KS-3000: An Application of DDUCKS to Bone-Marrow Transplant Patient Support

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Abstract

At the Fred Hutchinson Cancer Research Center (FHCRC), we are developing technology to support research nurses staffing a telephone consultation service for long-term bone-marrow transplant follow-up care. In this paper, we describe the design of KS-3000, an application of the DDUCKS development environment that will combine techniques from knowledge-based systems with those of decision analysis.

1. INTRODUCTION: BONE MARROW TRANSPLANTS AT FRED HUTCHINSON

The Long Term Follow-up Unit (LTFU) at the FHCRC provides a telephone consultation service for physicians caring for bone marrow transplant patients. Since its inception 21 years ago, the Seattle Marrow Transplant Team has carried out more than 4,200 transplants. Of these more than 2,000 patients across the United States and abroad require LTFU support. The Unit also serves as a national/international resource since the smaller bone marrow transplant units have the same long-term responsibilities to their patients but often lack extensive experience or expertise in aftercare. Advice is regularly requested on behalf of an undetermined number of patients who have been transplanted at other centers.

The LTFU receives between 50 and 60 consultation calls each day. The few experts at the LTFU are in high demand and their work load continues to grow with the completion of more successful transplants. Because the attending physician, the key expert, is a limited resource, it is not feasible for him to be directly available for telephone contact. LTFU communications are managed by two nurse experts who meet with the attending physician on a daily basis for rounds. in problem solving. Common consultations address experimental treatment protocols, immunodeficiency and infection (including varicella zoster virus and pneumonia), fever of unknown origin, sexual and gonadal dysfunction, chronic Graft Versus Host Disease (GVHD), immunosuppressive therapies, late complications of chemoradiotherapy including second malignancies, and recurrent leukemia (Nims & Strom, 1988; Sullivan et al, 1988a, b, c; 1991).

To date the LTFU has provided support to primary care physicians largely on a reactive basis; that is, it responds to requests for assistance. Although the team can predict many complications on the basis of past research and existing data, its current resources do not allow it to predict which patients carry specific risks at specific times. Neither can it formally provide office and primary care guidelines for diagnosis and management of life threatening or debilitating complications. As a result, early warning signs of serious complications may go unrecognized by physicians in the home community.

We have recently begun a project that will lead to the development of a prototype knowledge-based system (KBS) to be used as a resource to the research nurses staffing the telephone consultation service. The LTFU consultation service seems well suited for the use of a KBS. The problems encountered, while complex, can be defined within a limited domain and many post-transplantation disorders are encountered repeatedly. The KBS will help prompt the nursing staff to request valuable information, thus increasing the accuracy and completeness of data gathering. In addition, we expect that a KBS will eventually help less-experienced nurses perform at a level approaching that of more experienced ones. The system will keep a log of contacts and transactions, maximizing the efficiency of information analysis and problem solving. Data which are scattered across many formal and informal documents and databases will become readily accessible from a central source.

In addition to its role as a nursing resource, the system will be useful to physicians, residents, fellows, and visitors who come to FHCRC to learn bone marrow transplantation. The KBS will offer problem-focused guidelines for care provision to primary providers. The problem-focused (individual patient) guideline function of the system will eventually permit the KBS to assemble tailored guidelines that fit the risks and circumstances of the individual case and omit superfluous or irrelevant information. The guideline capability will encompass office practice and also include specifications for optimizing management of long term life-threatening or debilitating complications in the home community.

2. COMBINING KNOWLEDGE-BASED SYSTEMS AND DECISION ANALYSIS

Knowledge-based systems have been applied with success in a number of problem domains. Unfortunately, typical knowledge-based approaches have their limitations. Rule-based methods have been shown to perform poorly in problems involving large amounts of uncertainty or risk, and the kinds of complex tradeoffs that inevitably emerge in important decisions (Henrion, Breese & Horvitz, 1991). Furthermore, knowledge-based approaches are not sufficiently flexible for many decisions, since risks and preferences may vary greatly across individual cases (Langlotz, Shortliffe, and Fagan, 1986). Finally, knowledge-based system development environments do not generally provide facilities for integrating and updating judgments provided by expert physicians with patient information contained in databases (Spiegelhalter, Franklin, and Bull, 1990).

