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# Ontology-based Diagnostic Decision Support in Radiology

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**Abstract.** The Radiology Gamuts Ontology (RGO) is a knowledge model of diseases, interventions, and imaging manifestations. RGO incorporates 16,822 terms with their synonyms and abbreviations and 55,393 relationships between terms. Subsumption defines the relationship between more general and more specific terms; causality relates disorders and their imaging manifestations. We explored the application of the RGO to build an interactive decision support system for radiological diagnosis. The Gamuts DDx system was created to apply the RGO's knowledge: it identifies a list of potential diagnoses in response to one or more user-specified imaging observations. The system also identifies a set of observations that allow one to narrow the diagnosis, and dynamically narrows or expands the list of diagnoses as imaging findings are selected or deselected. The functionality has been implemented as a web-based user interface and as a web service. The current work demonstrates the feasibility of exploiting the RGO's causal knowledge to provide interactive decision support for diagnosis of imaging findings. Ongoing efforts include the further development of the system's knowledge base and evaluation of the system in clinical use.

**Keywords.** Decision support, knowledge representation, ontology, radiology, diagnosis

## Introduction

The Radiology Gamuts Ontology (RGO) is a large and growing knowledge model of diseases and their associated imaging observations [1]. It has been constructed from several sources of differential diagnosis information [2-5] to serve as a form of "computable knowledge" to aid in radiological diagnosis. RGO includes the names of disorders (e.g., "Aase-Smith syndrome"), interventions (e.g., "steroid therapy"), and observations (e.g., "hydrocephalus") with their synonyms and abbreviations. The subsumption ("is a") relation and its inverse ("has subtype") define a conventional hierarchy among more general and more specific concepts. The ontology incorporates knowledge across organ systems, patient populations (adults and children), and imaging modalities.

RGO is unique among current biomedical ontologies in that it specifies a causal relation ("may cause") and its inverse ("may be caused by") to relate entities to their imaging manifestations; for example, "hepatitis may cause cirrhosis," and "cirrhosis may cause portal venous hypertension." Unlike conventional "gamuts" listings, the representation of knowledge in the RGO model allows automated inference on that knowledge. This study describes the development of a platform for differential-

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diagnosis decision support using RGO's knowledge, called "Gamuts DDx." The platform has been applied to build an automated system for differential diagnosis of imaging observations.

## 1. Methods

As of January 2014, RGO included 16,822 terms, 1,755 subsumption relations, and 53,638 causal relations. A web-based user interface (*www.gamuts.net/ddx*) was developed to apply the RGO's knowledge. A web service using the Representational State Transfer (REST) architecture [6] and JavaScript Object Notation (JSON) was created to allow the system to be linked to other information systems.

Rather than using only direct links between entities, the Gamuts DDx system applied transitive closure over the ontology's subsumption relation,

$$\boldsymbol{isa}^{+}(X,Y) := \begin{cases} \boldsymbol{isa}\,(X,Y) \\ \boldsymbol{isa}\,(X,T),\ \boldsymbol{isa}^{+}(T,Y) \end{cases} \tag{1}$$

where **isa** $(X,Y)$ means "$X$ is a $Y$." Thus, if one knows "adenocarcinoma is a carcinoma" and "carcinoma is a neoplasm," the system can infer "adenocarcinoma is a neoplasm." Transitive closure over causality, where **causes** $(X,Y)$ means "$X$ may cause $Y$," incorporated transitive closure over subsumption:

$$\boldsymbol{causes}^{+}(X,Y) := \begin{cases} \boldsymbol{causes}\,(X,Y) \\ \boldsymbol{causes}\,(X,T),\ \boldsymbol{causes}^{+}(T,Y) \\ \boldsymbol{isa}^{+}(X,T),\ \boldsymbol{causes}^{+}(T,Y) \\ \boldsymbol{causes}^{+}(X,T),\ \boldsymbol{isa}^{+}(T,Y) \end{cases} \tag{2}$$

As a result, Gamuts DDx can follow chains of relations. For example, from the statements "hepatitis B is a viral hepatitis, which may cause cirrhosis, which may cause portal hypertension, which may cause splenomegaly, which is a splenic disease," the system can infer that hepatitis B may cause splenic disease.

