# Cancer Deep Phenotype Extraction from Electronic Medical Records (DeepPhe)

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# DeepPhe

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**NCI U24 CA132672 Cancer Deep Phenotyping from Electronic Medical Records (Savova and Jacobson, MPIs)**

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# Background: eMERGE, PGRN, i2b2, SHARP

## Manual chart review

EHR Notes

HPI: 48 woman with mam

Final diagnosis: Breast, Left, Needle Biopsy: In Ca

Patient currently on neoadjuvant therapy with Taxol. Due to cardiomyopathy, patient not candidate for Transtuzumab…

Phenotype Label

- positive/negative

## Automated chart review

EHR Notes

HPI: 48 woman with mam

Final diagnosis: Breast, Left, Needle Biopsy: In Ca

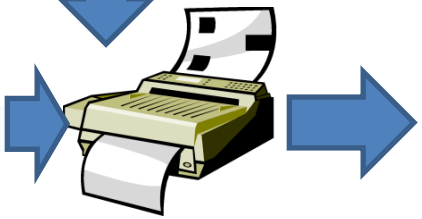
Patient currently on neoadjuvant therapy with Taxol. Due to cardiomyopathy, patient not candidate for Transtuzumab…

cTAKES

Doc1, 0, 2, 3…

Doc2, 0, 0, 1…

Doc3, 1,4,0…



Classifier

Phenotype Label

- positive/negative

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# DeepPhe Project

http://cancer.healthnlp.org

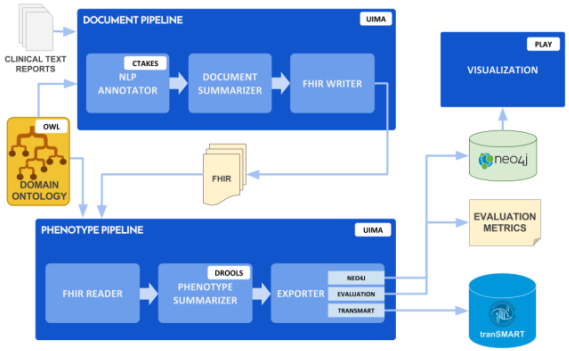
- Goal is to develop next generation cancer deep phenotyping methods
  - No longer dichotomization for a particular phenotype of interest
  - Rather, ***all phenotypes associated with a patient***
- Addresses information extraction but also representation and visualization
- Support **high throughput approach**
  - process and annotate all data at multiple levels (from mention to phenotype) and across time
- Combine IE with structured data (cancer registry)
- Driven by translational research scientific goals as well as surveillance (SEER supplement)

# DeepPhe

HPI: 48 woman with right breast mam

Final diagnosis: Breast, Left, Needle Biopsy: In Ca

Patient currently on neoadjuvant therapy with Taxol. Due to cardiomyopathy, patient not candidate for Transtuzumab…




NEOPLASM 1

Subject: Patient

Infilatrating Ductal Carcinoma (+3d)

Location: Right Breast

Nuclear grade: 2 (+3d)

ER: negative (+3d)

PR: negative (+3d)

Her2/Neu: positive (+3d)

Size: 2.9 x 2.5 x 2.0 (+3d)

Stage:

T2N0M0 (interval, +3d, +119d)

T2N0M1 (+656d)

Lymphadenopathy:

Negative, Clinical exam (+0d)

Negative, MRI (+1d)

Metastasis: Brain (+656d)

TREATMENT 1:

Neoadjuvant Chemotherapy

Agents: Pacitaxel (interval, >+3d, >+119d)

TREATMENT 2:

Her2Neu MAB

DISEASE 1:

Subject: patient

Cardiomyopathy

NEOPLASM 2:

Subject: mother

Cancer

…….

…….

