Diagnostic Strategies in the Hypothesis-Directed PATHFINDER System

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Abstract
PATHFINDER is a developing expert system to assist pathologists in the interpretation of findings noted on microroscopy examination of lymph node tissue. We describe PATHFINDER's hypothesis-directed reasoning approach with an emphasis on intelligent question selection strategies, techniques for managing data uncertainty, and explanation methods for justifying questions asked of the pathologist. Although this work was originally inspired by the INTERNIST-1 approach to hypobrosis strong and question selection, we have made several modifications to the INTERNIST-1 approach in having an expert system for pathology.

Introduction
PATHFINDER is a hypothesis-directed expert system for the diagnosis of lymph node pathology based upon the appearance of microscopic features in lymph node tissue. Major questions addressed in our research include the investigation of (a) alternative methods for combining evidence in support of possible hypotheses, (b) useful diagnostic problem-solving strategies, and (c) appropriate question justification schemes. In this paper, we discuss our research on strategies for refining a set of plausible disease hypotheses through the generation of appropriate questions and the management of potential data uncertainty. We also describe our current approach to question justification.

Motivation for the expert system
A working expert system that could give general pathologists easy access to the diagnostic reasoning capabilities of experts within the lymph node pathology domain would be a useful clinical innovation. Over 30,000 new cases of lymphomas (malignancies of the lymphatic system) are reported each year in the United States. As most lymphomas have a distinct natural history and specific therapy, precise diagnosis is crucial. Unfortunately, the diagnosis of lymph node disease is often error-prone and is considered one of the most difficult tasks in pathology. Experts is the diagnosis of lymph node pathology (especially lymphomas) is used to diagnose diagnostic-based general pathologists. Several studies have shown that expert diagnosis often agree on one another whereas the diagnoses offered by general pathologists are varied in as many as 50% of the cases receiving secondopin review by experts.

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The problem
As in many areas of medicine, a central problem-solving task within the lymph node pathology specialty is the classification of sets of symptoms into disease categories. Expert pathologists estimate that approximately 15% low- and high-magnification microscopic features are used in reasoning about lymph node disease. There are over eighty lymph node disease, fifty of which are malignant. The malignant diseases include primary malignancies (lymphomas) that arise from cells of hematologic origin and hematologic malignancies arising from intratumoral lymphoid cells. The great variability of abnormal lymph node sections can be attributed to thirty different benign diseases ranging from hematopoietic to rheumatologic arthritis. A source of difficulty in this domain is that many of the benign lymph node diseases closely resemble the malignant lymphomas in appearance.

The choice of methodology
Two symbolic reasoning approaches were considered in the initial design stages of an expert system for lymph node pathology: the INTERNIST-1 hypothesis-directed approach and the MYCN rule-based production system approach. Early informal "process tracing" involving discussions with experts and observation of expert diagnostic procedures suggested that the diagnosis of lymph node pathology often involves iterative hypothesis refinement. The hypothesis-directed model of physician problem-solving (as described in INTERNIST-1) attracted our attention as a potentially useful way to simulate diagnostic strategies in pathology. INTERNIST-1 is an expert system for internal medicine initiated at the University of Pittsburgh 10 years ago. It is the core of a continuing research program, CADUCEUS.

The method of sequential diagnosis
PATHFINDER and INTERNIST-1 are based on the method of sequential diagnosis. With this approach, a set of related disease manifestations is initially presented to the program. A list of plausible disease hypotheses (a differential diagnosis) is then formed based on these manifestations and questions are selected that can help narrow the number of diseases under consideration. After the user answers these questions, a new set of hypotheses is formulated and the process is repeated until a diagnosis is reached. The method of sequential diagnosis is hypothesis-directed in that the questions are selected by strategies of either that consist of a correct list of hypotheses. The INTERNIST-1 approach to the method of sequential diagnosis uses several diagnostic strategies for selecting questions in conjunction with a set of heuristics for making decisions about using the alternatives strategies.

