errors of omission that have been viewed as a prominent cause of medical errors. In conclusion this paper investigated the histological features used in the diagnosis of breast diseases and proposed an integrated knowledge base system based on the features.

Index Terms— Knowledge Base Systems, Case-Based Reasoning, Rule-Based Reasoning, Artificial Intelligence, Diagnosis

I. Introduction

Integrating computer technology and artificial intelligence is a promising approach in the provision of quality health delivery services in medicine. Artificial intelligence (AI) is a branch of computer science concerned with the design and implementation of programs which are capable of emulating human thinking skills, such as problem solving, visual perception and language understanding. It is concerned with the creation of computer programs to perform activities which, if performed by a person, would require intelligence.

Artificial Intelligence in Medicine (AIM) as a field emerged in the early 1970's in response to several simultaneous needs, opportunities, and interests [1]. An increased demand for high-quality medical services coupled with the explosive growth of medical knowledge has led to the suggestion that computer programs could be used to assist physicians and other health care providers in discharging their clinical roles in diagnosis, therapy and prognosis [2].

One of the first uses of AI on a practical level was the coupling of expert medical knowledge with computer-based technology. As early as the 1960s, computer scientists and physicians recognized the possibility that computers could assist doctors in the diagnosis and treatment of diseases [3].

The field of AI includes the areas of natural language processing, robotics, machine vision and expert systems [4].

An Expert System (ES), sometimes called a Knowledge Base System (KBS) is a computer program that contains some of the subject specific knowledge of one or more human experts. ES automates expert's tasks, which require specialized skills and training. Examples of these tasks include medical diagnosis, equipment repair, computer configuration and financial planning [5].

The aim of this study is to design an integrated knowledge-based system, which is capable of making use of heuristic knowledge and previous cases to improve its performance. The idea is to use rule-based reasoning to generate a diagnosis for Histopathological Breast Diseases (HBD) and to use case-based reasoning to handle exceptions to the rules. A characteristic of a rule-based system is handling problems from a well-defined knowledge base that contains rules. In an only partially-understood domain, this approach may become impractical. Therefore one approach for improving rule-based systems is to extend the rule set by integrating the rule-based system with a case-based reasoning system. A case-based reasoning system is used to solve problems by incorporating past experiences in a partially-understood domain.

The remainder of this paper is organized as follows: Section 2, 3 and 4 describe the rule base reasoning, the case base reasoning and object oriented design respectively. Section 5 presents the related works on automatic diagnosis of breast diseases, section 6 discusses method used, section 7 explains the result of the integrated architecture for HDBD. Conclusion is given in section 8.

II. Rule-based Systems

The idea of rule-based systems is to represent a domain expert's knowledge in a form called rules [6]. In a typical rule-based expert system, a rule consists of several premises and a conclusion. If all the premises are true, then the conclusion is considered true. That is, a rule consists of two parts: condition (antecedent) part and conclusion (action, consequent) part, i.e.: IF (conditions) THEN (actions).

Figure 1 below illustrates the components of a rule-based system.
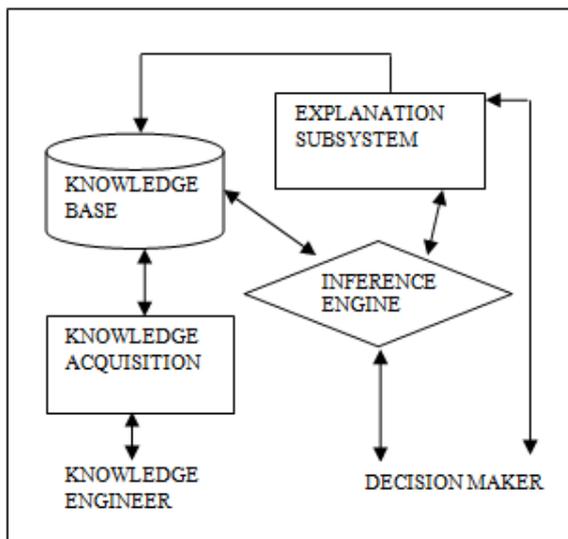
Knowledge base. The permanent knowledge of an expert system is stored in a knowledge base. It contains the information that the expert system uses to make decisions. This information presents expertise gained from top experts in the field. This knowledge comes in the form of facts and rules. Facts are minimal elements of the knowledge which must be identified before anything else. For example, 'fibroadenoma is a breast disease' is a fact.

