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Using CommonKADS to Build an Expertise Model for Breast Cancer Prognosis and Therapy

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▶ **To cite this version:**

Roberto Sacile. Using CommonKADS to Build an Expertise Model for Breast Cancer Prognosis and Therapy. RR-2737, INRIA. 1995. <inria-00073956>

HAL Id: inria-00073956
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Submitted on 24 May 2006

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Éditeur

Inria, Domaine de Voluceau, Rocquencourt, BP 105 LE CHESNAY Cedex (France)

ISSN 0249-6399

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  Institut Pasteur
- http://www.med.nyu.edu/nih-guide.html
  NIH GUIDE INDEX
- http://cancer.med.upenn.edu/
  OncoLink, The University of Pennsylvania Cancer Resource
- http://wwwicic.nci.nih.gov/jnci/jnci_issues.html
  Current JNCI issues available on-line

9.2.2. On Knowledge Acquisition

- http://camis.stanford.edu/protege/
  PROTÉGÉ's Home Page
- http://arti.vub.ac.be/www/kads/welcome.html
  CommonKADS in the VUB AI lab
- ftp://swi.psy.uva.nl/pub/CommonKADS
  Remote file swi.psy.uva.nl/pub/CommonKADS
- http://www.swi.psy.uva.nl/projects/Kactus/toolkit/about.html
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9 Appendix D: further references

The references which are reported here have been divided in different subsections. The first subsection refers to the courses attended during this vising period; the second subsection refers to a selection of WWW sites which have been frequently accessed during this work. Finally, the other two subsections refers to a greater list of references on CommonKADS and on breast cancer prognosis and treatment which might be useful for readers interested in this field.

9.1 Attended courses and publication produced in relation to this work

European School of Oncology - Advanced Course: Breast Cancer, 2nd-4th October, 1995, Milan, Italy. Chairman of the Scientific Committee Prof. U.Veronesi. Chairman of the Course/Seminar Prof. J-Y. Petit, Dr. D.W.Kinne.

Sacile, R., Ruggiero, C., Dieng, R., Applicazione ed uso di CommonKADS per creare un modello concettuale per la prognosi del tumore della mammella. Congresso Annuale Aica (Associazione Italiana per l'Informatica ed il Calcolo Automatico), vol.2, pp. 691-696.

9.2 List of WWW server

9.2.1. On Cancer Information

- http://golgi.harvard.edu/biopages/medicine.html
  The World-Wide Web Virtual Library: Biosciences - Medicine
- http://nysernet.org/bcic/
  Breast Cancer Information
- gopher://gopher.ncc.go.jp/
  National Cancer Center, Tokyo JAPAN
- http://galaxy.einet.net/galaxy/Medicine/Medical-Specialties/Cancer.html
  Cancer (Medical Specialties)
- gopher://gan1.ncc.go.jp/11/CNET/Physicians
  For Physicians
- http://biomed.nus.sg/Cancer/welcome.html
  CancerNet

```
    type : primitive ;
    sub-tasks : cover ;
    control-structure :
    generate(c:initial_complaint -> h:hypothesis) =
        cover(c:initial_complaint -> h:hypothesis) ;

task test ;
task-definition
    goal : «test the risk» ;
    input : initial_complaint : «risk value» ;
    output : hypothesis : «risk value» ;
task-body
    type : primitive ;
    sub-tasks : match ;
    control-structure :
    test(c:risk1 -> h:risk2) =
     match(c:risk1 -> h:risk2);
```

```
--inference establish
    --operation-type : backwardall ;
    --input-roles : initial_complaint -> state ;
    --output-roles : hypothesis -> state ;
       --static-roles : necessary_condition -> cause in
causal_model ;
    --specification : «une» ;

task-knowledge

task bc_prognosis ;
task-definition
    goal : «define the bc risk» ;
    input : initial_complaint : «a» ; biol_manifestation :
«b» ;
    output : prognosis : «c» ;
    specification : «assess the bc risk, confirm by addi-
tional biol_manifestation» ;
task-body
    type : primitive ;
    sub-tasks : generate_biol , generate ;
    additional-roles : hypothesis : «» ;
    control-structure :
    bc_prognosis(c:initial_complaint, m:biol_manifestation
-> h:prognosis) =
       generate_biol(m:biol_manifestation -> d:complaint) ;
         generate(d:complaint -> h1:hypothesis) ;
         generate(c:initial_complaint -> h2:hypothesis) ;
         test(h1:hypothesis -> h: prognosis);
         test(h2:hypothesis -> h: prognosis);

task generate_biol ;
task-definition
    goal : «generate a biol risk fact» ;
    input : initial_complaint : «» ;
    output : hypothesis : «» ;
task-body
    type : primitive ;
    sub-tasks : cover ;
    control-structure :
    generate(c:initial_complaint -> h:hypothesis) =
        cover_biol(c:initial_complaint -> h:hypothesis) ;

task generate ;
task-definition
    goal : «generate a possible risk» ;
    input : initial_complaint : «» ;
    output : hypothesis : «» ;
task-body
```

```
status of Thymidine_labeling_index = high

status of Proliferative_capacity = low
has_biol_manifestation
status of S_phase_fraction = low

status of Proliferative_capacity = high
has_biol_manifestation
status of S_phase_fraction = high

status of Proliferative_capacity = high
has_biol_manifestation
status of S_phase_fraction = medium
;

domain-model : risk_model ; uses : breast_cancer ;
rules :

status of final_risk = high
caused_by_risk
status of risk = high

status of final_risk = low
caused_by_risk
status of risk = low
;

inference-knowledge


inference cover
    operation-type : backward ;
    input-roles : initial_complaint -> state ;
    output-roles : hypothesis -> state ;
       static-roles  :  potential_cause  ->  caused_by  in
causal_model;
    specification : «any» ;

inference cover_biol
    operation-type : backward ;
    input-roles : initial_complaint -> state ;
    output-roles : hypothesis -> state ;
   static-roles : biol_cause ->  has_biol_manifestation in
behavioral_model;
    specification : «any» ;

inference match
    operation-type : backward;
    input-roles : risk1 -> state ;
    output-roles : risk2 -> state ;
   static-roles : produce ->  caused_by_risk in risk_model;
    specification : «any» ;
```

```
relation has_biol_manifestation ;
    argument-1 : state ;
                 argument-role : cause ;
    argument-2 : biol_manifestation ;
                 argument-role : effect ;

relation caused_by_risk;
    argument-1 : state ;
                 argument-role : cause ;
    argument-2 : state ;
                 argument-role : effect ;

domain-model : causal_model ; uses : breast_cancer ;
--status of Size = little and--status of axillary_nodes =
negative and--status of ER = positive and--status of
Proliferative_capacity = low--cause--status of risk = low
rules :

status of risk = high
caused_by
status of Size = big

status of risk = high
caused_by
status of axillary_nodes = positive

status of risk = high
caused_by
status of ER = negative

status of risk = high
caused_by
status of Proliferative_capacity = high
;

domain-model : behavioral_model ; uses : breast_cancer ;
rules :

status of Proliferative_capacity = low
has_biol_manifestation
status of Ploidy = aneuploid

status of Proliferative_capacity = high
has_biol_manifestation
status of Ploidy = diploid

status of Proliferative_capacity = low
has_biol_manifestation
status of Thymidine_labeling_index = low

status of Proliferative_capacity = high
has_biol_manifestation
```

```
        status : {low, high} ;
                                          differentiation-of
state_variable(Primary_tumor_prognostic_factor) ;

concept Thymidine_labeling_index ;
    sub-type-of : Primary_tumor_prognostic_factor ;
    properties :
        status : {low, high} ;
                                          differentiation-of
observable_variable(Primary_tumor_prognostic_factor) ;

concept S_phase_fraction ;
    sub-type-of : Primary_tumor_prognostic_factor ;
    properties :
        status : {low, medium, high} ;
                                          differentiation-of
observable_variable(Primary_tumor_prognostic_factor) ;

concept Ploidy ;
    sub-type-of : Primary_tumor_prognostic_factor ;
    properties :
        status : {diploid, aneuploid} ;
                                          differentiation-of
observable_variable(Primary_tumor_prognostic_factor) ;

expression state ;
    description : «status of Size = big» ;
                  operand     :     state_variable     of
Primary_tumor_prognostic_factor ;

expression biol_manifestation ;
                operand    :    observable_variable    of
Primary_tumor_prognostic_factor ;

expression risk_factor ;
description : «status of risk = high» ;
operand : status of risk;

relation cause ;
    inverse : caused_by ;
    argument-1 : state ;
                 argument-role : cause ;
    argument-2 : state ;
                 argument-role : effect ;

relation caused_by ;
    inverse : cause ;
    argument-1 : state ;
                 argument-role : cause ;
    argument-2 : state ;
                 argument-role : effect ;
```

8 Appendix C: a simple CommonKADS model for breast cancer therapy

```
expertise-model BcPrognosis ;

domain-knowledge
ontology breast_cancer ;
definitions :
concept Primary_tumor_prognostic_factor ;
    properties :
        observable_variable : universal ;
        state_variable : universal ;

concept risk ;
    sub-type-of : Primary_tumor_prognostic_factor ;
    properties :
        status : {high, low} ;
                                        differentiation-of
state_variable(Primary_tumor_prognostic_factor) ;

concept final_risk ;
    sub-type-of : Primary_tumor_prognostic_factor ;
    properties :
        status : {high, low} ;
                                        differentiation-of
state_variable(Primary_tumor_prognostic_factor) ;
concept Size ;
    sub-type-of : Primary_tumor_prognostic_factor ;
    properties :
        status : {big, little} ;
                                        differentiation-of
state_variable(Primary_tumor_prognostic_factor) ;

concept axillary_nodes ;
    sub-type-of : Primary_tumor_prognostic_factor ;
    properties :
        status : {positive, negative} ;
                                        differentiation-of
state_variable(Primary_tumor_prognostic_factor) ;

concept ER ;
    sub-type-of : Primary_tumor_prognostic_factor ;
    properties :
        status : {positive, negative} ;
                                        differentiation-of
state_variable(Primary_tumor_prognostic_factor) ;

concept Proliferative_capacity ;
    sub-type-of : Primary_tumor_prognostic_factor ;
    properties :
```

```
    ARGUMENT2  :CONCEPT Size
    AXIOMS     :
    axiom 1    :IF Size(level) = [0-1]
               THEN Positive axillary nodes(level) = 20
    axiom 2    :IF Size(level) = [1-2.9]
               THEN Positive axillary nodes(level) = 39
    axiom 3    :IF Size(level) = [2.9-infinite]
               THEN Positive axillary nodes(level) = 69
END RELATION (Positive axillary nodes) depend from (Size)

 Relation
```

```
                [Size(level) = unknown]
   ND RELATION (Size) depend from (S-phase fraction)

   Relation

   *

  RELATION (Positive axillary nodes) depend from (Ploidy)
      SOURCES    :Cancer 68:(1469)
      ARGUMENT1  :CONCEPT Positive axillary nodes
      ARGUMENT2  :CONCEPT Ploidy
      AXIOMS     :
      axiom 1    :IF Ploidy(status)=diploid
                  THEN {with probability=0.64}
                  [Positive axillary nodes(status) = null]
                  OR {with probability=0.36}
               [Positive axillary nodes(status) = low/high]
      axiom 2    :IF Ploidy(status)=aneuploid
                  THEN {with probability=0.59}
               [Positive axillary nodes(status) = null]
                  OR {with probability=0.41}
             [Positive axillary nodes(status) = low/high]
  END RELATION (Positive axillary nodes) depend from (Ploi-
dy)

   Relation

   *

   RELATION (Positive axillary nodes) depend from (S-phase
fraction)
      SOURCES    :Cancer 68:(1469)
      ARGUMENT1  :CONCEPT Positive axillary nodes
      ARGUMENT2  :CONCEPT S-phase fraction
      AXIOMS     :
      axiom 1    :IF S-phase fraction(status)=low
                  THEN {with probability=0.65}
               [Positive axillary nodes(status) = null]
                  OR {with probability=0.35}
             [Positive axillary nodes(status) = low/high]
      axiom 2    :IF S-phase fraction(status)=high
                  THEN {with probability=0.58}
               [Positive axillary nodes(status) = null]
                  OR {with probability=0.42}
             [Positive axillary nodes(status) = low/high]
   END RELATION (Positive axillary nodes) depend from (S-
phase fraction)

   *
   RELATION (Positive axillary nodes) depend from (Size)
      SOURCES    :Neoplasie della mammella(622)
      ARGUMENT1  :CONCEPT Positive axillary nodes
```

```
RELATION (Size) depend from (Ploidy)
   SOURCES    :Cancer 68:(1469)
   ARGUMENT1  :CONCEPT Size
   ARGUMENT2  :CONCEPT Ploidy
   AXIOMS     :
   axiom 1    :IF Ploidy(status)=diploid
               THEN {with probability=0.34}
               [Size(level) = [0-2]
               OR {with probability=0.41}
               [Size(level) = [2-4]
               OR {with probability=0.24}
               [Size(level) = [4-infinite]
               OR {with probability=0.1}
               [Size(level) = unknown]
   axiom 2    :IF Ploidy(status)=aneuploid
               THEN {with probability=0.23}
               [Size(level) = [0-2]]
               OR {with probability=0.44}
               [Size(level) = [2-4]]
               OR {with probability=0.32}
               [Size(level) = [4-infinite]]
               OR {with probability=0.1}
               [Size(level) = unknown]
END RELATION (Size) depend from (Ploidy)

Relation

*

RELATION (Size) depend from (S-phase fraction)
   SOURCES    :Cancer 68:(1469)
   ARGUMENT1  :CONCEPT Size
   ARGUMENT2  :CONCEPT S-phase fraction
   AXIOMS     :
   axiom 1    :IF S-phase fraction(status)=low
               THEN {with probability=0.32}
               [Size(level) = [0-2]
               OR {with probability=0.44}
               [Size(level) = [2-4]
               OR {with probability=0.23}
               [Size(level) = [4-infinite]
               OR {with probability=0.1}
               [Size(level) = unknown]
   axiom 2    :IF S-phase fraction(status)=high
               THEN {with probability=0.25}
               [Size(level) = [0-2]
               OR {with probability=0.43}
               [Size(level) = [2-4]
               OR {with probability=0.32}
               [Size(level) = [4-infinite]
               OR {with probability=0}
```

```
   RELATION (Nuclear grade) depend from (Ploidy)
      SOURCES    :Cancer 68:(1469)
      ARGUMENT1  :CONCEPT Nuclear grade
      ARGUMENT2  :CONCEPT Ploidy
      AXIOMS     :
      axiom 1    :IF Ploidy(status)=diploid
                  THEN {with probability=0.27}
                  [Nuclear grade(status) = poor]
                  OR {with probability=0.72}
                  [Nuclear grade(status) = good]
                  OR {with probability=0.1}
                  [Nuclear grade(status) = unknown]
      axiom 2    :IF Ploidy(status)=aneuploid
                  THEN {with probability=0.44}
                  [Nuclear grade(status) = poor]
                  OR {with probability=0.55}
                  [Nuclear grade(status) = good]
                  OR {with probability=0.1}
                  [Nuclear grade(status) = unknown]
   END RELATION (Nuclear grade) depend from (Ploidy)

   Relation

   *

   RELATION (Nuclear grade) depend from (S-phase fraction)
      SOURCES    :Cancer 68:(1469)
      ARGUMENT1  :CONCEPT Nuclear grade
      ARGUMENT2  :CONCEPT S-phase fraction
      AXIOMS     :
      axiom 1    :IF S-phase fraction(status)=low
                  THEN {with probability=0.28}
                  [Nuclear grade(status) = poor]
                  OR {with probability=0.71}
                  [Nuclear grade(status) = good]
                  OR {with probability=0.1}
                  [Nuclear grade(status) = unknown]
      axiom 2    :IF S-phase fraction(status)=high
                  THEN {with probability=0.45}
                  [Nuclear grade(status) = poor]
                  OR {with probability=0.54}
                  [Nuclear grade(status) = good]
                  OR {with probability=0.1}
                  [Nuclear grade(status) = unknown]
   END RELATION  (Nuclear grade) depend from (S-phase frac-
tion)

   Relation

   *
```

```
                OR {with probability=0.44}
                [Grading(status) = 3]
END RELATION (Grading) depend from(ER)

Relation

*

RELATION (Age) depend from (Ploidy)
   SOURCES    :Cancer 68:(1469)
   ARGUMENT1  :CONCEPT Age
   ARGUMENT2  :CONCEPT Ploidy
   AXIOMS     :
   axiom 1    :IF Ploidy(status)=diploid
               THEN {with probability=0.3}
               [Age(level) = [0-49]]
               OR {with probability=0.7}
               [Age(level) = [50-150]]
   axiom 2    :IF Ploidy(status)=aneuploid
               THEN {with probability=0.33}
               [Age(level) = [0-49]]
               OR {with probability=0.67}
               [Age(level) = [50-150]]
END RELATION (Age) depend from (Ploidy)

Relation

*

RELATION (Age) depend from (S-phase fraction)
   SOURCES    :Cancer 68:(1469)
   ARGUMENT1  :CONCEPT Age
   ARGUMENT2  :CONCEPT S-phase fraction
   AXIOMS     :
   axiom 1    :IF S-phase fraction(status)=low
               THEN {with probability=0.31}
               [Age(level) = [0-49]]
               OR {with probability=0.69}
               [Age(level) = [50-150]]
   axiom 2    :IF S-phase fraction(status)=high
               THEN {with probability=0.33}
               [Age(level) = [0-49]]
               OR {with probability=0.67}
               [Age(level) = [50-150]]
END RELATION (Age) depend from (S-phase fraction)

Relation

