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Role and use of expert systems within the clinical laboratory

Pierre Marie Valdiguié*

Laboratoire de Biochimie, Hôpital Universitaire de Rangueil, 1 Avenue J. Poulhès, 31403 Toulouse Cedex 4, France

Abstract

Artificial intelligence can be used, mainly in the form of knowledge based systems, for different parts of clinical laboratory activity. Most of the iterative tasks for control and validation, or for maintenance or repair of automated instruments can be assisted by specialized software. There are now specific programmes (i) for control and validation of the request, where the goal is to modify the requesting behaviour of the physician, using protocol driven requests and immediate feedback, incorporating simultaneously a check of test request redundancy, (ii) for helping in equipment trouble-shooting, (iii) for technical and biological validation because too many QC data are issued from large equipment to be checked and used properly by the technologist whilst the pathologist can be assisted for the final revision of reports and (iv) for assistance in the interpretation of laboratory reports, one of the most valuable aspects of the pathologist's participation in the patient care process.

Keywords: Knowledge based systems; Specialized software; Control; Validation; Trouble-shooting

1. Introduction

There are many different steps in clinical laboratory activity where iterative tasks can be assisted by specialized software using artificial intelligence; i.e., automated algorithms, neural networks or knowledge based systems, often called expert systems.

Following the usual fate of a patient sample within a clinical laboratory, we have first to control the sample identification and to consider the corresponding

*Tel.: + 33-5-6132-2808; fax: + 33-5-6132-2953; e-mail: valdiguie@rangueil.inserm.fr

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request. Many efforts have already been made to rationalize and improve the suitability of the clinicians' demands.

During the analytical phase, automated equipment is mainly used and its maintenance or repair failure can also be sometimes helped with specific programmes for automated troubleshooting.

The validation process will have to occur later at the bench level where the technologist has to check the data from the analytical batches. We know that in large laboratories, using large multitest analysers, the technologists are inundated with a flood of QC data which cannot be dealt with manually with the best performance and profit and therefore the implementation of a specialized programme will be welcome.

Afterwards the biological or clinical validation occurs where the coherence and the medical acceptability of the results are properly ensured by the senior supervisor, the clinical chemist or the pathologist who can also be helped by specialised software.

Finally, and particularly for complex reports or uncommon analyses or rare diseases, interpretative assistance can be helpful, provided again by knowledge based systems.

2. Control and validation of the test request

This task should be carried out firstly at the reception area where the sample quality check and its identification have to be done. Moreover, we have now to deal also with a possible validation of the physician's request due to abnormal or irrational demands for laboratory tests or profiles.

The financial constraints, in spite of the relatively low cost of laboratory medicine, are the reason why physicians have to be rational when requesting tests in order to contain the costs of patient management. Moreover, the great number and the expanding complexity of laboratory tests produce an information overload for clinicians who are faced with masses of data rather than information.

Several types of intervention strategy have been proposed, with the aim to promote suitability and effective use of laboratory tests. We can mention the following: (i) education and guidelines: (Pannal et al. [1], Lyon et al. [2]), followed by a ban on test-panel ordering, with written justification to accompany a test request (Novich et al. [3]), restriction to standard panels (Werner et al. [4]), (ii) workstation at the clinical site, (Connelly et al. [5]), (iii) rule based clinical decision support and protocols (Peters [6]), (iv) interactive expert system residing on a physician's office computer (McNeely [7]), (v) feedback and peer review for GP orders (Hasman et al. [8]), (vi) computer program for time monitoring between two requests (Bao et al. [9]).

The efficiency of these approaches is unfortunately very variable, and all successful attempts at reducing laboratory utilization are labour-intensive, involving both laboratory and medical staff. Cost containment has been overemphasized as the main objective, the clinicians being more likely to cooperate if improvement in patient care is stressed.

Therefore the goal is to modify the requesting behaviour of the physician, using protocol driven requests and the feedback system, incorporating simultaneously a check of test request redundancy with control of the time elapsed between two identical requests for the same patient.

