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Validating the semantics of a medical iconic language using ontological reasoning

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ABSTRACT

To help clinicians read medical texts such as clinical practice guidelines or drug monographs, we proposed an iconic language called VCM. This language can use icons to represent the main medical concepts, including diseases, symptoms, treatments and follow-up procedures, by combining various pictograms, shapes and colors. However, the semantics of this language have not been formalized, and users may create inconsistent icons, e.g. by combining the "tumor" shape and the "sleeping" pictograms into a "tumor of sleeping" icon. This work aims to represent the VCM language using DLs and OWL for evaluating its semantics by reasoners, and in particular for determining inconsistent icons.

We designed an ontology for formalized the semantics of VCM icons using the Protégé editor and scripts for translating the VCM lexicon in OWL. We evaluated the ability of the ontology to determine icon consistency for a set of 100 random icons. The evaluation showed good results for determining icon consistency, with a high sensitivity. The ontology may also be useful for the design of mapping between VCM and other medical terminologies, for generating textual labels for icons, and for developing user interfaces for creating VCM icons.

1. Introduction

The enormous growth of knowledge and the increasing availability of online resources have made access to medical information an important issue. Clinicians can be overwhelmed by the amount of medical knowledge available; they have very limited time to read clinical guidelines and drug dictionaries, and may have difficulties in accessing large patient records. Reading medical information and knowledge is particularly problematic as it is traditionally presented in a textual format, although it is well established that a graphical presentation can be more efficient. Indeed, Paivio [1] showed that verbal (i.e. textual) and non-verbal (i.e. image) information are treated by different cognitive processes, with different abilities. Various works have shown that graphical presentations can be more efficient than textual ones in medicine [2–4]. In a previous study [5], we proposed VCM (*Visualisation des Connaissances Médicales*, French acronym for Medical Knowledge Visualization), an iconic language for representing major medical concepts: patients' clinical conditions, symptoms, diseases, physiological states, risks or antecedents of diseases, drug and non-drug treatments, lab tests and follow-up procedures. VCM has subsequently been used in a graphical interface for accessing drug knowledge, and we have shown that it allowed physicians to access drug knowledge faster and with fewer errors than through a textual interface [6]. VCM was initially devoted to drug knowledge, but has been recently extended for other medical applications [7], including Electronic Health Records (EHRs), decision support systems and search engines.

The VCM language provides a graphical combinatory grammar for generating icons from a restricted set of shapes, pictograms and colors. For example, the icon for representing "tumor of the stomach" is generated by combining a pictogram representing the stomach, a red color (meaning current patient state), and a square (meaning pathological state) with two cells in the process of dividing (meaning tumor). The use of a combinatory grammar makes it possible to generate billions icons from a hundred of primitive shapes, pictograms and colors. However, *inconsistent* icons, i.e. icons that are absurd from a medical point of view, may also be generated. For example, the two cells in division (meaning tumor) can be combined with the pictogram with a "Z" in a bubble (meaning sleep): the resulting icon would be interpreted as "tumor of sleeping" which has no medical meaning and is thus inconsistent.

Unfortunately, such inconsistent icons are problematic, because VCM allows the user to create icons by combining the various pictograms, shapes and colors. Examples of situations in which users may have to create icons are: (a) a physician creating icons for indicating the patient's clinical conditions, diseases or antecedents in an EHR, (b) a medical expert associating VCM icons to a reference document, e.g. a clinical guideline, to improve the readability of the document, and (c) a terminology expert developing mappings

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between VCM and a medical terminology, to associate icons with the terms of the terminology. In these situations, inconsistent icons are not desired, and could only result from a slip (e.g. the user clicked on the wrong button when choosing the icon) or a misunderstanding of the VCM language. Additionally, among all the possible VCM icons that could be created by the combinatory process (e.g. in a cache on a server), a large proportion would be inconsistent.

Consistency checking has been widely studied for auditing medical terminologies [8], and tracking inconsistent terms. Zhu et al. [9] distinguished two categories of methods for searching for inconsistent terms in a medical terminology: *linguistic-based methods* searching for lexical inconsistency (e.g. is the word "congenital" used consistently across a terminology of diseases?), and *ontological methods* searching for inconsistent classifications (e.g. is there a term classified as both a plant and an animal?). Both of these types of method can rely either on *extrinsic knowledge*, i.e. the terminology is compared to another source of knowledge such as another terminology, or on *intrinsic knowledge*, i.e. the terminology's consistency is checked with regards to knowledge inferred from the terminology itself, either manually or automatically. Zhu et al. distinguish between *manual* auditing methods, *automated heuristic* methods (which still require a manual validation of the inconsistencies found) and *automated systematic* methods (no manual intervention at all is required).

However, linguistic methods, and in particular string-based methods, are not well-suited for iconic languages, and the large number of possible icons in VCM makes manual operations impractical. Therefore we preferred automated systematic ontological methods for checking icon consistency. Such methods typically consist of (1) formally defining *restrictions* (also called *rules* or *constraints*) that are derived from another terminology (in the case of extrinsic knowledge) or that are implicit in the terminology (in case of intrinsic knowledge), and then (2) searching for terms or concepts violating these restrictions [9]. Ontologies represented using formal languages, such as Description Logics (DLs) [10], have been frequently used for expressing the restrictions (mainly for restricting the domains and ranges of relations) in these methods. For example, diseases could be described as concepts that have for finding site only anatomical sites, such that: "have finding site" is the relation, "disease" is the domain, "anatomical sites" is the range and "only" is the restriction on the range. The use of DLs has several advantages including the possibility of exploiting advanced inference services (satisfiability, subsumption, classification, consistency checking, instantiation and realization) [11] provided by reasoners.

During the GALEN project [12], these methods were applied by Rector et al. [13] in the GALEN Representation And Integration Language (GRAIL) for restricting medical terminologies to *sensible* (i.e. not non-sense) concepts. Similar methods have been applied, alone or in combination with others, to many medical terminologies including the Medical Subject Heading (MeSH) [14], the Standardized Nomenclature of Medicine Clinical terms (SNOMED CT) [15–17], the International Classification of Diseases 10th release (ICD10) [18], the Foundational Model of Anatomy (FMA) [19,20] and the National Cancer Institute (NCI) thesaurus [21,22]. Several studies have also checked the consistency of the Unified Medical Language System (UMLS) [23–25]. In particular, these methods have been used for verifying the consistency of *post-coordinated* terms. In some terminologies, *post-coordination* is a mechanism that lets the user create new terms by combining existing terms (e.g. combining the terms "anemia" and "severe" for creating "severe anemia"). This mechanism is very similar to the construction of a VCM icon, and can also lead to inconsistent terms. Both Navas et al. [26] and Cornet [27] proposed using rules expressed in DLs for verifying the consistency of post-coordinated terms.

Many of these studies use the Ontology Web Language (OWL) for representing DLs. OWL is the W3C standard for ontologies on the Semantic Web [28]. It has several advantages for ontologies in medicine: interoperability, semantics and reasoning services (see [29] for an overview of biomedical information services that can be supported by medical ontologies). Another practical benefit of OWL is that it allows the multitude of existing tools freely available online to be exploited, including in particular ontology editors such as Protege [30] and several powerful reasoners such as HermiT [31] and Pellet [32].

The objective of the work reported here is to represent the VCM language using DLs and OWL for evaluating its semantics by reasoners, and in particular for identifying inconsistent icons. We will first introduce the VCM language briefly. Then we will describe the modeling choices for the ontology and the evaluation methodology. In the results section, we will describe the ontology and give the evaluation results. Finally, we will discuss the difficulties encountered when formalizing this iconic language, and the perspectives for the VCM icon ontology beyond the determination of icon consistency.

2. Background: the VCM iconic language

The VCM language proposes icons for representing the patient's main clinical conditions, including symptoms, diseases, physiological states (e.g. age class or pregnancy), risks and history of diseases, drug and non-drug treatments, lab tests and follow-up procedures. However, it does not aim to achieve the same level of detail as possible with textual language. VCM includes a set of graphical primitives (shapes, pictograms and colors), and a graphical grammar to combine these elements for creating icons.

Fig. 1 illustrates graphical combinations of the various elements. A VCM icon can be described by a color,[1] a basic shape and a set of shape modifiers, a central pictogram, a top-right color and one or two top-right pictograms; Fig. 2 shows the VCM syntax in Backus-Naur Form (BNF). A simple icon can be created by combining (1) a color indicating the temporal aspect of the icon: red for current states of the patient, orange for risk of future states, and brown for past states (*i.e.* antecedents or history), (2) a basic shape: a circle for physiological states or a square for pathological states (diseases or symptoms), and (3) a central white pictogram indicating the anatomico-functional location (e.g. heart, lung, etc.) or the patient characteristic (e.g. pregnancy) involved. Anatomic structures and their corresponding functions are usually represented by the same pictogram (e.g. lung and respiration share the same pictogram).

