A Document Engineering Environment for Clinical Guidelines

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Outline

- Context of the work
- G-DEE
  - Environment dedicated to the study of Clinical Guidelines incorporating text processing functions
- Potential applications in the context of the computerization of clinical guidelines
Clinical Guidelines’ Content

- Clinical Guidelines are medical documents that contain best practice recommendations based on the concept of *Evidence-Based Medicine* [Sackett et al, 1996])

- Clinical Guidelines have a characteristic structure and style and they are organized around the notion of recommendations

In case of an angiotensin converting enzyme inhibitors or angiotensin receptor blockers treatment prescribed, it is recommended to prescribe a bilan associating kaliemie and creatinin in 7 to 15 days, after the beginning of the treatment.

Posologies should be increased progressively specifically for bitherapies using insulin due to the fact of the risk of hypoglycemia incurred.
Rationale for the Computerization of Clinical Guidelines

- Documents are often too long to be used in practice, sometimes complex and not so clear [Patel et al, 2001]

- Texts can be semantically complex, as well as structural plan, containing often sequence of procedures with causal or temporal relations that are also complex [Patel et al, 2001]

- Variability of structures that can be tend to difficulties to understand [Elkin et al, 2000]

- Reading the clinical guidelines and reminding the different recommendations can appear unrealistic within sight of the effort which it requires [Grimshaw & Eccles, 2004; Kavanagh, 2002; Patel et al, 2001]
Life Cycle of Clinical Guidelines

1. Authoring
2. Diffusion
3. Reading
4. “paper” version
5. Updating
6. “electronic” version

Clinical Guidelines

Decision Support System
Computerization of Clinical Guidelines

Translation of guideline into computer-executable statements is complex [Shiffman et al, 1999]

Approaches centered on knowledge formalization

- Description of decision process that contents in clinical guidelines
  - GLIF [Greenes et al, 1999]
  - PROforma [Fox & Rahmanzadeh, 1998]
  - GUIDE [Ciccarese et al, 2003]
  - PRODIGY [Purves et al, 1999]

  - Aimed at **elaborating decision systems**

Approaches centered on document engineering

- Methods using document as a representation support
  - HGML [Hagerty et al, 2000]
  - GEM [Shiffman et al, 2000]

  - Aimed at **managing the document**
Encoding Clinical Guidelines

Clinical Guidelines

Interpretation

Expert

Manual encoding

Structured Document (e.g. GEM)
Document-based Approaches

- Adding information on text using marking-up

- GEM (Guideline Elements Model) is the most known model and has been recognized as a standard to structure clinical guidelines
  - Developed by the Yale team, and approved as a standard ASTM E2210-02 (Shiffman et al., 2000)
Guideline Elements Model (GEM)

- GEM is an XML-based guideline document model that can store and organize the heterogeneous information contained in practice guidelines.

- Facilitate translation of natural language guideline documents into a format that can be processed by computers

- Hierarchy of more than 100 elements with 10 major branches
Description of the GEM Model

Specific terms have been defined by the National Clearinghouse¹, a control source of vocabulary, to improve text structure (Bernstam et al., 2000)

¹http://www.guideline.gov
Description of the Knowledge Components

Guideline Document

Knowledge Components

- Recommendation
  - Conditional
  - Imperative
- Definition
- Background Information
- Research Agenda
- Algorithm
  - Action Step
  - Conditional Step
  - Branch Step
  - Sync Step

Term
  - Term Meaning
GEM-Cutter: Editor to Assist Encoding of Clinical Guidelines

1. **EVALUATION: IMAGING Recommendation 11**
   - Infants and young children 2 months to 2 years of age with UTI who do not demonstrate the expected clinical response within 2 days of antimicrobial therapy should undergo ultrasonography promptly, and either voiding cystourethrogram (VCUG) or radionuclide cystography (RNC) should be performed at the earliest convenient time. Infants and young children who have the expected response to antimicrobials should have a sonogram and either VCUG or RNC performed at the earliest convenient time (strength of evidence: good).

