Original Article

Application of Text Information Extraction System for Real-Time Cancer Case Identification in an Integrated Healthcare Organization

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Received: 28 July 2017 Accepted: 1 November 2017 Published: 14 December 2017

Abstract

Background: Surgical pathology reports (SPR) contain rich clinical diagnosis information. The text information extraction system (TIES) is an end-to-end application leveraging natural language processing technologies and focused on the processing of pathology and/or radiology reports. **Methods:** We deployed the TIES system and integrated SPRs into the TIES system on a daily basis at Kaiser Permanente Southern California. The breast cancer cases diagnosed in December 2013 from the Cancer Registry (CANREG) were used to validate the performance of the TIES system. The National Cancer Institute Metathesaurus (NCIM) concept terms and codes to describe breast cancer were identified through the Unified Medical Language System Terminology Service (UTS) application. The identified NCIM codes were used to search for the coded SPRs in the back-end datastore directly. The identified cases were then compared with the breast cancer patients pulled from CANREG. **Results:** A total of 437 breast cancer concept terms and 14 combinations of "breast" and "cancer" terms were identified from the UTS application. A total of 249 breast cancer cases diagnosed in December 2013 was pulled from CANREG. Out of these 249 cases, 241 were successfully identified by the TIES system from a total of 457 reports. The TIES system also identified an additional 277 cases that were not part of the validation sample. Out of the 277 cases, 11% were determined as highly likely to be cases after manual examinations, and 86% were in CANREG but were diagnosed in months other than December of 2013. **Conclusions:** The study demonstrated that the TIES system can effectively identify potential breast cancer cases in our care setting. Identified potential cases can be easily confirmed by reviewing the corresponding annotated reports through the front-end visualization interface. The TIES system is a great tool for identifying potential various cancer cases in a timely manner and on a regular basis in support of clinical research studies.

Keywords: Breast cancer, case identification, natural language processing, pathology reports, text information extraction system

Introduction

Recent innovations in computer technology have resulted in the exponential expansion of electronic information in various industries, including the rapid growth of electronic medical records (EMR) in health-care systems.[1,2] EMR systems capture and store patient health information in structured and unstructured formats electronically in place of paper charts. The resulting structured healthcare data have been extensively used to support clinical operations, decision-making, and biomedical research.[3] However, clinical narrative captured in clinician notes is the most natural and efficient way to capture communication between patients and clinicians, nuanced clinical details, and explanation for medical decision-making.[4] These free text notes capture substantial and rich information related to patients' health conditions; however, the unstructured format can make it difficult to use this information directly in patient care management and medical research without further information processing.[5] To resolve these challenges, over the past several decades, the field of clinical natural

Access this article online

Quick Response Code:

Website:
www.jpathinformatics.org

DOI:
10.4103/jpi.jpi_55_17

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How to cite this article: Xie F, Lee J, Munoz-Plaza CE, Hahn EE, Chen W. Application of text information extraction system for real-time cancer case identification in an integrated healthcare organization. J Pathol Inform 2017;8:48.

Available FREE in open access from: http://www.jpathinformatics.org/text.asp?2017/8/1/48/220747

language processing (NLP) has been focused on developing various methods for semantic processing and analysis of these clinical texts, and can thus be applied to a variety of clinical applications. In fact, a number of clinical NLP systems have been successfully developed and implemented in a myriad of medical domains with varying focuses.[6-11]

Surgical pathology reports (SPRs) contain valuable medical information embedded in the narrative free text, including information on the gross and microscopic description of tissue. SPRs are a vital research resource, in particular, for cancer-related research.[8,10,12-22] However, extracting information from SPR is generally time-consuming, laborious, costly, and requires manual processes and significant domain expertise. Alternatively, automating the application for information extraction (IE) provides a method for radically increasing the speed and scope with which this data can be accessed quickly.[4] A series of NLP methods and applications have been developed to retrieve this type of information from pathology reports.[8,10,12-15,17,18,20,21,23] For example, the text information extraction system (TIES) released by the University of Pittsburgh School of Medicine[8] was initiatively focused on extracting cancer information from SPR and later extended to radiology reports to support multi-center collaborative translational medical research through a federated network model.[21] Yip *et al*. developed an N-gram model for concept discovery from pathology reports.[18] The iterative online machine learning-based IE system (IDEAL-X) was introduced by Zheng *et al*.[10] to incrementally process pathology reports to improve the learning model. The medical knowledge analysis tool pipeline (MedKATp), a system established by the Open Health Natural Language Processing Consortium,[23] automatically extracts cancer-specific characteristics from unstructured clinical reports. The pathology extraction pipeline (PEP), built on MedKATp by University of California at Irvine, was also developed for extracting data elements and relationships from pathology reports.[20] Additional examples and the details of these NLP systems were documented in the review article by Burger *et al*.[12]

The TIES system leverages the Noble coder[22] and other well-known NLP methods and algorithms to process pathology and radiology reports.[8] One of the advantages of the TIES system is the capacity to share de-identified data and tissue through coded SPRs among a federated research network of institutions under bundle of restrict security regulations and compliances. As of 2015, this federated TIES system had been implemented in four institutions[21] and accumulated >5 million coded pathology reports and 25 million radiology reports between January 2003 and January 2017.[24] As an end-to-end application for processing both pathology and radiology reports, the TIES system is increasingly of interest to biomedical research communities and healthcare maintenance organizations to facilitate translational medical research and clinical operations.[25,26] The TIES system attracted our attention due to its potential for rapid cancer case ascertainment in support of research studies. Especially, it offers detailed technical documentation and real-time online support, as well as other needed functionalities (such as deidentification and restricted secured model). On the other hand, the other systems such as MedKATp, PEP, and IDEAL-X are capable of effectively processing SPRs, but they are more focused on IE rather than case identification. Additional detail documentation and appropriate technical support are important for successful implementation of these comprehensive systems.