Rules consist of 'if….then' statements, where a given set of conditions will lead to a specified set of results.

Inference Engine. The inference engine is a computer program that controls the execution, and uses rules to respond to a query and determine whether a suitable match can be found in the fact list, through backward or forward chaining. It determines which rules will be applied to a given question and in what order by using information in the knowledge base.

Backward- and/or forward-chaining reasoning models are typically implemented in rule-based expert systems: Backward chaining is an approach that starts with a goal, e.g., "Which HBD is it?" and works through a potential thesis until it reaches the fact that supports the thesis.

Forward-chaining inference engines are goal-oriented in the sense that they try to prove a goal or rule conclusion by confirming the truth of all the premises. These premises may themselves be conclusions of other rules. This method begins with a set of known facts or attributes values, and applies these values to rules that use them in their premise.

Knowledge Acquisition. Most expert systems continue to evolve over time. New rules can be added to the knowledge base by using the knowledge acquisition sub-system.

Fig. 1: General structure of an expert system
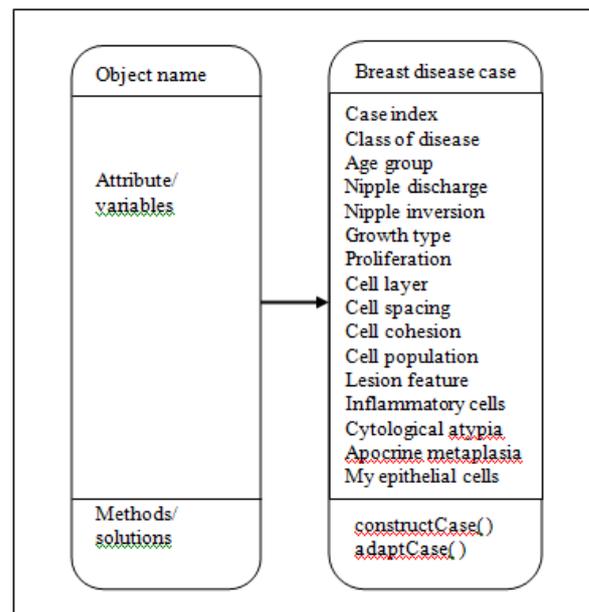
Fig. 2: Structure of Objects

III. Case Based Reasoning

According to [7], CBR is a problem solving technique which complements the solution, acting as a memory of past cases which can be consulted in order to identify similar cases for the new problem. CBR is described as a cyclical process comprising of the four 'Re's [8]. These are: (1) retrieve the most similar case, (2) re-use the case to attempt to solve the problem, (3) revise the proposed solution if necessary and (4) retain the solution as part of the new case.

CBR is an approach to incremental sustained learning, since a new experience is retained each time a problem has been solved. After identifying a given breast disease, an expert is reminded of another disease that he had come across some time ago. Assuming that the reminding was caused by a similarity of important characteristics, the expert uses the diagnosis to the previous disease to determine the disease at hand.

A CBR works in much the same manner as our memories. We learn new things, we learn more about old things, and we retain and reuse new information. It will differ from logic or rules based engine in aspects of recording and retrieving cases.

A case is a contextualised piece of knowledge representing an experience. It contains a past lesson, that is, the content of the case and the context in which the lesson can be used [9]. Typically a case comprises: the problem, the solution to the problem, and the outcome after the solution has been applied to the problem.

In a case-based system, a problem is matched against cases in the case base, and one or more similar cases are retrieved. Case indexing [10] involves assigning indices to cases to facilitate their retrieval. A solution suggested by the matching cases is then reused. Unless the retrieved case is a close match, the solution will probably have to be revised, producing a new case that can be retained. For example if the past experience was a disease called intraductal papilloma, and the disease that is current is a multiple papilloma, that means the case that is nearest to the new disease is intraductal papilloma, and hence the revised content will have the characteristics of the intraductal papilloma as the base, as well as the additional characteristics that are peculiar to multiple papilloma. Therefore inductive indexing is basically a search for similarities among a series of instance and categorization based on these similarities.

The components of a case-based system are the input module, the case memory, retriever, the case adapter and a module to update cases.

