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Creation and Usage of a "Micro Theory" for Long Bone Fractures: An Experience Report

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We seek to leverage enhanced expressivity in OWL 1.1 via property chain axioms with right identities in order to organize and constrain anatomic concepts for use in clinical descriptions. Anatomic knowledge represented in SNOMED CT uses SEP triplets; we anticipate that property chains will allow a more parsimonious organization of anatomic concepts. However, these constructs may lead to unanticipated inference, especially when scaling to large numbers of concepts [1]. We used a bottom-up approach based on targeted use case questions to iteratively develop a "micro theory" that both identifies the sensible locations of fractures in long bones and also supports logic-based classification of fractures. Alternative representations of the statement "fractures occur in bone" were explored with the aim of creating rich clinical descriptors that support classification for inference and data mining. The process of creating this micro theory is discussed, where pragmatic decisions were made with an intention of both constraining data entry and enabling inferences within the scope of the use cases.

INTRODUCTION

OWL and other forms of description logics have been used extensively to model spatial relationships for anatomical knowledge [1-6]. The focus of these efforts has been either to investigate the computational properties of the description logic or to develop a generalized set of axioms or theories to support classification inferences for a wide variety of clinical decision support use cases. We seek to leverage the enhanced expressivity of OWL 1.1 [7] to organize anatomic concepts for use in creating clinical descriptions. In particular, we explore the use of property chain axioms with right identities to simplify a knowledge base of anatomy without limiting the inferences that can be computed. It has previously been demonstrated that for anatomical descriptions, inferences after addition of these axioms can remain computationally tractable [3]. In contrast with other approaches, such as SEP triplets [2], we anticipate that property chains will allow a more parsimonious organization of anatomic concepts. The downside to using property chains and transitivity, however, are that these constructs may lead to unanticipated inference, especially when scaling to large numbers of concepts [1].

For our initial investigation, we focused on a single use case limited to fractures of long bones. We adopted an iterative bottom-up process to developing a "micro-theory"—an axiomitization that yields sensible and logically correct inference in a limited domain. At each stage, we tested the incremental theory against the use case scenario. We re-used content from the Foundational Model of Anatomy (FMA) [8]. The various distinctions introduced in the FMA to model partonomy, i.e., systemic-part-of, regional-part-of and constitutional-part-of were explored. We attempted to design a theory that was compact and understandable and also gave us the correct intended behavior. The model accounts for both anatomic perspectives and functional clinical perspectives. We tested the model by computing the appropriate inferences based on the use cases.

Locative transfer over pathophysiologic processes is a fundamental property for ontologies that will be used for clinical decision support or data warehousing applications. Given the sheer number of anatomic concepts present in systems such as SNOMED CT, it is critical that modeling idioms yield predictable results in order to scale. An important goal of the current work is begin to understand the characteristics of these idioms in a limited domain.

Clinical Scenario and Use Case Questions

Typically, a physician creates a clinical descriptor that is of sufficient granularity to support a management plan—the clinical descriptor is an index for the general management plan for a given pathology. Within the contemporary electronic health record, the clinical descriptor may be reused as data to drive point-of-care decision support, or as warehouse data to support reporting. For instance, if we need to report the number of patients who had a fracture of the proximal femur, we should include the number of patients who had a fracture of the femoral neck. In both cases, the original descriptor should support detailed classification schemes.

With respect to bone fractures, it is desirable to describe fractures in detail with respect to the bone features involved—the clinical detail drives the management plan. The clinical detail may describe either a fracture involving an anatomic landmark or a functional region where all fractures act similarly. It is equally important that the clinical descriptor not admit any nonsensical description. While fractures may involve bony landmarks, we generally do not describe fractures of the periosteum—the bone lining—or the bone marrow. While these are parts of bones, they are not generally parts through which fractures are described to occur. The GALEN project used constraints called *sanctions* to specify the values that could sensibly be applied to relations such as *has-location* [6]. Similarly, we constructed our ontology fragment with the intent of logically defining the set of all and only locations for fractures.

Given a need to document, to classify, and possibly to obtain reference information, useful questions that might be posed include[†]

1. What bone regions and features are contained in the Distal Epiphysis of the Femur?
2. What parts of the Distal Epiphysis of the Humerus are covered by Articular Cartilage?
3. Is a fracture of the Femoral Neck also a fracture of the Proximal Femur (i.e., is a fracture through an anatomic feature a fracture of a functional region)?
4. Is a fracture of the Trochlea a fracture of the Distal Epiphysis of the Humerus?
5. Is a fracture of the Trochlea an intra-articular fracture?
6. Is a fracture of the Trochlea an intra-articular fracture of the Distal Epiphysis of the Humerus?

