A FrameNet for Cancer Information in Clinical Narratives: Schema and Annotation

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Abstract
This paper presents a pilot project named Cancer FrameNet. The project’s goal is a general-purpose natural language processing (NLP) resource for cancer-related information in clinical notes (i.e., patient records in an electronic health record system). While previous cancer NLP annotation projects have largely been ad hoc resources to address a specific and immediate information need, the frame semantic method employed here emphasizes the information presented in the notes themselves and its linguistic structure. To this end, three semantic frames (targeting the high-level tasks of cancer diagnoses, cancer therapeutic procedures, and tumor descriptions) are created and annotated on a clinical text corpus. Prior to annotation, candidate sentences are extracted from a clinical data warehouse and de-identified to remove any private information. The frames are then annotated with the three frames totaling over thirty frame elements. This paper describes these steps in the pilot project and discusses issues encountered to evaluate the feasibility of general-purpose linguistic resources for extracting cancer-related information.

Keywords: clinical information extraction, cancer, frame semantics

1 Introduction
Important medical information about cancer patients is often only available in free text (natural language) notes in electronic health records (EHRs). This information is frequently needed for research, quality improvement, surveillance, and other important functions. However, the manual abstraction of this information can be incredibly time-consuming and expensive, often making it infeasible for both early-stage research and clinical quality improvement projects. Thus, natural language processing (NLP) approaches can offer a tremendous service in oncology.

Existing NLP systems for cancer-related information generally fall under a type of biomedical NLP task known as phenotyping, which is the task of identifying patients that meet a certain set of criteria. Phenotyping specifications are often highly task-specific, which frequently yields one-off NLP datasets and algorithms that do not generalize to similar phenotyping tasks. For example, one phenotype method may identify lung cancer patients with a tumor of at least 2cm in diameter, while another method may identify lung cancer patients with at least two tumors that are 1cm in diameter. Such methods are quite similar, yet often produce incompatible annotations and algorithms.

The key insight is that phenotyping methods often conflate extraction (identifying relevant portions of text) and reasoning (determining if the extracted text fulfills the task’s needs). By separating these steps and focusing on general-purpose extraction, it will be possible to easily and rapidly develop phenotyping methods. This is because the bulk of the effort is typically spent in the extraction step (annotating data and developing NLP algorithms), while the reasoning step is often a straightforward set of rules. Continuing the example above, an NLP system capable of extracting all tumor references and their sizes from text would easily meet the needs of both phenotyping methods (along with potentially many others).

The challenge then becomes how to develop general-purpose extraction algorithms for clinical text, especially when it isn’t necessarily clear a priori what information needs to be extracted. Luckily, frame semantics provides a useful framework for developing such a resource. In frame semantics, a word or phrase evokes a frame of semantic knowledge that describes the characteristic attributes associated with a concept. For example, for tumor, the frame would likely contain elements that describe the size, location, and morphology of the tumor. The set of frame elements can either be defined a priori by a subject expert or added iteratively based on the data (this work combines both approaches).

The specification of a set of frames combined with annotated examples is referred to as a FrameNet, the best known being Berkeley FrameNet (Baker et al., 1998). But other FrameNets exist as well, notably domain-specific FrameNets. This paper describes a pilot project to build such a domain-specific resource—referred to hereafter as Cancer FrameNet—that focuses on cancer-related information. The goal of the pilot is to test the feasibility of a much larger resource covering the depth and breadth of cancer information in patient records. Even as a pilot, however, this resource is still sizable, covering three important frames, 22 lexical units, and nearly 8 thousand annotated sentences.

There are several potential pitfalls for frame annotation in clinical notes, thus the need for a feasibility pilot. These issues include the consistency of cancer-related information in clinical notes: is cancer too complex with too many variables to be reliably annotated (both manually and by an automatic NLP system)? Another issue is the overlapping information of frames: are there really semantically distinct
concepts that can be formed into different frames? Finally, frame annotation is typically limited to sentence and clause context (excluding implicit information), but does this apply to cancer-related information in clinical notes?