2. **UTI in young children serve as a marker for abnormalities of the urinary tract. Imaging of the urinary tract is recommended in every febrile infant or young child with a first UTI to identify those with abnormalities that predispose to renal damage. Imaging should consist of urinary tract ultrasonography to detect dilatation secondary to obstruction and a study to detect VUR.**

   - **Ultrasonography**
   - **Urinary tract ultrasonography consists of examination of the kidneys to identify hydronephrosis and examination of the bladder to identify dilatation of the distal ureters, hypertrophy of the bladder wall, and the presence of ureteroceles. Previously, excretory urography (commonly called intravenous pyelography) was used to reveal these abnormalities, but now ultrasonography shows them more safely, less invasively, and often less expensively. Ultrasonography does have limitations, however. A normal ultrasound does not exclude VUR. Ultrasonography may show signs of acute renal inflammation and established renal scars, but it is not as sensitive as other renal imaging techniques.**
Difficulties to encode Clinical Guidelines

Substantial variation is observed in the GEM encoding of a given Clinical Guideline by different users\(^2\)

- Example: difficulties with the identification of decision variables and text inserted into certain GEM elements varied considerably

Translation of text to document models faces limitations

- Documents are subject to variations in style
- Interpretation problems affecting encoding

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Key Ideas

- Automatic text structuring through the recognition of documents specific linguistic content ("recommendations")

- Method
  - Automatic recognition of deontic operators\(^1\) (linguistic formulation of recommendations)
  - Using shallow Natural Language Processing (NLP) methods

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Part I

A Document Engineering Environment
G-DEE (Guidelines Document Engineering Environment)

- A software environment for the study of Clinical Guidelines that incorporates automatic text processing functions

- Automatically performs XML encoding of guidelines based on the recognition of the guideline’s linguistic content

- These processing functions recognize specific natural language expressions corresponding to the linguistic formulation of recommendations (deontic operators)
III.2. Examens complémentaires.

Il est proposé de vérifier la stérilité des urines par bandelette urinaire. *En cas de signe évocateur ou d’antécédent d’infection urinaire, il est recommandé de pratiquer un ECRU (accord professionnel)* (1).

Le dosage de la créatininémie n’est pas proposé à titre systématique. Il n’est recommandé que chez les patients présentant des facteurs de risque d’insuffisance rénale, celle-ci n’étant affirmée que sur le calcul de la clairance de la créatinine (accord professionnel). La débitmétrie urinaire n’est pas proposée en première intention dans le bilan initial d’une HBP symptomatique. C’est un examen optionnel pratiqué dans un centre spécialisé (accord professionnel). L’échographie de l’abdomen par voie abdominale n’est pas proposée à titre systématique dans le bilan initial de l’HBP symptomatique (accord professionnel). Cet examen peut être utile pour le diagnostic de vésicule de lutte, de calcul vésical ou de dilatation du haut appareil. Il a été démontré que la mesure du résidu postmictionnel et du volume prostatique par échographie sus-pubienne n’était pas fiable.

Le bilan urodynamique n’est pas recommandé systématiquement dans le bilan initial de l’HBP symptomatique. Cet examen invasif peut être utile en cas de comorbidité, notamment neurologique, et pour préciser les indications thérapeutiques en mise en place spécialisé (accord professionnel). Une échographie prostatique par voie transrectale n’est pas recommandée lors du bilan initial de l’HBP symptomatique. Cet examen n’a aucune place dans le diagnostic, le bilan ni la surveillance d’une HBP.

**Règle**

SI *signe évocateur ou d’antécédent d’infection urinaire*

ALORS *pratiquer*

*un ECRU (accord professionnel)*
Recommendations

- It is the essence of clinical guidelines to convey specific advice which has scientific authority.

- Such advice is formulated through specific statements known as recommendations.
  - “In case of extension to pedicle lymph nodes, if surgical accessibility falls into Class I, surgery cannot be contraindicated, but this decision should nevertheless be part of a multi-disciplinary consultation.”

- These recommendations constitute the backbone of the guideline documents.
Recommendations have a specific linguistic expression

Deontic propositions are the most characteristic linguistic structures of normative texts [Kalinowski\(^1\)]

- Previous work on legal texts by Moulin et al.\(^2\)

These are based on deontic operators such as (in French)\(^3\):

- *pouvoir* (to be allowed to or can/may),
- *devoir* (should or ought to),
- *interdire* (to forbid)

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\(^1\) Kalinowski G. La Logique Déductive. Presses Universitaires de France (in French); 1996.