For a given set of findings $F = \{ F_i \}$, the set of diagnoses is defined as the set of all entities $X$ that satisfy $\mathbf{causes}^{+}(X, F_i)$ for every finding $F_i$. We defined a "discriminator" as an observation that is caused by entities in a proper subset of the diagnoses. Thus, asserting the presence of a discriminator allows one to reduce the set of diagnoses.

## 2. Results

Gamuts DDx instantaneously and correctly identifies a list of potential diagnoses and a set of discriminators in response to user-specified imaging observations. Asserting the presence of a discriminator allowed users to refine the list of diagnoses. The lists of diagnoses and discriminators are narrowed or expanded dynamically as the user selects or deselects observations. The system accommodates an arbitrary number of specified findings.

Consider, for example, a patient in whom the initial finding is hypertelorism. Specifying the finding "hypertelorism" produces a list of 148 diagnoses, listed alphabetically from Aarskog syndrome to XXXXY syndrome. Among the 976 discriminators are observations such as acro-osteolysis, abnormal sternum, clubfoot, tracheomalacia, and Wormian bones. Selecting the additional observation "abnormal sternum" narrows the differential diagnosis to six entities: Brachmann-de Lange syndrome, cleidocranial dysostosis, Noonan syndrome, Rubinstein-Taybi syndrome, Seckel syndrome, and XXXXY syndrome. The list of discriminators is reduced to 278 possible observations. If the user then indicates that Wormian bones are present, the system identifies cleidocranial dysostosis as the only diagnosis in which all three of the observations are present.

On the web site, the user specifies an initial finding, such as "hypertelorism" (Figure 1). The discriminators are grouped by organ system and/or imaging modality, and are presented as a set of checkboxes. When checked, that finding is added to the list of the patient's findings. The lists of diagnoses and discriminators are updated accordingly. Selected findings can be unchecked. Additional information about each disorder is available through a hyperlink from the differential diagnosis listing. Figure 2 shows part of the web service response for hypertelorism and Wormian bones.

