CADIAG-IV/Rheumatology—
An Internet-Based Consultation System for Differential Diagnosis in Rheumatology

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Abstract
CADIAG-I, -II and -III (Computer-Assisted DIAGnosis) are diagnostic consultation systems, which, given a list of symptoms, signs, test results, and clinical findings for a patient, provide diagnostic hypotheses (confirmed, possible, and excluded) and proposals for further examinations (Adlassnig, 1980; Adlassnig et al., 1985b, 1986). One of their most important features is that the physician gains a greater awareness of rare diseases. In addition to being a consultation system, CADIAG-IV, the latest version of the CADIAG series supports comprehensive patient management and administration by use of the integrated patient data and medical knowledge base, MedFrame (Bögl, 1997; Kolousek, 1997). This framework consists of two major components: a class library for storing patient data and medical knowledge on the one hand, and a set of tools for implementing Client/Server-based medical consultation systems on the other.

CADIAG-IV/Rheumatology is a part of the project CADIAG-IV. Its goal is to develop an Internet-based consultation system for decision support in the field of rheumatic diseases. A further goal that is closely linked with CADIAG-IV/Rheumatology is the design and development of the medical consultation system shell, MedFrame/CADIAG-IV.

Keywords: Artificial Intelligence, Computing Systems, Information Systems, Soft Computing, Medical Expert System.

1 Introduction

The goal of the CADIAG-IV project is to develop Internet-based consultation systems for medical decision support. Its main purpose is to derive confirmed diagnoses, positive and negative hypotheses, excluded diagnoses, as well as recommendations for therapy and further examinations. The data used by the system are symptoms, signs, test results, clinical and laboratory findings. The system is intended to make physicians more aware of rare diseases.

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While a number of decision support systems for the interpretation of laboratory test results are currently in existence, the quantity of available software for the assessment of clinical symptoms is relatively scarce (Kolarz and Adlassnig, 1986). This is due to the fact that it is much more time consuming for the physician to document the clinical symptoms of a specific patient. Consequently, the acceptance of such systems is less. Nevertheless, the need for such decision support systems is evident, as they would clearly improve the standard of treatment and the quality of medical services. It is a challenge to work at a project that would meet these requirements and to design software that supports decision-making in fields of medicine that depend on large quantities of medical data, including clinical symptoms.

The task of CADIAG-IV is to investigate how the previous work can be improved in terms of increasing the sensitivity and specificity of the inferred diagnostic and therapeutic proposals and how these concepts can be implemented by the use of modern software technology.

Section 2 provides a summary of the extensive previous work on this subject while section 3 describes the objectives of the project. The objectives of these tasks will be presented in section 4, followed by the current results in section 5 and a discussion including comparisons with other rheumatological consultation systems as well as some ideas for further advancements in section 6. Section 7 will provide a brief conclusion.

2 Background

2.1 CADIAG: Consultation Systems for Internal Medicine

CADIAG-I, CADIAG-II, and CADIAG-III are diagnostic consultation systems, which, given a list of symptoms, signs, test results, and clinical and laboratory findings for a patient, provide diagnostic hypotheses and suggestions for therapy and further examinations. This series of systems was started with the implementation of a system based on Boolean logic in 1968 (Spindelberger and Grabner, 1968). Subsequent versions are based on fuzzy set theory and fuzzy logic to represent vagueness, uncertainty, and incompleteness of medical knowledge (Adlassnig, 1986; Adlassnig et al., 1985b, 1986; Zadeh, 1965). Currently, CADIAG-III (Schuh 1992) is used by the Vienna General Hospital.

The CADIAG systems have been designed to support diagnostic decision-making in various sub-domains of internal medicine (gastroenterology, hepatology, rheumatology (Adlassnig et al., 1985a, 1993; Leitich et al., 1996a), gallbladder diseases (Adlassnig and Akhavan-Heidari, 1989), and radiology (Bögl et al., 1995)).