Identification of specific syntactic structures for deontic operators

Deontic operators depend on deontic verbs (examples for French):

- **recommander** (to recommend) - **éviter** (to avoid)
- **conseiller** (to advise) - **prescrire** (to prescribe)
- **préférer** (to prefer) - **proposer** (to propose)
- **envisager** (to consider) - **traiter** (to treat)
We described a grammar of deontic expressions to support their automatic recognition from free text.

Extended corpus of 17 documents to maximize syntactic coverage (clinical guidelines / consensus conferences / medical teaching material)
Syntactic formalism

- The whole text is scanned using Finite-State Transition Networks\(^1\) (FSTN) dedicated to the recognition of deontic operators

- FSTN are a convenient way to define specialized structures, including their morphological variants

- 170 syntactic patterns described from our corpus analysis (corresponding to 65 deontic operators)*

- 12,000 FSTN* once morphological variants are taken into account

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* Latest version
Structure of Deontic Expressions

Deontic expressions naturally structure a sentence in terms of deontic operators and its operands which are textual elements within the scope of the operator.

Investigation for secondary hypertension (with specific laboratory tests or imaging) should be considered in young hypertensive patients (under 30 years old).

Scopes correspond to the operands of deontic operators

Front-Scope: the scope that precedes a deontic operator

Back-Scope: the scope that follows the operator
This natural structure can be the basis of document encoding using an XML format.

```
<FrontScope> Investigation for secondary hypertension (with specific laboratory tests or imaging) </FrontScope>
<OpDeont> should be considered </OpDeont> <BackScope> in young hypertensive patients (under 30 years old) </BackScope>.
```

The encoding can serve as a basis for further processing:
- The extraction of decision rules under textual format
- The encoding using GEM categories
FSTN Implementation

- FSTN for individual deontic expressions are grouped into larger FSTN sharing common syntactic patterns
- Parsing uses 10+ such aggregated FSTN
In case of symptoms of urinary tract infection, it is recommended to perform urinalysis.
In case of symptoms of urinary tract infection, it is recommended to perform urinalysis.

In case of symptoms of urinary tract infection, it is recommended to perform urinalysis.

In case of symptoms of urinary tract infection, it is recommended to perform urinalysis.
In case of symptoms of urinary tract infection, <Op Reco> it is recommended to perform </Op Reco> urinalysis.
<Front Scope> In case of symptoms of urinary tract infection, </Front Scope> <Op Reco> it is recommended to perform </Op Reco> <Back Scope> urinalysis </Back Scope>.
Third Step: Marking Up Conditional Expressions

<Front Scope> <cond> In case of </cond> <condition> symptoms of urinary tract infection </condition>, </Front Scope>
<Op Reco> it is recommended to perform </Op Reco> <Back Scope> urinalysis </Back Scope>.
The radiotherapy is not either recommended to patients less than 60 years, like treatment of the sclerodermiforms CBC, on specific zones (ears, hands, feet, legs, genital organs). If the diabetes is diagnosed in an elderly patient, an objective of HbA1c ranging between 6.5% and 8.5% can be used as a reference but it is essential to individualize this objective according to the medical and social context.
Part II

Encoding-Based Transformations of Guidelines Documents
..... En cas de signe évocateur ou d'antécédent d'infection urinaire, il est recommandé de pratiquer un ECBU (accord professionnel). ..... 

Clinical Guidelines

Automatic content processing

Clinical Guidelines marked-up

<?xml version="1.0" encoding="ISO-8859-1"?>
<FrontScope><cond> En cas de </cond> <condition> signe évocateur ou d'antécédent d'infection urinaire </condition> <SubScope>, <SubScope> </SubScope> </SubScope> 

XML file

XSLT processor

XSL for extraction

XSL for visualization
We defined XSL style sheets for highlighting:
- Deontic operator
- Front-scope and back-scope
- Conditional elements

Visualization facilitates immediate access to recommendations.