The aim is to gather these different approaches within an expert system located on a PC at the laboratory reception and networked with the PC of the care unit where the order is generated.

2.1. Protocol driven request

Considering that the same frequent diseases are often encountered in specialised wards, the objective has been to establish, by dialogue between clinicians and pathologists, the optimized order in every case of frequent disease or in the most classical semiological syndromes. It can be slightly different from one clinician to another in a given medical or surgical specialty. This protocol must be respected, it must be coded as a simple four digit number and sent directly by the local network to a dedicated PC within the laboratory, housing the knowledge based system controlling the testing orders.

The protocol includes profiles or predetermined patterns, but also particular or specific requests, on the condition that the requesting doctor has been authorized.

2.2. Ordering outside any protocol

Of course it is possible to request any test or profile outside any preliminary protocol and in these conditions different intervention strategies for influencing test requesting behaviour will be necessary:

- Clinical or semiological information will have to be added,
- Feedback will be, if necessary, employed to discuss with the physician, considering the traditional and consensual rules in use within the institution. In the case of non-usual or very expensive tests, the cost of the individual requested analysis will also be signalled to the ward and a reconfirmation of the order will be awaited.
- Senior house staff will be the only authorized persons to use this method of ordering, in non-emergency situations.

2.3. Check of order redundancy

Two identical requests concerning a patient from the same ward or from two different wards must be rejected if a short time has elapsed between the two orders. Therefore it must be assessed: (a) what is the acceptable time between two routine profiles according to the various patients in a given medical discipline, also taking into consideration the tradition and the professional habits of the different physicians, (b) which kind of analysis or profile can be accepted without any time limit. This approach concerns mainly the ICU or emergency rooms where reanimation care needs frequent repetitive monitoring of biological data.

Preceding results must be retrieved to be sent back in the case of request rejection. Moreover the microcomputer will also have to inform the technologist, through the mainframe computer, about any information or problem related to a sample coming from the ward (risk of infectious hazard, particular therapy, abundant myeloma protein etc . . .).

All these items will be automatically controlled using a knowledge based system embedded in a PC connected to the hospital network on one hand and to the Laboratory Information System on the other. Specific software for the automated prescription at the ward can be provided nowadays by manufacturers.[1]

3. Technical validation

Over the past twenty years, many studies and papers have been dedicated to quality control within clinical laboratories or between laboratories as regional, national or international quality assurance programmes. However very few articles, mainly from the Westgard's team, have proposed practical and efficient solutions to deal with the daily problems. The advances in this domain came particularly from simulation and modelling. Furthermore proficiency testing (PT) in this time of health care expenses containment must be performed with the highest cost-effectiveness.

These approaches explain the need for a reasonable and rational quality assurance protocol using various types of control materials. However too many data are then issued from large equipment in clinical chemistry, immunoanalysis and haematology (cytology or coagulation) to be checked and used manually and carefully within an acceptable time, particularly when various multitest analysers are run simultaneously.

Therefore the necessity for an automated system, capable of detecting and signalling any disturbance or abnormality, is to be emphasized, with software

[1]Bayer Diagnostics, 13 rue Jean Jaurès, 92807 Puteaux Cedex, France.

that can cope efficiently with the flood of QC data and is capable of deciding whether to accept or reject a series of analyses.

A knowledge based system for assisted technical validation has thus been designed, taking into consideration the previous experience from Groth and Modèn [10].

The details concerning the hardware and software and their implementation in a big hospital laboratory of chemical pathology in Toulouse has been already published in this journal [11]. We use data from patient results and from control sera simultaneously for automated QC.

Data from external quality assessment programmes are also used to characterize the reliability of the laboratory with regard to bias problems. These data are particularly valuable in our interlaboratory weekly programmes where telecommunications provide an immediate look at reference results previously stored in the server computer [12].

Signals and alarms from the analysers have also to be integrated within the system in order to achieve a comprehensive system.

The check of the mean of normals is a complementary tool used for validating or non-validating the conclusions of the algorithms in charge of the evaluation of data from control sera. In cases of disagreement between the two protocols, the system refuses to decide and the delta check will then be performed, if previous data are available.

