Ontology Driven Decision Support Systems for Medical Diagnosis: An interactive form for consultation in patients with plasma cell disease

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INTRODUCTION

- Previous work shows how to create an ontology driven rules base for expert system (Bertaud-Gounot, Donfack Guefack, Lasbleiz, Bourdé, & Duvaufrier, 2011)

- **Aim:**
  - Operationalize an ontology for plasma cells diseases
  - Construct an interactive form aiding in the medical diagnosis
  - Validate and evaluate on sixty-three medical reports
MATERIALS

- **NCI-T (v10.7)**: 80,000 classes, 187 properties (relations), 57,000 restrictions

- **Protégé 3.4.2**

- **OWL and SWRL languages**

- **OWL and Jess API’s with Java language**

- **Pellet reasoner 1.5.2**

- **Sixty-three medical reports**
METHODS (1/3)

- Extracting a subontology (plasma cell disease) from NCI-T
- Concept reorganization
Methods (2/3)

Concept addition

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Disease definition</th>
</tr>
</thead>
</table>
| Monoclonal gammopathy of undetermined significance (MGUS) | All three criteria must be met:  
- Serum monoclonal protein < 3 g/dL  
- Clonal bone marrow plasma cells < 10%  
- Absence of end-organ damage such as hypercalcemia, renal insufficiency, anemia, and bone lesions (CRAB) that can be attributed to the plasma cell proliferative disorder; or in the case of IgM MGUS, no evidence of anemia, constitutional symptoms, hyperviscosity, lymphadenopathy, or hepatosplenomegaly that can be attributed to the underlying lymphoproliferative disorder. |

- Plasma_Cell_Neoplasm
- Disease_Has_Associated_Anatomic_Site only Hematopoietic_System
- Disease_Has_Finding only Monoclonal Paraproteinemia Present in Lower than Myeloma Levels
- Disease_Has_Finding only Neoplastic_Plasmacellular_Cells_Under_10_Percent_of_Bone_Marrow_Nucleated_Cells
- Disease_Has_Finding only Stable_Disease
- Disease_Has_Normal_Cell_Origin only Bone_Marrow-Homing_Plasmacellular
- Disease_May_Have_Molecular_Abnormality some Clonal_Immunoglobulin_Gene_Rearrangement
Methods (3/3)

- Adding a SWRL rule layer for abductive reasoning according to (Bertaud-Gounot, Donfack Guefack, Lasbleiz, Bourdé, & Duvaufrier, 2011)

- Storing production rules in a relational database

- Building the form according to the ontology contains (signs observed in patients)
RESULTS (1/7)

- Concept reorganization

(1)

- Hematopoietic_System_Disorder
- Hematologic_Disorder
- Hematopoietic_Cell_Neoplasm
- Leukemia
- Lymphocytic_Neoplasm
- B-Cell_Lymphocytic_Neoplasm
- Mature_B-Cell_Lymphocytic_Neoplasm
- Plasma_Cell_Neoplasm
- Monoclonal_Gammopathy_of_Undetermined_Significance

(2)

- Precancerous.Condition
- Precancerous.Condition_by_Site
- Premalignant_Hematologic.Condition
- Atypical_Lymphoproliferative_Disease
- U936_Monoclonal_Gammopathy_MGUS
- Monoclonal_Gammopathy_of_Undetermined_Significance_MGUS_Not_IgM_Or_Not_Light_Chain_MGUS
- U936_IgM_Monoclonal_Gammopathy_of_Undetermined_Significance_Or_IgM_MGUS
- U936_Light_Chain_Monoclonal_Gammopathy_Of_Undertermined_Significance_Or_Light_Chain_MGUS
RESULTs (2/7)

- Concept addition

Serum monoclonal protein < 3g/dl

Hypercalcemia
RESULTS (3/7)

- Adding new roles and SWRL rule

- Finding_Absence_Excludes_Diagnosis
- Finding_Absence_Has_Diagnosis
- Finding_Excludes_Diagnosis
- Finding_Has_Diagnosis


\[
\begin{align*}
&\text{Finding}(?y) \land \text{Disease\_May\_Have\_Finding}(?x, ?y) \rightarrow \text{Finding\_Has\_Diagnosis}(?y, ?x) \\
&\text{Finding}(?y) \land \text{Disease\_Excludes\_Finding}(?x, ?y) \rightarrow \text{Finding\_Excludes\_Diagnosis}(?y, ?x) \\
&\text{Finding}(?y) \land \text{Disease\_Has\_Finding}(?x, ?y) \rightarrow \text{Finding\_Absence\_Excludes\_Diagnosis}(?y, ?x) \\
&\text{Finding}(?y) \land \text{Disease\_Excludes\_Finding}(?x, ?y) \rightarrow \text{Finding\_Absence\_Has\_Diagnosis}(?y, ?x)
\end{align*}
\]
RESULTS (4/7)