This marking-up enables document structure analysis by users.
VI. TRAITEMENT PHARMACOLOGIQUE (150).
VI.1. Choix des antihypertenseurs (151).
La réduction du risque cardio-vasculaire est avant tout dépendante de la baisse de la pression artérielle, quelle que soit la classe d'antihypertenseur utilisée (grade A) (86).
Dans l'HTA essentielle non compliquée, les 5 classes d'antihypertenseurs majeurs [les diurétiques thiazidiques, les bêta-bloquants, les inhibiteurs calciques, les inhibiteurs de l'enzyme de conversion (IEC) et les antagonistes des récepteurs de l'angiotensine II (ARAI)] ont montré un bénéfice sur la morbi-mortalité cardio-vasculaire, dans les essais cliniques (87). Ces 5 classes d'antihypertenseurs peuvent donc être proposées en première intention dans la prise en charge d'un hypertendu essentiel non compliqué (grade A) (88). Le choix d'un traitement médicamenteux sera adapté à chaque patient en fonction des indications préférentielles de certaines classes dans des situations cliniques articulées (cf (89), infra) (en accord avec les études cliniques), de l'efficacité et de la tolérance des médicaments déjà pris par le patient, de l'existence de comorbidités pouvant justifier ou contre-indiquer certains antihypertenseurs, et du coût du traitement et de sa surveillance, en sachant que le diurétique thiazidique fait partie des classes dont le coût journalier est le plus faible (90). En cas de prescription d'un traitement par IEC ou ARA-II, il est recommandé de prescrire un bilan associant kaliémie et créatininémie dans un délai de 7 à 15 jours, après le début du traitement (91). Si la créatininémie s'élève de plus de 20 à 30 %, il est recommandé d'arrêter l'IEC ou l'ARA-II et de demander un avis spécialisé (92). Pour favoriser l'observance, une prise unique quotidienne (monoprise) utilisant un médicament de longue durée d'action sera préférée (93).
A partir d'études menées chez des patients afro-américains et africains des Caraïbes, il apparaît que l'HTA chez ces patients, est plus sensible aux diurétiques et aux inhibiteurs calciques qu'aux classes thérapeutiques agissant sur le système rénine-angiotensine (IEC, ARA-II) ou qu'aux bêta-bloquants (94).
VI.2. Stratégie d'adaptation du traitement médicamenteux (152).
Il est recommandé de débuter par une monothérapie (95). Une association fixe d'antihypertenseurs à doses faibles, ayant l'AMM en première intention pour l'indication HTA, peut également être proposée (96).
En deuxième intention, une bithérapie sera instaurée dans un délai d'au moins 4 semaines, en cas de réponse tensionnelle insuffisante au traitement initial (97).
Une bithérapie pourra être instaurée dans un délai plus court, dans les cas suivants chez le patient ayant une PA = 180-110 mmHg quel que soit le nombre de facteurs de risque cardio-vasculaire associés, chez le patient ayant une PA de 140-179/90-109 mmHg et à risque cardio-vasculaire élevé (98).
We defined XSL style sheets (based on domain knowledge) that enable to identify:

- The scope corresponding to the condition
- The scope corresponding to the action

Specific visualization modes can be supported, e.g., GEM format, or decision rules.
Investigation for secondary hypertension (with specific laboratory tests or imaging) should be considered in young hypertensive patients (under 30 years old).
Investigation for secondary hypertension (with specific laboratory tests or imaging) should be considered in young hypertensive patients (under 30 years old).

Règle

IF young hypertensive patients (under 30 years old)

THEN consider

Investigation for secondary hypertension (with specific laboratory tests or imaging)
G-DEE Demo: Analysis of a sentence
G-DEE Demo: Analysis of a complete Guideline
Part III

Evaluation of G-DEE
Preliminary Evaluation

- Evaluate the marking-up generated by G-DEE on a test set of clinical guidelines with respect to the manual marking-up of deontic operators.

- Test set of 5 Clinical Guidelines (83,997 words / 1003 sentences / 311 deontic operators).

- None of these 5 texts has been used for the definition of our deontic operators’ grammar!

- 97% of documents are correctly marked up in this test set and 3% identified as errors arise from a few specific syntactic phenomena (limits of syntactic coverage).
Evaluation of G-DEE by Experts

- Complete Analysis of Clinical Guidelines by G-DEE to be evaluated by experts
  - Guidelines for the “Early management of adult stroke patients Medical aspects – September 2002”
  - Guidelines for the “Management of adults with essential hypertension - 2005 update”

- Evaluation of the entire marking-up of recommendations of clinical guidelines by 4 experts (physicians involved in the authoring of clinical guidelines)
Criteria for the evaluation of G-DEE (1/2)

- **True positive (TP):** sentence correctly marked-up and corresponding to an actual recommendation

  *In case of symptoms of urinary tract infection, it is recommended to perform urinalysis.*

- **True negative (TN):** sentence that is not a recommendation and has not been marked-up as one

  *Isolated systolic hypertension is more common in the elderly.*
Criteria for the evaluation of G-DEE (2/2)

➢ False positive (FP) : sentence marked-up which is not an actual recommendation

The NIH Scale is the reference scale in the occurrence of fibrinolysis.

