

Implementing an Observables Ontology for SNOMED CT and LOINC Decision Support

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Outline

- The role of Observable entities in interoperability
- Harmonized LOINC - SNOMED CT observables ontology
- Decision support use cases from QRDA reporting, genomic treatment selection and guidelines
- Observables 'groupers' for Epic decision support
- Observables ontology in i2b2 and Neo4j



ONC Terminology Model for Semantic Interoperability

- Demographics: LOINC, HL7/OMB code set
- Social and medical history: SNOMED CT
- Problem list/encounter diagnoses: SNOMED CT / ICD-10-CM
- Lab results (observables): Lab LOINC
- Physical findings: LOINC, SNOMED CT observables
- Medication orders: RxNORM, SNOMED CT
- Laboratory Orders: LOINC
- Immunizations: CVX, MVX
- Procedures: CPT, HCPCS
- Documents: LOINC



ONC Terminology Model for Semantic Interoperability

: How it relates SNOMED CT and LOINC

- Demographics: (Clinical) Observables code set
- Social and medical history: Findings and Situations
- Problem list/encounter diagnoses: SNOMED CT / Findings, Events and Situations
- Lab results (observables): (Laboratory) Observables
- Physical findings: (Clinical) Observables CT observables
- Medication orders: RxN Events, Social context, Qualifiers
- Laboratory Orders: (Laboratory) Orderables
- Immunizations: CVX, MVX
- Procedures: CPT, HCPCS
- Documents: LOINC



Introducing: Observable entity...What?

➤ IHTSDO

“Observables are considered to be partial observation results, where there is a defined part of the observation missing.”

“Concepts in this hierarchy can be thought of as representing a question or procedure which can produce an answer or a result”

“Observable entity + Evaluation (test) result = Finding”

➤ Regenstrief institute: LOINC

“...a set of universal names and ID codes for identifying laboratory and clinical test results”

“...master file of standard ‘test’ names and codes that will cover most of the entries in these files of operational laboratory systems”

“...organization of LOINC is divided first into four categories, ‘lab’, ‘clinical’, ‘attachments’ and ‘surveys’ ” (Lab and clinical are semantically equivalent to observables)



