Expressing Medical Image Measurements using the Ontology for Biomedical Investigations

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Agenda

1. Measurements in radiology and pathology
2. Expressing measurements using OBI
    1. OBI value specifications
    2. Size measurements
    3. Density measurements
    4. Ratio measurements
3. Normal size, density and ratio specifications
4. Applications
    1. Information Extraction
    2. Normality Classification
    3. Inference of Change
5. Demo

Typical Measurements in Radiology

Not comprehensive

Size
length (1D, 2D, 3D), area, volume
index (e.g. spleen index = width*height*depth)

Density measured in Hounsfield scale (Hu):
mainly in CT images
minimal, maximal and mean density values for Regions of Interest (ROIs)

Angle
e.g. bone configurations or fractions

Blood flow
e.g. PET: myocardial blood flow and blood flow in brain

…

Measurements in Pathology

Not comprehensive

Size

length (1D, 2D, 3D), area

Weight

weight of resected tissue, nodule or tumor
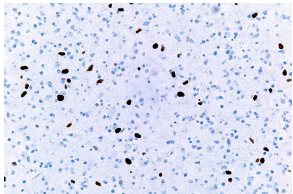
Ratios

immunohistochemical staining of tumor cells

Other measurements

viscosity of blood, serum, and plasma

mitotic rate

serum concentration

...

Expressing Measurements using OBI

obi:value specification

Shared structure in different contexts

The element "1.8cm" can occur in many different parts of a biomedical investigation.
It might be part of:

- the data resulting from a measurement of one of John's lymph nodes, made on January 12, 2014 in Berlin
- a protocol, i.e. a specification of a plan to make some measurement
- a prediction of the result a measurement planned for the future
- a rule for classifying measurements
- many more...

OBI uses the "value specification" approach to capture the shared structure across different uses and allow for easy comparison between them.

obi:value specification

Definition: An information content entity that specifies a value within a classification scheme or on a quantitative scale.

Example of usage: The value of 'positive' in a classification scheme of "positive or negative"; the value of '20g' on the quantitative scale of mass.

A scalar value specification has a numeric value and a unit of measurement. We connect them together with these relations:

- obi:has value specification: connect some particular measurement datum, prediction, etc. to a value specification
- iao:has measurement unit label: determine the unit of measurement for the value specification
- obi:has specified value: determine the numeric value for the value specification

Ontologies

Besides OBI the following ontologies are used to express measurements.

OBO Library

Basic Formal Ontology (BFO)

Relations Ontology (RO)

Information Artifact Ontology (IAO)

Ontology for General Medical Science (OGMS)

Units Ontology (UO)

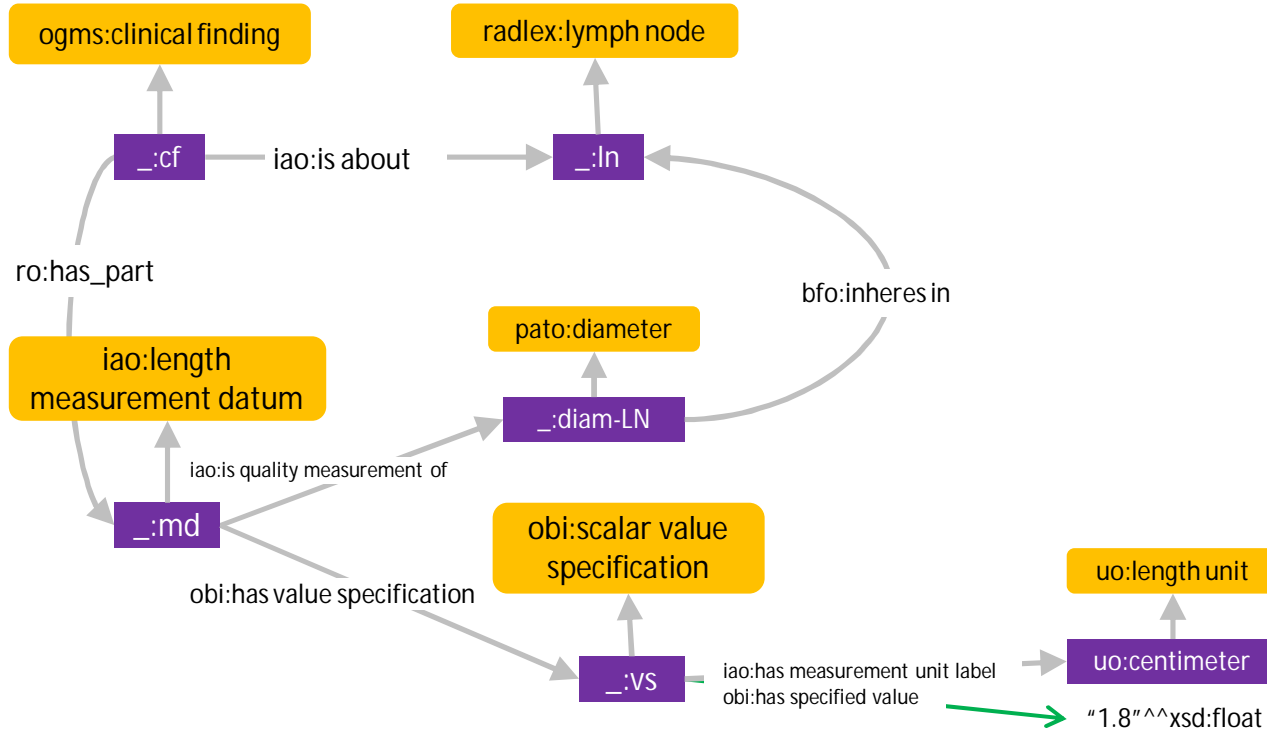Phenotypic quality (PATO)

Biological Spatial Ontology (BSPO)

Other

Radiological Lexicon (RadLex)

Model of Clinical Information (MCI)

Length measurements

Example: Enlarged lymph node with diameter 1.8 cm.

Length measurements

Example: Transverse diameter of kidney 5.2 cm.

Legend:

Note: Instances with underscore represent blank nodes

2D Measurements

Example with RECIST

Source: http://www.recist.com/recist-in-practice/19.html

RECIST
(Response Evaluation Criteria In Solid Tumors)

"First you need to identify the longest [in plane] diameter of a lymph node or nodal mass (here 56.0mm) and then choose the longest perpendicular diameter to that as the short axis (here 45.3mm)."