CADIAG-IV is currently under development at the Department of Medical Computer Sciences, University of Vienna Medical School. In addition to being a consultation system it will support comprehensive patient management and general administrative tasks. It is intended to be a framework of tools for developing medical consultation systems as well as for the specific implementations of consultation systems for several sub-domains of internal medicine.

2.2 MedFrame: Integrated Patient Data and Medical Knowledge Base

CADIAG-IV is based on MedFrame, an integrated patient data and medical knowledge base designed for the storage of medical knowledge as well as administrative data. MedFrame is a framework consisting of two major components: a class library for storing data on the one hand, and a set of tools for implementing Client/Server-based medical consultation systems on the other.

Classes included in MedFrame that are suitable for modeling and storing administrative data are, for instance, *Patient*, *Department*, or *StayInHospital*, classes for medical knowledge are, e.g., *MedicalEntity*, *FuzzySet*, or *SymptomDef*, and classes for the construction of a knowledge base are, for example, *Operator*, *Facet*, or *KnowledgeItem*. The second component of MedFrame provides an interface for implementing RMI- or CORBA-based consultation systems with a Client/Server architecture in a straightforward fashion. A detailed description of the architecture of MedFrame has been published previously in (Kolousek, 1997).

Because MedFrame is implemented in the object-oriented language Java, it meets the requirements of state-of-the-art software: multi-user capability, platform independence, Client/Server architecture, and multiple language support implemented by the use of flexible object-oriented programming and modeling techniques (Sageder et al., 1997). The underlying storage system is the object-oriented database management system Poet. The communication between MedFrame and Poet is based on the Object Query Language (OQL), a counterpart of the Structured Query Language (SQL).

2.3 Inference Mechanism

A mathematical framework formalism improved the inference methodology of CADIAG-II (Brein, 1997), which, principally, is a production system. It also uses fuzzy sets and fuzzy logic, but with the important additional merit of two fuzzy qualifiers for each rule: the *strength of evidence* and the *strength of counter-evidence* (instead of using one value, which can be interpreted as evidence, where the strength of counter-evidence then is the complement of this evidence). Additional formalisms provide the possibility to explain the deductive result and give suggestions for further examinations, which would lead to more specific diagnosis.

The first step of the inference is so-called *data-to-symbol conversion*, in which quantitative data (e.g. test results) are converted into qualitative fuzzy linguistic concepts (Adlassnig 1988, Leitich et al., 1996b). These symbols constitute the layer of symptoms (i.e. a collection of medical entities representing symptoms) and are used to deduce diagnoses, which are represented in another layer. A third layer containing therapies can be used for therapeutic proposals, which may be inferred from diagnoses in the same manner as diagnoses are inferred from symptoms. The explanation is then a listing of deduction steps, or—in mathematical terms—the explanation of the proof of diagnosis or therapy.

2.4 Terminology

To unify data representation, a concept for a unique terminology to be used within CADIAG-IV has been defined (Smutny, 1996). Its main concepts are facets and qualifiers based on SNOMED (Côté et al., 1993) and ICD-10 (WHO, 1994), two approaches for an international standardization of medical terms.

2.5 Knowledge Acquisition

KBuilder (Bögl, 1997) is the prototype of a knowledge acquisition framework developed for the creation and maintenance of medical knowledge by medical experts without any support from knowledge engineers.

ToxoBuilder (Kopecky, 1999) is a tool for modifying knowledge bases consisting of decision graphs and has been developed as part of the MedFrame/ToxoNet system for the decision support of toxoplasmosis. MedFrame/ToxoNet is an implementation that is specifically designed as a Web-based decision support system for routine clinical use in connection with toxoplasma gondii infections.

2.6 Knowledge Base for Rheumatology

As part of the previous CADIAG projects, a large data and knowledge base for rheumatology has been developed and successfully tested (Adlassnig et al., 1985a, 1993; Kolarz and Adlassnig, 1986; Leitich et al., 1999). It includes 250 complex diagnosis rules, about 50,000 simple diagnosis rules (i.e. rules with a single symptom on the left side), 437 diagnoses, 1,128 symptoms, and 3,252 patients with a total of 3,607 stays in hospital.