Input module. The input module takes new cases. The case is forwarded to the indexing/matching module.

The case memory. The cases are stored in the case memory and may be represented as objects. The case memory is a hierarchy of objects. Any real world entity is uniformly modeled as an object. Every object is an entity that has a state, that is, the set of values for the attributes of the object; and behaviour, that is, a set of methods which operate on the state of the object. The object-oriented paradigm is based on encapsulating the variables and the methods that operate on them into a single object. Conceptually, all interactions between an object and the rest of the system are via messages. Thus, the interface between an object and the rest of the system is defined by a set of allowed messages.

In CBR, the object attributes represent the internal characteristics of an object that facilitate the complete description of the case, and can be used to retrieve, reuse and interpret the case. The list includes attributes needed for classifying and indexing cases, attributes needed for interpreting the cases, attributes serving as the basis for decision-making and performance evaluation and attributes related to recognisable changes in scenarios that can be reused by others. Figure 2 is an example of an object on a breast disease.

Retriever. In its most basic form, the case retrieval procedure consists of searching the case base to find historical cases that most closely resemble the current problem. The comparison consists of matching attributes of the current problem with those of each historical case.

Case adaptation. It is possible that the most similar case in the case base is significantly different from the current problem. Alternatively, there may be subtle but critical differences between them that invalidate the application of the old solution to the current problem. In such cases, it may be necessary to modify the historical solution to fit the current problem.

Case update. Once the current problem has been solved through the retrieval and adaptation of a historical case, the current case can be integrated into the case base as a new historical.

Following are the advantages of CBR:

1. The problem of the knowledge-elicitation bottleneck is surpassed, since elicitation is a simpler way of acquiring past cases.
2. CBR systems can propose a solution quickly.
3. CBR systems can learn by acquiring new cases, making maintenance easier to demonstrate.
4. Unlike RBR systems, CBR systems can grow to reflect their organisation's experience by acquiring new episodic cases.

IV. Object-oriented Design

The object oriented paradigm is well-covered in literature [11] and [12]. Objects are autonomous entities that have a state and respond to messages. All objects communicate using the same mechanism of message passing, and the processing activity takes place inside the objects. Inheritance allows the classification of ob

jects which permits their properties to be shared [13][14][15].

Abstraction in terms of object-oriented concepts is a technique that involves the selective examination of certain aspects of an application. It has the goal of isolating those aspects that are important for an understanding of the application, and suppressing those aspects that are irrelevant. Forming an abstraction in terms of classes and objects is one of the fundamental tenets of the object-oriented paradigm.

Re-using already available software components facilitates rapid software development and promotes the production of additional components. Taking components created by others is better than creating new ones. If a good library of re-usable components exists, browsing components to identify opportunities for re-use should take precedence over writing new ones from scratch.

Inheritance is an object-oriented technique that boosts re-usability [16] and [17].

V. Related Works

Many publications have covered the development of knowledge-based systems using case-based reasoning in the areas of conceptual design [18], aircraft conflict resolution [19], military decision support systems [20], helpdesk operations [21], customer service management [22], legal systems [23] and [24], diagnosis [25], design [26] and planning [27]. It is seen that the applications of CBR in developing knowledge-based systems have been widely adopted in various industries and areas.

There are a number of expert systems that have been developed using rule-based reasoning. This covers areas such as mining [28], commerce [29], diagnosis [30], medicine [31], and robotics [32].

Also, the use of expert systems in the diagnoses of breast cancers is not new, the earliest study encountered was by Cook and Fox [33], where mammographic image analysis was investigated using a decision table to represent all the parameters and possibilities in 41 rules that were created, all centered upon masses and lesions. The other related works were mostly based on Artificial Neural Networks (ANN) for decision making in the diagnoses of breast cancer and some of the work are related to breast mammographic decisions ([34], [35], [36], [37], [38] and [39])

In the like manner [40] proposed an artificial intelligent algorithm for tumor detection in screening mammogram; [41] proposed a multiple circular path convolution neural network system for detection of mammographic masses; [42] classified mammographic breast density using a combined classifier paradigm, [43] worked on the automatic classification of mammography parenchyma patterns in breast cancer; [44] presented an automatic mammographic diagnosis

system for detecting breast cancer based on association rules (AR) and neural network (NN) and [45] worked on frame-based decision support system for histopathological diagnosis of breast diseases in women.