The final conclusion appears either as a written comment on the appropriate graph on the screen, or as a printed message with an alarm sound, indicating the rejection of the run.

If there are no problems, the QC report is printed out at a predefined time with or without the Levy–Jennings graph.

Nevertheless, the implementation of multirule QC programmes in the daily work of big hospital laboratories remains a tedious and difficult task due mainly to the presence of various multitest analysers which do not always have the same analytical technology and thus the same behaviour when running control specimens where the matrix effect is variably important.

Our experience on the assistance provided by specific programmes to optimize the QC performance, like the QC Validator[2] proposed by Westgard [13] is still insufficient to be presented here.

4. Automated maintenance and troubleshooting

This is related to feedback control mechanisms and auto-diagnostic routines, useful in troubleshooting and in fault identification for automated analysers whose mechanical, fluidic and electronic complexity has become very great.

[2]Westgard Quality Corporation, PO box 2026, Ogunquit ME 03907, USA.

At the instrument level, the embedded microcomputer may automatically detect physical abnormalities and self-test its own circuits and features. In 1989 and 1991 two examples had already been developed for a knowledge-based trouble-shooter and advisor devoted to a Prisma analyser [10] and an Hitachi analyser [14].

However, if the failure cannot be solved on site, the assistance of the manufacturer is required, usually thanks to "hot lines" that allow technical specialists to deliver advice for repair by telephone.

These technical assistance center specialists are often responsible for support of multiple products and the trend is to consolidate laboratory activities in a system that can merge chemistry, haematology, coagulation, immunochemistry and urine analysis into a single, highly efficient, cost effective, work management system, where there are a lot of different machines and robots automatically performing sorting, preanalytical processing (centrifugation, decapping, aliquoting) of mixed pathology specimens as well as automatically loading them onto the various analysers. Therefore the on-line assistance needs expert systems to achieve its role.

An example is given by BRITE, (Bringing Resources and Information to Employees), an expert information retrieval system implemented at Chiron, Ciba-Corning Diagnostics in Norwood, MA, USA, [15]. It permits the technical specialists to access information in less than 3 s. The expert system makes electronically available manuals, technical bulletins, parts lists and also administrative tools such as word processing and network fax.

The extension of its technology to customers in the laboratory and manufacturer personnel in the field will provide the ability to capture and dynamically incorporate information.

5. Clinical validation

Flooded by the tedious work of validation or supervision of laboratory reports from a big hospital laboratory of chemical pathology, we decided in 1988 to use artificial intelligence and to carry out an expert system project to aid decision making and to develop an automated validation of data.

The expert system VALAB [16,17] was first designed for an electrolyte profile but has been rapidly further expanded to handle 22 tests commonly run in the clinical chemistry laboratory. Right now the system is able to deal with 48 usual tests, including a specific programme for pH and blood gases.

5.1. Short description

The ES operates on a microcomputer IBM-compatible Pentium PC. The software runs under MS–DOS and uses an ES generator (inference engine)

KHEOPS from the Laboratoire d'Automatique et d'Analyse des Systèmes, an institute of the Centre National de la Recherche Scientifique in France. KHEOPS uses forward chaining as the reasoning process that is applied to the knowledge base represented in the form of production rules.

The production rules (more than 5000) are expressed in conditional (if–then) form. There are three sets of rules:

(a) the ones representing the core of the system are devoted to the *various criteria selected to help decide* whether to validate laboratory data. VALAB uses the following information for every patient report: acceptable limits, internal coherence between analyte results which are physiologically related, delta check, origin of the sample, i.e. identification of the ward and the medical specialty, stat analysis or not, Out- or in-patient, age, sex, comments on the sample quality.

(b) some rules (*weighing rules*) are dynamically defining acceptability thresholds for each patient as various trends for that patient are noticed.