A majority of retrospective cancer research studies rely on local or national cancer registries (CANREGs) for cohort identification. This presents a significant challenge, especially for prospective studies such as clinical trials, because CANREG data are often delayed at least several months due to the lengthy manual process involved in collecting and coding registry data. Methods to quickly identify newly diagnosed cancer patients are critically needed to expedite prospective studies. In this paper, we will demonstrate the implementation and application of the TIES system in a large integrated health maintenance organization, Kaiser Permanente Southern California (KPSC), and the performance of the TIES application for rapid case ascertainment. Furthermore, the limitations and the caveats of the system learned through our processes will be shared to shorten the learning curves of potential future users.

Methods

Implementation of the text information extraction system

Natural language processing software

The TIES system, an open-source system formerly known as caTIES, was originally developed for the Shared Pathology Informatics Network to enable translational research within a federated network of institutions.[8,21] TIES has evolved over time through many iterations with the latest available version being V5.4 at the time of our implementation.[24] The TIES system consists of clients, services, and datastores connected and implemented under the Globus grid service architectures with a restricted regulatory model for federated data sharing (relying on Institutional Review Board (IRB) protocols and honest brokers). The unique TIES components used in our study are described below.

1. Back-end Datastores: The private datastore is the recipient of data and stores the original free text reports with identifiers while the research datastore contains de-identified free text reports for the NLP Pipeline Services, which creates and stores annotations for each de-identified report
2. Data preparation services: The HL7 data importer loads the identified reports with HL7 specification format into the private datastore. The de-identifier recognizes and removes the identifiers protected by the Health Insurance Portability and Accountability Act. De-identification was achieved by using the built-in MGH scrubber. The concept coding service performs a sequence of NLP processing[8] to produce conceptual annotations and codes based on free-text reports. The indexing service creates an index for quick access to reports based on the text and conceptual codes being searched

3. Information retrieval services: The data access and integration service provide web service which interacts with data sources. The search service communicates the user entered search criteria to the TIES server
4. The restrict security enforcement layers guard the resources and authorize access based on roles of users.

The detailed components, functionalities and evaluations of the TIES system have been described in the published paper of the system[8] and the TIES official website.[24] The developers of the TIES system created a helpful user manual[27] and built a TIES community forum for technical discussions, support, user feedback, logs of issues and improvements.[28]

Deployment of the text information extraction system

Our initial implementation of TIES version 4.01 on a Window-based server started in 2008. Due to the rapidly increasing volumes of SPRs, we adopted version 5.4 in 2016, the latest version at the time of implementation. The new version was implemented on a Linux server. After a lengthy installation and configuration process described below, the implementation was a success. Although the TIES system has the capability for integration into a federated research network, our deployment was restricted to our local network without any outside communication activities.

Installation and configuration

The required hardware was prepared and software was downloaded according to the TIES system's installation guideline.[27] The components included: (1) configuration and installment of the Linux server and disk space allocation for data storage; (2) third-party software installed were JAVA, MySQL database server, Tomcat web server, Apache Ant, and NCI Metathesaurus; and (3) The zip executable files for TIES application, TIES Java Message Services (JMS) services for supporting parallel coding, and ActiveMQ required by the TIES JMS services.[24] All downloaded software packages described above were first unzipped and installed into the designed folders in the Linux server. The configuration files of each installed package were then examined and adjusted to the corresponding installation settings as required.

Launching text information extraction system application, MySQL server, text information extraction system java message services, and ActiveMQ

A configured and executed script was stored at the configuration or common bin folder for each service. These scripts were submitted through a command line to launch a series of processes that brought up the TIES application, the MYSQL server, TIES JMS services, and ActiveMQ. The logs of the launching processes and the execution statues were stored in the corresponding log files. It is critical to check the log files to make sure the launching processes are error-free. The launching process could also be performed through a job scheduler.

Launching text information extraction system client

The TIES application embeds the security model of the Globus Toolkit, which uses Grid Security Infrastructure based on public key encryptions and certificates for enabling secure authentication and communication over an open or intra network.[8] Therefore, the Globus security certificates should first be copied into the corresponding and designated folder in the user's computer, which is used to launch the TIES client. Because the TIES client is a JAVA application based on JAVA WebStart, the client machine is also required to install/update a comparable JAVA version (currently V1.7 or higher) before launching the TIES client. Using the administrator's account to login into the TIES system, we examined all administrative functionalities, such as study protocols, user access, and password. The account for an honest broker, researcher, and the preliminary user was each used to login into the TIES system to examine whether the functionalities for each role performed as designed.