*
```

```
   Relation

   *

    RELATION (Grading) depend from (Peritumoral lymphatic
vessel invasion)
      SOURCES    :Cancer 58:(2665)
      ARGUMENT1  :CONCEPT Grading
      ARGUMENT2  :CONCEPT Peritumoral lymphatic vessel in-
vasion
      AXIOMS     :
       axiom 1     :IF Peritumoral lymphatic vessel inva-
sion(status)=Positive
                   THEN {with probability=0.28}
                   [Grading(status) = 1]
                   OR {with probability=0.48}
                   [Grading(status) = 2]
                   OR {with probability=0.24}
                   [Grading(status) = 3]
       axiom 2     :IF Peritumoral lymphatic vessel inva-
sion(status)=negative
                   THEN {with probability=0.18}
                   [Grading(status) = 1]
                   OR {with probability=0.49}
                   [Grading(status) = 2]
                   OR {with probability=0.33}
                   [Grading(status) = 3]
   END RELATION (Grading) depend from (Peritumoral lymphat-
ic vessel invasion)

   Relation

   *

   RELATION (Grading) depend from(ER)
      SOURCES    :Cancer 58:(2665)
      ARGUMENT1  :CONCEPT Grading
      ARGUMENT2  :CONCEPT ER
      AXIOMS     :
      axiom 1    :IF ER(status)=Positive
                  THEN {with probability=0.29}
                  [Grading(status) = 1]
                  OR {with probability=0.52}
                  [Grading(status) = 2]
                  OR {with probability=0.19}
                  [Grading(status) = 3]
      axiom 2    :IF ER(status)=negative
                  THEN {with probability=0.12}
                  [Grading(status) = 1]
                  OR {with probability=0.44}
                  [Grading(status) = 2]
```

```
node)

   Relation

   *

   RELATION (Grading) depend from (Menopause)
      SOURCES    :Cancer 58:(2665)
      ARGUMENT1  :CONCEPT Grading
      ARGUMENT2  :CONCEPT Menopause
      AXIOMS     :
      axiom 1    :IF Menopause(status)=pre
                  THEN {with probability=0.21}
                  [Grading(status) = 1]
                  OR {with probability=0.48}
                  [Grading(status) = 2]
                  OR {with probability=0.31}
                  [Grading(status) = 3]
      axiom 2    :IF Menopause(status)=post
                  THEN {with probability=0.24}
                  [Grading(status) = 1]
                  OR {with probability=0.50}
                  [Grading(status) = 2]
                  OR {with probability=0.26}
                  [Grading(status) = 3]
   END RELATION (Grading) depend from (Menopause)

   Relation

   *

   RELATION (Grading) depend from (Size)
      SOURCES    :Cancer 58:(2665)
      ARGUMENT1  :CONCEPT Grading
      ARGUMENT2  :CONCEPT Size
      AXIOMS     :
      axiom 1    :IF Size(status)=T1
                  THEN {with probability=0.28}
                  [Grading(status) = 1]
                  OR {with probability=0.47}
                  [Grading(status) = 2]
                  OR {with probability=0.25}
                  [Grading(status) = 3]
      axiom 2    :IF Size(status)=T2-3
                  THEN {with probability=0.18}
                  [Grading(status) = 1]
                  OR {with probability=0.50}
                  [Grading(status) = 2]
                  OR {with probability=0.32}
                  [Grading(status) = 3]
   END RELATION (Grading) depend from (Size)
```

```
                [Size(status) = T0-1]
                OR {with probability=0.46}
                [Size(status) = T2]
                OR {with probability=0.22}
                [Size(status) = T3]
                OR {with probability=0.6}
                [Size(status) = T4]
   axiom 2     :IF Age(level)=[34-40]
                THEN {with probability=0.34}
                [Size(status) = T0-1]
                OR {with probability=0.44}
                [Size(status) = T2]
                OR {with probability=0.18}
                [Size(status) = T3]
                OR {with probability=0.4}
                [Size(status) = T4]
    axiom 3    :IF Age(level)=[40-150]
                THEN {with probability=0.31}
                [Size(status) = T0-1]
                OR {with probability=0.46}
                [Size(status) = T2]
                OR {with probability=0.17}
                [Size(status) = T3]
                OR {with probability=0.6}
                [Size(status) = T4]
END RELATION (Size) depend from (Age)

Relation

*

RELATION (Grading) depend from (Positive axillary node)
   SOURCES     :Cancer 58:(2665)
   ARGUMENT1   :CONCEPT Grading
   ARGUMENT2   :CONCEPT Positive axillary node
   AXIOMS      :
   axiom 1     :IF Positive axillary node(status)=low
                THEN {with probability=0.26}
                [Grading(status) = 1]
                OR {with probability=0.46}
                [Grading(status) = 2]
                OR {with probability=0.28}
                [Grading(status) = 3]
   axiom 2     :IF Positive axillary node(status)=high
                THEN {with probability=0.18}
                [Grading(status) = 1]
                OR {with probability=0.52}
                [Grading(status) = 2]
                OR {with probability=0.30}
                [Grading(status) = 3]
END RELATION (Grading) depend from (Positive axillary
```

```
*

RELATION (Positive axillary node) depend from (Age)
   SOURCES    :The Lancet 1990:335:(1566)
   ARGUMENT1  :CONCEPT Positive axillary node
   ARGUMENT2  :CONCEPT Age
      AXIOMS  :
      axiom 1 :IF Age(level)=[0-29]
               THEN {with probability=0}
               Positive axillary node(level) > 0
               OR {with probability=1}
               Positive axillary node(level) = 0
      axiom 2 :IF Age(level)=[30-39]
               THEN {with probability=0.12}
               Positive axillary node(level) > 0
               OR {with probability=0.87}
               Positive axillary node(level) = 0
      axiom 3 :IF Age(level)=[40-49]
               THEN {with probability=0.12}
               Positive axillary node(level) > 0
               OR {with probability=0.88}
               Positive axillary node(level) = 0
      axiom 4 :IF Age(level)=[50-59]
               THEN {with probability=0.7}
               Positive axillary node(level) > 0
               OR {with probability=0.93}
               Positive axillary node(level) = 0
      axiom 5 :IF Age(level)=[60-69]
               THEN {with probability=0.8}
               Positive axillary node(level) > 0
               OR {with probability=0.92}
               Positive axillary node(level) = 0
      axiom 6 :IF Age(level)=[70-150]
               THEN {with probability=0}
               Positive axillary node(level) > 0
               OR {with probability=1}
               Positive axillary node(level) = 0
END RELATION (Positive axillary node) depend from (Age)

Relation

*

RELATION (Size) depend from (Age)
   SOURCES    :The Lancet(1040)
   ARGUMENT1  :CONCEPT Size
   ARGUMENT2  :CONCEPT Age
   AXIOMS     :
   axiom 1    :IF Age(level)=[0-33]
               THEN {with probability=0.26}
```

```
                OR {with probability=0.56}
                [ER(level) not determined
      axiom 2 :IF  Age(level)=[34-40]
                THEN {with probability=0.30}
                [ER(level) > 250 fmol/mg
                OR {with probability=0.13}
                [ER(level) < 250 fmol/mg
                OR {with probability=0.57}
                [ER(level) not determined
      axiom 3 :IF  Age(level)=[40-150]
                THEN {with probability=0.31}
                [ER(level) > 250 fmol/mg
                OR {with probability=0.11}
                [ER(level) < 250 fmol/mg
                OR {with probability=0.58}
                [ER(level) not determined
END RELATION (ER) depend from (Age)

Relation

*

RELATION (PR) depend from (Age)
   SOURCES    :The Lancet 1993:341:1040
   ARGUMENT1  :CONCEPT PR
   ARGUMENT2  :CONCEPT Age
   AXIOMS     :
      axiom 1 :IF Age(level)=[0-33]
                THEN {with probability=0.41}
                [PR(level) > 250 fmol/mg
                OR {with probability=0.26}
                [PR(level) < 250 fmol/mg
                OR {with probability=0.33}
                [PR(level) not determined
      axiom 4 :IF Age(level)=[34-40]
                THEN {with probability=0.52}
                [PR(level) > 250 fmol/mg
                OR {with probability=0.20}
                [PR(level) < 250 fmol/mg
                OR {with probability=0.28}
                [PR(level) not determined
      axiom 7 :IF Age(level)=[40-150]
                THEN {with probability=0.51}
                [PR(level) > 250 fmol/mg
                OR {with probability=0.20}
                [PR(level) < 250 fmol/mg
                OR {with probability=0.29}
                [PR(level) not determined
END RELATION (PR) depend from (Age)

Relation
```

