Causal Reasoning in Nuclear Medicine

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Abstract

Qualitative (causal) reasononing has been one of the most interesting new approaches to artificial intelligence in medicine in the last ten years. The search for deep knowledge that captures the relationships and causal interactions between the different elements of a system, seemed to be able to overcome some of the limitations of using heuristics in expert systems. In this report, we explore the use of causal models for a diagnostic expert system in cardiology and the current constraints of this direction, due to the lack of detailed physiological knowledge in present medicine.

1. *Introduction.*

For the past several years, a rule-based expert-system ("PERFEX") for interpreting 3D myocardial perfusion distributions has been under development at Georgia Tech. This system is designed to provide diagnostic assistance using Thallium-201 tomographic images and has been developed at the Medical Informatics lab Georgia Tech, in collaboration with the Department of Radiology, Emory University both in Atlanta, GA.

The present project tries to build useful clinical tool incorporating knowledge in cardiac nuclear medicine imaging in order to perform the interpretation of the areas affected by decrease of myocardial perfusion.

As the system nears completion, some of the typical limitations of medical expert systems have been encountered and partially addressed, such as limited explanation capabilities, difficulty associated with knowledge acquisition and treatment of uncertainty. Although PERFEX has been successfully tested in the clinical environment, there is interest in exploring newer approaches and capabilities. As a result, we studied the possibility to extend and refine PERFEX by applying several new methods that could improve performance and system usability.

More specifically, we considered the application of qualitative reasoning methods to improve the diagnostic performance of the system, and to incorporate new strategies for prognosis. The basic idea was to incorporate a qualitative model of the underlying physiological and pathological mechanisms of the disease. This will be used as the module of justification/explanation of the complete system, using text and graphics, to facilitate user interaction and support inferences made by the system in a specific consultation. This task of clarification and justification is extremely important, and has classically been one of the strongest criticisms made with regards to expert systems in medicine, since physicians usually do not accept their use for medical decision-making largely because of the insuffiency of explanation. Instead, reasoning has been justified usually by tracing rules and only showing a list with the rules fired or associated texts.

For all of these reasons, it was deemed appropriate to consider the use of qualitative reasoning methods for supporting explanation mechanisms, and we began a detailed bibliographic search in order to identify the best possible approaches.

2. *Background and Rationale.*

Medical decision making is one of the fundamental topics in medical informatics, and a number of different approaches and techniques have been developed in the last 25 five years in this field. The first attempts were purely algorithmic and statistical methods, which did not enjoy success but showed that computers could play a new and fundamental role in this area. It was during the 70's that Artificial Intelligence, until then only a laboratory science, came to the world of practical applications, with the emergence of expert systems, and a new field, knowledge engineering. (Clancey and Shortliffe, 1984; Reggia, 1985).

Since the first expert system, Dendral (Buchanan et al.,1969), in the field of chemistry, a great number of expert systems have been developed in medicine, from MYCIN (Shortliffe, 1976), INTERNIST (Pople, 1982) and others to numerous more recent systems. This first generation of expert systems was based on the heuristic knowledge of experts in the field, with the use of the so- called rules of thumb or surface knowledge. The method that was used to weight the relations between findings and hypothesis was the use of certainty factors, a scaled conditional probability of the diagnosis given the confidence of the conclusion.

This produced a considerable lack of knowledge, since most medical expert systems diagnosed by naming a disease rather than causally relating states and processes.

At the beginning of the eighties, several reports centered in the use of another kind of knowledge, "deeper" than that related to heuristics. This new approach was labeled as the 2nd generation of medical expert systems.

This generation introduced the concept of deep knowledge, related to the association between causes and effects in medicine, in aspects related to physiology or pathophysiology. Two general types of description are used in this new model:

- QUANTITATIVE: a description in terms of mathematical expressions.

- QUALITATIVE (causal): a description of a system in terms of the behavior of each component and its effects on the rest of the system.