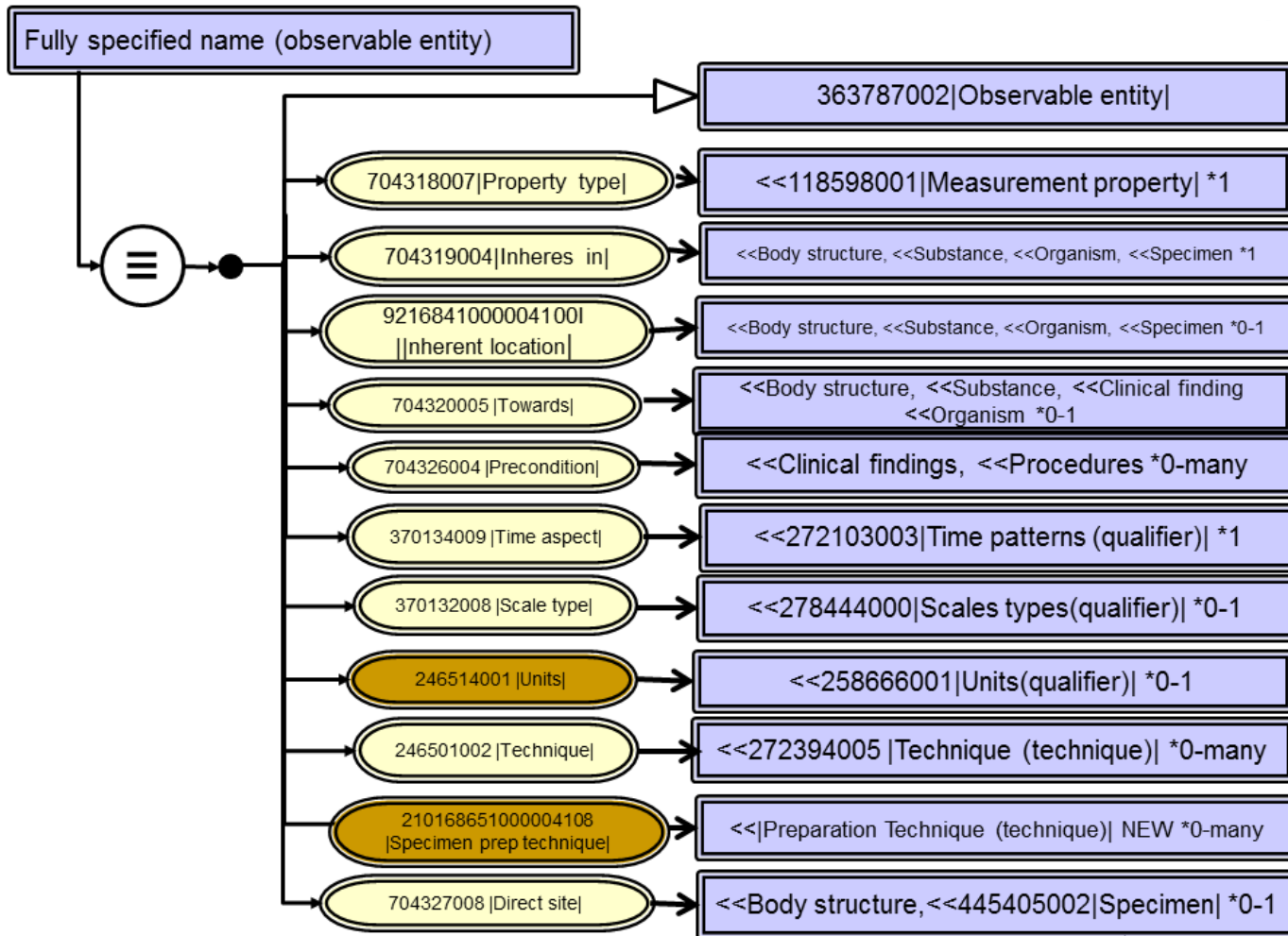
LOINC – SNOMED CT

Harmonization of Observable entities

- 2008 agreement between Regenstrief (RI) and IHTSDO
 - <https://loinc.org/collaboration/ihtsdo/agreement.pdf>
 - Extend and harmonize a shared concept model for 363787002|Observable entity|
 - Map and instantiate LOINC parts in SNOMED CT content
 - Jointly publish expression data set defining (lab) LOINC concepts within the harmonized concept model
 - Technology preview alpha January 2016
- Assertion: What is needed to support clinical decision making and research with big data is a unified domain ontology for Observable entities spanning clinical and research content including genomics



Observables Project: Concept model draft



Step by step to create an Observables Ontology

- Implement SNOMED CT International release using SNOW OWL authoring platform
- Install Nebraska Lexicon© SNOMED CT extension; author new content needed for expanded SNOMED CT concept model
- Convert Observables technology preview to OWL format and install
- Import OWL axioms for gene and protein ontology from NCBI
- Run SNOMED CT and extensions through a description logic classifier
- VOILE!



Decision criteria which cannot be answered by aggregate query of LOINC or SNOMED CT

- Identify all diabetic patients with no hemoglobin A1C in the last 6 months
- Pull all cases records of colon cancer patients that have reports of tumor budding
- Find all patients who have tested positive for sickle related hemoglobinopathy
- Pull all historical cases for research of (colon) cancer with any gene biomarker testing completed



Decision queries which cannot be answered by query of LOINC or SNOMED CT

- Meaningful Use QA reporting: Identify all diabetic patients with no hemoglobin A1C in the last 6 months
- PathM: Pull all cases records of colon cancer patients that have reports of tumor budding
- LM: Find all patients who have tested positive for hemoglobin other than HbA
- PersM: Pull all historical cases of colon cancer with BRAF gene testing for research



Quality reporting criteria: Hemoglobin A1C values

- Common lab test assessing diabetic control; an outcome measure followed for quality of diabetic care
- RELMA code review: “Hemoglobin A1C”
- NLM valueset authority center: 17855-8, 17856-6, 4548-4, 4549-2
- Frequent confusion in proper code leads to miscoding in the clinical laboratory in the face of seven possibilities