Verifying the features for query construction and result visualizations

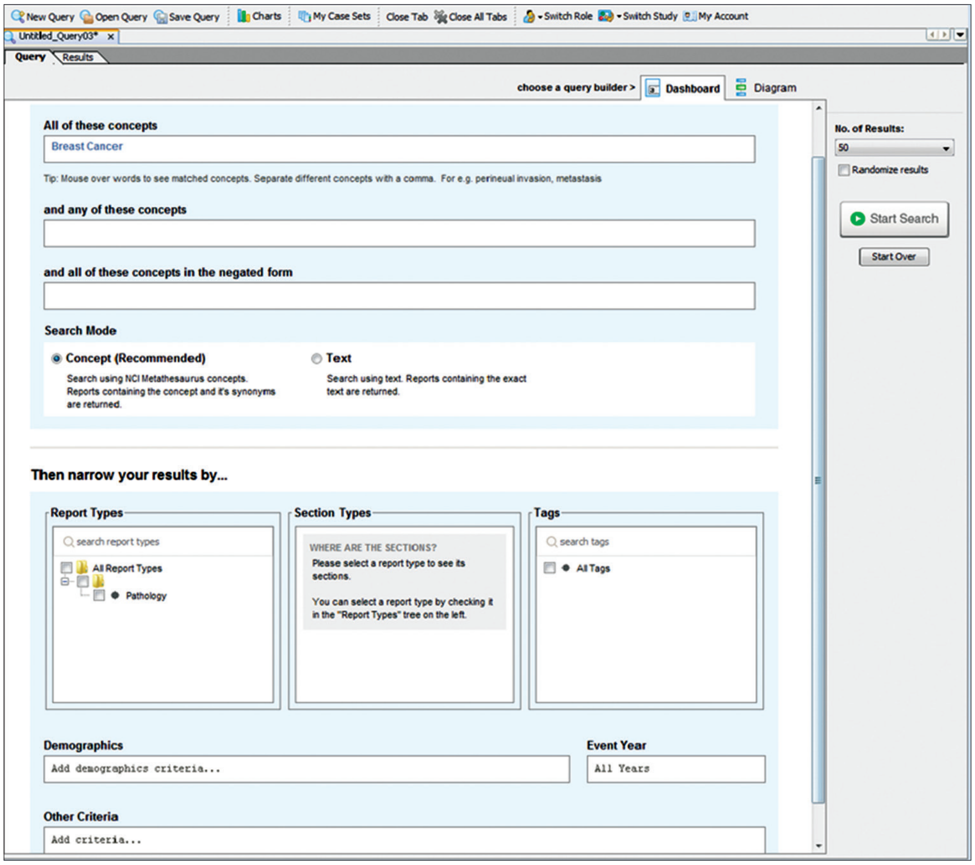
The TIES system provides two approaches for users to construct queries. The first approach is using a user-friendly interface to create queries based on concepts or texts (text strings), as shown in Figure 1. Users can type one or multiple keywords in the concept box, and the specific negated form in the negated box. The application shows up the corresponding concepts and National Cancer Institute Metathesaurus (NCIM) codes as the user types the searching terms. The results can be narrowed down by specifying pathology report section (s), demographics and event year. The second approach (referred to as the diagram method), demonstrated in Figure 2, provides more flexibility and can be used to formulate complex queries consisting of multiple events with a temporal relationship. For example, the query demonstrated in Figure 2 was to search for all patients who had breast cancer in 2013 and had a recurrent case within 1 year.

Search results are presented nicely with a list of individual reports to the left of the results screen, and a summary by demographics and year, utilizing either a bar or pie chart format on the right side [Figure 3]. When each report listed to the left is clicked, the annotated report opens with highlighted Diagnosis, Procedure, Organ, Negated Diagnosis, Negated concept, General concept, as shown in Figure 4 (a de-identified sample, with"xxxx" replaced the identifiable information). However, visualization of individual reports is limited to only two types of users as follows: Researcher and honest broker. Furthermore, researchers can only view the de-identified reports, in which all identified information is masked by the de-identification process in the TIES system.

Operation of the text information extraction system at Kaiser Permanente Southern California

Data source

The CoPathPlus system, an interactive and comprehensive system of Cerner Corp, manages accessioning and handles specimens at the Kaiser Permanente national anatomic pathology laboratories. In the past few years, the system has processed more than a half million specimens annually.



All of these concepts: Breast Cancer

Tip: Mouse over words to see matched concepts. Separate different concepts with a comma. For e.g. perineual invasion, metastasis

and any of these concepts:

and all of these concepts in the negated form:

Search Mode

◉ Concept (Recommended)
Search using NCI Metathesaurus concepts. Reports containing the concept and it's synonyms are returned.

○ Text
Search using text. Reports containing the exact text are returned.

WHERE ARE THE SECTIONS?
Please select a report type to see its sections.
You can select a report type by checking it in the "Report Types" tree on the left.

Demographics: Add demographics criteria...