It should be noted that there is a second major challenge in the generalizability of clinical NLP systems. This involves the portability of algorithms from one institution’s clinical notes to another, as oftentimes these can be drastically different. While we acknowledge the critical importance of this problem, we make no attempt to solve it here. All data described in this paper come from a single institution. It is our hope, however, that upon establishing a general-purpose resource, annotated frames from additional institutions can be added in order to improve inter-institutional generalizability.

The rest of this paper is structured as follows: Section 2 outlines previous work in both domain-specific FrameNets and cancer-related information extraction. Section 3 describes the pre-annotation process: where the data came from, how it is extracted and prepared for annotation, including how it is de-identified to protect patient privacy. Section 4 lays out the frames covered in the pilot project: what they are, why they were chosen, and the current frame elements. Section 5 details the annotation process. Finally, Section 6 discusses the potential ramifications of Cancer FrameNet on cancer information extraction, including its strengths and weaknesses, and how it might or might not overcome some of the aforementioned pitfalls.

2 Background

The theory of frame semantics has spawned many practical natural language resources. Most prominent is the Berkeley FrameNet project (Baker et al., 1998; Baker et al., 2015), which is intended to be an open-domain encoding of common knowledge (commercial transactions, transportation, crime, international affairs, etc.). The FrameNet construction methodology has been ported to many other languages (Heppin and Gronostaj, 2014; Lin et al., 2015; Rezhake and Kuerban, 2015; Ohara, 2016). More interesting, many domain-specific FrameNets exist, ranging from soccer (Schmidt, 2006; Torrent et al., 2014) to sentiment (Ruppenhofer, 2013) to disability (Savova et al., 2005) to cellular pathways (Dolbey et al., 2006; Dolbey, 2009). No such resource targets the types of cancer-related information found in EHR notes.

While not explicitly based on a FrameNet-style approach, a significant amount of work has focused on NLP systems for extracting cancer-related information from EHRs. A sampling of the types of information extracted include: a frame-like representation of radiological findings (Taira et al., 2001); procedures, tumor stages, and various biomarker scores (Xu et al., 2004); tumor and node staging (McCowan et al., 2007); Gleason score, tumor stages, and margin status (D’Avolio et al., 2008); histology, site, dimension, and various tumor types (Coden et al., 2009); tumor progression (Cheng et al., 2010); colonoscopy status (Denny et al., 2010); colonoscopy quality measures (Harkema et al., 2010); Gleason score, Clark level, and Breslow depth (Napolitano et al., 2010); cancer history (Wilson et al., 2010); counts of examined and positive tumors and nodes (Martinez and Li, 2011); pancreatic cancer predictors (Zhao and Weng, 2011); tumor staging and biomarkers (Segagni et al., 2012); pain in prostate cancer patients (Heintzelman et al., 2013); highest level of pathology, number of removed adenomas (Imler et al., 2013); tumor, node, metastases, and ACPS stages (Martinez et al., 2013); liver cancer status (Ping et al., 2013); change of event state (Vanderwende et al., 2013); twenty-two staging indicators (Ashish et al., 2014); volume, size, and location (Wang et al., 2014); and diagnosis, hormone receptor status, tumor size, and number of positive nodes (Napolitano et al., 2016). This synopsis understates the number of extracted information types, but it is still clear that there is a significant breadth of information as well as consistent areas of overlap.

A more direct comparison to our work is the recent work in the DeepPhe project (Savova et al., 2017). DeepPhe takes a document-level approach to extracting cancer information, which is more appropriate for certain data types than the sentence-based approach proposed below. Most crucially, it is unknown how well their document-level approach generalizes to other institution’s data. On the other hand, while the pilot project discussed in this paper focuses on a single institution as well, we hypothesize that a frame-based method targeting information at the sentence level will result in greater potential for generalization across institutions.