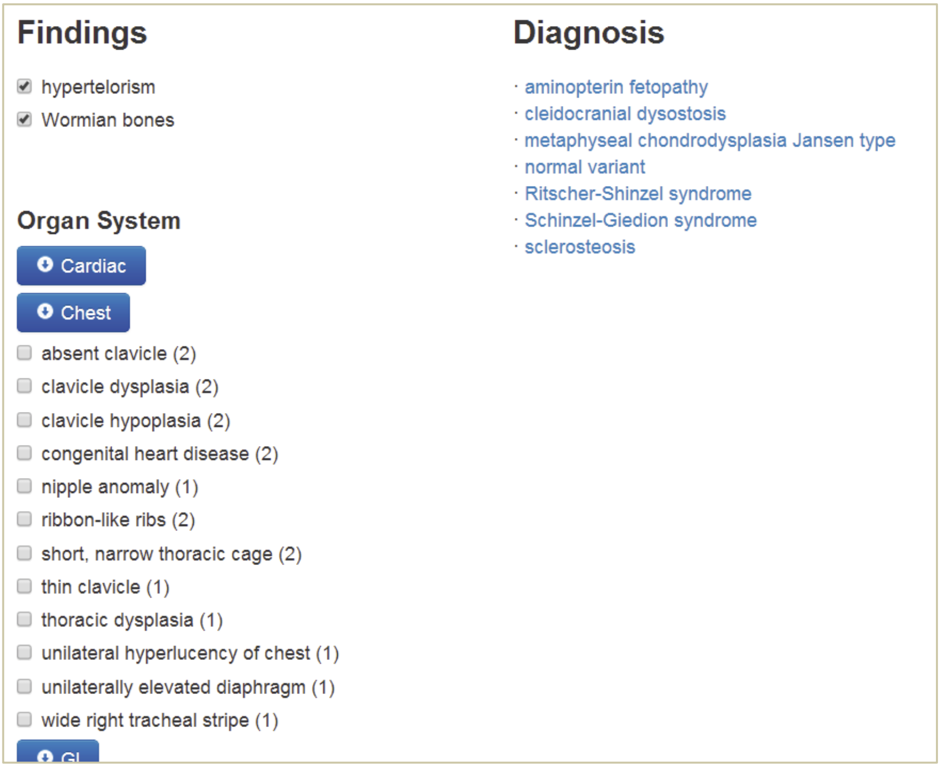


**Figure 1.** Screen shot of Gamuts DDx web-based user interface. Two observations (hypertelorism and Wormian bones) have been asserted. The seven diagnoses that exhibit both of these features are displayed at the right. Discriminators are grouped by organ system and imaging modality.

```
{
  "status": {
    "code": 200,
    "message": "Success",
    "createdAt": "2013-12-02T02:36:44Z"
  },
  "response": {
    "license": "Copyright (c) 2013 by the Authors. ALL RIGHTS RESERVED",
    "count": {
      "finding": 2,
      "diagnosis": 7,
      "discriminator": 258
    },
    "finding": [
      "hypertelorism",
      "Wormian bones"
    ],
    "diagnosis": [
      "aminopterin fetopathy",
      "cleidocranial dysostosis",
      "metaphyseal chondrodysplasia Jansen type",
      "normal variant",
      "Ritscher-Shinzel syndrome",
      "Schinzel-Giedion syndrome",
      "sclerosteosis"
    ],
    "discriminator": [
      {
        "name": "abnormal fibula",
        "n": "1"
      },
           . . .
      {
        "name": "widespread predominantly medullary osteosclerosis",
        "n": "1"
      }
    ]
  }
}
```


**Figure 2.** Example JavaScript Object Notation (JSON) output from differential diagnosis web service. For the two observations (hypertelorism and Wormian bones), seven diagnoses and 258 discriminators are identified.

## 3. Discussion

The Radiology Gamuts Ontology provides a large knowledge base of diseases and their imaging manifestations. The RGO incorporates information about a large number of rare diseases, such as metabolic disorders and skeletal dysplasias, including the Bone Dysplasia Ontology [7]. As defined by the U.S. National Institutes of Health, a rare disease is one whose prevalence is less than one in 1,500 (0.06%). There are 6,000 to 7,000 rare diseases, which in aggregate affect 25 to 30 million persons in the United States. The ontology is made available as a publically available web site (*www.gamuts.net*) and a web service [1]. Although useful for identifying potential causes of imaging findings, the original web site does not allow one to easily explore the intersection of more than one differential-diagnosis list.

One limitation of the Gamuts DDx system is the premise that a diagnosis must cause of all of the specified findings. As such, if the user asserts the presence of an imaging finding that is not linked a particular disease, that disease is eliminated from the differential diagnosis. The system also is limited by the extent of RGO's knowledge of diseases and their associated imaging observations. Because the RGO currently lacks information about prevalence of the various disorders, it cannot rank diagnoses in order of likelihood, nor can it identify those imaging features that have the greatest discriminatory power.

One of the goals for the RGO is to incorporate the prior probability (prevalence) of each disorder in the knowledge model. The envisioned future work includes incorporating conditional probabilities into the RGO as well to express quantitatively the relationships between disorders and their imaging manifestations. Such information should allow better determination of the more likely diagnosis and more accurate ranking of the most informative imaging features. By linking to other biomedical ontologies and incorporating tools from platforms such as the National Center for Biomedical Ontology (NCBO), Gamuts DDx seeks to provide a sophisticated, semantically-aware platform for clinical decision support [8].

The current work demonstrates the feasibility of exploiting the RGO's causal knowledge to provide an interactive decision support tool for radiological diagnosis. Ongoing efforts include the further development of the system's knowledge base and evaluation of the system for clinical use.

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