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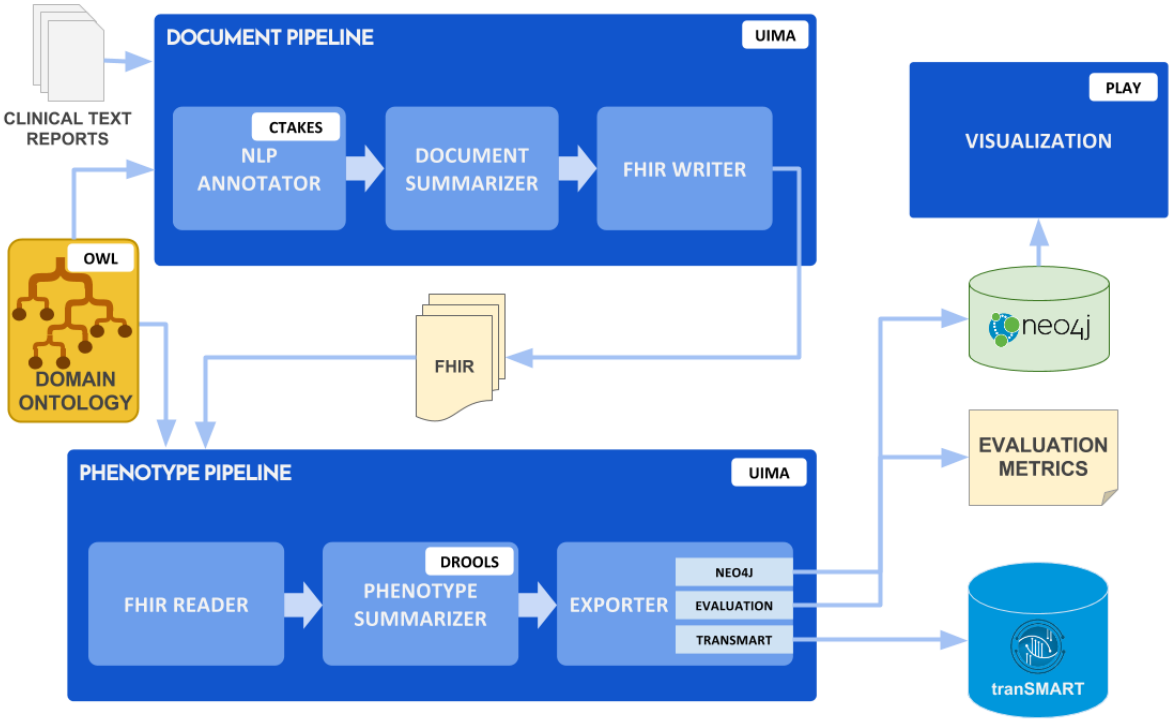
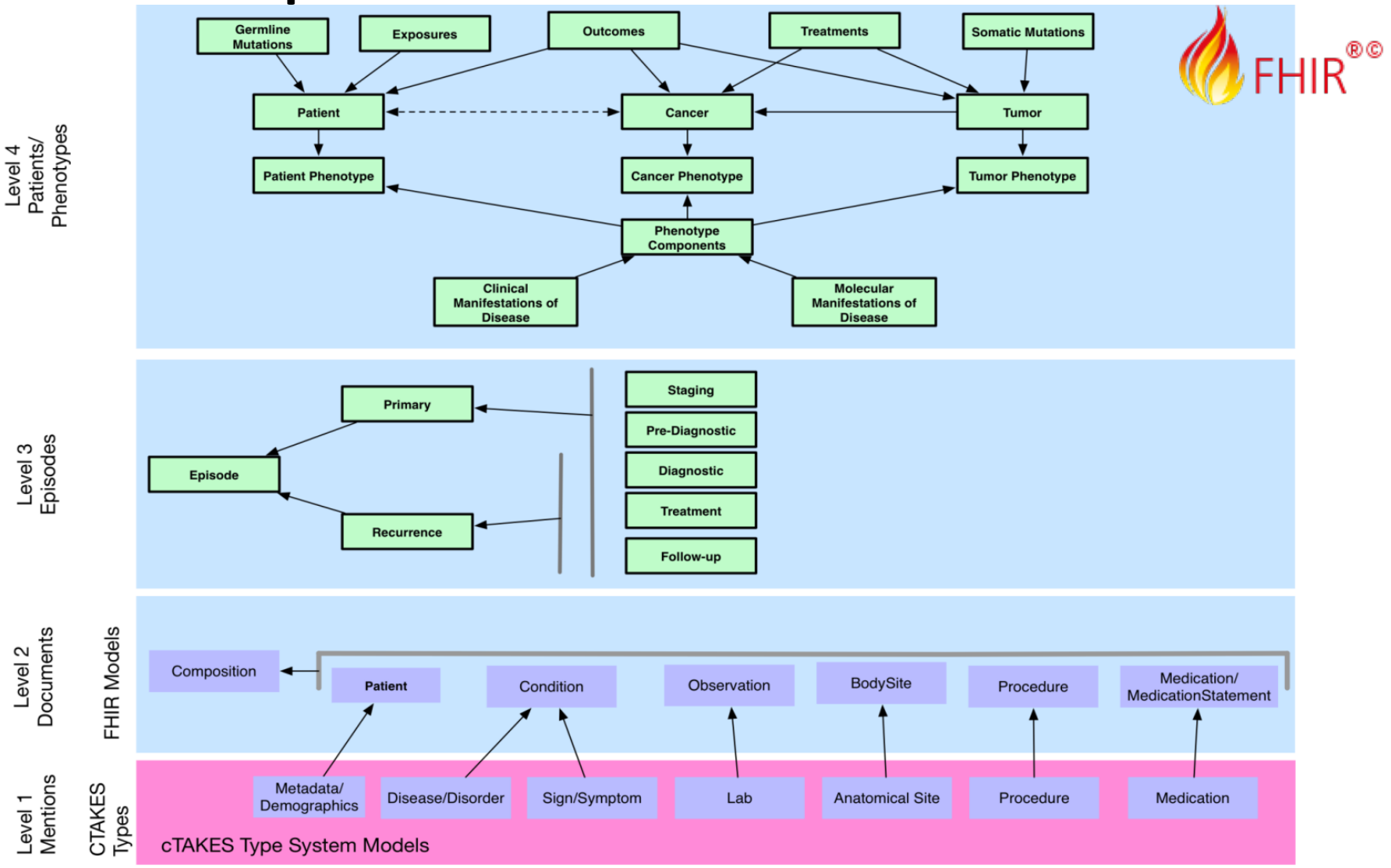
# Architecture