(c) particular rules are coping with *clinical or therapeutical data.* All these rules are divided into rule groups, each rule group containing between 50 and 200 elementary rules which are related to a similar topic. Groups of rules are compiled resulting in the construction of a decision network that can be more rapidly processed than the rules in their original form. This "pretreatment" of the internal representation of the knowledge base results in a total inference time for each report of about 50 ms.

The evaluation protocol [18,19] consists in comparing the clinical chemist's and pathologist's consensus that is the reference decision, to the VALAB's one. The control process is conducted with the epidemiological method used to assess the semiological value of a medical sign. Thus sensitivity, specificity and predictive values can be calculated and compared between the ES and the other observers. Sensitivity is greatly enhanced because its calculation formula contains "false negative" results (that is falsely validating an incorrect report) which are unacceptable.

Furthermore, the system has also been submitted to a national multicentred evaluation in five different laboratories, with four big hospital laboratories of clinical chemistry and one big private laboratory of clinical pathology.

5.2. Results

VALAB is presently dealing with 48 common biochemical tests, with pH and blood gases, cellular haematology and coagulation.

It runs silently according to the following various steps: presentation of the laboratory report on the microcomputer monitor, identification of the data in the report and syntax analysis, performance of the expert function, local display of the decision to accept or reject the reported data with indication of the abnormality, transmission of the decision to the mainframe computer which

either prints out an accepted report or stores it again, if rejected, for a human validation that will be helped by the conclusion of the VALAB's expertise.

Statistical data are presented concerning the activity and the performance of VALAB, with emphasis on the results considered invalid and the main causes of rejection by the programme.

The conditions of operation can be adapted for every user:

(i) definition on the mainframe computer (LIS), on which the ES is connected as an analytical instrument, of the reports to be submitted to the ES, i.e. either only pathological reports or any report if the limits of normality are strictly narrowed,

(ii) assessment and settlement of the parameters which can be adjusted by the user.

Finally, VALAB can be considered as a screening programme dedicated to the selection of biochemical or haematological reports needing a human evaluation in order to either accept them as valid or have them rerun after dialogue with the physician.

6. Assisted interpretation of laboratory data

Computer assisted medical decision-making may be the solution to deal optimally with the flood of data and explosion of knowledge occurring in the medical area [20]. Moreover in a survey with ten clinician experts investigating the opportunities and obstacles involved in introducing computerized decision support systems, Hoffmann [21] pointed out that experts cited few attractive opportunities, and among them interpretation of results in specific area.

Pro.M.D. is one of the oldest programmes, presented by Trendelenburg and Pohl [22,23] which is able to deal with various diseases and corresponding laboratory data, in clinical chemistry, serology or infectious diseases. Its large use, mainly in Germany, explains that the integration within a LIS or hospital information system can be easily achieved and that future trends look ahead to intranet/internet technology [24].

PEIRS [25] is based on a novel acquisition technique, called "ripple down rules" that enables rapid and simple knowledge acquisition by the domain expert without knowledge engineering or programming skills and the expert system may be maintained and updated by pathologists without the need of knowledge engineering expertise. It can thus provide a comprehensive automated interpretative service mainly for thyroid diseases and acid–base disorders.

REPCAT [26] is designed for urine determination of epinephrine and norepinephrine for pheochromocytoma diagnosis. In full time use in the authors' laboratory, it has proven a fast, highly functional tool, providing the performance of an experienced expert in this domain of clinical pathology.

Moreover it is situated half way between the validation of laboratory data and results interpretation.

7. Conclusion

We must be convinced that, in spite of a considerable interest in artificial intelligence in laboratory medicine, expert systems development has not be as huge as expected at the end of the eighties. Few systems are actually widely used and spread over the western world. As Winkel said [27], tools other than expert systems may be often more appropriate for most of the problems that are mainly confined to laboratory data and therefore should be solved by the clinical pathologist. Furthermore, routine cases do not require much expertise and only the difficult cases could be handed over to the expert system.

However, iterative tasks, control of the testing request appropriateness, help in instrument troubleshooting will certainly continue to be considered as important functions to be dealt with by expert systems.

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