Annotation and Image Markup: Accessing and Interoperating with the Semantic Content in Medical Imaging

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Interest in applying Semantic Web technologies to the life sciences continues to accelerate. Biomedical research is increasingly an online activity as scientists combine and explore different types of data in cyberspace, putting together complementary views on problems that lead to new insights and discoveries. An e-Science paradigm is thus emerging; the biomedical community is looking for tools to help access, query, and analyze a myriad of data in cyberspace. Specifically, the biomedical community is beginning to embrace technologies such as ontologies to integrate scientific knowledge, standard syntaxes, and semantics to make biomedical knowledge explicit, and the Semantic Web to establish virtual collaborations. These technologies are showing promise in tackling the information challenges in biomedicine, and a variety of applications are quickly appearing. Although researchers can now access a broad diversity of biomedical data, a critical type of data—images—is much more difficult to leverage.

Challenges for Images in E-Science

Those wanting to access and use imaging in their work face difficulties similar to the rest of the e-Science community—namely, to manage, find, and use the voluminous amounts of imaging data accruing at an explosive pace. However, imaging poses unique challenges that hinder direct translation of the informatics methods currently applied to non-imaging biomedical data:

- Image content isn’t explicit and machine-accessible. Images contain rich information about anatomy and the abnormal structures within the images; however, this is implicit knowledge that is deduced by the person viewing them. For example, a researcher might want to indicate where particular areas of interest lie in an image and whether they are abnormal (see Figure 1 on the next page). This information, the semantic image content, is often considered “image metadata,” including observations about images, interpretations, and conclusions. Generally, this information isn’t recorded in a structured
manner or directly linked to the image. Thus, researchers can’t easily search images for their semantic content (that is, to find all images containing particular anatomy or representing particular abnormalities).

• No controlled image terminology or standard syntax is used for image information. Standard terminologies aren’t generally used for describing medical image contents—the imaging observations, the anatomy, and the pathology—and the syntax varies with no widely adopted standards, resulting in limited interoperability. Descriptions of medical images are most frequently recorded in free-text in an unstructured manner, limiting the ability of computers to analyze and access this information. Schemes for annotating images have been proposed in nonmedical domains;3 however, no comprehensive standard appropriate to medical imaging has yet been developed. The syntax used to encode image data and metadata also varies; current standards include the Digital Imaging and Communications in Medicine (DICOM) standard for images acquired from imaging devices, Health Level Seven (HL7) for information in electronic-medical-record systems, and the World Wide Web for images labeled with HTML or RDF, although not with consistent semantics across the Web.

• Context-dependent annotation requirements. The particular information researchers want to annotate in medical images depends on the context—users can obtain different types of images for various purposes—and the types of annotations that should be created (annotation requirements for images) depends on that context. For example, in images of a cancer patient’s abdomen (the context is cancer and abdominal region), we would want annotations to describe the liver (an organ in the abdominal region), and if there is a cancer in the liver, then there should be a description of the margins of the cancer (the appearance of the cancer on the image). Such context dependencies must be encoded somehow so that an annotation tool can prompt the user to collect the proper information in different imaging contexts.

We seek to tackle these challenges to achieve semantic integration of images across hospital information systems and the Web. Our approach, the Annotation and Image Markup (AIM) Project, adopts knowledge representations for what people viewing images want to say about them: the entities observed in images (anatomy and abnormalities), the annotation contexts and image annotation requirements in those contexts to ensure the proper information is collected in the different contexts, and an annotation tool to create the annotations. AIM is a project of the National Cancer Institute’s Cancer Biomedical Informatics Grid (caBIG, https://cabig.nci.nih.gov/tools/AIM), designed to establish standards for recording semantic-image information that will enable cancer centers to interoperate with these data nationally.

We distinguish between image annotation and markup (see Figure 1). Image annotations are explanatory or descriptive information, generated by humans or machines, directly related to the content of a referenced image (generally non-graphical, such as abnormalities seen in images and their locations). Image markup refers to graphical symbols that are associated with an image and optionally with one or more annotations of that same image. Accordingly, the key information content about an image lies in the annotation; the markup is simply a graphical presentation of the information in the annotation. The AIM project provides methods for representing and handling both image annotations and markups.

