

# Lecture Notes in Medical Informatics

---

Vol. 1: Medical Informatics Europe 78. Proceedings 1978. Edited by J. Anderson. XI, 822 pages. 1978.

Vol. 2: D. Fenna, S. Abrahamsson, S. O. Lööv and H. Peterson, The Stockholm County Medical Information System. VI, 163 pages. 1978.

Vol. 3: Long-Term Studies on Side-Effects of Contraception – State and Planning. Symposium 1977. Edited by U. Kellhammer and K. Überla. VI, 240 pages. 1978.

Vol. 4: Clinical Trials in 'Early' Breast Cancer. Proceedings 1978. Edited by H. R. Scheurlen, G. Weckesser and I. Armbruster. VI, 283 pages. 1979.

Vol. 5: Medical Informatics Berlin 1979. Proceedings 1979. Edited by B. Barber, F. Grémy, K. Überla and G. Wagner. XXIII, 970 pages. 1979.

Vol. 6: Health Care Technology Evaluation. Proceedings, 1978. Edited by J. Goldman. VII, 118 pages. 1979.

Vol. 7: Technology and Health: Man and his World. Proceedings, 1978. Edited by G. Wagner, P. L. Reichertz and E. Masè. VI, 243 pages. 1980.

Vol. 8: Mathematical Aspects of Computerized Tomography. Proceedings 1980. Edited by F. Natterer. VIII, 309 pages. 1981.

Vol. 9: Computers and Mathematical Models in Medicine. Proceedings, 1977. Edited by D. Cardús and C. Vallbona. VIII, 315 pages. 1981.

Vol. 10: B. Fries, Applications of Operations Research to Health Care Delivery Systems. V, 107 pages. 1981.

Vol. 11: Medical Informatics Europe 81. Proceedings 1981. Edited by F. Grémy, P. Degoulet, B. Barber, and R. Salamon. XXIII, 975 pages. 1981.

Vol. 12: G. Wiederhold, Databases for Health Care. VI, 75 pages. 1981.

Vol. 13: The Computer and Blood Banking. Proceedings, 1981. Edited by J. R. Möhr and A. Kluge. X, 275 pages. 1981.

Vol. 14.: F. Wingert, Medical Informatics. X, 247 pages. 1981.

Vol. 15: Digital Image Processing in Medicine. Proceedings 1981. Edited by K. H. Höhne. VIII, 197 pages. 1981.

Vol. 16: Medical Informatics Europe 82. Proceedings, 1982. Edited by R.R. O'Moore, B. Barber, P.L. Reichertz, and F. Roger. XX, 938 pages. 1982.

Vol. 17: Biomedical Images and Computers. Proceedings, 1980. Edited by J. Sklansky and J.-C. Bisconte. VII, 332 pages. 1982.

Vol. 18: D.P. Pretschner, Engymetry and Personal Computing in Nuclear Medicine. V, 129 pages. 1982.

Vol. 19: R. L. Blum, Discovery and Representation of Causal Relationships from a Large Time-Oriented Clinical Database: The RX Project. XIX, 242 pages. 1982.

Vol. 20: S. Biefang, W. Köpcke, M. A. Schreiber, Manual for the Planning and Implementation of Therapeutic Studies. V, 100 pages. 1983.

Vol. 21: Influence of Economic Instability on Health. Proceedings, 1981. Edited by J. John, D. Schwefel, and H. Zöllner. VIII, 528 pages. 1983.

Vol. 22: Objective Medical Decision-making; Systems Approach in Acute Disease. Proceedings, 1983. Edited by J. E. W. Beneken and S. M. Lavelle. VIII, 243 pages. 1983.

# Lecture Notes in Medical Informatics

Edited by P.L. Reichertz and D.A.B. Lindberg

32

---

Glenn D. Rennels

A Computational Model  
of Reasoning from  
the Clinical Literature

---



Springer-Verlag

Berlin Heidelberg New York London Paris Tokyo

## **Editorial Board**

J. Anderson J. H. van Bommel M. F. Collen F. Grömy S. Kaihara A. Levy  
D. A. B. Lindberg (Managing Editor) H. Peterson A. Pratt  
P. L. Reichertz (Managing Editor) E. H. Shortliffe W. Spencer K. Überla C. Valbona

## **Author**

Glenn D. Rennels, M. D., Ph. D.  
Medical Information Sciences Program  
Stanford University, Medical School Office Building  
Stanford, CA 94305 – 5479, USA

ISBN-13: 978-3-540-17949-8 e-ISBN-13: 978-3-642-93363-9  
DOI: 10.1007/978-3-642-93363-9

This work is subject to copyright. All rights are reserved, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, re-use of illustrations, recitation, broadcasting, reproduction on microfilms or in other ways, and storage in data banks. Duplication of this publication or parts thereof is only permitted under the provisions of the German Copyright Law of September 9, 1965, in its version of June 24, 1985, and a copyright fee must always be paid. Violations fall under the prosecution act of the German Copyright Law.