Creation the prototypical cases

Terminological and assertional definition of MGUS
**RESULTS (5/7)**

- Generation and storage of semiological rules

OWL Ontology → Jess engine → 1710 production rules

**4 SWRL rules (1st order logic)**

- $\rightarrow$ Finding(?y) ∧ Disease_May_Have_Finding(?x, ?y) → Finding_Has_Diagnosis(?y, ?x)
- $\rightarrow$ Finding(?y) ∧ Disease_Excludes_Finding(?x, ?y) → Finding_Excludes_Diagnosis(?y, ?x)
- $\rightarrow$ Finding(?y) ∧ Disease_Has_Finding(?x, ?y) → Finding_Absence_Excludes_Diagnosis(?y, ?x)
- $\rightarrow$ Finding(?y) ∧ Disease_Excludes_Finding(?x, ?y) → Finding_Absence_Has_Diagnosis(?y, ?x)
## Results (6/7)

### Query Form

<table>
<thead>
<tr>
<th>Finding</th>
<th>Present</th>
<th>Absent</th>
<th>Undecided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oesophageal Disorder</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Rectal Cleft</td>
<td></td>
<td></td>
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<tr>
<td>Hyperkalemia</td>
<td></td>
<td></td>
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<tr>
<td>Haemolysis</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Light Chain Deposition</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Renal Insufficiency</td>
<td></td>
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<tr>
<td>Monoclonal Paraproteins_Present_in_Lower_than_Myeloma_Level</td>
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<tr>
<td>Thrombocytosis</td>
<td></td>
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<tr>
<td>U936_Hemoglobin_Measurement_F0m_Men_Between_11_and_17_0_FrEd</td>
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</tr>
<tr>
<td>U936_Hemoglobin_Measurement_F0m_Men_Between_10_and_19_0_FrEd</td>
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<tr>
<td>U936_Hemoglobin_Measurement_F0m_Men_Between_9_and_15_0_FrEd</td>
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<tr>
<td>U936_Hemoglobin_Measurement_F0m_Men_Under_11_0_FrEd</td>
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<tr>
<td>U936_Hemoglobin_Measurement_F0m_Men_Under_2_0_FrEd</td>
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</tr>
<tr>
<td>U936_Hemoglobin_Measurement_Not_Pregnant_WoMen_Between_11_and_17_0_FrEd</td>
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<tr>
<td>U936_Hemoglobin_Measurement_Not_Pregnant_WoMen_Under_2_0_FrEd</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>U936_Hypokalemia</td>
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<tr>
<td>U936_IgA_Serum_Measurement_Between_3_and_5_0_FrEd</td>
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<tr>
<td>U936_IgA_Serum_Measurement_Under_2_0_FrEd</td>
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<tr>
<td>U936_IgA_Serum_Measurement_More_Than_2_0_FrEd</td>
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<tr>
<td>U936_IgA_Serum_Measurement_More_Than_5_0_FrEd</td>
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<tr>
<td>U936_IgA_Serum_Measurement_Under_3_0_FrEd</td>
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<tr>
<td>U936_IgA_Serum_Measurement_Under_5_0_FrEd</td>
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<tr>
<td>U936_IgA_Serum_Measurement_Under_3_0_FrEd</td>
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<tr>
<td>U936_IgA_Serum_Measurement_Under_5_0_FrEd</td>
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<tr>
<td>U936_IgG_Serum_Measurement_Between_3_and_5_0_FrEd</td>
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<td>U936_IgG_Serum_Measurement_More_Than_5_0_FrEd</td>
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<tr>
<td>U936_IgG_Serum_Measurement_Under_3_0_FrEd</td>
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<tr>
<td>U936_IgG_Serum_Measurement_Under_5_0_FrEd</td>
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<tr>
<td>U936_IgM_Serum_Measurement_More_Than_6_Equal_3_0_FrEd</td>
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<tr>
<td>U936_Kappa_Fosc_Gradient_Small_More_Than_3_63</td>
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</table>
### RESULTS (7/7)