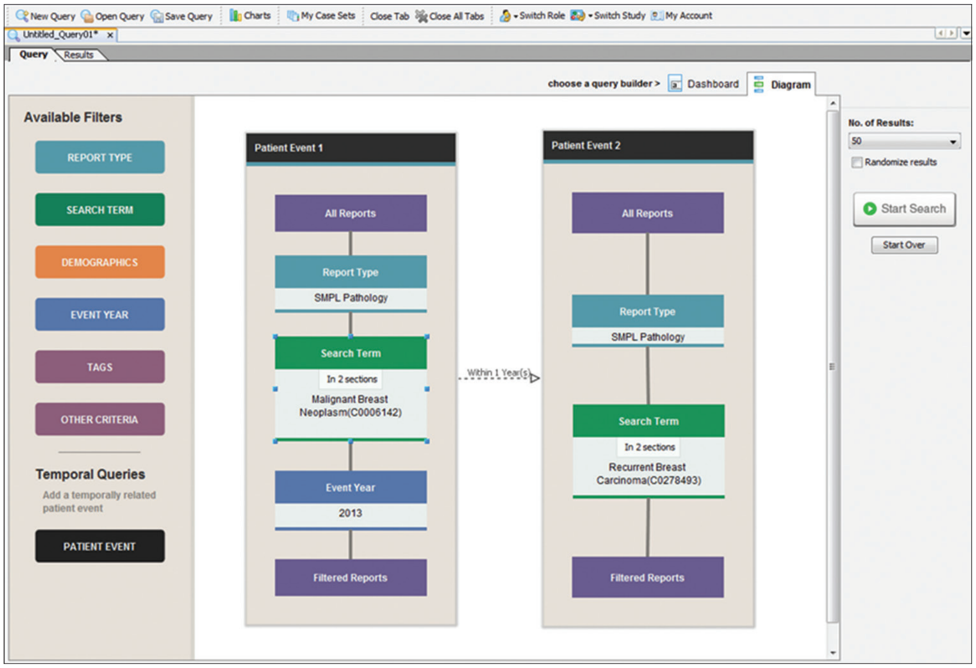
Event Year: All Years

Other Criteria: Add criteria...

No. of Results: 50

□ Randomize results

Figure 1: User interface for query construction in the text information extraction system application



No. of Results: 50

□ Randomize results

Figure 2: A demo of constructing a temporal query using a diagram method to search for patient who had breast cancer in 2013, and recurrent within one year

Pathology reports are generated for all processed surgical accessions. The final diagnosis, based on the pathologist assessment, is in the form of free text and is a mandated section of any report. All the pathology reports are loaded into the KPSC Research Data Warehouse (RDW) on a daily basis, and these reports are further loaded into the TIES system.

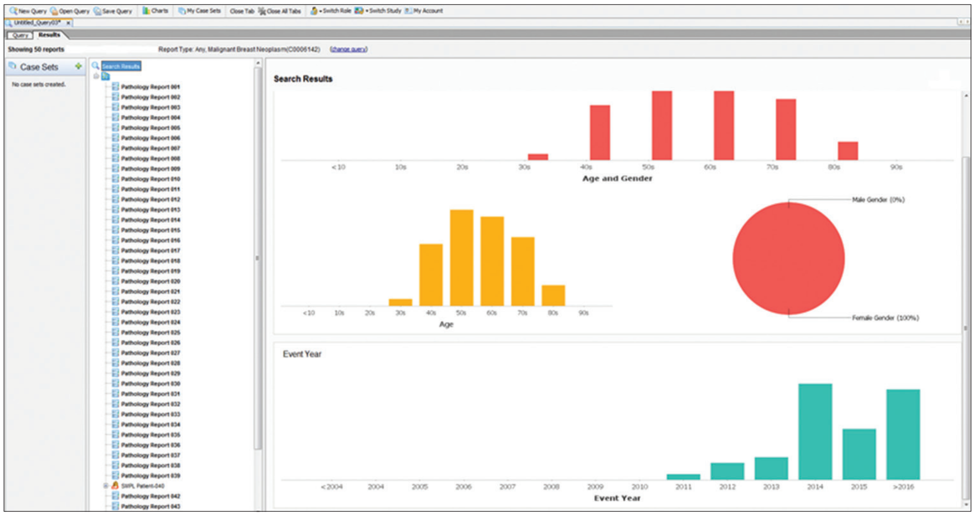
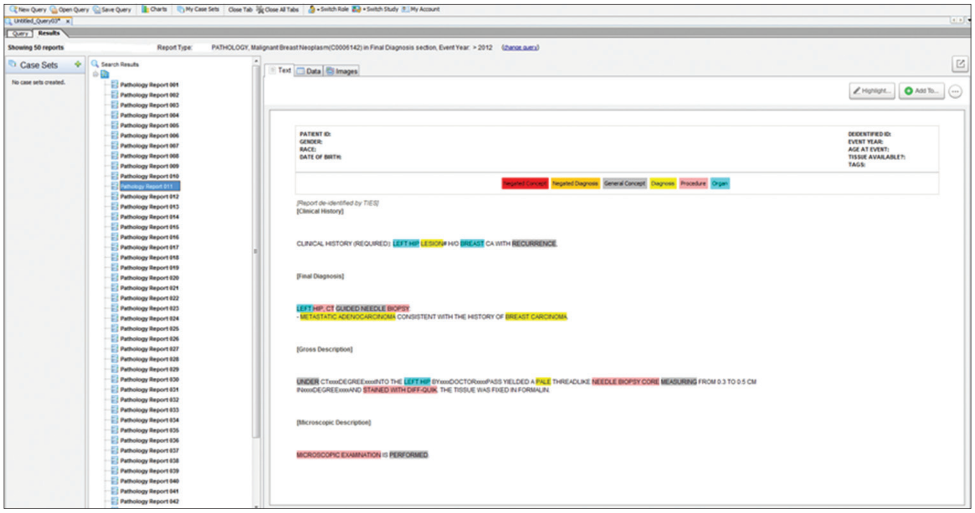


Figure 3: Searched results of example 50. Individual lists were on the left side, and statistical summaries were on right



Showing 50 reports

Report Type: PATHOLOGY, Malignant Breast Neoplasm(C0006142) in Final Diagnosis section, Event Year: > 2012 (change query)

PATIENT ID:
GENDER:
RACE:
DATE OF BIRTH:

DEIDENTIFIED ID:
EVENT YEAR:
AGE AT EVENT:
TISSUE AVAILABLE?:
TAGS:

[Report de-identified by TIES]
[Clinical History]

CLINICAL HISTORY (REQUIRED): LEFT HIP LESION# H/O BREAST CA WITH RECURRENCE.