The method of sequential diagnosis is an agreement on older Bayesian statistics programs that require all relevant
findings in a patient case at once to make an accurate diagnosis. As there are often dozens of relevant clinical findings, the Bayesian approach has been considered less suitable for application in a clinical setting than systems using the method of sequential diagnosis.

In PATHFINDER, a crucial task in the formulation of differential diagnoses is the assignment of a numerical score to each disease based on the given disease manifestations. We will not discuss details of scoring or formation of the differential in this paper. The scoring procedures make use of expert estimates of the associations between diseases and disease manifestations. In PATHFINDER and INTERNIST-I, there are two estimates attached to each disease-manifestation pair: an evolving strength and a frequency. The evolving strength for a disease-manifestation pair answers the question: "If I see one of these findings, how strongly should I consider this disease to be its explanation?" The frequency is an estimate of how often the disease under consideration is associated with the finding. The evolving strength and frequency estimates are similar to the formal statistical concepts of predictive value and sensitivity.

Disease manifestations in lymph node pathology are microscopic features. In PATHFINDER, features are each subdivided into a mutually exclusive and exhaustive list of values. For example, the feature paraffin-clear can take on any one of the values absent, slight, moderate, or prominent. Features are evaluated by the selection of a value that reflects the severity of the feature. We refer to a particular feature and value as a feature-value. Every feature-value is, the PATHFINDER knowledge base is associated with an evolving strength and frequency for each disease.

Problems with the method of sequential diagnosis

The INTERNIST-I effort demonstrated the utility as well as the limitations and problems with the method of sequential diagnosis in internal medicine. After summarizing some problems with INTERNIST-I, we will discuss each in the context of lymph node pathology.

While INTERNIST-I was shown to reason admirably within the defined problem area using general diagnostic strategies, deficiencies were identified in the system's inability to consistently focus on an accurate set of diseases. Specifically, INTERNIST-I researchers have identified four problems:

1. The program performs poorly when several disease processes coexist and single manifestations can be explained by more than one disease.

2. Inappropriate questions are sometimes asked because of a lack of explicit knowledge about problem-solving strategies.

3. Diagnoses are sometimes incorrect because of a lack of deep pathophysiologic and anatomical knowledge.

4. Diagnoses are sometimes incorrect because important information may be overlooked when there is a preponderance of unimportant information.

Applying the method of sequential diagnosis to lymph node pathology

We believe that the INTERNIST-I approach is in several aspects more appropriate for reasoning about lymph node disease than it is for diseases of internal medicine. We will now describe PATHFINDER's relative immunity to the first three problems listed above. Later, in our discussion of PATHFINDER's confirmation mode strategy for selecting questions, we will address the fourth issue.

1. The multiple disease problem: Within internal medicine, the presence of concurrent diseases in a single patient is not uncommon. Two or more diseases can co-exist in lymph node pathology as well. However, they are by definition limited to spatially discrete areas in one or more lymph node specimens from the same patient. Although it is understood that co-sustaining lymph node diseases could grow to become adjacent and continue to spatially adhere, there is no concept of spatially superimposed diseases. Experts believe that the resulting morphological patterns are too difficult to classify. Since PATHFINDER can process each area of lymph node tissue separately, it is free from the multiple disease deficiencies of INTERNIST-I.

2. Diagnostic problem-solving strategy: INTERNIST-I's developers attribute the generation of poor questions in part to the system's deficiency of explicit knowledge about problem-solving strategies in internal medicine. Diagnostic strategies in internal medicine are complex. There exist no simple diagnostic strategies that can be used to solve problem formulation. Unlike internal medicine, the domain of lymph node pathology appears to have a diagnostic strategy based on a simple disease ontology. The current version of PATHFINDER uses this knowledge in question selection. This will be described in detail below as the section on PATHFINDER methods for question selection.