Results form

<table>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1261_Serum_Calcium_Measurement_More_Than_2.6_Or_3_Mmole/L</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
<td>1261_Serum_Calcium_Measurement_More_Than_2.6_Or_3_Mmole/L</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
<td>1261_Serum_Calcium_Measurement_More_Than_2.6_Or_3_Mmole/L</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
</tr>
<tr>
<td>1261_Bicarbonate_Measurement_Below_16_Mmole/L</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
<td>1261_Bicarbonate_Measurement_Below_16_Mmole/L</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
<td>1261_Bicarbonate_Measurement_Below_16_Mmole/L</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
</tr>
<tr>
<td>1261_Range_Measurement_Sodium_Below_135_Mmole/L</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
<td>1261_Range_Measurement_Sodium_Below_135_Mmole/L</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
<td>1261_Range_Measurement_Sodium_Below_135_Mmole/L</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
</tr>
<tr>
<td>1261_Range_Measurement_K_Or_K_</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
<td>1261_Range_Measurement_K_Or_K_</td>
<td>Finding</td>
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<td>1261_Range_Measurement_K_Or_K_</td>
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<td>Age, Gender</td>
<td>Finding</td>
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<tr>
<td>1261_Range_Measurement_Potassium_Below_3_Mmole/L</td>
<td>Finding</td>
<td>Age, Gender</td>
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<td>1261_Range_Measurement_Potassium_Below_3_Mmole/L</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
<td>1261_Range_Measurement_Potassium_Below_3_Mmole/L</td>
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<td>Age, Gender</td>
<td>Finding</td>
</tr>
<tr>
<td>1261_Range_Measurement_Alt</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
<td>1261_Range_Measurement_Alt</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
<td>1261_Range_Measurement_Alt</td>
<td>Finding</td>
<td>Age, Gender</td>
<td>Finding</td>
</tr>
</tbody>
</table>

Available at: [http://nautilus.univ-rennes1.fr:8080/AppDiagnosticRatioWithDetail/saveDiagnostic.do](http://nautilus.univ-rennes1.fr:8080/AppDiagnosticRatioWithDetail/saveDiagnostic.do)
CONCLUSION

❖ Formal ontology in medical diagnosis process
  ➢ Diagnostic accuracy 90% (90% well classified, 10% misclassified)
  ➢ Presentation of explanation (diagnosis with his present, absent and missing signs)
  ➢ Entry form developing on demand (based on ontology)
  ➢ Availability of tools for consistency checking (like Pellet)

❖ Improvements are needed
  ➢ Better classification of possible diagnoses with the use of probability
  ➢ Multi-centric evaluation
Thank you for your attention


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METHODS

• Abductive reasoning

  – Ontology classifiers (Pellet, FACT ...): deductive reasoning.
    • IF (a → b) and (a is true), THEN (b is true)

  – Diagnostic process needs abductive reasoning (Vertue & Haig, 2008) (Fischer & Heidelberg, 1978)
    • IF (a → b) and (b is true), THEN (a is possibly true)

⇒ SWRL rules to introduce abductive reasoning in compliance to (Bertaud-Gounot, Donfack Guefack, Lasbleiz, Bourdé, & Duvaufrierer, 2011)
METHODS

OWL Ontology

SWRL rules (1st order logic)

Jess engine

Rules (0 order logic)

Knowledge base (Database)

User entry form

John SMITH’s possible diagnoses

John SMITH’s findings

John SMITH’s findings

Methods
### Signs

<table>
<thead>
<tr>
<th>Clinical Signs</th>
<th>Present</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aggressive_Clinical_Course</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone_Pain</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Impotence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable_Disease</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Systemic_Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unfavorable_Clinical_Outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gynecomastia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### List of diagnoses:
- Solitary_Osseous_Plasmacytoma_0 (signs number: 2/6)
- Extramedullary_Plasmacytoma_0 (signs number: 1/4)
- Solitary_Plasmacytoma_0 (signs number: 1/3)
- Plasmacytoma_0 (signs number: 1/2)
- Monoclonal_Gammopathy_of_Undetermined_Significance_0 (signs number: 1/4)
- Stage_III_Multiple_Myeloma_0 (signs number: 1/6)
- Chest_Wall_Solitary_Plasmacytoma_0 (signs number: 1/2)

#### List of excluded diagnoses:
- Smoldering_Myeloma_0 (signs number: 2)
- Indolent_Myeloma_0 (signs number: 2)