- Portability
- Extensibility
- Modularity
- Ontology driven



# DeepPhe Information Model

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# DeepPhe NLP Pipeline


Boundary detection
Tokenization
Normalization
POS tagging

Entity Recognition

Entity Properties

deepPHE

Relation Extraction

Document Summary

Phenotype Summary

Invasive Ductal Carcinoma. 4.4 cm
Tumor is ER-, PR-, Her2-.

Path

| Tumor is ER -, PR -, HER2 -. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Tumor | is | ER | - | , | PR | - | , | HER2 | - | . |
| Tumor | is | ER | neg | , | PR | neg | , | HER2 | neg | . |
| NN | VBZ | NNP | JJ | | NNP | JJ | | NNP | JJ | |

Neoplasm C3273930 | Estrogen Receptor C0034804 | Progesterone Receptor C0034833 | erbB2 protein C0069515

Tumor → ER, PR, Her2

Tumor | ER Neg | PR Neg | Her2 Neg

58 yo F presents to the ER with slurred speech.
Patient has triple negative breast cancer.

ER

| Patient has triple negative breast cancer. | | | | | | |
|---|---|---|---|---|---|---|
| Patient | has | triple | negative | breast | cancer | . |
| Patient | has | triple | negative | breast | cancer | . |
| NN | VBZ | JJ | JJ | NN | NN | |

Patient C0030705

Malignant Neoplasm of Breast C0006142

Triple-Negative Tumor → ER Neg, PR Neg, Her2 Neg, Tumor

Tumor Phenotype: ER Receptor negative; PR Receptor negative; Her2 receptor negative

Tumor Phenotype: ER Receptor negative; PR Receptor negative; Her2 receptor negative

Tumor Phenotype: ER Receptor negative; PR Receptor negative; Her2 receptor negative

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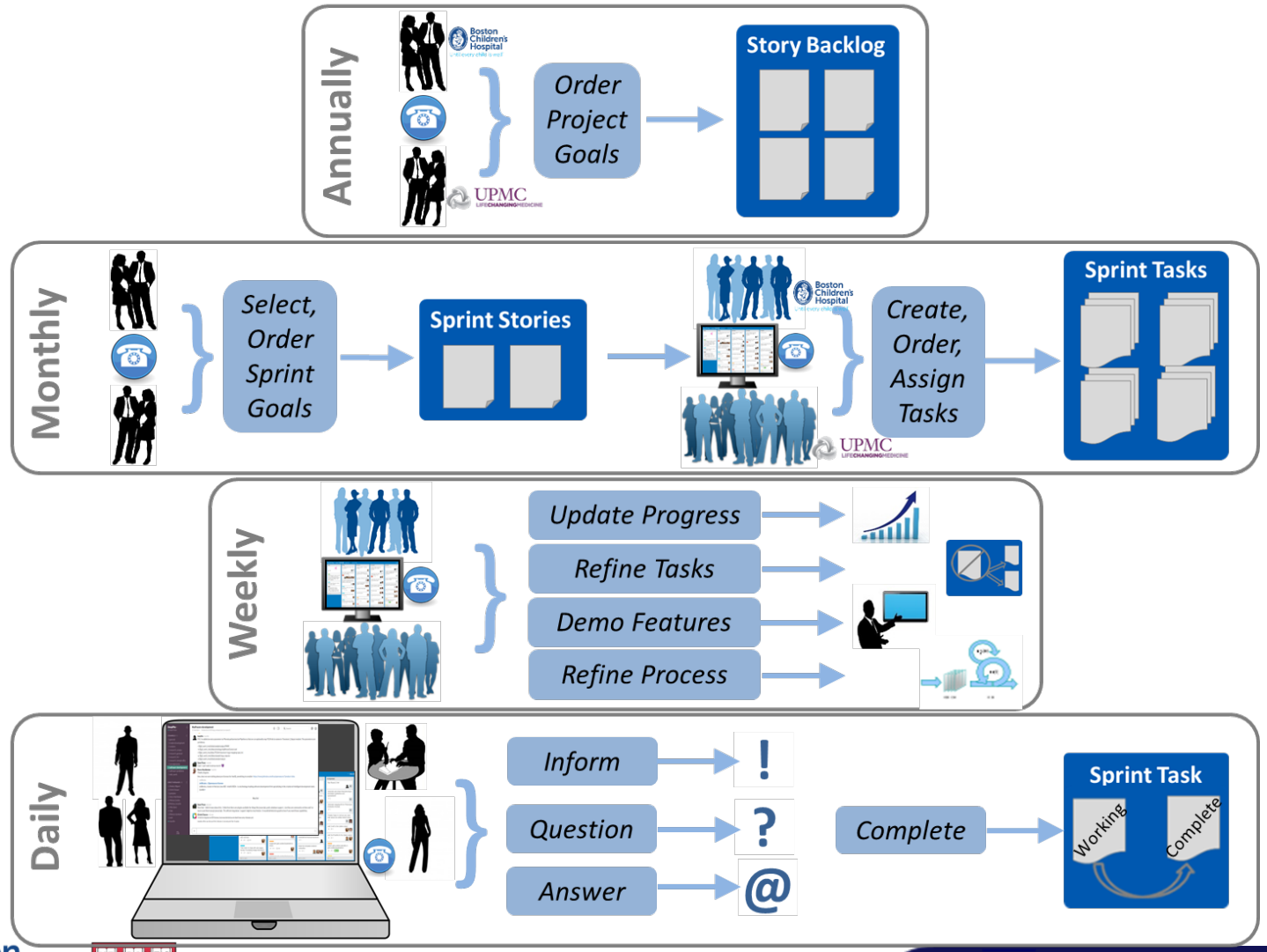
# Software Development Process

