

Haematological validation of a computer-based bone marrow reporting system

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Abstract

Aims—To prove the safety and effectiveness of “Professor Belmonte”, a knowledge-based system for bone marrow reporting, a formal evaluation of the reports generated by the system was performed.

Methods—Three haematologists (a consultant, a senior registrar, and a junior registrar), none of whom were involved in the development of the software, compared the unedited reports generated by Professor Belmonte with the original bone marrow reports in 785 unselected cases. Each haematologist independently graded the quality of Belmonte’s reports using one of four categories: (a) better than the original report (more informative, containing useful information missing in the original report); (b) equivalent to the original report; (c) satisfactory, but missing information that should have been included; and (d) unsatisfactory.

Results—The consultant graded 64 reports as more informative than the original, 687 as equivalent to the original, 32 as satisfactory, and two as unsatisfactory. The senior registrar considered 29 reports to be better than the original, 739 to be equivalent to the original, 15 to be satisfactory, and two to be unsatisfactory. The junior registrar found that 88 reports were better than the original, 681 were equivalent to the original, 14 were satisfactory, and two were unsatisfactory. Each judge found two different reports to be unsatisfactory according to their criteria. All 785 reports generated by the computer system received at least two scores of satisfactory or better.

Conclusions—In this representative study, Professor Belmonte generated bone marrow reports that proved to be as accurate as the original reports in a large university hospital. The haematology knowledge contained within the system, the reasoning process, and the function of the software are safe and effective for assisting haematologists in generating high quality bone marrow reports.

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generating interpretive reports, the software must be judged to be accurate, safe, reliable, and effective. In addition, the system should allow the professional to utilise their own judgment when making decisions.¹ To prove the quality of a medical knowledge-based system, formal validation studies must be carried out, preferably by reviewers who were not involved in the design of the system.

“Professor Belmonte” is a haematology knowledge-based system for bone marrow reporting. Belmonte is the third module in a comprehensive system for haematology laboratory diagnosis including “Professor Petrushka” for peripheral blood interpretation, and “Professor Fidelio” for flow cytometry immunophenotyping. Professors Petrushka and Fidelio are commercially available as part of the Coulter FACULTY Knowledge-Based System Software.

The three modules are designed to be used in concert on a haematology workstation or on several networked workstations. The modules share relational databases that act as a communication link between the programs.² The structure and function of the three modules has been thoroughly described in the literature.³⁻⁶

Professor Belmonte follows a logical approach to bone marrow diagnosis, classifying cases based on the patterns listed in table 1. As more than one pattern can coexist, a hierarchy has been established based on standard haematology principles. The “non-specific” pattern corresponds to the condition where no other pattern definition is met. If more than one pattern remains after the first evaluation of the data, an algorithm is applied to exclude all but the pattern with the highest ranking in the hierarchy. Each pattern corresponds to a list of differential diagnoses. The final diagnosis is established by using rules, specific to a given pattern, which take into consideration the clinical history, the peripheral blood pattern retrieved from Professor Petrushka’s database, the morphological findings in the bone marrow, the results of cytochemical stains, and, when appropriate, the immunophenotyping data retrieved from Professor Fidelio’s database. When the findings are non-diagnostic, Belmonte defaults to a descriptive diagnosis. Before printing the report, the contents of Belmonte’s report can be edited, if desired, by the haematologist.

It is important to incorporate peripheral blood findings into the interpretation. Therefore, Belmonte automatically searches the peripheral blood database and displays the pertinent blood count and manual differential

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Before healthcare providers can justify using a knowledge-based system or “decision support system” in preference to their usual methods of

Table 1 Bone marrow patterns

Normocellular
Hypocellular
Erythroid predominance/hyperplasia
Hypercellular, myeloid predominance/hyperplasia
Megakaryocytic hyperplasia
Lymphocytosis/plasmacytosis
Mononuclear cell infiltration
Foreign cell infiltration
Granulomatous
Bi-hyperplasia
Non-specific

data at the beginning of the consultation. Based on the peripheral blood findings, specific suggestions are made for the bone marrow specimen, including reminders for appropriate adjunctive tests such as immunophenotyping and cytogenetics.