[Final Diagnosis]

LEFT HIP, CT GUIDED NEEDLE BIOPSY
- METASTATIC ADENOCARCINOMA CONSISTENT WITH THE HISTORY OF BREAST CARCINOMA.

[Gross Description]

UNDER CTxxxxDEGREExxxxINTO THE LEFT HIP BYxxxxDOCTORxxxxPASS YIELDED A PALE THREADLIKE NEEDLE BIOPSY CORE MEASURING FROM 0.3 TO 0.5 CM INxxxxDEGREExxxxAND STAINED WITH DIFF-QUIK. THE TISSUE WAS FIXED IN FORMALIN.

[Microscopic Description]

MICROSCOPIC EXAMINATION IS PERFORMED.

Figure 4: A de-identified report with highlighted concept terms

Architecture of the Kaiser Permanente Southern California text information extraction system and data loading

The architecture of the TIES system within the KPSC research environment is illustrated in Figure 5. The column to the left demonstrates the flow of data extraction from CopathPlus, to RDW, and finally to the reports formatted in the HL7 specification. The middle part consists of the TIES application server, MySQL database server and web server, whereas the right side shows client requests through the TIES's web-based client interfaces or querying directly against the back-end datastores.

First, the historic pathology reports were retrieved and converted into HL7 specification format and transferred into the HL7 data folder in the TIES server where the HL7 importer automatically loaded these reports into the back-end datastores of the TIES system. Second, a process was set up to extract and load the pathology reports on a daily basis. To handle large daily volumes of pathology reports (~4000/day), the TIES JMS service was implemented to process the reports in parallel. Currently, the KPSC TIES system contains over 3 million pathology reports dating back to 2013. For security control, we followed our internal operational procedures and the TIES built-in security protocol to manage and monitor the authorized access and other activities through the web-based administrative interface.

Searching cases by using a flexible time window

Instead of allowing users to specify time windows on a daily basis (e.g., 1/2/2015–1/8/2015), the front-end window of installed TIES system only supports the search of time windows on an annual basis at this point. This limitation prevents the effective use of the TIES system for timely cancer identification. For example, if a user is interested in identifying breast cancer patients evidenced by pathology reports last week, he/she is not able to rely on the front-end application to do so. Therefore, we developed a query process to search against the TIES back-end datastore through a batch mode (referred to as the direct method) to support our study application described below.

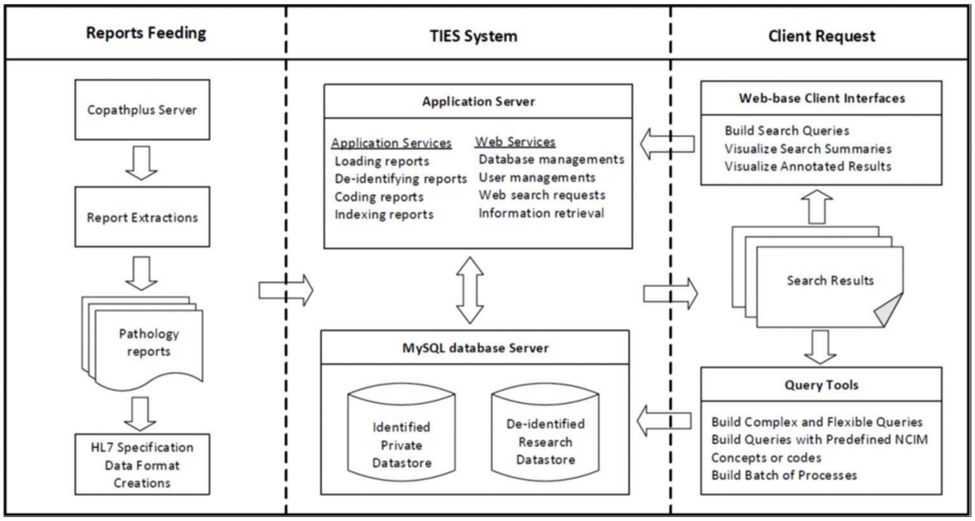


Figure 5: Architecture of the text information extraction system within the Kaiser Permanente Southern California research environment

Application of the text information extraction system

We conducted a validation study to examine the ability of the TIES system to identify potential breast cancer cases diagnosed in December of 2013, using the KPSC CANREG as the gold standard. This is part of a large-scale internal initiative to develop efficient processes to prospectively identify newly diagnosed cancer patients for enrolment into clinical studies. The methods and results described below are limited to the validation study only. The KPSC CANREG contains information on patients who were diagnosed or received at least part of their first course of treatment for cancer at KPSC hospitals for all reportable cancers. The diagnosis date in CANREG was based on multiple sources, including diagnostic mammograms; thus, it could be potentially different from the reported date of a pathology report. Therefore, the TIES searching time window was extended to the end of 2014 from December 2013. Because the TIES system is based on the NCIM, we first used the online the Unified Medical Language System terminology service (UTS) web application[29] to search all potential NCIM codes describing breast cancer and the terms described in the Buckley *et al*. study[19] to create the initial list of breast cancer terms and corresponding NCIM codes. This list was then reviewed and finalized by the study team. These selected NCIM terms and codes were then used to search against the TIES back-end datastores through the direct method described above. The search was limited to only the final diagnosis section, assuming such a section could be detected by the TIES system; otherwise, the search was applied to the entire pathology reports (the TIES system defines it as report section). Potential reasons for the failure of identifying final diagnosis sections are provided in the Discussion Section. After discovering that a majority of reports negative for breast cancer only contained negated cancer concepts (these are identified by the codes starting with the character "N"), only concepts that were not negated (the codes starting with the character "A") were included for query extractions.