Recently, several researchers have begun working on ways of adapting decision analysis techniques to overcome the limitations of typical knowledge-based systems (Wellman, Breese, & Goldman, 1991). Knowledge-based decision analysis model construction systems make decision analysis techniques practical and cost-effective for a wider range of problems (Bradshaw, Covington, Russo & Boose, 1990, 1991; Holtzman, 1989). The key to success of such systems is that each component contributes to the portion of the process it does best: the knowledge-based components guide the interaction by using rough rules-of-thumb that can help to quickly scope, categorize, gather information, structure, and interpret important aspects of the problem; the decision analysis components rely on carefully crafted assessments of uncertainty and utility to provide specific answers to questions about a particular patient's situation in a rigorous manner. Szolovits and Pauker (1978) express the complementary nature of these knowledge-based system and decision analysis methods in this way:

> "When the complex problems need to be addressed—which treatment should be selected, how much of the drug should be given, etc.—then… probabilistic models are necessary. The essential key to their correct use is that they must be applied in a limited problem domain where their assumptions can be accepted with confidence. Thus, it is the role of [knowledge-based system] methods to discover what the central problem is and to limit it as strongly as possible; only then are probabilistic techniques appropriate for its solution."

In section 3, we will describe the high-level system architecture contemplated for KS-3000. Following this, we will explain the design, organization, and use of specific components of the knowledge base (section 4).

3. SYSTEM ARCHITECTURE

We will extend a Boeing-developed framework called DDUCKS (Decision and Design Utilities for Comprehensive Knowledge Support) to serve as the foundation for KS-3000 (Bradshaw, Chapman & Sullivan, 1992; Bradshaw, Ford, Adams-Webber & Boose, in press). DDUCKS is based on a three-schema architecture and the client-server model. This approach is discussed in more detail in Bradshaw, Ford, & Adams-Webber (1991), Ford, Bradshaw, Adams-Webber, & Agnew (in press) and van Griethusen & King (1985). A diagram representing the major components of KS-3000 is shown in Figure 1.

3.1. Virtual notebook

We have found the concept of a virtual notebook to be an effective paradigm for recording and extending group memory (Bradshaw, Holm, Kipersztok & Nguyen, 1992). The virtual notebook facility in DDUCKS will help team members collect and organize the diverse materials associated with a particular set of patients. It will provide access to data and capabilities for external applications by means of MANIAC (MANager for Inter-Application Communication), a custom program-to-program interface developed by Seattle University as part of a Boeing-sponsored activity (Bradshaw, Holm, Kipersztok, Nguyen, Russo & Boose, 1991). It also will help manage changes between different versions and views of informal and formal information as it evolves.

DDUCKS notebooks are usually opened in double-page mode, displaying a page on the right and one on the left as in a paper notebook. Like a real notebook, the virtual notebook divides the material into tabbed sections and subsections, automatically generating various notebook “organizers” (i.e., pages containing table of contents and indexing information). Unlike a real notebook, related items can be linked electronically so they can be accessed rapidly and continuously kept up-to-date. Users move from page to page by selecting a “tab” on the side of the notebook or selecting an item in the table of contents view. Alternatively, the user can query the notebook to bring up pages meeting user-defined criteria.

In KS-3000, virtual notebooks provide the interface between the nurses and the information available through the KBS. They function somewhat like the current LTFU book of facts. Each ‘page’ of the notebook contains one or more ‘views’ that can display and accept data concerning general information on patient care or specific items of interest about a particular case. As progress notes and patient data are entered, formal knowledge structures will be created in the background (cf. Campbell & Musen, 1992). Learning mechanisms allow the notebook to adapt over time to specific users and tasks (Bradshaw & Boy, 1993). From time to time, public versions of the notebook will be ‘published’ to allow selected information on patient care to be made available to physicians. This publication could be in hardcopy form, or electronically through remote network access to the public notebook interface.