Icons for treatments and follow-up procedures are created from the icon for the disease treated or the risk of disease followed-up, by adding a top-right pictogram in green (for treatment) or blue (for follow-up procedure). The shape of the top-right pictogram indicates the type of treatment (drug treatment, oral drug or surgery, for example) or follow-up procedure (including lab tests and medical imaging).

More details can be added to a simple disease or symptom icon. We distinguished two types of disease and symptom: (1) those specific to an anatomico-functional location, and they are represented by using a modified central pictogram (e.g. vomiting is a symptom specific to the stomach) and (2) those that are general and involve a morphology that can occur in many anatomico-functional locations (e.g. tumor, infection or functional deficiency); these are represented by adding a shape modifier to the square basic shape (for instance, tumor is represented by two cells in

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[1] For interpretation of color in Fig. 1, the reader is referred to the web version of this article.

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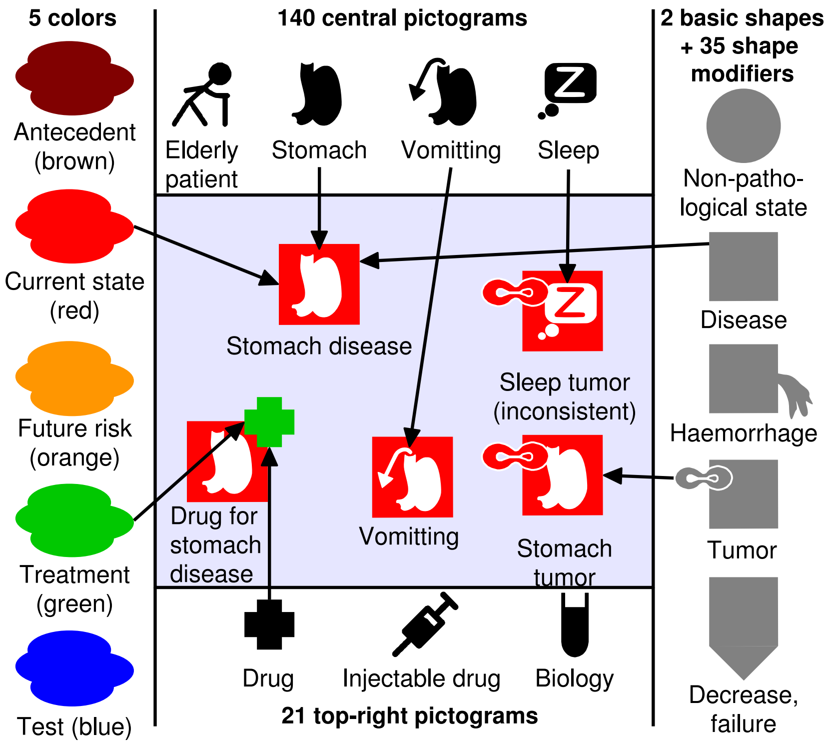

Fig. 1. Examples of VCM icons, created by combining various shapes, pictograms and colors. The simple "stomach disease" icon is created by assembling the red color (meaning current state), the square (meaning disease) and the stomach pictogram. It can then be further modified to create (a) the "Drug for stomach disease" icon by adding a green cross top-right pictogram (meaning drug treatment), (b) the "Vomiting" icon by using a more precise pictogram (meaning vomiting), or (c) the "Stomach tumor" icon by adding a shape modifier showing two cells in division (meaning tumor).

```
<icon> ::= <main color> + <shape> + [<central pictogram>] + [<first top-
right element>] + [<second top-right element>]
<main color> ::= <current disease color> | <risk color> | <antecedent color>
<current disease color> ::= red
<risk color> ::= orange
<antecedent color> ::= brown
<shape> ::= circle | (square + [{<pathological shape modifier>}]) + [{<non pathologi-
cal shape modifier>}]
<pathological shape modifier> ::= <etiologic shape modifier> | <generic dis-
ease shape modifier>
<etiologic shape modifier> ::= virus shape modifier | bacteria shape modifier |...
<generic disease shape modifier> ::= failure shape modifier | pain shape modifier |...
<non pathological shape modifier> ::= blood vessel shape modi-
fier | metabolism shape modifier |...
<central pictogram> ::= <anatomico-functional pictogram> | <anatomic region pic-
togram> | <patient characteristic pictogram> | <specific disease pictogram>
<anatomico-functional pictogram> ::= heart pictogram | sleep pictogram |...
<anatomic region pictogram> ::= head pictogram | thorax pictogram |...
<patient characteristic pictogram> ::= male pictogram | child pictogram |...
<specific disease pictogram> ::= vomiting pictogram | diabetes pictogram |...
<first top-right element> ::= (green + <treatment pictogram>) | (blue + <exam pic-
togram>)
<treatment pictogram> ::= drug pictogram | surgery pictogram |...
<exam pictogram> ::= lab test pictogram | imagery pictogram |...
<second top-right element> ::= health professional pictogram | medical document pic-
togram
```

Fig. 2. Syntax of VCM icons expressed in Backus-Naur Form (BNF).

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division, bacterial infection by a small bacterium and functional deficiency by a downward arrow).

Anatomical structures belonging to "transversal" systems that are present in many anatomico-functional locations (such as blood vessels and nerves that are present in most organs) are also represented by shape modifiers. This allows a blood vessel located in a specific organ to be represented (e.g. coronary vessels are blood vessels located in the heart). A central pictogram expressing a specific disorder can be combined with shape modifiers, and several shape modifiers can be applied to the same icons as long as they do not overlap spatially.

Finally, a second top-right pictogram can be added to represent health professionals or medical documents, e.g. the cardiologist icon is created by adding the health professional top-right pictogram to the cardiac disease icon.

More details can be found in the article describing the VCM language [5].

3. Materials and methods

3.1. Materials

We used the Protégé ontology editor version 4.1 beta for editing the OWL-DL ontology, and the HermiT OWL reasoner version 1.2.4 for detecting inconsistent concepts. Python scripts were used for generating OWL files from text files.

3.2. Building the ontology

The ontology needs to take two types of constraints into account: (a) *graphical constraints* (e.g. the shape modifiers meaning "tumor" and "virus" are placed at the same location on a VCM icon, and thus they cannot be used simultaneously), and (b) *medical constraints* similar to those encountered when verifying medical terminologies (e.g. a tumor "is a" morphology that can occur in an anatomical structure, but not in a biological function). Consequently, the ontology has been developed in three parts: a first part describing VCM icons with their graphical constraints, a second part describing medical concepts and constraints, containing anatomical structures and biological functions, and a third part including no new concepts but linking graphical and medical concepts with "represents" and "is represented by" relations (e.g. the lung-shaped pictogram represents the lung organ or the respiratory biological function).

The first part, the graphical part, was automatically generated from the lexicon of VCM colors, pictograms and shape modifiers. The OWL file generated was then manually edited with Protégé for adding the graphical constraints. The second part of the ontology, the medical part, was modeled manually using the Protégé editor. The medical concepts and relations were limited to a low level of precision similar to that of VCM, i.e. an upper level. The third part was automatically generated from a text file listing pairs of the form (graphical concept, medical concept), each concept being present in one or several pairs (e.g. (lung-shaped pictogram, lung organ) and (lung-shaped pictogram, respiration) for the previous lung example).

The ontology was built using an iterative process, each iteration consisting of the following steps: (1) enriching the ontology with new medical concepts and relations, (2) adding a few consistent and inconsistent icons to a test set, (3) executing the reasoner, (4) verifying the consistency of the test icons, and (5) fixing any problems encountered.