2.7 CADIAG-II/Rheuma

The rheumatologic application CADIAG-II/Rheuma consists of a consultation system for rheumatologic differential diagnoses being used to provide consultation for patients visiting a rheumatologic hospital or a rheumatologic outpatient clinic (Adlassnig et al., 1985a, 1985b; Kolarz and Adlassnig, 1986; Leitich et al., 1994, 1999). The specific tasks of CADIAG-II/Rheuma in the consultation process are to offer a complete and correctly ranked list of diagnostic hypotheses. It was implemented in an IBM mainframe environment (Adlassnig et al., 1986, Grabner, 1985).

2.8 MedFrame/Browser

A tool for direct browsing and editing of the data contained in MedFrame is required. The tool has to be suitable for both medical and technical staff. MedFrame/Browser (Heisz et al., 2000) is able

- to present data and knowledge of the entire database,
- to show structural details for technical purposes,
- to retrieve data without the need for technical background knowledge, and

- to provide advanced views for analyzing data.

One possible use of the browser is to develop and inspect a new or migrated knowledge base. However, physicians or departments should also be able to use it to get information by views, which can be adapted in any desired way.

This discrepancy is resolved by a generic representation of the object and the possibility to use special views instead. Generic views can represent any object stored in MedFrame by a list of its properties together with technical details (see Fig. 1). For specific objects, additional views can be added; these have to be explicitly implemented. The advantage is that any representation of this kind of object (class), including combinations of several objects, will be possible.

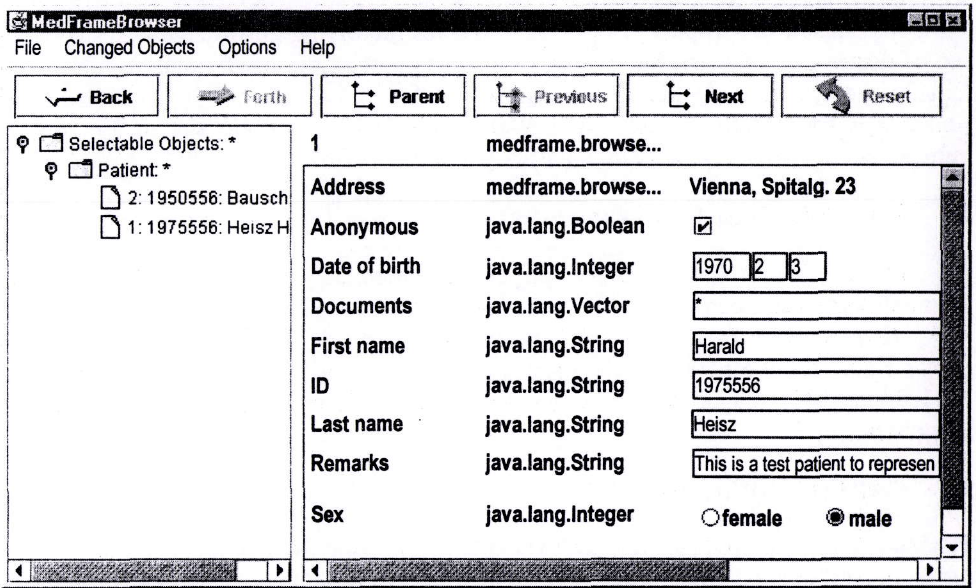

Fig. 1: The data of a patient stored in MedFrame visualized by a generic representation of a prototype of MedFrame/Browser.

3 Objectives of CADIAG-IV/Rheumatology

The aim of the CADIAG-IV/Rheumatology project is methodological research, design, development, and clinical evaluation of an Internet-based consultation system for decision support in the field of rheumatic diseases within the CADIAG-IV project.

Its development, currently being in an intermediate stage, is tightly coupled with the further improvement and advancement of MedFrame/CADIAG-IV which will serve as a shell for medical consultation systems.