Quality reporting criteria: Hemoglobin A1C values

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hemoglobin a1c Units Search 

Use Standard Search

No Common Limits

Row	Score	LOINC	Component	Property	Timing	System	Scale	Method	ExUCUM...	ExUnits	Rank	SIRank	LForms
1	15.8838	43150-2	HbA1c measurement device panel	-	Pt	^Patient	-						
2	28.1114	41995-2	Hemoglobin A1c	MCnc	Pt	Bld	Qn		g/dL	g/dL			
3	29.5607	4548-4	Hemoglobin A1c/Hemoglobin.total	MFr	Pt	Bld	Qn		%	%	81	81	
4	26.9771	17855-8	Hemoglobin A1c/Hemoglobin.total	MFr	Pt	Bld	Qn	Calculated	%	%			
5	26.9771	4549-2	Hemoglobin A1c/Hemoglobin.total	MFr	Pt	Bld	Qn	Electrophoresis	%	%			
6	26.9771	17856-6	Hemoglobin A1c/Hemoglobin.total	MFr	Pt	Bld	Qn	HPLC	%	%	215	215	
7	26.9771	62388-4	Hemoglobin A1c/Hemoglobin.total	MFr	Pt	Bld	Qn	JDS/JSCC	%	%			
8	26.9771	71875-9	Hemoglobin A1c/Hemoglobin.total	MFr.DF	Pt	Bld	Qn						
9	26.9771	59261-8	Hemoglobin A1c/Hemoglobin.total	SFr	Pt	Bld	Qn	IFCC	%	mmol/...			

Find all hemoglobin A1C/Hgb measurements for patient

➤ ?Observable entity:

- Component = 259690008|Glycosylated hgb-c fraction(substance)|
- Direct site<<<119297000|Blood specimen(specimen)|
- Property type = 118542001|Mass fraction(property)|
- Relative to = 38082009|Hemoglobin (substance)|



Find all hemoglobin A1C/Hgb measurements for patient

➤ ?Observable entity:

The screenshot displays a software interface for managing medical concepts. On the left, a tree view under 'SNOMED CT' shows a search for 'Hgb A1C', with 'Hemoglobin A1C fraction of blood hemoglobin' selected. Below this, a 'Parents' pane shows it is an 'Observable entity'. The main pane shows the details for 'Hemoglobin A1C fraction of blood hemoglobin', including its fully specified name, synonym, and various properties such as 'Is a: Observable entity', 'Component: Glycosylated hemoglobin', and 'Direct site: Blood specimen'. The 'SNOMED CT Properties' section lists the concept ID, module, effective time, status, and definition status.

Property	Value
Fully specified name:	Hemoglobin A1C fraction of blood hemoglobin (observable entity)
Synonym:	Hemoglobin A1C fraction of blood hemoglobin
Is a:	Observable entity
Component:	Glycosylated hemoglobin
Direct site:	Blood specimen
Inheres in:	Blood
Relative to:	Hemoglobin
Concept ID:	441596301000004106
Module:	Nebraska Lexicon extension module
Effective time:	Unpublished
Status:	Active
Definition status:	Defined



Decision queries which cannot be answered by query of LOINC or SNOMED CT

- MU: Identify all diabetic patients with no glycated hemoglobin in the last 6 months
- Clinical Pathology: Pull all case records of colon cancer patients that have reports of tumor budding
- LM: Find all patients who have tested positive for hemoglobin other than HbA
- PersM: Pull all historical cases of colon cancer with BRAF gene testing for research



What is Tumor budding?

- A microscopic finding by the pathologist noting focal extension of tumor mass into surrounding tissue
- Not found in LOINC 2.54 or US Ed SNOMED CT 20160901
- Requested by one of our senior pathologists as part of a research protocol
- CAP Cancer synoptic standards treat this as an optional data element



Nebraska Lexicon for CAP Cancer checksheets

- 629949841000004100|Number of tumor buds per high power field observed in excised carcinoma (observable entity)|:
 - Inheres in: Malignant neoplasm
 - Direct site: Formalin-fixed paraffin embedded tissue specimen
 - Property type: Histologic invasiveness
 - Technique: Light microscopy
 - Towards: Tumor budding observed