The potential breast cancer cases identified by the TIES were manually examined and compared against the CANREG data. Error analysis was performed. The study was approved by KPSC IRB.

Results

A total of 437 specific NCIM terms and codes associated with breast cancer were identified through the UTS application. These specific terms contained the combination of the anatomical location (lobular or duct), malignant disorder (carcinoma or cancer), and severity (infiltrating or metastatic). The detailed list was included in Appendix 1. Some positive pathology reports were not identified through breast cancer concepts because breast and cancer were mentioned separately in different sentences or places. Therefore, an additional list was created, including 14 cancer concepts that were required to occur along with the breast concept [Appendix 2].

There were a total of 249 breast cancer cases diagnosed in December 2013 based on CANREG records. Of these, 241 cases (457 pathology reports) were found by using the preidentified concept codes listed in Appendices 1 and 2. Out of the eight false negative cases, negated terms were found in the pathology reports for 3 cases. Table 1 displays the number of the identified patients and the number of pathology reports by the concept codes used. A total of 13 preidentified concepts were found to have 10 or more reports while the "other terms" (all concepts with <10 reports combined) had 46 reports. Among the concepts for which 10 or more reports were found, the top three were "Ductal Breast Carcinoma *in situ*" (274 reports, and 171 patients), "Invasive Ductal Carcinoma, NOS" (197 reports and 124 patients), and "Carcinoma *in situ*" (156 reports and 119 patients), respectively. Nearly 56% of the diagnosis dates and pathology report dates were within 1 month, and the median of the difference of these two dates was within one and half months. The differences between the report sign-off dates and the diagnosis dates derived from the CANREG were shown in Table 2.

The TIES system also identified additional 277 potential cases with the report sign-off dates within December of

Table 1: Distribution of pathology reports identified by text information and extraction system with the predefined breast cancer concepts and codes for patients diagnosed with breast cancer in December, 2013 based on the cancer registry

NCIM code and term	Total number of pathology reports*	Total number of patients*
C0007124 - ductal breast carcinoma *in situ*	274	171
C1134719 - invasive ductal carcinoma, NOS	197	124
C0007099 - carcinoma *in situ*	156	119
C1176475 - ductal carcinoma	92	73
C1334274 - invasive carcinoma	74	70
C0279563 - lobular breast carcinoma *in situ*	70	53
C1384494 - metastatic carcinoma	46	43
C0678222 - breast carcinoma	40	34
C0853879 - invasive breast carcinoma	26	19
C0206692 - lobular breast carcinoma	24	20
C0442835 - atypical lobular breast hyperplasia	19	17
C0334384 - invasive ductal and lobular carcinoma *in situ*	14	13
C0006826 - malignant neoplasm	12	11
C2732747 - infiltrating carcinoma with ductal and lobular features	10	9
Other terms	46	37

*One patient may have multiple reports and one report may contain one or more NCIM codes. The total of unique report was 457, which belonged to 241 unique patients. NCIM: National Cancer Institute Metathesaurus, NOS: Not otherwise specified

Table 2: The difference between the pathology report signoff date and the breast cancer diagnosis date by the preidentified concepts and codes for patients diagnosed with breast cancer in the December, 2013 based on the cancer registry

NCIM code and term	Difference between pathology report signoff date-breast cancer diagnosis date in cancer registry		
	Total	Median	Range (minimum–maximum)
C0007124 - ductal breast carcinoma *in situ*	274	28.0	0-352
C1134719 - invasive ductal carcinoma, NOS	197	20.0	0-352
C0007099 - carcinoma *in situ*	156	28.5	0-245
C1176475 - ductal carcinoma	92	17.0	0-274
C1334274 - invasive carcinoma	74	32.5	0-245
C0279563 - lobular breast carcinoma *in situ*	70	28.0	0-245
C1384494 - metastatic carcinoma	46	35.5	0-274
C0678222 - breast carcinoma	40	3.0	0-81
C0853879 - invasive breast carcinoma	26	16.5	0-234
C0206692 - lobular breast carcinoma	24	22.5	0-213
C0442835 - atypical lobular breast hyperplasia	19	42.0	1-347
C0334384 - invasive ductal and lobular carcinoma *in situ*	14	16.5	0-234
C0006826 - malignant neoplasm	12	44.5	0-351
C2732747 - infiltrating carcinoma with ductal and lobular features	10	17.5	0-41
Other terms	46	24.0	0-121

NCIM: National Cancer Institute Metathesaurus, NOS: Not otherwise specified

2013 for whom the corresponding records were not found in the subset of breast cancer patients diagnosed in December of 2013 based on the CANREG. Table 3 shows the number of reports, as well the number of patients which fall under this category. Further research revealed that 84.8% (235) of these patients were found in the CANREG with diagnosis dates between January and November of 2013 and 1.4% (4) were found in the CANREG with diagnosis dates in 2012. Nearly 13.8% (38) of these patients were not found in the CANREG in 2012 or 2013. After manually examining the detail pathology reports, we concluded that 31 cases were highly likely to be identified by the concepts "Atypical Lobular Breast Hyperplasia," "Ductal Breast Carcinoma *in situ*," "Invasive Ductal Carcinoma, NOS." Only seven were misclassified (false positive) due to the failure of recognizing historical or negated cases.