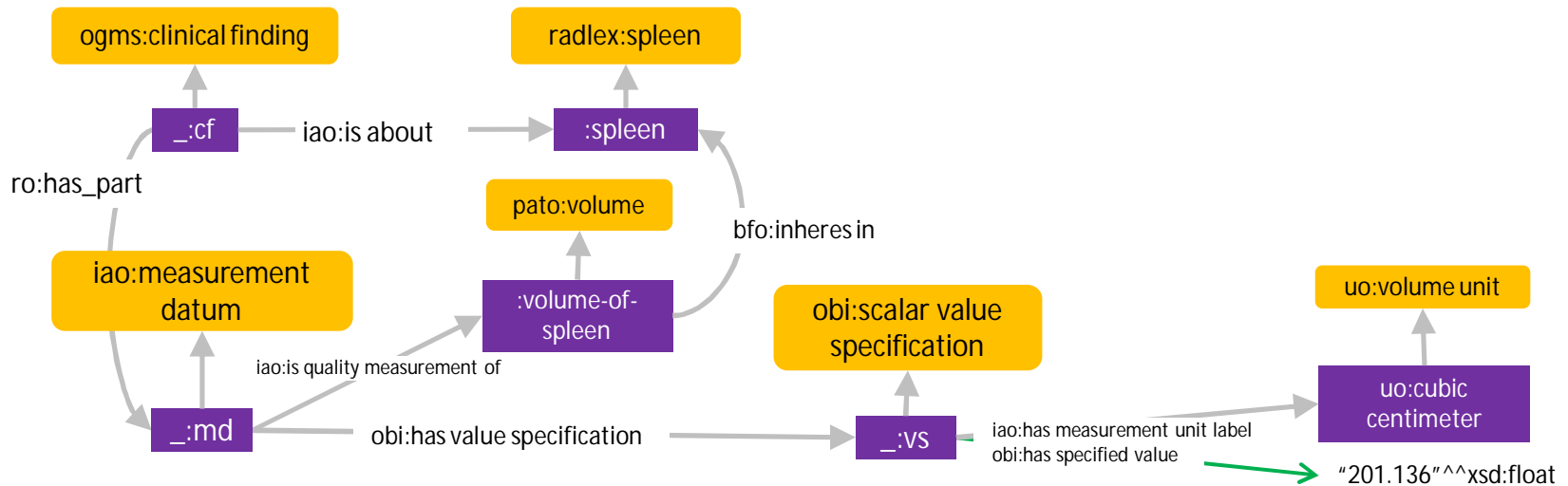# 2D Measurements

Example: Lymph node with diameter 56.0 x 45.3 mm.
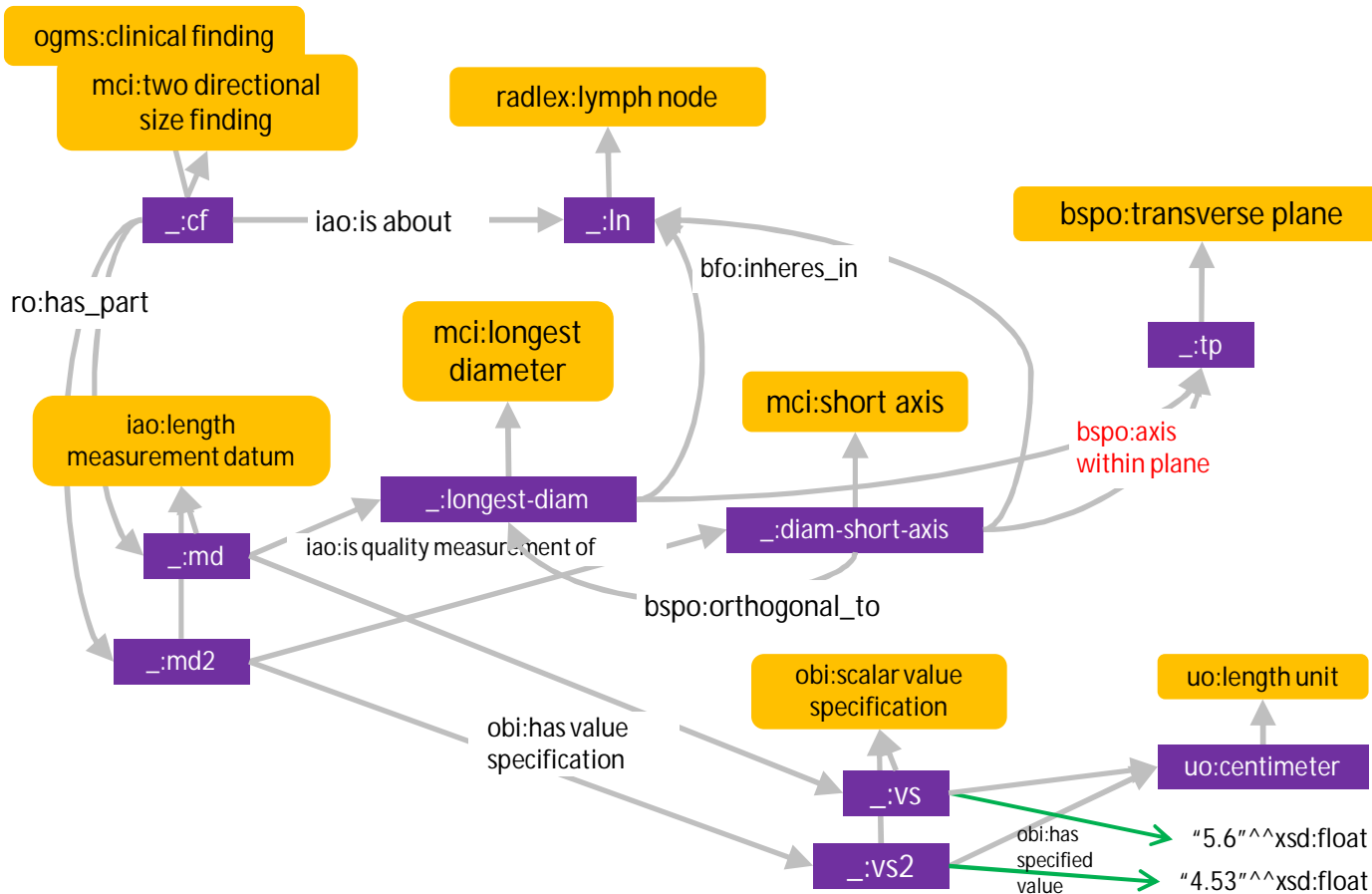
Volume Measurements
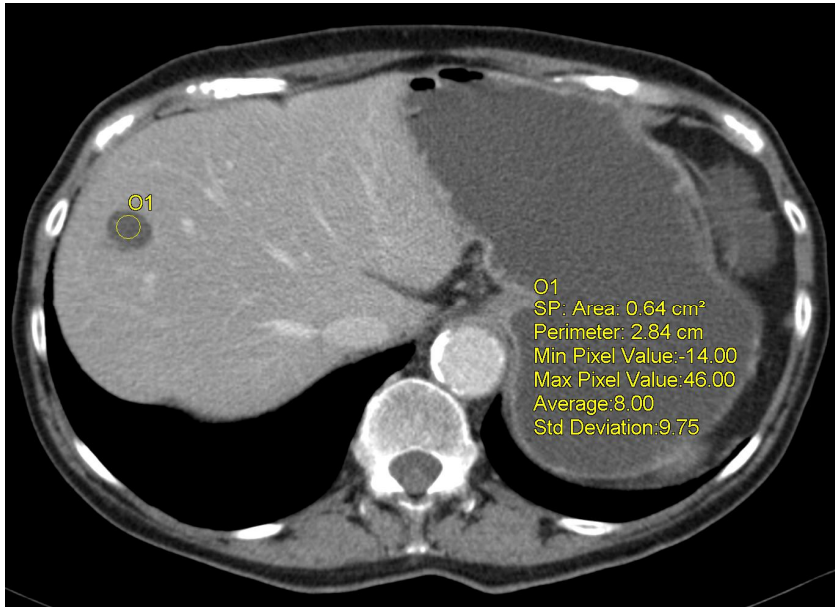
Example: Volume of spleen 201.136 cm³.

Milzvolumen
201,136 cm³

Source: "Automatische Detektion und volumetrische Segmentierung der Milz in CT-Untersuchungen" – M. Hammon, P. Dankerl,M. Kramer, S. Seifert,A.Tsymbal,M. J. Costa, R. Janka,M. Uder, A. Cavallaro
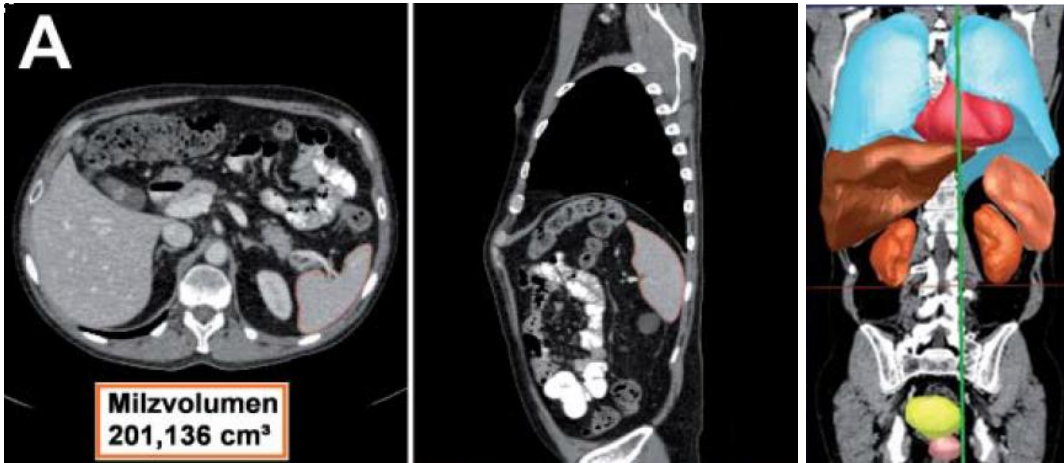
Segmentation algorithms used to determin the volume of organs.