VI. Method

An initial familiarization with the subject of histological diagnosis was carried out through the study of the standard breast pathology textbooks. Journals were also used to obtain detailed information in specific areas.

Further investigation was carried out through interviews with a participating pathologist. These allowed specific diagnostic points to be clarified and potentially problematic areas of diagnosis to be identified. Such interviews have continued regularly throughout the duration of this study, providing valuable feedback. There are several important items of diagnostic knowledge that are used by all pathologists in the identification of histological types. These include information about the possible clinical symptoms of a disease, its rate of occurrence, and microscopic characteristics.

Detailed discussions were held from time to time with the consultant pathologist to ensure that the work progresses in an acceptable frame of reference. Finally, the characteristics contained in the table1 were obtained with the consensus of the pathologists.

6.1 Knowledge Elicitation (KE)

The method used for Knowledge Elicitation in this study is interview method. This stage, involved interviews held with the expert, a pathologist specialized in breast diseases, where several aspects of the problem were discussed. Furthermore, a broad bibliographical material on breast diseases was covered by the knowledge engineer, in order a) to acquire background knowledge on the subject, so that the engineer could go along with the pathologist, and b) to obliterate the subjectivity of the single expert.

During the early stages of the knowledge acquisition, materials of a general nature were also covered. The objective was to uncover key concepts and general problem-solving methods used by the expert in the histopathological diagnosis of breast diseases.

The knowledge acquired from the domain experts is presented in table 1which shows the clinical and microscopic features used by pathologists in diagnosing breast diseases. These characteristics underwent numerous changes until the consultant pathologist was satisfied.

Table 1: Features used in HDBD

Features	Possible Outcomes
Age group	Pre-menopausal, menopausal, post menopausal, not applicable
Nipple discharge	watery, cloudy, bloody
Nipple inversion	yes, no, not applicable
Lesion class	benign, malignant
Growth type	infiltrating, non–infiltrating
Proliferation	stromal, epithelial
Cell layer	double, multiple
Cell spacing	regular, irregular, not applicable
Cell cohesion	tightly, loosely
Cell population	Monomorphic (complete, incomplete), pleomorphic
Lesion feature	necrosis, hemorrhage, not applicable
Inflammatory cells	present, absent, not applicable
Cytological atypia	yes, no, not applicable
Apocrine metaplasia	present, absent, not applicable
Myoepithelial cells	present, absent, not applicable

Note: when diagnosing a disease, the outcome of a feature is tagged 'not applicable' when that feature is not a diagnostic factor in the differential diagnosis of such disease.

6.2 The Rule-Based Expert System Components for HDBD

The facts in the knowledge base of the rule-based expert system include breast diseases, their class, the clinical and histological characteristics of each of the breast diseases etc.

Knowledge is represented in the form of rules as shown in table 2

Table 2: Sample IF – THEN Rules obtained from the knowledge elicited

S/No	Antecedence	Status	Consequence
1.	Pre-menopausal Benign lesion Non-infiltrating growth Double cell layer Apocrine metaplasia.	TRUE TRUE TRUE TRUE TRUE	FIBROADENOMA
2.	Benign lesion Epithelial proliferation Non-infiltrating growth Multiple cell layer Myoepithelial cells	TRUE TRUE TRUE TRUE TRUE	EPITHELIAL HYPERPLASIA
3.	Bloody discharge Benign lesion Epithelial proliferation Non-infiltrating growth Double cell layer Myoepithelial cells Hemorrhage.	TRUE TRUE TRUE TRUE TRUE TRUE TRUE	SCLEROSING ADENOSIS
4.	Pre-menopausal Bloody discharge Benign lesion Epithelial proliferation Non-infiltrating growth Double cell layer Myoepithelial cells Necrosis	TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE	INTRADUCTAL PAPILLOMA
5.	Post-menopausal Malignant Epithelial proliferation Non-infiltrating growth Myoepithelial cells Pleomorphic Tight cohesion periductal fibrosis Necrosis.	TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE	COMEDO CARCINOMA

6.3 The case-based expert system components for HDBD

Let us consider the example of the INTRADUCTAL PAPILLOMA and SCLEROSING ADENOSIS diseases of the breast. Except for the differences in the lesion feature of the diseases, the rest of the characteristics are similar. Supposing that the rule-based expert system has captured only INTRADUCTAL PAPILLOMA, then if the disease detected proves to be SCLEROSING ADENOSIS that would mean that its characteristics have to be captured in the case-based reasoning expert system. SCLEROSING ADENOSIS will inherit the characteristics of the INTRADUCTAL PAPILLOMA, and in addition, the lesion feature is modified. To represent the inheritance in object- oriented terms.

