# Motivation and Organizational Principles for Anatomical Knowledge Representation: the Digital Anatomist Symbolic Knowledge Base

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## ABSTRACT

**Objective:** Conceptualization of the physical objects and spaces that constitute the human body at the macroscopic level of organization, specified as a machine-parseable ontology which, in its human-readable form, is comprehensible to both expert and novice users of anatomical information.

**Design:** Conceived as an anatomical enhancement of the UMLS Semantic Network and Metathesaurus, the anatomical ontology was formulated by specifying defining attributes and differentia for classes and subclasses of physical anatomical entities based on their partitive and spatial relationships. The validity of the classification was assessed by instantiating the ontology for the thorax. Several transitive relationships were used for symbolically modeling aspects of the physical organization of the thorax.

**Results:** By declaring *Organ* as the macroscopic organizational unit of the body, and defining the entities that constitute organs and higher level entities constituted by organs, all anatomical entities could be assigned to one of three top level classes (*Anatomical structure*, *Anatomical spatial entity* and *Body substance).* The ontology accommodates both the systemic and regional (topographical) views of anatomy, as well as diverse clinical naming conventions of anatomical entities.

**Conclusions:** The ontology formulated for the thorax is extendible to microscopic and cellular levels, as well as to other body parts, in that its classes subsume essentially all anatomical entities that constitute the body. Explicit definitions of these entities and their relationships provide the first requirement for standards in anatomical concept representation. Conceived from an anatomical view point, the ontology can be generalized and mapped to other biomedical domains and problem solving tasks that require anatomical knowledge.

## INTRODUCTION

Human anatomy is a fundamental science that underlies all fields of medicine. Indeed, it is difficult to make a statement in any medical context without explicitly or implicitly invoking anatomical concepts. The physical examination, medical imaging and other procedures, as well as the basic elements of the medical history, all generate clinical data that pertain to anatomical entities in the human body. The interpretation of these data relies on an implicit understanding of anatomy. The inferences entailed in such reasoning call upon cognitive or computational processing of abstractions about physical entities of the body, making use of relationships that exist among anatomical concepts.

Continuing advances in imaging, coupled with the growing use of imaging in diverse fields of patient care, have highlighted anatomy as an information domain critical for clinical medicine. Although the number of anatomical terms in current use is large, and their occurrence in hard copy sources and controlled medical vocabularies is extensive, there is little consistency in their representations. Each of the current major medical vocabulary projects arranges anatomical terms according to its own conceptualization. [1-4] Such disparity in approach is perhaps not surprising, since the organizational principles which could provide the foundation for a reusable anatomical information resource have not been articulated.

Since many types of clinical data may be regarded as attributes manifested by various classes of anatomical entities, we argue that standards in anatomical concept representation could facilitate the establishment of standards in clinical concept representation. The need for a formalized, canonical model of anatomy has, in fact, been advocated as a prerequisite for clinical concept representation [5, 6]. This need can best be met by a coordinated research effort focussed on developing symbolic representations of anatomical knowledge; an effort that should parallel the intense interest and research activity currently directed toward visualizing human anatomy.

We have been developing a symbolic knowledge base in anatomy as one of the information resources in the Digital Anatomist distributed framework for anatomical information. [7-9] Our objective is a system in which conceptualizations of anatomical entities, and the relationships among them, are specified as an ontology that models the physical organization of the body. We argue that, in order for such a knowledge base to be reusable in different fields of patient care, biomedical education and research, it should be developed from an anatomical viewpoint.

### Structure of this Paper

We begin by defining the term *anatomy* (Section 2). We next consider the types of physical objects and spaces that constitute the body, an essential step in formulating a symbolic model of the body's physical organization. Section 2 ends with an assessment of currently available representations of anatomical concepts. In Section 3, we state the requirements of a knowledge base of anatomy and propose defining attributes according to which anatomical entities may be classified. We support the proposed classification by type definitions and examples. A description of the granularity of concept representation, term assignments, and relationships is followed by the implementation of the ontology. Finally, we consider the emergent properties and the evaluation of the knowledge base, and conclude the section with the evolutionary enhancements we currently envision for the knowledge base. Section 4 summarizes the features of the Digital Anatomist Knowledge Base that distinguish it from other symbolic representations of anatomy, and considers its contribution to the setting of standards in anatomical concept representation. In conclusion, we describe ways in which the availability of the knowledge base may facilitate the development of problem-targeted applications that require anatomical knowledge.

## ANATOMY AND ANATOMICAL ENTITIES

### Definitions of Anatomy

A contraction of two Greek roots, *ana- (*up), and *temnein* (to cut), hence *anatemnein* (to cut up or dissect), the term *anatomy* was used historically to denote either dissection of a cadaver (e.g., performing or attending an *anatomy*, such as that depicted by Rembrandt in 1632 [10]), or a treatise on the same subject (e.g., Vesalius' *Anatomy*, 1543 [11]). With the advancement of methods for analyzing the human body, such as the introduction of the microscope, the term began to acquire broader meanings.

For the purposes of developing the knowledge base, we define *anatomy* in terms of two distinct concepts. These definitions assert that anatomy is:

1. the ordered aggregate of physical objects and spaces that are assembled according to predetermined spatial relationships or patterns that are influenced by the coordinated

expression of groups of genes, and thereby constitute an organism and its physical subdivisions; in other words, the organizational structure that, in the material sense, constitutes a living organism and its parts. To distinguish this concept from that of the second definition, we designate it as *anatomy(structure)*, when so doing serves the purpose of clarity.

2. the science concerned with the discovery, analysis and representation of anatomy(structure), and the processes responsible for its establishment, along with the conceptual entities required for understanding, explaining and drawing conclusions from anatomical observations. To distinguish this concept from anatomy(structure), we designate it *anatomy(science).*

The second definition implies that a primary objective of anatomy(science) is the conceptualization of physical entities that constitute anatomy(structure). It is a peculiarity of anatomy(science) that most of the concepts it deals with are physical entities (e.g., thorax, heart, gland, lymphocyte), whereas the chief concept domain in other biomedical sciences involves nonphysical entities (inflammation, nausea, diabetes mellitus, tachycardia, schizophrenia, pregnancy). Nonetheless,the underlying physical entities with which these other biomedical sciences are concerned are, in fact, anatomical entities. Thus conceptualizations of anatomy(structure) are critical for modelling biomedical concept domains in fields other than anatomy, as well as in anatomy itself.

## Physical Anatomical Entities

The cell theory, formulated in 1838 and 1839 by Schleiden and Schwann, defined the cell as the fundamental organizational unit of plants and animals [12, 13]. The human body is formed from a single cell, the zygote, in which the nuclei of a male and a female gamete fuse and mingle their genetic material. The progeny of the zygote, generated by successive cell divisions, are constituted of organelles and macromolecules synthesized by the parent cells. Cells also produce molecules that act as signals for inducing and regulating the assembly of newly formed cells into aggregates according to spatial patterns that are genetically conserved. Governed by these genetic and molecular processes, the cell aggregates become folded and rearranged into microscopic and macroscopic physical objects. Spaces are generated within and between them, and become filled with body substances. The physical objects, spaces and substances formed by these cellular and morphogenetic processes range in size from molecules to major body parts and the entire body (organism) itself; together, they constitute anatomy(structure).

All these anatomical entities manifest both physical and functional attributes, according to which they may be characterized and classified. The great diversity of anatomical entities that exists in the body accounts for its structural complexity. An understanding of this complexity requires conceptualization of a hierarchy of physical units or parts, and of the relationships that hold among them. Such conceptualization is the domain of anatomy(science), and more particularly, the purpose of a knowledge base.

Organizational units and relationships at the molecular level can be defined with quantitative methods of physics, and physical chemistry (e.g., x-ray crystallography and NMR spectroscopy), as well as with assays of molecular and cellular functions. In contrast, the criteria by which multicellular units of anatomical organization can be defined and characterized are more subjective. Consequently, there is a good deal of ambiguity in the current definitions of microscopic and macroscopic anatomical entities and in the names by which groups or classes of them are identified. The emergence of computer-based methods for knowledge representation and information processing calls for an evaluation and possible modification of the classification schemes which, for more than a century, have served to represent and communicate anatomical knowledge.

Owing to the large body and scope of information, the subject domain of the knowledge base must initially be restricted, for practical reasons, to one organizational level of anatomy(structure). Since the anatomical data that are generated in clinical practice pertain predominantly to anatomical entities visible to the unaided eye, we have restricted the subject domain of the knowledge base to the macroscopic anatomy of the human body. We use the term *macroscopic anatomy* to include anatomical entities visible with the unaided eye in both the living and the deceased human body; it is distinct from *gross anatomy*, which implies cadaver anatomy alone. The distinction between these terms is relevant to the further subdivision of macroscopic anatomy into *canonical* and *instantiated anatomy*, discussed below.

**Representations of Macroscopic Anatomy**

We have previously drawn distinctions between spatial (or graphical) and symbolic representations of physical anatomical entities and have proposed that such reusable representations be developed in parallel, with methods best suited for each, together with methods that link the two representations.[7, 14] This approach has been adopted by others [15,16] and is also being pursued by the Visible Human project [17]. Both spatial and symbolic representations may be concerned with either canonical or instantiated anatomy.

**Canonical and Instantiated Anatomy**

Knowledge of macroscopic anatomical entities is based on the historical exploration of the body and its parts by qualitative methods (e.g., cadaver and surgical dissection, the physical examination, physical and optical sectioning). These methods, however, can be applied only to individual instances of anatomical structure. The anatomical data that have resulted have not been systematically recorded; rather, generalizations deduced from such qualitative observations have been propagated by generations of anatomists. A synthesis of such generalizations, sanctioned implicitly by accepted usage, may be regarded as *canonical anatomy*. Because of the highly conserved nature of morphogenetic processes, the canonical model has sufficed for learning anatomy and for applying this knowledge by humans to clinical problems. The current canonical model of anatomy, therefore, is a useful conceptualization of physical anatomical entities. Such a model is implicit in the graphics and narrative texts that constitute the recorded legacy of anatomy(science), and it also exists as an abstraction in the mind of humans who understand anatomy.

In contrast to canonical anatomy, *instantiated anatomy* comprises the anatomical data generated by invasive and non-invasive methods in clinical practice. These data are systematically documented in the clinical record, and amount to a new field which deals with the macroscopic anatomy(structure) of individual, living, human subjects. When problem-targeted applications need to rely on anatomical knowledge for sorting data of instantiated anatomy, and making inferences based on these data, the ranges of variation in size, shape, spatial relations and other anatomical attributes, which seem trivial in terms of the canonical model, assume practical importance. Such sorting and inference, however, must rely on knowledge of canonical anatomy and therefore the canonical model must serve as a foundation for a knowledge base in anatomy.

It is one of our objectives to formulate a canonical symbolic model which also accommodates instantiated anatomy.

**Symbolic Representations**

A large number of anatomical terms are embedded in controlled medical vocabularies.[1-3, 18] However, the development of these resources is motivated largely by the need to computerize the clinical record. Thus they were not developed from a strictly anatomical viewpoint, and lack concepts and semantic relationships that are required for modeling the physical organization of the body. A review of some of the available representations is warranted in order to justify the creation of yet another anatomical knowledge source.

*Nomina Anatomica* [19], written in Latin and available only in hard copy, was published originally in 1895. Now in its sixth edition, it is the only comprehensive compendium of anatomical terms that has been developed from an anatomical viewpoint and sanctioned by the International Nomenclature Committee. Nonetheless, the specificity and granularity of its terms are inadequate for meeting the needs of scholarly treatises in anatomy or many fields of clinical practice. Terms in *Nomina Anatomica* (NA) are organized according to the study of so called systems of the body (e.g., Osteologia, the study of bones; Splanchnologia, the study of internal organs). However, it fails to define the systems adequately and does not attempt a classification of the concepts denoted by its terms, shortcomings that may account for some inconsistencies evident in its organization. Splanchnologia, for example, includes the liver but not the heart, which is included in Angiologia, the study of blood vessels.