Density Measurements

Density measurement of a liver cyst

Density is measured in Hounsfield unit (HU)

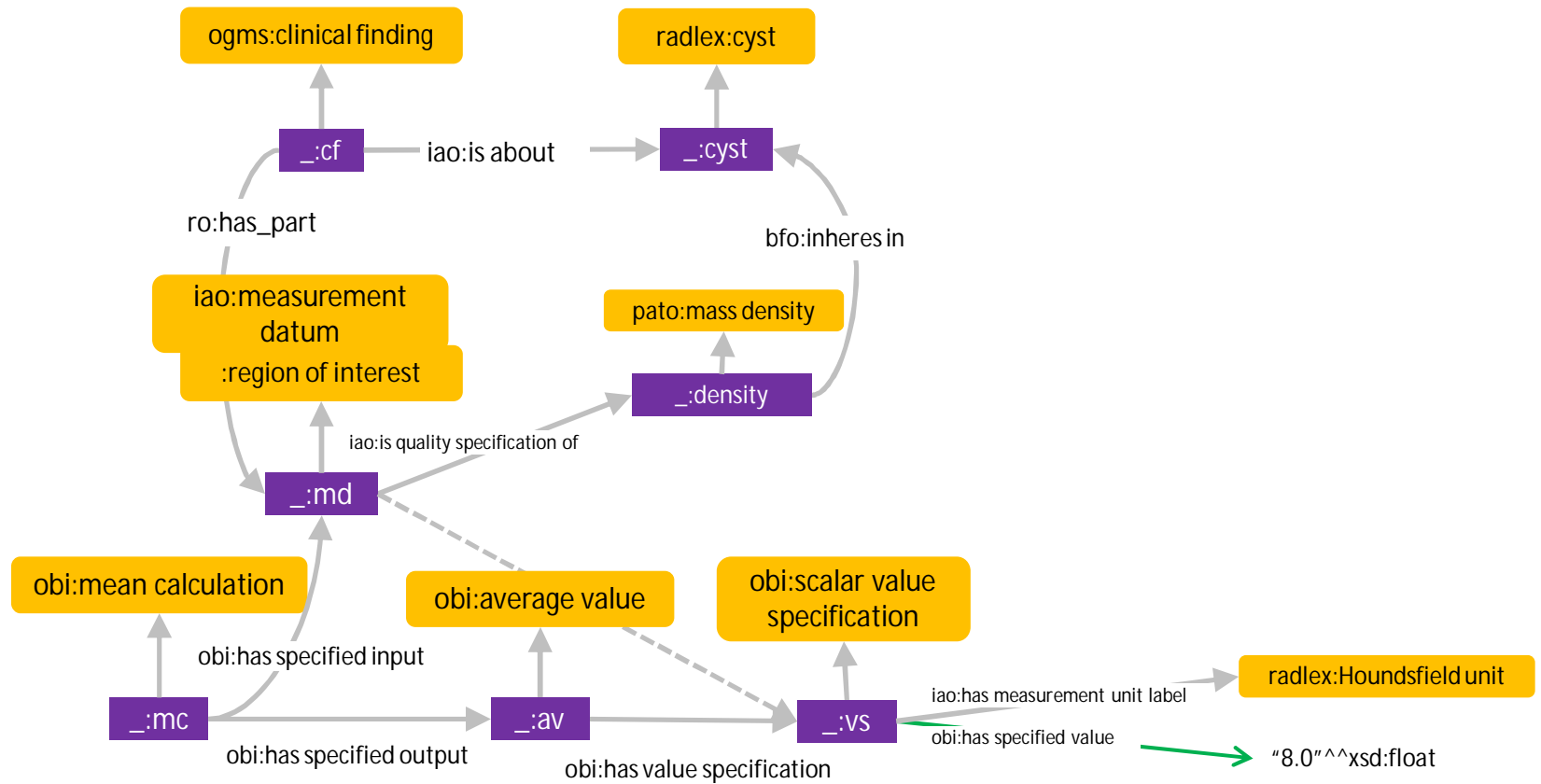Density measurements given for a region of interest (ROI)

Minimal, maximal and mean values for the pixels of the ROI
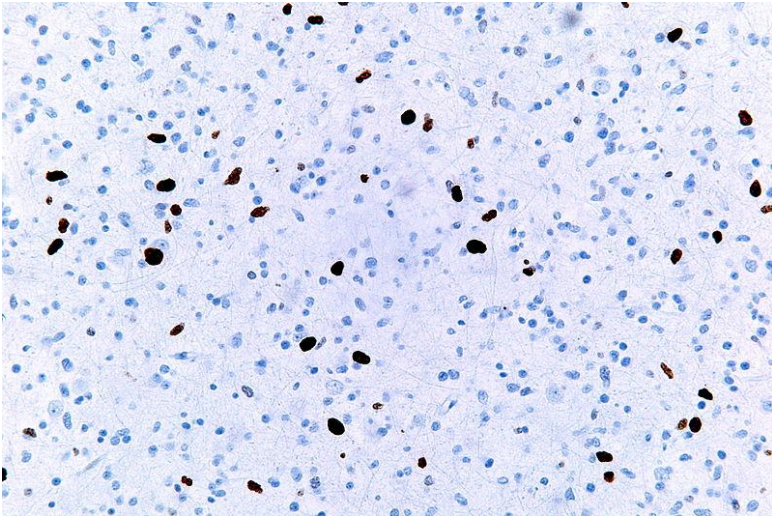
Examples:

"Density of a liver cyst 8 HU"

Density Measurement

Representation with obi:mean calculation
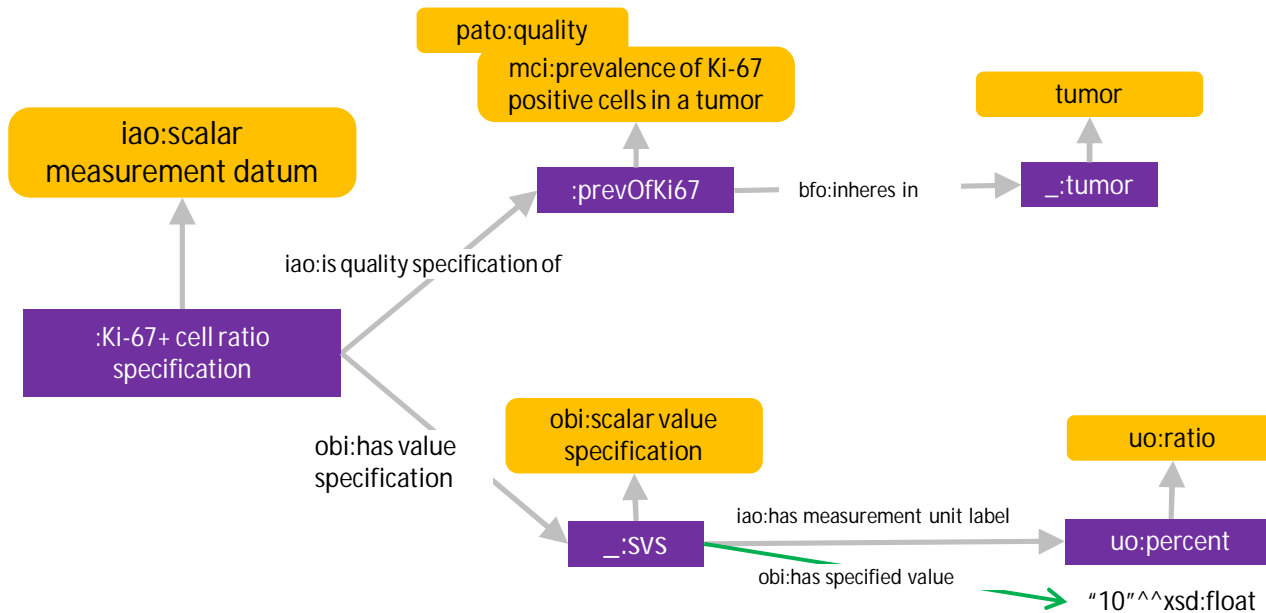
Ratio Measurements

Ki-67 immunostaining of brain tumor cells
Source: Wikipedia

Percentage of Ki-67 positive tumor cells

Ki-67 is a protein in cells that increases as they prepare to divide into new cells. A staining process can measure the percentage of tumor cells that are positive for Ki-67. The more positive cells there are, the more quickly they are dividing and forming new cells. In breast cancer, a result of less than 10% is considered low, 10-20% is intermediate/borderline, and more than 20% is considered high.