Some relations in the domain model

```
Relation

go to prognostic factor

   (Menopause) depend from (Age)
   (ER) depend from (Age)
   (PR) depend from (Age)
   (Positive axillary node) depend from (Age)
   (Size) depend from (Age)
   (Grading) depend from (Positive axillary node)
   (Grading) depend from (Menopause)
   (Grading) depend from (Size)
   (Grading) depend from (Peritumoral lymphatic vessel in-
vasion)
   (Grading) depend from(ER)
   (Age) depend from (Ploidy)
   (Age) depend from (S-phase fraction)
   (Nuclear grade) depend from (Ploidy)
   (Nuclear grade) depend from (S-phase fraction)
   (Size) depend from (Ploidy)
   (Size) depend from (S-phase fraction)
   (Positive axillary nodes) depend from (Ploidy)
  (Positive axillary nodes) depend from (S-phase fraction)
   (Positive axillary nodes) depend from (Size)

   *

   RELATION (Menopause) depend from (Age)
      ARGUMENT1  :CONCEPT Menopause
      ARGUMENT2  :CONCEPT Age
      AXIOMS     :IF Age(level)=[0-50]
                  THEN [menopause(status) = pre]
                  IF Age(level)=[50-150]
                  THEN [menopause(status) = post]
   END RELATION (Menopause) depend from (Age)

   Relation

   *

   RELATION (ER) depend from (Age)
      SOURCES    :(The Lancet 1993:341:1040)
      ARGUMENT1  :CONCEPT ER
      ARGUMENT2  :CONCEPT Age
      AXIOMS     :
         axiom 1 :IF Age(level)=[0-33]
                  THEN {with probability=0.28}
                  [ER(level) > 250 fmol/mg
                  OR {with probability=0.16}
                  [ER(level) < 250 fmol/mg
```

```
          (T*  and  N3  and  M0)
     IV:(T*  and  N*  and  M1)
END CONCEPT TNMstage

Concept
```

```
      status    :{normal,amplified}
END CONCEPT P53

Concept

*

CONCEPT Her2/neu
   DESCRIPTION: oncogene whose level is measured by
                immunoperoxidase procedure
   SYNONYMS: erbB-2; HER2/neu;
   SOURCES    :Cancer Research 52,1107-1113,1992
                Journal of Clinical Oncology 10(7):1044-
1048,1992
            Journal of Clinical Oncology 8(1):103-112,1990
   SUB TYPE OF:Oncogene expression
   PROPERTIES:
      status    :{positive ,negative}
      level     :{-,+,++}
   AXIOMS:
      positive:level = {++}
      negative:level = {-,+}
END CONCEPT Her2/neu

Concept

*

CONCEPT TNMstage
     DESCRIPTION:clinical classification of brast cancer
(1992)
                -T:primary Tumor size
                -N:lymph Node status
                -M:distant metastasis
   SOURCES    :G.Bonadonna, Breast neoplasia(622)
   SUB TYPE OF:Size AND Axillary nodes AND metastasis
   PROPERTIES:
      stages    :{0,I,IIA;IIB,IIIA,IIIB,IV}
   AXIOMS:
      0:(Tis and  N0  and  M0)
      I:(T1  and  NO  and  M0)
  IIA:(T0 and N1 and M0) or
    (T1 and N1 and M0) or
       (T2  and  N0  and  M0)
    IIB:(T2  and  N1  and  M0) or
       (T3  and  N0  and  M0)
   IIIA:(T0  and  N2  and  M0) or
       (T1  and  N2  and  M0) or
       (T2  and  N2  and  M0) or
       (T3  and  N1  and  M0) or
       (T3  and  N2  and  M0)
   IIIB:(T4  and  N*  and  M0) or
```

```
      status:{low,middle,high}
   AXIOMS:
      low   :(0-7)
      middle:(7-11.9)
      high  :(12-100)
END CONCEPT  S-phase fraction

Concept

*

CONCEPT Ploidy
   DESCRIPTION:prolification indicator
   SOURCES    :Cancer 68:1465-1475,1991
   SUB TYPE OF:proliferative capacity
   PROPERTIES:
      status    :{diploid,aneuploid}
END CONCEPT Ploidy

Concept

*

CONCEPT Oncogene expression
  DESCRIPTION:whatever agent which is able to cause cancer;
it is generally used for proteins whose presence is related
to cancer.
   SUB TYPE OF:biologic
END CONCEPT Oncogene expression

Concept

*

CONCEPT C-myc
   DESCRIPTION:oncogene
   SOURCES    :Cancer Research 52,1107-1113,1992
   SUB TYPE OF:oncogene expression
   PROPERTIES:
      status    :{normal,amplified}
END ONCEPT C-myc

Concept

*

CONCEPT P53
   DESCRIPTION:protein oncogene
    SOURCES     :Journal of Clinical Oncology 12(3):454-
466,1994
   SUB TYPE OF:Oncogene expression
   PROPERTIES:
```

```
                8(6):1025-1035,1990
   SUB TYPE OF:Hormonal receptor
   PROPERTIES:
      unit       :{fmol/mg}
      level      :NUMBER-RANGE(0-infinite)
      status      :{positive,negative}

   AXIOMS:
      positive:INTEGER-RANGE(0-9)
      negative:INTEGER-RANGE(10-infinite)
END CONCEPT PR

Concept

*

CONCEPT Proliferative capacity
   DESCRIPTION:proliferative activity gives information on
the reproduction speed of the tumoral cells.
      SOURCES       :The  New  England  Journal  of  Medi-
cine(322):1045-1053
   SUB TYPE OF:Biologic
   PROPERTIES:
      status    :{low,high}
END CONCEPT Proliferative capacity

Concept

*

CONCEPT Thymidine labeling index
   DESCRIPTION: proliferative index given by the thymidine
index
   SUB TYPE OF:Proliferative capacity
   PROPERTIES:
      status    :{low,high}
END CONCEPT Thymidine labeling index

Concept

*

CONCEPT  S-phase fraction
   DESCRIPTION: proliferative index given by
                the fraction of cells in phase S.
               (Flow cytometric measurements)
   SOURCES    :Cancer 68:1465-1475,1991
               The New England Journal of Medicine(322)
               :1045-1053
   SUB TYPE OF:Proliferative capacity
   PROPERTIES:
      unit:{%}
```

```
*

CONCEPT Biologic
   DESCRIPTION: biologic prognostic factors
   SUB TYPE OF:Histologic
END CONCEPT Biologic

Concept

*

CONCEPT Hormonal receptor
   DESCRIPTION:descriptors of hormonal substances
   TYPE OF:Biologic
END CONCEPT Hormonal receptor

Concept

*

CONCEPT ER
    DESCRIPTION:estrogen are hormonal substances which fa-
vour the female growth, whose level is related to the mor-
tality of breast cancer. A risk level (10 fmol/mg) has been
so defined.
   SOURCES    :Breast Cancer Research and Treatment
               7(3):147-160,1986
               Journal of Clinical Oncology
               8(6):1025-1035,1990
   SUB TYPE OF:Hormonal receptor
   PROPERTIES:
      unit       :{fmol/mg}
      level      :NUMBER-RANGE(0-infinite)
      status      :{positive,negative}
   AXIOMS:
      positive:INTEGER-RANGE(0-9)
      negative:INTEGER-RANGE(10-infinite)
END CONCEPT ER

Concept

*

CONCEPT PR
   DESCRIPTION:progesteron is an hormonal substance, whose
               level is related to the mortality of breast
              cancer. A risk level (10 fmol/mg) has been so
                defined.
   SOURCES    :Breast Cancer Research and Treatment
               7(3):147-160,1986
               journal of clinical oncology
```

```
   DESCRIPTION:
        Nearly quantitative evaluation of the grade of ma-
lignant of the tumor based in terms of histologic parame-
ters on a microscopic point of view. The following parame-
ters are evalueted:tubular formation, nuclear polymorphism
(irregularity in the dimension) and mitosi
      Specifically:
      Tubular formation:T
      1 score:well-defined
      2 score:medium
      3 score:low
      Polymorphism:P
      1 scorepunto:isomorph
      2 score:low in dimension, form and structure
      3 score:high
      Mitosi:M
      (peripheric exam in the sites of the tumor in which
       neoplastic tissue is present)
      1 score:occasional mitotic patterns
      2 score:two or three mitotic pattern observed
      3 score:high number of mitotic patterns
    SOURCES     :Cancer 65:2121-2128,1990;Cancer 58:2662-
2670,1986
   SUB TYPE OF:Morphologic
   PROPERTIES:
      T level:INTEGER RANGE(1-3)
      P level:INTEGER RANGE(1-3)
      M level:INTEGER RANGE(1-3)
      level  :INTEGER RANGE(3-9)
      status :{I,II,III}
   AXIOMS:
      level = T level+P level+M level
      I  :level=[3-5]
      II :level=[6-7]
      III:level=[8-9]
END CONCEPT Grading

Concept

*

CONCEPT Cellular
  DESCRIPTION:Semiquantitative evaluation of cytologic pa-
rameters
    SOURCES     :Cancer 65:2121-2128,1990;Cancer 58:2662-
2670,1986
   SUB TYPE OF:Primary tumor prognostic factor
   PROPERTIES:
      status:{poor,good,unknown}
END CONCEPT Cellular

Concept
```

```
   SUB TYPE OF:Morphologic
   PROPERTIES:
      status:{positive,negative};
      region: NOMINAL;
END CONCEPT Necrosis

Concept

*

CONCEPT Serial sectioning of ipsilateral axillary lymphn-
odes
   SOURCES    :Lancet(335);1565-1568,1990
   SUB TYPE OF:morphologic
   PROPERTIES:
      status:{positive,negative};
      lynph node: NOMINAL;
END CONCEPT Serial sectioning of ipsilateral axillary lym-
phnodes

Concept

*

CONCEPT Tumor microvessels density
    SOURCES     :Journal of Clinical Oncology 12(3):454-
466,1994
   SUB TYPE OF:morphologic
   PROPERTIES:
      status:{positive,negative};
END CONCEPT Tumor microvessels density

Concept

*

CONCEPT Peritumoral lymphatic vessel invasion
   DESCRIPTION:nearly the 30% of breast cancers have an in-
vasion of the peritumoral lymphatic vessels (external to
the tumor) in the form of tumor embol. The tumor embol are
groups of neoplastic cells come off from tumor mass.
   SOURCES    :G.Bonadonna, Breast neoplasia(622)
   SUB TYPE OF:morphologic
   PROPERTIES:
      status:{positive,negative}
END CONCEPT Peritumoral lymphatic vessel invasion

Concept

*

CONCEPT Grading
```

```
Concept

*

CONCEPT metastasis
   DESCRIPTION: reproduction of the tumor at distance, due
to the infiltration of cancer cells in the lymphantic or
circuation system.
   SOURCES    :Lancet(335);1565-1568,1990
   SUB TYPE OF:Anatomic stage
   PROPERTIES:
      status :{N0,N1,N2,N3,MX,M0,M1 }
   AXIOMS :
      N0  :no metastasis in regional lymph nodes
      N1  :metastasis in mobile homolateral axillary lymph
nodes
     N2  :metastasis in fix homolateral axillary lymph nodes
      N3  :metastasis in omolateral internal mammary lymph
nodes
      Mx  :distant metastasis not checked
      M0  :no distant metastasis
      M1  :distant metastasis.
END CONCEPT metastasis

Concept

*

CONCEPT Histologic
   DESCRIPTION: histologic (that is regarding the tissue)
prognostic factors
   SUB TYPE OF:primary tumor prognostic factor
END CONCEPT Histologic

Concept

CONCEPT Morphologic
    DESCRIPTION: morphologic (that is regarding the forme
and the structure) prognostic factors
   SUB TYPE OF:histologic
END CONCEPT Morphologic

Concept

*

CONCEPT Necrosis
   DESCRIPTION:necrosis is a complex of irreversible alter-
ations of cellular, tissue, organ structure which implies
their loss of living activity
    SOURCES     :journal of clinical oncology 11(10):1929-
1935, 1993
```

```
CONCEPT Anatomic stage
   DESCRIPTION:Prognostic factors from an anatomic point of
view. Anatomy studies the form and the structure of living
being both from a microscopic and from a macroscopic point
of view.
   SUB TYPE OF:Primary tumor prognostic factor
END CONCEPT Anatomic stage

Concept

*

CONCEPT Positive axillary nodes
   DESCRIPTION:it is the most powerful prognostic factor;
               it describes the presence of lymphnodes in
the axillary areas, which have been affected by the tumor,
and as a consequence, in the dimension. In the case a lymph
node is not affected, is classified as negative.
   SOURCES    :Lancet 335(8705):1565-1568,1990
   SUB TYPE OF:Anatomic stage
   PROPERTIES:
      level         :INTEGER-RANGE(0-infinite);
      status        :{null,low,high}
   AXIOMS:
      null  :NULL
      low   :INTEGER-RANGE(1-3)
      high  :INTEGER-RANGE(4-INFINITE)
END CONCEPT Positive axillary nodes

Concept

*

CONCEPT Size
   DESCRIPTION:dimension of the primary tumor, expressed in
cm.
   SUB TYPE OF:Anatomic stage
   PROPERTIES:
      unit          :{cm}
      level         :NUMBER-RANGE(0,infinite);
    status      :{T0,T1,T1a,T1b,T1c,T2,T3,unknown}
   AXIOMS:
         T0 :NULL
         T1 :INTEGER-RANGE(0-2)
         T1a:INTEGER-RANGE(0-0.5)
         T1b:INTEGER-RANGE(0.5-1)
         T1c:INTEGER-RANGE(1-2)
         T2:INTEGER-RANGE(2-5)
         T3:INTEGER-RANGE(5-infinite)
          T4:whatever dimension, but with direct extension
to the
            chest wall or to the skin.
END CONCEPT Size
```

The primary tumor prognostic factor domain

```
Concept

go to Prognostic factor

go to relation

   Primary tumor prognostic factor
      Anatomic stage
         Size
            TNMstage
         Positive axillary nodes
            TNMstage
         metastasis
            TNMstage
      Histologic
         Morphologic
            Grading
            Cellular
            Necrosis
            Serial sectioning of ipsilateral axillary lym-
phnodes
            Microvessels density
            Peritumoral lymphatic vessel invasion
         Biologic
            Hormonal receptor
               ER
               PR
            Proliferative capacity
               Thymidine labeling index
               S-phase fraction
               Ploidy
            Oncogene expression
               C-myc
               P53
               Her2/neu

*

CONCEPT Primary tumor prognostic factor
    DESCRIPTION:Prognostic factors related to the primary
tumor. Primary tumor generally refers to the cancer tissue
which has been surgically removed in the first surgical op-
eration.
   SUB TYPE OF:Breast cancer prognostic factor
END CONCEPT Primary tumor prognostic factor

Concept

*
```

```
CONCEPT  Brca-1
   DESCRIPTION:a gene whose mutation is related to the he-
           redity of breast cancer. A gene is a unit in a
           chromosome which controls heredity.
                (chromosome 17q21)
   SOURCES    :Science 266(5182):66-71,1994
   SUB TYPE OF:Tumor related prognostic factor
   PROPERTIES:
      status:{positive,negative}
   AXIOMS:
      positive : germ-line mutation=on
      negative : germ-line mutation=off
END CONCEPT Brca-1

Concept

*

CONCEPT Brca-2
   DESCRIPTION:a gene whose mutation is related to the he-
           redity of breast cancer. A gene is a unit in a
           chromosome which controls heredity.
                (chromosome 13q12-13)
   SOURCES    :Science 266(5182):66-71,1994
   SUB TYPE OF:Tumor related prognostic factor
   PROPERTIES:
      status:{positive,negative};
   AXIOMS:
      positive : germ-line mutation=on
      negative : germ-line mutation=off
END CONCEPT  Brca-2

Concept
```

```
END CONCEPT  Hormonal therapy

Concept

*

CONCEPT  Other therapy
   DESCRIPTION:
   SOURCES    :
   SUB TYPE OF:  Therapy prognostic factor
   PROPERTIES:
       status:{positive,negative};
END CONCEPT  Other therapy

Concept

*

CONCEPT Breast cancer prognostic factor
   DESCRIPTION:Prognostic factors which refers to the dis-
ease in itself.
   SUB TYPE OF:Prognostic factor
END CONCEPT Breast cancer prognostic factor

Concept

*

CONCEPT Tumor-related prognostic factor
  DESCRIPTION:Prognostic factors which are related to can-
cer itself but not to the cancer tissue.
   SUB TYPE OF:Breast cancer prognostic factor
END CONCEPT Tumor related prognostic factor

Concept

*

CONCEPT Recurrent tumor prognostic factor
  DESCRIPTION:Prognostic factors which are related to the
              recurrent tumor; generally the recurrence of
               a secondary tumor (not metastasis) does not
                affect survival in prognosis.
   SUB TYPE OF:Breast cancer prognostic factor
END CONCEPT Recurrent tumor prognostic factor

Concept

*
```

```
       SUB TYPE OF: Therapy prognostic factor
       PROPERTIES:
          status:{positive,negative};
          cycle: {1, 2 ... n};
          drug: NOMINAL;
          quantity: REAL mg;
          frequence: {1,2 ... n weeks};
          date: DATE;
          elapsed time: {1,2 .... n days};
END CONCEPT  Chemotherapy

Concept

*

CONCEPT  Radiotherapy
  DESCRIPTION: It is a therapy which focuses on the use of
             X-rays, in order to produce a biologic action
on the human tissue, which can be selective since the tissue
cells are characterised by a different radiosensitivity ac-
cording to their activity and their development stadium.
   SOURCES    :G.Bonadonna, Breast neoplasia
   SUB TYPE OF: therapy prognostic factor
   PROPERTIES:
        status:{positive,negative};
        cycle: {1, 2 ... n};
        drug: NOMINAL;
        power: REAL Gy;
        frequence: {1,2 ... n weeks};
        target: NOMINAL;
        date: DATE;
        elapsed time: {1,2 .... n days};
END CONCEPT  Radiotherapy

Concept

*

CONCEPT  Hormonal therapy
  DESCRIPTION: It is a therapy which focuses on the use of
            hormones; thias therapy was the only treatment
before chemotherapy and radiotherapy were available.
   SOURCES    :G.Bonadonna, Breast neoplasia
   SUB TYPE OF:  Therapy prognostic factor
   PROPERTIES:
        status:{positive,negative};
        cycle: {1, 2 ... n};
        drug: NOMINAL;
        dose: REAL;
        frequence: {1,2 ... n weeks};
        date: DATE;
        elapsed time: {1,2 .... n days};
```

```
      date: DATE;
END CONCEPT Blood transfusion

Concept

*

CONCEPT Relative with breast cancer
   DESCRIPTION:relatives of the patient who are/were
               breast cancer affected
  SOURCES   :G.Bonadonna, Breast neoplasia:649-651
   PROPERTIES:
      level:INTEGER-RANGE(0-infinite)
   SUB TYPE OF:External factor
END CONCEPT Relative with breast cancer

Concept

*

CONCEPT Therapy prognostic factor
   DESCRIPTION:the treatment which is given to the patient
is obviously one of the most important
               prognostic factor
   SOURCES    :G.Bonadonna, Breast neoplasia
   SUB TYPE OF: Prognostic factor
END CONCEPT Therapy prognostic factor

Concept

*

CONCEPT Surgical  operation
   DESCRIPTION:Surgical operation already undergone
               by the patient
   SOURCES    :G.Bonadonna, Breast neoplasia
   PROPERTIES:
      status:{positive,negative};
      recorrunces:{0,1,... n};
      technique: {mastectomy, lampectomy, quadrantectomy}
   SUB TYPE OF: Therapy prognostic factor
END CONCEPT Surgical  operation
Concept

*
CONCEPT  Chemotherapy
   DESCRIPTION: It is a therapy which focuses on the use of
chemical drugs to treat diseases, specifically cancers.
Chemotherapy is characterised by a chemotherapy index,
which is obtained by the maximum toleration dose and the
minimum curative dose ratio.
   SOURCES    :G.Bonadonna, Breast neoplasia
```

```
                        - more than 25 year-old.
                        - more than 30 year-old.
   SOURCES   :G.Bonadonna, Breast neoplasia:649-651
    SUB TYPE OF:Physic characteristic
    PROPERTIES:
       status:{Null,I,II};
END CONCEPT Pregnancy

Concept

*

CONCEPT Race
   DESCRIPTION:race of the patient
   SOURCES    :Journal of the National Cancer Institute
               81(24):1879-1886,1989
   SUB TYPE OF:Physic characteristic
   PROPERTIES:
      status:{black,white,oriental};
END CONCEPT Race

Concept

*

CONCEPT stress
   DESCRIPTION:process for which harmful stimula produce a
collection of reactive modifications of defence in the or-
ganism in order to annihilate them.This reponse is princi-
pally based on the action of the hormones produced in the
cortex part of the surkidney gland. If this action lasts
longtime, this may cause the «general syndrome of adapta-
tion».
   SUB TYPE OF:External factor
   PROPERTIES:
      status:{positive,negative};
END CONCEPT Stress

Concept

*


CONCEPT Blood transfusion
   DESCRIPTION:therapeutic process which consists of
               the introduction in the circulation system
               of a certain amount of blood which has
               been taken from another fellow.
   SOURCES    :Surgery 106(5):836-841,1989
   SUB TYPE OF:External factor
   PROPERTIES:
      status:{positive,negative};
```

```
      level:INTEGER-RANGE(0,150);
END CONCEPT Age

Concept

*

CONCEPT Menopause
   DESCRIPTION:time when a woman ceases to menstruate, usu
          ally around the age (45,50)
   SOURCES   :G.Bonadonna, Breast neoplasia:649-651
    SUB TYPE OF:Physic characteristic
    PROPERTIES:
       status:{positive, negative};
END CONCEPT Menopause

Concept

*

CONCEPT Overweight
   DESCRIPTION:the patients who weights too much
               may have a worst prognosis
   SOURCES   :Annals of Internal Medicine 120(1):18-25,1994
    SUB TYPE OF:Physic characteristic
    PROPERTIES:
       status:{positive,negative};
END CONCEPT Overweight

Concept

*

CONCEPT General health
    DESCRIPTION:general health assessed by a specialistic
          visit
   SUB TYPE OF:Physic characteristic
   PROPERTIES:
      status:{good,bad};
END CONCEPT General health

Concept

*



CONCEPT Pregnancy
   DESCRIPTION:pregnancy
               null:the patient has never had labour;
               first term pregnancy:
               two groups:
```

```
CONCEPT Prognostic factor
   DESCRIPTION:Factors which allow to predict
               the course of the disease
END CONCEPT Prognostic factor

Concept

*

CONCEPT Patient prognostic factor
   DESCRIPTION:Prognostic factors dealing with the
               host (patient) characteristics
   SUB TYPE OF:Prognostic factor
END CONCEPT Patient prognostic factor

Concept

*

CONCEPT External factor
   DESCRIPTION:Prognostic factors external to the host
   SUB TYPE OF:Patient prognostic factor
END CONCEPT External factor

Concept

*

CONCEPT Physic characteristic
   DESCRIPTION:Prognostic factors dealing with the
            physic characteristics of the host. In general,
               as a latest results, these characteristics
                are not very related with prognosis, but
                may be very related to the risk factors to
                become ill.
   SUB TYPE OF:Patient prognostic factor
END CONCEPT Physic characteristic

Concept

*

CONCEPT Age
   DESCRIPTION:the age of the patient is related to prog-
          nosis;specifically, prognosis in patients aged
          (0, 33) is usually worst; this is due to the
          greater frequence of positive axillary lymph
          nodes and high proliferative index cases.
   SOURCES    :Lancet 341(8852):1039-1043,1993
   SUB TYPE OF:Physic characteristic
   PROPERTIES:
```

7 Appendix B: the CommonKADS domain model for breast cancer prognosis

In this first part of our approach to the CommonKADS, we have obviously focused more on the domain knowledge. In this Appendix the last version of the domain knowledge is presented. In order to give a more structurated version of the domain model, an HTML version is available in http://www.inria.fr/acacia/personnel/rsacile/roberto.html.