Figure 2 shows a screen snapshot of a DDUCKS virtual notebook containing an influence diagram. The diagram represents a generic medical decision making template. The problem is to determine the best treatment alternative for a cancer patient, taking treatment risks and other diagnostic uncertainties into account. The treatment strategy is composed of two decisions (Test, Treatment), represented by square nodes on the diagram. Round nodes represent treatment uncertainties (Results, Therapeutic Effect, Side-Effect), diagnostic uncertainties (Patient Demographics, Observable Symptom, Hypothetical Disorder, Physiological Need), and Cost. The eight-sided node labeled “Value” has been designated as the criterion to maximize in evaluating the model to determine the best treatment strategy.

3.2. Consultation tools and views

Certain types of pages in the notebook will contain views designed for the use of nurses and others interacting with the system to enter patient information or gain answers to questions. By defining virtual notebook templates, teams and individuals can tailor the contents of a “boiler plate” virtual notebook to be consistent with their own preferences for accessing, viewing, and using the information. For example, the LTFU team's blank notebook can come pre-configured with information about standard definitions and procedures (e.g., required steps in a protocol), just as a real notebook can be pre-loaded with labeled dividers and forms. Within a particular view,

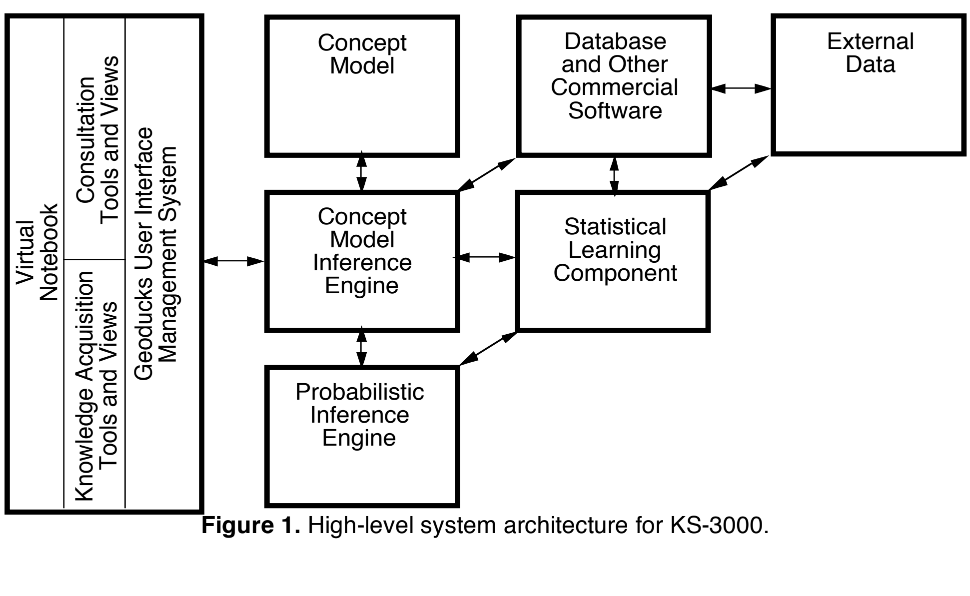


Figure 1. High-level system architecture for KS-3000.

information entered by the nurse can be intermixed freely with information accessed from the patient database or inferred by the knowledge-based system.