Representation of Ratio Measurements

Example: 10 % of Ki-67 positive tumor cells

Representation of Ratio Measurements

Example: 10 % of Ki-67 positive tumor cells

Numerator and denominator should be explicit and could be represented as 'iao:measurement data item' or 'iao:scalar measurment datum' or stato:count similar to the definition in STATO. This has the advantage that dimensional and dimensionless ratios can be represented in the same form.
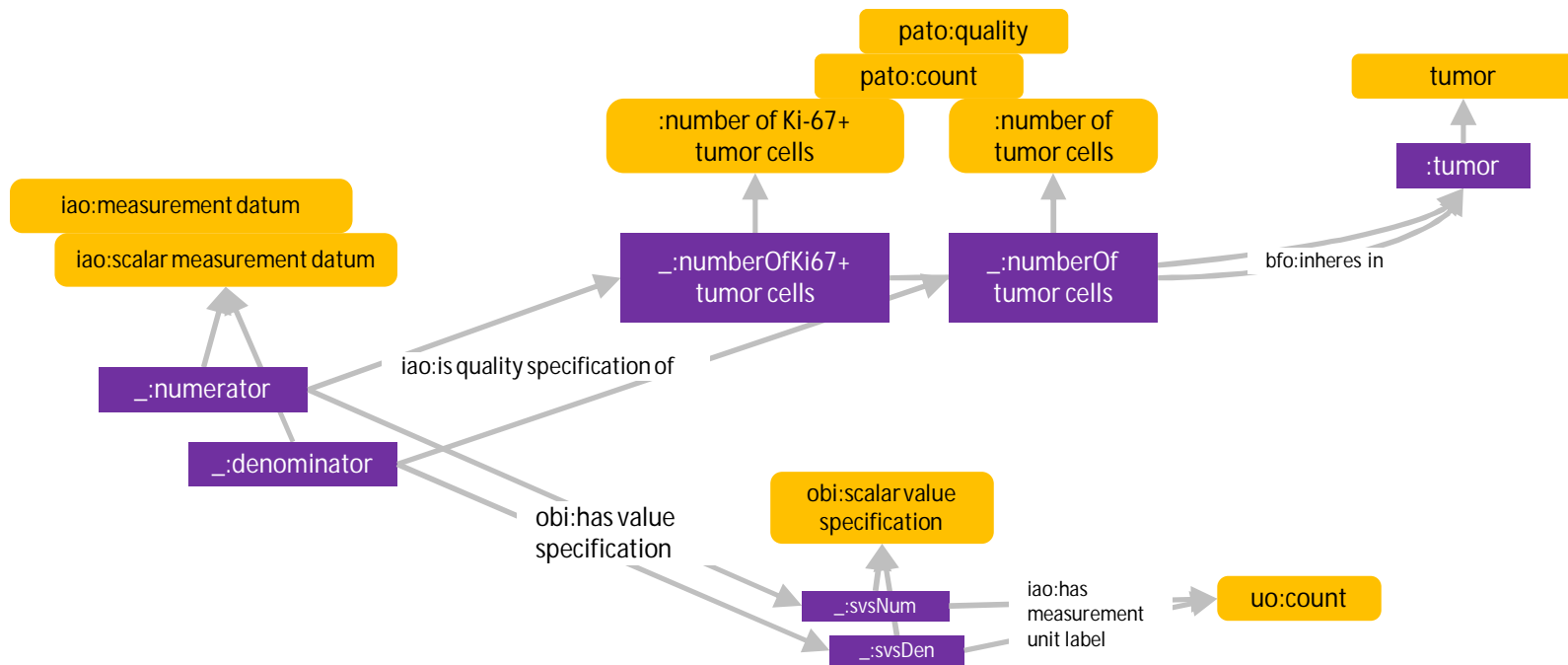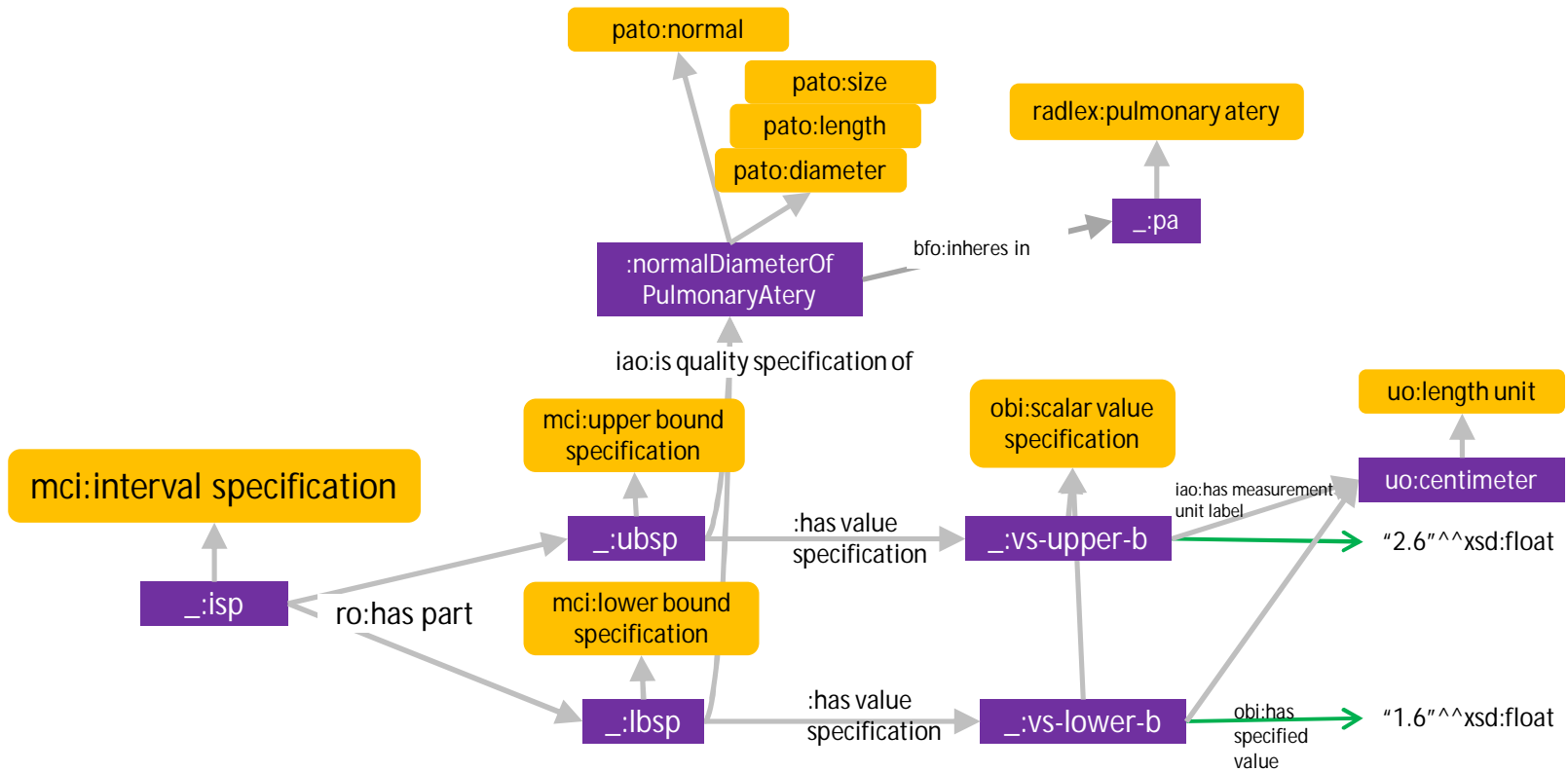
Normal Specifications