To a varying extent, the same shortcomings are to be found in the large body of published anatomical information. As a result, the specificity in available sources is insufficient for defining classes of anatomical entities and their relationships in ways that would meet the requirements for logic-based knowledge representation. More important, the principles for formulating such definitions in narrative text, as well as the definitions themselves, have only been implied and not explicitly articulated. A few examples will underscore the relevance of this point.

Which class of entity is the heart? The answer is likely to be, an organ, rather than a blood vessel, as specified by NA. If it is *Organ*, presumably so are the spleen and the uterus; but according to what criteria? Are the sciatic nerve, the abdomen, the biceps and the knee joint also members of the class *Organ*? Is the right atrium an organ? If it is not *Organ* but a part of an organ (the heart), is the myocardium (which forms the muscular wall of the heart, as well as that of the right atrium) also a member of the same class? Should this class be designated as *Organ part*? Should the cavity of the right atrium also be classified as an *Organ part*?

The anatomical terms in these examples denote concepts that manifest sets of morphological and functional properties - in other words, anatomical attributes. On the basis of these attributes, anatomists intuitively conceptualize differences and similarities between the concepts, even though these attributes are not explicitly defined.

Because of this state of affairs, *ad hoc* attempts at anatomical knowledge representation are forced to resort to other arbitrary classification schemes (e.g. classes such as *simple structure*, *paired structure*, *symmetrical structure* [20], *conventional cavity, true cavity, actual cavity*[21], *thoracic structure*, *cardiovascular structure* [4]), or they simply omit assigning terms to classes. Segments of anatomical information have been incorporated as illustrative examples into knowledge representation methods (see for instance, Lucas [22]), or as indispensable components of clinical applications.[23-26] Of the large controlled vocabularies, SNOMED [2] includes an extensive and detailed compendium of terms in axes that relate them to anatomy. However, type definitions do not assign these terms to classes, nor are the relationships among these terms specified, and the fixed, code-dependent hierarchy is too limiting to accommodate a consistent conceptualization of anatomy.

The GALEN [3] and the Read Codes[18] projects adopt a more flexible approach. Each, however, develops an independent and different representation scheme for anatomical concepts.[4, 21] Moreover, the anatomical principles on which the schemes are based are not defined, leading to inconsistencies in the classification. For instance, in the anatomical symbolic knowledge base of the Read Codes [4], the list of subordinate concepts of the *Chambers of the heart* includes the fibrous pericardium and the pericardial cavity.[27] It is hard to see how a membrane and a space, both of which are outside the heart itself, can be subordinated to a set of entities that are part of the heart proper (the cardiac chambers).

The other project, GALEN,[3, 21] regards anatomical entities primarily as the location of disease processes; consequently its anatomy module lacks sufficient specificity and taxonomic structure for a coherent symbolic representation of anatomy. The Representation and Integration Language of GALEN,[3] however, seems well suited for generating expressions about anatomical concepts by the compositional approach, as well as associating diverse attributes with these concepts.

The UMLS Metathesaurus [1, 28] provides text definitions for a modest number of anatomical concepts and specifies their semantic type and their relations. These classes, however, are too broad for the purposes of modeling a knowledge domain as complex as anatomy. Nevertheless, the nodes and relationships in the UMLS Semantic Network have served us well as useful starting points for structuring anatomical knowledge.

As this review indicates, there is currently a substantial duplication of effort in the compilation of anatomical terms within various ongoing projects concerned with clinical concept representation. We contend that the problem lies in the failure of traditional knowledge sources to define concepts of anatomical entities with sufficient specificity and consistency. A standardized representation of anatomy(structure) in the clinical concept representation projects is impeded by the primary orientation of these projects: they are directed toward the clinical user rather than toward anatomy(science). Fundamental concepts, according to which anatomical entities may be organized, cannot be culled from radiological or clinical discharge reports, or from publications in diverse fields of clinical medicine. Writers of such communications assume a certain level of anatomical knowledge and understanding in the reader, but the basic concepts that support that understanding remain unarticulated and are therefore lacking from the respective controlled vocabulary projects.

The first requirement for standardizing anatomical knowledge representation seems to be an ontology generated from an anatomical viewpoint. Domain ontologies have been widely advocated as the first requirement for developing logic-based formalisms that can model defined information domains of medicine. [29-34] In addition to comprehensive concept representation, an anatomical ontology should also model the structure of anatomical knowledge itself. In order to assure its soundness and reusability, such a resource must be based on explicit definitions of anatomical entities and the relationships that hold among them.

## THE EVOLVING DIGITAL ANATOMIST SYMBOLIC KNOWLEDGE BASE

Our work on symbolic representation of anatomical knowledge began as an enhancement of the UMLS Semantic Network and Metathesaurus.[1, 28] Rather than adopting one of the more complex knowledge representation systems and languages, we retained and extended the semantic net of the UMLS and enhanced it with well defined semantics. This strategy allowed us to define the requirements for representing anatomical knowledge. Currently, the Digital Anatomist symbolic knowledge base consists of hierarchies, constructed on the basis of defined relationships, and definitions. Our experimental approach to developing the knowledge base has focussed on anatomical entities that comprise the thorax. The foundation of the knowledge base is the *-is a-* hierarchy, in which over 8700 concepts have been assigned to more than 200 classes and subclasses; we refer to this hierarchy as the anatomical ontology.

### Requirements of the Anatomical Ontology

At the outset, we imposed a number of requirements that the ontology had to satisfy. These requirements have been met and are listed below.

1. The subject of the anatomical ontology had to be restricted to anatomy(science). Anatomy(science) is defined in section 2.1, and on-

tology has been defined, in the broadest sense, as an explicit specification of a conceptualization.[31] For the time being, the scope of the ontology has been further restricted to entities pertaining to *macroscopic anatomy*.

2. The anatomical ontology had to specify, first of all, conceptualizations of the physical entities that constitute the body. This requirement must be met before such concepts as states, processes, and activities can be associated with physical anatomical entities. For the time being, we have limited the ontology to the static state of physical anatomical entities.

3. The ontology had to model *canonical anatomy* and provide ways for the knowledge base to accommodate and organize data pertaining to *instantiated anatomy*.

4. The ontology had to define the physical units that constitute anatomy(structure), in order to model the physical organization of the body. Although the ontology is currently limited to the macroscopic level of organization, physical units that constitute macroscopic entities had to be defined at the microscopic level, as well.

5. Generic, partitive and certain spatial relationships which exist, both horizontally and vertically, among the macroscopic and microscopic units of physical organization, had to be defined.

6. Although developed for macroscopic anatomy, the ontology had to be scalable and extendible to other fields of anatomy (embryology and developmental biology, microscopic anatomy, cellular and molecular biology, and neuroanatomy).

7. The representations of anatomical entities had to be parseable by machine and comprehensible, in their human-readable form, to both expert and novice users of anatomical information.

8. The ontology had to include all macroscopically discernible anatomical entities arranged in a type hierarchy. Therefore, the defining attributes of classes or subclasses in this hierarchy had to be stated in terms of anatomical attributes which are inherited by members of a class or subclass; likewise, the differentia between members of a class or subclass had to be defined in terms of anatomical attributes.

9. A symbolic model had to rearrange entities of the anatomical ontology according to various defined relationships that describe the physical organization of the entire organism (in the current context, the human body).

10. To assure consistency of the classification and the evaluation of the ontology by teachers and students of anatomy, the constraints imposed on the meaning of terms had to be formulated as definitions in human-readable text, and subsequently transcribed in logic-based notation.

An ontology that meets these requirements is distinct from knowledge itself and also from its existing representations in narrative text, in that it puts explicit constraints on the terms and the structure of the knowledge.[32] These constraints emerge largely from the conceptualization of the units of anatomical organization and their relationships.

### Defining Anatomical Attributes

In medical dictionaries [35, 36] and textbooks of anatomy (see for example [37, 38]), definitions of anatomical entities tend to be formulated in terms of functional attributes*. These attributes, however, fail to specify the constraints by which anatomical entities may be grouped together or distinguished from one another. In order to model the physical organization of the body, defining attributes of anatomical entities need to be stated in terms of their constituent parts, and in terms of the entities which they, in turn, constitute. A physical unit of anatomical organization must, therefore, be defined in terms of the parts of which it is composed and the higher order units of which it, in turn, is a part.

We have, therefore, formulated definitions of physical anatomical entities by specifying constraints in terms of the units that make up the body, and the relationships that hold among these units. In doing so, we have found it necessary to restrict and specify the meaning of several terms that denote partitive relationships (subdivision, part, component). Differentia are specified in the definitions primarily by the relationships -*consists of*-, and its inverse, -*constitutes*-. We use these relationships with a minor modification of their UMLS definitions**.

### Classification and Definitions

Since the objective of the anatomical ontology is to model the physical organization of the body, we declared *Physical anatomical entity* as the top level concept of the ontology. We classify all physical anatomical entities into one of three classes: *Anatomical structure, Anatomical spatial entity* and *Body substance* (Fig.1). These classes are also referred to as root concepts because we assign, based on the -*is a*- relationship, all physical entities in the body, as concepts, to these three classes. These assignments result in three parallel type hierarchies.

In each type hierarchy, several generations of subclasses link the root concept (class) to leaf concepts or instances. We distinguish between leaf concepts of *canonical anatomy* and *instantiated anatomy* (defined in Section 2.3.1). When desirable, a canonical leaf concept may itself serve as a parent for leaf concepts of instantiated anatomy: the canonical instance becomes a subclass. For example, "Left tibia" is a canonical instance and includes among its parents such subclasses as *Tibia, Long bone, Bone(organ)* and *Organ*, as well as the class *Anatomical structure.* The "Left tibia" of an individual subject (e.g., that of John Doe), however, is a leaf concept of instantiated anatomy; when designated with an appropriate extension (e.g., "Left tibia[JD]") it becomes a child of the subclass *Left tibia*. Classes and subclasses in the anatomical ontology correspond to semantic types of the UMLS Semantic Network, which are higher level nodes in the net.

The remainder of this section provides the definitions of the three classes (root concepts) of the anatomical ontology and those of some of their offspring. For each class and subclass, the definition states the genus and the defining anatomical attributes that distinguish its members (the entities included within the class or subclass) from those of the parent class or subclass. We have evaluated and revised the subclasses and their definitions during the process of making concept assignments in the ontology, pursuing in parallel top-down and bottom-up approaches.

Although our approach so far has been largely limited to the thorax, this body part actually includes almost all subclasses of anatomical entities that are found in the body. Thus the three root concepts and their immediate offspring, illustrated in Figure 1, subsume virtually all macroscopically visible entities in the body. It should, therefore, be possible to assign to these classes and subclasses all physical entities in the living or deceased body, regardless of whether or not they have been named previously. The same holds true for representations of macroscopic anatomical entities in medical images (e.g., groups of pixels and voxels).

Although concentrating predominantly on the thorax, we have found it necessary to include examples from other body parts to clarify and validate the classification and definitions. Some of these examples are cited in the following sections.