3 Preparing Clinical Narratives

Several steps are necessary to prepare clinical narratives for frame annotation: clinical notes must be retrieved from the clinical data warehouse, lexical units (see Section 2) and their proper context must be extracted, then private patient information must be de-identified. All of this must be done within a secure HIPAA-compliant environment.

The clinical notes are derived from the UT Physicians clinics, a chain of outpatient clinics in the Houston area. The snapshot available from the data warehouse contains more than 260,000 notes with more than 175 million tokens. While by no means a large corpus by EHR standards, it contains sufficient data for a pilot evaluation. This project was deemed exempt by the Committee for the Protection of Human Subjects, the UTHealth Institutional Review Board, under protocol number HSC-SBMI-13-0549.

For each lexical unit (see Section 2), every sentence containing the lexical unit is extracted from the note corpus. Sentence segmentation is by no means a simple task in clinical data (Miller et al., 2015; Zweigenbaum et al., 2016). Stanford CoreNLP (Manning et al., 2014) was used to identify initial sentences, but due to the lack of punctuation in clinical notes, these often constituted multiple (sometimes dozens) of sentences (newlines are often used as end-of-sentence markers, but frequently newlines do not end sentences). As a result, several high-precision rules were used to prune down sentence length. Ultimately, a human annotator was required to remove words not part of the lexical
unit’s proper sentence boundary. This was done in conjunction with the de-identification stage below.

Clinical notes contain significant amounts of copy-pasting and templated sentences, so a random sample of sentences might contain substantial numbers of duplicates and near-duplicates. To maximize the diversity of the annotations, the sentences were sorted by TF-IDF cosine distance.

The final preparation step is to de-identify the notes, removing any protected health information (PHI) and replacing it with a placeholder. In the United States, the Health Insurance Portability and Accountability Act (HIPAA) mandates the de-identification of 18 categories of information:

1. names
2. geographic localities smaller than a state
3. dates and ages over 89
4. telephone numbers
5. fax numbers
6. e-mail addresses
7. Social Security numbers
8. medical record numbers
9. health plan numbers
10. account numbers
11. certificate/license numbers
12. vehicle & license numbers
13. device identifiers
14. web URLs
15. IP addresses
16. biometric identifiers
17. full face photographic images
18. any other identifying number/characteristic/code

We expanded on this to cover all ages and geographic localities, as well as other types of identifying information as described in Stubbs and Uzuner (2015). Furthermore, one of our lexical units is frequently a surname in the data: these sentences are completely discarded. Both human annotation and an in-house automatic system (Lee et al., 2017) were used. To reduce bias, the human de-identification occurred first, then the automatic system provided additional suggestions that the human may have missed. The automatic de-identifications were all manually verified to reduce the proliferation of false positives common with de-identification systems. Finally, at future stages of the annotation, as detailed below, annotators always have the option of identifying further PHI missed by this process.

4 Initial Frame Schemas

Based on the existing literature, three common phenotyping tasks were selected: (1) identification of patients with a particular cancer diagnosis, (2) identification of patients with a particular cancer treatment, and (3) identification of patients with particular tumor characteristics. To reduce the complexity of the second task, and to focus on data more likely to be found in outpatient notes, treatments are limited to surgical procedures (i.e., excluding medications, chemotherapy, etc.). These three tasks yield three frames (i) CANCER_DIAGNOSIS, (ii) CANCER_THERAPEUTIC_PROCEDURE, and (iii) TUMOR_DESCRIPTION. We also define an abstract root frame, CANCER_MASTER_FRAME, from which all three inherit elements. This enables frame elements (attributes) that are universal, such as negation and certainty. For each of these frames, an expert in cancer informatics (EVB) helped devise a list of lexical units:

**CANCER_DIAGNOSIS**: adenocarcinoma, cancer, carcinoma, leukemia, lymphoma, malignancy, malignant, melanoma, myeloma, sarcoma

**CANCER_THERAPEUTIC_PROCEDURE**: colectomy, hysterectomy, lymphadenectomy, mastectomy, palliative, pancreatectomy, prostatectomy, radiation, whipple

**TUMOR_DESCRIPTION**: lesion, mass, tumor

For each of these lexical units, the process described in Section 3 was followed until up to 500 de-identified sentences were available for each lexical unit. Five of the lexical units (lymphadenectomy, myeloma, pancreatectomy, sarcoma, and whipple) had fewer than 500 sentences in the corpus.