In Figure 5, the rectangle represents the inheritance. This means that SCLEROSING ADENOSIS object will inherit all the characteristics of the INTRADUCTAL PAPILLOMA and will additionally have a method to reset the lesion feature of the disease, resulting in the SCLEROSING ADENOSIS.

6.4 The Integrated Architecture

The architectural goal is to improve rule-based reasoning by augmenting it with case-based reasoning.

This augmentation is done by taking the rules as a starting point of problem-solving, i.e. using rules to generate a first approximation to the diagnosis for a target disease and then invoking case-based reasoning to handle exceptions to the rules.

The idea is to fine-tune the performance of the rules. Another advantage is that if the case-based reasoning misses a similar case, the architecture will at least have a reasonable default answer generated by the rule-based system.

The architecture of the integrated expert system is shown in Figure 3, while the flow in the system is as shown in Figure 4. Each subsystem is essentially an individual problem solver. If a case-based solution is available, case-based reasoning can learn by acquiring new knowledge. The input uses disease characteristics and produces a casual network of possible diagnosis that lead to those diseases. When a disease arises, the system tries to find diseases with similar, but not identical, properties. The system adapts the diagnosis by considering the differences in characteristics between the old and new cases. The component to add a new case is generated.
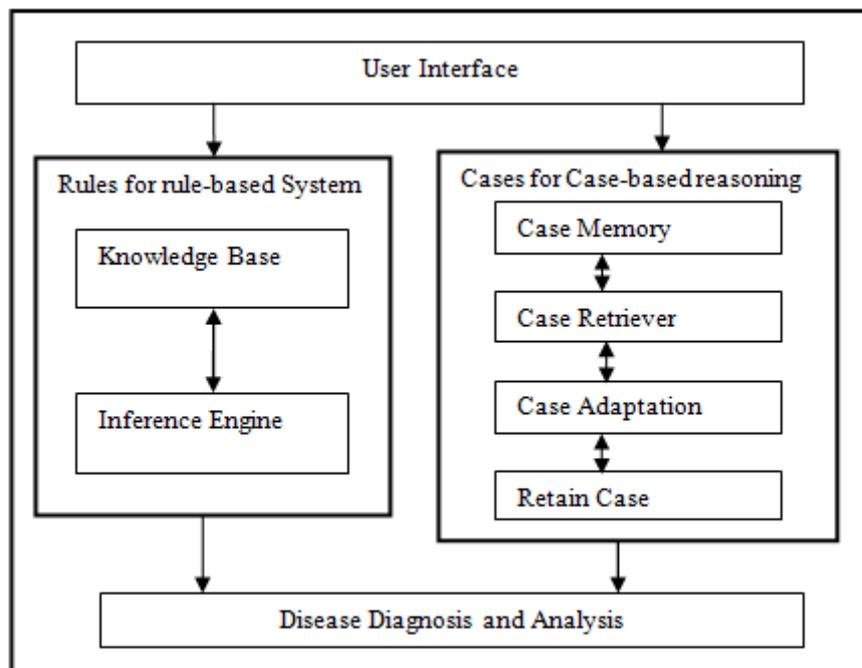
Fig. 3: Integrated architecture for HDBD
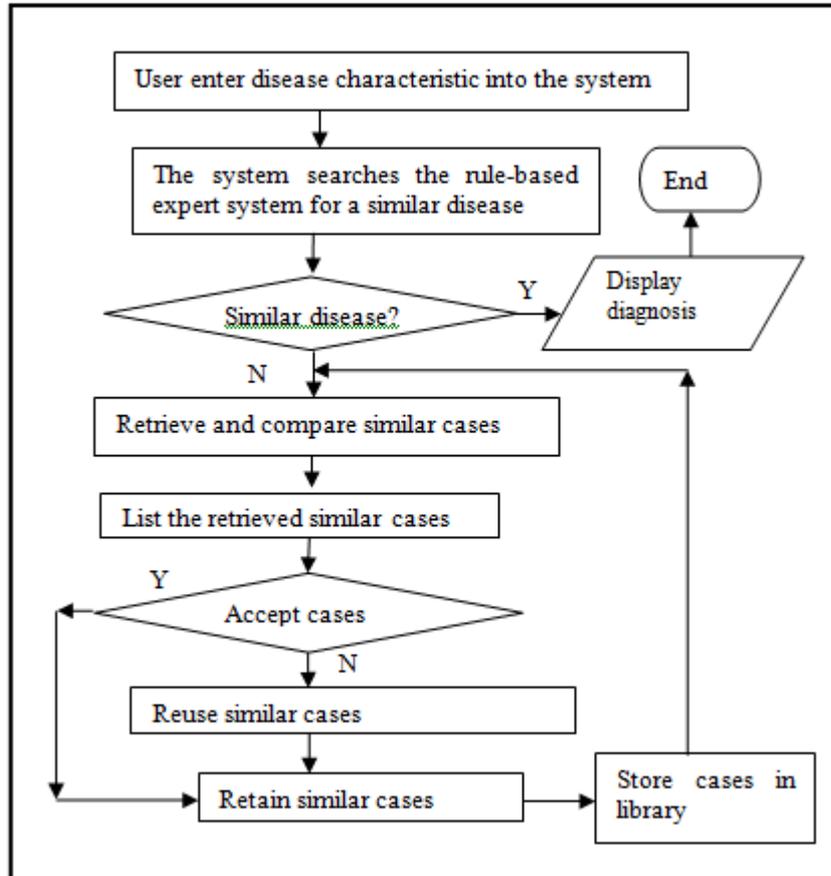
Fig. 4: Flow of data in the integrated architecture for HDBD