MATERIALS

We looked at the following two sources for creating the fracture ontology: (a) The SNOMED CT hierarchies spanning the femur and the humerus; and (b) The FMA hierarchies corresponding to the femur and the humerus. A brief description of the portion of these two knowledge sources is described below.

SNOMED CT

SEP-triplets are extensively employed in the anatomical part of SNOMED CT. For each SNOMED anatomical class representing one entire entity, called *entity (or entire)* class (E-class), there are two auxiliary classes, the *structure* class (S-class) and the *part* class (P-class). For example, in the femur hierarchy, we ideally would have the following classes defined:

StructureOfFemur
EntireFemur $\sqsubseteq$ StructureOfFemur
FemurPart $\sqsubseteq$ StructureOfFemur $\sqcap$ $\exists$partOf.EntireFemur
BoneStructureOfDistalFemur $\sqsubseteq$ FemurPart
EntireDistalFemur $\sqsubseteq$ BoneStructureOfDistalFemur
DistalFemurPart $\sqsubseteq$ BoneStructureOfDistalFemur $\sqcap$ $\exists$partOf.EntireDistalFemur
StructureOfDistalEpiphysisOfFemur $\sqsubseteq$ DistalFemurPart
EntireDistalEpiphysisOfFemur $\sqsubseteq$ StructureOfDistalEpiphysisOfFemur

The E-class is instantiated by entire anatomical objects (such as the entire femur), and the P-class by the proper parts of the referred objects (such as the distal femur). The S-class, finally, is instantiated by instances that are either entire objects or their parts. This definition explains the *is-a* links from the E-class and the P-class to the S-class, as well as the partOf link from the P-class to the E-class. The main idea underlying the SEP-triplet approach is to represent a part-whole relationship between two entity classes not by a part-of link between the E-classes, but rather by an is-a link between the S-class of the "part" and the P-class of the "whole". This is, however, sufficient to simulate transitivity of part-of through the inherently transitive relation is-a:

EntireDistalEpiphysisOfFemur
$\sqsubseteq$ StructureOfDistalEpiphysisOfFemur
$\sqsubseteq$ DistalFemurPart
$\sqsubseteq$ BoneStructureOfDistalFemur
$\sqsubseteq$ FemurPart
$\sqsubseteq$ $\exists$partOf.EntireFemur

This allows us to conclude that every Distal Epiphysis of the Femur is part of some Femur. Since characteristics are inherited along the is-a hierarchy, the SEP-triplet encoding also allows us to simulate inheritance of characteristics along the part-of hierarchy. In our example, by connecting a fracture via the findingSite property to the S-class, we can ensure that a fracture located in the Distal Epiphysis of the Femur is classified as a fracture located in the Femur. Another advantage of the SEP encoding is that one can suppress such inheritance along the part-of hierarchy by connecting via findingSite to the E-class.

There are, however, several problems with the SEP-triplet encoding. First, from a formal ontological point of view, it partially conflates the is-a hierarchy with the part-of hierarchy, which may lead to unintended consequences since the two relationships are completely different by nature [9]. In SNOMED, it has indeed turned out that is-a links can be ambiguous, i.e., it is not always clear whether they are

[†] 1) The medial and lateral condyles of the Femur; 2) Trochlea and Capitellum; 3) Yes; 4) Yes; 5) Yes; 6) Yes.

introduced as part of the SEP-triplet approach, or are supposed to represent a genuine generalization relationship. Second, the SEP-triplet approach is error prone since it works correctly only if it is employed with a very strict modeling discipline. In SNOMED, triplets are often modeled in an incomplete way; in particular, the P-class and the part-of link to it from the E-class are missing in most cases. For example, the following axioms presented earlier were not actually asserted in SNOMED, but were included for pedagogical purposes (DistalFemurPart does not currently exist in SNOMED):

DistalFemurPart ⊑ BoneStructureOfDistalFemur
⊓ ∃partOf.EntireDistalFemur
StructureOfDistalEpiphysisOfFemur ⊑ DistalFemurPart

In addition, the auxiliary S-class is sometimes incorrectly used as if it were an *entire* entity class. Third, the approach introduces for every proper class in the ontology two auxiliary classes, which results in a significant increase in the ontology size. Finally, the SEP approach makes it much more difficult to define and maintain the set of sensible locations for fractures.