### Classes of Physical Anatomical Entity

The definition of *Physical anatomical entity* is implied by that of anatomy(structure) in Section 2.1. Of the three root concepts or classes of the ontology (Fig.1), *Anatomical structure* plays a dominant role; the other two, *Anatomical spatial entity* and *Body substance*, are defined in relation to *Anatomical structure*.***

**Anatomical structure** *is a* **physical anatomical entity** and **a physical object** which is *generated by* processes that are *affected by* the coordinated expression of groups of genes; it *consists of*

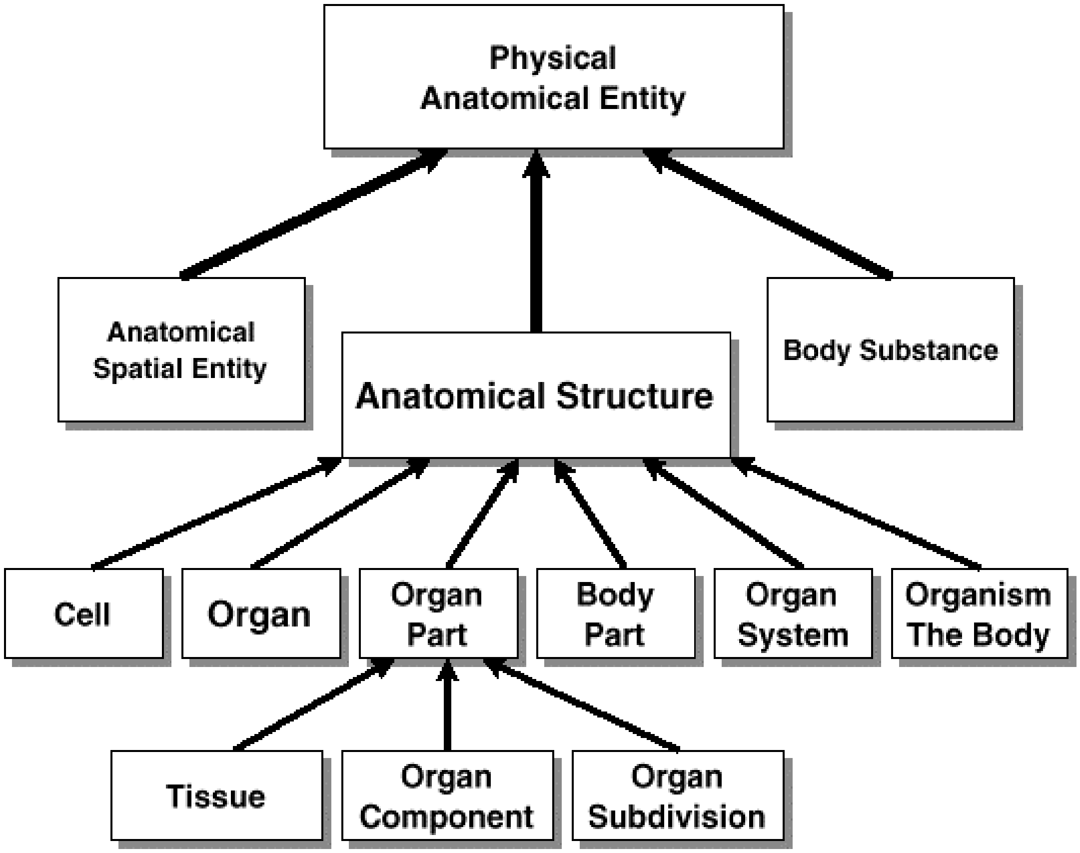


**Figure 1** The classification of physical anatomical entities based on the -*is a*- relationship. The first-generation offspring of *Anatomical structure* and *Organ part* are also shown

parts that are themselves **anatomical structure**s. The parts are *spatially related to* one another according to patterns which are also *affected by* the coordinated expression of groups of genes.

The largest anatomical structure is the whole **organism**; the smallest (for the current purpose of developing the knowledge base), is a **cell**, which is the fundamental organizational unit of plants and animals. (Examples: heart, right ventricle, mitral valve, myocardium, endothelium, lymphocyte, fibroblast, thorax, cardiovascular system.)

**Anatomical spatial entity** *is a* **physical anatomical entity** and a **spatial entity** of three or fewer dimensions, which is *associated with* the exterior or interior of **anatomical structure**s. (Examples: thoracic cavity, pericardial cavity, epigastrium, femoral triangle, diaphragmatic surface of heart, transpyloric plane, midclavicular line, midinguinal point.)

**Body substance** *is a* **physical anatomical entity** and a **substance** § in gaseous, liquid, semi-solid or solid state, with or without the admixture of cells, which is *produced by* **anatomical structure**s or *derived from* inhaled and ingested substances that become *modified by* **anatomical structure**s as they pass into or through the body. (Examples: intercellular matrix, saliva, semen, cerebrospinal fluid, inhaled air, urine, feces, blood, lymph.)

Arbitrarily limiting the definition of *Anatomical structure* to objects that are constituted by cells is justifiable in the present circumstances because the immediate purpose of the knowledge base is to model macroscopic anatomy. It will be necessary, however, to extend the symbolic model, with the collaboration of appropriate domain experts, to cell components (organelles such as mitochondrion, ribosome), large and small molecules, (e.g., myoglobin, T-cell receptor, cyclic AMP), and embryonic structures (developmental stages of fully-formed structures as well as transient structures that are transformed or eliminated by the morphogenetic process), since these entities also satisfy the definition of *Anatomical structure*.

The definition of *Anatomical structure* that we propose is more restrictive than that of UMLS, whose definition of the same term includes "pathological part of anatomy" (e.g. tumors, abscess).[1] Since such pathological entities are not generated by the processes responsible for establishing normal anatomy, we have excluded them from the anatomical ontology. The most specific semantic type for macroscopic anatomy in UMLS is *Body Part, Organ or Organ Component,* defined as a collection of cells and tissues which are localized to a specific area or combine and carry out one or more specialized functions of an organism.[1] (Examples: thorax, vagus nerve, heart, left ventricle, myocardium, anterior leaflet of mitral valve.) This semantic type is subsumed by *Anatomical structure* in the anatomical ontology that we are developing. Most of our work has entailed giving depth and specificity to members of the class *Body Part, Organ, Organ Component* of the UMLS semantic network.

### Subclasses of *Anatomical Structure*

Whereas the cell is usually considered the fundamental organizational unit of the body, assigning this role to the concept *Cell*, does not serve a useful purpose for formulating abstractions of macroscopic anatomy. Rather, we have hypothesized that of the subclasses of *Anatomical structure* shown in Figure 1, *Organ* be regarded as the basic organizational unit of macroscopic anatomy. We have proposed definitions of other subclasses of *Anatomical structure* in terms of the relationships they hold to *Organ*. We have tested this hypothesis by populating the ontology with anatomical structures located in the thorax. Although making these assignments called for a cyclic revision of the proposed definitions and the nodes of the ontology, the validity of *Organ* as the basic organizational unit of macroscopic anatomy was, in the final analysis, upheld.

We have assigned macroscopic and microscopic anatomical structures that constitute organs to the subclass *Organ part,* and we have defined *Body part* and *Organ system* as those subclasses of *Anatomical structure* that are constituted by organs. We have formulated the differentia that distinguish all these concepts from one another in terms of the anatomical structures that constitute each of them and the structures that they, in turn, constitute. All these subclasses of *Anatomical structure* also inherit the second defining attribute of their parent; namely, the parts that constitute members of each of the subclasses manifest spatial patterns of organization that are characteristic of each.

The next section states the constraints for *Organ* and *Organ part* in narrative text, supported by relevant examples; the following section defines *Body part* and *Organ system*.

### <u>Organ and Its Parts.</u>

**Organ** *is an* **anatomical structure** that *consists of* the maximal set of **organ part**s so *connected to* one another that together they *constitute* a self-contained unit of macroscopic anatomy, distinct both morphologically and functionally from other such units. Together with other organs, an organ *constitutes* an **organ system** or a **body part**. An organ is <u>*divisible into*</u> **organ part**s but not organs.(Examples: femur, biceps, liver, heart, aorta, sciatic nerve, ovary.)

In the current iteration of the anatomical ontology, three members of the subclass *Organ* are canonical instances (brain, spinal cord, skin) and the others are subclasses (Fig. 2). The latter subsume one or more generations of additional subclasses; only those of *Viscus* are displayed in Figure 2. There are no canonical instances of *Organ part*; its subclasses include *Tissue*, *Organ component,* and *Organ subdivision* (Fig. 1).

**Organ part** *is an* **anatomical structure** that *consists of* one or more types of **cell**s and intercellular matrix (which *is a* **body substance**); **organ part**s are *connected to* one another to *constitute* **anatomical structure**s of increasing size and structural complexity, which together *account for* the emergent morphological and functional attributes of an **organ**. An organ part is *divisible into* other organ parts, the smallest of which is a **tissue**. (Examples: endothelium, osteon, cortical bone, neck of femur, bronchopulmonary segment, middle lobe of right lung).

**Tissue** *is an* **organ part** that *consists of* similarly specialized **cell**s and intercellular matrix, aggregated according to specific spatial relationships; together with other tissues, it *constitutes* an **organ component**. [Examples: epithelium, muscle(tissue), connective tissue, neural tissue, lymphoid tissue.]

In addition to tissues, similarly specialized cells may also aggregate in body substances (e.g., cell aggregates and sediments in blood and urine). Spatial relationships in these aggregates, however, are not specified; therefore, these aggregates do not satisfy the definition of *Tissue*.

Tissues do not exist as discrete anatomical structures in the body. Accumulation of a particular tissue leads to spatial associations with one or more additional tissue types, resulting in the formation of anatomical structures of a higher order, which we have designated as *Organ component*.

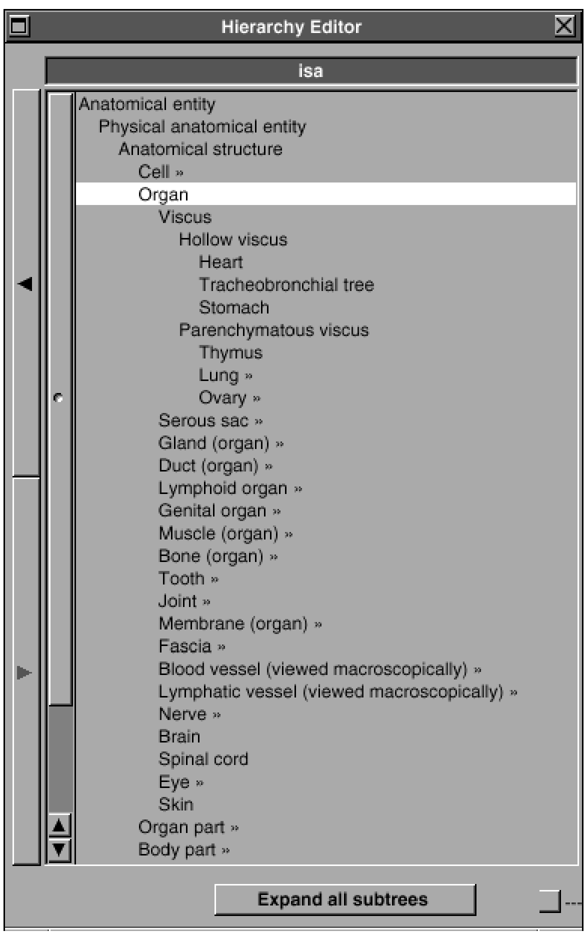


**Figure 2** The subclasses of *Organ* and its subclasses, displayed in a screen capture from the hierarchy editor of Knowledge Base Manager, the authoring program for the symbolic knowledge base. The symbol >> indicates that the node in the hierarchy (formed in this instance by the -*is a*- relationship) has at least one generation of children that is not shown. Double clicking on a term displays its immediate offspring by one tab indentation. Some of the terms denoting organ subclasses are extended by the qualifier "(organ)" because these terms are also used to designate members of other subclasses of *Anatomical structure*, such as Bone (tissue), Muscle (tissue). The tree is opened up for *Viscus*, the first *Organ* subclass, in which examples of canonical instances are displayed to illustrate the classification.