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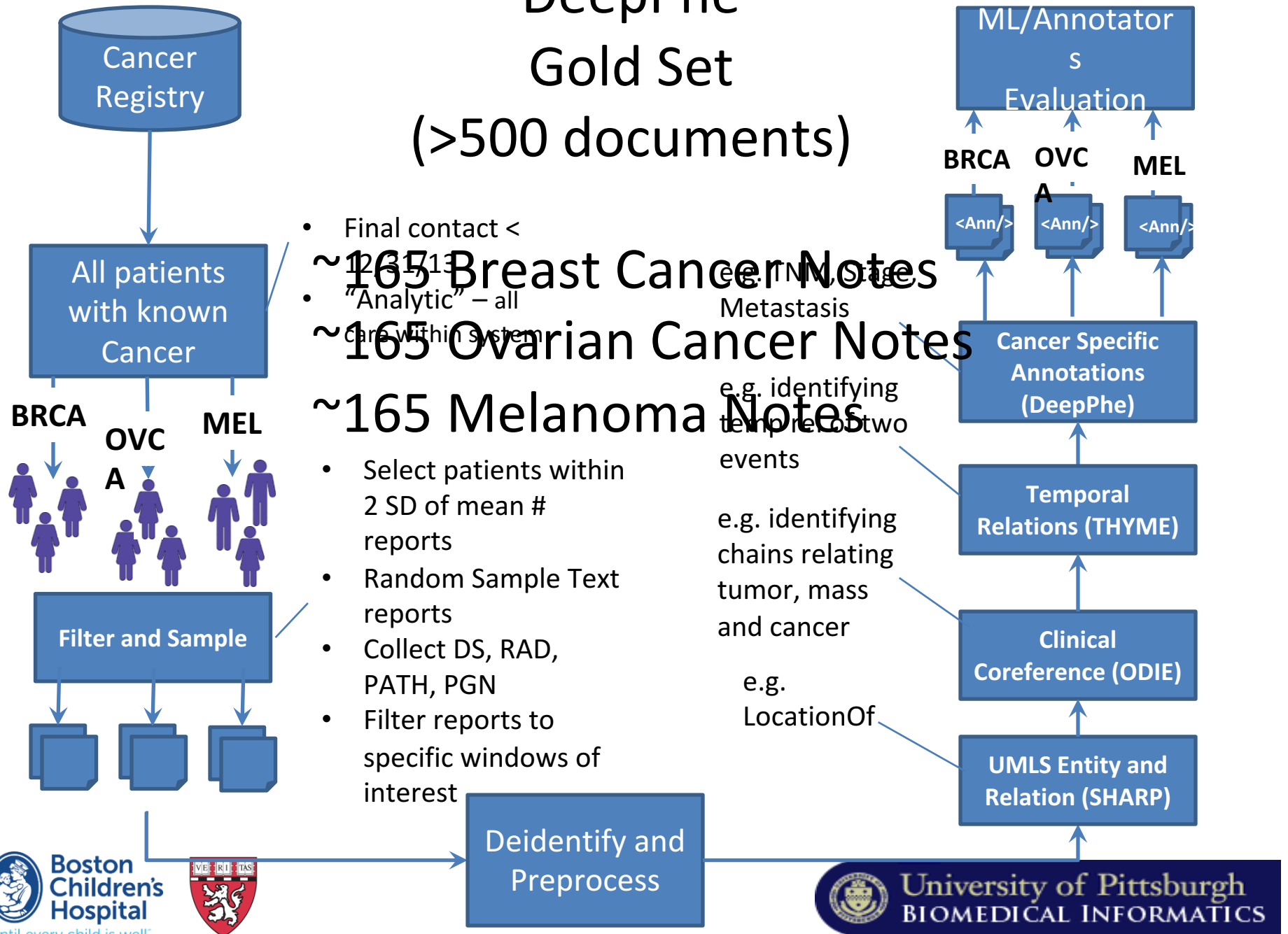
# Y3 Developments