Foundational Model of Anatomy
The FMA ontology defines a set of partonomic relationships discussed in [10,11] for guiding the representation of anatomical parts. This is a smaller set than that used in GALEN [6], and thus one of the questions we seek to answer is whether it is sufficient for clinical modeling, Refinements of the generic part-whole relationships for anatomical structures are proposed, as anatomical structures have been decomposed based on several different contexts. A partition is defined as the decomposition of the entire body or any anatomical structure in a given context or viewpoint.

A *constitutional part* is defined as a primary partition of an anatomical structure into its compositionally distinct anatomical elements. In the context of the whole, an element is any relatively simple component of which a larger, more complex anatomical structure is compounded; i.e., the partition is compositional rather than spatial. For example, a stomach may be viewed as being partitioned into its wall and cavity. A *regional part* on the other hand is defined as a primary partition that spatially subdivides an anatomical structure into sets of diverse constitutional parts that share a given location within the whole; i.e., the partition is spatial rather than compositional. For example, a stomach may be viewed as being partitioned into its fundus, body and pyloric antrum to name a few of such parts. Constitutional parts are genetically determined, whereas regional parts are defined not only by genetically regulated developmental processes (e.g., lobe of lung, cortex of kidney, finger), but also by arbitrary landmarks or coordinates, such as used for demarcating the thoracic and abdominal parts of the aorta and the fundus of the stomach from adjacent parts of the corresponding wholes. A *systemic part* is defined as a secondary partition of an anatomic structure in accord with functional systems.

The distinction between regional parts determined by well defined genetically regulated processes and arbitrary landmarks and coordinates, is represented by associating the attributes *anatomical* or *arbitrary* with regional parts. Furthermore, these attributes provide the basis for the different views of regional partitions, as in the case of the liver, where its traditional partition into lobes based on *arbitrary* landmarks constitutes an arbitrary kind of regional view, while another partition based on the distribution of the tributaries of the hepatic veins or branches of the hepatic artery constitutes an *anatomical* regional view.

The FMA also supports topologic relationships supporting connectedness and containment. Connectedness describes whether structures are continuous with, attached to, or synapsed with other structures. Containment deals exclusively with the containment of a material anatomic entity within an anatomic space, e.g., Right lung -*contained in*- Right half of thoracic cavity. Connectedness and containment are orthogonal to regionality and constitutionality and do not confer parthood [12].

METHODS

We now present our approach to developing the long bone fracture ontology. We draw on the FMA as a primary source of anatomic content.

Regional vs. Constitutional Partitions
As previously discussed, the FMA ontology draws a distinction between a regional partition and a constitutional partition. We reviewed this content to determine whether it was suitable for reuse within our ontology fragment.

1. The ***regional partition*** of long bones is exemplified by the following regional parts of the Femur (regPartOf):

   ProximalEpiphysisOfFemur ⊑ ∃ regPartOf.Femur
   DiaphysisOfFemur ⊑ ∃ regPartOf.Femur
   DistalEpiphysisOfFemur ⊑ ∃ regPartOf.Femur
   FemoralNeckOfFemur ⊑ ∃
   regPartOf.ProximalEndOfFemur

Regional parts of the femur include true anatomic parts (epiphyses, diaphysis) as well as functional parts defined by fiat boundaries (proximal end of femur), illustrating the FMA's anatomic and arbitrary types.

2. The ***constitutional partition*** of long bones is exemplified by the following constitutional parts of the Femur (constPartOf):

   BonyPartOfFemur ⊑ ∃constPartOf.Femur
   BoneOfFemur ⊑ ∃constPartOf.BonyPartOfFemur
   PeriosterumOfFemur ⊑
   ∃constPartOf.BonyPartOfFemur
   MedullaryCavityOfFemur ⊑
   ∃constPartOf.BonyPartOfFemur
   VasculatureOfBonyPartOfFemur ⊑
   ∃constPartOf.BonyPartOfFemur
   ArticularCartilageOfDistalEpiphyisOfFemur ⊑
   ∃constPartOf.Femur
   ArticularCartilageProximalEpiphysisOfFemur ⊑
   ∃constPartOf.Femur
   VasculatureOfFemur ⊑ ∃constPartOf.Femur
   CavityOfFemur ⊑ ∃constPartOf.Femur

The constitutional parts of the femur include the multiple tissue types that combine to form a long bone—the bone proper, the articular cartilage, etc. Note the bone proper also decomposes to include the bone material itself, the periosteum, and the medullary cavity.

