Computer assisted diagnosis of fine needle aspirate of the breast

H A Heathfield, N Kirkham, I O Ellis, G Winstanley

Abstract
The development of the National Breast Screening Programme has created a demand for the widespread availability of fine needle aspiration cytology services. To meet this demand there must be a rapid increase in the number of pathologists and laboratories able to offer this service. In turn there is a need for improved training methods. The technique of fine needle aspiration cytology is not inherently complicated. The number of possible conclusions is essentially limited to four: unsatisfactory, benign, suspicious and malignant. A computer based expert system, designed to assist pathologists in the diagnosis of fine needle aspirates of the breast, has been developed. The system prompts pathologists to categorise a number of variables in the aspirate including nuclear and cytoplasmic features, and the degree of cellular cohesion, and uses these data to reason about possible conclusions. The final diagnosis is displayed with a detailed explanation listing the factors supporting it.

Initial trials with this system have been encouraging and it is envisaged that this system will be of value both in training and as an aid to routine diagnosis.

Fine needle aspiration cytology has become an essential part of the preoperative assessment of suspected mammary carcinoma. It offers several advantages over alternative techniques. Firstly, current evidence indicates that cytopathological investigation can result in a significant reduction in the number of biopsies performed with consequent financial savings. Secondly, definitive surgery for carcinoma may be decided preoperatively on combined findings from mammography, clinical examination, and cytology, avoiding intraoperative frozen sections in most cases.

With the introduction of the National Breast Screening Programme, the demand for fine needle aspirate cytology services has risen dramatically. A great deal of effort has been directed towards the problem of training pathologists in aspiration cytology techniques in sufficient numbers to meet the growing demand. Attention has therefore been focused on the need for new and improved training methods in this area.

The technique of fine needle aspiration cytology of the breast is not inherently complicated. The number of possible conclusions is essentially limited to four: unsatisfactory, benign, suspicious and malignant—these being based on limited cytological features. Such a well defined problem area, with only limited numbers of conclusions, lends itself readily to the application of "artificial intelligence" techniques.

This paper describes a computer-based expert system, designed to assist pathologists in the examination and diagnosis of fine needle aspirates of the breast.

Methods
SYSTEM DEVELOPED
This system was developed using a commercially available expert system shell (KES, Rule-Based Production System), running on an IBM PC/XT/AT or clone.

Expert systems typically comprise three modules; an inference mechanism which performs reasoning; a user interface which directs dialogue with the user; and a knowledge base holding application information. Expert system shells provide both the inference mechanism and the user interface, leaving the system developer to write the knowledge base.

Knowledge may be represented formally in various ways, including rules, frames, and semantic networks. The expert system shell used here requires knowledge to be expressed as rules. These are seen as a convenient method of representation, comprising modular "chunks" of knowledge about a domain, in a form that is easily comprehensible to clinicians. They have been used successfully in several medical fields.

THE KNOWLEDGE BASE
Knowledge acquisition was carried out using text books and references and through detailed discussion with pathologists. The range of possible diagnostic conclusions included in the system are shown in table 1.

A list of all aspirate features considered important in reaching a diagnosis is shown in table 2.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Possible diagnostic conclusions included in expert system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade</td>
<td>Diagnosis</td>
</tr>
<tr>
<td>+2</td>
<td>Malignant</td>
</tr>
<tr>
<td>+1</td>
<td>Suspicious of malignancy</td>
</tr>
<tr>
<td>0</td>
<td>No comment, inadequate or unsatisfactory sample</td>
</tr>
<tr>
<td>-1</td>
<td>Probably benign</td>
</tr>
<tr>
<td>-2</td>
<td>Benign</td>
</tr>
</tbody>
</table>
Table 2 Aspirate features important in diagnosis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Benign epitelial</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuclear shape</td>
<td>Oval</td>
<td>Rounded (not oval)</td>
</tr>
<tr>
<td>Nuclear size</td>
<td>Small</td>
<td>May be increased</td>
</tr>
<tr>
<td>Chromatin</td>
<td>Normal coarse</td>
<td>Finer or coarser</td>
</tr>
<tr>
<td>Nucleolar numbers</td>
<td>Single</td>
<td>May be multiple</td>
</tr>
<tr>
<td>Nucleolar size</td>
<td>Small</td>
<td>May be increased</td>
</tr>
<tr>
<td>Nucleolar shape</td>
<td>Regular</td>
<td>May be irregular</td>
</tr>
<tr>
<td>Cytoplasm</td>
<td>Moderate amount</td>
<td>May be abundant</td>
</tr>
<tr>
<td>Pleomorphism</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Apocrine cytoplasm</td>
<td>May be present</td>
<td>Absent</td>
</tr>
<tr>
<td>Bipolar/stromal cells</td>
<td>Usually present</td>
<td>Absent</td>
</tr>
<tr>
<td>Cellular cohesion</td>
<td>Good</td>
<td>Absent</td>
</tr>
<tr>
<td>Punched out holes in nuclei</td>
<td>Absent</td>
<td>May be present</td>
</tr>
<tr>
<td>Cellularity</td>
<td>Sparse</td>
<td>Highly cellular</td>
</tr>
</tbody>
</table>

Finally, the significance of each of these features was assessed as being in favour of a benign or malignant diagnosis, and a number of rules expressing this were formulated. An example of two such rules is shown below.