**Organ component** *is an* **organ part** that *consists of* a principal and one or more subsidiary **tissue**s; *connected to* other organ components, it *constitutes* an **organ subdivision**. (Examples: osteon, acinus, submucosa, capillary, papillary muscle, anterior leaflet of mitral valve, capsule of kidney, cortical bone, muscle fasciculus, anterior rootlet of spinal nerve.)

The associations of a principal tissue with subsidiary tissues delineate organ components which manifest great morphological diversity in terms of size, shape and patterns of spatial organization. One or more types organ components connected together form an organ part of a higher order, which we have designated as *Organ subdivision.*

**Organ subdivision** *is an* **organ part** that *consists of* two or more **organ component**s*; connected to* other organ subdivisions, it *constitutes* an **organ**. An organ subdivision is demarcated from other subdivisions of the same organ by one or more **anatomical feature**s. (Examples: right atrium, mitral valve, left lobe of liver, neck of femur, short head of biceps, arch of aorta).

Spatial relationships among organ components and organ subdivisions account for the shape, internal architecture and some of the physiological properties of an organ, as a whole. Different subclasses of *Organ* have different kinds of subdivisions (e.g., shaft, lobe, chamber), and different kinds of organ components.

The definitions of *Organ* and *Organ part* resolve the conundrum cited above. regarding the classification of the heart and its parts. Figure 3 illustrates these definitions and provides exam-

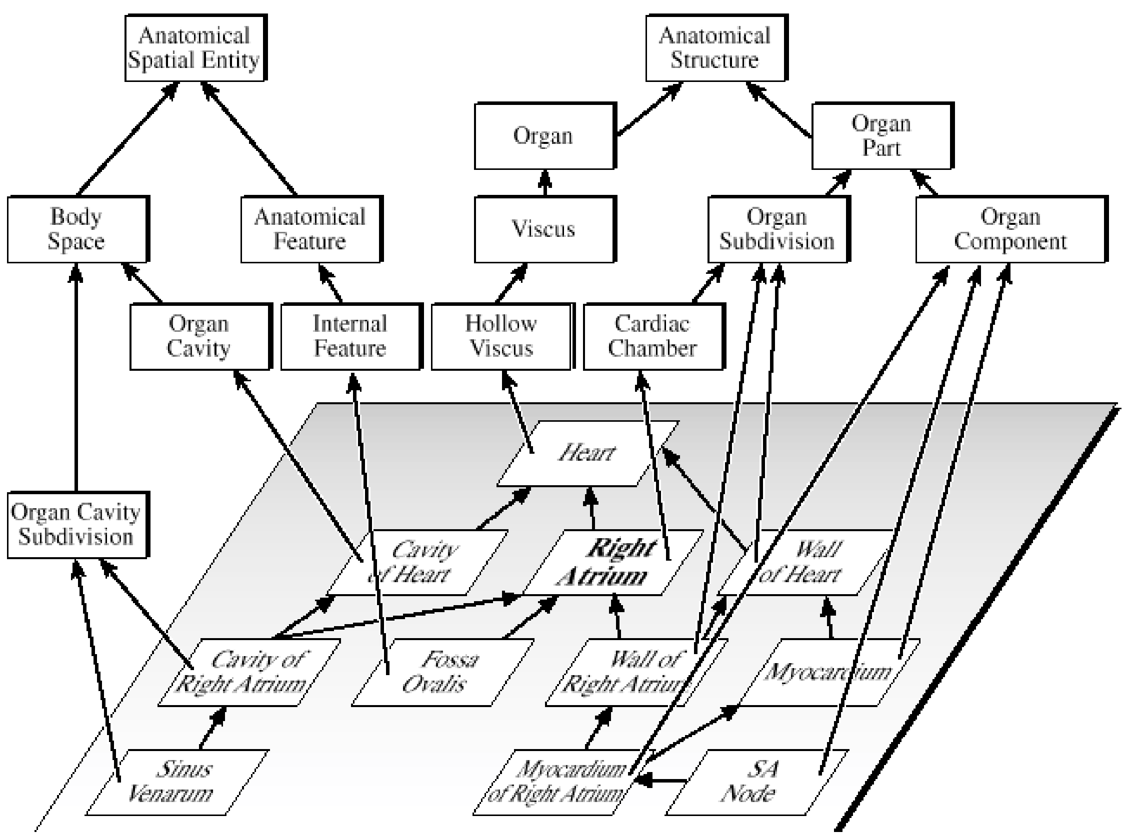


**Figure 3** Semantic network constructed with *-is a-* (solid lines) and *-part of-* (interrupted lines) relationships to model aspects of knowledge pertaining to the right atrium. Terms denoting parts of the heart are shown in the plane of the shaded quadrangle; the subclasses to which these entities are assigned are displayed above this plane.

ples for the relationships that exist between an organ and its various organ parts.

The heart is a *Hollow viscus*, [§§] which is a *Viscus*, which in turn is an *Organ* (Fig.2). The right atrium is not an organ, because it is not a maximal set of organ parts that constitute a self-contained, distinct unit of macroscopic anatomy (constraints that are satisfied by the heart itself). For instance, the myocardium (or heart muscle, forming the middle layer of the trilaminar wall of the heart), is a constituent not only of the right atrium but of other parts of the heart as well. The right atrium is an instance of *Cardiac chamber*, a subclass of *Organ subdivision*. On the exterior of the heart, the right atrium is demarcated from other cardiac chambers by the coronary and interatrial sulci, which are anatomical features. Moreover, the right atrium is not an *Organ component*, because it can be further subdivided into anatomical structures that are more complex than a tissue. As noted earlier, one such *Organ component* is the myocardium, which consists of myocardial fiber bundles or fasciculi of varying size. These fasciculi, in turn, consist of cardiac muscle (the principal tissue), and connective tissue. The latter serves as a subsidiary tissue, which ensheathes aggregations of cardiac muscle and defines the myocardial fasciculi and their spatial pattern of disposition. Thus myocardial fasciculi of different sizes and heart muscle itself are also organ components.

The spatial organization of the fasciculi manifest in part as the muscular ridges on the interior surface of the wall of the heart) is characteristic of a given cardiac chamber (*Organ subdivision*). For instance, as a consequence of abnormal developmental processes, the right atrium or the right ventricle may be located on the left rather than the right side of the heart. In such a case, these chambers can still be identified as the right atrium and right ventricle, based on their myocardial fiber architecture, and are indeed so designated ("anatomical right ventricle" located on the left).

The cavity of the heart, and that of the right atrium, do not satisfy the constraints of *Organ subdivision*, even though they are parts of the heart and may be related to it by the *-part of-* relationship. The cavity of the heart is classified as an *Organ cavity*, and the cavity of the right atrium as an *Organ cavity subdivision*, both of which are subclasses of *Anatomical spatial entity* (Fig.3), discussed below.

Similar introspective analysis has led us to establish subclasses of *Organ*, shown in Figure 2, and to assign other anatomical structures as subclass of *Organ part.* As a result we have classified as *Organ* several anatomical structures that are not usually thought of as such, whereas other structures conventionally regarded as organs are classified as *Organ subdivision.*

For instance, we classify skin as an organ rather than an organ system, because no part of the skin is a self-contained anatomical unit, its subdivisions (skin of the chest, skin of the palm) are demarcated by anatomical features, and its other constituent parts best meet the definition of *Organ component*. Similar reasoning justifies the classification of *Fascia* as a subclass of *Organ.* On the other hand, the rectum, colon and cecum are each classified as *Organ subdivision*, rather than *Organ*. In no case do the organ parts of these structures constitute a self-contained, distinct unit of macroscopic anatomy; the structures are demarcated from one another by anatomical features on the large intestine, and the spatial organization of their organ components manifests differences that are characteristic of each of these anatomical structures. It is the large intestine that satisfies the constraints for the definition of *Organ*. A similar argument may be made for classifying the trachea and bronchi as *Organ subdivision*, and only the full tracheobronchial tree as *Organ.*

The classification of *Joint* has presented a particular difficulty.[¶] Its constituent parts include subdivisions of two or more bones, each of which is a distinct organ. However, all constituent parts of a joint satisfy the constraints for *Organ subdivision* and *Organ component*; therefore, a joint is classified as *Organ*.

In addition to their defining attributes, organs and organ parts exhibit a number of other attributes that characterize them and assist in making class assignments and distinctions among the members of these two subclasses. Embryological derivation, location, anatomical feature, and physiologic function are such attributes. Organs are located in body parts, and may be represented as -*part of*- a body part, whereas organ parts are located only in organs, and may be represented as -*part of*- an organ. Organs are not located within other organs and do not form parts of other organs. Exceptions to this assertion are bone(organ) which, as already noted, contributes to the formation of joints, and blood vessels, lymphatic vessels and nerves (each a subclass of *Organ*), which arborize within other organ types. Another exception is a subdivision of a serous sac (the visceral layer of the serous membrane that forms the sac), which may be so adherent to the adjacent viscus that it is regarded as part of the viscus wall, as well as a subdivision of the sac itself (e.g., epicardium is the visceral layer of the serous pericardium; serosa of the small intestine is the visceral layer of the peritoneum). In each case, it is a subdivision of these organs (bone, blood vessel, nerve, serous sac) that is incorporated in another organ.

The differentia for distinguishing between various organ subclasses can be formulated by filling in values for different organ parts and their spatial relations. The result will be the assignment of some organs to more than one subclass. For instance, the ovary is classified as both a parenchymatous viscus and a genital organ. Likewise, the thymus is classified as a lymphoid organ and a parenchymatous viscus. Similar examples can be cited for subclasses of nerve. Such multiple assignments establish the basis for multiple inheritance.

Body Part and Organ System

The two higher level organizational units of the body are constituted of organs, as specified by their definitions.

**Body part** *is an* **anatomical structure** that *consists of* members of diverse subclasses of **organ**, one of which is a set of bones, and another is skin, a subdivision of which completely or partially *surrounds* the body part; together with all other body parts, a body part *constitutes* the body. (Examples: head, trunk, thorax, upper limb, forearm, finger, body wall.)

**Organ system** *is an* **anatomical structure** that *consists of* all members of one or more organ subclass; these members are *interconnected by* **anatomical structure**s or **body substance**s. (Examples: skeletal system, cardiovascular system, gastrointestinal system, immune system.)

Both terms, *Body part* and *Organ system*, are used by anatomical sources and structured vocabularies, and both carry various connotations. Nomina Anatomica, together with most other anatomical and clinical sources, uses *Body part* synonymously with *Body region* or *region*. For instance, the thorax is regarded as both a body part and a region, as are the upper limb and the hand. As already cited in section 3.3.1, UMLS provides one inclusive definition for a semantic type designated "Body Part, Organ or Organ Component". Anatomical sources do not define organ system explicitly but use the term in the same sense as NA (see Section 2.3.2). UMLS defines Body System as: "A complex of anatomical structures that performs a common function".[1] Both *Organ system* (e.g., cardiovascular system) and *Body part* (e.g., upper limb, or hand) satisfy the constraints of this definition. The definitions we propose constrain the meanings of the terms *Organ system* and *Body part*. Furthermore, both terms are distinguished from *Body region*, which is dealt with in the next section.

That defining attributes of *Body part* are inherited by members of the subclass can be appreciated if one considers that each is supported by a specific skeletal frame, each contains various types of organs (e.g., muscles, nerves, blood vessels, viscera), and most of the surfaces of each are covered by skin. Differentia of the members of the subclass will be given by filling in the values for the defining attributes, particularly those for the set of bones.