The prognostic factor domain

```
*

Concept

go to relation

   prognostic factor
      Patient prognostic factor
         Physic characteristic
            Age
            Menopause
            General health
            Overweight
            Pregnancy
            Race
         External factor
            Stress
            Relative
            Blood transfusion
      Therapy prognostic factor
         Surgical operation
         Chemotherapy
         Radiotherapy
         Hormonal therapy
         Other therapy
      Breast cancer prognostic factor
         Tumor-related prognostic factor
            Brca-1
            Brca-2
         Primary tumor prognostic factor
         Recurrent tumor prognostic factor

*
```

- biochemical test for liver function before starting adjuvant chemotherapy and after the third cycle.

At completion of adjuvant chemotherapy

- repeat biochemical tests if adjuvant chemotherapy is delivered for more than 3 cycles
- gynecological work-up with pelvic u.s. before starting tamoxifen.

Two months after completion of adjuvant chemotherapy + breast irradiation

- physical examination
- chest X-ray
- mammography (bilateral if conserving surgery)
- cardiac work-up (examination plus ECG)
- biochemical test if not performed at completion of adjuvant chemotherapy.

During the first five years from surgery (in the absence of suspicious findings)

- bone scan after 6 months from completion of adjuvant chemotherapy
- every 6 months
- physical examination
- CBC with differential and platelets
- biochemical tests
- chest X-ray

-every 12 months

- bone scan
- mammography (bilateral, if conserving surgery)
- ECG
- gynecologic examination plus pelvic ultrasounds (up to the first two years from completion of tamoxifen)

In all patients subjected to adjuvant CMF, Tamoxifen will be delivered at the dose of 20mg/day for 5 consecutive years, starting at the end of CMF.

In all patients subjected to conservative surgery followed by postoperative CMF, breast irradiation (max 60 Gy) will be delivered at the end of chemotherapy, either concomitantly or before tamoxifen.

ADJUVANT CHEMOTHERAPY IN OPERABLE BREAST CANCER IN WOMEN NOT SUBJECTED TO PRIMARY CHEMOTHERAPY

At surgery: FULL AXILLARY DISSECTION, TUMOR GRADE, CELL PROLIFERATIVE ACTIVITY, ESTROGEN RECEPTORS

Within 14 days after surgery

- if N- and POSITIVE ER and LOW PROLIFERATIVE ACTIVITY andDIFFERENTIATED TUMOR (variables measured at diagnosis and at major surgery)
  NO SYSTEMIC THERAPY
  BREAST IRRADIATION (max 60 Gy) AFTER CONSERVATIVE SURGERY
- if N- and NEGATIVE ER or HIGH PROLIFERATIVE ACTIVITY or UNDIFFERENTIATED TUMOR (variables measured at diagnosis and atmajor surgery)
  ADJUVANT CMF (C 600 mg/m2 , M 40 mg/m2 i, F 600 mg/m2 , days 1 and 8, iv q. 4 weeks) for 3 or 6 cycles

- if N+ 1 to 3, regardless of other variables
  ADJUVANT CMF as above
- if N+ > 3, regardless of other variables
  ADJUVANT CMF (same dose and schedule) for 6 cycles.

FOLLOW-UP STUDIES

During adjuvant chemotherapy administration:

- complete blood counts with differential and platelets before each iv administration
- physical examination before starting any new cycle

FINE NEEDLE ASPIRATION (cell diagnosis, ER-ICA, PgR-ICA, Ki-67, nuclear grade)

Within 7 days from mammography:

- Day1Epirubicin 120 mg/m2 iv
- Day22Epirubicin 120 mg/m2 iv
- Day43Epirubicin 120 mg/m2 iv
- Day63Repeat mammography, breast u.s., chest x-ray
- Day64SURGERY

- if at operating room T ≤ 2.5 - 3 cm, no scattered foci outside quadrant area: CONSERVATIVE SURGERY
- if at operating room AT > 3 cm, or scattered foci outside quadrant area: MASTECTOMY

For both technical procedures: FULL AXILLARY DISSECTION, TUMOR GRADE, CELL PROLIFERATIVE ACTIVITY, ESTROGEN RECEPTORS

Within 14 days after surgery

- if N- and POSITIVE ER and LOW PROLIFERATIVE ACTIVITY and DIFFERENTIATED TUMOR (variables measured at diagnosis and at major surgery)
  NO SYSTEMIC THERAPY
  BREAST IRRADIATION (max 60 Gy) AFTER CONSERVATIVE SURGERY
- if N- and NEGATIVE ER or HIGH PROLIFERATIVE ACTIVITY or UNDIFFERENTIATED TUMOR (variables measured at diagnosis and at major surgery)
  ADJUVANT CMF (C 600 mg/m2 , M 40 mg/m2 i, F 600 mg/m2 , days 1 and 8, iv q. 4 weeks) for 3 or 6 cycles
- if N+ 1 to 3, regardless of other variables
  ADJUVANT CMF as above
- if N+ > 3, regardless of other variables
  ADJUVANT CMF (same dose and schedule) for 6 cycles

If axillary nodes are histologically negative (or if surgery has not been performed) consider other variables determined either at diagnosis or at surgery:

- if NEGATIVE ESTROGEN RECEPTOR or HIGH PROLIFERATIVE ACTIVITY or UNDIFFERENTIATED TUMOR
  adjuvant chemotherapy should be delivered. A non-cross resistant adjuvant regimen is highly advisable (e.g. CMF days 1 and 8 q. 4 weeks for 3 or 6 cycles);

- if POSITIVE ESTROGEN RECEPTOR and LOW PROLIFERATIVE ACTIVITY and DIFFERENTIATED TUMOR
  no adjuvant systemic therapy should be delivered.

In patients subjected to adjuvant chemotherapy, tamoxifen can be delivered at the dose of 20 mg/day for 5 consecutive years, starting at the end of adjuvant chemotherapy.

In all patients subjected to conservative surgery, breast irradiation (max 60 Gy) will be delivered. When adjuvant chemotherapy is planned, breast irraA conceptual information retrieval system for the production
of guidelines on prognostic factors of breast cancerA conceptual information retrieval system for the production
of guidelines on prognostic factors of breast cancerA conceptual information retrieval system for the production
of guidelines on prognostic factors of breast cancerdiation should be started at the end of chemotherapy to avoid dose-intensity reductions.

PRIMARY CHEMOTHERAPY IN OPERABLE BREAST CANCER

OPERATIONAL FLOW

At palpation: T>2.5 cm, N0-2, M0

1) MAMMOGRAPHY

if T ≤ 2.5 cm --> conservative approach

if T> 2.5 cm

2) BREAST U.S.

TATTOO OF BREAST LESION

- PERFORM FINE NEEDLE ASPIRATION with sufficient material to allow determination of

    - cell diagnosis (malignant cells must be documented prior to start chemotherapy)

    - nuclear grade, estrogen and progesterone receptors with immunocytochemistry, cell proliferation activity (primary chemotherapy can achieve pathologic complete remission of the tumor and knowing about these variables can allow to assess whether patients need postoperative systemic treatment).

b. Within 7 days from diagnosis: start primary chemotherapy (e.g. epirubicin 120 mg/m2 iv q.3 weeks for 3 cycles)

c. Within 3 weeks from the end of primary chemotherapy: repeat mammography and breast ultrasounds and compare imagins with those performed at diagnosis.

- if primary tumor measures <2.5 cm and no scattered foci at distance, consider conservative approach (e.g. quadrantectomy or lumpectomy with full axillary dissection)

- if primary tumor measures >3cm or scattered foci at distance are present, consider modified radical mastectomy with full axillary dissection

SURGERY (conservative or radical) must be performed within 3 weeks from the last dose of primary chemotherapy.

At surgery, if residual tumor is present in adequate quantity, tumor grade, cell proliferative activity and steroid receptors must be determined.

Within 14 days from surgery, postoperative systemic treatment, if needed, should be started.

In the presence of positive axillary nodes, postoperative chemotherapy should be delivered regardless of other prognostic variables and degree of primary tumor reduction. A non-cross resistant adjuvant regimen is highly advisable (e.g. CMF i.v. days 1 and 8 q. 4 weeks for 6 cycles).

6 Appendix A: skeleton of a guideline commonly used for breast cancer treatment in Italy

The following documents are in relation to the operational procedures in two "protocols" for breast cancer treatment, one for primary chemotherapy and the second for adjuvant chemotherapy.

The following is copy as written by oncologists.

MULTIDISCIPLINARY TREATMENT IN OPERABLE BREAST CANCER

a. At mammography:

- if, regardless of primary tumor diameters, scattered foci are present outside a quadrant; consider conventional surgical approach (e.g. modified radical mastectomy with full axillary dissection);

- if maximum tumor diameter is < 2.5 cm and no scattered foci at distance: consider conservative approach (e.g. quadrantectomy or lumpectomy with full axillary dissection + breast irradiation);

- if maximum tumor diameter is > 2.5 cm and no scattered foci at distance; consider primary chemotherapy to facilitate conservative approach and reduce the risk of local recurrence.

PRIMARY CHEMOTHERAPY IN OPERABLE BREAST CANCER

a. Following mammography and breast ultrasound:

- TATTOO OF BREAST LESION (primary chemotherapy can reduce the size of the primary and thus will facilitate surgeons to consider initial shape of the primary)

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10. Tu, S.W., Kahn, M.G., Musen, M.A., Ferguson, J.C., Shortliffe, E.H. and Fagan, L.M. (1989) Episodic skeletal-plan refinement based on temporal data. Communication of the ACM, 32, 12, 1439-1455.
11. Gaglio, S., Ruggiero, C., Spinelli, G., Bonadonna, G., Valagussa, P. and Nicolini, C. (1986) BREASTCAN: an expert system for postoperative breast cancer thera-

ified, as well its reliability (in this case also the term “axiom” should be revised); the introduction of some kind of function should be allowed to avoid long lists of similar axioms, like in TNM_stage. The task knowledge does not provide any representation to decompose tasks in sub-tasks which are not sequential; such as, for example, in the prognostic task, it is not easy to represent the assessment deriving from literature consultation, even if this updating is intrinsic to a possible model of a human expert in oncology.

In conclusion, although the work presented here may be interpreted just as an exercise of CommonKADS application in the medical domain, the conceptual model we have obtained seems to reflect well the new trends of breast cancer prognosis; besides, we are still far from a design model of the prognostic system, and from verifying the gap between conceptual and design model which has been addressed in [19] as one of the worse features of KADS-I methodology. From this experience, we can conclude that CommonKADS has been a good support for conceptualisation, although its standardisation process has not finished yet, and a standard, leading tool is needed to support it.

The guideline (GL) database is the real core of the system; specifically its formalism as well as its level of abstraction has to be defined in order to comply a trade-off between natural language and computer language structure. The need of a representation which is not distant from the natural language is due to the very fact that a guideline should always have a correspondant in natural language (a sort of guideline "book"). Besides, it is feasible that in the next few years multimedia and/or networking techniques will be used to describe guidelines; in this case, although guidelines are still expressed in natural language, a greater effort in structuring the GL contents will be performed. Finally, guidelines might become object of the inferring of knowledge based systems (KBS) as well as of other applications, so in this case GLs should be expressed in a language which is highly structured in order to infer on it and to allow a fast access to a specific content; moreover a highly structured language will be necessary to automatate the guideline building process. CML may be a good candidate for this representation.

4.2 Conclusions

Our conclusion is that CommonKADS was a satisfactory methodology to conceptualise prognosis, since it guided us to approach the problem in a structured way; first, we decomposed the prognostic task into subtasks which were already defined in the CommonKADS library; subsequently, we defined the domain knowledge involved, following CML; then we defined the inference layer following the library, and finally we defined the task knowledge. Following this conceptualisation, we have found a significant help; specifically, exploding the prognostic process has allowed us to find a problem definition which fits well the needs of a modern definition of prognosis, and which can reuse the models already developed in the library; the domain knowledge and its CML definition allows a good definition of a glossary of the terminology used and it is also a good way to approach knowledge acquisition both from literature and from human experts; in the latter case, CML has been found an easy language to have a dialogue with experts, who could directly evaluate the evolution of the work. The inference knowledge and the task knowledge have given us a trace of models that can be reusable for our aim.

On the other hand, CommonKADS is not a cookbook for building expert systems [19], yet. The research in the CommonKADS library of generic models is not easy, since some models have not been developed to a great extent (i.e. the qualitative model); in some cases (i.e. prediction model) the reader has to refer to the work done in previous releases (KADS-I) thus facing in changes of terms and approaches. Besides, the CML is commonly used in a grammar that is more practical in some aspects than the one we have referred to; in our opinion, further work is needed also in CML; for example, concept and relation axioms are a central issue in modelling a domain when starting from a knowledge acquisition process and their role should be stressed and deeply formalised; for example, the source of an axiom should be spec-

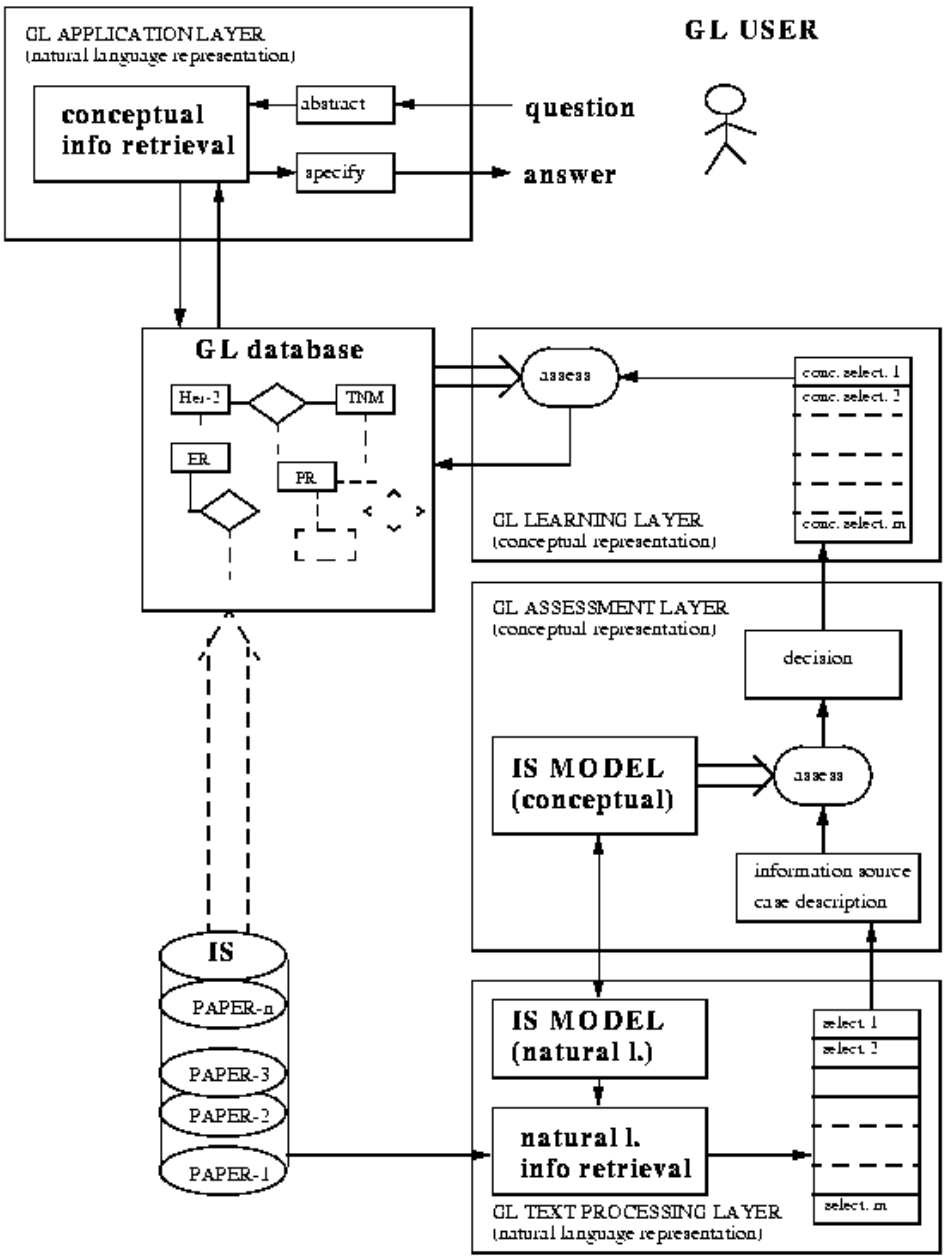


Figure 11 : A guideline system architecture.