3.3. Evaluating the ontology with regards to icon consistency

We evaluated the ontology of VCM icons by determining the consistency of a set of 100 random VCM icons. The consistency of each of these icons was reviewed by four experts with both a medical and a computer science background. Two of them (AV and CD) were involved in the design of the VCM language (but not directly in the design of the ontology). The two other experts had not contributed to the development of VCM; they were trained to the use of VCM with the VCM training software and they were given a paper lexicon of the pictograms used in VCM. Each expert was asked to indicate the consistency of each icon, with two possible values (consistent or inconsistent). The inter-expert agreement was evaluated using Fleiss' Kappa. Disagreements between experts were resolved by seeking a consensus by collective discussion. Sensitivity and specificity were computed. Sensitivity indicates the percentage of inconsistent icons that were found to be inconsistent by the ontology and the reasoner. Specificity indicates the percentage of consistent icons that were found to be consistent by the ontology and the reasoner. The following formulae were used:

$$\text{sensitivity} = \frac{|true\ positives|}{|true\ positives| + |false\ negatives|} \tag{1}$$

$$\text{specificity} = \frac{|true\ negatives|}{|true\ negatives| + |false\ positives|} \tag{2}$$

True positives are icons classified as inconsistent by the ontology and considered to be inconsistent by the experts. *True negatives* are icons classified as consistent by the ontology and considered to be consistent by the experts. *False positives* are icons classified as inconsistent by the ontology, but considered to be consistent by the experts. *False negatives* are icons classified as consistent by the ontology, but considered to be inconsistent by the experts.

In addition, we tested the ability of the ontology to detect inconsistent icons in a real case: the validation of the 521 icons present in the VCM training software. This training software has previously been validated by three VCM experts (JBL, AV and CD) during the design of the VCM language. Thus, it is expected to contain only consistent icons. The ontology was thus used to search for inconsistent icons among these 521 icons.

4. Results

4.1. The ontology of VCM icons

The ontology of VCM icons includes 609 classes, 41 relations and 3,934 axioms. It is represented with the OWL-DL language and belongs to the ALCRIQ Description Logics family. It has been shown that this DL family is decidable [33].

The ontology is composed of three parts: The first part of the ontology describes the VCM icons, and contains 240 classes, 21 relations and 2597 axioms. It includes concepts for the pictograms, shapes and colors used in the VCM language, and graphical constraints for assembling them into icons. In particular, graphical constraints prevent icons with too many components (e.g. an icon with two central pictograms) or overlapping shape modifiers (e.g. the "tumor" and "virus" shape modifier are overlapping). Fig. 3 shows the top of the first part of the ontology.

The second part describes the medical concepts represented by VCM pictograms, shapes and colors: anatomic locations, biological functions, patient characteristics (e.g. age class) and categories of medical treatments, exams and procedures. This second part contains 369 classes, 18 relations and 828 axioms. The basic medical concepts can be used for describing more complex medical concepts, such as patient's clinical conditions, diseases, risks and antecedents, drug treatments, lab tests, medical procedures and health services (e.g. stomach tumor can be described as a disease that affects the stomach and that involves a tumoral process). The

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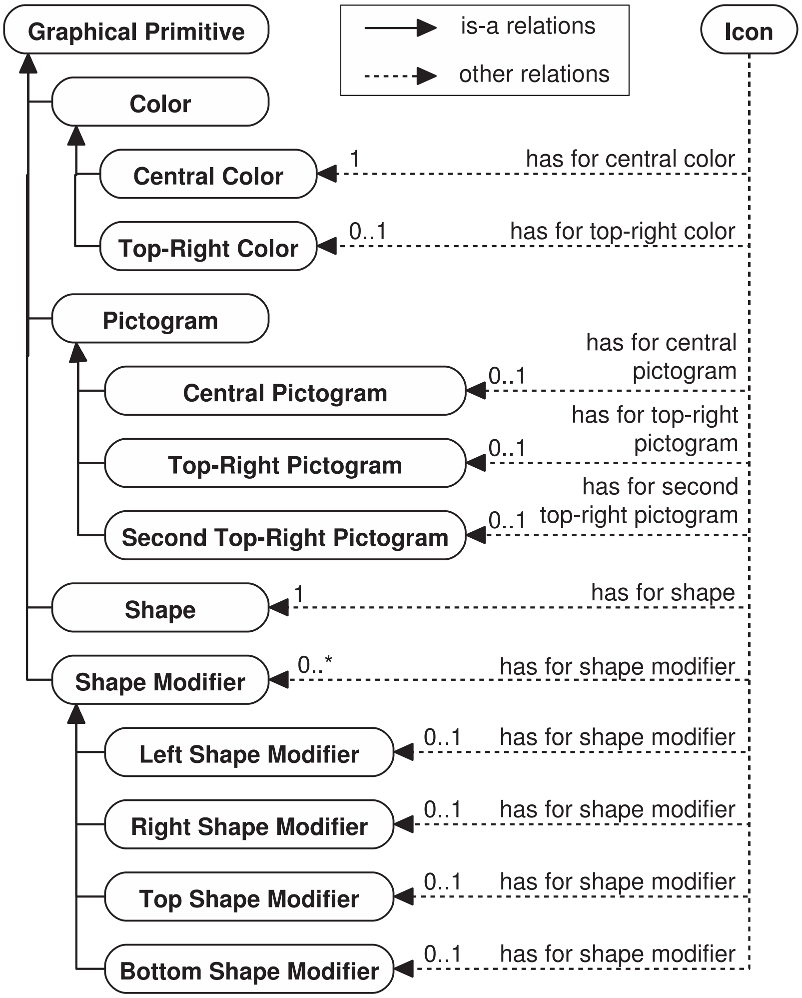

Fig. 3. The top of the first part of the VCM icon ontology, which describes the VCM icons.

medical part of the ontology includes the medical constraints for assembling the basic concepts into complex ones, but not the complex concepts themselves (i.e. the ontology includes the "stomach" and "tumor" concepts, and constraints for post-coordinating them, but not the "stomach tumor" concept). Fig. 4 shows the top of the second part of the ontology, and Fig. 5 shows a sub-part of the TBox describing the two first parts of VCM icon ontology.

The third part of the ontology relates the two other parts with "represent" and "is represented by" relations, including constraints on these two relations. For instance, the central pictogram "heart" is only present in icons that represent medical concepts related to the "heart" organ or the "heart function". The third part contains no classes, two relations and 509 axioms.

Figs. 6–9 show how the "tumor of stomach" and "tumor of sleep" icons can be represented in the ontology. By propagating the constraints of the various parts of the ontology, a reasoner like HermiT determines the consistency of an icon described in the ontology. For instance it deduces that the "tumor of stomach" icon is consistent and that the "tumor of sleep" icon is inconsistent. Supplementary data file "vcm_icon_ontology_example.owl" contains the OWL definitions corresponding to Figs. 6 to 9; it has been tested with Protégé 4.1 and HermiT 1.3.5.

4.2. Evaluation results

The consistency of 100 randomly selected VCM icons was determined by 4 experts. The inter-expert Fleiss' Kappa was 0.47 (moderate agreement). For 61 icons, all the experts were of the same opinion. For the remaining 39 icons, a consensus was obtained by collective discussion. A total of 27 icons were considered as consistent by the experts, 19 of these 27 icons were found consistent by the ontology; 73 icons were scored by the experts as inconsistent and 67 of these 73 were found by the ontology to be inconsistent. Thus, the ontology displayed a sensitivity of 91.8% (CI: 83–96%) and a specificity of 70.4% (CI: 52–84%). The experts and the ontology agreeded on the icon consistency for 86 of the 100 icons (and for 58 of the 61 icons for which all four experts agreed).

Examples of icons scored as inconsistent by experts but as consistent by the ontology (*i.e.* false negatives) included: (a) an icon associating the pregnancy pictogram with the dependency shape modifier, (b) an icon associating the dental pulp pictogram with the nerve shape modifier, for which the evaluators considered that dental pulp was nervous tissue and thus the nerve shape modifier was redundant, (c) icons associating a radiotherapy or a graft treatment exponent with a disease that was considered by evaluators as unlikely to be treated by radiotherapy or grafting (e.g. drug dependence), (d) an icon associating the metabolism shape modifier with a pictogram representing an anatomical location that has limited metabolic activity (e.g. throat and nose).