This new methodology had an immediate appeal because it seemed powerful to be able to model causal mechanisms in medicine.
This created a great deal of research interest, and deep models appeared to be an ideal way to overcome the previous limitations of classical systems.

Some theoretical (cognitive) justifications were given to explain this new trend. Earlier, some researchers (Kassirer, Gorry, 1978) reported that, using protocol analysis, physicians seemed to use mental models and explanations of physiological processes of the human body in terms of qualitative expressions of continous variables and the constraints among them. This insight generated research centered on qualitative reasoning about physical systems (De Kleer, 1977; Kuipers, 1985) on medical diagnosis.

Several reports have appeared in recent years proposing the use of causal methods in medicine. We will summarize some of the most interesting and influential research to date.

- (1) CASNET. It is possible to place CASNET (Kulikowsky, 1982) as the first expert system designed to include some causal aspects, by means of a semantic network for the diagnosis and treatment of glaucoma. It used multiple increasing levels of detail, with a function for the calculus of the likelihood in all pathways.

- ABEL. After this first attempt, other researchers continued looking for the representation of causal relations. In this way, ABEL (Patil et al., 1981), constructed a model to represent causal explanations in the context of acid-base and electrolyte disorders. Abel uses three levels of description, from a high, simple level to a low, specified one, with some characteristics represented in all levels.

- (3) CHF. CHF Advisor.

This program (Congestive Heart Failure) was designed to assist the physician in the diagnosis of patients with manifestations of heart failure. The appeal of this approach is that a number of diseases can produce similar features, suggesting the use of a causal reasoning approach (Long et al., 1987).

This model used a truth-maintenance system to deal with the relations defined within the model, propagating the effects of the change in one parameter value to the rest of the model, because of the causal relations among states, and then observe how that model reacts. A Bayesian probabilistic network was also introduced for inferring causes. At the same time, a case-based reasoning system, CASEY (Koton, 1988) was developed to complete the characteristics of CHF.

- (4) QSIM.

Kuipers has tried to study the problem of qualitative model-based reasoning, for its possible predictive value (Kuipers, 1985). The following graph summarizes his idea:

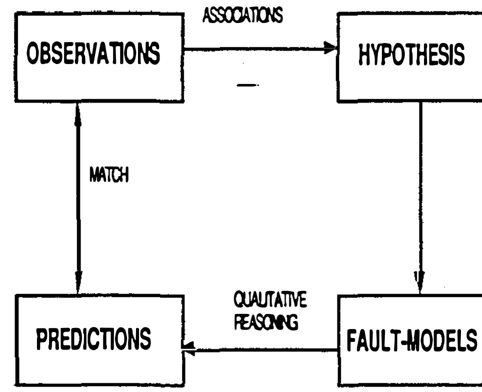

FIG. 1: MODEL-BASED REASONING IN A GENERATE-AND-TEST CYCLE FOR DIAGNOSTIC PROBLEM SOLVING.

He observed that the use of weighted associations between findings and hypotheses made it impossible for traditional expert systems to express causal mechanisms. Also, he and his colleagues analyzed verbatim transcripts of expert physicians solving selected clinical problems, and this resulted in a knowledge representation and a qualitative simulation algorithm (QSIM). Within this representation, he built a structural description for the mechanism studied in the transcripts, and the simulation seemed to produce the same qualitative prediction made by the physicians. The key concept is the use of landmark values for variables (values at which the functions change behavior).

One of the biggest constraints of this approach is that the explanation of the knowledge representation refers only to a small set of objects and relations.

- (5) Cardiovascular modeling (Widman, 1988)

Widman has built a system to represent some aspects of the cardiac circulation) that, briefly, consists of:

- semiquantitative descriptions of findings.
- qualitative analysis of the findings.
- simulation of the model, by means of differential equations.
- the results of the semiquantitative simulation are mapped back to qualitative terms.