In this respect, the results of the knowledge acquisition process may be viewed as a guidelines (GL) database which can be used to produce guidelines as well as to be accessed by computers applications (see fig.10).

With respect to GL productions, a system which guides the conceptualisation of the knowledge contained in a paper should represent a valid help in the production of a guideline. In a future development of this work, the definition of a conceptual information retrieval system for the production of guidelines on prognostic factors of breast cancer should be also addressed.

There are several medical models that have been implemented which address different aspects of this domain, such as, for example, ICD9 (International Classification of Diseases with Clinical Modifications), GMN (Gabrieli Medical Nomenclature) and GALEN (Generalized Architecture for Languages, Encyclopaedias and Nomenclatures in Medicine).

A possible architecture of the global system we propose is shown in fig.11. We propose a four-layered architecture. The text processing layer processes the information source (IS) database in order to select the papers which contain the topics addressed by the guideline. This can be performed by a traditional information retrieval (IR) system which can select from IS the papers which address a specific topic (modelled in an IS model, in the form of boolean expressions of keywords). The service given to the upper layer is a queue of papers which satisfy the information needs of the addressed GL modelled in the IS model.

The assessment layer performs the conceptualisation of the papers selected at the text processing layer. Each selected paper is abstracted and compared with an IS conceptual model, which defines the syntax, the relations and the constraints of the concepts which should be contained in the current selected paper in an abstract formalism. The services provided to the upper layer is the result of this comparison, which is assessed in a decision which contains the abstracted structure of the selected paper as well as parameters indicating its compliance with quality criteria.

The learning layer stores the decisions given from the assessment layer. The service of this layer is to update the guideline. An assessment task compares the GL database with each element of the queue; the result of the assessment may be either an updating of the GL database with the results presented in the paper or a decision of not taking into account those results.

4 Future developments and conclusions

4.1 A conceptual information retrieval system for the production of guidelines on prognostic factors of breast cancer

The first steps of a guideline production are the reading of the literature on a specific topic, the conceptualisation and the understanding of it, and the assessment whether the concepts contained in it are proper to be added or to modify the guidelines which concern this topic (such as, for example, according to criteria about the quality of the research). The key point of this process is the knowledge conceptualisation and the result understanding.

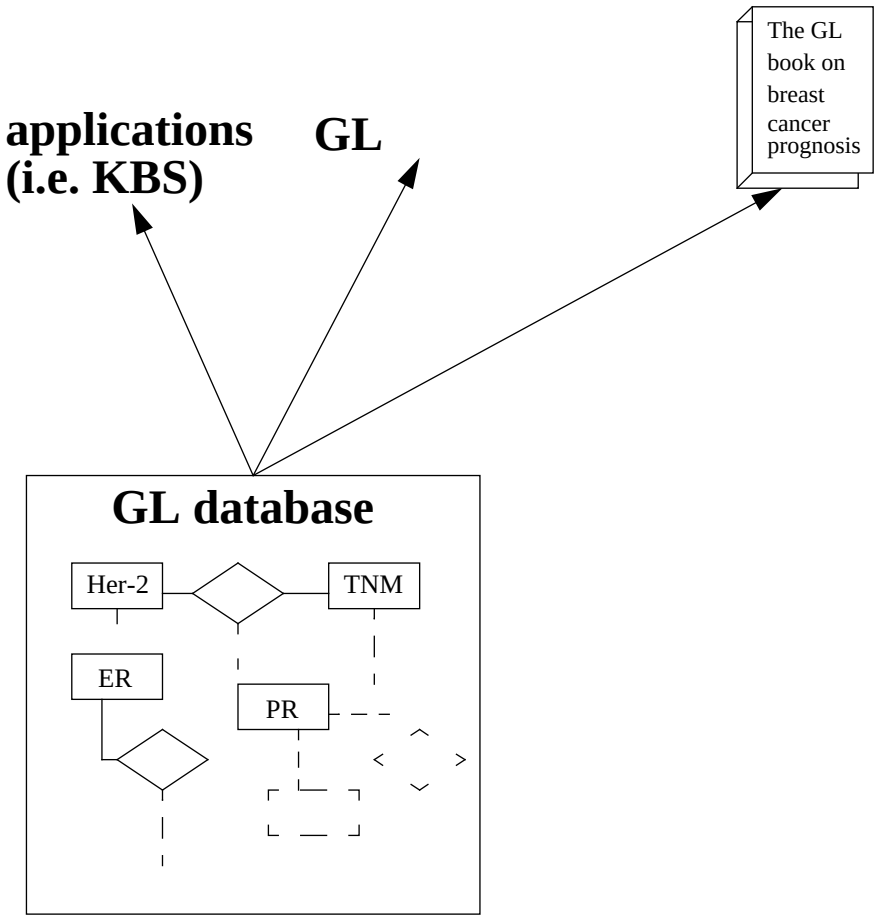


Figure 10 : A guideline database containing the conceptual structure of the breast cancer prognosis (and therapy) domain should have different applications, such as, for ex. the production of guidelines, the consultation by KBS, the management of guidelines for updating...

3.4 A simplified model for breast cancer treatment in CML

One of the main problems of actual release of CommonKADS methodology is that it lacks of a standard, leading tool which can guide the user in the application of the whole methodology. Other methodology, such as Protege from Stanford University, do not have this problem since the methodology has followed the evolution of a related software tool.

For CommonKADS, the KADS_tool is one of the best known tools to use CommonKADS, but it presents many features from KADS-I which has been overcome in CommonKADS.

It is the author's opinion that a CommonKADS-dedicated tool should be strictly adherent to the CommonKADS standard and, first of all, to CML, the conceptual modelling language which has been reccomended to CommonKADS.

The KACTUS toolkit, by the University of Amsterdam and Cap Programator (Stockholm), supports CML. KACTUS is an interactive environment for browsing, editing and managing (libraries of) ontologies. The toolkit is currently under development. One of the aims of KACTUS is to support reuse of ontologies, in other to support this, the toolkit can handle various ontology formalisms (CML, EXPRESS and Ontolingua) and can perform (partial) translations between these formalisms.

Specifically, in the group ACACIA, a CML-supporting tool, COKACE (CommonKADS Centaur) is under development. This tool has been developed with the CENTAUR environment, also developed at INRIA. COKACE, allows to develop a CML model according to the CML standard definition, to check its consistency and to interpret it. Since a first version of the tool has been available in these last few days, and anyway it is always better to test tools on easier examples, a simplified example of the breast cancer prognostic problem has been developed. In this example, some factors have been regarded as a biological manifestation; this biological manifestation can produce risk factors. The combination of risk factors produced as well as risk factors given as user input, can produce a risk as a result, which may assume the high value and the low value. In section 8 page 72 (Appendix C), this model has been reported.

Obviously, the advantage of using a tool is that it constrains the knowledge engineer to a more realistic version of its conceptual model. Besides, the risk of a tool very related to a language is to become nothing but a shell for software production. It is the author's opinion, that to overcome this risk, the next step to be performed in the COKACE tool, is to give the user a collection of reusable models (specifically, inference and task knowledge) to be «cut & pasted» in the user application.

TASK bc_prognosis

TASK-DEFINITION

GOAL: to predict the evolution of breast cancer (bc) disease at least in terms of survival and disease-free time

INPUT:

prognostic factors: the set of prognostic factors about bc in a patient model description: set of parameter/value pairs to define a partial bc description

therapy: previous, actual and proposed therapy for that bc

OUTPUT:

evolution of the disease: survival time, disease free, recurrences ....

messages: needs of other prognostic factors, needs of controlling unprobable values...

TASK-BODY

TYPE: composite

sub-taskS: bc_assess, bc_update, bc_predict

ADDITIONAL-ROLES:

decision: a set of data, referring to the input prognostic factor,for ex., the value of the prognostic factor, if the procedures to determine it were fitted to guidelines, whether considering or not this prognostic factor...

model of prognostic factors: abstracted guideline on prognostic factors

model description: description of bc on which evolution should be predicted

CONTROL-STRUCTURE:

bc_prognosis (prognostic factors + model description + therapy → evolution + messages) =

REPEAT
; assess the value and reliability of a specified prognostic factor
bc_assess (prognostic factor + model of prognostic factors → decision);
UNTIL there are any input specification for prognostic factors
; update the model description, both from input description and from decisions
bc_update (model description + decision → model description)
; predict the evolution of bc, thus predicting also evolution and giving control messages
bc_predict (model description → model description + evolution + messages);

END TASK bc_prognosis

Figure 9 : The task knowledge of the prognostic system.

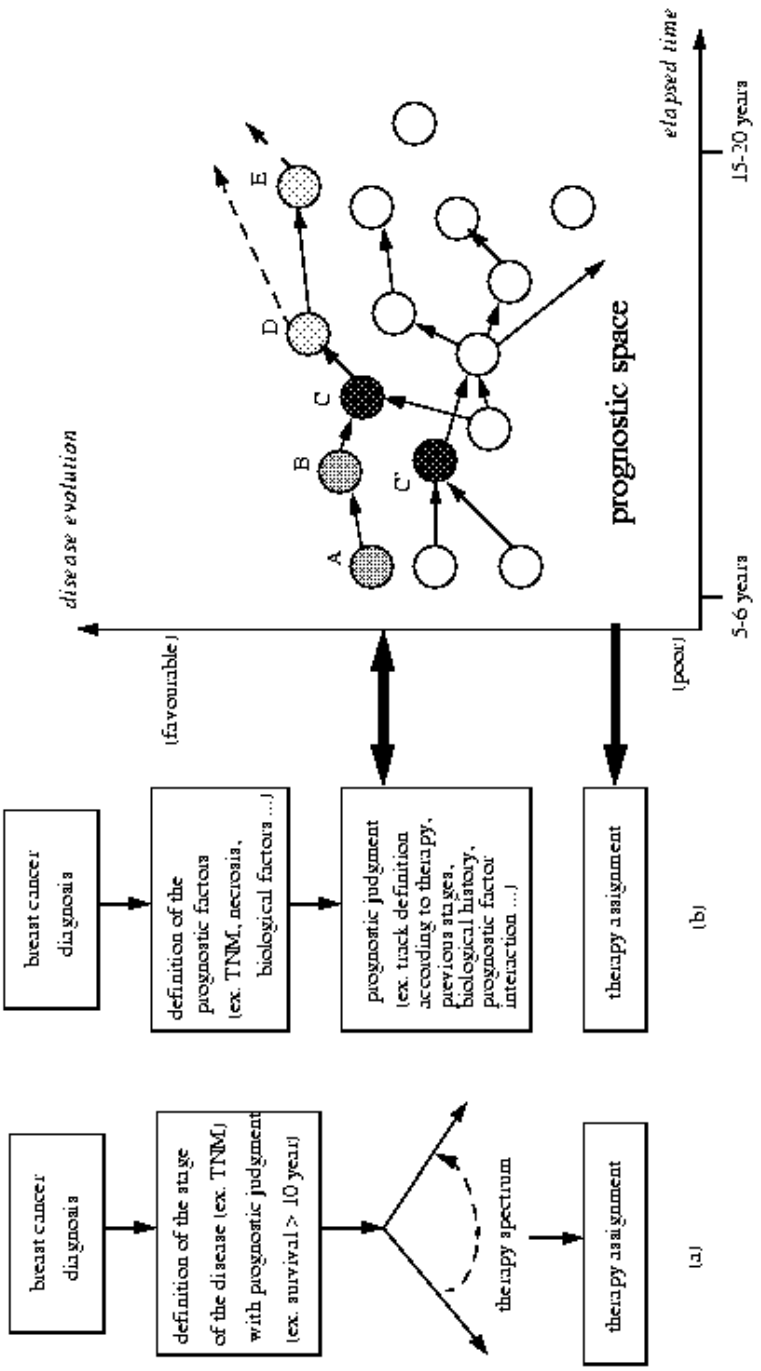

breast cancer diagnosis
definition of the stage of the disease (ex. TNM) with prognostic judgment (ex. survival > 10 year)
therapy spectrum
therapy assignment
(a)
breast cancer diagnosis
definition of the prognostic factors (ex. TNM, necrosis, biological factors ...)
prognostic judgment (ex. track definition according to therapy, previous stages, biological history, prognostic factor interaction ...)
therapy assignment
(b)
disease evolution
(favourable)
(poor)
A
B
C
C'
D
E
prognostic space
elapsed time
5-6 years
15-20 years

FIGURE 8

Starting from this, past states (A, B) and future states (D, E) should be predicted, thus defining the track (A, B, C, D, E). The choice of the proper therapy will come from this track definition.

In this case, the addition of information from literature to the system should not need a reinterpretation of the qualitative model or of the assessment model, but an upgrade of the primitive inferences.

3.3.5. The task knowledge

Oncology is perhaps one of the more knowledge structurated domain of medicine, in which task as diagnosis, assessment, scheduling are continuously studied and applied.

Specifically, the primitive task knowledge involved in prognosis are assessment and prediction (as defined by fig2d); fig.9 shows the root task knowledge of the prognostic task, which can be decomposed in an assessment, a prediction and an updating task. As refers to assessment and prediction task, their refinement reflects the correspondent CommonKADS library of generic models, while the updating task is just a combination of “specify” inferences on the system model.

Besides, when dealing with task knowledge, we should focus on two separate modules: an assessment task for the updating of the prognostic system from literature and the prognostic system itself composed by assessment and prediction. The connection between these two modules is not really straightforward; in the sense that updating may depend on prognosis, but it can also “run” independently, that is when some “stimulus” is present. Some techniques currently not provided by CommonKADS should be needed to solve the problem; fig.9 does not take into account the updating from literature.