Examples of icons scored as consistent by experts but as inconsistent by the ontology (i.e. false positives) included: (a) icons for abdominal tumor, thoracic tumor, etc.; in the ontology, the tumor shape modifier was only allowed with organs and cells, but not

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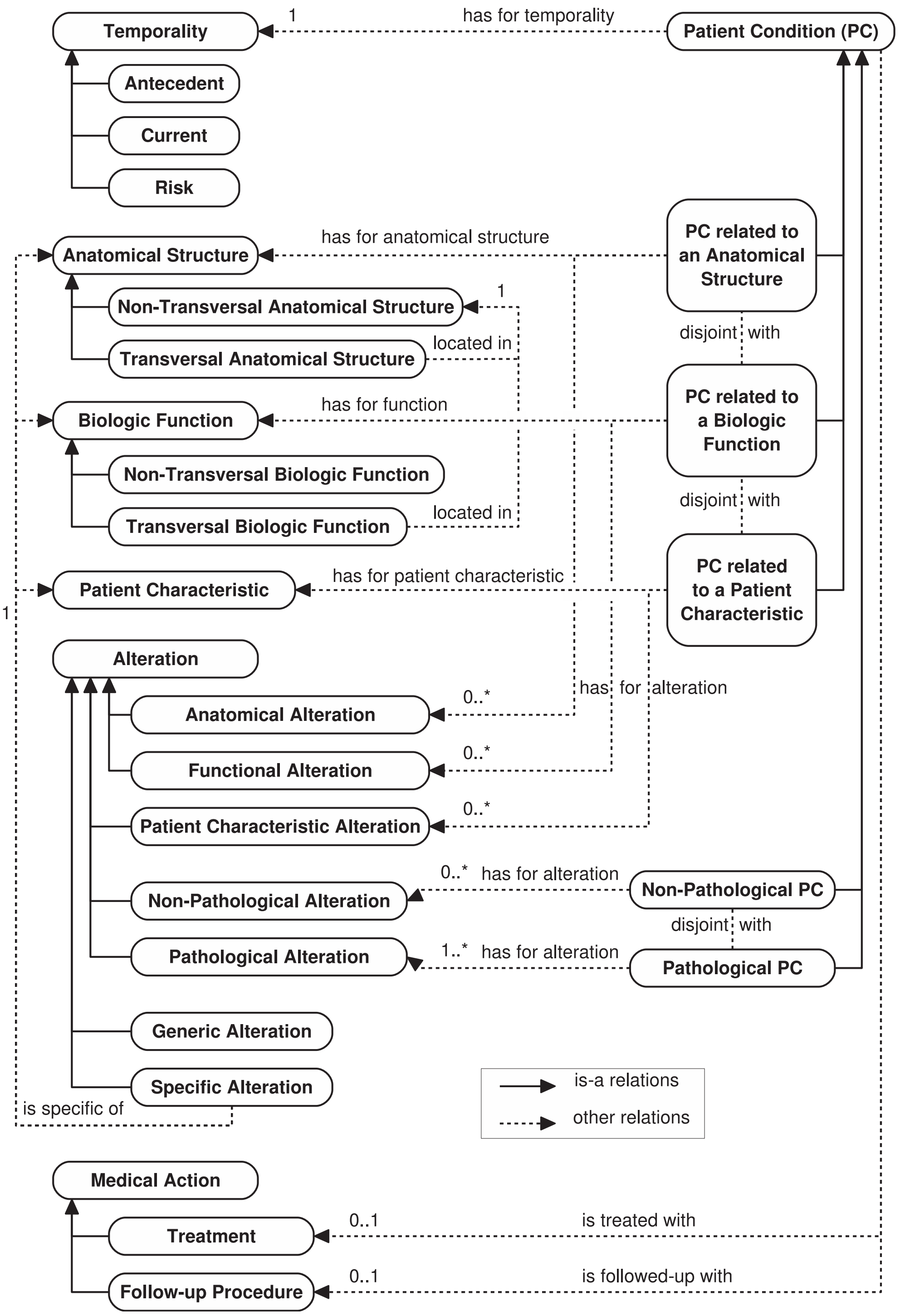

Fig. 4. The top of the second part of the VCM icon ontology, which describes the medical concepts. Patient Condition (PC) related to an Anatomical Structure, PC related to a Biological Function and PC related to a Patient Characteristic are mutually disjointed, as are Pathological PC and Non-Pathological PC. However PC related to an Anatomical Structure is not disjointed from a Pathological PC and Non-Pathological PC, e.g. a given PC can be both related to an Anatomical Structure and Pathological.

with anatomical region, (b) an icon associating the throat and nose pictogram with a functional alteration; the throat and nose pictogram was not considered by the ontology to be able to represent a function, but the evaluators considered that it can represent deglutition, (c) icons including a pictogram specific to a disease (e.g. photosensitization or Paget's disease) combined with additional shape modifiers; in the ontology these pictograms were considered to define the disease fully, such that adding more detail was not allowed, (d) an icon including a patient characteristic pictogram (e.g. weight) and a shape modifier indicating an etiology, and (e) an icon with the patient's entourage pictogram associated with the pathological square shape.

The consistency of the 521 icons of the VCM training software was tested using the ontology; these icons were expected to be consistent. However, the reasoner identified 25 of these icons as being inconsistent; a manual review of these inconsistencies showed that 14 of them were erroneous icons in the training software, five were incomplete (and thus inconsistent) icons that were

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$$
\begin{aligned}
\mathit{Icon} &\sqsubseteq \forall\, \mathit{represents}.\mathit{PC}\\
&\sqcap \forall\, \mathit{has\_central\_color}.\mathit{CentralColor}\\
&\sqcap \forall\, \mathit{has\_central\_pictogram}.\mathit{CentralPictogram}\\
&\sqcap \forall\, \mathit{has\_shape}.\mathit{Shape}\\
&\sqcap \forall\, \mathit{has\_shape\_modifier}.\mathit{ShapeModifier}\\
\mathit{Graphical\_primitive} &\sqsubseteq \top\\
\mathit{Color} &\sqsubseteq \mathit{Graphical\_primitive}\\
\mathit{CentralColor} &\sqsubseteq \mathit{Color}\\
\mathit{TopRightColor} &\sqsubseteq \mathit{Color}\\
\mathit{Pictogram} &\sqsubseteq \mathit{Graphical\_primitive}\\
\mathit{CentralPictogram} &\sqsubseteq \mathit{Pictogram}\\
\mathit{TopRightPictogram} &\sqsubseteq \mathit{Pictogram}\\
\mathit{SecondTopRightPictogram} &\sqsubseteq \mathit{Pictogram}\\
\mathit{Shape} &\sqsubseteq \mathit{Graphical\_primitive}\\
\mathit{Shape\_modifier} &\sqsubseteq \mathit{Graphical\_primitive}\\
\mathit{Left\_shape\_modifier} &\sqsubseteq \mathit{Shape\_modifier}\\
\mathit{Right\_shape\_modifier} &\sqsubseteq \mathit{Shape\_modifier}\\
\mathit{Top\_shape\_modifier} &\sqsubseteq \mathit{Shape\_modifier}\\
\mathit{Bottom\_shape\_modifier} &\sqsubseteq \mathit{Shape\_modifier}\\
\mathit{is\_represented} &\doteq (\mathit{represents})^{-}\\
\mathit{is\_central\_color} &\doteq (\mathit{has\_central\_color})^{-}\\
\mathit{is\_central\_pictogram} &\doteq (\mathit{has\_central\_pictogram})^{-}\\
\mathit{is\_shape} &\doteq (\mathit{has\_shape})^{-}\\
\mathit{is\_shape\_modifier} &\doteq (\mathit{has\_shape\_modifier})^{-}
\end{aligned}
$$

$$
\begin{aligned}
\mathit{PC} &\sqsubseteq \forall\, \mathit{has\_temporality}.\mathit{Temporality}\\
\mathit{Temporality} &\sqsubseteq \top\\
\mathit{PC\_rel\_to\_anat\_str} &\doteq \mathit{PC}\\
&\sqcap \forall\, \mathit{has\_anat\_str}.\mathit{Anatomical\_structure}\\
&\sqcap \forall\, \mathit{has\_alteration}.\mathit{Anatomical\_alteration}\\
\mathit{Anatomical\_structure} &\sqsubseteq \forall\, \mathit{is\_anat\_str}.\mathit{PC\_rel\_to\_anat\_str}\\
\mathit{Anatomical\_alteration} &\sqsubseteq \mathit{Alteration}\\
&\sqcap \forall\, \mathit{is\_alteration}.\mathit{PC\_rel\_to\_anat\_str}\\
\mathit{PC\_rel\_to\_biol\_funct} &\doteq \mathit{PC}\\
&\sqcap \forall\, \mathit{has\_function}.\mathit{Biologic\_function}\\
&\sqcap \forall\, \mathit{has\_alteration}.\mathit{Functional\_alteration}\\
\mathit{Functional\_alteration} &\sqsubseteq \mathit{Alteration}\\
&\sqcap \forall\, \mathit{is\_alteration}.\mathit{PC\_rel\_to\_bio\_func}\\
\mathit{Alteration} &\sqsubseteq \top\\
\mathit{PC\_rel\_to\_anat\_str} \sqcap \mathit{PC\_rel\_to\_bio\_func} &\sqsubseteq \bot\\
\mathit{Pathological\_PC} &\doteq \mathit{PC}\\
&\sqcap \forall\, \mathit{has\_alteration}.\mathit{Pathological\_alteration}\\
\mathit{Pathological\_alteration} &\doteq \mathit{Alteration}\\
&\sqcap \forall\, \mathit{is\_alteration}.(\mathit{PC} \sqcap \forall\, \mathit{is\_represented}.(\mathit{Icon} \sqcap \exists\, \mathit{has\_shape}.\mathit{Square}))\\
\mathit{is\_temporality} &\doteq (\mathit{has\_temporality})^{-}\\
\mathit{is\_anat\_struct} &\doteq (\mathit{has\_anat\_struct})^{-}\\
\mathit{is\_function} &\doteq (\mathit{has\_function})^{-}\\
\mathit{is\_alteration} &\doteq (\mathit{has\_alteration})^{-}
\end{aligned}
$$

Fig. 5. A sub-part of the TBox describing the VCM icon ontology: icon concepts related to medical concepts and their respective roles. The TBox contains primitive and defined concepts and roles expressed in Description Logics. For example, the concept *Icon* has a *central color*, which is a *color*, and it represents a *PC* (Patient Condition). "rel_to" is an abbreviation for "related to", "anat_str" for "anatomical structure", and "bio_func" for "biological function".

used as intermediary results for explaining how to create icons, and six were actually consistent.