Normal Upper Bound Specification

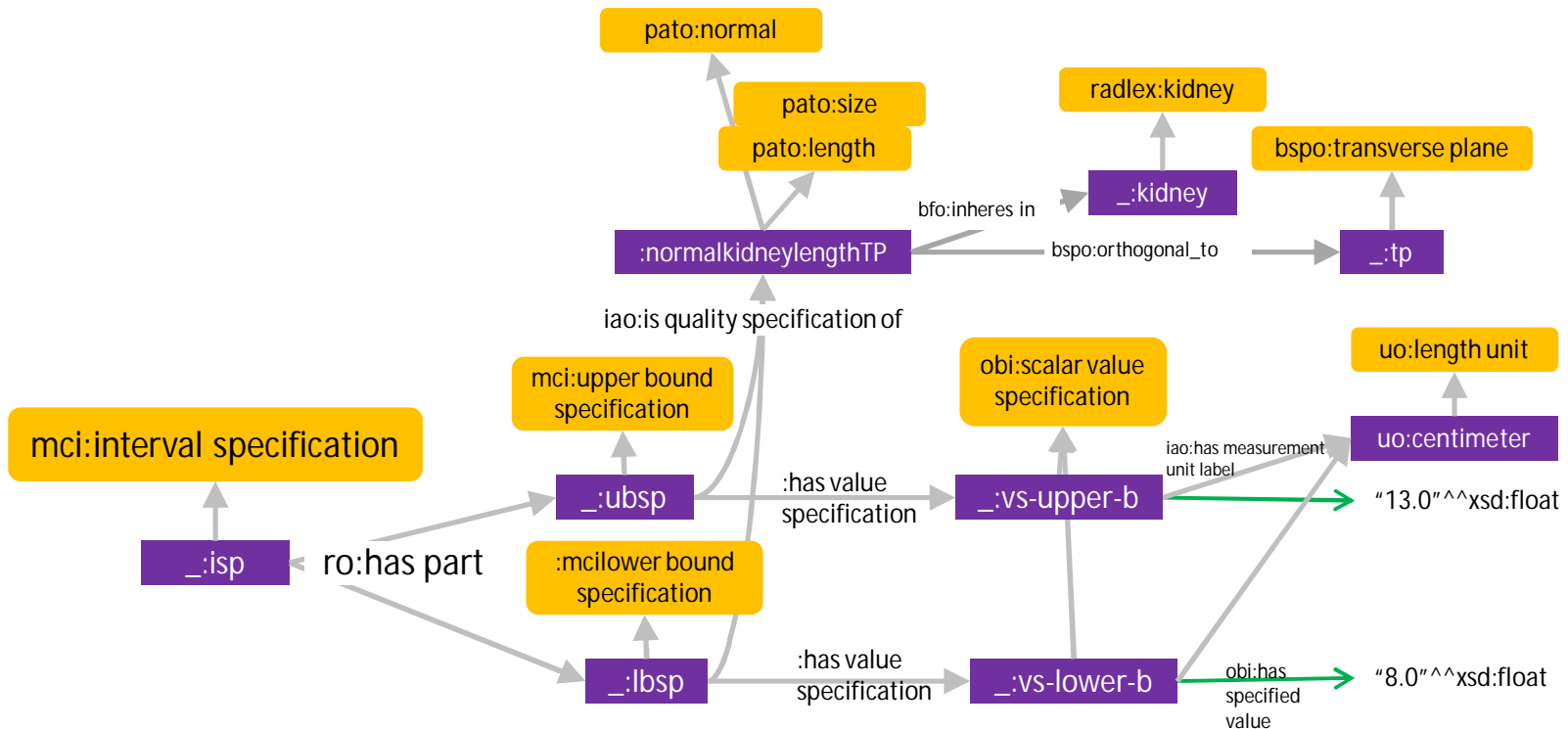**Example:** Lymph nodes are normally up to 1 cm.
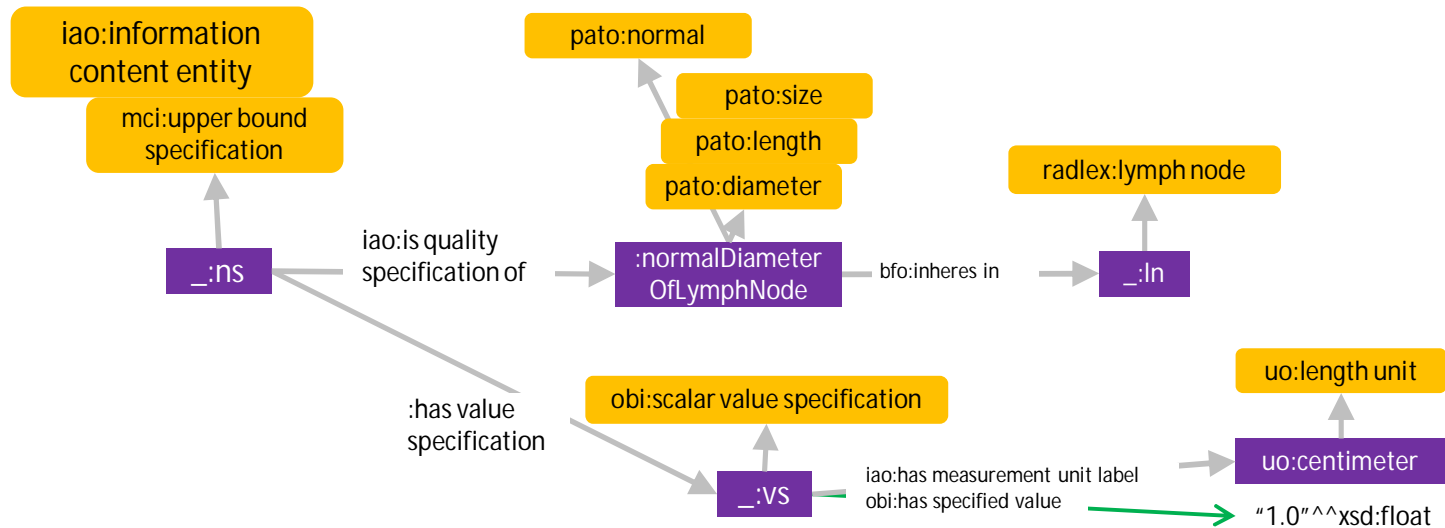
Normal Interval Specification

Example: Normal diameter of the pulmonary atery is between 1.6 and 2.6 cm.

Normal Interval Specification

Example: Normal length of kidney along craniocaudal axis: 8.0 – 13.0 cm.

Normal Interval Specification

Example: Normal mass density of the spleen in Hounsfield scale: 40-50 HU.
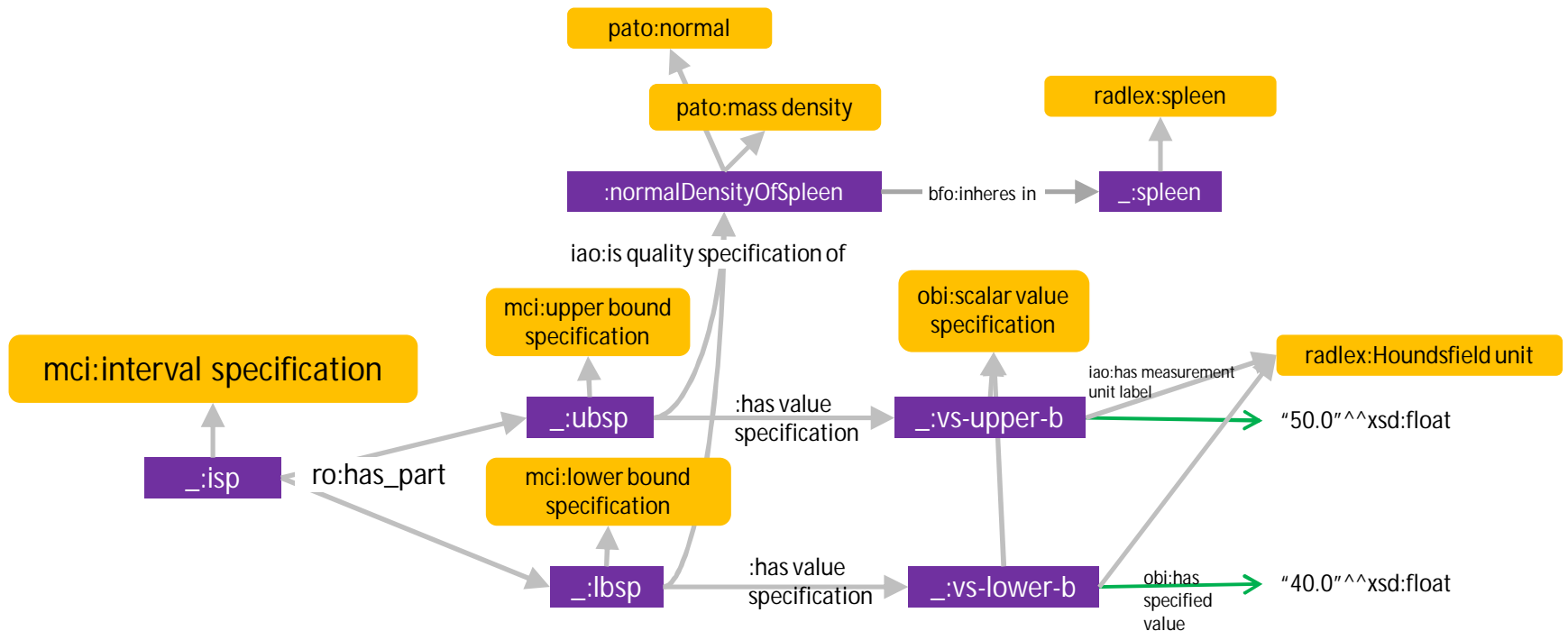
Expressing a Reference Population

Use punning of PATO qualities

Populations, defined by certain qualities (e.g., age or gender) are represented by punning the respective PATO qualities.
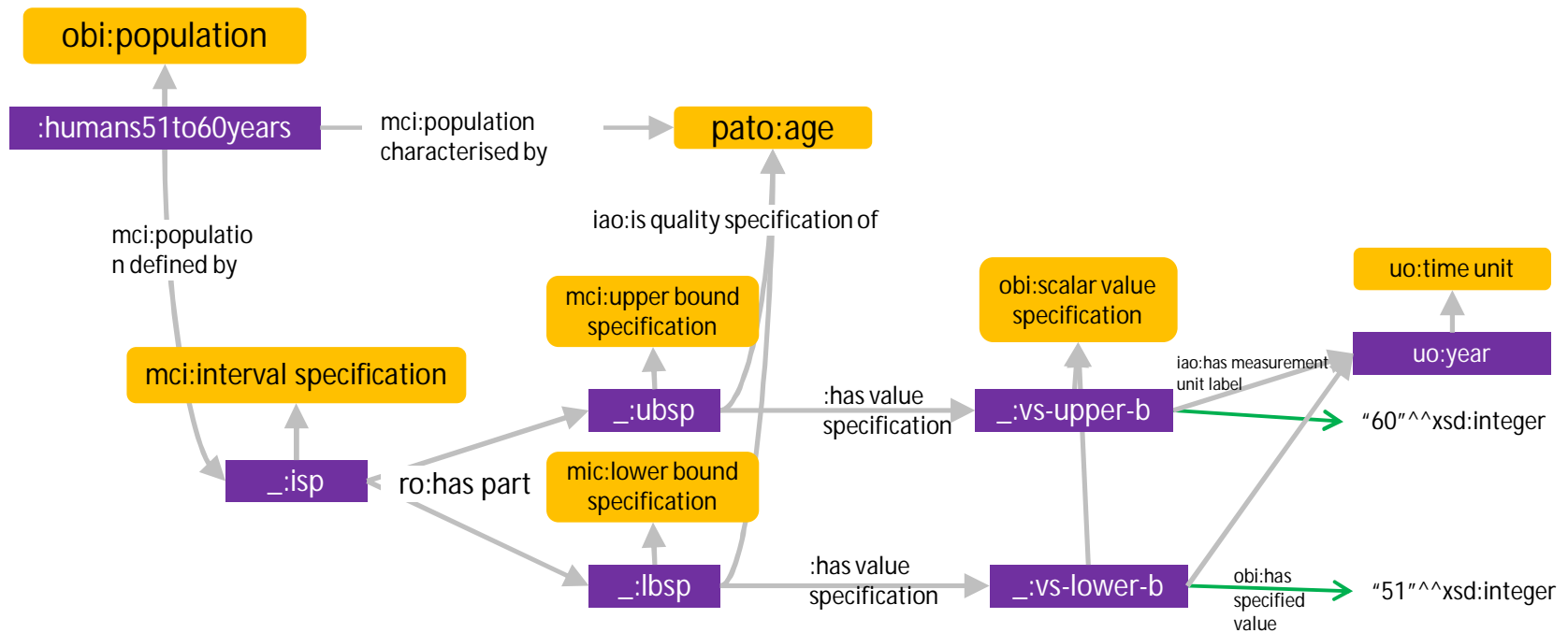
Link Normal Specifications to Reference Population