The elements (attributes) of each frame were determined by an iterative process. First, an initial set of elements was proposed by the cancer expert. During the course of the annotation, new elements were frequently proposed by the annotators. Elements with sufficient frequency and importance—as determined by the cancer expert—were added to the frame schema. For example, FAMILY-HISTORY (for the CANCER_DIAGNOSIS frame), EXTENT (for CANCER_THERAPEUTIC_PROCEDURE), and RECURRENCE (for TUMOR_DESCRIPTION) were added after the start of annotation. It is expected that further annotation will yield additional changes to the schema. The set of frame elements, including brief definitions, is shown in Table 1. Note that some elements (e.g., STATUS, PATIENT) are part of all three frames, but not the CANCER_MASTER_FRAME as these are not expected to necessarily apply to future frames.

5 Annotation

The annotation process largely followed standard linguistic annotation practices (Pustejovsky and Stubbs, 2013). Notably, the sentences containing candidate lexical units were double-annotated then reconciled with the help of a third individual. All frame annotation was performed in Brat (Stenetorp et al., 2012). See Figure 1 for examples.

Two special annotations, whose functionality was briefly mentioned earlier, deserve more attention here. First, as shown in Table 1, there is a special “???” element that annotators can use to indicate potentially useful information that may later result in the creation of a new element. (see Figure 1 for an example). As the disease is so complex, there is simply too much information associated with cancer to include elements for all possible types of information. So the “??” element allows for the prioritization of information based on the actual frequency in the clinical notes. Second, the annotation denoted as ERROR is used by
Table 1: Cancer FrameNet pilot frames and their elements.
Table 4: Annotation agreement.

(a) Frame Agreement

| Frame                           | Observed Agreement | Expected Agreement | $\kappa$ |
|--------------------------------|--------------------|--------------------|---------|
| CANCER_DIAGNOSIS                | 0.96               | 0.73               | 0.84    |
| CANCER_THERAPEUTIC_PROCEDURE   | 0.88               | 0.77               | 0.46    |
| TUMOR_DESCRIPTION              | 0.89               | 0.74               | 0.58    |

(b) Frame Element Agreement

| Element            | Overall $F_1$ |
|--------------------|---------------|
| AGENT              | 0.30          |
| CERTAINTY          | 0.69          |
| COMPLICATION       | 0.33          |
| DATE_TIME          | 0.69          |
| EXTENT             | 0.87          |
| FAMILY_HISTORY     | 0.84          |
| HISTOLOGY          | 0.66          |
| LOCATION           | 0.82          |
| MALIGNANCY         | 0.87          |
| MARGIN_STATUS      | 0.61          |
| METASTASIS         | 0.57          |
| MORPHOLOGY         | 0.56          |
| PATIENT            | 0.83          |
| POLARITY           | 0.77          |
| QUANTITY           | 0.41          |
| RECURRENCE         | 0.70          |
| RESECTABILITY      | 0.88          |
| RESULT             | 0.34          |
| SIZE               | 0.83          |
| SIZE_TREND         | 0.60          |
| STAGE              | 0.80          |
| STATUS             | 0.75          |

Table 2: Frequencies of frame instances in the corpus.

Annotators to mark both PHI that was missed (thankfully a rare occurrence) and sentence boundaries that should have been removed by the process described in Section 3. Thus ERRORS indicate “sentences” that must be altered before the annotations can be considered final.