The differentia for members of the subclass *Organ system* can be specified in terms of the organ subclasses that constitute the system, and in terms of the particular anatomical structures or substances that interconnect them. For instance, the skeletal system consists of all members of the *Bone(organ)* subclass, which are interconnected by all members of the *Joint* subclass. In this instance, the interconnecting entity is an integral component of this particular organ system itself. This is the case in the majority of organ systems (e.g. respiratory, cardiovascular, gastrointestinal). In the hematopoietic and immune systems, however, the constituent organs are spatially separated and the interconnection between them is provided by blood and lymph, body substances contained in the cardiovascular and lymphatic systems. In all cases, the interconnections are as important for the manifestation of physiologic function as are the organs that constitute the system.

A number of body systems do not satisfy the definition of *Organ system* that we propose. For instance, we classify the conduction system of the heart as an *Organ component* (see Fig.5), and the portal system as an *Organ system subdivision*. The defining attribute of *Organ system subdivision* is that it consists of a specific set, rather than all members, of an organ subclass. For instance, the rib cage is an organ system subdivision, because its constituent organs are a set of bones consisting of thoracic vertebrae, ribs and the sternum, rather than all bones. The portal system includes that set of veins that are spatially associated with the gastrointestinal system; it is a subdivision of the cardiovascular system. The definition also specifies that the central, peripheral, and autonomic nervous systems each be classified as *Organ system subdivision*, rather than as *Organ system*.

The classification of anatomical structures that we propose, deviates in some respects from generally held views. Traditionally, anatomy(structure) has been described along one or the other of two axes. On the one hand, systemic anatomy(science) organizes anatomical structures into systems on the basis of the physiologic functions they share, and is sometimes called functional anatomy; on the other, regional or topographical anatomy(science) organizes anatomical structures on the basis of their location in "regions", that is, body parts, and is sometimes also called morphological anatomy. Some textbooks and treatises describe anatomy(structure) along the systemic axis;[38,39] others along the regional axis.[37, 40] Such different views or axes have dominated the conceptualization of several symbolic models of anatomy (e.g. Read Codes,[4] Voxelman [16]).

The structural ontology we propose, and the definitions that support it, unify these two axes of anatomy(science). The unification results from regarding *Organ* as the basic organizational unit of macroscopic anatomy, and from specifying relationships among members of the same or different organ subclasses in ways that constitute the higher order anatomical structures of *Organ system* and *Body part.* This conceptualization allows an association of attributes, such as physiologic and pathologic function, not only with *Organ system*, but also with *Body part*, *Organ*, and *Organ part* as well.

### Subclasses of *Anatomical Spatial Entity*

*Anatomical spatial entity* is defined in section 3.3.1. Many anatomical terms relate to spatial concepts about the body, but neither specific definitions nor an ontology of these concepts have been proposed. Some symbolic models do not distinguish them from structures. UMLS defines two semantic types for spatial entities: 1. *Body Space or Junction*, "an area enclosed or surrounded by body parts or organs or the place where two anatomical structures meet or connect"; 2. *Body Location or Region*, "an area, subdivision or region of the body demarcated for the purpose of topographical description".[1] These definitions include such diverse entities as the midinguinal point, midclavicular line, sagittal plane, epigastrium, diaphragmatic surface of heart, pleural cavity, sinus venarum of right atrium, orifice of right coronary artery, and mediastinum. The examples illustrate the heterogeneity of one-, two-, or three-dimensional spatial concepts. Our purpose is to sort these entities into classes according to the attributes they manifest in relation to anatomical structures.

The subclasses of *Anatomical spatial entity* are shown in Figure 4. The first generation of subclasses include *Body space*, *Body region*, *Anatomical landmark*, *Anatomical junction*, and *Anatomical feature*. All have second or third generation subclasses as parents of canonical

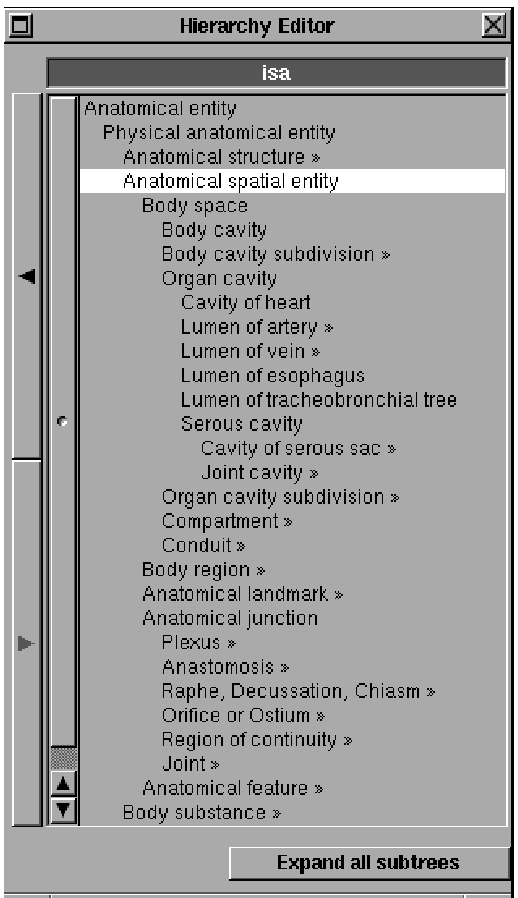


**Figure 4** Members of the class *Anatomical spatial entity*, displayed by KB Manager. The first generation subclasses of *Anatomical spatial entity* are comprehensive; trees are partially opened up for *Body space* and *Anatomical junction* to show their subclasses and some canonical instances of *Body space*.

instances. Here we provide definitions for those subclasses of *Anatomical spatial entity* that require explanation.

Body Space.

**Body space** *is a* three-dimensional **anatomical spatial entity**, which is *generated by* morphogenetic or other physiologic processes that *generate* anatomical structures; it is *enclosed by* **anatomical structure**s and *contains* one or more **anatomical structure**s or **body substance**s. (Examples: celom, thoracic cavity, lesser sac of peritoneum, cavity of right atrium, lumen of blood vessel, mediastinum, anterior compartment of forearm, intervertebral foramen.)

The constraints of the definition exclude spaces generated by pathological processes, such as the cavities of abscesses and cysts, but include pathological enlargement of anatomical body spaces. Members of the subclass are shown in Figure 4. The following examples illustrate the differentia on the basis of which members of the subclass may be distinguished in terms of embryological derivation, location, boundaries and contents.

**Body cavity** *is a* **body space** that is *embryologically derived from* the intraembryonic celom, is *located in* the trunk, is *enclosed by* the body wall, and *contains* **serous sac**s, **viscera** and other **organ**s. There is only one body cavity; it is a canonical instance of body space.

**Body cavity subdivision** *is a* **body space** that is *part of* the body cavity, it is *enclosed by* a **body wall subdivision** and is *demarcated from* another body cavity subdivision by an **anatomical structure** or a **conduit**; it *contains* one or more **serous sacs**, **viscera** and other **organ**s; together with the other body cavity subdivisions, it *constitutes* the body cavity. Canonical instances: thoracic cavity, abdominopelvic cavity, abdominal cavity, pelvic cavity.

The specificity of these definitions may be judged by comparing them with those of sibling subclasses of *Body space* (Fig. 4). Anatomically and clinically, a distinction needs to be made between a *Body cavity subdivision*, such as the thoracic cavity and the cavity of the serous sac that lines that body cavity subdivision: in this case the pleural cavity. The pleural cavity is a subclass of *Organ cavity,* since it is the cavity of a serous sac, which is an organ (Fig. 2). The definitions illustrate the use of differentia for constraining the meaning of anatomical spatial entities in relation to anatomical structures.

**Organ cavity** *is a* **body space** that is <u>enclosed by</u> **organ part**s and *contains* one or more **body substance**s; in the case of bone(organ), it contains bone marrow. (Examples: lumen of blood vessel or tracheobronchial tree, pericardial cavity, cavity of stomach or heart, uterine cavity, medullary cavity of femur.)

**Serous cavity** *is an* **organ cavity** that is <u>enclosed by</u> a **serous membrane** and *contains* **serous fluid**. (Examples: pleural cavity, peritoneal cavity, subdeltoid bursa, synovial cavity of hip joint.) Serous membrane is an *Organ part* of two organ types : *Serous sac* (e.g., pleural sac, peritoneal sac, bursa) and of synovial joint, a subclass of *Joint*. Therefore only serous sacs and synovial joints have serous cavities. Accordingly, a joint cavity is a serous cavity, which is distinct from *joint space*, a term used in radiology. The joint space is filled by articular cartilage (an organ component, which is translucent to x-rays), rather than by serous fluid. Therefore, *joint space* needs to be represented as a radiological attribute of both articular cartilage and synovial joint.

<u>Body Region and Anatomical Landmark</u>.

In contrast to body spaces, body regions and landmarks are rather arbitrarily defined spatial concepts. Their extensive use in both anatomical and clinical descriptions, however, requires that the terms denoting these concepts be specified. *Body region,* in particular, calls for clarification because, as noted in section 3.3.2.2., the term has been used synonymously with *Body part*.

**Body region** *is a* two-dimensional **anatomical spatial entity**, that is <u>*demarcated by*</u> **anatomical feature**s or **anatomical landmark**s on the external or internal surfaces of anatomical structures. It serves the purpose of topographical description, and *contains* **anatomical feature**s and the surface projections of anatomical structures and spatial entities that are located subjacent to the area. [Examples: epigastrium, precordium, palm of hand (region), axilla (region), triangle of Koch, right iliac fossa.]

The examples will suggest that the names of members of this subclass are frequently used to imply 3-D rather than 2-D spatial entities. For instance, "the epigastrium contains the stomach and the liver", or "the palm of the hand contains the lumbrical muscles". The first example is an incorrect assertion (the epigastrium contains the surface projections of viscera located within the abdominal cavity); the second example implies a compartment rather than a region. Therefore, the term "palm of hand" has two meanings, a region and a compartment, both of which can be specified by the values of the defining attributes of the two subclasses of *Anatomical spatial entity*. When necessary, an extension associated with the term should indicate the relevant concept [palm of hand(compartment), palm of hand(region)].

Anatomical landmarks include visible and palpable anatomical entities as well as arbitrary lines, planes and points. For example, the umbilicus, nipple and cardiac impulse are visible landmarks, and the sternal angle and apex beat are palpable landmarks. A number of arbitrary planes, lines and points, defined in relation to a variety of anatomical structures, have been sanctioned by long term usage (e.g., coronal plane, subcostal plane, vertebral level, midaxillary line, Nelaton's line, McBurney's point).

<u>Anatomical Junction</u>.

An anatomical junction implies physical continuity rather than adjacency, exemplified by the inosculation of blood vessels and hollow viscera with one another, or the intermingling of organ components of muscles, aponeuroses, nerves and nerve fiber tracts in such junctions as raphés, plexuses and decussations.

**Anatomical junction** *is a* two-, or three-dimensional **anatomical spatial entity** where two or more anatomical structures or body spaces meet and establish physical continuity with one another or with the exterior, or intermingle their organ components. [Examples: brachial plexus, optic chiasm, anococcygeal raphé, linea alba, orifice (ostium) of left coronary artery, anus, gastroesophageal junction, pylorus, knee joint.]

The differentia for the subclasses shown in Figure 4 can be stated as those anatomical entities that intermingle or establish continuity at the various junctions. The definition is best satisfied by the junction of body spaces (*Orifice* and *Anastomosis*), and the branching points of nerves, blood vessels and ducts. However, it is not entirely satisfactory to limit *Anatomical junction* to body spaces, because distinct anatomical structures (objects) are also formed by the junction of anatomical structures: plexuses of nerves and vessels, as well as raphés and decussations, are objects, which consist of the commingling of anatomical structures. For this reason, in addition to assigning such anatomical entities to the spatial concept *Anatomical junction*, we have also assigned them to the subclasses of *Anatomical structure* according to the defining attributes they satisfy. For instance, *Nerve plexus* and *Vascular plexus* satisfy the definitions of both *Organ system subdivision* and *Anatomical junction*. As discussed in section 3.3.2.1, *Joint* satisfies constraints in the definitions of *Organ* and *Anatomical junction*.