Methods

As we recently described,4 our approach to making the semantics of image content explicit and accessible to machines is to create an ontology to provide controlled terminology for describing the contents of medical images, and a standard image information model for recording semantic annotations. We developed an image annotation tool to collect user annotations as instances of the ontology, providing intelligent feedback to inform the user about annotation information requirements given the image annotation context. And we serialized the annotation instance data to DICOM, HL7 CDA (XML), and OWL representation languages to enable semantic integration and let agents access the image annotations across hospital systems and the Web.

Ontology for Image Annotation

We created the AIM ontology in OWL-DL to represent the entities associated with medical images. The AIM ontology includes anatomic structures that researchers can see in images (such as the liver and lung), the observations that radiologists make about images (such as opacity and density of struc-
tions contained in the images), and the spatial regions that can be visualized in images, as well as other image metadata (see Figure 2). The anatomic structures and observations are obtained from RadLex, a controlled terminology for radiology. We imported RadLex into the AIM ontology to provide these entities with a way in which to describe anatomy and observations in images.

The AIM ontology also represents knowledge about annotation requirements—the information required to create image annotations (see Figure 2). These annotation requirements are analogous to minimum information requirements in annotation tasks in other domains, such as in the microarray community. Annotation requirements comprise two aspects: the context and the requirement for annotation. The contexts for annotations comprise a set of pre-enumerated image types and scenarios in which images are used, for example, in assessing the anatomy and observations present in images when evaluating nodules in the lungs as part of the Lung Imaging Database Consortium (LIDC) study. The contexts are represented as a set of defined classes, specifying the various aspects of annotation appropriate for that context. For example, abnormal opacity is an imaging observation seen in lungs, so an existential restriction is added to the AbnormalOpacity class (see Figure 2). We also created restrictions to describe anatomic composition, such as the fact that the lungs are in the thorax. A context is encoded by creating a defined class, specifying all necessary and sufficient conditions for the context.

We encode annotation requirements by adding the appropriate class descriptions to define the context classes in the AIM ontology. For example, a computed tomography (CT) chest image obtained to assess a nodule (LIDCChestCTNoduleContext) should have annotations describing anatomic entities located in the thorax along with any imaging observations that occur in the lung. OWL represents these requirements using the following assertions:

(a) Given a context, the AIM ontology can be used to determine the annotation information requirements using DL classification. First, the appropriate context class is asserted to be a subclass of the context class in the asserted ontology (see Figure 3). After asserting the context, a DL classifier is applied, and the annotation tool can determine the annotation information requirements from the inferred ontology by looking at the newly classified subclasses of each subclass of the context classes. Following classification, the annotation tool determines the information requirements for annotation by querying the ontology for the subclasses of the annotation context class (see Figure 3). The annotation tool uses the names of the classes in the ontology to determine the corresponding data fields in the AIM schema to use for collecting annotation information for that context. For example, the LIDC Chest CT Nodule context has two information requirements (anatomic entity and imaging observation), and following DL classification, we can determine from the ontology that image annotations for anatomic entities in this context should be thoracic entities and that imaging observations should be types of abnormal opacity (see Figure 3 on the next page).

We produced an API to enable image annotation tools to enforce annotation requirements. We wrote the API in Java, and it provides an input argument that specifies the image annotation context (such as in the LIDC Chest CT Nodule Context example). The output from the API provides a list of anatomic entities and imaging observations that are required for the given annotation context. These anatomic entities and imaging observations constitute the annotation requirements.

We implemented the AIM ontology in Protégé-OWL. We use Pellet (http://pellet.owldl.com) to classify the ontology and to infer the requirements for annotation given an imaging context that was asserted at the time we created an annotation. We created an API to the ontology to encapsulate the functionality of determining annotation requirements, providing a single function that is called by image annotation tools needing to access this information. The
function takes an input integer argument specifying the context, and it makes the appropriate class assertion in the ontology, calls the Pellet classifier, and returns the inferred annotation requirements as the function’s output.