Nebraska Lexicon for CAP Cancer checksheets

- 629949841000004100|Number of tumor buds per high power field observed in excised carcinoma (observable entity)|:

The screenshot displays a software interface with three main panes. The top-left pane shows a search for 'tumor buds' and a tree view of SNOMED CT concepts, with 'Number of tumor buds per high power field observed at leading edge of excised carcinoma' selected. The top-right pane shows 'Ungrouped Properties' for the selected concept, including 'Is a:', 'Direct site:', 'Inherent location:', 'Inheres in:', 'Property type:', 'Technique:', 'Time aspect:', 'Towards:', and 'Towards:'. The bottom-left pane shows 'Parents' for the selected concept, including 'Status of tumor budding from excised carcinoma'. The bottom-right pane shows 'SNOMED CT Properties' for the selected concept, including 'Concept ID:', 'Module:', 'Effective time:', 'Status:', 'Definition status:', and 'Subclass definitions:'. The bottom status bar shows 'cambell@unmc.edu connected to localhost' and 'No task activated'.

Ungrouped Properties

- Is a: Status of tumor budding from excised carcinoma
- Direct site: Formalin-fixed paraffin-embedded tissue specimen
- Inherent location: Morphologically abnormal structure
- Inheres in: Malignant Neoplasm (Morphology)
- Property type: Histologic invasiveness property
- Technique: Light microscopy
- Time aspect: Single point in time
- Towards: Local tumor spread
- Towards: Tumor budding observed

SNOMED CT Properties

- Concept ID: 629949841000004100
- Module: Nebraska Lexicon extension module
- Effective time: 2016-01-30
- Status: Active
- Definition status: Defined
- Subclass definitions: Non-disjoint

Overview | Descriptions | Source relationships | Destination relat... | Value domain memb... | Mappings | References 1

cambell@unmc.edu connected to localhost | No task activated

Terminology development summary: CAP Colorectal and Breast Cancer checksheets

SNOMED CT hierarchy	Anatomic Pathology Concepts/Primitives	Molecular Genetic Concepts/Primitives	Exemplar molecular extension concepts
Observable entities	61/1	32/3	“BRAF nucleotide sequence detected in excised malignancy”
Body Structures	10/9	29/3	“BRAF gene locus”
Clinical findings	6/2	7/3	“BRAF V600E variant identified in excised malignancy”
Procedures	2/1	0	
Techniques	4/4	7/7	“Pyrosequencing”
Property types	8/8	2/2	“Sequence property”
Scale types	0	9/9	“Variant call format”
Situations	1/0	0	
Substances	0/0	11/11	“BRAF human cellular protein”
Attributes	2/2	3/3	
Qualifiers	2/2	0	
TOTALS	88/29	100/41	



Decision queries which cannot be answered by query of LOINC or SNOMED CT

- MU: Identify all diabetic patients with no glycated hemoglobin in the last 6 months
- PathM: Pull all cases records of colon cancer patients that have reports of tumor budding
- Laboratory Medicine: Find all patients who have tested positive for sickle related hemoglobinopathy
- PersM: Pull all historical cases of colon cancer with BRAF gene testing for research



ACIP Guidelines for Pneumococcal Vaccination: Case of Hemoglobinopathy

- Special populations: Asplenia; Immunosuppressed; Sickle cell disease or Hemoglobinopathy; ...
- NLM VSAC: SNOMED CT clinical findings
- Hemoglobinopathy:

Computable Phenotypic criteria:

- Problem list contains active problem <<|Hemoglobinopathy(disorder)|
- Lab testing verifies abnormal hemoglobin?