3. Deep models: We mentioned above that INTERNIST-I does not use deep means of disease processes in clinical problem-solving. Evaluators of INTERNIST-I have speculated that use of more complete knowledge about causal relations could raise the confidence of later versions of INTERNIST-I. While this is undoubtedly true in the domain of internal medicine, lymph node pathology apparently makes little use of deep causal or etiological models. Knowledge relating the complexity observed in lymph node patterns to underlying fundamental patterns is sparse. As deep models seem to have little importance in reasoning about lymph node patterns, the addition of deep models would likely yield little or no improvements in PATHFINDER's performance.

In summary, properties of the lymph node pathology application area that minimize the problems attributed to the INTERNIST-I methods are the domain's lack of recognizable superimposed diseases, the existence of a simple globally-applicable problem-solving hierarchy, and the lack of accepted deep models of lymph node disease.

PATHFINDER hypothesis-directed question selection strategies

As mentioned above, a crucial feature of sequential diagnostic systems is their ability to pose questions that give the user to collect useful data. We will now describe PATHFINDER hypothesis-directed strategies for selecting questions that can minimally reduce the uncertainty in the differential diagnosis.

PATHFINDER generally applies different modes depending on the nature of the current differential diagnosis list. The current system uses three different modes for question selection. We call these modes group-discriminate node, entropy-discriminate node, and confirmation mode. We will describe these modes, the heuristics used in the selection to apply them, and the motivation for their development.
Early PATHFINDER question selection strategies

Earlier versions of PATHFINDER used questionning modes similar to those found in INTERNIST-1. The modes used in INTERNIST-1 were named "preamble mode", "diagnose mode", and "rule-out mode". The selection of modes in INTERNIST-1 is a function of the number of diseases and corresponding scores of the diseases on the differential diagnosis list. If there is only one disease on the differential diagnosis, INTERNIST-1 immediately concludes the disease at the first diagnosis. Otherwise, INTERNIST-1 determines those diseases which are "true" to the disease with the highest score. Two diseases are "true" if their scores differ by less than some carefully chosen threshold. Depending upon how many diseases are close to the leader, INTERNIST-1 enters one of the three modes:

1. Preamble mode: If there are no diagnoses close to the leader, INTERNIST-1 pursues the leading diagnosis. That is, the user is asked to report on patient findings that would confirm the diagnosis. These findings have associated high existing attentiveness for the disease being pursued.

2. Diagnose mode: If one or two diseases have scores close to the score of the leading diagnosis, INTERNIST-1 enters diagnose mode. In this mode, questions are asked which best discriminate between the two leading contenders.

3. Rule-out mode: If there are three diseases with scores close to the score of the leading diagnosis, INTERNIST-1 goes into rule-out mode. In this mode, each disease on the differential diagnosis, questions are asked that would tend to eliminate further consideration of the disease.

The first several versions of PATHFINDER used the preamble and diagnose modes. We did not implement a rule-out mode because the pathologist on our team believed that clinical-pathologists very rarely attempt to pursue the differential diagnosis list by methodically ruling out unlikely contenders. This is based on the frequent occurrence of very large differential diagnoses in lymph node pathologies.

Later PATHFINDER question selection strategies

After some experimentation with preamble and diagnose discriminate modes, we decided to eliminate preamble mode in favor of a "confirmation mode" which is described below. Our experimentation also revealed the utility of putting questions that could discriminate among more than two diseases. We thus began to explore new diagnostic strategies that could supply the missing stage of hypothesis in the differential diagnosis. We first implemented a selected question that could rule out the largest number of diseases on a differential diagnosis. Later, focus mode was introduced by the more general "entropy-discriminate mode". The testing of entropy-discriminate mode uncovered an important hypothesis-specific strategic hierarchy used by experienced pathologists in the diagnosis of lymph node pathology. Integrating the strategic hierarchy into the entropy-discriminate mode yielded group-discriminate mode. We will discuss the new modes and the reasoning behind their development.