**Information Model for Image Annotation**

We also created an information model (AIM schema) to provide a standard syntax for creating and storing instances of image annotations (see Figure 4). The AIM schema is in UML, and it distinguishes image annotation and markup. Annotations describe the meaning in images, whereas markup is the visual presentation of the annotations. In the AIM schema, all annotations are either an annotation on an image (ImageAnnotation) or an annotation on an annotation (AnnotationOnAnnotation). Image annotations include information about the image as well as their semantic contents (anatomy, imaging observations, and so on). Annotation on annotations let users make statements about groups of preexisting annotations, such as commenting on multireader image evaluations, or to make statements about a series of images. In this article, our tools focus on using ImageAnnotation.

We converted the AIM schema in UML to XML schema (XSD file) to enable creation of AIM annotations as XML files and allow validation of AIM files. To enable interoperability of AIM between hospital and Web environments, we also converted the AIM UML information model to OWL using CIMTool (http://cimtool.org) so that annotation instances in AIM could be created in OWL. In Semantic Web applications, AIM annotations would then be created as new individuals of the ImageAnnotation or AnnotationOnAnnotation class (see Figure 5 on page 62).

**Image Annotation Tool**

We created an image annotation tool to collect annotations from users as they review images, adopting AIM and its knowledge of annotation contexts to enable users to make image information explicit. The annotation tool provides an image-viewing pane so that users can scroll through images. The tool also provides an annotation palette with drop-down boxes and text fields the user accesses to record semantic information about the images (see Figure 6 on page 62). The tool implements the AIM schema so that annotations created with the tool are stored in AIM-compliant syntax. The annotation tool accesses the ontology to guide users as to annotation requirements during the annotation process. The annotation tool makes assertions in the ontology about the annotation context, and queries the ontology to determine subclasses of the appropriate context classes (which indicate the annotation requirements for the context). For example, if the user selects the LIDC Chest CT Nodule context (see LIDCChestCTNoduleContext in Figure 3), the annotation tool can access the ontology to determine that all thorax anatomic entities and abnormal opacity imaging observations are appropriate for this image annotation (children of the AnatomicEntity and ImagingObservation class in the inferred hierarchy).

**Serializing Annotations to Diverse Formats**

The image annotations are initially stored as AIM XML. Regardless of whether they
aim

exist on hospital systems or the Web, all images thus have uniform AIM XML synta

for representing the metadata in a common information model. We created a soft

tware module to serialize the AIM XML into other formats depending on the type

of environment (hospital or Web) storing the image. This ability to serialize AIM to
different storage formats provides interoperability and semantic integration across
diverse hospital systems and the Web. To date, we have created applications to trans
form the AIM XML into DICOM-SR and HL7-CDA XML. We also adapted an ap
lication previously developed that maps between XML and OWL to transform our
AIM XML files into OWL. The application reads XML documents and automatically
transforms them to an OWL ontology representing the document. Researchers can
directly publish their OWL-encoded AIM annotations on the Web, and Semantic Web
agents can reference their content.

Applications can validate AIM XML documents against the AIM XSD. Because the
XSD directly encodes the semantics of image annotations, this validation approach
ensures interoperability of the semantic content of images regardless of whether the
images are located within hospital information systems or cyberspace.

Evaluation and Use Case

We evaluated our work by using AIM to annotate radiological images from 10 pa
tients. The images were CT images of the abdomen in cases where the patients had
abnormal lesions in the liver. Two radiologists viewed the radiological images and
used the AIM schema to create annotations describing the major abnormalities in the
images. We assessed completeness of the AIM schema to capture the annotation infor
mation that the radiologists sought to rec
ord. We also assessed the completeness of the AIM ontology with respect to its ability
to provide the knowledge necessary to define the annotation contexts the radiologists
required.

We created a use case related to image query as an example of the potential utility of AIM in real-world applications. AIM annotation files in XML were loaded into a relational database, and SQL queries were created to support a user case to test the utility of expressing semantic image information in AIM. The use case queried the images from the cases annotated to identify

images of the liver showing a mass. This query required semantic access to the anat
omy (liver) and observations (mass) in the image.

Results

We have been using AIM and our annota
tool to make the semantics of radiologi
c images explicit so that image data can be processed with other machine-accessible biomedical data. We describe our results related to using AIM for image annotation, the AIM-compliant annotation tool, and results of our evaluation to date.