<u>Anatomical Feature</u>.

There are a large number of named anatomical entities which are rather difficult to classify either as *Anatomical structure* or *Anatomical spatial entity*, and are best designated as *Anatomical feature*. These concepts are widely used for describing anatomical structures. Because the anatomical attributes that are shared by these concepts can be stated most satisfactorily in terms of spatial concepts, we classify anatomical features as a subclass of *Anatomical spatial entity*.

**Anatomical feature** *is an* **anatomical spatial entity** which *is a* modulation of the external or internal surface, or of the internal organizational pattern, of body parts, organs and organ parts. (Examples: facet, surface, margin, border, apex, pole, hilum, tubercle, spine, gyrus, sulcus, metameric segmentation, multipennate fascicular architecture, acinar architecture.)

Most anatomical features are related to body parts, organs and organ parts by the *-part of-* relationship (e.g., the apex of the heart is a part of the heart). They serve descriptive purposes and as such, do not exhibit physiologic functions.

We have subdivided this subclass into *External feature, Internal feature* and *Organizational pattern*, in order to enhance the specificity of representations of anatomy(structure). Descendants of *External feature* are such modulations of an external surface as border or margin, apex or pole, base, prominence (e.g., spine, crest, tubercle, gyrus) and depression (e.g., fossa, fissure, sulcus or groove). *Internal feature* includes similar modulations of the internal surface. Distinctions between internal and external features are required if the anatomical ontology is to model the physical organization of the body. For instance, the knowledge captured by assigning the *fossa ovalis* as an internal feature to the right atrium (Fig.3), and the *coronary sulcus* as an external feature to the heart, is more useful, both clinically and anatomically, then if both concepts were entered in the ontology as canonical instances of *Anatomical feature* of the heart.

Spatial concepts such as lobulation, segmentation, metamerism, trabeculation, acinar architecture and fascicular architecture capture the spatial relationships according to which anatomical structures are organized into higher level units. We include these concepts in the subclass *Organizational pattern*.

### Body Substance

Body substance is defined in section 3.3.1.The definition is based on that of the same semantic type in the UMLS Semantic Network.[1] The Digital Anatomist definition specifies body substances in relation to anatomical structures, making it possible to state the differentia for members of the subclass in terms of the anatomical structures that produce or contain them. Most of the examples cited to illustrate the definition satisfy the constraints of the definition without ambiguity. Our assignment of blood and lymph to Body substance, however, calls for justification.

Blood and lymph have traditionally been regarded by anatomical sources as Tissue. Other fluids of the body, however, in which cells are suspended (e.g., cerebrospinal fluid, semen, synovial fluid) have not been classified as Tissue. In the anatomical ontology,we assign blood, lymph and all other body fluids in which cells are suspended to Body substance, because all satisfy the constraints of the definition of Body substance. We do not assign these body fluids to Tissue, because none of them satisfies one of the defining attributes we proposed for Tissue; namely, specific spatial organization of its constituent parts.

### Concept Representation

We have entered in the anatomical ontology, as unique concepts, all physical entities that are macroscopically discernible in the thorax. A granularity of greater resolution calls for microscopic methods to analyze anatomy(structure). Associating every concept with a discrete physical entity in the body allowed us to safeguard against representing one physical entity by more than one concept, even if a concept is known by several names. Once this constraint was satisfied, we assigned each unique concept to one or more classes or subclasses in the ontology for which it satisfied the type definition.

Our commitment to represent each visible entity explicitly, as a unique concept is one of the notable features that distinguish the Digital Anatomist ontology from available hard copy and machine-parsed sources of anatomical information. An example may help to illustrate what we believe is the advantage of our approach. Genetically determined organizational patterns conserved in the vertebrate body dictate that certain subclasses of anatomical structures occur not only bilaterally but also in metameric sets or other segmental patterns that are based on acinar architectures. In contrast to ours, several structured vocabularies take a predominantly compositional approach [2-4] and provide procedures for joining a term (e.g., rib) to numerical and laterality modifiers in order to represent members of a set. We chose an enumerative approach and have entered a unique concept in the ontology for each discrete, visible entity, and have associated it with a unique concept identifier and a preferred term. For instance, the *Right third rib* is a unique concept in the ontology, as is the *Superior articular facet of the head of the right third rib*.

Although macroscopic anatomical entities are numerous, their number is finite and can be readily managed by commercial database programs. Thus, for the purposes of an ontology that models the physical organization of the body, the comprehensiveness and veracity of a symbolic model obtainable by an enumerative approach outweigh the procedural disadvantage which, after all, has to be overcome only once. A compositional approach is suited for making statements about anatomy(structure) by those who have a knowledge of anatomy, but it fails to satisfy the objective of our ontology: a comprehensive and coherent, symbolic model of anatomy(structure) which, in its human-readable form, is comprehensible to both novice and expert users. Meeting this objective is a practical requirement for evaluating the ontology by teachers and students of anatomy.

Entering concepts at the level of granularity that we have chosen, leads to a heightened awareness of differences and variations in recurring anatomical entities and their parts. An example involves the 11 pairs of intercostal nerves and their distribution pattern: although each pair resembles other members of the set, each has branches that innervate different subdivisions of the skin and serous membranes associated with the body wall (pleura, pericardium, peritoneum). Unless each nerve is represented independently, the particular nerves that send branches to the breast, for example, or to the diaphragm, or to the peritoneum apposed to the diaphragm's abdominal surface, may be readily overlooked. In other words, unless the members of a set are represented as distinct concepts, it will be procedurally intractable to associate branches of different members of the set with different anatomical structures.

Such detailed representations can provide the knowledge necessary to make inferences about sources of referred pain, for instance, without having to provide a problem-targeted application concerned with the differential diagnosis with all possible manifestations of referred pain. Likewise, the specific morphological differences between the 12 thoracic vertebrae may not have an obvious clinical relevance but the spatial relations that change from vertebra to vertebra certainly do, and these relationships cannot be represented unless each vertebra exists as a distinct concept. Knowledge of these different relations is necessary in order to deduce which of the adjacent anatomical structures will be affected by lesions of a particular vertebra. Knowledge-based applications that target problems requiring such detail in anatomy(structure) will call for the explicit representation of these concepts. Entering such information in the knowledge base when the need for it arises is economically inefficient and is likely to result in inconsistencies.

Notwithstanding these justifications for the approach we have taken, we recognize the value and advantages of the compositional or generative approach. In expressive representation systems such as Ontolingua [29] and GALEN, [3, 21] common relationships can be described by axioms that hold for enumerated sets of anatomical concepts without having to repeat those axioms for each member of the set. It is indeed desirable to merge enumerative and generative representations once we migrate the simple frame system we have implemented to a more expressive system, such as Ontolingua.

In order to assure that the canonical symbolic models we generate can also accommodate instantiated anatomy, we have assigned variants of normal anatomy(structure) to a *Variant* subclass of particular anatomical concepts. For instance, *Third coronary artery* is assigned to *Variant artery*, a child of *Artery* in the ontology. At this stage, however, anatomical variants have not been systematically instantiated. Our experience argues for comprehensive representation of anatomical variants in the anatomical ontology.

Anatomical variants result from modulation of the processes that establish the canonical anatomical pattern of organization, without adversely affecting physiologic function. In some cases (e.g., coronary arteries, bronchopulmonary segments), the incidence of variants may be higher than that of the canonical pattern. When the modulation or disruption of morphogenetic processes leads to the persistence of embryonic structures that are normally eliminated during morphogenesis, or an abnormal structure develops that interferes with physiologic function, the structure should be classified as a *Congenital abnormality*. An atrial septal defect, or an ileal (Meckel's) diverticulum, for instance, is classified as *Congenital abnormality* of the interatrial septum or ileum, respectively. Such a semantic type already exists in UMLS.

### Term Assignments

We have assigned 14,916 terms to the 8,763 concepts we have entered to date in the ontology. Preferred terms were based on widely used American [37] and European [38] textbooks of anatomy. We disallowed homonyms. Where two concepts have been traditionally denoted by the same term, we associated, in parenthesis, a different modifier with each term to assure the uniqueness of preferred terms [e.g., muscle(organ), muscle(tissue)]. We also entered as synonyms all other terms that we could identify as having been associated with the concept (see

Fig.5); in some instances there are as many as six synonyms, but usually not more than two. Segmentally recurring concepts and their parts (e.g., branches of arteries and nerves), as a rule, have no synonyms.

We have cross referenced the terms that we have entered with three sources: Nomina Anatomica,[19] SNOMED [2] and the UMLS Metathesaurus [1] (Fig.5). Of the 15,000 terms, 1,850 occur in SNOMED, and less than 700 in NA. Since NA tends to record the name of sets of entities as a