© Springer-Verlag Berlin Heidelberg 1987

2127/3140-543210

## Foreword

As research on expert systems has moved well into its second decade, it has become popular to cite the limitations of the phenomenologic or associational approach to knowledge representation that was typical of first generation systems. For example, the Internist-1 knowledge base represents explicitly over 600 diseases, encoding associated disease manifestations (signs, symptoms, physical findings, and lab abnormalities) but failing to deal with the *reasons* that those findings may be present in the disease [Miller, R. A. 82]. In recent years Pople has sought to add detailed causal models to the knowledge base in a revised version of the program known as CADUCEUS [Pople 82]. Similarly, a typical production rule in the MYCIN system states inferences that may be drawn when specific conditions are found to be true [Buchanan 84], but the underlying explanations for such relationships are not encoded. Clancey has argued that MYCIN needs such "supporting knowledge" represented, especially if its knowledge base is to be used for teaching purposes [Clancey 83].

By the late 1970s, artificial intelligence researchers were beginning to experiment with reasoning systems that used detailed mechanistic or causal models of the object being analyzed. Among the best early examples were a program to teach students how to analyze electronic circuits [Brown 82] and a system for diagnosing problems with mechanical devices [Rieger 76]. Such developments were not lost on the medical expert system community, and by the early 1980s we were beginning to see systems that analyzed medical problems based on detailed symbolic models of pathophysiology [Patil 81].

At about this time Glenn Rennels, a physician who had interrupted post-graduate medical training to obtain a degree in Medical Information Sciences at Stanford, was beginning to search for a Ph.D. dissertation topic. Impressed though he was in the exploratory work using medical causal models of pathophysiology, his medical training and experience persuaded him that the approach would be applicable to only a small percentage of the clinical problems that beset physicians in practice. When he observed consultants giving advice in clinics or on the wards, only occasionally did he notice that mechanistic explanations were a key element of the analysis. More typically the experts would cite the literature, mentioning data from clinical trials that were judged pertinent to the question at hand. Even more importantly, it was clear that for many areas of medicine our understanding of pathophysiologic

details is so limited that it would be *misleading* to use a mechanistic model, rather than empiric data from well-controlled studies, to guide decision making.

The management of primary breast cancer is a particularly good example of this latter point. Although physicians have a superficial model of disease progression and spread via the blood or lymphatics, those models have proved inappropriate and hence useless for therapeutic decision making. Instead it is a careful analysis of studies reported in the literature, with expertise in statistical interpretation and matching of patient populations, which is the basis for selecting therapy for breast cancer. Even so, there is ample opportunity for disagreement, as the ongoing controversy regarding alternative surgical approaches and the role of adjuvant radiotherapy reveals.

The Roundsman system subsequently developed by Rennels is a novel and clever effort to develop a consultant program that gives advice based on an explicit representation of the content of articles from the clinical literature. Rather than seeking a mechanistic explanation of observed phenomena, Roundsman must select the studies that are relevant to a specific question, isolate the pertinent data for the population of patients best matched to the current case, and then generate advice in the form of free text that is understandable, tactful, and persuasive. Rennels' success in this effort is the subject of the current volume. Although the system is specific to breast cancer management at present (due to the generous collaboration of an eminent oncologist, Dr. Frank Stockdale), the approach is general and should be broadly applicable in other medical domains where empirical data are the cornerstone of expert decision making (for example, the management of hyperlipoproteinemia).

Rennels' work on this project has been a source of considerable excitement for me. Glenn is the first doctoral graduate from a novel interdisciplinary degree program in Medical Information Sciences that we began in 1982. Sitting as it does at the interface between computer science, clinical medicine, biostatistics, and artificial intelligence, Roundsman is in the best tradition of high quality interdisciplinary research. It helps show, by example, the unique confluence of scholarly activities that help define medical informatics as a distinct emerging academic discipline. I will not soon forget the gratifying discussion after Glenn's Ph.D. oral examination when the other members of his examination committee (a computer scientist, biostatistician, and internist) each acknowledged that the work was original and fully worthy of the doctorate although none felt the scope, content, and emphasis would have matched precisely with the advanced degree requirements of their own department.