Fig. 10 shows some examples of inconsistent icons found during the design of the ontology and the evaluation. Categories of inconsistency could be defined, and some of the major categories were: (1) graphical inconsistencies, i.e. icons with overlapping graphical primitives (see icon (a) in Fig. 10), (2) icons with a blue follow-up procedure exponent and a red central color meaning "current state"; by definition only risks are monitored in VCM (e.g. (b) in Fig. 10), (3) icons including both the non-pathological circle shape and pathological shape modifiers (e.g. (c) in Fig. 10), (4) icons including a shape modifier for a transversal anatomical structure (i.e. meaning "blood vessel of" or "peripheral nervous structure of") but associated to a central pictogram that is not an organ or a tissue (e.g. (d) in Fig. 10), (5) icons with a shape modifier corresponding to a pathological alteration that cannot be applied to the medical concept represented by the central pictogram of the icon (e.g. the "tumor of sleeping" icon, and (e), (f) and (g) in Fig. 10), and (6) icons including a treatment exponent but not associated to a pathological state, or a non-pathological alteration such as pregnancy (e.g. (h) in Fig. 10).

5. Discussion

In this article, we present a method for formalizing an iconic language, i.e. a language that is graphical and not a textual, in

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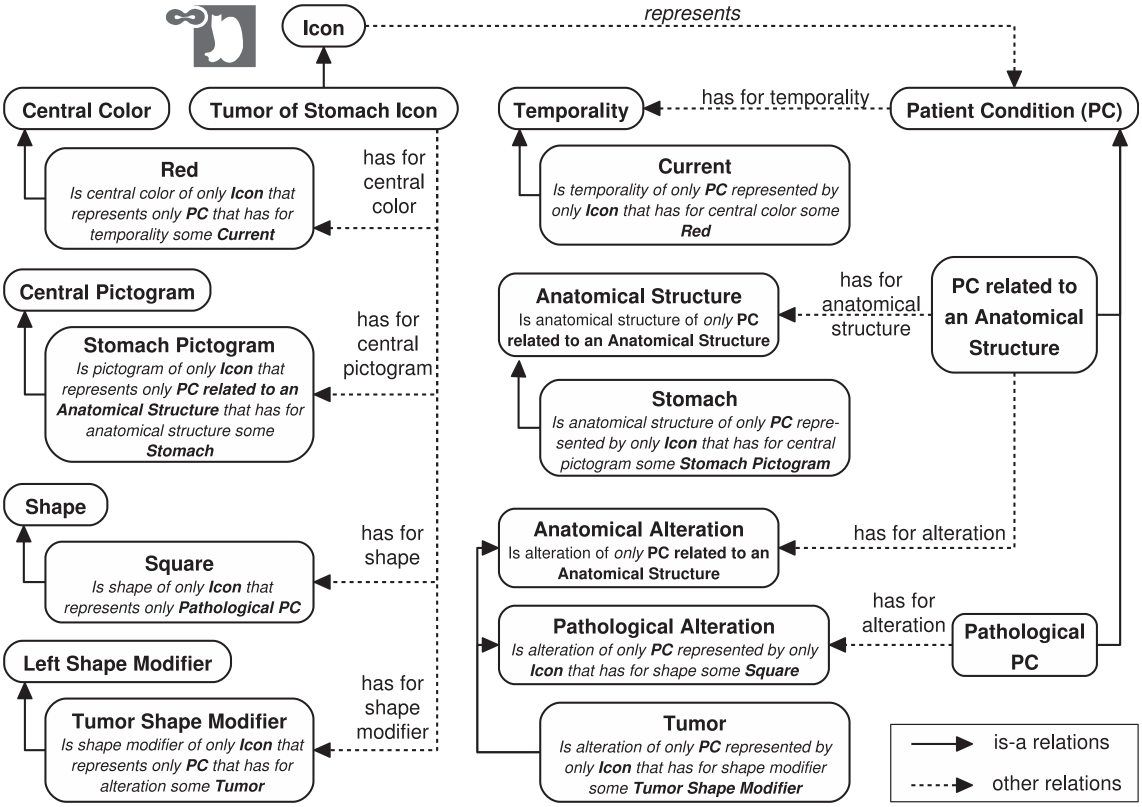

Fig. 6. Example showing how to represent the "tumor of stomach" icon in the VCM icon ontology. The first, graphical, part of the ontology is shown on the left, the second, medical, part on the right, and the third part relating the first two is in italics. Inverse relations are not shown, but can be easily deduced, e.g. "is alteration of" is the inverse relation of "has for alteration". Some restrictions are shown in the boxes and are expressed in English, using a syntax similar to that used in the Protégé editor.

$$
\begin{aligned}
Tumor\_stomach\_icon \doteq\ & Icon \\
\sqcap\ & \forall\, has\_central\_color.Red \\
\sqcap\ & \forall\, has\_central\_pictogram.Stomach\_pictogram \\
\sqcap\ & \forall\, has\_shape.Square \\
\sqcap\ & \forall\, has\_shape\_modifier.Tumor\_shape\_modifier \\
Red \doteq\ & CentralColor \\
\sqcap\ & \forall\, is\_central\_color.(Icon \sqcap \forall\, represents.(PC \sqcap \exists\, has\_temporality.Current)) \\
Stomach\_pictogram \doteq\ & CentralPictogram \\
\sqcap\ & \forall\, is\_central\_pictogram.(Icon \sqcap \forall\, represents.(PC\_rel\_to\_anat\_str \sqcap \exists\, has\_anat\_str.Stomach)) \\
Square \doteq\ & Shape \\
\sqcap\ & \forall\, is\_shape.(Icon \sqcap \forall\, represents.Pathological\_PC) \\
Tumor\_shape\_modifier \doteq\ & Left\_shape\_modifier \\
\sqcap\ & \forall\, is\_shape\_modifier.(Icon \sqcap \forall\, represents.(PC \sqcap \exists\, has\_alteration.Tumor)) \\
\\
Current \doteq\ & Temporality \\
\sqcap\ & \forall\, is\_temporality.(PC \sqcap \forall\, is\_represented.(Icon \sqcap \exists\, has\_central\_color.Red)) \\
Stomach \doteq\ & Anatomical\_struture \\
\sqcap\ & \forall\, is\_anat\_str.(PC \sqcap \forall\, is\_represented.(Icon \sqcap \exists\, has\_central\_pictogram.Stomach\_pictogram)) \\
Pathological\_alteration \doteq\ & Alteration \\
\sqcap\ & \forall\, is\_alteration.(PC \sqcap \forall\, is\_represented.(Icon \sqcap \exists\, has\_shape.Square)) \\
Tumor \doteq\ & Anatomical\_alteration \\
\sqcap\ & Pathological\_alteration \\
\sqcap\ & \forall\, is\_alteration.(PC \sqcap \forall\, is\_represented. \\
& (Icon \sqcap \exists\, has\_shape\_modifier.Tumor\_shape\_modifier))
\end{aligned}
$$

Fig. 7. A sub-part of the TBox related to the concept *Tumor_stomach_icon*, corresponding to the example given in Fig. 6. The concept *Tumor_stomach_icon* is defined as an *Icon* that has *central_color Red*, has a *central_ pictogram Stomach_Pictogram*, has a *Square* as *Shape* and has a *Tumor_shape_modifier* as *shape_modifier*.