3.1 MedFrame/CADIAG-IV: Shell for Medical Consultation Systems

A consultation system shell that will be suitable for designing and implementing differential diagnostic consultation systems, monitoring systems, and systems for the knowledge-based interpretation of laboratory test results is currently being developed.

As the inference mechanism uses fuzzy logic, medical items, e.g. medical concepts, are being formulated by the use of fuzzy sets. A knowledge acquisition tool to support the acquisition of such medical items is being devised. The tool will be such that it can be used by medical experts without assistance from a knowledge engineer.

A further feature is the possibility to communicate with other systems via a computer network such as an Intranet or the Internet. It will permit the exchange of data between different medical computer systems, either within the hospital, within a larger organization or worldwide.

To promote this aim, several subprojects have to be undertaken:

The general inference mechanism for CADIAG-IV, as described in the previous section will have to be enhanced and implemented.

For data that are not structured as heavily as those for medical knowledge, views of the browser can be used to implement prototypical user interfaces. These interfaces can be adapted by specialized applications, which usually have more sophisticated requirements. Thus, a large amount of implemented software can be reused.

Knowledge acquisition and evaluation of medical knowledge bases: For the most important kinds of knowledge representation in computational medicine, it is necessary to have user interfaces that support input and output of medical data, depending on the kind of representation. For example, tables, rules, or decision graphs are easily maintained when there is a vivid graphical user interface supporting their respective features. This simple mode of data acquisition is especially suitable for the administration of existing knowledge. In addition, the system will permit statistical processing of medical data in a hospital, and thus enable the user to extract medical knowledge in an automatic process (Schuerz, 2000). As a matter of course, tools to evaluate the sensitivity and specificity of the implemented medical knowledge base and to verify and upgrade their usability will also have to be included.

Patient data management and general administration: Independent of the implementation of specific consultation systems, components for managing patient data, departments and other administrative entities are required.

Graphical user interface for CADIAG-IV: An application that would serve as a frame offering the possibilities of the CADIAG-IV consultation system shell to create new consultation systems and specific user interfaces is needed.

3.2 Specific Implementations of Medical Consultation Systems

Developing this shell together with the consultation system CADIAG-IV/Rheumatology will serve the following purposes:

- to support the shell by utilizing the experiences gained from the development of the specific systems,

- to evaluate the usability of already available subparts for CADIAG-IV,
- and finally—yet important—to devise applications which can be used by departments of the Vienna General Hospital or by users of the Internet.

Since the medical consultation system CADIAG-II is being used in rheumatology since several years, extensive experience has been gained in regard of its specific computational knowledge representation, its deployment in the clinic, and the special needs of its subject area. In addition, it is a great advantage to have a rheumatology knowledge base of guaranteed quality from the CADIAG-II/Rheuma (Adlassnig et al. 1985a; Kolarz and Adlassnig 1986).

4 Material and Methods of CADIAG-IV/Rheumatology

4.1 Subtasks of CADIAG-IV/Rheumatology

Certain subtasks which are a part of the development of CADIAG-IV/Rheumatology will have to be undertaken in order to achieve the described goals:

- *Migration* of data from CADIAG-II: The rheumatologic knowledge base available in CADIAG-II/Rheuma is being migrated from WAMIS—the medical information system of the Vienna General Hospital (Adlassnig et al., 1985a; Grabner, 1985; Leitich et al., 1999)—into the integrated patient data and medical knowledge base, MedFrame.
- In addition, an *inference engine* is needed.
- The existing *rheumatologic knowledge base* has to be updated with respect to the new inference method for CADIAG-IV.
- The *graphical user interface for CADIAG-IV* must be designed and implemented.
- The *browser* still has to be amended in terms of features like improved selection, vivid and sophisticated views for many of the MedFrame classes.
- In addition, *tools for patient administration* will be developed.
- *A test and an evaluation* of the resulting prototype of CADIAG-IV/Rheumatology will have to be carried out and corrections made.