AIM Ontology and Knowledge Representation for Image Annotation

The annotation contexts were successfully represented in OWL in the AIM ontology
by specifying assertions and defined classes (see Figure 2). In addition, the ontology
correctly specified the annotation information requirements given the annotation con
cepts evaluated. For example, consider the context LIDCChestCTNoduleContext
representing a CT chest image for assessing a nodule. This class was defined using two
classes in AIM ontology: one specifying that the anatomic entities appropriate for
annotation are located in the thorax, and the other specifying that the imaging observa
tions appropriate for annotation are those that are seen in the lung. At runtime, when
users indicate they are annotating an image in the context LIDCChestCTNoduleContext,
the annotation application asserts the class LIDCChestCTNoduleContext in the AIM ontology, then calls Pellet to reclassify the ontology, and finally queries the ontology to infer the portions of the AIM ontology that are subclasses of the asserted LIDCChestCTNoduleContext class, indicating the portions of

Figure 4. AIM schema and annotation instance. A portion of the AIM schema (gold) and example instance of ImageAnnotation (blue) are shown. Only is–a and instance–of relations are depicted. The figure shows that the annotation describes an image that visualizes the liver, and contains a mass in the liver measuring 2 cm in size.
the AIM schema needed for annotation in this context (see Figure 3). That knowledge was used by the annotation tool to prompt the user as to the annotation information required for that image.

On the basis of our experience annotating radiological images with AIM schema, we considered the information model sufficient to capture the semantic contents that the radiologists sought to describe. The AIM ontology also contained sufficient knowledge to define the annotation contexts the radiologists required.

**Annotation Tool**

As the user interacts with our annotation tool, such as by drawing lines or making entries to describe anatomy and findings, the tool records this information using the AIM ontology and controlled terminology, hiding the structured form of the information from the user (see Figure 6). For example, if the user draws a line and labels it region 1, the annotation tool creates an AIM annotation with the line coordinates, length, and name (region 1) in a data structure compliant with AIM schema. Users can annotate entire images or regions of images, and images can have multiple annotations.

When beginning an image annotation, the user first provides the tool with the context for annotation (specified using a drop-down box). The annotation tool then asserts the user-specified context in the AIM ontology as a set of defined classes, and it executes the classifier to infer the appropriate data fields from the AIM schema for annotating the image in that context (see Figure 3). The tool then presents the user with terms appropriate for the annotation task.

**Evaluation**

The annotations the radiologists created comprised a set of instances of the AIM schema (see Figure 4). When the user created an annotation using the AIM image annotation tool, the annotation information was initially stored in XML, compliant with the AIM XML schema. The AIM XML annotations were successfully transformed to DICOM-SR by the application developed for this purpose. The DICOM-SR could be stored in hospital image information systems, and the system’s contents were semantically interoperable with AIM annotations published in cyberspace. The
AIM schema contains a unique identifier to the image available in all the representation languages, so the image is linked to the annotation regardless of whether the annotation is serialized to DICOM-SR, HL7 CDA XML, or OWL.

To interoperate with the Semantic Web, the AIM annotations can be serialized to OWL. The XML was successfully transformed to OWL using the tool mapping between XML and OWL.7 The annotations in OWL could then be viewed in Protégé-OWL (see Figure 5) by selecting instances of the classes representing types of annotation classes in AIM (ImageAnnotation and AnnotationOnAnnotation). For example, all AIM annotations on images are instances of the ImageAnnotation class (see Figure 5). With the image annotation in OWL, the semantic contents were accessible on the Semantic Web.

The process by which users viewed images and created AIM annotations was similar to the current process radiologists use to perform this task, by drawing or notating directly on images (see Figure 1). However, the annotation tool creates semantic structure (hidden from the user during annotation), which is stored in computer-accessible formats. Thus, AIM and the annotation tool provide a means to conceptually link the image to its semantic contents for subsequent data analysis or access on the Semantic Web.

The AIM-enabled image query required for the use case in our study ensured that the images annotated with AIM could be searched according to any of the AIM semantic fields. The radiologists who annotated the images had posed a few example queries, such as “find images of the liver that show a mass.” Such queries would be impossible without AIM because the semantic content of images annotated without AIM aren’t explicit and machine accessible (see Figure 1). On the other hand, such queries were straightforward with AIM, letting users retrieve images according to their query criteria (see Figure 7).