Link to Normal Specifications

Normal Ratios

Example: Normal levels of creatinine in the blood are 0.6-1.2 mg/dL in adult males

Applications

Representing Context Information

Links to examinations, images and reports.
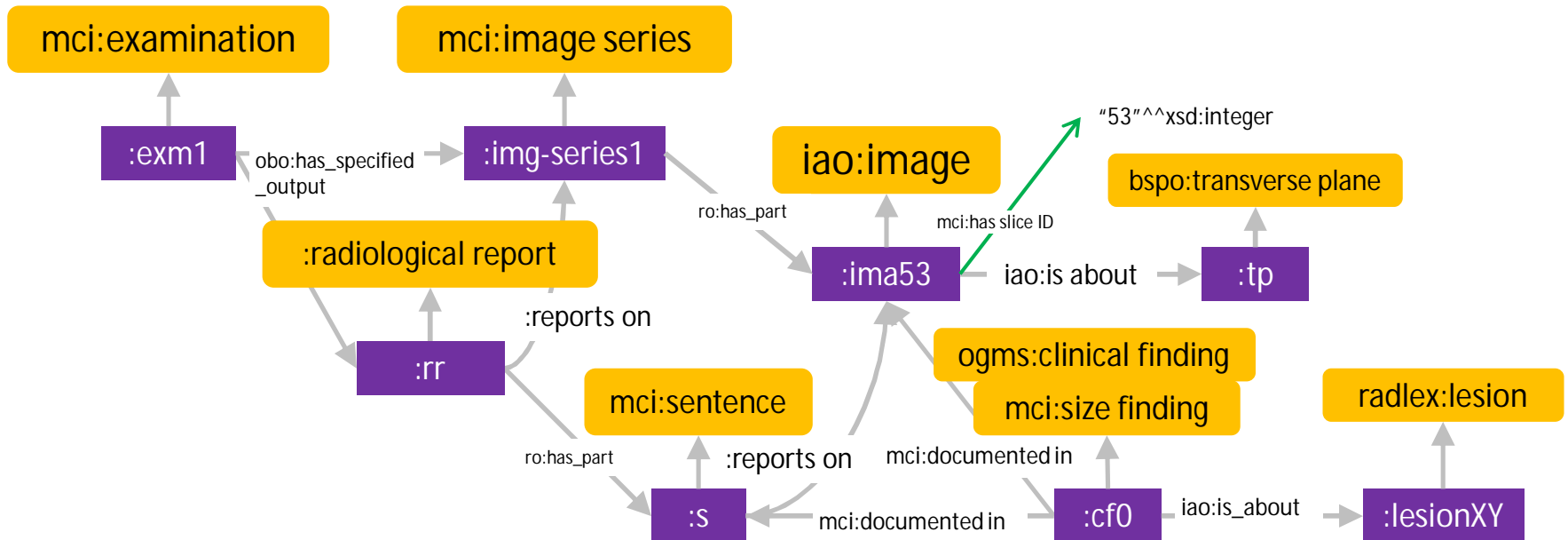
Knowledge Model with Size Specifications

Manually created with radiologist.

Content:

- 50 size specifications about 38 different RadLex concepts:

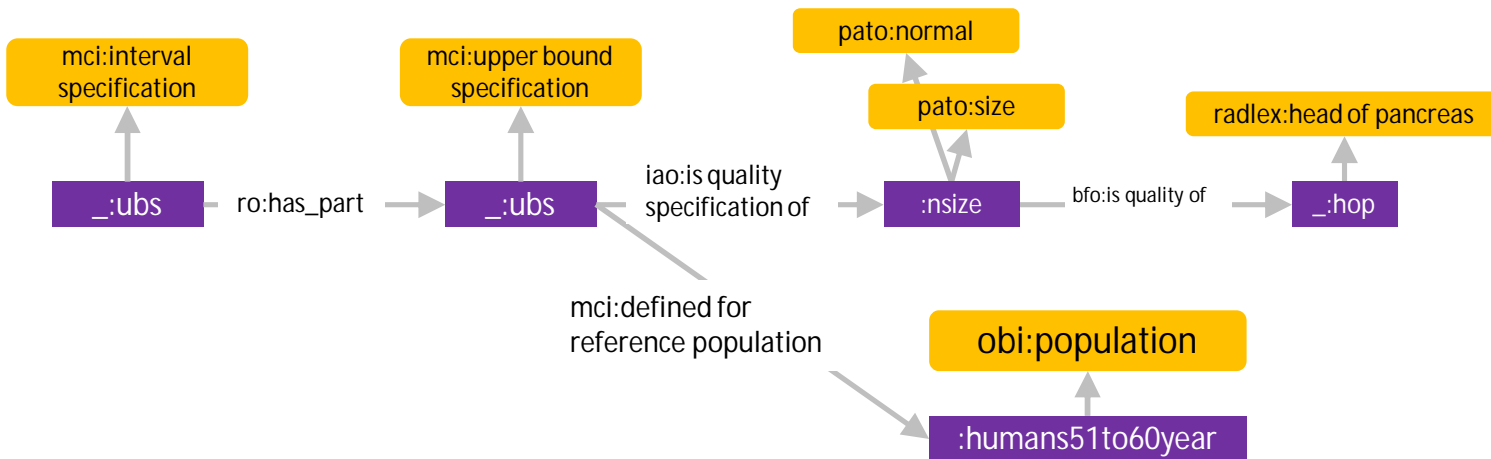   e.g. spleen, kidney, gallbladder, pancreas, lymph nodes, aorta, lesion, cyst, bile ducts etc.

- Some of them are patient-specific.

Sources:

- A book about normal findings[1]
- Radiopedia[2]

Data Sets:

- Lymphoma patients: 2584 German radiology reports (27 different readers) of 377 patients
  Imaging modality: CT, MRI, US

- Internistic patients: 6007 German radiology reports (27 different readers)
  Imaging modality: CT

[1] T. B. Möller and E. Reif, CT- und MRT-Normalbefunde. Thieme, 1998.
[2] http://radiopaedia.org/

Application 1: Information Extraction

Using normal size specification to extract size findings from text.

Example: "Enlarged lymph node right paraaortal below the renal pedicle now 23 mm."

Annotations:

| radlex:enlarged | radlex:lymphadenopathy | radlex:lymph node | radlex:right | radlex:paraaortic |

| radlex:lateral aortic lymph node | radlex:inferior | radlex:inferior para-aortic lymph node |

| radlex:kidney | radlex:renal pedicle |

| 2.3 | uo:centimeter |

Measurement relation resolution:
1. Knowledge based:
   1. Filter annotations
   2. Create spanning tree along RadLex subclass hierarchy
   3. attach available size specifications
   4. compare size specifications with measurement
   5. compute ranking value including the concept position in Radlex
2. Sentence distance
3. Statistics (based on 1000 manually annotated sentences)
→Final ranking integrates results from all three approaches

Result: 2.3 cm describes the size of the inferior para-aortic lymph node.