**Benign cell rule if:**
- pleomorphism = none or
- pleomorphism = benign and
- nuclei = normal and
- nucleoli = normal and
- chromatin = normal and
- cytoplasm = scanty or moderate then,
  - cell type = benign.

**Benign diagnosis rule if:**
- cell type = benign and
- cellularity = sparse or moderate and
- cellular cohesion = good or moderate and
- bipolar cells = present and
- punched out holes = absent then,
  - diagnosis = benign.

Rules identifying a limited number of histopathological subtypes were also incorporated into the knowledge base. These are intended only to give a tentative suggestion as to histopathological type in situations where highly characteristic features are present.

Modifications were made to take account of several exceptions to these general rules. For example, rules were incorporated to allow for lobular carcinoma in which bipolar cells can coexist with malignant epithelial cells; for fibroadenoma in which high cellularity is found in younger women; and to take account of those tumours which have malignant nuclear features but lack abundant cytoplasm.

This initial rule set was tested and its performance assessed by pathologists. Errors and omissions in the knowledge were corrected. The whole process was repeated several times until a reasonably robust rule set had been produced.

While our system can interpret the clinical importance of bipolar cells alongside malignant characteristics, it should be cautioned that it cannot assess the situation where bipolar cells reflect only the benign tissue through which the needle transversed, and where suction was not applied while the needle tip was within the neoplastic area.

**RUNNING THE SYSTEM**

On start-up the system displays information describing the purpose of the system and the possible conclusions which can be drawn. A main menu is then presented. This gives the user the option of beginning with a diagnostic session or viewing the structure of the knowledge base in various ways.

**System menu**
1. Next diagnostic session
2. View attributes
3. Display rules
4. Display rule tree
5. Information
6. Exit system

Selecting number 1 from the main menu begins a new diagnostic session. Before beginning with the session, the system first attempts to establish the adequacy of the sample by asking the user if the smear is scanty or the preparation poor. If either of these is true then a verdict of “inadequate” is given and the session terminated. Unlike the cytopathologists, who carry out their own needling, the system does not have access to the additional valuable information which is necessary to interpret a scanty smear and so makes no attempt to do so.

The user is then prompted to categorise each of the variables in the aspirate. For each question the system gives several possible answers from which the user can choose—for example,

**How cellular is the sample?**
1. Sparse
2. Moderate
3. Highly cellular

If at any time during the consultation the user requires an explanation of the meaning of a particular question this can be obtained by typing “explain”—for example,

**How much cohesion is shown by the epithelial cells?**
1. Good
2. Moderate
3. Absent

? = explain

At low power, an indication of malignancy is the lack of cellular adhesion resulting in clusters and sheets of loosely attached cells.

When all relevant information has been gathered, the system displays a short conclusion, giving the diagnostic decision. If the data were suggestive of any particular histological subtype this is also commented on—for example,

**Recommended diagnosis**

BENIGN < -2>

The sample may be an inflammatory lesion resulting from fat necrosis or abscess. This is suggested by the presence of inflammatory cells.

Finally, the user can obtain a detailed justi-
SUSPICIOUS OF MALIGNANCY \langle +1 \rangle
THE EVIDENCE SUPPORTING A DIAGNOSIS OF MALIGNANCY IS:
Cells showing some but not all features of malignancy
No bipolar cells
Punched out holes in the nuclei
A moderately cellular sample

THE EVIDENCE AGAINST A DIAGNOSIS OF MALIGNANCY IS:
Age of patient: 21
Benign pleomorphic cells
Moderate cellular cohesion

Discussion
Trials of this system have been carried out as part of a training course designed to instruct pathologists in fine needle aspiration techniques. Although most users were initially reticent about using the system, this can be attributed to an unfamiliarity with computer operation. They quickly gained confidence in its use. Results using a test set of samples were encouraging, with a high proportion of conclusions given by the system corresponding to those found at biopsy. Although many of the criticisms aimed at the system were directed at the user interface, and have since been resolved, a more fundamental inadequacy lies in the inability to reason quantitatively. In practice, pathologists attach different degrees of importance to the various diagnostic features of breast aspirate. To recreate this process numerical weights have to be attached to rules in the knowledge base. The problem lies in determining accurately the weighting factors used by pathologists as each has his or her own biases. To reach a consensus would need vast amounts of statistical data which are not presently available, but they may be provided in the future by the quality assurance monitoring of the Breast Screening Programme. This aims to establish a cytology database with particular emphasis on relating cytological reports to subsequent histological findings. Such information will be important if we are to enhance and extend the capabilities of our system. So that the system could apply historical knowledge to extrapolate back to what caused the nature and content of an individual aspirate smear, it would also be necessary to incorporate a pathological disease model into the system.

With the advent of the National Breast Screening Programme, the need for increased numbers of pathologists able to perform fine needle aspiration cytology has placed a considerable burden on those centres involved in training. While not providing a complete answer to training problems, the system described in this paper can, by acting in a consistent and reliable manner, be used as a training tool. By teaching an awareness of the need for a structured approach to data gathering, identifying aspirate features important in diagnosis, and providing explanations for all questions and conclusions, it can be used in conjunction with more traditional teaching methods.

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