PATHFINDER Focus mode

As the testing of early versions of PATHFINDER proceeded, deficiencies in the discriminate-discriminate mode became apparent. For example, if a differential diagnosis contained several small cell intermediately-differentiated cell, large cell disease, our initial version of PATHFINDER would use discriminate mode to identify questions that could discriminate between the two diseases rather than proposing that the user answer a more globally discriminating question about the site of the cell that is in zero to be probabilistic. In such cases, reasoning on just two diseases was more appropriate than using expert hematopathologists. This strategy is viewed as being too narrowly biased at the top of the differential diagnosis. These considerations led to the formulation and implementation of focus mode.

Focus mode considers all of the diseases on the differential diagnosis. The most selective question among the set of features is used to minimize the number of diseases that remains on the differential diagnosis after values for these features are reported. The mode operates by estimating the number of diseases that will remain on the differential diagnosis when the user requests a feature and value. The mode then selects those features which yield the maximum final disease estimate.

The expected number of remaining diseases for a feature is calculated by summing, over all values for that feature, the product of:

• the probability that a value will be reported, and
• the number of diseases that will remain if that value is reported.

The probability that a value will be reported is estimated by taking the average of the frequency of that value for each disease on the current differential diagnosis. This assumes that each disease in the differential diagnosis is equally likely. Although usually not the case, this assumption is used to help select questions that discriminate equally among the diseases on the differential diagnosis. The pathologist in our group believes that this is an appropriate strategy for this domain.

The exact number of disease remaining on the differential diagnosis after a feature and value are reported in the discriminate-discriminate mode is unsatisfactory. Instead, focus mode uses approximations that only some of the diseases in the differential diagnosis that are assigned a feature-value frequency score of 0 by experts will be removed from the differential diagnoses if that feature and value is reported.

The focus mode strategy has a simple conditional deterministic reasoning. If we define the utility of a question to be proportional to the number of diseases removed from the differential diagnosis after the question is answered, we are simply looking for the question with the maximum utility. This definition of utility is reasonable in that smaller number of diseases on a differential diagnosis reflects more certain knowledge about the diagnosis. Thus, a question with a high utility corresponds to a question that can lead to a large increase in certainty.

The basis and behavior of the mode was well-accepted by expert hematopathologists. However, it had a major problem that was caused in the use of a threshold on frequency values to determine the number of diseases remaining in the differential diagnosis. If a feature has one or more values that are zero with low (but non-zero) frequency in every disease on the differential, focus mode will overlook this feature as a useful question even though evaluating the feature could highly discriminate many diseases on the differential. This problem with focus mode led us to the formulation of the PATHFINDER entropy-discriminate mode.

PATHFINDER Entropy-discriminate mode

In focus mode, the utility of a question is related to the number of diseases removed from the differential diagnosis. This change in number of diseases on the differential diagnosis reflects a difference in the uncertainty of the differential diagnosis.
Entropyp indiscriminate mode makes use of a more general form of uncertainty than in information theory. In this mode, a quantity called entropy is used as the measure of uncertainty. The value of this measure is derived from the differential diagnosis, which is inspired by a program developed by Gyorv for diagnosis of acute renal failure. In this context, entropy is equal to the sum of entropy per each disease in the differential diagnoses where \( p_i \) is the probability that a disease is in diagnoses. Instead of reducing the number of diagnoses remaining on the differential diagnosis when a particular value is reported for a feature, we calculate the entropy of the resulting differential diagnosis. For a potential question, we must calculate for each value, the probability that each disease will be on the final differential diagnosis. We use Bayes' theorem to calculate the probabilities and assume that each disease on the initial differential diagnoses is equally likely (as we do in focus mode).

The entropy distinguishing mode was judged by experts to be an improvement over focus mode. However, there were still occasions when the questions were not viewed as optimal.

**PATHFINDER Group-discriminate mode** Preliminary testing showed that the rationale for questions selected by the powerful entropy-discriminate mode was often not easily understood by experts. Although these questions were undoubtedly the most discriminating among the diseases on the differential diagnosis, we found that they were not natural questions to ask in relation to the problem-solving process followed by the human experts.