Evaluation of pure Knowledge based Approach

F-measure results:
lymphoma dataset: 0.85
internistic dataset: 0.79

Details (to be published): "Knowledge-based Extraction of Measurement-Entity Relations from German Radiology Reports". H. Oberkampf, C. Bretschneider, S. Zillner, B. Bauer, M. Hammon. IEEE International Conference on Healthcare Informatics 2014.
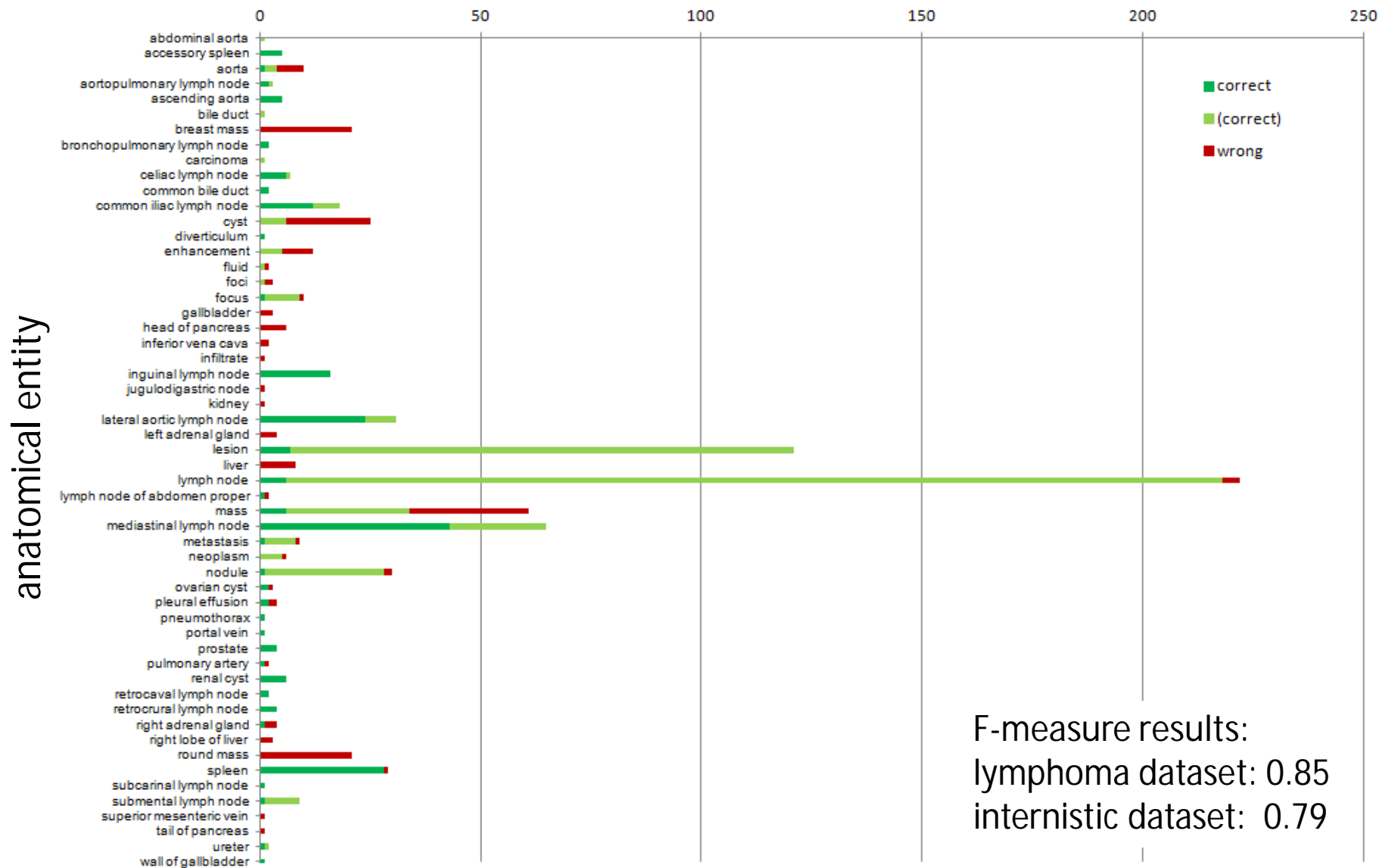
Application 2: Normality Classification

Patient-specific classification of normal and abnormal size findings.

Example: 52 years old patient

Given a size finding: 1D, 2D or 3D with corresponding anatomical entity.

mediastinal lymph node	1.6 x 1.2 cm
inguinal lymph node	1.4 cm
spleen	10 x 4.8 cm
head of pancreas	2.8 cm

Retrieve all patient-specific normal size specifications for closest superclass:

mediastinal lymph node → normal diameter of lymph node up to 1 cm
inguinal lymph node → normal diameter of inguinal lymph node up to 1.5 cm
spleen → normal spleen: depth 4-6 cm, width 7-10 cm, length 11-15 cm
head of pancreas → normal size of head of pancreas (for patients from 51-60 years): 21-27 mm

Check whether the values are within normal interval
abnormal: mediastinal lymph node 1.6 x 1.2 cm
normal: inguinal lymph node 1.4 cm
normal: spleen 10 x 4.8 cm
abnormal: head of pancreas 2.8 cm

Application 3: Inference of Change

We use SPARQL to classify size findings as progressive, regressive or stable.
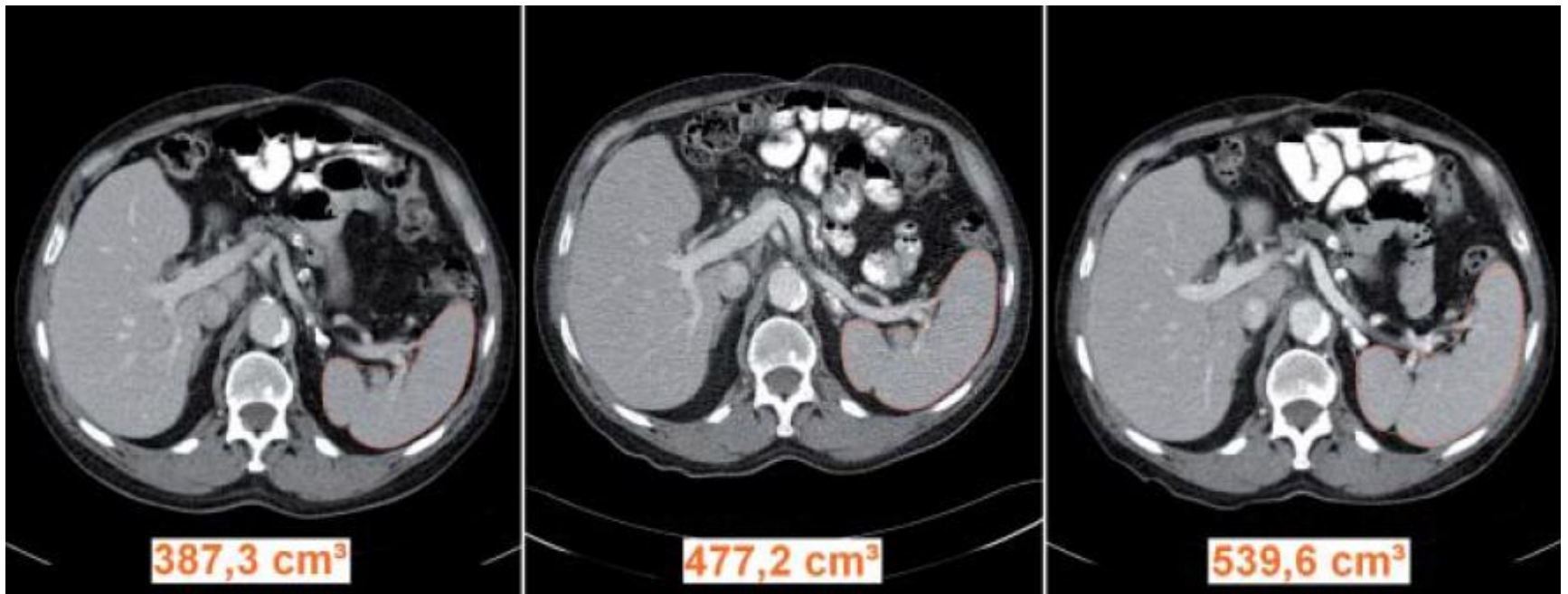

387,3 cm³   477,2 cm³   539,6 cm³

Image source: "Automated Detection and Volumetric Segmentation of the Spleen in CT Scans" M. Hammon, P. Dankerl, M. Kramer, S. Seifert, A. Tsymbal2, M. J. Costa2, R. Janka1, M. Uder1, A. Cavallaro

- Scalar measurements can be compared directly.
- For two/three directional length measurements we compare the index (e.g. spleen index: width x depth x length).