- IE methods
  - Coreference
  - Temporal relations
  - Template filling improvement
- Additional templates for Procedures, Medications, Tumor size
- Breast imaging reporting and data system (BIRADS) annotations
- Clinical genomics – gold standard
- New model for Melanoma
- Visualization of patient data from graph db
- Tooling for faster, more efficient evaluations

# DeepPhe Gold Set (>500 documents)

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# Evaluation Results: Entity Level (BrCa)

| Results on BrCa Test Split | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | *overlapping span of template anchor (mention instance)* | | | | | | | | |
| | *stage* | *TNM* | *receptors* | *metastasis* | *size* | *procedures* | *neoplasms* | *medications* | *docTimeRel* |
| #instances in test split | 10 | 48 | 79 | 42 | 55 | 728 | 217 | 121 | 713 |
| computational method | dictionary lookup | patterns | patterns | dictionary lookup | patterns | dictionary lookup | dictionary lookup | dictionary lookup | machine learning |
| precision/PPV | 1 | 0.98 | 1 | 1 | 1 | 0.81 | 0.87 | 0.62 | 0.67 |
| recall/sensitivity | 0.9 | 0.94 | 0.66 | 0.79 | 0.75 | 0.93 | 0.86 | 0.94 | 0.67 |
| F1 | 0.95 (1) | 0.96 (1) | 0.79 (0.89) | 0.88 (0.46) | 0.85 | 0.87 | 0.86 (0.91) | 0.75 | 0.67 (0.65) |
| | *attribute accuracy* | | | | | | | | |
| *conditional | 1 | n/a | 1 | 1 | n/a | 0.37 | 1 | 0.33 | |
| *uncertainty | 1 | 1 | 1 | 0.72 | n/a | 0.99 | 0.97 | 1 | |
| *negation | 1 | n/a | 1 | 0.99 | n/a | 0.77 | 0.98 | 0.96 | |
| *subject | 1 | n/a | 1 | 1 | n/a | 0.67 | 1 | 1 | |
| *generic | 1 | n/a | 1 | 0.39 | n/a | 0.28 | 0.98 | 0.46 | |
| associated neoplasm | 0.67 | 0.78 | 0.67 | 0.27 | 0.17 | n/a | n/a | n/a | |
| body location | n/a | n/a | n/a | 0.65 | n/a | n/a | 0.59 | n/a | |
| test method | n/a | n/a | 0.62 | n/a | 0.61 | n/a | n/a | n/a | |
| value | n/a | n/a | 1 | n/a | n/a | n/a | n/a | n/a | |
| ** indicates weighted accuracy per SemEval 2015 to take into account default value prevalance rates* | | | | | | | | | |

# Extended Test Set Evaluation

# Evaluation Results: Phenotype Level Cancer

| Cancer Template Distribution: BrCa | |
|---|---|
| | #instances in corpus |
| cancer | 52 |
| body location | 52 |
| body location side | 52 |
| clinical stage | 35 |
| cT value | 34 |
| cN value | 34 |
| cM value | 32 |
| pT value | 34 |
| pN value | 34 |
| pM value | 15 |
| corpus: 50 patients, 1881 documents | |

| Results on BrCa Test Set: Phenotype System vs. Gold (results in parentheses are for inter-annotator agreement) | | | |
|---|---|---|---|
| | **Precision/PPV** | **Recall/Sensitivity** | **F1 measure** |
| cancer | 0.87 (1) | 0.83 (1) | 0.85 (1) |
| body location | 1.00 (1) | 1.00 (1) | 1.00 (1) |
| body location side | 1.00 (n/a) | 1.00 (n/a) | 1.00 (n/a) |
| clinical stage | 0.35 (0.80) | 0.93 (1) | 0.51 (0.89) |
| cT value | 0.42 (0.89) | 0.89 (1) | 0.57 (0.94) |
| cN value | 0.71 (0.89) | 0.96 (1) | 0.82 (0.94) |
| cM value | 0.90 (0.89) | 1.00 (1) | 0.95 (0.94) |
| pT value | 0.80 (0.89) | 0.93 (1) | 0.86 (0.94) |
| pN value | 0.66 (0.78) | 0.83 (0.88) | 0.74 (0.82) |
| pM value | 0.92 (0.62) | 0.85 (1) | 0.88 (0.77) |