Description Logics, focusing on the evaluation of its semantics by reasoners and the determination of the consistency of the icons used. This method is based on a three-part ontology, the first part describing the icons, the second part describing the concepts they mean, and the third part linking the icons to the concepts they represent. The method was successfully applied to the VCM medical iconic language. The evaluation indicated that it gave satisfactory results for determining icons consistency. The fact that we were able to formalize the iconic language with success is an argument in favor of the validity of the construction of the VCM

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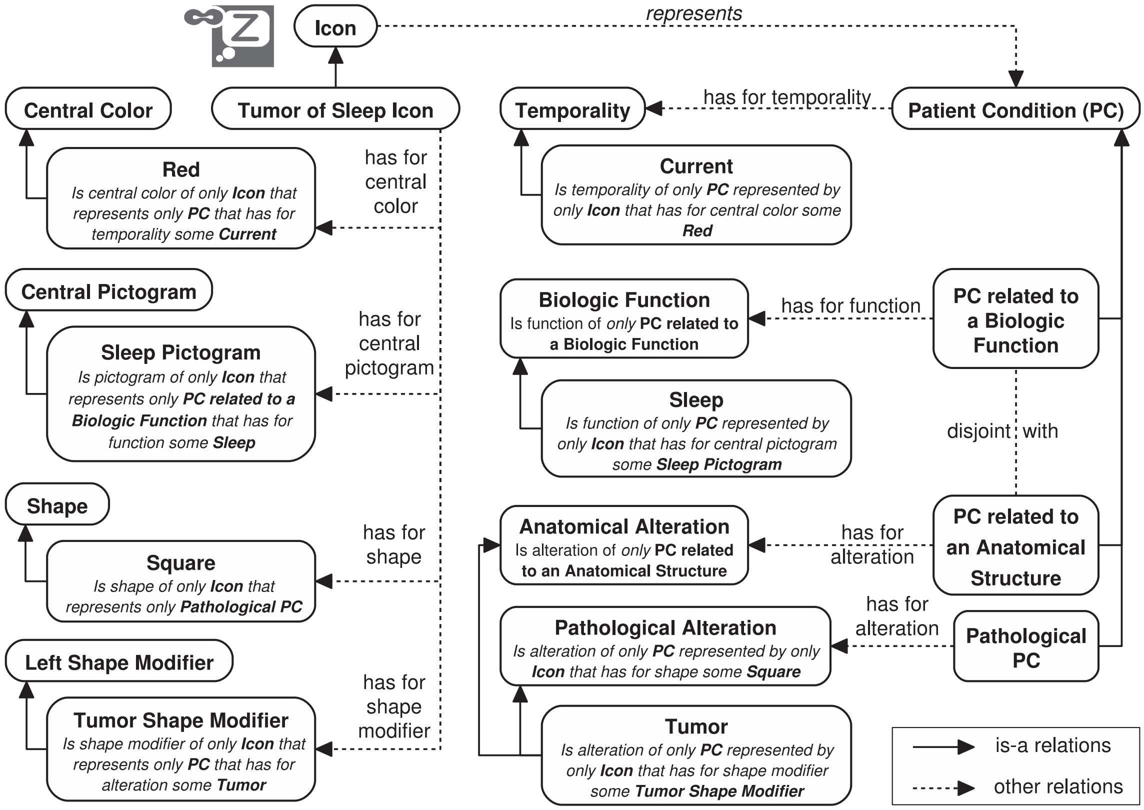

Fig. 8. Example showing how to represent the inconsistent "tumor of sleep" icon in the VCM icon ontology. The inconsistency of the "tumor of sleep" icon can be deduced from the restrictions: (a) the icon has a sleep pictogram, and thus it represents only patient conditions (PC) related to biologic functions, (b) the icon has a tumor shape modifier, and thus it represents only PC that have for alteration a tumor, (c) tumor is an anatomical alteration, and thus is an alteration of only PC related to an anatomical structure, and (d) however, PC related to a biologic function and PC related to an anatomical structure are disjointed.

$$
\begin{aligned}
Tumor\_sleep\_icon \doteq\ & Icon\\
\sqcap\ & \forall\, has\_central\_color.Red\\
\sqcap\ & \forall\, has\_central\_pictogram.Sleep\_pictogram\\
\sqcap\ & \forall\, has\_shape.Square\\
\sqcap\ & \forall\, has\_shape\_modifier.Tumor\_shape\_modifier\\
Red \doteq\ & Color\\
\sqcap\ & \forall\, is\_central\_color.(Icon \sqcap \forall\, represents.(PC \sqcap \exists\, has\_temporality.Current))\\
Sleep\_pictogram \doteq\ & Pictogram\\
\sqcap\ & \forall\, is\_pictogram.(Icon \sqcap \forall\, represents.(PC\_rel\_to\_biol\_funct \sqcap \exists\, has\_function.Sleep))\\
Square \doteq\ & Shape\\
\sqcap\ & \forall\, is\_shape.(Icon \sqcap \forall\, represents.Pathological\_PC)\\
Tumor\_shape\_modifier \doteq\ & Left\_shape\_modifier\\
\sqcap\ & \forall\, is\_shape\_modifier.(Icon \sqcap \forall\, represents.(PC \sqcap \exists\, has\_alteration.Tumor))\\
\\
Current \doteq\ & Temporality\\
\sqcap\ & \forall\, is\_temporality.(PC \sqcap \forall\, is\_represented.(Icon \sqcap \exists\, has\_central\_color.Red))\\
Pathological\_alteration \doteq\ & Alteration\\
\sqcap\ & \forall\, is\_alteration.(PC \sqcap \forall\, is\_represented.(Icon \sqcap \exists\, has\_shape.Square))\\
Tumor \doteq\ & Anatomical\_alteration\\
\sqcap\ & Pathological\_alteration\\
\sqcap\ & \forall\, is\_alteration.(PC \sqcap \forall\, is\_represented.\\
& (Icon \sqcap \exists\, has\_shape\_modifier.Tumor\_shape\_modifier))\\
Sleep \doteq\ & Biologic\_function\\
\sqcap\ & \forall\, is\_function.(PC \sqcap \forall\, is\_represented.(Icon \sqcap \exists\, has\_central\_pictogram.Sleep\_pictogram))
\end{aligned}
$$

Fig. 9. A sub-part of the TBox related to the concept *Tumor_sleep_icon*, corresponding to the example given in Fig. 8. This concept is inconsistent according to the concepts definitions in the TBox

language, which was initially partly intuitive. The ontology has already contributed to the identification of several erroneous icons in the VCM training software. In addition, the proposed method seems to be sufficiently generic to be applied to other medical and even non-medical iconic languages.

The problem of determining the consistency of icons is similar to the detection of inconsistencies in medical terminologies, but we also encountered several difficulties related to the graphical nature of VCM. First, linguistic approaches are not well-suited to iconic languages, and indeed they have mostly been applied to tex-

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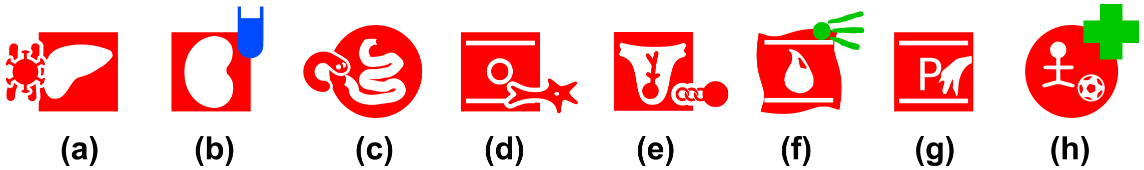

Fig. 10. Various examples of inconsistent VCM icons: (a) genetic viral hepatic disease (while the medical concept might be consistent, the icon is not because the "genetic" and "viral" shape modifiers overlap, producing an unreadable icon), (b) biological test for detecting an already known renal disease, (c) non-pathological parasitic infection of the small intestine, (d) disease of the red cells localized in the peripheral nervous system, (e) dependency on pregnancy, (f) radiotherapy of a congenital malformation of lipemia, (g) edema of phosphoremia, and (h) drug for treating a child (with no associated disease or risk).

tual languages. Second, it is necessary to consider two different types of inconsistency: medical inconsistencies as in medical terminologies, and graphical inconsistencies, e.g. when several parts of an icon overlap. Finally, icons are less precise than text, and thus an iconic language has a lower level of granularity and generates much more polysemy than a typical textual terminology. The use of an ontology including both a medical part and a graphical part resolved these problems; Pisanelli et al. [34] previously highlighted the value of ontologies for dealing with polysemy.