Annotation Statistics The annotation was completely performed in 90 hours, taking approximately one minute per sentence, and additional time for reconciliation. Descriptive statistics of the annotated corpus are provided in Table 2. A total of 7,961 sentences are annotated with 7,163 frame-evoking lexical units (out of a total of 8,206 candidate lexical units). Specifically, there are 3,577 CANCER_DIAGNOSIS frames, 2,204 CANCER_THERAPEUTIC_PROCEDURE frames, and 1,382 TUMOR_DESCRIPTION frames. In terms of frame elements (e.g., LOCATION, PATIENT, HISTOLOGY), CANCER_DIAGNOSIS had an average of 3.2 elements per frame instance, CANCER_THERAPEUTIC_PROCEDURE had an average of 1.7, and TUMOR_DESCRIPTION had an average of 1.1 elements. The most common elements which are shared across frames are PATIENT (2,749 instances), STATUS (2,214), LOCATION (2,190), CERTAINTY (999), and POLARITY (638). See Table 2 for more frame element details.

Annotation Agreement Inter-annotator agreement results are shown in Table 3. While observed agreement for frames—shown in Table 3(a)—is high (around 90%) for all three frames, the fairly high levels of expected agreement (73-77%) result in at best moderate $\kappa$ agreement for CANCER_THERAPEUTIC_PROCEDURE and TUMOR_DESCRIPTION (0.46 and 0.58, respectively). However, $\kappa$ agreement for CANCER_DIAGNOSIS is excellent (0.84). The reason for the high expected agreements is the lack of ambiguity in many of the lexical units (e.g., adenocarcinoma is almost always used to indicate a diagnosis), but each of the frames have at least one lexical unit that has high levels of ambiguity (e.g., cancer, radiation, and mass). Table 3(b) shows the $F_1$ agreement for frame elements. It is unsurprising to see a wide range of agreements, from the very high (e.g., RESECTABILITY, EXTENT, LOCATION) to the quite low (e.g., RESULT, COMPLICATION, AGENT). Notably, the elements with lowest agreement tend to be relatively rare in the corpus (e.g., 6 AGENTS and 71 COMPLICATIONS compared to 553 EXTENTS and 2,190 LOCATIONS), so low agreement was likely due to a lack of data for calibration.

6 Discussion & Conclusion

In this paper, we presented Cancer FrameNet, a pilot project focuses on building a cancer-related clinical narrative resource for developing NLP systems. We introduced an annotation schema consisting of three frames (CANCER_DIAGNOSIS, CANCER_THERAPEUTIC_PROCEDURE, and TUMOR_DESCRIPTION), as well as a corpus annotated according to the schema which consists of almost eight thousand sentences. Our primary goal is to inform the developmental process for an extended Cancer FrameNet resource, with the secondary goal of informing the develop-
Table 3: Frequencies of frame elements in the corpus.

(a) CANCER_DIAGNOSIS elements

| Lexical Unit     | Certainty | DateTime | Polarity | Family History | Histology | Location | Patient | Stage | Quantity | Status |
|------------------|-----------|----------|----------|----------------|-----------|----------|---------|-------|---------|--------|
| adenocarcinoma   | 112       | 10       | 16       | 46             | 91        | 3/16     | 119     | 134   | 1       | 84     |
| cancer           | 61        | 8        | 30       | 85             | 12        | 335      | 197     | 25    | 0       | 101    |
| carcinoma        | 98        | 0        | 24       | 15             | 49        | 419      | 176     | 133   | 5       | 92     |
| leukemia         | 37        | 7        | 15       | 167            | 6         | 4        | 96      | 1     | 0       | 91     |
| lymphoma         | 87        | 16       | 28       | 56             | 41        | 77       | 202     | 22    | 0       | 142    |
| malignancy       | 192       | 5        | 209      | 9              | 2         | 122      | 195     | 6     | 1       | 46     |
| malignant        | 6         | 1        | 3        | 0              | 0         | 5        | 3       | 0     | 0       | 1      |
| melanoma         | 55        | 17       | 43       | 96             | 19        | 197      | 181     | 49    | 9       | 156    |
| myeloma          | 38        | 4        | 18       | 46             | 0         | 10       | 73      | 2     | 0       | 44     |
| sarcoma          | 20        | 3        | 5        | 34             | 2         | 101      | 69      | 3     | 0       | 63     |