VII. Result and Discussion

The system was tested using two set of samples: the first comprising 10 retrospective samples (table 3, appendix section) of breast disease in the form of slide preparations obtained from the Department of Morbid Anatomy, Obafemi Awolowo Teaching Hospital, Ile–Ife, Nigeria. The second consisting five hypothetical cases of breast diseases (table 4, appendix section) which were included to represent interesting and demanding diagnostic areas in which the consultant pathologist wished to explore the system's behavior.

The aim of this evaluation was to determine if the system can assist an inexperience pathologist in making accurate, consistent and timely diagnoses.

A consultant pathologist evaluated the system's recommendation which was summarized in table in the appendix section. The diagnoses made by the system were classified by the consultant pathologist into one of three categories:

Fig. 5: Inheritance in objects.

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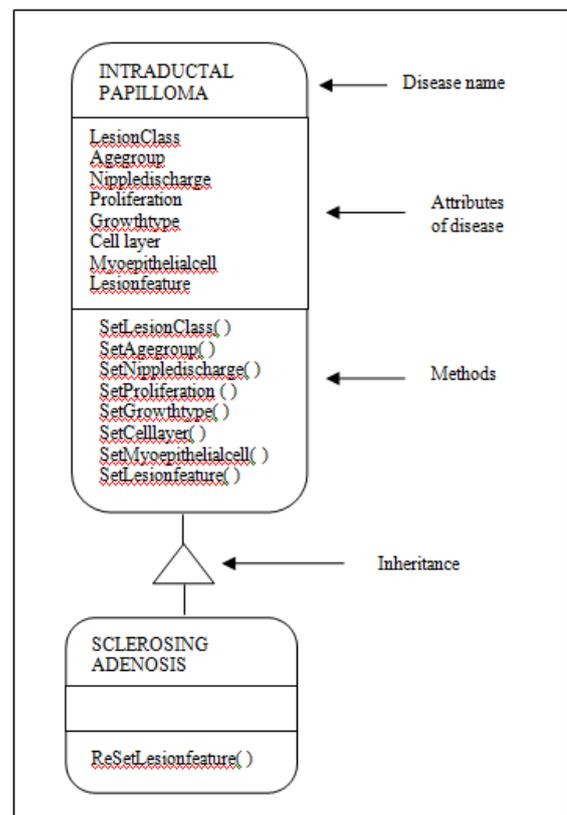
1. Correct: The system's recommendation was identical with the pathologist's own diagnosis.