The main problem we encountered when modeling the VCM icon ontology was the incapacity of the OWL-DL language to model relations on object properties (except inverse and is-a relations). For instance, in medicine, etiologies cause diseases, and in VCM, etiological shape modifiers are located at the left side of the icons. We can state in OWL that etiologies are represented by etiological shape modifiers, and that diseases are represented by icons. However we cannot state that the "cause" relation is represented by the "is located at the left side of" relation. A way to work around this problem was to apply the "represent" relation only between icons and diseases, and to state that diseases caused by etiologies are represented by icons with etiological shape modifiers located on the left side of the icons.

Various formalisms have been proposed for representing the semantic and/or syntactic constraints of a language, and in particular for natural language. The *sublanguage theory* [35,36] considers that to each specialized domain (e.g. the medical domain or part of it) corresponds a *sublanguage* of the natural language. A sublanguage is defined by syntactic structures as specified by the grammar of the natural language, but also by domain-specific semantic constraints. For example, in the pharmacy sublanguage, when speaking about "delivery", it is understood that it is a drug that is delivered, whereas in the gyneco-obstetric sublanguage, it is a baby. For formalizing sublanguages, Johnson [37] proposed the use of conceptual graphs extended with syntactic constraints.

For the particular case of pictures, two-dimensional grammars have also been proposed [38], such as tile rewriting grammars [39] or random picture grammars [40]. However, these grammars were developed for picture-recognition, and they consider pictures as rectangular arrays of small squares (e.g. pixels). However, VCM icons are vector images with several pictograms and shape modifiers that can overlap slightly; it would be very difficult to describe them in terms of rectangular arrays.

We chose to formalize the structure of VCM using an ontology rather than a grammatical formalism. Our choice was motivated by the need for rich semantic constraints, for several of the main categories of inconsistencies identified (see the end of the results section). Category (1), graphical inconsistencies (e.g. overlapping shape modifiers), could easily be dealt with using grammatical constraints. By contrast, dealing with categories (4), (5) and (6) is more difficult. Many VCM pictograms can represent several medical concepts depending on the context (e.g. the "lung" pictogram represents the lung organ but also respiration), such that a context-sensitive grammar would be required. Additionally, these categories of inconsistency require domain-specific knowledge. For example, to determine that icon (d) in Fig. 10 (disease of the red cells localized in the peripheral nervous system) is inconsistent, one needs to know that (i) the "red cell" pictogram represents red cells, (ii) nerves are transversal anatomical structures that can only be associated to an innervated organ or tissue, and (iii) red cells are cells but not organ or tissue. The issue can be seen as a classification problem: is the "red cells" pictogram a pictogram that can represent something that is an innervated organ or tissue? This led us to use ontologies. This choice is comparable with the one of Johnson [37], who chose a semantic formalism as a basis for formalizing sublanguages.

Instead of creating the medical part of our ontology from scratch, we could have reused an existing ontology. One possibility was to start from a top ontology. Several upper-level ontologies have been developed and are being maintained, e.g. BFO (Basic Formal Ontology) [41], DOLCE (Descriptive Ontology for Linguistic and Cognitive Engineering) [42], SUMO (Suggested Upper-Merged Ontology) [43], and GFO (General Formal Ontology) [44]. Some authors have used these ontologies for detecting inconsistencies in medical terminologies [15,22]. However, the restrictions included in top-level ontologies are very general, and they do not include restrictions specific to the medical domain. For instance, a top-ontology states that only *endurant* concepts have a duration, but not that tumors occur only in anatomical structures and not in biological functions.

Another possibility would have been to use the UMLS Semantic Network, which is available in OWL [45] and has been used in previous studies for auditing terminologies [24,21]. The Semantic Network includes the main classes of medical concepts and their relations: for example, it states that neoplastic processes have for location only anatomical abnormality, but the various anatomical abnormalities or locations are not included. However, Vizenor et al. [24] has noted that there are many inconsistencies between the semantic network and the UMLS metathesaurus, and thus the semantic network should not be considered as a "medical top-ontology" but rather as a "loose reference". Consequently, it was easier to create the medical part of the ontology from scratch, especially as it includes only a very limited number of concepts (368 concepts and 18 relations).

We did not reuse domain ontologies because (a) many of these ontologies are not well adapted to our requirements, e.g. the FMA for anatomical concepts is very large (about 70,000 concepts compared to the 53 anatomical pictograms in VCM, with thus a very different level of granularity) and its representation in OWL has not yet been debugged and still includes inconsistencies [19], and (b) there is no existing ontology for all the domains covered by the VCM pictograms and shapes, e.g. there is no ontology for biological functions [46]. However, the development of application-oriented domain ontologies, such as the OBO ontologies (Open Biomedical Ontologies) [47], have led to the proposal of a kind of intermediate level. OBO is a collaborative initiative guided by ontological principles whereas BioTop [48] is an upper-level ontology for the biomedical domain founded upon strict ontological principles using OWL-DL as a formal representation language. Schulz

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et al. [49] mapped the UMLS Semantic Network [50] with BioTop to make logic-based reasoning available for the resources annotated or categorized with the Semantic Network. It may be useful similarly to align the VCM ontology with BioTop, the UMLS Semantic Network, or other medical ontologies and terminologies.

The top levels of the VCM ontology and the top levels of other medical terminological systems, such as the UMLS Semantic Network or SNOMED CT, share several similarities. Many concepts are common, including anatomical structures (called topography in SNOMED CT), biologic functions, etiologies, etc. In addition, the distinction between transversal and non-transversal anatomical structures in the ontology allows several anatomical structures to be combined in an icon; this mechanism is similar to the multiple inheritance used in some terminological systems. For instance, "coronary vessels" are represented in VCM by combining two graphical primitives: the "heart" pictogram and the "blood vessels" shape modifier. This is similar to what SNOMED CT does: the "coronary artery structure" concept (ID 41801008) has two is-a relations, with "heart part" and with "artery of mediastinum" (which is a blood vessel). Distinguishing traversal and non-transversal anatomical structures prevents meaningless combination of anatomical structures (e.g. kidney and liver have no overlapping structures; as both are non-transversal anatomical structures in the VCM ontology, it is not possible to combine them).

However, it appears that in some situations, the VCM ontology goes further in the decomposition of medical concepts. For example, renal failure is represented in VCM by combining two graphical primitives: the kidney pictogram and a downward arrow meaning "failure of a biologic function". By contrast, in SNOMED CT, the "renal failure syndrome" concept (ID 42399005) is only described as being a "renal impairment" which has for finding site the "kidney structure". Indeed, SNOMED CT includes no concept equivalent to "failure of a biologic function".

The ability of the VCM icon ontology to determine icon consistency was evaluated over a random set of 100 icons. The evaluation suggested a high sensitivity (91.8%), indicating that the ontology is good at detecting inconsistent icons. The evaluation also identified a few errors in the ontology (such as considering as inconsistent icons for tumor located in general anatomical region like the thorax or abdomen); these errors have subsequently been fixed. It was difficult to find evaluators for evaluating icon consistency, because they needed both a medical and a computer science background, and they also needed to be trained in the use of VCM. In the near future, both user-created and randomly-generated icons will be used for a more complete evaluation of the ontology, and all such evaluations should involve several users (for generating icons) and evaluators (for manually determining icon consistency).

6. Conclusion

In the VCM iconic language, medical concepts are represented by icons, these icons being created by combining several graphical primitives such as pictograms and colors, according to a grammar. However, VCM allows inconsistent (self-contradictory or meaningless) icons to be created. In this work, we have developed a method for representing iconic languages by ontologies using Description Logics and OWL, which allows a language's semantics to be evaluated by reasoners, and in particular inconsistent icons to be identified. This method was successfully applied to VCM.

The VCM icon ontology has several potential applications that we plan to develop. Our next step will be to map VCM icons with the various medical terminologies (e.g. SNOMED CT, ICD10, etc). The ontology can help to detect inconsistent icons in such mappings. Additionally, for multiaxial terminologies and ontologies like SNOMED CT, the various axes of the terminology, or the various relations of the ontology, could be mapped to the VCM ontology, and then the terms could be projected and translated into VCM icons. Another advance would be the automatic generation of textual labels for VCM icons, as an aid to helping physicians to learn the icons. In this context, the VCM ontology could contribute to disambiguating icons. A third possibility is the design of graphical interfaces for creating VCM icons by combining several graphical primitives; the ontology could by used by any such interface to prevent users creating inconsistent icons.

Author contributions

JBL designed the VCM icon ontology.
GK worked on mappings between VCM and medical terminologies, which were used as test sets during the design of the ontology.
JBL, AV and CD designed the VCM iconic language.
LS wrote the TBox of the various parts of the ontology.
JBL and LS drafted the article.
JBL, LS, GK, AV and CD approved the final version of the article.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jbi.2012.08.006.