The pathologist on our team was a simplifying problem-solving strategy for managing complexity in the domain. While entropy-discriminate mode selects diagnoses that best discriminate among all diseases on a differential diagnosis, we found that the pathologist's judgment about the number of diagnostic categories. For example, if there are benign and malignant diagnoses on a differential diagnosis, the pathologist might ask whether diagnoses that are likely to be malignant rather than benign contribute less to the differential diagnosis than are primary malignant and metastatic diagnoses. Our pathologist finds questions that discriminate among various natural groupings of diagnoses on the differential diagnosis than the question that could best discriminate among all the diseases.

Our guiding strategy for creating the diagnostic hierarchy was to identify similar cases in other medical domains. The existence of a small set of questions that can be asked to change the diagnostic strategy led to the formulation of group-discriminate mode. For a given differential diagnosis, the group-discriminate mode identifies the most specific groupings possible and then selects diagnoses that best discriminate among the diseases in a group. This mode is analogous to the INTERNIST-1 discriminate mode except that groups of diagnoses, rather than diagnoses, are discriminated.

**PATHFINDER**

**Primary Malignancy**

**Benign**

**Metastasis**

**Hodgkin's Lymphoma**

**Figure 1: Lymph Node Disease Strategic Hierarchy**

**PATHFINDER Confirmation mode** Recall that the INTERNIST-1 partial mode selects questions that lead to the confident diagnosis. These questions are those with high evoking strengths for the disease under consideration. In place of partial mode, we have designed confirmation mode. This mode is similar to partial mode in that questions are asked when a single disease is being considered as the diagnosis. Confirmation mode differs from partial mode in that the questions selected are marked by our expert pathologist as being "important" to the disease under consideration. For example, the presence of Sternberg-Reed cells is an important feature of Hodgkin's disease. If Hodgkin's disease is to be excluded by the progress of Sternberg-Reed cells has not been evaluated, PATHFINDER will ask the user to evaluate this feature. Confirmation mode upon expert knowledge as a safeguard that contains the tendency of the method of sequential diagnosis to focus the differential diagnosis. In terms of computational problem solving, this mode will lead to the generation of the "backtrack problem" associated with hill-climbing algorithms. Such a mode serves as the function of the traditional review of systems used by physicians when interviewing a patient. One objective of the traditional medical review of systems and PATHFINDER confirmation mode is to ensure that the conclusions reached are not completely off target. A confirmation strategy addresses these issues in which a preponderance of unimportant information leads an INTERNIST-like expert system to a diagnostic diagnosis.

**PATHFINDER heuristics for mode application**

In reasoning about a case, PATHFINDER tries attempts to classify diseases on the differential diagnoses into two groups at the most specific level of the strategic hierarchy for diseases of lymph node diagnosis. If the disease group can be determined, group-discriminate mode is applied to the differential diagnosis. If there are two or more diagnoses on the differential diagnosis and all the diseases can be classified in a group at our leaf or the strategic hierarchy, group-discriminate mode is applied. Finally, if our disease remains on the differential, confirmation mode is applied. If the same single disease remains at the completion of confirmation mode, the disease is concluded as
While a pathologist is training or an expert interested in PATHFINDER's reasoning might desire understandable questions, matched by group-discriminate mode, where users are less interested in reaching a diagnosis as quickly as possible. For this reason, we allow the user the option of disabling group-discriminate mode. When group-discriminate mode is disabled, every mode is applied in its place. Although, the questions generated in many cases by the explain-discriminate mode may not be understandable, they are often superior in their ability to discriminate among all the disease hypotheses. Some questions usually lead the user to a diagnosis more quickly than those generated by group-discriminate mode.