# Evaluation Results: Phenotype Level Tumor

| Tumor Template Distribution: BrCa | |
|---|---|
| | #instances in corpus |
| tumor | 127 |
| body clock face | 44 |
| body quadrant | 27 |
| diagnosis | 127 |
| tumor type (primary; regional or distant metastasis; local, regional, distant recurrence) | 127 |
| er interpretation | 51 |
| pr interpretation | 51 |
| her2 interpretation | 48 |
| calcifications | 127 |
| corpus: 50 patients, 1881 documents | |

| Results on BrCa Test Set: Phenotype System vs. Gold (results in parentheses are for inter-annotator agreement) | | | |
|---|---|---|---|
| | **Precision/PPV** | **Recall/Sens.** | **F1 measure** |
| tumor | 0.56 (0.79) | 0.36 (0.88) | 0.44 (0.84) |
| body clock face | 0.50 (0.89) | 0.02 (0.73) | 0.05 (0.80) |
| body quadrant | 0.52 (0.73) | 0.57 (0.80) | 0.54 (076) |
| diagnosis | 0.77 (0.93) | 0.78 (0.93) | 0.77 (0.93) |
| tumor type | 0.92 (1) | 0.92 (1) | 0.92 (1) |
| er interpretation | 0.91 (1) | 0.93 (1) | 0.92 (1) |
| pr interpretation | 0.84(1) | 0.84 (1) | 0.84 (1) |
| her2 interpretation | 0.61 (1) | 0.55 (1) | 0.58 (1) |
| calcifications | 0.67 (n/a) | 0.67 (n/a) | 0.67 (n/a) |

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# SEER Dev Subset Evaluation

# Evaluation Results: Phenotype Level Cancer

| Cancer Template Distribution: BrCa | |
|---|---|
| | #instances in corpus |
| cancer | 240 |
| body location | 239 |
| body location side | 218 |
| clinical stage | 8 |
| cT value | 2 |
| cN value | 2 |
| cM value | 2 |
| pT value | 79 |
| pN value | 72 |
| M value | 12 |
| corpus: 231 patients, 254 documents | |

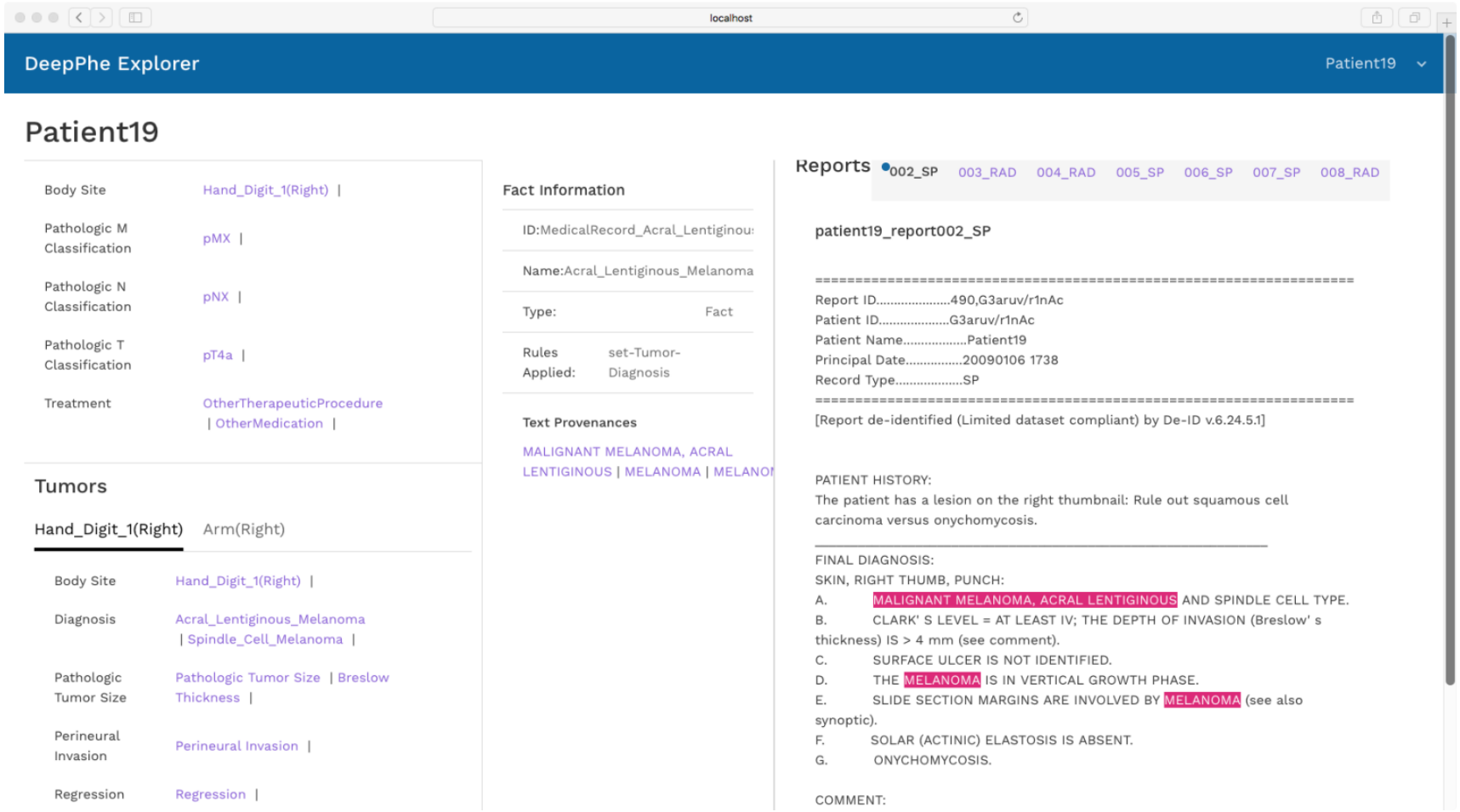
| Results on BrCa Simple Train/Dev: Phenotype System vs. Gold (results in parentheses are for inter-annotator agreement) | | | |
|---|---|---|---|
| | **Precision/PPV** | **Recall/Sensitivity** | **F1 measure** |
| cancer | 0.68 (1) | 0.63 (1) | 0.65 (1) |
| body location | 1.00 (1) | 1.00 (1) | 1.00 (1) |
| body location side | 1.00 (n/a) | 1.00 (n/a) | 1.00 (n/a) |
| clinical stage | 1.00 (0.80) | 1.00 (1) | 1.00 (0.89) |
| cT value | 1.00 (0.89) | 0.50(1) | 0.67 (0.94) |
| cN value | 1.00 (0.89) | 0.50(1) | 0.67 (0.94) |
| cM value | 0.33 (0.89) | 0.50(1) | 0.40 (0.94) |
| pT value | 0.67 (0.89) | 0.70 (1) | 0.69 (0.94) |
| pN value | 0.61 (0.78) | 0.69 (0.88) | 0.65 (0.82) |
| pM value | 0.75 (0.62) | 1.00 (1) | 0.86 (0.77) |