The regional partition includes the structures where clinicians locate fractures and the relationships between these structures. The constituents of long bone such as the periosteum, where fractures are not described to occur, are conveniently sequestered in the constitutional partition. We adopted the relevant portions of the regional partition for use in our model. However, we adopted a simpler representation for the incorporation of articular cartilage into the model for this initial iteration.

Modeling Design Choices
We now present some high-level classes and object properties that characterize the entities in which we are interested.

Bone
LongBone ⊑ Bone
Femur ⊑ LongBone
Humerus ⊑ LongBone
ObjectProperty(regionalPartOf)
reflexive(regionalPartOf)
transitive(regionalPartOf)
BoneRegion ⊑ ∃regionalPartOf.Bone
ObjectProperty(findingSite)
domain(findingSite) = Disorder
Disorder
Fracture ⊑ Disorder ⊓ ∃findingSite.BoneRegion

The class Bone is effectively the class BoneOrgan in the FMA. Within this initial iteration, we are neutral regarding the alignment of Bone with the Upper Ontology of FMA, i.e., aligning with the is-a hierarchy consisting of CavitatedOrgan, Organ, AnatomicalStructure, MaterialAnatomicalEntity, and AnatomicalEntity, as we did not see an impact of this in the context of the application at hand. The property findingSite aligns with the SNOMED CT relationship which assigns locations to clinical conditions

We declare the property regionalPartOf to be reflexive, thereby inducing Bone to be a BoneRegion. This has the important effect of unifying the treatment of entire long bones and bony landmarks with respect to findingSite—fractures may be declared to occur equally within the entire bone or at the landmark. We declare regionalPartOf to be transitive to support the interrelationships between discrete landmarks, larger regions of bone, and the entire bone.

Anatomical vs. Functional Partition
We add the following subclasses of BoneRegion into the model:

AnatomicBoneRegion ⊑ BoneRegion
FunctionalBoneRegion ⊑ BoneRegion

In clinical practice, pathology may be attributed to a true anatomic entity or a functional entity where unique pathologies behave similarly, are responsive to similar treatments, are aggregated for epidemiologic purposes, etc. In orthopedics, for example, several unique fractures all aggregate to fractures of the proximal femur. As previously noted, the FMA incorporates true anatomic regions and functional regions. We partition bone regions into either anatomic or functional components to support the independent enumeration of these features, as described in the use case.

Propagation of Locative Relationships
A key functionality that is required to support the use case questions discussed earlier is the ability to propagate the location of a fracture from a given region to all the regions to which it has regionalPartOf relationships. For instance, if a fracture is located in the femoral neck, it is also located in the proximal metaphysis of the femur as the femoral neck is a regional part of the proximal metaphysis of the femur. This is represented using the following axiom:

findingSite ∘ regionalPartOf ⊑ findingSite

It may be noted that the transfer of locative relationships is also propagated transitively due to the transitive nature of regionalPartOf.

regionalPartOf ∘ regionalPartOf ⊑ regionalPartOf

Articular Bone Regions
In order to explore articular fractures—the fracture of a bone region covered by articular cartilage, we incorporated the following concepts :

ArticularCartilage
ObjectProperty(coveredBy)
ArticularBoneRegion≡ BoneRegion ⊓
∃coveredBy.ArticularCartilage
ArticularFracture ≡ Fracture ⊓
∃findingSite.ArticularBoneRegion

This representation provides a simple method to distinguish between articular and non-articular bone regions.

RESULTS

Using the initial ontology, we were able to create a series of detailed clinical descriptions which classified as expected. Some examples are discussed next.

Locative Transfer over Regional Parts
rA facture of the Femoral Neck is classified as a fracture of the Proximal Femur.

FemoralNeckFx ≡ Fracture ⊓ ∃findingSite.FemoralNeck
⊑ Fracture ⊓

∃findingSite.(∃regionalPartOf.ProximalEndOfFemur)
(Since FemoralNeck ⊑
∃regionalPartOf.ProximalEndOfFemur)
⊑ Fracture ⊓ ∃findingSite.ProximalEndOfFemur
(Since findingSite ∘ regionalPartOf ⊑ findingSite)
⊑ ProximalFemurFx

Transitive Locative Transfer
A fracture of the Femoral Neck is classified as a fracture of the Femur. Let's revisit the earlier example and begin with the following reformulation of FemoralNeck.