The specific morphological features found in the bone marrow aspirate and trephine are entered by the haematologist after microscopic review. The presence or absence of particles in the aspirate, an estimate of the cellularity, the relative number of megakaryocytes, and the presence of cells foreign to the bone marrow can be assessed at low power. Higher magnification is used for a bone marrow differential count and cytological evaluation of the erythroid and myeloid precursors.

If the bone marrow differential is judged to be normal, qualitative estimates of the relative numbers of erythroid and myeloid precursors can be entered instead of a detailed bone marrow differential. The characteristics (pattern and cytology) of any lymphoid infiltrate present on the trephine can be input. Choices are also available to indicate that no abnormal cells are present on the aspirate or trephine. When these selections are used, Belmonte appends the comment, "No evidence of infiltration", to appropriate sections of the report. Special stains, such as iron storage and incorporation, reticulin, and stains for myeloid and monocytic precursors, are entered when appropriate.

Professors Petrushka, Fidelio, and Belmonte have been installed on a five computer network in the haematology laboratory at St Bartholomew's Hospital in London, UK. Petrushka and Fidelio have been in live operation since January 16, 1996. Belmonte was added on June 17, 1996 after the computer-generated report was customised (fig 1) to closely resemble the reports previously issued by the department. The formal evaluation reported here was performed shortly after activating Professor Belmonte.

Methods

Cases with accession numbers from 1 to 800 in 1995 (January 2 to August 31) were chosen. During this time, 14 accession numbers were skipped because of clerical errors. Of the remaining 786 cases, one was excluded from the study because it was a postmortem trephine of poor quality.

For the 785 cases in the study, the demographic data (patient identification number, date of birth, and sex) and the clinical history obtained from the original bone

marrow report were entered into the appropriate database using a Windows utility.⁷ The blood count and peripheral blood film findings (including the manual differential, if available) were collected from the laboratory computer system or from an archive on microfiche. The full blood counts were entered using the manual data entry utility supplied with Coulter FACULTY and processed with Professor Petrushka. In cases with flow cytometry immunophenotyping, the findings were processed with Professor Fidelio.

The microscopic findings (aspirate and/or trephine) contained in the original bone marrow reports were entered into Professor Belmonte. The 785 unedited reports generated by the system were printed and assembled into two binders (cases 1–400 and cases 401–800) analogous to the two bound volumes containing the laboratory's copies of the original reports.

Three haematologists, a consultant (JAA), a senior registrar (JDC), and a junior registrar (RP) compared Belmonte's report with the original report. None of the three was involved in the development of the software. Neither of the two registrars was responsible for any of the original reports.

The haematologists independently judged the quality of Belmonte's reports using four grades: "A+", "A", "S", and "U". The grade "A+" was given when Belmonte's report was judged to be better than the original (for example, when Belmonte's report contained useful information or a comment not included in the original). The grade of "A" was assigned when the two reports were equivalent. An "S" meant that Belmonte's report was satisfactory, but was either missing information that should have been included, or contained an unnecessary comment. When Belmonte's report was judged to be unsatisfactory, a grade of "U" was assigned. Each reviewer had a separate score sheet with space available for comments. The haematologists were instructed to indicate their reasons for assigning the grade "S" or "U". The results were tabulated from the score sheets.

In order to judge the overall quality of Belmonte's reports, a numerical score was assigned to each grade as follows: A+ = 1.25, A = 1.00, S = 0.70, and U = 0. A score for the overall quality of the reports was calculated for each judge. A mean score of 1.00 indicates that the overall quality of the reports is the same as that of the original reports.