ACIP Guidelines for Pneumococcal Vaccination: Case of Hemoglobinopathy

- Special populations: Asplenia; Immunosuppressed; Sickle cell disease or Hemoglobinopathy; ...
- NLM VSAC: SNOMED CT clinical findings



Value Set Name	Sickle Cell Disease SNOMEDCT		
OID	2.16.840.1.113762.1.4.1029.33		
Type	Extensional		
Definition Version	20160722		
Steward	The Joint Commission		

****This update was generated by VSAC to align with code changes published by SNOMEDCT****

Expanded Code List			
Code	Description	Code System	Code System Version
127040003	Hereditary hemoglobinopathy disorder homozygous for hemoglobin S (disorder)	SNOMEDCT	2016-09
127041004	Sickle cell-beta-thalassemia (disorder)	SNOMEDCT	2016-09
127045008	Sickle cell anemia with coexistent alpha-thalassemia (disorder)	SNOMEDCT	2016-09
127047000	Sickle cell-hemoglobin Lepore disease (disorder)	SNOMEDCT	2016-09
127048005	Sickle cell-Hemoglobin O Arab disease (disorder)	SNOMEDCT	2016-09
23269001	Double heterozygous sickling disorder (disorder)	SNOMEDCT	2016-09
25472008	Sickle cell-hemoglobin D disease (disorder)	SNOMEDCT	2016-09
35434009	Sickle cell-hemoglobin C disease (disorder)	SNOMEDCT	2016-09
36472007	Sickle cell-thalassemia disease (disorder)	SNOMEDCT	2016-09
38589006	Mixed hemoglobin disorder (disorder)	SNOMEDCT	2016-09
416290001	Hemoglobin S sickling disorder without crisis (disorder)	SNOMEDCT	2016-09
416417002	Hereditary hemoglobin S (disorder)	SNOMEDCT	2016-09
416826005	Sickle cell-thalassemia disease with crisis (disorder)	SNOMEDCT	2016-09

Sickle cell hemoglobin measurements

➤ ?Observable entity:

- Component: <<<50095005 Hemoglobin S (substance)
- Direct site = 119297000 Blood specimen(specimen)
- Technique = 258035006 High pressure liquid chromatography(technique) OR 743050007 Electrophoresis(technique)



Decision queries which cannot be answered by query of LOINC or SNOMED CT

- MU: Identify all diabetic patients with no glycated hemoglobin in the last 6 months
- PathM: Pull all cases records of colon cancer patients that have reports of tumor budding
- LM: Find all patients who have tested positive for hemoglobin other than HbA
- **Personalized Medicine: Pull all historical cases of colon cancer for research which had any tumor biomarker testing**