I accordingly commend to you this excellent book. Roundsman is good computer science, offering an impressive synthesis of recent ideas regarding object centered programming, statistical reasoning, heuristic problem solving, and text generation. It is also good medicine, showing how domain knowledge evolves over time and addressing important issues of how medical experts must integrate new knowledge and data with what they already know. But, perhaps most importantly, it is superb medical informatics and is accordingly a worthy addition to this influential series of research notes.

Edward H. Shortliffe

Palo Alto

March 1987

## Acknowledgments

This work was supported in part by training grant LM-07033 from the National Library of Medicine and ONR contract N00014-81-K-0004. Computing resources have been provided by the Biomedical Research Technology Program under grant RR-00785 and by the Hewlett-Packard Company.

The research described in this book was possible only with the help of many colleagues and friends. I am especially grateful to Ted Shortliffe, Frank Stockdale, Perry Miller, and Brad Efron.

Portions of this work have been published or are in press in the *Encyclopedia of Artificial Intelligence* [Rennels 87a], *Medical Decision Making* [Rennels 87b], *Computer Methods and Programs in Biomedicine* [Rennels 87c], *Proceedings of the Fifth World Congress on Medical Informatics* [Rennels 86a], *Proceedings of the AAMSI Congress 86* [Rennels 86b], *Proceedings of the Tenth Annual Symposium on Computer Applications in Medical Care* [Rennels 86c], and the *Proceedings of the AAMSI Congress 87* [Rennels 86d].

# Table of Contents

<b>1. Introduction</b>	<b>1</b>
1.1. Introduction to the Problem	1
1.2. Research Themes	3
1.3. The Roundsman System: Examples	5
1.4. Research Contributions	9
1.5. Guide to the Reader	10
<b>2. Background</b>	<b>13</b>
2.1. A Review of Artificial Intelligence in Medicine	13
2.1.1. Introduction	13
2.1.2. Theoretical Basis	14
2.1.3. Research Themes	19
2.1.4. Summary of Roundsman's Relationship to Prior AIM Research	21
2.2. Consultation Systems for Biostatistics	22
2.3. Computer Databases	25
2.3.1. Bibliographic Retrieval Systems	25
2.3.2. Databases of Patient Records	26
2.4. Decision Analysis	27
2.5. Scope of the Biomedical Reports in Roundsman's Library	29
2.6. Guides to Clinical Application of Biomedical Reports	31
2.7. Management of Primary Breast Cancer	32
2.7.1. Treatment Options	32
2.7.2. Treatment Objectives	35
2.7.3. Controversy	36
<b>3. Overview of the Research and the Roundsman System</b>	<b>37</b>
3.1. Informal Protocol Analysis	37
3.2. The Development of Target Scripts	39
3.3. Selection of Publications to Include in Roundsman	41
3.4. Hardware and Software Support	42
3.5. An Overview of the Roundsman System	42
<b>4. Modeling Distance from Study to Decision</b>	<b>55</b>
4.1. Representing a Study's Basic Statistical Results	55
4.2. A Taxonomy of Distance	58
4.3. Calibration of Distance	66
4.4. Distance Estimators	72
4.5. Work Related to Roundsman's Distance Metric	73
4.6. Summary	77
<b>5. Choice and Explanation</b>	<b>79</b>
5.1. Introduction	79
5.2. Multiattribute Decision Making	80
5.3. The Importance of Modelling Both Choice and Explanation	81



## Table of Contents

5.4. Four Strategies for Choice and Explanation	82
5.5. Lexicographical Ordering	82
5.5.1. Operational Definition	82
5.5.2. Examples	83
5.5.3. Assumptions	86
5.5.4. Explanation	86
5.6. Satisficing	86
5.6.1. Operational Definition	86
5.6.2. Examples	87
5.6.3. Assumptions	88
5.6.4. Explanation	88
5.7. Dominance	89
5.7.1. Operational Definition	89
5.7.2. Examples	89
5.7.3. Assumptions	90
5.7.4. Explanation	90
5.8. Trade-Off	90
5.8.1. Operational Definition	90
5.8.2. Examples	91
5.8.3. Assumptions	93
5.8.4. Explanation	94
5.9. Comparison Strategies Under Uncertainty	95
5.10. Implementation in Roundsman	96
5.11. Summary	102
<b>6. Interactions Between Studies</b>	<b>103</b>
6.1. Updating Roundsman Over Time	103
6.2. Conflict Between Study Results	108
6.2.1. Bayes' Estimates and Meta-Analysis	109
6.2.2. Explicit Use of Inter-Study Domain Knowledge	115
6.3. Summary and Future Directions	116
<b>7. Text Generation</b>	<b>119</b>
7.1. Introduction	119
7.2. Examples	121
7.3. Programming Language Primitives: Objects and Messages	125
7.4. Overview of the Implementation	126
7.5. Operational Description of the Objects	126
7.5.1. Prose Fact	127
7.5.2. Start-State	127
7.5.3. Pop-State	129
7.5.4. Cond-State	129
7.5.5. Option-State	130
7.5.6. Sequence-State	131
7.5.7. Push-Arc	132
7.5.8. Jump-Arc	133
7.5.9. Text-Arc	134