Results

A summary of the grades assigned by the haematologists and the mean score for the overall quality of the reports is shown in table 2. Between 86.7% and 94.1% of the reports were found to be equivalent to the original reports. Although each judge found two reports (0.3%) to be unsatisfactory, there was no consistency in the faults recorded, and no single report received more than one unsatisfactory score. Thus, each of the 785 reports received a grade of satisfactory or better from at least two of the three haematologists. Depending on the judge,

the pathology encountered in the university setting including evaluation of unexplained anaemia, new patients presenting with acute and chronic leukaemias, and staging or follow up of patients with a variety of malignancies. The evaluation included both routine cases as well as difficult cases.

Each of the 785 reports generated by Professor Belmonte earned a score of satisfactory, or better, from at least two of the three judges. As the system correlated the peripheral blood findings with the bone marrow findings assiduously, and generated diagnoses with consistent wordings, the judges considered a substantial number of Belmonte's reports (3.7–11.2%) to be better than the original reports. In addition, the mean calculated scores for overall quality showed that each judge found Professor Belmonte's reports to be as accurate as the original reports.

Although several groups have reported using knowledge-based systems and computer networks to improve the efficiency of reporting full blood counts,^{8–10} few laboratories have applied this technology to bone marrow reporting. Smith and Gyde developed two systems aimed at improving bone marrow reporting.^{11 12} The first is a prototype rule-based expert system using a multiparameter approach for the diagnosis of leukaemia. The program, which incorporates clinical data including general laboratory tests, immunophenotype, morphology, and cytogenetics, was evaluated on 43 cases, demonstrating an agreement between the system diagnosis and the true diagnosis in 82% of cases.¹¹ Although their system was designed only for leukaemia diagnosis, its multiparameter approach is similar to Professor Belmonte. Belmonte is only one module in a comprehensive system for diagnostic haematology which includes Professor Petrushka for peripheral blood interpretation, and Professor Fidelio for flow cytometry immunophenotyping (both commercially available in the Coulter FACULTY Knowledge-based Systems). Our systems are designed to correlate all available information including the clinical history and laboratory data related to haematology. The second program by Smith and Gyde is a rule-based bone marrow reporting system for generating the descriptive portion of the bone marrow report via a series of questions which the user answers by selecting choices from menus.¹² Unlike Professor Belmonte, however, this system does not provide an interpretation of any kind.

The efficiency of a knowledge-based system is an important feature in addition to safety and accuracy. Comparison of the turnaround time of reports typed by secretaries to that of reports generated by Professor Belmonte demonstrated that the system nearly halved the bone marrow reporting time at St Bartholomew's

Hospital (from a mean of 10.08 days to 5.34 days for all reports), eliminating the previously existing four to five day delay caused by the backlog of reports and the limited availability of secretaries.¹³ The system is now routinely used for issuing bone marrow reports in the laboratory. If desired, the haematologist can edit the computer-generated report prior to printing. Currently, the main delay in issuing bone marrow reports is the expected time for batch-processing trephine specimens in the histopathology department. Up to 60% of the aspirates are now reported either on the day of the procedure or within one day. In the near future, it will be possible to interface Professor Belmonte to the hospital patient management system for electronic transmission of the complete reports to the appropriate wards, further speeding the communication of laboratory results.

Origins of the unusual names of the three knowledge-based systems— Professors Petrushka, Fidelio, and Belmonte are named after a parrot, a walrus, and a bottlenose dolphin, respectively. The actual names come from the world of classical music. Petrushka (a ballet by Stravinsky) was assigned to the peripheral blood interpretation module because the parrot is very colourful, like the hues in a Romanovsky stained peripheral blood film. Immunophenotyping by flow cytometry (in a liquid medium) is the domain of Fidelio (Beethoven's only opera) because a walrus spends much of his life in water and his brown colour reminds one of the nickname ("brown stain") used by pathologists for immunohistochemistry. The bone marrow module is the responsibility of Belmonte (a principal character in Mozart's opera, *The Abduction from the Seraglio*) because the shape of the bottlenose dolphin, in particular his rostrum, is reminiscent of a bone marrow needle.

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