Managing the collection of unreliable data

The discriminating power of questions is not the only important factor in question selection. INTERNET-1, for example, considers the cost and invasiveness of tests. We do not consider invasiveness; if lymph node pathology, invasion occurs only at biopsy. Within the lymph node pathology domain, we found it useful to consider the reliability, fieldness, and extent associated with the evaluation of a particular feature. PATHFINDER uses these features in combination with the abilities assigned to potential features by the question selection nodes to generate a final utility for each question. The final utilities are used for selecting the best questions to ask. The details of the PATHFINDER cost-benefit utility equation will not be discussed here. We will only mention the reliability factor as it relates to a technique for minimizing the collection of unreliable data.

The collection of data is especially important in reasoning about symptomatic pathology. Dilemmas with experts hemopoesia or about the expert-dependent problems with the recognition and quantification of lymph node features suggested that the questions selected by PATHFINDER at each point in a case should be tailored to different levels of user expertise. We have found that the need for customizing question-generation and relevance to a user's expertise to minimize the collection of unreliable data is an important yet relatively unexplored area. Such methods could enable medical expert systems to adapt the selection of questions to maximize the accuracy of the inference process.

PATHFINDER considers the level of expertise of the system user in generating questions. After scanning the user's level of expertise, PATHFINDER uses three sets of expert estimates of expected reliability to modify the questions asked of users having different levels of expertise. The expected reliability is the amount of brain placed by an expert in the values reported for each feature by system users in different expertise groups. We believe that the expert's reliability estimate is a cogeneration of the relative frequencies of false positives and false negatives for both the recognition of a feature and for the selection of a feature-value pair. Sets of expected reliability estimates for the experts, hemopoesia, non-pathologists, and pathologists in training are used by PATHFINDER's utility equation. The different sets of estimates enable PATHFINDER to first offer questions to users that they are more likely to answer reliably. The current version of PATHFINDER prompts the user for his level of expertise and incorporates the appropriate set of feature reliability equations in the utility equation. We are currently exploring techniques to dynamically assess the reliability of data-filling inconsistencies in input data.

Justification of question selection

Surveys of potential users of medical advice systems have suggested that the capability of the system to explain its reasoning strategies may be one of the most important factors determining its eventual clinical acceptance. Unfortunately, explanation systems for frame-based systems such as PATHFINDER are uncommon. For example, INTERNET-1 only informs the user about the current question-generating strategy in progress. More specific reasons as to why a particular finding is being requested are absent.

We have experimented with several question justification schemes. We first implemented a free text system that evaluated the questions selected in terms of discriminating power, fieldness, reliability, and cost. Early versions simply reported that a question was "good" or "very good" for discriminating benign diseases from the differential diagnosis based on the compiled utility. We later decided to offer the system user more specific information about the discriminating abilities of a question. The present version of PATHFINDER displays information about the relative impact of alternative responses on a particular differential diagnosis in a graphical format.

Figure 2 depicts the justification offered by PATHFINDER when two diseases or disease groups are being considered. In this sample case, the feature architecture has been recommended by the system as having the ability to reflect a particular differential diagnosis (not shown) containing a number of benign and malignant diseases. The positions of the set of features is used to indicate the degree to which each group of diseases is favored by each possible feature value. In the example below, the values preserved and partially obliterated strongly support diagnoses on the differential diagnosis that are in the benign group, while the value completely obliterated strongly supports the malignant disease hypotheses. The value greatly obliterated is not very useful for discriminating between the two disease groups. If more than two diseases from one category are on the differential diagnosis, a justification format exists for each possible value, the diseases that will likely become strong contenders if their value is reported. This format is displayed in the sample PATHFINDER transcript in the appendix. The graphical justification format has been extremely useful in offering insights about the impact of questions on a differential diagnosis and in facilitating the refinement of the knowledge-base data.

why ARCHITECTURE

feature Architecture

<table>
<thead>
<tr>
<th></th>
<th>Malignant</th>
<th>Benign</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>preserved</td>
<td>partially obliterated</td>
</tr>
</tbody>
</table>

Figure 2: Sample Graphical Justification

Summary

In this paper, we have presented several aspects of our research on the PATHFINDER expert system. Our conclusions are as follows:
2. When selecting questions to refine the differential diagnosis, it is often necessary to be able to discriminate among more than two disorders.