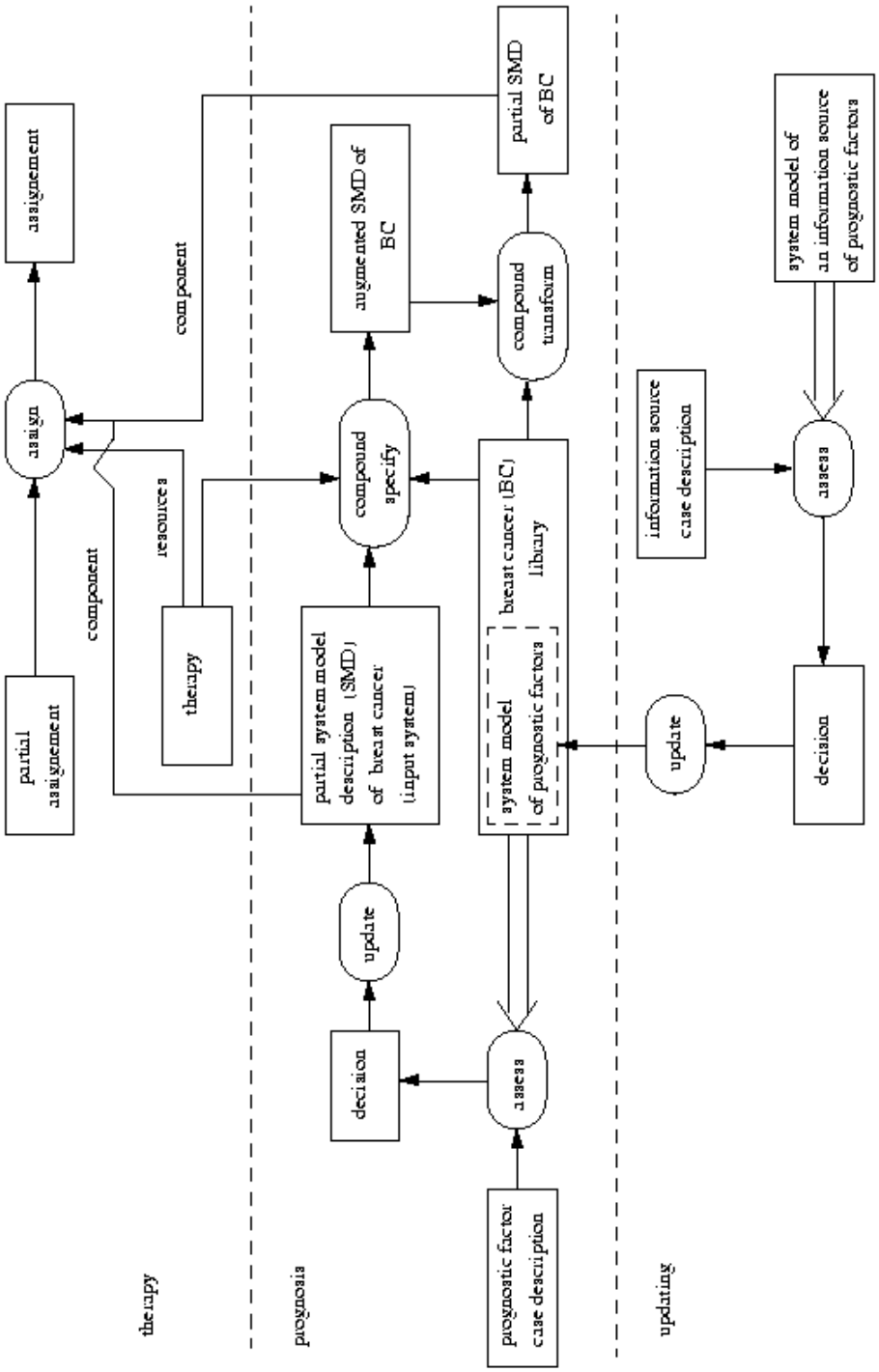

therapy
prognosis
updating
partial assignement
assignement
assign
component
component
resources
therapy
partial system model description (SMD) of breast cancer (input system)
compound specify
augmented SMD of BC
compound transform
partial SMD of BC
breast cancer (BC) library
system model of prognostic factors
update
decision
assess
prognostic factor case description
update
decision
assess
information source case description
system model of an information source of prognostic factors

FIGURE 7

In theory, the addition to the system of information from literature should not need a reinterpretation of the domain, if a good work of abstraction has been done in considering all the possible classes of prognostic factors and the possible influences on the behaviour of the tasks. As an easy example, if the HER2 prognostic factor were not included in the model, its super-concept "oncogene" must be present, thus allowing a new instantiation of it, as well as of the referring axioms. In the case a prognostic factor is already present, but a different (or in agreement) interpretation is given from literature, the system should "properly" update the axioms and the relations involved. In section 7 page 43 (Appendix B), the skeleton of the domain knowledge of breast cancer prognosis is shown. This information can be easily read by consulting http://www.inria.fr/acacia/personnel/rsacile/roberto.html.

3.3.4. The inference knowledge

The inference structure (fig.7) reflects the prediction inference knowledge by [21], the assessment inference knowledge by [16, chap.7]; and the preliminary definition of the assignment inference knowledge by [16, chap.11]. Besides, following the CommonKADS library of generic models, we should have a guide to describe our conceptual model in more detail.

Prognosis is in the middle layer of fig.7, that is an assessment task on prognostic factors of the patient and a prediction task of breast cancer behaviour; the assessment on prognostic factors extracted from literature is in the lower layer, while therapy is in the upper layer. The system model of prognostic factor is a static role when referred by prognosis, but it can be updated by the assessment on information source. The prediction is strongly related to the development of a qualitative model of breast cancer, since the relations and the parameters in this domain are "naturally" qualitative rather than quantitative; this model is currently being in phase of development, following [21, 22] and some specific previous work [23, 24]. The transition between one state and another of the qualitative model is determined both by the biological features of the tumour and by the values of prognostic factors, including therapy. The qualitative model should predict the future state (and the therapy will be the variable that should optimise prognosis) as well as the past states (identified also by other previous information, such as for example, the clinical card of the patient). The identification of the past states will be used for a better identification of the track corresponding to the tumour evolution (fig.8), and, as a consequence, to an improved definition of the current stage. A qualitative model of breast cancer should cover the prognostic space with states and transitions. Nowadays, prognosis is not only the result of an assessed stage of the disease, but it may be regarded as the research in the prognostic space (defined as "disease evolution x elapsed times" from the cancer birth) of the evolution track related to the current patient. As a first step, prognosis should consist of assessing breast cancer stage and prognostic factors; this should define probable milestones of the track (fig.8b, C, C').

CONCEPT *TNM_stage*

DESCRIPTION: "This staging system provides a strategy for grouping patients with respect to prognosis. Therapeutic decisions are formulated in part according to staging categories but primarily according to lymph node status, ER and PR receptor levels in the tumour tissue, menopausal status, and the general health of the patient. TNM stages are defined by primary tumour (T), regional lymph nodes (N) and pathologic classification (pN), distant metastasis (M)."

SOURCES: 1. Breast. In: American Joint Committee on Cancer: Manual for Staging of Cancer. Philadelphia: JB Lippincott Company, 4th ed., 1992, pp 149-154.

SUB-TYPE-OF: size, axillary nodes, metastasis

PROPERTIES:

stage
VALUE-SET stages;
TYPE: NOMINAL;
VALUE-LIST:=, I, IIA, IIB, IIIA, IIIB, IV;
VALUE-SPEC:text;
END VALUE-SET stages

AXIOMS:

∀ T:size N:axillary_node M:metastasis TNM:TNM_stage

has_status(T, Tis) ∧ has_status(N, N0) ∧ has_status(M, M0)
→ has_status (TNM, 0);
has_status(T, T1) ∧ has_status(N, N0) ∧ has_status(M, M0)
→ has_status(TNM, I);
(has_status(T, T0) ∧ has_status(N, N1) ∧ has_status(M, M0)) ∨
(has_status(T, T1) ∧ has_status(N, N1) ∧has_status(M, M0)) ∨
(has_status(T, T2) ∧ has_status(N, N0) ∧ has_status(M, M0))
→ has_status(TNM, IIA);
(has_status(T, T2) ∧ has_status(N, N1) ∧ has_status(M, M0)) ∨
(has_status(T, T3) ∧ has_status(N, N0) ∧ has_status(M, M0))
→ has_status(TNM, IIB);
(has_status(T, T0) ∧ has_status (N, N2) ∧ has_status (M, M0)) ∨
(has_status(T, T1) ∧ has_status (N, N2) ∧ has_status (M, M0)) ∨
(has_status(T, T2) ∧ has_status (N, N2) ∧ has_status (M, M0)) ∨
(has_status(T, T3) ∧ has_status (N, N1) ∧ has_status (M, M0)) ∨
(has_status(T, T3) ∧ has_status (N, N2) ∧ has_status (M, M0))
→ has_status (TNM, IIIA);
(has_status (T, T4) ∧ has_status (M, M0)) ∨
(has_status (N, N3) ∧ has_status (M, M0))
→ has_status (TNM, IIIB);
has_status (M, M1)
→ has_status (TNM, IV);

END CONCEPT TNM_stage

FIGURE 6

CONCEPT *HER2*

DESCRIPTION: "a proto-oncogene whose overexpression is likely to have a direct impact on cellular growth control and to the aggressiveness of the tumour."

SYNONYMS: erbB-2; HER2/neu

SOURCES: 1. Bacus S., Zelnick C., Plowman G. and Yarden Y. "Expression of the erbB-2 family of growth factor receptors and their ligands in breast cancer".....

SUB-TYPE-OF: proto-oncogene

PROPERTIES:

overexpression
VALUE-SET qualitative_value;
TYPE: NOMINAL;
VALUE-LIST: +, -
VALUE-SPEC:text;
END VALUE-SET overexpression
...

END CONCEPT HER-2

CONCEPT *Immunoperoxidase*

DESCRIPTION: "Paraffin sections are cut from tissue blocks on poly-L-lysine coated slides. After the sections are dewaxed and rehydrated, they are treated with 0.1% protease for 20 minutes at 20˚C to 22˚C. This is followed by incubation with a mouse monoclonal antibody (4 mg/mL overnight at 4˚C) to the external domain of the HER-2 protein. Bound antibodies are demonstrated by the avin-biotin-peroxidase sequence. The sections are counterstained with methyl green."

SOURCES: 1. Toikkanen S. et al.. "Prognostic significance of HER-2 oncoprotein expression in breast cancer: a 30-year follow-up".....

SUB-TYPE-OF: prognostic laboratory test

PROPERTIES:

stain_intensity
VALUE-SET qualitative_value;
TYPE: NOMINAL;
VALUE-LIST: -, +, ++
VALUE-SPEC:text;
END VALUE-SET stain_intensity
...

END CONCEPT Immunoperoxidase

FIGURE 6 (following in the next page)

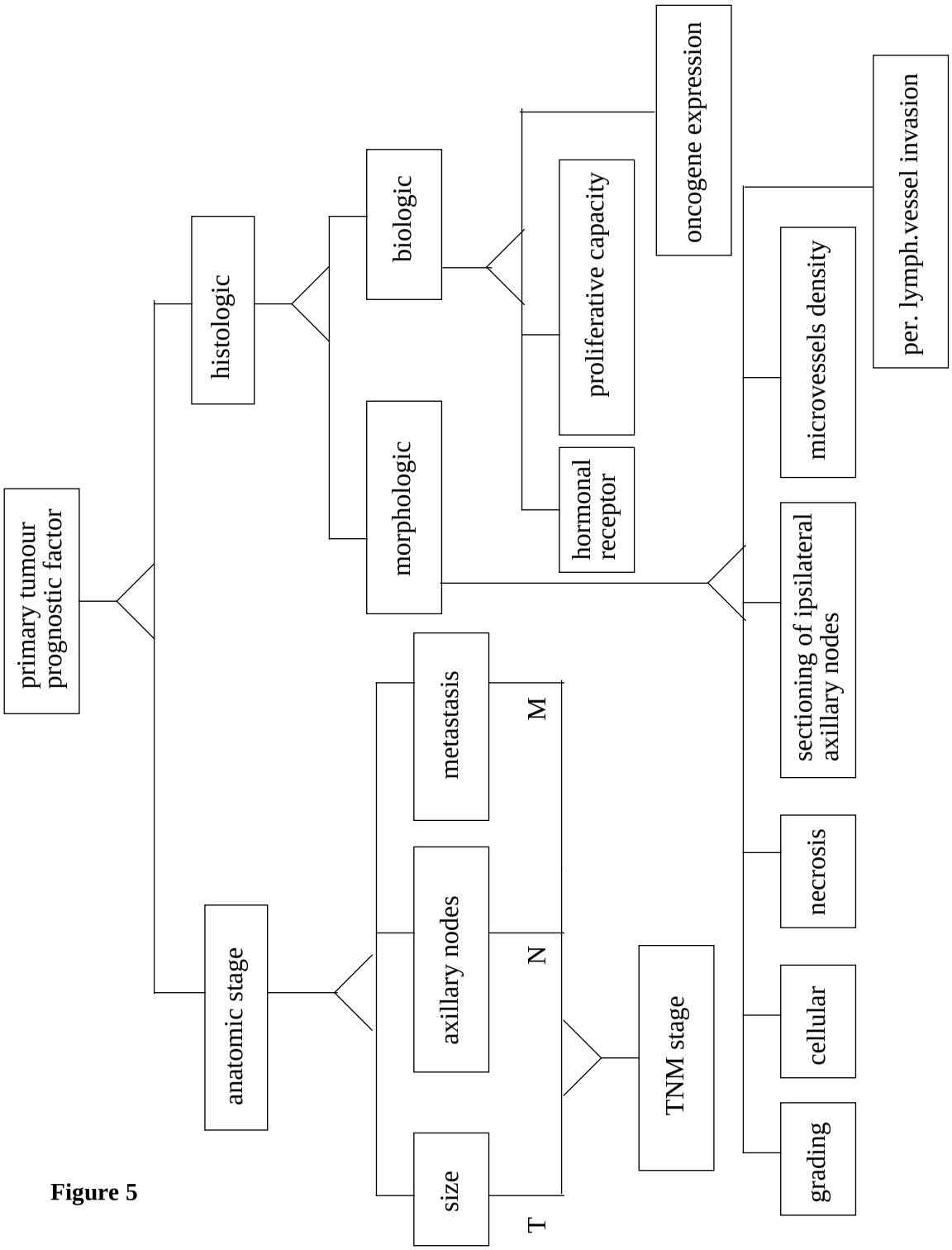

primary tumour prognostic factor
histologic
biologic
morphologic
proliferative capacity
oncogene expression
hormonal receptor
anatomic stage
metastasis
axillary nodes
size
M
N
T
TNM stage
microvessels density
per. lymph.vessel invasion
sectioning of ipsilateral axillary nodes
necrosis
cellular
grading

Figure 5

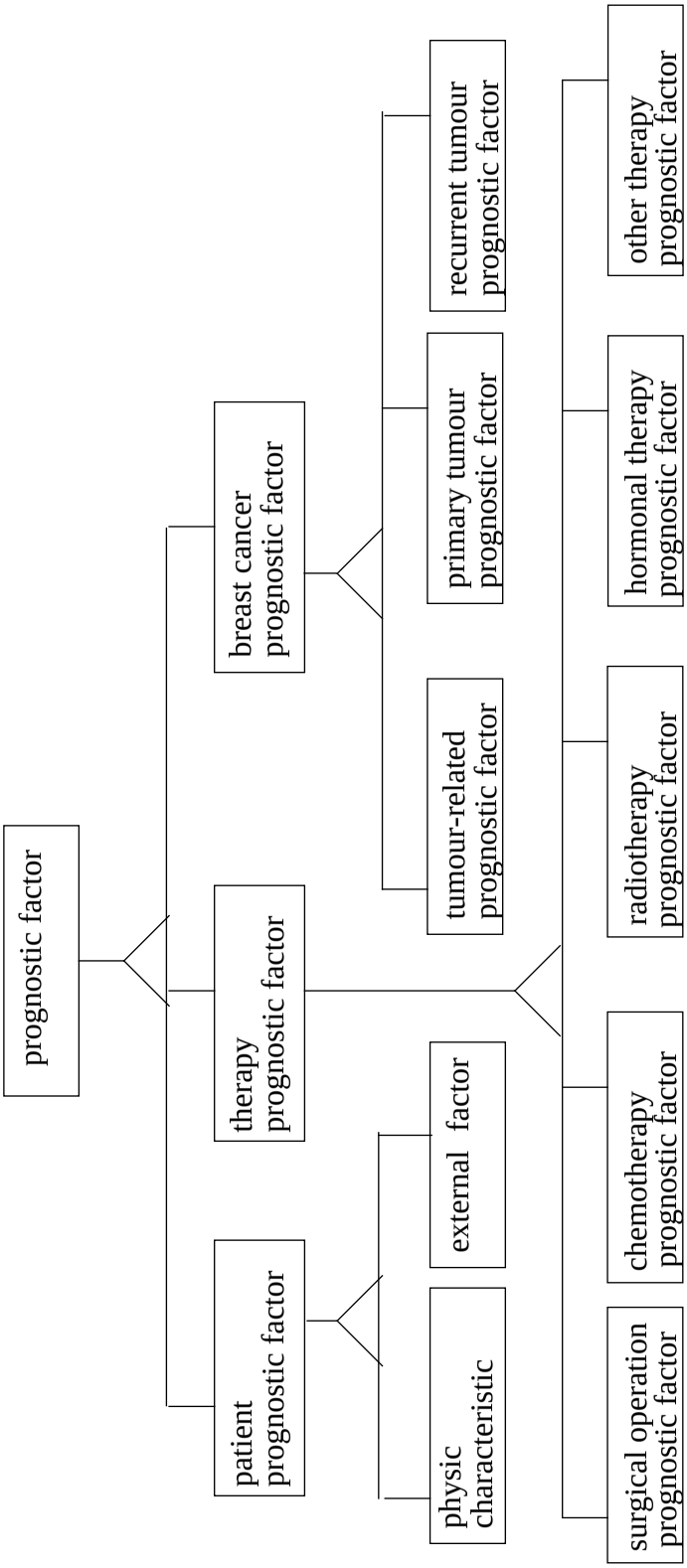

prognostic factor
patient prognostic factor
physic characteristic
external factor
therapy prognostic factor
surgical operation prognostic factor
chemotherapy prognostic factor
radiotherapy prognostic factor
hormonal therapy prognostic factor
other therapy prognostic factor
breast cancer prognostic factor
tumour-related prognostic factor
primary tumour prognostic factor
recurrent tumour prognostic factor

Figure 4

port, etc.; so, it should also be assessed whether it is worthwhile to add the knowledge deriving from this article to the assessment and prediction system models in order to improve the prognostic judgement and, as a consequence, a proper therapy. This assessment task does not take part of the chain of the expert tasks for patient management; it is in a certain way an optional task (a task in which the whole system is updated), or a task which is performed “now and again”, that is at sample periods or when a case needs a better evaluation.