(b) CANCER_THERAPEUTIC_PROCEDURE

| Lexical Unit      | Certainty | DateTime | Polarity | Agent | Complication | Extent | Location | Patient | Result | Status |
|-------------------|-----------|----------|----------|-------|--------------|--------|----------|---------|--------|--------|
| colectomy         | 7         | 7        | 4        | 4     | 197          | 66     | 1        | 194     |        |        |
| hysterectomy      | 21        | 14       | 13       | 1     | 9            | 53     | 40       | 183     | 1      | 237    |
| lymphadenectomy   | 3         | 7        | 2        | 0     | 3            | 48     | 20       | 0       | 38     |        |
| mastectomy        | 15        | 15       | 5        | 2     | 7            | 191    | 188      | 223     | 16     | 306    |
| palliative        | 18        | 6        | 0        | 1     | 0            | 3      | 72       | 6       | 64     |        |
| pancreatectomy    | 1         | 2        | 0        | 0     | 3            | 15     | 25       | 8       | 24     |        |
| prostatectomy     | 9         | 12       | 5        | 0     | 34           | 89     | 65       | 109     | 6      | 208    |
| radiation         | 25        | 11       | 90       | 2     | 10           | 5      | 117      | 253     | 3      | 149    |
| whipple           | 3         | 5        | 1        | 0     | 4            | 0      | 2        | 27      | 2      | 41     |

(c) TUMOR_DESCRIPTION elements

| Lexical Unit | Certainty | DateTime | Polarity | Margin Status | Metastasis | Morphology | Patient | Quantity | Recurrence | Reces- | Reces- | Size | Size | Stage | Status |
|--------------|-----------|----------|----------|---------------|------------|------------|---------|-----------|-------------| Ability| Ability|      |      |       |--------|
| lesion       | 64        | 8        | 2        | 10           | 7          | 60         | 145     | 14       | 0           | 25    | 51     | 95   | 94   | 15    | 73     |
| mass         | 50        | 7        | 48       | 10           | 3          | 18         | 115     | 0        | 2           | 25    | 54     | 12   | 2    | 16    |        |
| tumor        | 77        | 6        | 37       | 42           | 5          | 18         | 246     | 2        | 11          | 96    | 34     | 27   | 15   | 73    |        |

Note: The table above shows the frequencies of frame elements in the corpus. The columns represent different elements of the frame and the rows show the corresponding data. The data includes the frequency of each element along with additional relevant details such as certainty, date-time, and status.
However, in this pilot project we limited ourselves to just the sentence-level scope for frame annotation, so determining better ways to handle this kind of data in future projects will be important.

On the other hand, our limitation to sentences provides a useful starting point for cross-institutional data sharing. The privacy concerns surrounding sharing of complete records largely goes away when individual sentences are manually stripped of their PHI and any potential linking information back to the original record. The ability to gather multiple institutions’ data, all organized according to the same frame semantic schema, into a single FrameNet would be highly valuable to the clinical NLP community. These frames could then be mapped to existing structured clinical data standards, such as FHIR and OHDSI.

The one notable exception to sentence-based annotation, and something we would strongly consider changing in a future such project, is the use of sentences at the frame identification stage. While individual frame elements can easily be annotated at the sentence level, the word sense disambiguation task of determining whether a phrase invokes a particular frame is sometimes difficult. This is usually limited to cases where the sentence is in fact a fragment (e.g., a single item in a bulleted list), but this is a common phenomenon in EHR text and therefore worth taking careful consideration in how to handle. It may be sufficient to provide a human annotator with the extra-sentential context, but limit the machine to simply the sentence itself for classification. Alternatively, we could relax the notion of sentences in the case of fragments to provide more context. These compromise strategies could overcome one of the primary issues the annotators struggled with, while likely not having that significant an impact on the resource for training NLP systems.

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