A Constraint-based Approach to Medical Guidelines and Protocols

Arjen Hommersom\textsuperscript{1}, Perry Groot\textsuperscript{1}, Peter Lucas\textsuperscript{1}
Mar Marcos\textsuperscript{2}, and Begoña Martínez-Salvador\textsuperscript{2}

\textsuperscript{1}University of Nijmegen
\{arjenh,perry,peterl\}@cs.ru.nl
\textsuperscript{2}Universitat Jaume I
\{marcos,bmartine\}@icc.uji.es

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Guidelines and Protocols

- Medical guidelines are systematically developed, structured documents, containing conclusions and recommendations, based on scientific evidence.
- Protocol is basically a restructured summary of the guideline recommendations with local modifications.
- Goal: obtaining differences between guidelines and protocols using formal methods.
Case Study

- Case study: breast cancer treatment
- Protocol: developed by Dutch Integral Cancer Centre East (IKO in Dutch)
- Guideline: developed by Dutch guideline development group CBO

Informally, some differences are the following:

1. IKO: ultrasound axilla is default during sentinel node procedure, while CBO does not provide such a default
2. IKO: first radiotherapy, then chemotherapy; CBO specifically no order
3. IKO: additional axillary treatment when isolated tumour cells are found in axilla; CBO recommends wait-and-see
Contraint-based Approach

- Guidelines are under-specified (constraints)
- Protocols are local adaptations most likely to be used in computerised decision support (program-like)
- Guidelines and protocols need interpretation (clinical context)
Breast Cancer Surgery

Surgery of breast cancer consists of two main decisions:

- Treatment of primary tumour: breast conserving (preferred) or mastectomy
- Treatment of axilla: staging (preferred) or dissection

Furthermore, the following needs to be decided:

- Order between interventions
- Influence of outcome of axilla staging and status of resection margins on subsequent interventions
Surgery for Invasive Breast Cancer [D.F. Roses, 2005]

- **T1-2,N0-1,M0**
- **CI-BCT**
  - **SN**
    - **SNneg**
    - **SNpos**
  - **¬ CI-BCT ∧ CI-SN**
- **MRM**
  - **tumour excision**
    - **TF**
      - **BCT**
      - **¬ TF**
    - **¬ TF**
      - **BCT+AD**
      - **¬ TF**
        - **MRM**
        - **¬ TF**
          - **BCT+AD**
          - **MRM**

- **CI-BCT**
  - **¬ CI-BCT ∧ CI-SN**

Specification Language

- Computational Tree Logic

\[\text{CTL} ::= \neg\text{CTL} \mid \text{CTL} \ast \text{CTL} \mid O \text{CTL}\]

where \(\ast\) a prop. connective and \(O \in \{\text{AG, AF, EG, EF}\}\)

- Linear Temporal Logic

\[\text{LTL} ::= \neg\text{LTL} \mid \text{LTL} \ast \text{LTL} \mid O \text{LTL}\]

where \(\ast\) a prop. connective and \(O \in \{\text{G, F}\}\)

- (Linear-Branching) Modular Model Checking

\[[\varphi]_M \langle \psi \rangle\]

where \(\varphi\) is an LTL formula and \(\psi\) a CTL formula
Guideline Constraints

- Constraints imposed by the guidelines as modular formulas:

\[
\begin{align*}
\top & \quad M \langle \text{AG}(\text{MRM} \rightarrow \text{AF AD} \land \text{AF mastectomy}) \rangle \\
\top & \quad M \langle \text{AG}(\text{excision} \rightarrow (\neg \text{TF} \leftrightarrow \text{AF MRM})) \rangle
\end{align*}
\]

- Constraints assumed (on the final model), e.g.:

\[
\top \quad M \langle \text{CI-BCT} \leftrightarrow \text{AG CI-BCT} \rangle
\]
Asbru Model of the Protocol

- **BCT surgery**
  - **SN procedure**
    - filter: neg sn−contraindications
    - abort: SN positive
  - **dissection−of−axilla**
    - filter: no contra−indications for bct
    - abort: margins not tumour free
  - **axilla surgery**
    - wait for SN or dissection−of−axilla
  - **BCT surgery**
    - wait for axilla surgery and excision
  - **MRM**
    - manual activation
  - mastectomy

- treatment
  - wait for BCT or MRM

- **BCT**
  - wait for BCT surgery or MRM

- **excision**
  - abort: margins not tumour free
  - manual activation
Two questions need to be resolved:

1. Is the protocol consistent with the description of management in practice?

2. Is the protocol, restricted to medical management in practice, consistent with the recommendations from the guideline?
Comparison Protocol and Management in Practice

Assume:

- no contra-indications for BCT or SN
- sentinel node is negative
- excision of the tumour was not successful

Treatment suggested by management in practice is mastectomy (and not axilla dissection). We check:

\[ \neg \text{CI-BCT} \land \neg \text{CI-SN} \land \text{EF}(\text{SN} \land \text{SNneg} \land \text{EF}((\text{excision} \land \neg \text{TF} \land \text{EF}(\text{mastectomy}) \land \text{AG}(\neg \text{AD})))) \]

and find it is false. Instead, the protocol/guideline recommends MRM (including axilla dissection).
Comparison Protocol and Guideline

Let $P$ be the set of LTL formulas describing medical management in practice, then each guideline constraint $[\varphi] M \langle \psi \rangle$ is verified by:

$$[P \land \varphi] M \langle \psi \rangle$$

Using this approach, we find that the protocol has a different recommendation in case isolated tumour cells are found in the axilla.
Summary

- The goal: obtaining differences between guidelines and protocols using formal methods
- Approach: by checking guideline constraints on a protocol model in a clinical context
- Case study: breast cancer surgery
- Results: feasible using modular model checking
Conclusions & Future Work

- First attempt to formally compare the guideline, protocol, and medical management in practice was successful.
- Constraint based approach generates interesting proof obligations which can be easily investigated using model checking.
- Future work
  - Mapping between background knowledge and modal logic
  - Generalisation of the approach