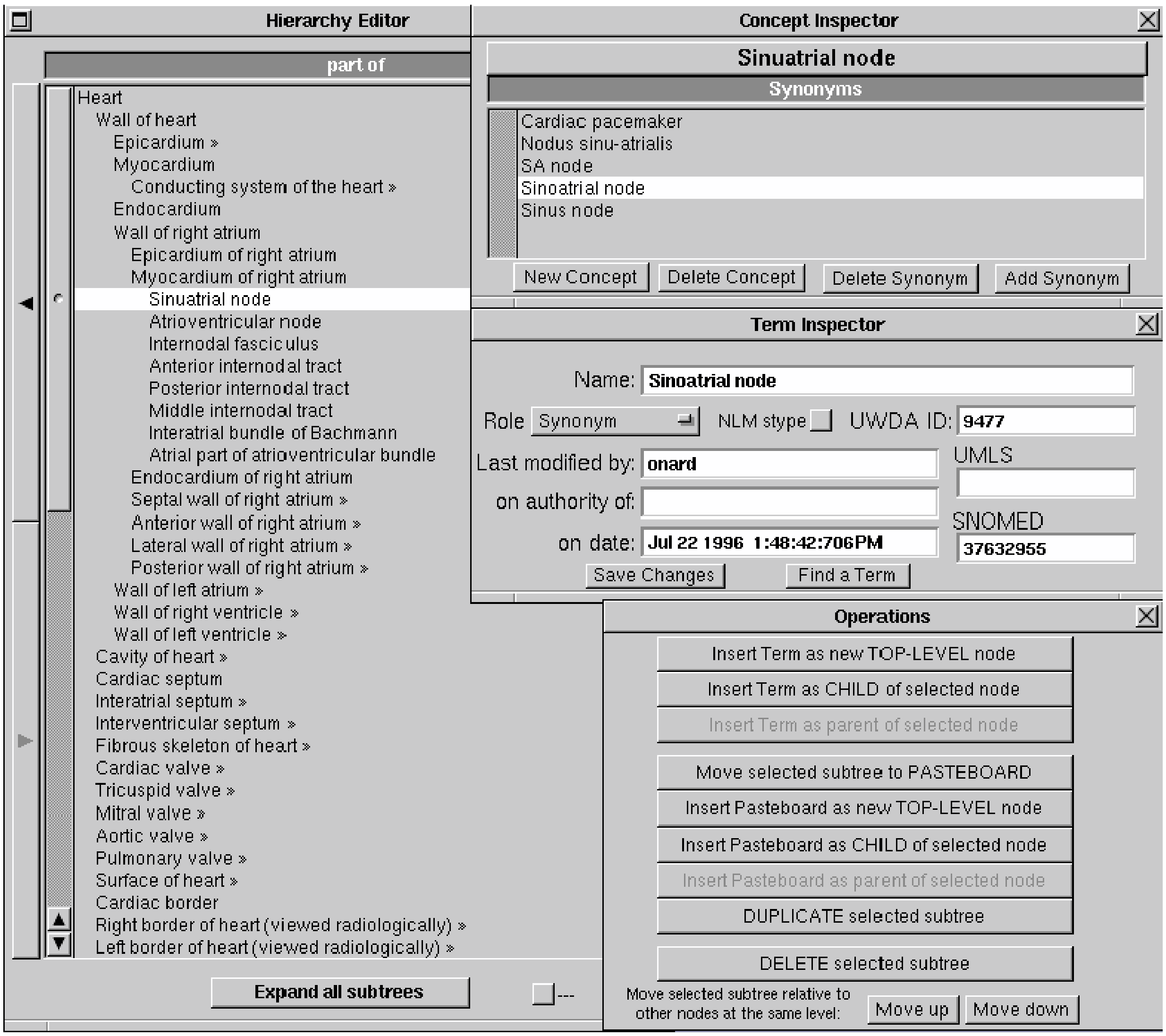


**Figure 5** Screen capture from the authoring program KB Manager, showing a segment of the *-part of-* hierarchy for the heart to illustrate concept granularity, term assignments and cross references with other vocabularies. The symbol >> indicates that the node in the hierarchy has at least one generation of children that is not shown. Immediate offsprings of a node are shown by one tab indentation. All components of the *Conducting system of the heart* could, for instance, be displayed by double clicking on the term and the successive generations of its children. Note that those components of the conducting system that are associated with the right atrium are displayed as parts of the *Myocardium of right atrium*, providing a symbolic representation of useful spatial information. The preferred name of a concept is highlighted in the Hierarchy Editor panel and also appears in the top bar of the Concept Inspector panel. Of the five synonyms associated with the concept, one is highlighted and appears in the Term Inspector panel, which provides information about the term: its role (synonym), concept identifier (UWDA ID) and its SNOMED identifier. Selecting *Nodus sinuatrialis* among synonyms would identify the authority for the terms as Nomina Anatomica.

Latin plural string, we have used the Latin singular string as a synonym for a member of the set, when doing so seemed appropriate (e.g., *Arteria intercostalis posterior dextra* for *Right posterior intercostal artery*, when the NA entry is limited to *Aa. intercostales posteriores)*.

### Relationships

The generic *-is a-* relationship has served for fully instantiating an ontology with canonical concepts for a major body part, the thorax. The ontology establishes type classes for anatomical physical entities. However, in order to model the physical organization of anatomy(structure), a number of other relationships must be represented explicitly. The definitions we have formulated imply that chief among these are partitive relationships, as defined by the UMLS.[1] Others are relationships of spatial adjacency and those that describe the branching and union of vessels and nerves.

We have formulated hierarchies using the transitive *-part of-* relationship. Figure 5 illustrates the high granularity of anatomical knowledge that can be represented with this relationship. For symbolically modelling relationships among instances of nerves, arteries, veins and lymphatic vessels, we have defined two anatomical relationships:

**-branch of-**, a smaller, peripheral anatomical structure, given off by a larger, central one, or into which a larger structure divides. Pertains in particular to the arborization of arteries, nerves, ganglia and bronchi. Inverse relationship: *-has branch-*.
**-tributary of-**, a smaller peripheral anatomical structure, particularly a vessel, that combines with another to form a larger more central one. Pertains in particular to the confluence of veins, lymphatic vessels and ducts. Inverse relationship: *-has tributary-*.

Using these two relationships, we have linked over 3,500 concepts of thoracic anatomy to 80 root concepts. Some of the trees extend to 7-8 generations of nodes in the *-branch of-* and *-tributary of-* hierarchies.

We are currently in the process of defining and implementing transitive anatomical relationships of spatial adjacency. In a fully segmented geometric anatomical dataset or model, such adjacencies can be represented quantitatively by sets of coordinates. Coordinate-free methods have also been proposed for describing in qualitative terms spatial relationships in 2-D medical images.[41] However, these descriptions, as well as coordinates, must also be stated in terms intuitive to humans, using the established naming conventions for spatial relationships. These are the terms that appear in standard anatomical and clinical publications, and in medical records.

Our current purpose is to represent canonical relationships of anatomical adjacency that have unambiguous semantics and a long history of established usage. The canonical spatial adjacencies are:

*-anterior-*, and its inverse, *-posterior-*
*-superior-*, and its inverse, *-inferior-*
*-lateral-*, and its inverse, *-medial-*

Any of these attributes may be joined to any other in the set, except to its own inverse, in order to describe with considerable precision binary spatial adjacencies between anatomical structures and anatomical spatial entities. Conjunction of an attribute with its inverse specifies direction, which pertains to orientation, viewing, or to passage of x-rays, projectiles, instruments, or of body substances and cells (including the spread of exudates, pus or cancer cells).

Our objective is to specify the conceptualization of canonical, as well as other, anatomical spatial relationships. The spatial adjacency ontology will represent the symbolic equivalents of a geometric constraint network,[42] which relates, and also predicts, the relative position of one anatomical entity to others. Representation of such spatial knowledge will be of particular value in the interpretation of medical images, in which the location of invisible anatomical entities must be inferred from those that are revealed by the imaging procedure.

We believe that a similar approach must be pursued for specifying other relationships that hold among anatomical entities and non-anatomical concepts of other biomedical domains. There is a need for developing domain ontologies that specify not only physiologic function associated with different anatomical entities, but also representations of anatomical entities with various medical imaging modalities, so that these ontologies can be mapped to the anatomical ontology.

## Process of Generating the Ontology

The conceptual framework of the ontology resulted largely from discussions that took place over an academic year in the context of a course at the University of Washington: Anatomical Knowledge Representation (CS 590BR); all the authors participated in the course. Principles for formulating symbolic representations of physical anatomical entities were proposed by one of the authors (CR) and were approved following rounds of discussions supplemented by presentations of publications from the relevant literature. The same process was followed for sanctioning narrative text definitions of classes, subclasses and relationships. The Knowledge Manager tool (designed by JFB) was used by JLM and CR for data entry. In general, this proceeded according to subclasses of physical anatomical entities (e.g, viscera, nerves, bones, serous cavities); in each case switching back and forth between the -*is a*- and -*part of*- hierarchies. Concept assignments to subclasses were strictly guided by the defining attributes specified in the definitions. Fully populating a specific subclass with instances present in the thorax tested the validity of the definitions not only for the subclass itself, but for entities of which it is constituted, and also for entities that the subclass in turn constitutes. Problematic instances were presented at weekly meetings of class CS 590BR, resulting at times in the modification of definitions, and reassignments of concepts. For instance, the initial assignment of *Joint* was to *Anatomical junction* in accord with the UMLS semantic type definition of this concept. As the definitions for various anatomical entities became clarified, *Joint* was reassigned to *Organ system subdivision*, and later to *Organ.* Once subclasses of *Anatomical spatial entity* were also defined, it was recognized that *Joint* also satisfied defining attributes of *Anatomical junction*. Currently it is assigned to both *Organ* and *Anatomical junction*, because it meets the definition of both these concepts.

Apart from those for segmentally recurring structures, all concept assignments were made one by one using the Knowledge Manager. When a subclass was completed, comprehensiveness of the entered data was checked by consulting the text book references, [37, 38] Nomina Anatomica and SNOMED.

## Implementation

The symbolic knowledge base is integrated in the Digital Anatomist distributed framework.[8,9] Currently, the knowledge base is represented by tables in a relational database, and by associated text files which describe definitions and other textual attributes. The terms table contains the preferred names and synonyms for all anatomical concepts, including the Nomina Anatomica Latin string. Each concept is assigned a unique ID, which remains constant. The terms table also records the associated SNOMED and UMLS ID, if the concept exists in these sources.

Terms are related by means of the links table, which records binary semantic relationships. The relational database is accessed by the Sybase commercial relational database server, which is in turn accessed by the Knowledge Base Manager authoring program, a tool for entering knowledge in the knowledge base. Figure 5 is a screen capture from the Knowledge Base Manager program, which is written in NeXTStep for the NeXT computer.

## Applications and Evaluation

The application that has driven the development of the symbolic knowledge base is the Atlas client program in the Digital Anatomist distributed framework.[9] Designed to support anatomy education, the program retrieves and integrates information from the spatial database and the symbolic knowledge base modules of the framework (Figure 6). Unlike clinical usage, which targets instantiated anatomy and is usually restricted to selected body parts and organ systems, education deals with the canonical anatomy of the whole body. Therefore, during the formative phase of the knowledge base, its educational uses are ideal for evaluating comprehensiveness of concept representation and the logical structuring of the information.

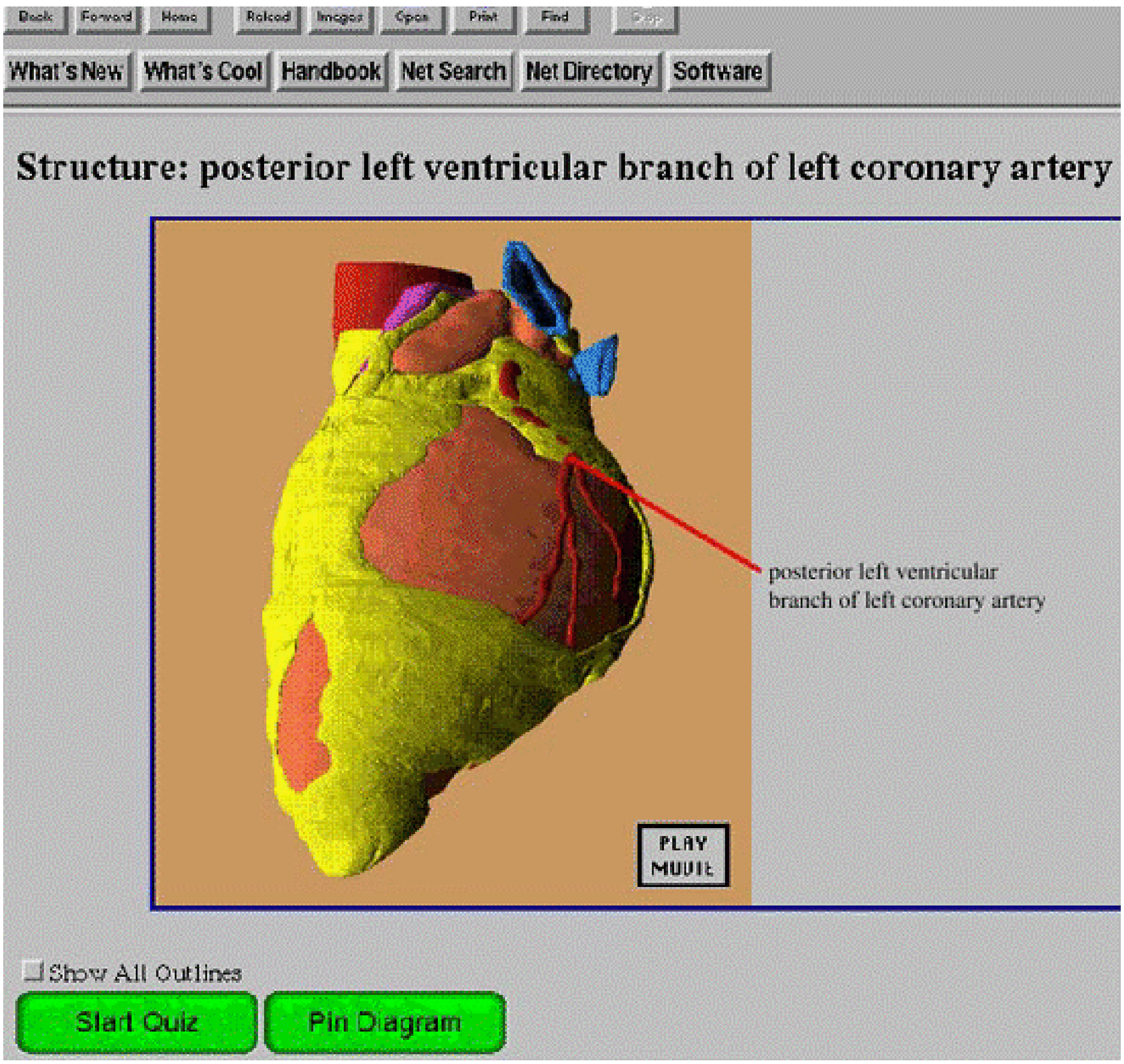


**Figure 6** Screen capture from the web atlas of Thoracic Viscera, illustrating the association of a term (retrieved from the Symbolic Knowledge Base by the Symbolic Knowledge Server), on the fly, with a structure present in a 3-D reconstruction (retrieved from the Spatial Database by the Web Server and CGI programs[9,43]). The term posterior left ventricular branch of left coronary artery was selected in the *-branch of* – hierarchy of the Symbolic Knowledge Base, accessed by the Web client; clicking on the term provides a list of images in which the concept is present. A lateral view of the heart, reconstructed by Skandha program[8] from 1-mm cryosections of a cadaver, [44,45] was chosen; a leader associates the selectd term (shown above the image) with the corresponding anatomical structure in the 3-D reconstruction.