Due to the positive findings reported above, the reported algorithm was implemented in an ongoing research study to prospectively identify newly diagnosed cancer patients for recruitment.

Discussions

The TIES system is an end-to-end clinical medical NLP application which can be used to support single or multiple institutional collaborative cancer research. It has evolved over time, resulting in numerous versions since it was introduced a decade ago. The system has garnered particular attention from the NLP cancer-focused research community since the publication of the caTIES system (its previous version) in 2010[8] and the establishment of the TIES Cancer Research Network among four research institutions.[21]

Table 3: Distribution of pathology reports identified by text information and extraction system with the predefined breast cancer concepts and codes for pathologist signoff date within December, 2013 for whom the corresponding records were not found in the subset of breast cancer patients diagnosed in December of 2013 based on the cancer registry

NCIM code and term	Total of pathology reports*	Total of patients*
C0007124 - ductal breast carcinoma *in situ*	178	173
C1134719 - invasive ductal carcinoma, NOS	110	108
C0279563 - lobular breast carcinoma *in situ*	43	43
C0007099 - carcinoma *in situ*	37	37
C1334274 - invasive carcinoma	26	26
C0442835 - atypical lobular breast hyperplasia	25	25
C1384494 - metastatic carcinoma	18	18
C1176475 - ductal carcinoma	15	15
C0678222 - breast carcinoma	15	15
C0206692 - lobular breast carcinoma	12	12
C0278488 - Stage IV breast cancer	10	10
C0853879 - invasive breast carcinoma	10	10
Other terms	32	32

*One patient may have multiple reports and one report may contain one or more NCIM codes. The total of unique report was 287, which belonged to 277 unique patients. NCIM: National Cancer Institute Metathesaurus, NOS: Not otherwise specified

Validation using with patients diagnosed in December 2013 extracted from the CANREG demonstrated that the TIES system has the capability to identify 96.8% (241 of 249) of breast cancer cases. Of the eight false negative cases, one case lacked any pathology report. The misclassification of the remaining seven false negative cases was due to the following reasons: (1) The pathology reports lacked any of the study's preidentified breast cancer concepts (n = 1). (2) The pathology reports contained the concepts being searched; however, they were either negated or appeared in the other report sections such as (addendum or gross description) instead of the final diagnosis (n = 6). The TIES system also identified additional potential breast cancer cases by searching pathology reports within December 2013. However, a majority of these cases (86%) were diagnosed in 2012 or 2013. The KPSC CANREG was based on multiple sources including diagnostic mammograms, biopsy pathology reports, etc. Therefore, there was a potential time lag between the diagnosed date and biopsy reporting date, which revealed that the diagnosis date could be the earlier date, while the biopsy date was the later confirmed date. However, the median of the date difference was within one and half months.

The developers of the TIES system provide a useful web-based online forum for knowledge sharing and issue discussion, as well as system support for a limited time.[28] However, the implementation or migration of the TIES system will continue to face challenges without a better understanding of the fundamental mechanism and framework of the system. First, trouble-shooting the errors requires a thorough understanding of the working mechanism, process flow and corresponding computer and NLP technologies. Second, the TIES default coder pipeline only runs in a single process. Thus, the performance is reasonable for small data volume but could be deteriorated as the data volume increases significantly. At KPSC, when we loaded the historic data into the TIES system, the coding process was relatively sluggish. After checking available information in the TIES online support, we realized that the TIES JMS component (optional component not included in the single download package) could be downloaded to speed up the coding process. Third, although the TIES system is an open source tool, it remains difficult to customize the design and improve the system without a deep understanding of the system and advanced technical expertise. Fourth, as the TIES system stands today, it lacks the proper components for disaster and error recovery. One error could potentially result in a full system failure, requiring a complete rebuild. In addition, although we noted that the TIES web application session can be timed out automatically after a certain period without activities, the front-end web interface lacks a user signoff/logout button. Given these identified challenges, we recommend that new versions focus on developing solutions to address these potential issues.

The study identified several limitations that could be considered for future enhancement. First, the search time window can only be specified annually. However, in real life, a more flexible time window is required. For example, if a user intends to identify cancer patients real-time using the system, he/she will need a narrower time window (e.g., month, week, or day). Second, the de-identified pipeline incorrectly de-identified some words or terms. For example, we noted that the word "mass" was constantly de-identified and resulted in an erroneous report. Third, when the TIES system codes the pathology report, a small percentage of reports erroneously combined all sections into a single "report section" rather than keeping the specific sections, such as "Clinical history," "Final diagnosis," "Gross description," etc. In this instance, the TIES system searched the entire context of the report and was unable to limit to the truly "Final diagnosis" section. Such a misclassification could result in either false negative cases or false positive cases when a user searches with a specific section in a pathology report. As a result, three historical cases identified from the actual "Clinical history" section were not identified as historic cases and therefore misclassified as current potential cases. This type of misclassification could be avoided by using the section detection functionality provided by the TIES to properly configure sections with new section headers. Fourth, it seems the TIES engine is unable to accurately exclude the historic cases when the history term and breast cancer concept term are located in different sentences. For example, the system failed to recognize the historical nature when "History of" appeared in the first sentence, and "breast carcinoma" appeared in the following sentence. Finally, there were cases in which the negation should be applied to two or more conditions while the TIES system can only negate the condition close to the negation term. For example, the negation term "negative for" in the description "negative for dysplasia and malignancy" should be negated for the conditions of "dysplasia" and "malignancy". However, the TIES system only highlighted "dysplasia" as negative diagnosis condition. Despite these limitations, our study demonstrated that the TIES system offers a robust and precise breast cancer case identification. In addition, the TIES system has the great potential to be easily applied to search for other cancer types, either single or multiple, with minimal development work.