3.3. Knowledge acquisition tools

Medical experts and knowledge engineers collaborate to build and test a knowledge base through the process of knowledge acquisition. Consensus exists among researchers that knowledge acquisition is the most difficult and time-consuming aspect of the KBS development process. Knowledge acquisition tools are designed to assist in the formulation, validation, verification, and maintenance of KBSs throughout their lifetime. (Bradshaw, Ford, Adams-Webber & Boose, in press) The intent is to reduce both the cost and the time of developing such systems while increasing their quality. We will draw from our experience in developing knowledge acquisition tools to develop and maintain the LTFU KBS (Boose & Bradshaw, 1987; Boose, Bradshaw, Koszarek & Shema, 1992; Bradshaw, Shema, Boose & Koszarek, 1992; Bradshaw, Covington, Russo & Boose, 1990, 1991; Bradshaw, Holm, Kipersztok & Nguyen, 1992).

3.4. *Geoducks* user interface management system

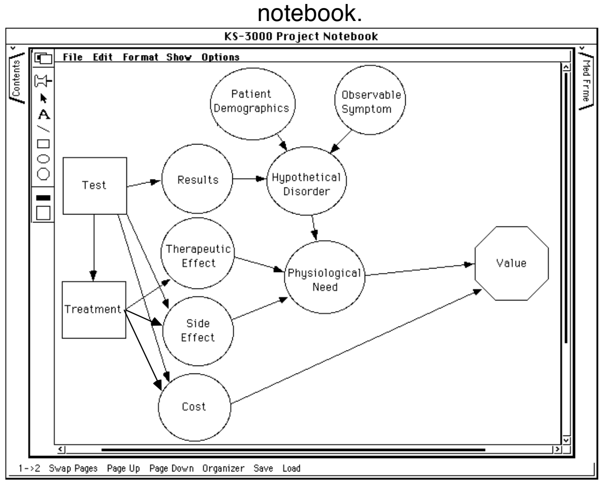
User-interface management systems (UIMSs) are becoming an essential part of interactive tool development and end-user tailoring (Hix, 1990). UIMSs allow graphical user-interfaces to be created or modified quickly from existing components. In DDUCKS, we have extended the capabilities of a Smalltalk-80-based direct-manipulation user-interface builder to construct a DDUCKS UIMS, called *Geoducks*.[1] *Geoducks* relies on the Smalltalk-80 MVC (model-view-controller) concept for managing different perspectives on data (Goldberg, 1990).

3.5. Concept model and concept model inference engine

The primary knowledge base in DDUCKS is called the concept model. (Bradshaw, Holm, Boose, Skuce & Lethbridge, 1992). A software component termed the concept model inference engine uses information in the concept model to answer questions and draw logical inferences based on some initial set of concepts, facts, and rules. DDUCKS employs a variant of CODE4 as the underlying conceptual representation (Skuce, 1991a, b). CODE4 will provide a rich paradigm for the definition of important concepts in the medical domain. A comprehensive lexicon allows references to concepts to be maintained automatically and accessed quickly. As part of the project, an existing simple natural language system in CODE4 will be extended to support semi-automated generation of textual reports and guidebooks. Definition of other facilities will support knowledge-based construction and interpretation of the probabilistic and decision models (Bradshaw, Covington, Russo & Boose, 1990, 1991; Wellman, Breese & Goldman, 1991). Concept libraries and default inferencing mechanisms can be augmented by users employing graphical views and an integrated scripting and query language.

We are interested in exchanging knowledge bases with other research groups (Bradshaw, Holm, Boose, Skuce, & Lethbridge, 1992; Almond, Bradshaw, & Madigan, 1993). Gruber's work on Ontolingua (Gruber, 1992) currently provides the most promising mechanism for sharing ontologies between different tools and formalisms. Ontolingua extends the knowledge interchange format (KIF; Genesereth & Fikes, 1992) defined by the DARPA knowledge sharing effort with standard primitives for defining classes and relationships, and organizing knowledge in object-centered hierarchies with inheritance. Ontolingua facilitates the translation of KIF-level sentences to and from forms that can be used by various knowledge representation systems (currently LOOM, Epikit, Algernon, and a canonical form of KIF). We are working with Gruber to define an Ontolingua interface for CKB, the CODE4 knowledge base file format (Lethbridge & Skuce, 1992)

Figure 2. Screen snapshot of the DDUCKS virtual notebook.