References

[1] Paivio A. Mental representations: a dual coding approach. Oxford University Press; 1990 [incorporated].
[2] Houts PS, Doak CC, Doak LG, Loscalzo MJ. The role of pictures in improving health communication: a review of research on attention comprehension recall and adherence. Patient Educ Couns 2006;61:173–90.
[3] Starren J, Johnson SB. An object-oriented taxonomy of medical data presentations. J Am Med Inform Assoc 2000;7(1):1–20.
[4] Chittaro L. Information visualization and its application to medicine. Artif Intell Med 2001;22(2):81–8.
[5] Lamy JB, Duclos C, Bar-Hen A, Ouvrard P, Venot A. An iconic language for the graphical representation of medical concepts. BMC Med Inform Dec Mak 2008;8:16.
[6] Lamy JB, Venot A, Bar-Hen A, Ouvrard P, Duclos C. Design of a graphical and interactive interface for facilitating access to drug contraindications, cautions for use, interactions and adverse effects. BMC Med Inform Dec Mak 2008;8:21.
[7] Lamy JB, Duclos C, Hamek S, Beuscart-Zéphir MC, Kerdelhué G, Darmoni S, et al. Towards iconic language for patient records, drug monographs, guidelines and medical search engines. Stud Health Technol Inform 2010;160:156–60.
[8] Geller J, Perl Y, Halper M, Cornet R. Special issue on auditing of terminologies. J Biomed Inform 2009;42(3):407–11.
[9] Zhu X, Fan JW, Baorto DM, Weng C, Cimino JJ. A review of auditing methods applied to the content of controlled biomedical terminologies. J Biomed Inform 2009;42(3):413–25.
[10] Yu AC. Methods in biomedical ontology. J Biomed Inform 2006;39(3):252–66.
[11] Baader F, Calvanese D, McGuinness DL, Nardi D, Pater-Schneider PL. The description logic handbook: theory, implementation and applications. 2nd ed. Cambridge University Press; 2007.
[12] Rector AL, Nowlan WA. The GALEN project. Comput Methods Programs Biomed 1994;45(1–2):75–8.
[13] Rector AL, Bechhofer S, Goble CA, Horrocks I, Nowlan WA, Solomon WD. The Grail concept modelling language for medical terminology. Artif Intell Med 1997;9:139–71.
[14] Soualmia LF, Golbreich C, Darmoni SJ. Representing the MeSH in OWL: towards a semi-automatic migration. In: Proceedings of the international workshop on

formal biomedical knowledge representation (KRMeD). Whistler, Canada; 2004. p. 81–7.

[15] Héja G, Surján G, Varga P. Ontological analysis of SNOMED CT. BMC Med Inform Dec Mak 2008;8(suppl. 1):8.

[16] Nadkarni PM, Marenco LA. Implementing description-logic rules for SNOMED-CT attributes through a table-driven approach. J Am Med Inform Assoc 2010;17(2):182–4.

[17] Ceusters W, Smith B, Kumar A, Dhaen C. Mistakes in medical ontologies: where do they come from and how can they be detected? Stud Health Technol Inform 2004;102:145–63.

[18] Héja G, Surján G, Lukácsy G, Pallinger P, Gergely M. GALEN based formal representation of ICD10. Int J Med Inf 2007;76(2–3):118–23.

[19] Cornet R, Abu-Hanna A. Two DL-based methods for auditing medical terminological systems. In: Proceedings of the AMIA Symposium; 2005. p. 166–70.

[20] Gu HH, Wei D, Mejino JL, Elhanan G. Relationship auditing of the FMA ontology. J Biomed Inform 2009;42(3):550–7.

[21] Mougin F, Bodenreider O. Auditing the NCI thesaurus with semantic web technologies. In: Proceedings of the AMIA Symposium; 2008. p. 500–4.

[22] Ceusters W, Smith B, Goldberg L. A terminological and ontological analysis of the NCI Thesaurus. Meth Inform Med 2005;44:498–507.

[23] Cimino JJ. Auditing the Unified Medical Language System with semantic methods. J Am Med Inform Assoc 1998;5(1):41–51.

[24] Vizenor LT, Bodenreider O, McCray AT. Auditing associative relations across two knowledge sources. J Biomed Inform 2009;42(3):426–39.

[25] Jiménez-Ruiz E, Cuenca Grau B, Horrocks I, Berlanga R. Logic-based assessment of the compatibility of UMLS ontology sources. J Biomed Semant 2011;suppl. 2(1):2.

[26] Navas H, Lopez Osornio A, Gambarte L, Elías Leguizamón G, Wasserman S, Orrego N, et al. Implementing rules to improve the quality of concept post-coordination with SNOMED CT. Stud Health Technol Inform 2010;160:1045–9.

[27] Cornet R. Definitions and qualifiers in SNOMED CT. Methods Inform Med 2009;48(2):178–83.

[28] Berners-Lee T, Hendler J, Lassila O. The semantic web. Sci Am 2001;284(5):34–43.

[29] Rubin D, Shah N, Noy N. Biomedical ontologies: a functional perspective. Brief Bioinform 2008;1(9):75–90.

[30] Knublauch H, Rector AL, Musen MA. Editing description logic ontologies with the Protégé OWL pluging. Descrip Log 2004.

[31] Motik B, Shearer R, Horrocks I. Hypertableau reasoning for description logics. J Artif Intell Res 2009;36:165–228.

[32] Sirin E, Parsia B, Grau BC, Kalyanpur A, Katz Y. Pellet: A practical OWL-DL reasoner. Web Semant Sci Serv Agents WWW 2007;5(2):51–3.

[33] Horrocks I, Sattler U. Decidability of SHIQ with complex role inclusion axioms. Artif Intell 2003;160:2004.

[34] Pisanelli DM, Gangemi A, Battaglia M, Catenacci C. Coping with medical polysemy in the semantic web: the role of ontologies. Stud Health Technol Inform 2004;107:416–9.

[35] Friedman C, Kra P, Rzhetsky A. Two biomedical sublanguages: a description based on the theories of Zellig Harris. J Biomed Inform 2002;35:222–35.

[36] Harris ZS. The structure of science information. J Biomed Inform 2002;35:215–21.

[37] Johnson SB. Conceptual graph grammar – a simple formalism for sublanguage. Meth Inform Med 1998;37(4–5):345–52.

[38] Giammarresi D, Restivo A. Handbook of formal languages. Beyond words, vol. 3. Springer; 1997. p. 215–67.

[39] Reghizzi SC, Pradella M. Tile rewriting grammars and picture languages. Theoret Comput Sci 2005;340(2):257–72.

[40] Ewert S. Manipulation of graphs, algebras and pictures. Hohnholt; 2009. p. 135–47.

[41] P. Grenon, BFO in a nutshell: a bi-categorial axiomatization for BFO and comparison with DOLCE. Tech. rep. Institute for Formal Ontology and Medical Information Science (IFOMIS); 2003.

[42] Gangemi A, Guarino N, Masolo C, Oltramari A, Oltramari R, Schneider L. Sweetening ontologies with DOLCE. In: Proceedings of the 13th international conference on knowledge engineering and knowledge management (EKAW '02). London: Springer-Verlag; 2002. p. 166–81.

[43] Pease A. Ontolinguistics. How ontological status shapes the linguistic coding of concepts. Vorbereitung Berlin, New York (Mouton de Gruyter); 2006. p. 103–14.

[44] Heller B, Herre H. Ontological categories in GOL. Axiomathes 2004;14(1):57–76.

[45] Kashyap V, Borgida A. Representing the UMLS semantic network in OWL. In: Proceedings of ISWC 2003 (International Semantic Web Conference); 2003. p. 1–16.

[46] Hoehndorf R, Ngonga Ngomo AC, Kelso J. Applying the functional abnormality ontology pattern to anatomical functions. J Biomed Semant 2010;1:4.

[47] Smith B, Ashburner M, Rosse C, Bard J, Bug W, Ceusters W, et al. The OBO foundry: coordinated evolution of ontologies to support biomedical data integration. Nat Biotechnol 2007;25(11):1251–5.

[48] Beisswanger E, Schulz S, Stenzhorn H, Hahn U. BioTop: an upper domain ontology for the life sciences. Appl Ontol 2008;3(4):205–12.

[49] Schulz S, Beisswanger E, van den Hoek L, Bodenreider O, van Mulligen EM. Alignment of the UMLS semantic network with BioTop: methodology and assessment. Bioinformatics 2009;25(12):i69–76.

[50] McCray AT. An upper-level ontology for the biomedical domain. Comp Funct Genom 2003;4:80–4.

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