➢ False negative (FN) : sentence corresponding to an actual recommendation which has not been correctly marked-up or has been ignored

In case of patients with essential hypertension (except patients with diabetes or renal failure), it is recommended to decrease the blood pressure values under 140 mm Hg for systolic blood pressure and 90 mm Hg for diastolic blood pressure.
### Results for Clinical Guidelines on Stroke

<table>
<thead>
<tr>
<th></th>
<th>Expert 1</th>
<th>Expert 2</th>
<th>Expert 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recall</td>
<td>0.99 (IC 95%: 0.96 - 1)</td>
<td>0.93 (IC 95%: 0.88 - 0.98)</td>
<td>0.81 (IC 95%: 0.74 - 0.88)</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.89 (IC 95%: 0.83 - 0.94)</td>
<td>0.93 (IC 95%: 0.89 - 0.98)</td>
<td>0.82 (IC 95%: 0.76 - 0.89)</td>
</tr>
<tr>
<td>Precision</td>
<td>0.92</td>
<td>0.96</td>
<td>0.92</td>
</tr>
<tr>
<td>Noise</td>
<td>0.11</td>
<td>0.07</td>
<td>0.18</td>
</tr>
<tr>
<td>F-measure</td>
<td>0.95</td>
<td>0.94</td>
<td>0.86</td>
</tr>
</tbody>
</table>

- The proportion of sentences correctly marked-up by G-DEE among the recommendations identified as such by experts [81% – 99%]

- The proportion of sentences not marked-up by G-DEE among the sentences that are not identified as recommendations by experts [82% - 93%]
## Results for Clinical Guidelines on Hypertension

<table>
<thead>
<tr>
<th></th>
<th>Expert 1</th>
<th>Expert 2</th>
<th>Expert 3</th>
<th>Expert 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recall</strong></td>
<td>0.91</td>
<td>0.86</td>
<td>0.83</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>(IC 95% : 0.86 - 0.95)</td>
<td>(IC 95% : 0.80 - 0.91)</td>
<td>(IC 95% : 0.77 - 0.89)</td>
<td>(IC 95% : 0.80 - 0.91)</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>0.84</td>
<td>0.93</td>
<td>0.96</td>
<td>0.88</td>
</tr>
<tr>
<td></td>
<td>(IC 95% : 0.78 - 0.90)</td>
<td>(IC 95% : 0.89 - 0.97)</td>
<td>(IC 95% : 0.93 - 0.99)</td>
<td>(IC 95% : 0.83 - 0.93)</td>
</tr>
<tr>
<td><strong>Precision</strong></td>
<td>0.88</td>
<td>0.95</td>
<td>0.98</td>
<td>0.92</td>
</tr>
<tr>
<td><strong>Noise</strong></td>
<td>0.16</td>
<td>0.07</td>
<td>0.04</td>
<td>0.12</td>
</tr>
<tr>
<td><strong>F-measure</strong></td>
<td>0.89</td>
<td>0.90</td>
<td>0.90</td>
<td>0.89</td>
</tr>
</tbody>
</table>
Automatic recognition of deontic operators using a dedicated FSTN parser can support the automatic structuring of the document.

Preliminary evaluation on 2 complete Clinical Guidelines:
- "Stroke": precision 92-96% / recall 81%-99%
- "Hypertension": precision 88%-98% / recall 83%-91%

The automatic detection of deontic operators can be a useful step to support Clinical Guidelines encoding in document-based approaches such as GEM.
G-DEE can be useful to help the structuring of clinical guidelines during their authoring.

G-DEE is currently integrated into the development process of French guidelines (managed by the French National Authority for Health (HAS)).

Impact of G-DEE

- Identification of document structure problems
- Re-writing recommendations which are not explicit enough, or ambiguous
- Production of summaries from marked-up clinical guidelines