3. The most discriminating question for refining a differential diagnosis list is not necessarily the "best" question to ask. Such highly discriminating questions are often difficult to quantitated by system input and difficult to justify. Expert pathologists/clinicians seem to use a simple, problem-solving hierarchy. Such a hierarchy can be used to select questions that are easily understood.

4. A strategy for question selection in the spirit of the medical "review of systems" is useful to ensure that a viable disease hypothesis has not been overlooked. This is a safeguard that ensures the scoring tendency of the method of sequential diagnosis.

5. It is useful for an expert system to avoid requests for data cell that can be expected to be unreliable. In this regard, knowledge about the expertise of the user is important in question selection.

6. Useful justification for selected questions is possible in a frame-based system.

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Appendix

Sample PATHFINDER Transcript

Morphologic features as reported from a random site obtained from the repository archive. Comments are in italics and not entered by the user is in bold face.

Welcome to PATHFINDER. Version 22 - 6/16/84.

Please state your expertise:
0. RESIDENT
1. NON-EXPERT
2. EXPERT
3. 1

The user enters values for salient features seen through the microscope.

- Follicles number

Follicles number
0
1-2
2.6-50
3.50-79
4-90
6

The number of tissues on the differential is 2.

- ask

- ask tells the program to select questions that refine the differential diagnosis. Since there are many and multivariate distances on the differential, group discriminate mode is used.

- discriminate

- malignant

Small cleaved, follicular lymphoma
Mixed, small cleaved and large cell.
Large cell, follicular lymphoma
Small noncleaved, follicular lymphoma
Follicular reaction follicular lymphoma

I recommend that the following features be evaluated:
1. Follicles present
2. Follicles present
3. Follicles (staining) predominating retic (1/2)?
4. Comparison of cytology inside and outside the follicles

- why

- which feature do you want justifying?

- #

The following table elucidates the discriminating power of this feature. The position of the asterisk indicates whether or not the two groups of diseases is favored by each value.

<table>
<thead>
<tr>
<th>#</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Absent</td>
</tr>
<tr>
<td>2</td>
<td>Present</td>
</tr>
<tr>
<td>3</td>
<td>Prominent</td>
</tr>
</tbody>
</table>

The following graph displays the three cost factor estimates on a 0 to 9 axis. The estimate impact on the final utility assigned to each potential question.

Propagated considerations in the evaluation of the feature, follicles mantle zone.

- #

The number of tissues on the differential is 4.

- ask

Here, entropy discriminates made in use because the differential consists solely of non-Hodgkin's lymphomas.

635
Rieger-neating
Small cleaved, follicular lymphoma
Mural, small cleaved and large cell,
Diffuse lymphoma
Large cell, follicular lymphoma
Small non-cleaved, follicular lymphoma

I recommend that the following features be evaluated:
- What is the size of the cells that predominate?
- Follicles (mostly) predominating cells [6,5]
- Medium sized lymphoid cells -- number
- Follicular lymphoma -- nuclear shape
- Are the follicular center cells monomorphic with chromatin structure?

- Why
- What feature do you want justified?

- 84

The following table elucidates the discriminating power of this feature. For each value, the diagnoses that will likely become strong contenders are listed.

Feature: What is the size of the cells that predominate?

None
Small, small cleaved and large cell,
follicular lymphoma
Medium [120]
Small, mixed, follicular lymphoma
Large [20]
Large cell, follicular lymphoma

Diagnostic considerations in the evaluation of this feature: What is the size of the cells that predominate?

- Unreliability
- Ion
- Cost

- 84

What is the size of the cells that predominate?
0: None
1: Small [120]
2: Medium [12-20]
3: Large [20]

The only disease remaining on the differential is Small cleaved, follicular lymphoma.

As there is only one disease left on the differential diagnosis, confirmation made is evolved.

contraining:
Small cleaved, follicular lymphoma

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