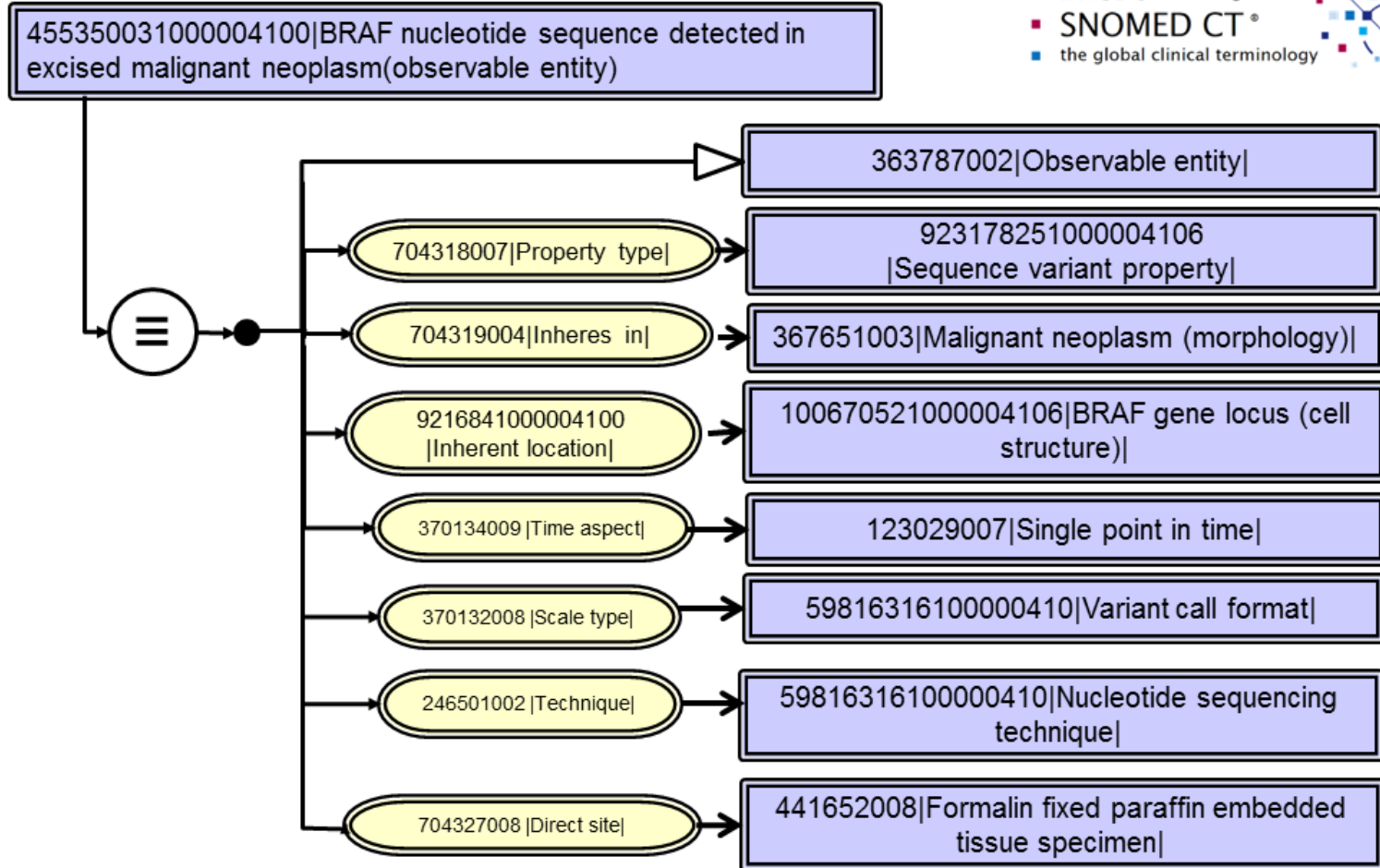
Molecular genetics testing of neoplasms

- Rapidly expanding field of research with nucleotide and chromosomal findings showing value for diagnosis, prognosis and treatment planning
- Large body of work in molecular genetics continuing to grow
- Expanded content model for Observables has SNOMED CT content to include genes and proteins defined by reference to NCBI scientific databases



Tumor biomarker Observable

IHTSDO delivering
SNOMED CT®
the global clinical terminology



Cancer case with tumor biomarkers accomplished

➤ ?Observable:

- Inherent location: <<< 367651003
Malignant neoplasm(morphology)
- Inheres in: <<< 590638411000004104
Nucleotide sequence(cell structure)
- Technique: <<< 708068002 Molecular genetics(technique)



Cancer case with tumor biomarkers accomplished

➤ ?Observable:

- Inherent location: <<< 367651003
Malignant neoplasm(morphology)
- Inheres in: <<< 590638411000004104

The screenshot displays the SNOMED CT interface for the concept 'Tumor biomarkers' (Concept ID: 628246651000004109). The interface is divided into several panes:

- Search and Navigation:** The top left pane shows a search for 'tumor biom' and a list of related concepts under 'Tumor biomarkers', including 'Degree of microsatellite instability' and 'Number of microsatellite markers exhibiting instability in excised neoplasm'.
- Concept Details:** The main pane shows the 'Tumor biomarkers' concept with the following information:
 - Descriptions:**
 - Fully specified name: Tumor biomarkers (observable entity)
 - Synonym: Tumor biomarkers
 - Properties:**
 - Ungrouped Properties:**
 - Is a: Tumor observable
 - Inherent location: Morphologically abnormal structure
 - Inherent location: Nucleotide sequence
 - Inheres in: Neoplasm
 - Property type: Measurement property
 - Technique: Anatomic pathology technique
 - SNOMED CT Properties:**
 - Concept ID: 628246651000004109
 - Module: Nebraska Lexicon extension module
 - Effective time: 2016-01-26
- Parents:** The bottom left pane shows the parent concept 'Tumor observable'.
- Navigation:** The bottom of the interface has tabs for 'Overview', 'Descriptions', 'Source relationships', 'Destination relationships', 'Value domain membership', 'Mappings', and 'References'.