# Evaluation Results: Phenotype Level Tumor

| Tumor Template Distribution: BrCa | |
|---|---|
| | #instances in corpus |
| tumor | 270 |
| body clock face | 78 |
| body quadrant | 15 |
| diagnosis | 269 |
| tumor type | 270 |
| er interpretation | 127 |
| pr interpretation | 125 |
| her2 interpretation | 96 |
| calcifications | 270 |
| corpus: 231 patients, 254 documents | |

| Results on BrCa Simple Train/Dev: Phenotype System vs. Gold (results in parentheses are for inter-annotator agreement) | | | |
|---|---|---|---|
| | **Precision/PPV** | **Recall/Sensitivity** | **F1 measure** |
| tumor | 0.64 (0.79) | 0.52 (0.88) | 0.57 (0.84) |
| body clock face | 0.67 (0.89) | 0.03 (0.73) | 0.06 (0.80) |
| body quadrant | 1.00 (0.73) | 0.77 (0.80) | 0.87 (0.76) |
| diagnosis | 0.68 (0.93) | 0.59 (0.93) | 0.63 (0.93) |
| tumor type | 0.96 (1) | 0.96 (1) | 0.96 (1) |
| er interpretation | 0.78 (1) | 0.26 (1) | 0.38 (1) |
| pr interpretation | 0.74 (1) | 0.27 (1) | 0.39 (1) |
| her2 interpretation | 0.67 (1) | 0.30 (1) | 0.41 (1) |
| calcifications | 0.86 (n/a) | 0.86 (n/a) | 0.86 (n/a) |

# Started Processing Melanoma

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# Visual Analytics Initial Prototype

- Support display of patient phenotype and all the reports available for the patient.
- Show cancer and tumor information with the ability to view evidence used to derive the information for each element.
- Highlight evidence in the report text.