4.2 Technical Details

At the present time, the first choice in terms of a programming language for Internet-based programming is Java. In addition to its object-oriented technology it has features, which assist or even enable applications, applets, or servlets needed to use the Internet and/or an Intranet. To access MedFrame Poet 6.1 is used. This is one of the most advanced DBMS (Database Management Systems) for the design and implementation of object-oriented databases.

5 Results

A large quantity of fundamental work has been accomplished. Currently some basic principles are still being improved and prototypes of the first consultation systems for rheumatology (CADIAG-IV/Rheumatology) and hepatology (CADIAG-IV/Hepa tology) will be implemented.

Two major types of results have been achieved. On the one hand, methodological fundamentals like MedFrame (Kolousek, 1997), KBuilder (Bögl, 1997) and theoretical work about inference has been accomplished (Brein, 1997); on the other hand, parts of CADIAG-IV like the MedFrame/Browser (Heisz, 2000) and a graphical user interface for CADIAG-IV have been implemented.

6 Discussion

The task of CADIAG-IV—how previous work can be improved to increase the sensitivity and specificity of the inferred suggestions and how these concepts can be implemented by the use of modern software technology—has been partially fulfilled. As no applicable consultation systems are in existence at the present time, the clinical usefulness and quality cannot be commented upon. However, a number of technical problems can be resolved by means of the integrated patient data and medical knowledge base MedFrame and by already implemented tools (see section 5). In addition, important theoretical enhancements have been achieved, which indicate a better approach to the vagueness, uncertainty, and incompleteness of medical knowledge (see section 2.3).

To permit comparison with other approaches in the development of computer-assisted diagnostic systems of rheumatologic diseases, it would be appropriate to give a brief overview of the same:

The objective of the project AI/RHEUM was to develop a computer-based rheumatology consultant system that could be applied by an expert rheumatologist in order to support practicing physicians with no special training in rheumatology (Kingsland et al., 1983). Criteria forms including "major" and "minor" decision elements extend its rule-based formalism. The knowledge base derives from formal criteria for 26 rheumatologic diseases using up to 877 symptoms and 1,029 production rules (Kingsland, 1988). The system has been tested against 1,570 clinical cases. The average sensitivity of the system in terms of the 26 diagnoses correctly triggered in cases in which the human expert's diagnosis was stated as definite was 76%, but varies widely (from 14% to 100% depending on the disease) (Bernelot Moens, 1992).

MESICAR is a rheumatological consultation system that integrates causal and associative reasoning (Horn, 1991). It uses extensive anatomical knowledge. Associative relations between diseases and manifestations are combined with expressions that define conditions on the manifestations. With MESICAR-LEARN its knowledge can be automatically refined and made more efficient by combining analytical and empirical generalization (Widmer et al., 1993).

The SEEK system (Politakis, 1984) provides AI methods for acquiring and verifying knowledge and demonstrates its performance with examples taken from the domain of rheumatic diseases.

CADIAG-IV, on the contrary, tries to extend the abilities of the existing systems by many features as described in section 3, such as the Client/Server-based integrated patient data and medical knowledge base MedFrame, enhancements in the inference mechanism, and new subsystems for knowledge acquisition and evaluation of medical knowledge bases with their respective graphical user interfaces.

There are still open questions, which presumably will not be answered by the present version of CADIAG-IV, but which should be taken into account for further enhancements:

- For proposing further examinations, it should be investigated whether the inference mechanism can be enriched by more sophisticated evaluation functions which would deal with several kinds of costs, e.g. the invasiveness of an examination, discomfort for the patient, financial costs, the required time, or even local settings.
- A further advancement would be the inclusion of prior medications. This can, for example, be done by considering the value of the symptom present before a drug therapy was administered. In the future, it will be meaningful to connect a drug database with information about effects and side effects.

7 Conclusion

In CADIAG-IV, a methodology for building consultation systems to support medical decision-making is under development. It subsumes the implementation of specific consultation systems (CADIAG-IV/Rheumatology and CADIAG-IV/Hepatology) as well as a shell for building such systems (MedFrame/CADIAG-IV). This methodology will make it possible to handle administrative patient data and medical knowledge about particular subjects by the use of MedFrame.

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