3.6. Probabilistic inference engine

The probabilistic inference engine can be used to answer questions and make specific predictions or recommendations for a particular patient and situation. It bases its conclusions on Bayesian network or influence diagram models for that patient that are individually formulated with help from the concept model inference engine. We will extend concepts and algorithms developed by Almond (1988, 1990), Madigan (1989; Madigan & Mosurski, 1992), and Zarley (1988; Zarley, Hsia & Shafer, 1988) to build a state-of-the-art probabilistic

[1] Pronounced "gooey-ducks".

inferencing facility capable of managing risk, uncertainty, and complex preferences in a rigorous manner.

3.7. Bayesian statistical learning component

By statistical learning, we mean the capability for a KBS to improve its knowledge base and hence its performance by taking advantage of accumulating patient data in addition to the subjective judgments initially supplied by medical experts. The approach we propose will make it convenient to combine probabilities derived from patient data with subjective probability assessments provided by medical experts (see e.g., approaches discussed by Bradshaw & Boose, 1990; Spiegelhalter, Franklin, and Bull, 1990). Before each consultation, expert probability assessments and data from past cases representing the experience base of the system are embedded in influence diagram networks. Following a consultation, staff can add new case data to the database for future use. New families of techniques, such as those proposed by Madigan & Raftery (1991; Madigan, Raftery, York, Bradshaw, & Almond, 1993), will allow the system to refine not only the quantitative assessments but also the qualitative structure of the networks.

4. Knowledge Base Design

It is useful to think of DDUCKS in terms of four “layers” of functionality: workbench, shell, application, and consultation. Starting with any layer in the system, a user can produce a set of tools and models that can be used to assist in configuration of a more specialized system at the layer below. The process for accomplishing this in the domain of bone-marrow transplant patient support is described below.

The first step in our approach involves building a methodology-specific shell by using the knowledge modeling facilities contained in the DDUCKS workbench. The first version of *Axotl* contained a shell for constructing decision analysis models using knowledge-based tools (Bradshaw, Covington, Russo & Boose, 1990, 1991; Holtzman, 1989; Wellman, Breese & Goldman, 1991). Using *Axotl*, we demonstrated prototype applications of such a shell in the domain of R&D project selection. Embedding similar facilities within DDUCKS will increase the power and flexibility of this approach. An application of DDUCKS in a different domain is described in (Bradshaw, Holm, Kipersztok, Covington & Nguyen, 1992).

A complete decision model, containing relevant items of problem-solving knowledge and their interrelationships, constitutes the *decision basis* (Howard and Matheson, 1984). Three things are represented in the decision basis: *information*, *preferences*, and *alternatives*. In a medical application, the information consists of the a physician’s description of relationships between symptoms and diseases; the preferences consist of factors that determine the desirability of a treatment alternative, such as cost, effectiveness, or risk; and the alternatives consist of the various possibilities for treatment. Using a variety of knowledge acquisition tools and techniques, we elicit and represent skeletal knowledge bases *(templates)* of information, alternatives, and preferences for particular classes of decisions within libraries of application-specific ontologies (Bradshaw & Boose, 1990; Bradshaw, Covington, Russo & Boose, 1990, 1991). Portions of this knowledge base will be combined with situation-specific information, alternatives, and preferences supplied by nurses or physicians at consultation time.

The generic *process* of knowledge-based decision analysis model construction and evaluation is shown in Figure 3. An application-specific version of this process model is available to assist users at consultation time. Knowledge-based tools assist in problem definition, information gathering, and model construction based on new and old patient data and the domain and problem-solving knowledge templates in the concept model. Rules for combining and modifying probabilistic model fragments are described using a specialized graph grammar (cf. Egar, Puerta, & Musen, 1992). Ultimately, a situation-specific probabilistic decision model is produced which can be evaluated by the probabilistic inference engine using decision-theoretic criteria to yield an expected utility on the alternatives. As part of the appraisal process, knowledge-based tools conduct appropriate forms of analysis (e.g., sensitivity analysis, value of information, control, or flexibility) and help to interpret the results. Insight gained through model appraisal can help users determine whether it is appropriate to take action or to further refine the model.