Observables Ontology Applications

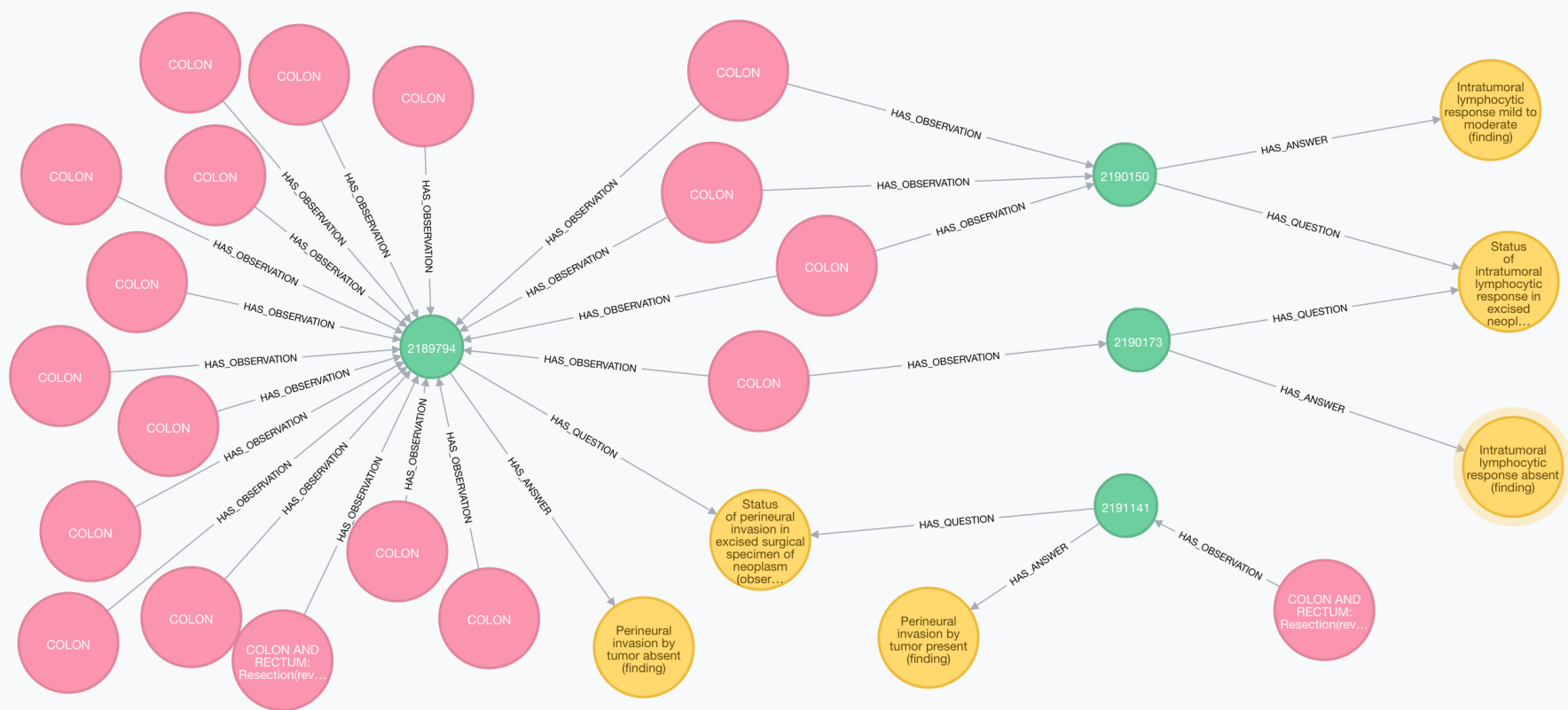
- Clinical decision support in Epic; creation of observables Groupers
- Indexing cancer biorepository using SNOMED CT and graph database
- Implementation of Observables ontology as i2b2 metadata



Observables Ontology Applications

\$ match p=(a:ObjectConcept{sctid:'66950952100004104'})--(b:SynopticObservation), q = (c:ObjectConcept{sctid:'82056361100004106'})--(d:SynopticObservation) return p,q

*(29) ObjectConcept(6) SynopticObservation(4) SynopticReport(19)
 *(31) HAS_ANSWER(4) HAS_OBSERVATION(23) HAS_QUESTION(4)



Questions?





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