2. Acceptable: The system's recommendation was different from that of the pathologist, but considered an acceptable alternative.

3. Incorrect: The system's recommendation was different from that of the pathologist and not an acceptable alternative i.e. contradictory to "gold standard" diagnosis of the consultant pathologist.

Table 3: System's performance using retrospective of breast disease

Case No	Differential problem	Pathologist's Recommendation	System's Recommendation	No of question	Evaluation
1.	Epithelial Hyperplasia atypical ductal hyperplasia atypical lobular hyperplasia	Epithelial Hyperplasia	Epithelial Hyperplasia	7	Correct
2.	Duct ectasia Fibrocytic change	Duct ectasia	Duct ectasia	5	Correct
3.	Unknown	Atypical Ductal Hhyperplasia	Atypical Ductal Hyperplasia	6	Correct
4.	Multiple papilloma Intraductal papilloma Papillary carcinoma in situ	Intraductal papilloma	Intraductal papilloma	6	Correct
5.	Cribriform carcinoma Comedo carcinoma Papillary carcinoma in situ	Comedo carcinoma	Comedo carcinoma Cribriform carcinoma	8	acceptable
6.	atypical ductal hyperplasia Lobular carcinoma in situ atypical lobular hyperplasia	Lobular carcinoma in situ	Lobular carcinoma in situ	6	Correct
7.	Complex Sclerosing lesion Sclerosing adenosis Intraductal papilloma	Sclerosing adenosis	Sclerosing adenosis	7	Correct
8.	Fibroadenoma Phyllode tumour	Complex fibroadenoma	Complex fibroadenoma	5	Correct
9.	Fibrocytic change Fibroadenoma	Ffibrocytic change	Fibrocytic change	5	Correct
10.	atypical ductal hyperplasia Invasive ductal carcinoma Ductal Carcinoma in situ	Medullary carcinoma	Comedo carcinoma	9	Incorrect

Table 4: System's performance using hypothetical cases of breast disease

Case No	Differential problem	Pathologist's Recommendation	System's Recommendation	No of question	Evaluation
1.	Epithelial hyperplasia atypical ductal hyperplasia	Epithelial Hyperplasia	Epithelial hyperplasia	5	Correct
2.	Fibrocytic change fibroadenoma	fibroadenoma	fibroadenoma	5	Correct
3.	Ductal Carcinoma in situ atypical ductal hyperplasia Invasive ductal carcinoma	Invasive ductal carcinoma	Invasive ductal carcinoma	6	Correct
4.	papilloma Papillary carcinoma in situ	intraductal papilloma	intraductal papilloma	5	Correct
5.	Cribriform carcinoma Comedo carcinoma Papillary carcinoma in situ	Comedo carcinoma	Comedo carcinoma	8	Correct

Testing proceeded in the following manner. The evaluating/consultant pathologist examined the slide (or slides) of each case microscopically, identified the perceived differential problem, if possible, and then used the system to direct data gathering. When all the questions generated by the system had been answered and the diagnosis was made, the pathologist compared the system's recommendations to his own diagnosis and classified it into one of the three categories described above.

From a total of 15 possible correct diagnoses, the system's recommendation was judged "correct" by the pathologist in 13 cases, acceptable in 1 case and incorrect in only 1 case.

VIII. Conclusion

The knowledge for interpreting slides of diseased breast tissue allows an experienced pathologist specialised in breast pathology to follow a systematic, orderly and logical line of reasoning that leads to a proper diagnosis. This system was developed to simulate the above logical reasoning, in order to facilitate inexperienced pathologists in the histological interpretation of the slides of diseased breasts.

The system's knowledge base has been evaluated positively by an experienced pathologist who is an expert in histopathological interpretation and diagnosis of breast diseases.

Based on the result obtained, the system is capable of assisting an inexperience pathologist to make accurate and timely decision, in the like manner, the system assists an experience pathologist in providing a substantial aid in eliminating the errors of omission that have been viewed as a prominent cause of medical errors thereby increasing the efficiency of his diagnostic skills. Also, automatic system such as this does not only have a role to play in enhancing decision making but also in the study of diagnostic protocol, education, self-assessment, and quality control in the domain of breast histopathology.

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