The configuration and tailoring process for developing a bone-marrow transplant patient support system can be described in terms of the layers of functionality described above. The first step involves building a knowledge-based decision analysis shell by using the knowledge modeling facilities contained in the DDUCKS workbench. The shell will consist of the following components:

- methodology-specific problem-solving task models (e.g., maximization of expected utility across decision alternatives, hierarchical constraint satisfaction using extended AND-OR graphs)
- methodology-specific mediating representations created out of the combination of generic interaction paradigms with a particular semantic and computational interpretation of the elements (e.g., influence diagrams, activity graphs);
- a methodology-specific ontology (a specification of the schema itself; e.g., taxonomies of concept descriptors for decision, chance, deterministic, and value nodes);
- methodology-specific model-building process models (i.e., knowledge about how to acquire application-specific knowledge within the context of decision analysis methodology);
- methodology-specific extensions to the inference and function library.

The bone-marrow transplant support application will be created by using the knowledge modeling facilities generated by the shell. It will be comprised of:

- application-specific mediating representations (e.g., specialized graphical or form-filling interfaces tailored to research nurses and physician-users, to be used in place of influence diagrams and activity graphs);
- an application-specific ontology (extensions to the schema that become the modeling primitives for the application; e.g., test and treatment decision nodes; risk factor, observable symptoms, and therapeutic effect chance nodes; cost deterministic nodes; canonical utility function value nodes);
- application-specific model-building process models (i.e., knowledge about how to conduct a consultation with research nurses or physician-users);
- application-specific extensions to the inference and function library.

Research nurses and physician-users will use the consultation facilities generated by the application to produce a situation-specific model comprised of:

- a situation-specific problem-solving task model (e.g., an influence diagram for the patient that is the subject of consultation).
- situation-specific mediating representations (e.g., text and graphical annotation of the graphical and form-filling views on the model);
- situation-specific model components (e.g., decision and chance nodes describing alternatives and outcomes for the patient);
- situation-specific facts and assertions (e.g., particular information about the patient's situation);
- situation-specific functions and inferences.

The complete situation-specific model represents the unique characteristics of a particular patient and situation and comprises all the information mentioned above. This model is formulated, evaluated, and analyzed during the consultation to produce recommendations for action or for further model refinement.

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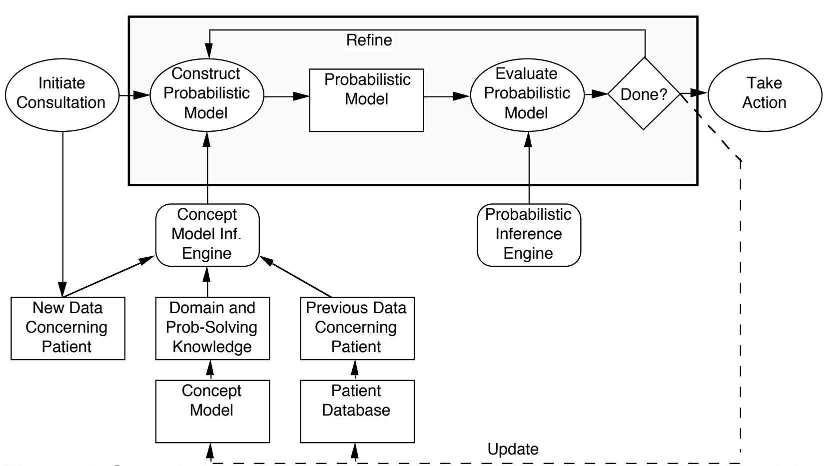

Figure 3. Steps in knowledge-based construction of the probabilistic model.

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