For instance, in addition to retrieving names of anatomical entities by clicking on the image, the web client version of Atlas also generates a so called "pin diagram" on the fly, which automatically displays the names of all entities contained in an image.[9, 43] Such labeling provides a check on the comprehensiveness of symbolic concept representation and also assures that not more than one preferred name is associated with each entity.

In addition to their use by health science students in a variety of courses at the University of Washington, the Digital Anatomist information sources are consulted world wide. For instance, during a recent one and a half year period, the web client Atlas was accessed by over 33,000 sites from 94 countries.[9] Feedback received from such extensive usage has been helpful in identifying errors and inconsistencies in term assignments.

As described in section 3.7, formative evaluation of the classification was an integral part of formulating and instantiating the ontology. Assisted by guidelines for structuring ontologies,[34, 46, 47] we have revised and validated candidate subclasses and their defining attributes as we entered specific data about a major body part. Parallel approaches from the top down and from the bottom up were indispensable in this cyclic process. The anatomical ontology has been evaluated by the National Library of Medicine and will be incorporated into the 1998 edition of UMLS. Since the anatomical information we have represented is stable, maintenance of the knowledge base does not pose a particular problem. The anatomy ontology and terminology will be maintained as a component of the Metathesaurus.

Availability of the Digital Anatomist Symbolic Knowledge Base through UMLS will open up the possibility for its empirical evaluation by knowledge base developers, independent of our group. Our motivation for describing the underlying principles and rationale for the anatomical ontology in this publication is to invite and promote such evaluation. Although our formative evaluation based on the classification of several thousands of concepts suggests to us that we have reached an asymptote in defining the ontology, a number of questions remain to be answered. For instance: How unambiguous is the ontology for knowledge base developers in different fields of medical informatics and how easy is it to adapt it to specific applications? How well do classes and subclasses of the ontology subsume anatomical concepts associated with body parts other than the thorax, and what is the error rate in such modelling?

## Emergent Properties

Although the current usage of the symbolic knowledge base is limited largely to the naming of anatomical entities, there are at least five properties of the representations we have generated that facilitate conceptualization of anatomy(structure):

1. Clarity. The explicit definitions of classes and subclasses in the context of the ontology have introduced a degree of clarity into the conceptualization and description of anatomy(structure) that is lacking from both hard copy and other machine-parsed sources of anatomical information. The representations seem promising for facilitating the learning of anatomy, a hypothesis that will be tested through the use of the Digital Anatomist Atlas.

2. Portability. The structural ontology is portable, can be made available on line, and readily lends itself for labeling and organizing any image dataset of human macroscopic anatomy, be it from a living or a deceased subject.[9] The ease of associating terms in the structural ontology with spatial representations of anatomical entities further facilitates conceptualization of anatomy(structure).

3. Display of information at different levels of granularity. The sheer wealth of anatomical information presents a difficult and longstanding conundrum in anatomy: how to filter and access anatomical detail at a level appropriate to each user's expertise and specific needs. Historically,

the problem has been addressed by producing textbooks and treatises that are specifically targeted for different user populations with widely disparate needs for detailed anatomical information (allied health students, medical and dental students, and trainees and practitioners in the clinical specialties). The possibility of opening up trees in the *-part of-*, *-branch of-*, and *-tributary of-* hierarchies, which display information at different levels of abstraction, solves this problem. For instance, if desired, the *-branch of-* hierarchy can display the smallest visible branch of an artery in relation to its parent vessel by clicking on successive generations of nodes; alternatively, the display can be limited to major branches of a parent artery, or similarly the parent artery itself. Such nodal levels can specify the granularity of anatomical spatial data that are required for the problem at hand. Display of greater detail becomes meaningful when differences in serially recurring structures (e.g., branches of intercostal nerves, as cited before) assume practical importance and are needed to support inference.

<u>4. Integration of systemic and regional anatomy.</u> By regarding *Organ* as the basic macroscopic organizational unit of the body, the knowledge base readily provides both a systemic and regional view of anatomy. The concepts defined by the anatomical ontology can be displayed in the *-part of-* hierarchy to model both systemic and regional organization of anatomical entities in a form that is intuitive to humans.

<u>5. Support for inference</u>. The high level of granularity in concept representation supports inference of a number of relationships which, without the requisite anatomical detail, would need explicit representation. For instance, as noted in Section 3.4, the nerve supply of the diaphragm can be inferred from the *-branch of-* hierarchy, obviating the need for explicitly representing the *-supplies-* relationship or attribute. It may readily be inferred that the right and left phrenic nerves and a subset of the right and left intercostal nerves supply the diaphragm, because these are the only nerves that are represented as having diaphragmatic branches.

### Evolutionary Enhancements

It will be evident from the preceding sections that the simple scheme of the *-is a-* ontology, supplemented by other hierarchies such as *-part of-*, can capture detailed anatomical knowledge. However, the lack of sufficient semantic expressivity for the concepts and relationships in a semantic net motivates us to consider more formal knowledge representation schemes.[48] Having represented a substantial body of anatomical knowledge enables us to evaluate available knowledge representation systems for extending and enhancing the Digital Anatomist Symbolic Knowledge Base.

The next step in the evolution of the symbolic knowledge base will be to commit to a representation language and scheme. Recognizing the advantages of an environment that enables reuse of domain knowledge and problem-solving methods, we are looking at systems that provide tools for promoting the reuse of the knowledge base we are building. A number of such systems have been advocated for biomedical knowledge representation and application development.[3, 29, 30] Reusable environments, such as those provided by PROTÉGÉ-II,[33] promote the development of domain ontologies, which are decoupled from the specific problem solving methods that use domain knowledge. The anatomical ontology could, therefore, be mapped onto the problem solving methods, which are described in terms of domain independent, abstract problem solving concepts.

The fundamental components of the Digital Anatomist Symbolic Knowledge Base we describe in this report were developed from an anatomical viewpoint based on our experience and expertise in anatomy. The next phase of our work will benefit from collaborations with investigators whose experience and expertise is in methodologies of knowledge representation.

## CONCLUSIONS AND DISCUSSION

Focusing on a single organizational level of the human body, the macroscopic level, we have proposed principles according to which we have implemented a consistent symbolic representation of the physical entities that constitute the human body. The anatomical ontology we have formulated is distinguished from other symbolic representations of anatomy in the following respects:

* it is formulated from an anatomical viewpoint;

* its nodes are defined by sets of anatomical attributes, which are also explicitly defined;

* it defines *Organ* as the basic organizational unit of macroscopic anatomy;

* it models the physical organization of the body and displays this organization in a manner that is both intuitive to humans and parseable by machine.

By fully instantiating the ontology for a major body part, the thorax, we have shown that all macroscopic entities can be assigned to one of three classes and their subclasses. The ontology is extendible, furthermore, to the microscopic organizational level, in that each cell in the body can be assigned to a canonical instance in one of the classes we have defined for macroscopic anatomical entities. In the ontology, defining attributes of a parent class or subclass are inherited by its descendants; these are, in turn, distinguished from their parent and their siblings by differentia, expressed as the defining anatomical attributes of each. We have used established anatomical terminology for denoting canonical instances of anatomical entities, and have assigned specific meaning to the terms that we have used to designate classes and subclasses of these entities.

Many elements of the knowledge structure we propose are implied in hard copy sources of canonical anatomy. However, when we have judged it to be both necessary and prudent, we have intentionally set some precedents in organizing anatomical knowledge. As a result, the semantics, definitions and the classification we propose remove many of the current ambiguities in anatomical information and establish the first requirements for logic-based notations of anatomy. The ontology should support the development of applications for reasoning along the horizontal axis of anatomy, an information domain fundamental to virtually all fields of medicine. Making use of the knowledge we have represented, such applications should provide the means for empirical evaluation of the knowledge base. The outcome of these evaluations, and the ensuing implemented revisions of the knowledge base, will establish standards for anatomical knowledge representation. Standardized representation of anatomical knowledge is an important objective for realizing standards in clinical data representation, because macroscopic anatomy is relatively stable and forms the basis for many types of clinical data, particularly those generated by the physical examination and medical imaging.

In addition to being available as a knowledge source that can be mapped to other domain ontologies, the Digital Anatomist Symbolic Knowledge Base has immediate practical applications in its current implementation. Through the Digital Anatomist Atlas client program, the knowledge base makes available over the Internet and the web well defined terminology for annotating spatial datasets such as the Visible Human [49] and various medical images. The synonyms associated with anatomical entities accommodate and unify different usages of terminology prevalent in different medical and surgical specialties. The knowledge base provides a structure for the classification of anatomical entities, which should assist in the storage, sorting and retrieval of medical and other anatomical image data. Its display in human-readable form can promote the conceptualization of anatomy. Anatomy is the first, and one of the most challenging and time consuming subjects introduced in the training of all health care professionals. There is a need for logic-based, machine-parsed representations of anatomical knowledge for the creation of intelligent educational programs in anatomy. The Digital Anatomist ontology establishes a basic requirement for such applications.

We hope that both the immediately realizable and the potential uses of the anatomical ontology we have generated will serve as persuasive arguments for investing in the representation of deep knowledge along the horizontal axis of the basic and clinical sciences. An approach that is oriented entirely toward solving problems is in danger of keeping its operation, even if narrowly targeted, on a superficial level. To paraphrase Blois,[50] medical problems, including the learning of anatomy, require vertical reasoning. Unless knowledge sources are developed along the horizontal axes of the basic and clinical sciences to support such reasoning, the *ad hoc* approaches to problems will be both shallow and costly. As demonstrated by our work, the properties that emerge from efforts focussed on representing deep knowledge in a defined domain, can yield immediate practical benefits. Their most important contribution, however, is that they empower applications by the inferences that are made possible through the reusable knowledge. It will be interesting to see whether the availability of a resource for symbolic anatomical knowledge will exert a motivating effect on the development of problem-targeted applications in biomedical education and patient care to an extent similar to that exerted by the availability of the Visible Human spatial dataset on approaches to visualizing anatomy. At the least, the work we have accomplished to date should facilitate the encoding of anatomical knowledge for the entire human body in a schema that makes this knowledge widely accessible and usable. We regard the ontology we have formulated as the first iteration and the foundation of a knowledge base in anatomy, and we invite comments and feedback to assist in its revision and refinement.

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