The way the system maps the values of qualitative variables into semiquantitative terms is by giving values to terms such as "normal", "elevated", "high", etc. , that are mapped into the internal system (-1......0......1), where 0 is "normal".

- (6) KARDIO .

Kardio is a qualitative model that simulates the electrical activity of the heart, and is used in an expert system for diagnosing cardiac arrhytmias from symbolic descriptions of electrocardiograms. The system incorporates a qualitative model which simulates the electrical activity of the heart. Bratko and his colleagues built a huge conjunct of Prolog clauses, and using inductive machine learning techniques (ID3, AQ11), formal rules were obtained for building a knowledge base. Thus, this approach tries to avoid the knowledge acquisition "bottleneck" (Bratko,1989)

These previous systems are the best known and extended models of qualitative reasoning in medicine at this moment. It is interesting to realize that most of them deal with cardiac features, probably due to the appeal of the heart as a research topic and the special characteristics of its physiology, which appears to be more adequate for this kind of research that other organs like the brain, for instance.

Although these approaches are representative of the state-of the-art of qualitative reasoning in medicine, at the moment, there are no real paradigms or widely accepted methodologies for the use of causal methods in medicine. Other approaches are also interesting, like XPLAIN (Swartout, 1981), a system that can generate explanations at multiple levels; NESTOR (Greg Cooper, 1984), that uses a causal tree associated with probability coefficients; RX (Blum,1986), with a statistical approach in large databases. Other systems that do not really use causal reasoning, but that could be considered to incorporate a knowledge also labeled as "deep", such as ROUNDSMAN (Rennels, 1986), which contains a "library"of knowledge about journal articles. It searches its own library for those articles most relevant to the case, selects the best match the patient and proposed plan, and compiles a list of the significant strengths and weaknesses.

3. Qualitative reasoning in Perfex: Preliminary assessment.

As a starting point, we tried to establish some levels of the knowledge domain, coronary artery disease, from a pathophysiological point of view.

The highest level would be myocardial infarction and the lowest level would be biochemical interactions, as follows:

1. Myocardial infarction (generalized)
2. Myocardial infarction (located)

3. Permanent myocardial perfusion
4. Angina pectoris.
5. Defects of myocardial perfusion
6. Coronary narrowing.
7. Atheroesclerotic disease
8. Atheroesclerotic collections
9. Alteration on the lipid transport
10. Alteration on the lipid metabolism
11. Biochemical alterations

Once this general idea was elaborated and the possible qualitative techniques studied, a discussion that included the cardiologists was carried out to consider the potential of this approach for its inclusion on Perfex.

We considered that the pros and cons of this approach were as follows:

1. Pros:

- Qualitative reasoning methods may be the best and most powerful techniques that are presently available to represent causal mechanisms in a cardiac expert system.

- Several reports have shown the wide range of possibilities
available to the researcher.

- The use of heuristics (only) in a cardiac expert system leads necessarily to an incomplete representation of knowledge, showing the need for other methods.

- It is possible to incorporate algorithmic, mathematical or probabilistic methods more accuratly than with the use of certainty factors to find the probability of a diagnosis (given some facts and causal relations). This fact has provoked the development of methods that improve the results of the 1st generation of medical expert systems.

2. Cons.

- Due to the characteristics of PERFEX, it would be necessary to include the upper levels of the list shown previously, leading to an enormous amount of information required to model the behavior of the system.

- All previous reports have been centered on narrower aspects than the one we are considering.

- There are no commonly accepted paradigms or methodologies. it is also difficult to accept that the concept of "deep" knowledge is only related to qualitative or causal, and even more, that classical expert systems did not incorporate this type of knowledge.

- Incomplete knowledge of cardiac pathophysiology. Some parts of the levels of figure 2 are still under development, and it would be difficult to model all the knowledge needed (for instance, the developers of QMR considered that 100 person-years would be necessary to build a "deep" QMR, not worthwhile for established researchers).

Based on these binding, we concluded that it vould he extremaly difficult to incorparate such a model in PERFEX.

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