Semantic technologies such as ontologies and knowledge representation syntaxes work well with nonimage data and are well suited to help scientists manage the information explosion. Biological and most medical data are of the nonimage type—laboratory data, gene sequences, proteomics, numerous assays, EKG, and much patient data are numeric or categorical variables, data types amenable to ontology-based annotation.8 However, images are a more complex data type, containing rich information of varying types (anatomy, physiology, morphology, and so on), and to date, there are no widely adopted methods for making the rich semantic content of images explicit.

Images on the Web generally have no semantic markup, nor do images residing within hospital information systems. On the Web, images and text are comingled, but not linked semantically. The closest thing to semantic annotation is social tagging of consumer images.9 However, such annotations generally don’t conform to a controlled terminology, and they don’t indicate particular regions within an image of interest—both attributes critical to biomedical imaging. Within hospital information

Figure 7. AIM image query.
In this use case to evaluate the potential utility of AIM, radiologists annotated images of the liver using AIM. A Web application was then created to search for images containing mass in the liver. The search was executed looking for AIM annotations in which the anatomic entity contains “liver” and the imaging observation field contains “mass.”
Semantic Scientific Knowledge Integration

systems, DICOM is a ubiquitous standard for the interchange of images, but even DICOM lacks a formalism for specifying the semantic contents of images. DICOM-SR provides a framework that enables encoding of imaging results in a structured format, but it lacks specification of particular image annotation information requirements.

If semantic information within images was made explicit and associated with images on the Web and in DICOM, developers could create many types of Semantic Web applications that access image data, ranging from simple image query programs and image classification to computer-reasoning applications. In addition, explicit semantic image contents would enable users to relate images to the nonimage data of e-Science that is pervasive on the Web. For example, researchers could mine images to discover patterns that predict biological characteristics of the structures they contain.

There is ongoing work to define methods to describe images on the Semantic Web. However, the efforts to date focus on describing the image as a whole, rather than particular regions within the image. In radiology, it's important to describe the semantics of individual regions within images; some regions in biomedical images might contain abnormalities, whereas other parts could be normal. An image annotation standard should let users describe regions in images and annotate the semantic content of those regions, in addition to the entire image.

Our work addresses the challenges for making the semantic contents of images explicit and accessible both within hospital systems and in cyberspace. There are, however, some remaining challenges. First, semantic interoperability between Web and hospital systems requires transformation of syntaxes (DICOM-SR, HL7 CDA, and OWL). It would clearly be preferable if all image annotation information were stored in a single format (that is, OWL); however, data standards in medicine predate the Web, are firmly entrenched, and are slow to change. We can facilitate integration with application interfaces for DICOM-SR and HL7 systems to enable them to access the necessary components of the AIM information model to interoperate more easily with data on the Web.

Another challenge is that the annotation contexts need to be prespecified and encoded in OWL. If there are many such annotation contexts, it could prove unwieldy to maintain them or for a user to select the context when annotating images. In the clinical-research settings in which we expect semantic annotation to take place, there are a manageable number of annotation contexts because they are generally determined by body region. In addition, we could create hierarchically driven user interfaces to manage large lists of selections. In the future, we will investigate ways to create “composed” annotation contexts and a more modular approach to representing their corresponding annotation requirements.

A final challenge is that it is possible the AIM ontology is insufficient for the semantic content of medical images to the nonimage data of e-Science to the medical domain; the AIM ontology is extensible, and we plan to augment it as needed as we encounter future imaging application areas. Another potential limitation is that the annotation tool might not be accepted in routine radiology workflow. For AIM annotations to succeed, users must have the ability to create annotations on images simply and quickly. Although our initial experience with user acceptance of our annotation tool is promising, we will continue evaluating the annotation tool with a larger group of radiologists and images. We are currently performing a formal evaluation of AIM with a large collection of images to ensure it is broadly applicable to the medical domain.

Our work herein focuses on making semantic contents of medical images explicit; however, our methods might be more broadly applicable to all types of images on the Web. Ultimately, many new Semantic Web applications could be created that exploit the rich information content latent in images once their semantic content is made explicit and accessible to agents. We believe that many new intelligent applications will appear to exploit the rich information in images as this content is made accessible in cyberspace.

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