FemoralNeckFx
⊑ Fracture ⊓
∃findingSite.(∃regionalPartOf.ProximalEndOfFemur)
⊑ Fracture ⊓ ∃findingSite.
(∃regionalPartOf.(∃regionalPartOf.Femur))
(Since ProximalEndOfFemur ⊑∃regionalPartOf.Femur)
⊑ Fracture ⊓ ∃findingSite.(∃regionalPartOf.Femur)
(Since regionalPartOf ∘ regionalPartOf⊑
regionalPartOf)
⊑ Fracture ⊓ ∃findingSite.Femur
(Since findingSite ∘ regionalPartOf ⊑ findingSite)
⊑ FemoralFx

The proof above indicates that we can represent direct relationships between bones and bone features and infer regional partonomy relationships between them.

Articular Fractures
Extending the model to describe and classify articular fractures is also accommodated by the model and creates no additional complications. The articular parts of the distal epiphysis of the humerus—trochlea and capitellum—are created as articular regions, while the non-articular parts—the medial and lateral epicondyle—are created as regular bone regions. The only caveat to this approach is that partially-covered regions are not considered articular regions; the distal epiphysis of the humerus is not considered an articular bone region by this criterion.

Fractures of the parts are created in the usual fashion by restricting the fracture finding site. Trochlear and capitellar fractures classify appropriately as articular fractures. General fractures of the distal humeral epiphysis and articular fractures are then created in the same way. Articular fractures of the distal humeral epiphysis are classified as subclasses of general fractures of the distal humeral epiphysis; trochlear and capitellar fractures are classified as further subclasses. Fractures of the epicondyles classify correctly as general fractures only. We did not specifically try to define non-articular fractures (fractures of parts not covered by articular cartilage).

Breach of the Model
We note one failure of the model in the subset of bones we examined. The FMA contains a regional part of the humerus, 'Nutrient Foramen of Humerus', literally, the hole where the nutrient artery enters the humerus. Because fractures are usually not described through this feature, this constitutes a failure of the model to constrain the set of sensible locations of fractures.

In the FMA, the nutrient foramen is a subclass of Immaterial Anatomic Entity. We can certainly remediate the model to additionally restrict bone regions to subclasses of Material Anatomic Entity. However, the appearance of the nutrient foramen as an arbitrary bone region bears further discussion.

DISCUSSION

We have begun to explore the creation of a 'micro-theory' for long bone fractures—an axiomitization that yields both sensible and logically correct inference. Using a set of framing axioms in combination with content from the FMA regional partition, we were able to describe and correctly classify a rich set of fractures, while maintaining a fairly parsimonious ontology. The resulting ontology is quite constrained as compared to an SEP triple approach.

Although this initial model successfully fulfills the use case, the breach raises significant questions. Because the FMA regional model admits arbitrary regions, there is no principled reason why an arbitrary region of a bone can sensibly be a fracture location. Our success seems to be an empirical finding—further analysis is necessary to see whether the model hold across all bones, or can extend to parenchymal organs such as the lung or the liver—organs made of the same 'stuff'.

Our model may succeed because bones exemplify a 'stuff/whole' partonomy, where arbitrary regions are compositionally homogenous. This does suggest that if regional parthood could be compositionally restricted, this would offer a more convincing model. One obvious possibility for implementing this restriction is to utilize the GALEN partitive attribute "hasSolidDivision", or perhaps a similar attribute with even more specialized meaning [13]. Currently, compositional properties are available through the constitutional partition of the FMA, i.e., if a part is composed of bone or a particular organ parenchyma, etc. Further work is necessary to reflect compositionality from constitutionality. We note that currently, wholes and parts have distinct roots in the FMA; in our model, it is important to treat parts and wholes similarly as bone regions.

This work provides initial insight into creating safe and effective inference over property chains for the purpose of creating and classifying clinical descriptions. Because of the tremendous change management implications of incorporating new idioms into terminologies such as SNOMED CT, it is important that we demonstrate that such idioms are safe, effective, and scale. Continuing work will investigate constraining the regional idiom with respect to homogenous compositionality, expanding our analysis to a larger set portion of the skeletal system, and examining the generalizability of the idiom to additional organ systems.

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