Work-in-Progress: Linking Findings

Linking findings from consecutive examinations based on anatomical entity.
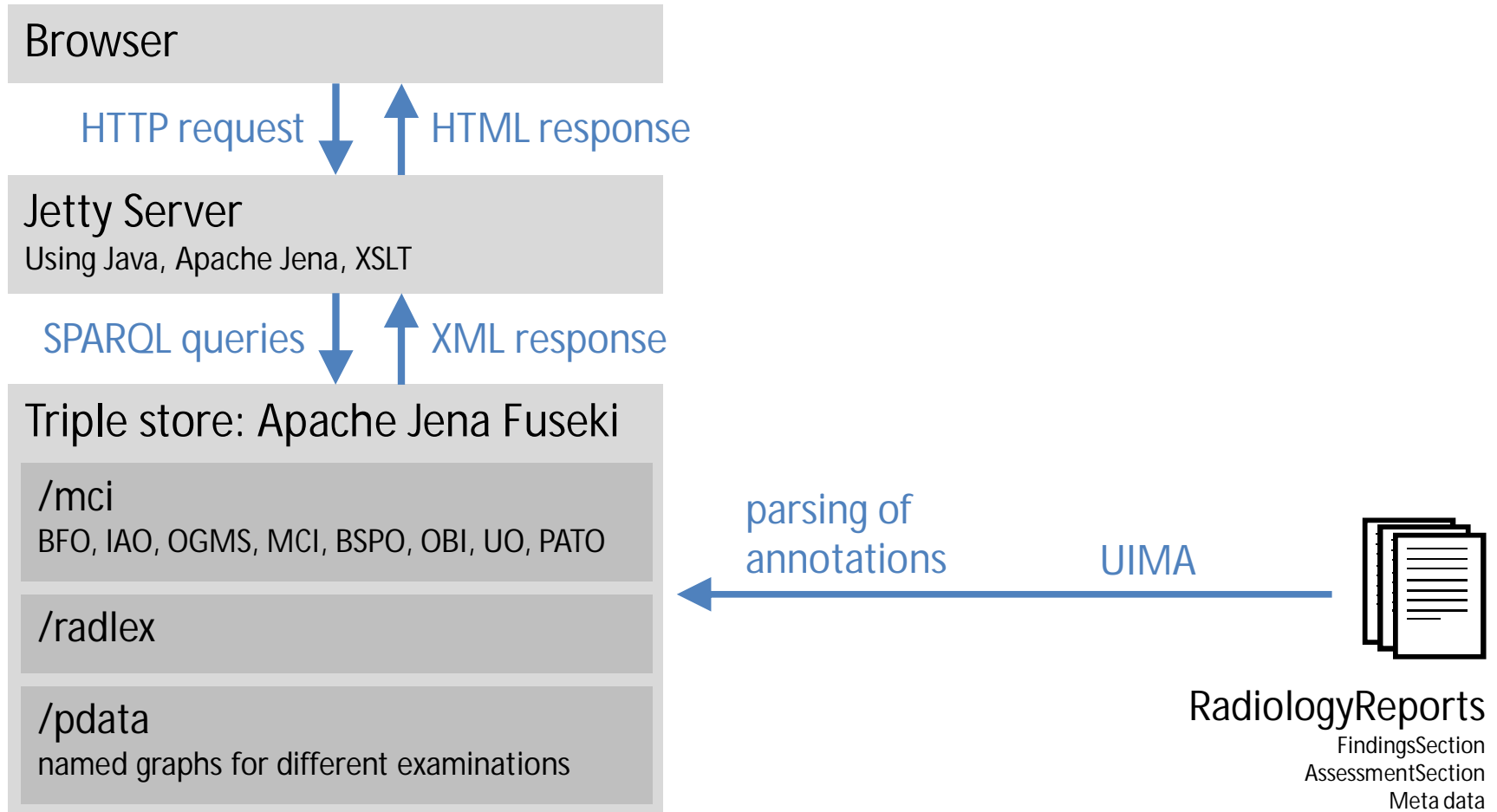
Problems: Two findings about "radlex:lymph node" do not necessarily describe the same lymph node.

preceeding finding/
related finding
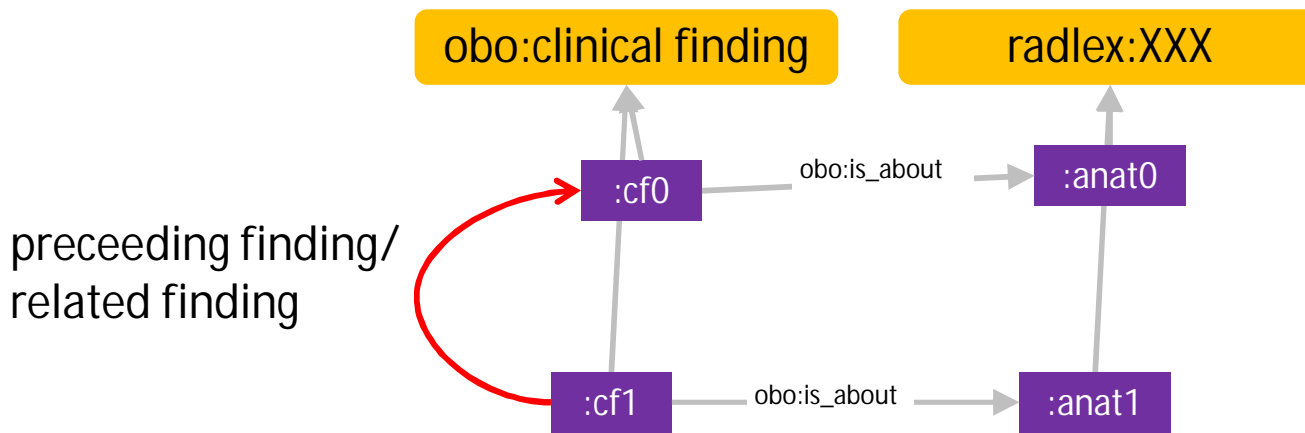
For the current demo we linked and compared only measurements occurring within one report sentence.

Demo

Architecture of Demo Implementation

Browser

HTTP request   HTML response

Jetty Server
Using Java, Apache Jena, XSLT

SPARQL queries   XML response

Triple store: Apache Jena Fuseki

/mci
BFO, IAO, OGMS, MCI, BSPO, OBI, UO, PATO

/radlex

/pdata
named graphs for different examinations

parsing of annotations   UIMA

RadiologyReports
FindingsSection
AssessmentSection
Meta data

Extracted and Classified Size Findings

2006-05-31 computed tomography	
Hals-, Thorax- und Abdomen-CT mit KM i.v	
1 cm lymph node	Weiterhin mehrere, deutlich unter 1 cm messende Lymphknoten entlang der Halsgefäßnervenscheiden bds..
1 cm axillary lymph node (1,3 cm)	Rechts axillär größenregredienter Lymphknoten jetzt 1 cm (IMA 9), vormals 1,3 cm.
1 cm axillary lymph node	Bei Z.n. B-NHL residualer, kleiner 1 cm großer Lymphknoten rechts axillär.

2006-02-28 computed tomography	
Hals-, Thorax- und Abdomen-CT mit KM i.v	
8 mm submental lymph node	Die vorbeschriebenen zervikalen Lymphknoten entlang der Halsgefäßnervenscheide bds. sowie submandibulär, submental und in den Kieferwinkeln sind in Größe und Anzahl deutlich regredient (aktuell noch Durchmesser bis 8 mm IMA 39 li unterhalb des M. sternocleidomastoideus).
1,4 cm axillary lymph node (3,5 cm)	Deutlicher Größenrückgang auch der axillären Lymphknoten, zuvor bis 3,5 cm durchmessende Lymphknotenpakete rechts axillär durchmessen aktuell noch maximal 1,4 cm.
5 mm	subpleural im Mittellappen rechts (IMA 35, Durchmesser 5 mm).
5 mm round mass 5 mm round mass 5 mm round mass 6 mm round mass	Im apikalen Unterlappen links zahlreiche Rundherde (IMA 20 bis 31, Durchmesser bis 6 mm), im rechten Unterlappen (IMA 34, Durchmesser 5 mm), im basalen Mittellappen (IMA 47, Durchmesser 5 mm) und in den Oberlappen bds. (jeweils IMA 12, Durchmesser 4 bzw. 5 mm).
1,2 cm lesion	Größenunveränderte, flau hypodense, subkapsulär im Segment 5 gelegene Leberläsion (IMA 66/67, Durchmesser 1,2 cm) mit randständig fraglich diskreter stäbchenförmiger KM-Mehranreicherung.
7 mm lesion	Eine weitere flau hypodense, 7 mm durchmessende Läsion im Segment 5 (IMA 65), die in der VA nicht sicher nachvollziehbar ist.
8,2 x 9,1 x 13 cm spleen	Milz homogen, ausgeprägter Größenrückgang bei vorbestehender Splenomegalie (aktueller Durchmesser 8,2 x 9,1 x 13 cm).
10,5 cm	Cranio-caudaler Durchmesser bds. 10,5 cm, im Vergleich zur VU hierbei rückläufige Schwellung des Nierenparenchyms bei verbesserter Abgrenzbarkeit zum umgebenden Fettgewebe.
8 mm	Bei liegenden Harnleiterschienen bds. mehrere kalkdichte Konkremente innerhalb des Nierenbeckenkelchsystems mit Durchmessern, bds. bis zu 7 bis 8 mm.

Age-specific Classification of Size Findings

Questions?

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Thanks:
OBI developers