In conclusion, we regard patient management as the collection of tasks of fig.2d (like in [16, chap.4], this chain, as well as the previous ones, reflects dependencies not an order of processing). This collection corresponds to 1) diagnosis, 2) prognosis 3) selection of therapy, 4) follow-up. The aim of our conceptualisation is 2).

After having defined the generic models which should be suited to our problem, we can conceptualise it; the CommonKADS conceptualisation of the breast cancer prognosis should be in terms, at least, of a description of the domain, inference and task knowledge involved in the problem.

3.3.3. The domain knowledge

Within the domain knowledge, we construct the axiomatic structure; this takes the form of producing a domain lexicon and a concept hierarchy. With respect to this and to our data sources, we have defined a hierarchy of ontologies [18]; fig.3 shows the root schema of the domain level; fig.4 shows the domain knowledge of the prognostic problem. As regards concepts, we have defined seven “primitive” concepts, that are: patient, breast cancer, information source, prognostic factor, prognosis, therapy and laboratory test (general, prognostic and therapy). Fig. 5 and 6 show the “is-a” concept hierarchy for the “prognostic factor” and for “primary tumour prognostic factor” concepts; fig.7 shows an example of definition of a prognostic factor (the HER2 growth factor receptor), of the related laboratory test (the immunoperoxidase test) and of the TNM stage. In TNM stage, an example of axioms appears.

In the following pages:

Figure 4 : The “is-a” hierarchy for the prognostic factor concept.

Figure 5 : The “is-a” hierarchy for the primary tumour prognostic factor concept

Figure 6 : Three examples of concept “leaves” of the concept hierarchy: the HER2 proto-oncogene, the Immunoperoxidase laboratory test and the TNM stage.

on whether we are looking for current properties of the breast cancer or whether we want to identify currently not observable states (i.e. past, present and future biological growing characteristics) of the breast cancer; in the first case, we should analyse breast cancer factors and determine a "stage" that is known to lead to a certain evolution of the disease; in the second case we should determine biological breast cancer history and evolution, by modelling the tumour activity and observing the biological characteristics of the disease. The first case corresponds to the task usually performed by oncologists during their work; the second case is the task more usually performed by researchers in cancer biology. The modern view of oncology joins the two cases, since nowadays the biological history of the tumour is more taken into account and prognosis is the consequence of analysing the interactions among "classical" prognostic parameters in relation to the biological activity of the tumour.

In the first case, following the cycle of patient management specified above and the suite of problem types in [16, chap.4], the management of breast cancer patient is the sequence of tasks shown in fig.2b. Connecting fig.2a and fig.2b, diagnosis includes initial diagnosis and its confirmation, assessment includes the evaluation of the disease (that is the stage considering certain prognostic factors and the associated prognosis), assignment includes the selection of therapy and monitoring includes the follow-up of the patient. With respect to this, prognosis is well distinguished from diagnosis: diagnosis is the task which establishes the presence or absence of the disease, while assessment determines its grade (stage) attribution. This parallels the approach normally adopted in clinical practice, in which normally the first step is diagnosis, and subsequently prognosis follows, possibly after further examinations. Moreover, monitoring is included in follow-up and it is not needed properly in prognosis; while prediction is not needed since the current stage of the disease (as well as a certain memory of the previously assessed ones) determines the proper therapy.

However, if we consider prognosis as a task in which the biological history of the cancer has to be reconstructed and predicted, the assessment task should be further specialised by the addition of a prediction task (fig.2c). In this case, the assignment of a therapy at a given instant is a parameter of the function which takes into account the global history - past, present and future - of the tumour (fig. 8). A proper therapy assignment should optimise the prediction in order to maximise some output parameter (such as, for example, the survival time); in this case, therapy is not a direct consequence of the stage of the disease, but it comes out from a sort of "propose and revise" task [16, chap.11], for example, by considering the identified states of the tumour history as different levels of abstraction of the disease. This optimization problem is not addressed in this work.

Moreover, diagnosis, prognosis, therapy and follow-up needs including new reliable research findings, but this is more perceived in prognosis. The knowledge which should update our guideline system for breast cancer prognosis also comes from an assessment task; that is, for example, after reading an article on breast cancer prognosis, it can be assessed that the presented results are reliable, maybe in contradiction with previous ones, that other previous results receive further sup-

Moreover, prognosis is not a task built upon static knowledge. A prognostic knowledge model should allow updating knowledge, by the introduction of new research results on prognostic factors. In this work, we do not intend to face the conceptualisation of knowledge extraction deeply, since it is anyway a process that is independent of prognosis, which is the objective of this work. The present model should be planned in order to allow the introduction of the output of this knowledge extraction process. So, while we assume that this knowledge extraction process is feasible (at least it is feasible to select the papers that deal with breast cancer prognosis with the help of a bibliographic research, i.e. by introducing proper keywords in a CD-ROM), we should provide both a "format" for this knowledge and the mechanism to allow for its insertion in the expert model.

Before starting with the description of the knowledge categories of the prognostic problem, it is worthwhile to check whether problem definitions already present in CommonKADS are also suitable for prognosis, in order to reuse elements of the CommonKADS modelling libraries that are already potentially modelled for breast cancer prognosis.

3.3.1. Definition of prognosis

We used the term "prognosis" with the meaning of judgement - assessed by a physician after a diagnosis - of the duration of a disease and the prediction of its future behaviour; in our case, at least in terms of survival time (such as, for example, 5-year and 10-year classes) and tumour recurrence. With respect to this, it is clear that we are dealing with an analysis problem [16, chap.4], which includes prediction, monitoring, diagnosis and assessment. Prediction seems the best aspect, since "prediction" is intrinsic to the definition of the problem, that is prognosis as prediction of the behaviour of the tumour. Anyway also monitoring (since we are interested in an "on line prognosis", that is, prognosis of a disease in a patient should be revised in time, specifically since we are considering long periods), diagnosis (since prognosis may be regarded as a more detailed diagnosis, that is, after a diagnosis of the disease, variables such as, for example, survival time should be estimated), and assessment (since a class/grade of the disease has to be identified) aspects may be considered as possible candidates for the application of the CommonKADS methodology.

3.3.2. Decomposition of prognosis in generic tasks

In order to identify prognosis tasks, we decomposed patient management in order to verify whether it consists of a mixture of generic tasks. Since reusability is also addressed by CommonKADS, we have searched if the subtasks obtained were already defined in the CommonKADS library.

The prognostic task ("evaluation of the disease" in fig. 2a) is the crucial point of the patient management. The task definition of the prognostic task mainly depends

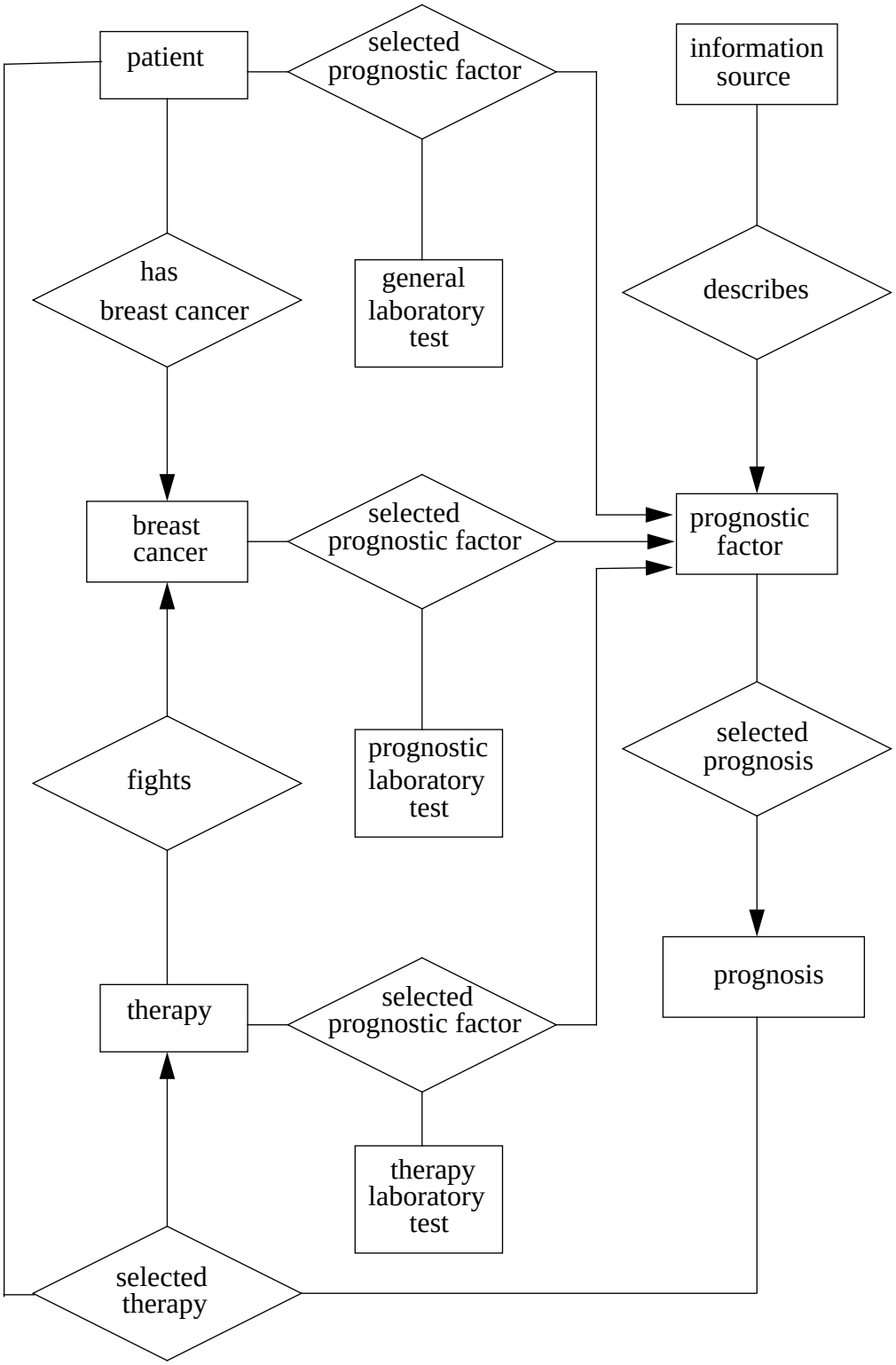
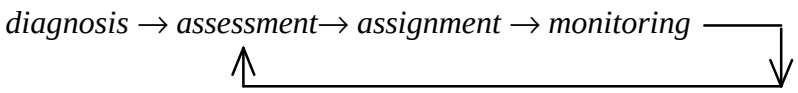


Figure 3 : The domain level at the root definition.

1.initial diagnosis ⇒ 2.confirmation of diagnosis ⇒
3.evaluation of disease ⇒ 4.selection of therapy ⇒ 5. follow up

(a)



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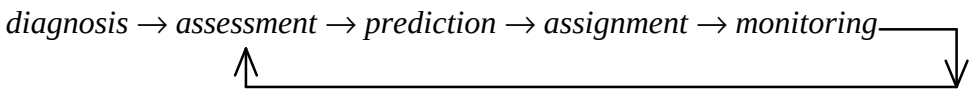
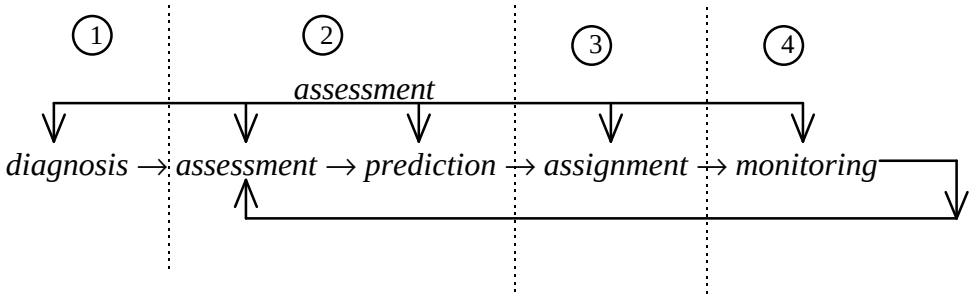


(c)



(d)

Figure 2 :
(a) Breast cancer patient management.
(b) Transferring of patient management to reusable tasks.
(c) The modern trend of breast cancer oncology, regarding prognosis not only as a stage assessment, but as a prediction of the biological history of the tumour.
(d) Updating of (c) tasks should be allowed, by extracting knowledge from literature, thus introducing an assessment task, which regards all the tasks of patient management, particularly the prognostic tasks.

- the task knowledge describes a recursive decomposition of a top-level task in subtasks, specifies these tasks, and describes when the subtasks are to be executed in order to achieve their parent task (control).

These descriptions are made by the CommonKADS Conceptual Modelling Language (CML) [18]. For many applications, these three layers are sufficient to build the system. Moreover, the CommonKADS modelling libraries capture knowledge engineering expertise in terms of reusable elements that are potentially modelled in a project. For example, the CommonKADS library of generic models offers models for diagnosis, design, planning, etc. These descriptions are made through the CommonKADS Conceptual Modelling Language (CML) [18].

3.2 The sources of experience

In our model, we deal with two types of knowledge:

- well assessed knowledge - which has already been included in prognostic guidelines - in order to produce the skeleton of the model for the prediction of the behaviour of breast cancer;
- new knowledge - which has not already been included in prognostic guidelines - in order to add new prognostic factors in the model.

In the first case, we followed the trace and the bibliography of the document "Breast Cancer" for physicians contained in the CancerNet Web info-server with PDQ (Physician Data Query) statements from National Cancer Institute USA (available at http://biomed/nus.sg). In the second case we should consider articles on breast cancer prognostic parameters taken from specialised journals.

Moreover, experts in oncology from IST (Genoa, Italy) have been consulted during the modelling construction process.

3.3 The general model

In order to transform the problem into a "well-defined" problem, we must find out how breast cancer prognosis is inserted in the patient management process. The management of breast cancer patients generally follows the task flow of fig.2a. In this work, we focus on the 3rd task. In general, 3rd, 4th and 5th tasks are iterated, that is the evaluation of the disease may be reassessed during follow-up, and therapy may be also reassessed in order to allow "ad hoc" changes in the selection of therapy; for example, after a surgical removal - which might be considered as an optional therapy (since it is not always necessary, although it is often performed) - an additional evaluation of the disease is certainly assessed.

3 Modelling breast cancer prognosis and treatment with CommonKADS

3.1 Conceptual modelling with CommonKADS

Our approach to the conceptualisation of the problem follows the CommonKADS (Knowledge Acquisition and Design Structuring) Library for Expertise Modelling, as described in [16]. KADS is a comprehensive methodology for the development of knowledge based systems (KBS); KADS was set up during European research projects (ESPRIT P1098 and P5248) and is becoming a “de facto” standard for KBS development in Europe; KADS methodology is currently under evolution and CommonKADS is the name of the last version which was available at the beginning of this work.