## Table of Contents

7.5.10. Endsequence-Arc	134
7.5.11. Function-Arc	135
7.6. Discussion	135
<b>8. Extended Examples and Evaluation</b>	<b>139</b>
8.1. Example 1	139
8.2. Example 2	142
8.3. Example 3	144
8.4. Example 4	146
8.5. Example 5	148
8.6. Example 6	149
8.7. Example 7	151
8.8. Example 8	152
8.9. Evaluation	153
8.9.1. Introduction	153
8.9.2. Methods	155
8.9.3. Results	155
8.9.4. Discussion	160
<b>9. Conclusions</b>	<b>167</b>
9.1. Summary	167
9.2. Limitations	169
9.3. Promising Areas for Extending the Research	170
<b>Appendix I. Internal Representation of the Studies in Roundsman's Library</b>	<b>173</b>
<b>Appendix II. Sample Distance Estimators</b>	<b>207</b>
<b>REFERENCES</b>	<b>213</b>
<b>Index</b>	<b>229</b>

## List of Figures

<b>Figure 1-1:</b>	Flow of control in the Roundsman system.	7
<b>Figure 2-1:</b>	Local Excision.	33
<b>Figure 2-2:</b>	Total Mastectomy.	34
<b>Figure 2-3:</b>	Halsted Radical Mastectomy.	35
<b>Figure 4-1:</b>	Comparisons are linked to treatments and outcomes.	58
<b>Figure 4-2:</b>	Partial hierarchy of distance metric components.	59
<b>Figure 4-3:</b>	Probability density function (pdf) over DP.	68
<b>Figure 4-4:</b>	Illustration of a <i>DP-change</i> .	69
<b>Figure 4-5:</b>	Illustration of an <i>SE-change</i> .	71
<b>Figure 5-1:</b>	The precedence scheme developed for EXPERT.	85
<b>Figure 6-1:</b>	Bayesian updating.	112
<b>Figure 6-2:</b>	Schematic of an averaging process.	114
<b>Figure 7-1:</b>	Sample net, called "Net-1".	122
<b>Figure 7-2:</b>	A sample net, called "Net-2".	124

## List of Tables

<b>Table 2-1:</b>	Research report classification scheme from [Bailar 84b].	30
<b>Table 3-1:</b>	The <i>patient-description</i> object for the example session.	45
<b>Table 3-2:</b>	The <i>intervention</i> object for this example session with Roundsman.	45
<b>Table 3-3:</b>	The hierarchy of <i>treatment</i> objects known to Roundsman.	46
<b>Table 3-4:</b>	The <i>decision-context</i> object for the example session with Roundsman.	47
<b>Table 3-5:</b>	An example <i>comparison</i> object from the Veronesi81 study.	48
<b>Table 3-6:</b>	Hierarchy of <i>outcome</i> objects known to Roundsman.	49
<b>Table 3-7:</b>	Example <i>stratum</i> from Veronesi81.	49
<b>Table 3-8:</b>	Example metric component: an <i>intervention-mismatch</i> object.	52
<b>Table 4-1:</b>	Example <i>comparisons</i> from Fisher85a.	57
<b>Table 4-2:</b>	Two "distance metric components".	65
<b>Table 4-3:</b>	A <i>population-distance-estimator</i> object.	72
<b>Table 5-1:</b>	Attributes used for choice of therapy in primary breast cancer.	83
<b>Table 5-2:</b>	Goals of the MYCIN revised therapy algorithm.	88
<b>Table 5-3:</b>	Summary of multiattribute interpretation of the strategies.	94
<b>Table 8-1:</b>	Form used for changes to a particular comment.	156
<b>Table 8-2:</b>	Form used to note general problems of a critique.	157
<b>Table 8-3:</b>	Number and type of evaluator corrections.	158
<b>Table 8-4:</b>	Possible sources of problems with output.	162