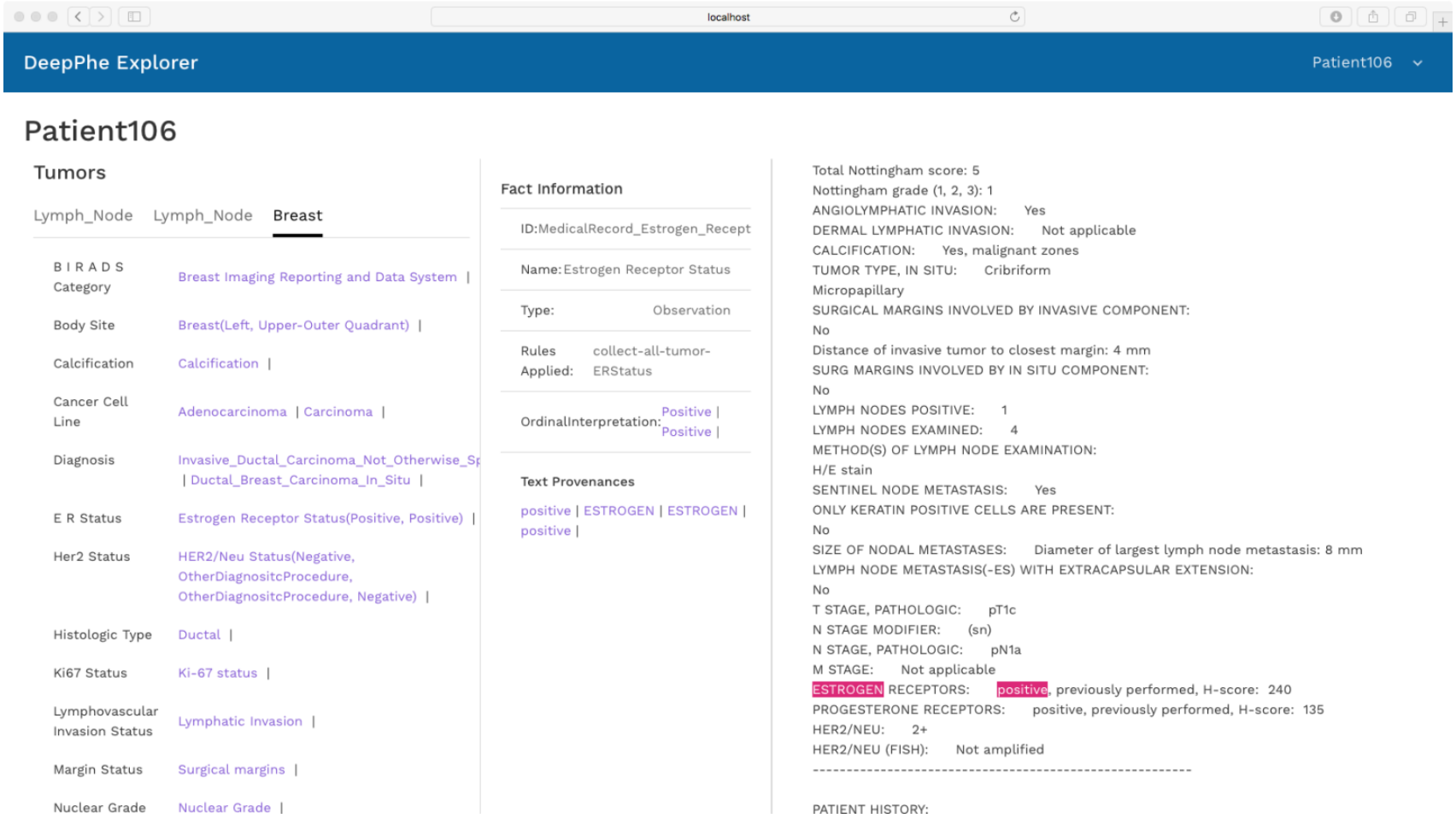
# Visual Analytics Architecture

Database: A Neo4J graph database was chosen to most naturally represent relationships between the clinical manifestations, phenotype components and the supporting evidence.

Backend Services: Play Framework. Allows for Java based controllers and backend code.

Front End: React Framework – Allows for modular frontend components.

# Screenshot

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# Publications and Collaborations


1. Chen, Lin; Miller, Timothy; Dligach, Dmitriy; Bethard, Steven; Savova, Guergana. 2016. Improving Temporal Relation Extraction with Training Instance Augmentation. BioNLP workshop at the Association for Computational Linguistics conference. Berlin, Germany, Aug 2016
2. Hochheiser, Harry; Castine, Melissa; Harris, David; Savova, Guergana; Jacobson, Rebecca. 2016. An Information Model for Cancer Phenotypes. BMC Medical Informatics and Decision Making.
3. Ethan Hartzell, Chen Lin. 2016. Enhancing Clinical Temporal Relation Discovery with Syntactic Embeddings from GloVe. International Conference on Intelligent Biology and Medicine (ICIBM 2016). December 2016, Houston, Texas, USA
4. Dligach, Dmitriy; Miller, Timothy; Lin, Chen; Bethard, Steven; Savova, Guergana. 2017. Neural temporal relation extraction. European Chapter of the Association for Computational Linguistics (EACL 2017). April 3-7, 2017. Valencia, Spain.
5. Towards Portable Entity-Centric Clinical Coreference Resolution (Journal of Biomedical InformaticsC
6. Castro SM, Tseytlin E, Medvedeva M, Mitchell KJ,Visweswaran S, Bekhuis T,**Jacobson RS**. Automated annotation and classification of BI-RADS assessment from radiology reports. Journal of Biomedical Informatics 2017 (in press). DOI: 10.1016/j.jbi.2017.04.011
7. DeepPhe system paper (submitted to Special Issue of Cancer Research)
8. Collaboration with THYME (thyme.healthnlp.org)


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# Goals for Next Year (Y4)

- Extraction of treatment regimens from constituent medications and procedures
- Episode classification and extraction (pre-diagn, diagn, treatment, followup)
- Clinical genomics result extraction
- Expanding to ovarian cancer
- Enhanced visualization including timeline
- Extrinsic evaluation of system with breast cancer clinical research questions

# Demo

[add link]