A CommonKADS model is a set of interrelated models from the CommonKADS model set. This model set specifies six model templates to describe different views on, or models of, a problem solving context [16]. The six models are:

1. the Organisation Model, which describes the organisational context in which the knowledge based activities that the project is concerned with occur;
2. the Task Model, which describes the tasks and activities that are executed to realise the organisational function;
3. the Agent Model, which collects the relevant properties of the different agents performing the previous defined tasks;
4. the Communication model, which describes transactions between agents;
5. the Expertise Model, which describes the knowledge of an agent relevant to a particular task;
6. the Design Model, which describes the realisation of the problem solving behaviours described in the Expertise and Communication models in computational and representational terms.

In this work we address the CommonKADS Expertise Model. Expertise modelling is founded on the Newell’s notion of knowledge level [17]. In CommonKADS the different roles are captured in three basic independent knowledge categories [16]:

- the domain knowledge specifies form, structure and contents of the specific domain which is relevant for an application (structures described through concepts and relations);
- the inference knowledge specifies the primitive steps in reasoning (inferences) in an application and the knowledge roles that refer to classes of domain knowledge statements manipulated by the inferences;

Modelling Language) [18] allows a structural approach to conceptualisation. Thus, in our opinion, it is worthwhile to use CommonKADS for our aim. The model presented here has been built following CommonKADS methodology according to [16] and [18]; at this stage, we have not used any specific CommonKADS tool. Later on, we tested COKACE (**Co**mmon**KA**DS-**Ce**ntaur), a tool developed in the ACACIA group. This tool supports the building and validation of CommonKADS expertise models, described in CML. We used this tool for the construction of a simplified model which regards the treatment of breast cancer; this model has been reported in section 8 page 72 .

The aim of this part of work is to provide a preliminary conceptualisation of the breast cancer prognosis while evaluating the efficacy of the CommonKADS methodology in facing the problem. In this respect, we wanted to build a conceptual knowledge model (in CommonKADS referred to as model of expertise) of the breast cancer prognosis, that is an intermediate knowledge representation understandable by the human expert and by the knowledge engineer, thus enriching communication and leading gradually to a shared understanding of the emerging conceptual model of the domain [8], as well as improving explanation, documentation and maintenance of the application. The definition of a conceptual knowledge model may be further used for the development of an expert system on the prognosis of breast cancer; therapy will also be addressed in terms of prognostic factor.

2.3 Related works from bibliography

In literature, there are several examples of expert systems on oncology patient management and diagnosis, such as, for example, ONCOCIN [9, 10], BREASTCAN [11], INC2 [12], SENEX [13] and others [14, 15]. Most of them focus on guiding the treatment of patients according to well assessed protocols, whereas the aim of the present work focuses on well assessed and new prognostic factors (extracted from recent literature), in order to give a prediction of the behaviour of the tumour which allows for the administration of an appropriate therapy. In this respect, we are not, actually, interested in patient management, but rather in producing an “intelligent” information system, that is a system which is able to inform and guide the physician in the analysis of recent findings and guidelines on breast cancer prognosis.

KADS has already been used for cancer treatment modelling in K-ONCOCIN [19] (specifically of Northern California Group Protocol 2083-1 for small-cell lung carcinoma treatment in ONCOCIN [9, 10]). The results of the application of the KADS methodology in K-ONCOCIN were not completely satisfactory; for example, the library of interpretation models (general models in CommonKADS) did not provide an inference structure that they could have used to model their task, the model transformation in KADS was found to be a poorly understood process, that is the technique did not assist the developer in overcoming the bias and information loss that can occur during the model-transformation phases.

Our approach to the model development is quite different from K-ONCOCIN. For example, we started conceptual modelling by a knowledge acquisition process, while K-ONCOCIN started from previous computational models, that, according to the author, may have provided them with biased preconceptions [19]; in addition, our model focuses on prognosis and information aspects, while K-ONCOCIN addresses the complex task of administering cancer therapy; moreover, better results have been achieved in other application fields (such as, for example, KNOP [16, chap. 11] and the VT task [20]); finally, the introduction of the CommonKADS CML (Conceptual

ry of the tumour, in order to select carefully groups of patients with unfavourable prognosis.

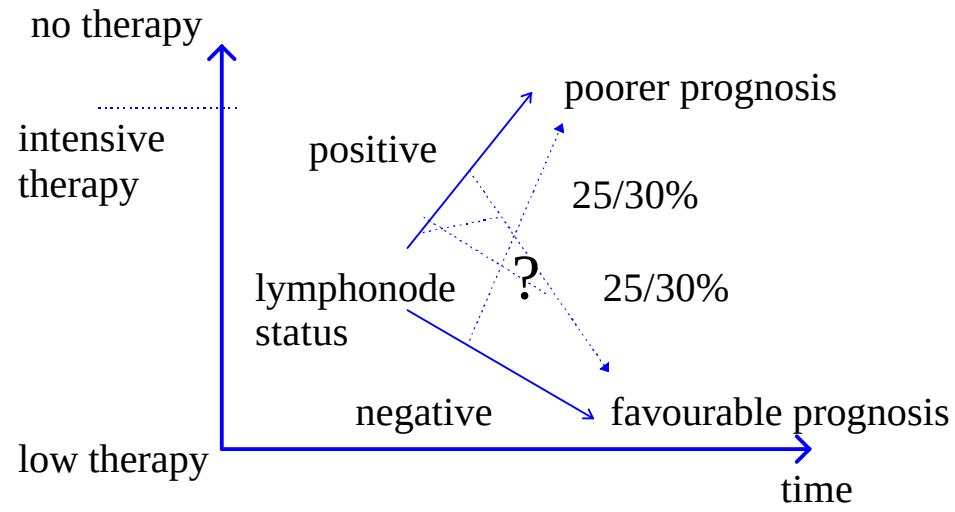


Figure 1 : Qualitative trend of breast cancer in function of the lymph node status of the primary tumour; positive status is likely to lead to a poorer prognosis while negative status is likely to lead to a favourable prognosis; 25/30% of the two categories of patients may have an opposite evolution.

A further problem originates by the fact that present day growth of cancer literature is of exponential nature (breast cancer is a typical example) [7]. Thousands of experimental and clinical researchers are actively engaged in cancer research. Specifically, one of the main aspects which is being increasingly investigated is the identification of prognostic factors for breast cancer, and specialised journals continuously report a flood of interesting results, at times conflicting; the evaluation of these results (whether, for example, there is not any bug due to the lack of some aspect of the research, or too much hurried conclusions) is also a very complex task which aims at producing a prognostic guideline.

In conclusion, the prognostic judgement, nowadays often constrained by rigid protocols, is likely to acquire a better flexibility in the near future, in order to face better the variability of breast cancer disease; in this case, a knowledge based system for prognostic decision which is able to manage a great amount of information will be certainly needed.

based system, but in our view, the most interesting application of this model is to be a base on which building guidelines from literature on cancer, in a future development.

2.2 Introduction to breast cancer prognosis and treatment

Breast cancer is an extremely various disease, especially as relates to its evolution. The course of the disease ranges from cases characterised by rapid growth and tendency to metastasis to cases characterised by low growth generally with favourable prognosis. Although breast cancer stage determined by diagnosis is one of the most important prognostic factors, it is known that within neoplasia categories which may seem homogeneous for clinic-pathological parameters, cases with different evolution can be observed.

Lymph nodes state (positive, N+, vs. negative, N-) is one of the most important prognostic factors in breast cancer patients and the one which determines post-surgical treatment. Patient survival percentage after 5 years in the N- cases is about 67-85%; this value decreases if lymph node metastasis are found (N+) and the decrease depends on the number of lymph nodes involved in the pathological process [1-4]. The research effort towards other prognostic factors is mainly due to the fact that within the more favourable category (N-) there is a group (about 25-30%) with unfavourable prognosis (less than 10 years survival) [2, 3] and, in parallel, within the less favourable category (N+) there is a group (about 25-30%) with favourable prognosis (more than 10 years survival) [4] (fig.1); so it is likely that an inadequate therapy is adopted - specially an “undertreatment” in the N- cases [2,3] - following the present therapy protocols.

At present, one major research aspect is the identification of one or more prognostic factors accurate enough to define different therapeutic decisions. Prognosis and selection of therapy are mainly influenced by the age of the patient, stage of the disease, pathology features of the primary tumour including the presence of tumour necrosis, oestrogen-receptor (ER) and progesterone-receptor (PR) levels in the tumour tissue, and measures of proliferative capacity, as well as by menopausal status and general health. Besides, it has been found that these parameters are not sufficient to define a proper prognosis if they are considered separately.

So, nowadays research mainly directs its efforts towards a characterisation of the natural history of the tumour, in terms of biological parameters. The biologic parameters seem to be very promising even if they are currently in phase of study; for example, ER and PR [5] have already been identified as important prognostic factors. Good results are expected from other biological parameters, such as, for example, growth factor receptors like erbB-2 [6]. Each prognostic factor on its own is not sufficient for the prediction of the biological behaviour of the tumour; but a combination of these parameters is necessary, taking in mind (that is modelling) the natural histo-

2 Introduction to conceptual modelling in breast cancer

2.1 Introduction to some oncologic problems

Cancer is a group of more than 100 different diseases. Cancer occurs when cells become abnormal and keep dividing and forming more cells without control or order. All organs of the body are made up of cells. Normally, cells divide to produce more cells only when the body needs them. If cells divide when new ones are not needed, they form a mass of excess tissue, called a tumour. Tumours can be benign (not cancer) or malignant (cancer). The cells in malignant tumours can invade and damage nearby tissues and organs. Cancer cells can also break away from a malignant tumour and travel through the bloodstream or the lymphatic system to form new tumours in other parts of the body. The spread of cancer is called metastasis. Cancer is treated with surgery, radiation therapy, chemotherapy, hormone therapy, or biological therapy. The doctor may use one method or a combination of methods. The choice of treatment depends on the type and location of the cancer, whether the disease has spread, the patient's age and general health, and other factors. Many cancer patients take part in clinical trials (research studies) testing new treatment methods. Such studies are designed to improve cancer treatment.

Clinical practise guidelines are more and more developing in order to decrease the delays in implementation of research findings into practise for similar pathology conditions. This trend is particularly felt in cancer domain, where the decrease in mortality should be deeply influenced by making state-of-art knowledge and best medical practices applied to each cancer patient.

Literature review in oncology is a very complex task, as well as the boot for guidelines development. The central problem originates by the fact that present day growth of cancer literature is of exponential nature (breast cancer is a typical example). Specifically, one among the many aspects which are being increasingly investigated is the identification of prognostic factors for cancer and for breast cancer in particular (the more common cancer in women); the evaluation of the flood of, sometimes in conflict, results reported by specialised journals (whether, for example, there is not any bug due to the lack of some aspect of the research, or too much hurried conclusions) aims at producing a prognostic guideline.

Although knowledge organisation is rapidly changing in the last few years by the introduction of hypertext and multimedia techniques, the knowledge resulting from a research activity is likely to be still presented and recorded by the very authors in natural language (usually English) for many years. This does not exclude that an electronic format of the paper, that is of the journal in which the paper has been published, will be given for many journals in a brief time.

In this work, we aimed at producing a conceptual model of breast cancer prognosis and treatment. This conceptual model may be used for building a knowledge

1 Introduction

The research work reported has been carried out in the context of a post-doctoral scientific visit in the ACACIA project at the INRIA research centre in Sophia-Antipolis (France). The ACACIA (Acquisition des Connaissances pour l'Assistance à la Conception par Interaction entre Agents) project is a multidisciplinary project that aims at offering models / methods / tools in order to help the knowledge engineer to acquire knowledge from multiple expertise sources (experts and documents). ACACIA project is interested either in capitalizing knowledge on a given domain or in building an explanatory knowledge based system. The aim is to offer new generic models in order to help the knowledge engineer to interpret the expertise documents (for example obtained after elicitation sessions); such models focus on solving problems of multiple expertises and of explanatory knowledge acquisition. For representation of expertise models or of acquired knowledge, the formalism adopted is commonly in terms of conceptual graphs as well following the methodological framework offered by CommonKADS. Various research is being done on knowledge acquisition from multiple experts: collective elicitation protocol, model of cognitive agents for guiding knowledge acquisition, management and comparison of multiple viewpoints, detection and solving of conflicts among several expertise models, comparison of knowledge graphs, generation of consensual rules among experts, architecture of cognitive agent, extension of CommonKADS for multi-expertise and for multi-agent systems. The project also works on modelling explanation task and activity, on explanation evaluation and on the integration of explanatory knowledge acquisition into a knowledge acquisition method such as KADS. The documentation aspect is tackled through the exploitation of hypertext techniques for knowledge acquisition and explanations based on electronic documents.

Moreover, although the knowledge acquisition process has mainly regarded the analysis of documents (papers, books ...), the research work described in this report has also been supported, when needed, by experts from the IST (Institute for the Study on Tumours) from Genoa.

In the context of this research visit, there have been two main objectives:

- defining a preliminary expertise model for breast cancer prognosis and therapy;
- verifying the potentiality of the CommonKADS methodology to define an expertise model in the medical domain.

Table of Contents

Remerciements

Je tiens à remercier:

Mme Rose Dieng, responsable scientifique du projet ACACIA qui m'a accueilli dans son groupe.

Tous les membres d'ACACIA.

Les experts de l'IST (Institut National pour la Recherche et l'Etude du Cancer) de Gênes - Italie, avec lesquels j'ai brièvement travaillé.

Je remercie également la COTRAO (COmmunauté du TRavail des Alpes Occidentales) qui a contribué au financement de cette visite post-doctorale à l'INRIA.

Utilisation de CommonKADS pour la construction d'un modèle d'expertise pour le pronostic et la thérapie du cancer du sein

Résumé : L'un des principaux aspects de la recherche sur le cancer du sein est l'identification de paramètres pronostiques suffisamment exacts pour permettre d'organiser des stratégies thérapeutiques différenciées ; aucun facteur pronostique n'est suffisant seul pour prédire le comportement biologique d'une tumeur, mais une combinaison de tels paramètres est indispensable. En outre, la littérature sur le cancer, en particulier sur ses aspects biologiques, croît actuellement de façon exponentielle, et la gestion des connaissances dérivant de la recherche sur le cancer aurait besoin d'une conceptualisation de ces connaissances pour simplifier le processus de production de guides pour le pronostic et la thérapie du cancer.
Les travaux décrits dans ce rapport se sont focalisés sur la définition d'un modèle conceptuel des connaissances sur le pronostic et la thérapie du cancer du sein. Nous avons suivi la méthode CommonKADS et, en particulier, la bibliothèque offerte par CommonKADS pour la modélisation de l'expertise. Le but de ces travaux était de fournir une première conceptualisation du pronostic et la thérapie du cancer du sein, tout en évaluant l'efficacité de la méthode CommonKADS dans ce cadre.

Mots-clé : CommonKADS, acquisition de la connaissance, cancer du sein, domaine médical.

Using CommonKADS to build an expertise model for breast cancer prognosis and therapy

Roberto Sacile*

Programme 3 : Intelligence artificielle,
systèmes cognitifs et interaction homme-machine

Projet ACACIA

Rapport de recherche n˚2737 - Novembre 1995

101 pages

Abstract: One of the major aspects in breast cancer research is the identification of prognostic factors accurate enough to define different therapeutic decisions; each prognostic factor on its own is not sufficient for the prediction of the biological behaviour of the tumour, but a combination of these parameters is necessary. Moreover, nowadays growth of cancer literature, specifically on biological aspects, is of exponential nature, and the management of the knowledge deriving from cancer research needs a knowledge conceptualisation in order to simplify the process of guideline production in cancer prognosis and therapy. The work described here focuses on the definition of a conceptual knowledge model of the prognosis and the therapy of breast cancer. Our approach to the conceptualisation of the problem follows the CommonKADS (Knowledge Acquisition and Design Structuring) Library for Expertise Modelling. The aim of this work is to provide a first conceptualisation of breast cancer prognosis and therapy, while evaluating the efficacy of the CommonKADS methodology in facing the problem.

Key-words: CommonKADS, knowledge acquisition, breast cancer, medical domain.

(Résumé : tsvp)

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Établissement public national à caractère scientifique et technologique - Décret N^{o} 85.831 du 2 août 1985

INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE

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Novembre 1995

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ISSN 0249-6399