Conclusions

We have successfully implemented the TIES system to import and process pathology reports on a daily basis. The validated results demonstrated that the TIES system can effectively identify the potential breast cancer cases within our care setting. All identified potential cases can be easily confirmed by reviewing the corresponding annotated reports through the front-end visualization interface. The TIES system is a useful NLP tool to identify cancer cases in a timely and efficient manner to support research studies and operational care management.

Acknowledgment

We would like to thank Philip Morales for the installation of the Linux server and the TIES system.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Appendices

Appendix 1: The breast cancer term lists and National Cancer Institute Metathesaurus codes identified by the Unified Medical Language System Terminology Service Metathesaurus browser web application

Term	Code
Malignant breast neoplasm	C0006142
Female breast carcinoma	C0007104
Ductal breast carcinoma *in situ*	C0007124
Malignant neoplasm of nipple and areola of female breast	C0024621
Paget disease of the breast	C0030185
Malignant neoplasm of central part of female breast	C0153549
Malignant neoplasm of upper-inner quadrant of female breast	C0153550
Malignant neoplasm of lower-inner quadrant of female breast	C0153551
Malignant neoplasm of upper-outer quadrant of female breast	C0153552
Malignant neoplasm of lower-outer quadrant of female breast	C0153553
Malignant neoplasm of axillary tail of female breast	C0153554
Malignant neoplasm of other specified sites of female breast	C0153555
Malignant neoplasm of nipple and areola of male breast	C0153558
Malignant neoplasm of other and unspecified sites of male breast	C0153559
Stage 0 breast cancer	C0154084
Lobular breast carcinoma	C0206692
Malignant neoplasm of female breast	C0235653
Male breast carcinoma	C0238033
Malignant neoplasm of male breast	C0242787
Stage I breast cancer AJCC v6	C0278485
Stage II breast cancer	C0278486
Stage III breast cancer AJCC v6	C0278487
Stage IV breast cancer	C0278488
Stage IIIA breast cancer	C0278489
Recurrent breast carcinoma	C0278493
Stage IIIB breast cancer	C0278513
Inflammatory breast carcinoma	C0278601
Invasive ductal breast carcinoma with predominant intraductal component	C0279556
Lobular breast carcinoma *in situ*	C0279563
Invasive lobular breast carcinoma with predominant *in situ* component	C0279564
Invasive lobular breast carcinoma	C0279565
Paget disease and intraductal carcinoma of the breast	C0279566
Paget disease of the breast with invasive ductal carcinoma	C0279567
Cellular diagnosis, breast cancer	C0279855
Bilateral breast carcinoma	C0281267
Secretory breast carcinoma	C0334371
Intraductal papillary breast carcinoma	C0334372
Intraductal papillary adenocarcinoma with invasion	C0334373
Intracystic papillary breast carcinoma	C0334376
Ductal breast carcinoma *in situ* and lobular carcinoma *in situ*	C0334383
Invasive ductal and lobular carcinoma *in situ*	C0334384
Scirrhous breast carcinoma	C0346151
Cancer en cuirasse	C0346152
Hereditary breast carcinoma	C0346153
Malignant breast phyllodes tumor	C0346154
Primary malignant neoplasm of skin of breast	C0346742
Breast melanoma	C0346787
Primary malignant neoplasm of nipple of male breast	C0346857
Primary malignant neoplasm of areola of male breast	C0346858
Malignant neoplasm of ectopic site of male breast	C0346860
Primary malignant neoplasm of nipple of female breast	C0346861
Primary malignant neoplasm of areola of female breast	C0346862
Malignant neoplasm of ectopic site of female breast	C0346865
Secondary malignant neoplasm of skin of breast	C0346986
Metastatic malignant neoplasm in the breast	C0346993
Carcinoma *in situ* of skin of breast	C0347152
Other carcinoma *in situ* of breast	C0348409
Malignant neoplasm, overlapping lesion of breast	C0348912
Breast sarcoma	C0349667
Breast lymphoma	C0349669
Atypical lobular breast hyperplasia	C0442835
Malignant neoplasm: Nipple and areola	C0496806
Malignant neoplasm of central portion of breast	C0496807
Malignant neoplasm of breast upper inner quadrant	C0496808
Malignant neoplasm of breast lower inner quadrant	C0496809
Malignant neoplasm of breast upper outer quadrant	C0496810
Malignant neoplasm of breast lower outer quadrant	C0496811
Malignant neoplasm of axillary tail of breast	C0496812
Carcinoma of axillary tail of breast	C0559063
Metastasis to breast of unknown primary	C0563510
Carcinoma of breast - upper, inner quadrant	C0564706
Carcinoma of breast - lower, inner quadrant	C0564707
Carcinoma of breast - upper, outer quadrant	C0564708
Carcinoma breast - lower, outer quadrant	C0564709
Breast carcinoma	C0678222
Malignant melanoma of skin of breast	C0684503
Carcinoma *in situ* of female breast	C0686288
Carcinoma *in situ* of nipple of female breast	C0686292
Secondary malignant neoplasm of nipple of female breast	C0686293
Carcinoma *in situ* of areola of female breast	C0686296
Secondary malignant neoplasm of areola of female breast	C0686297
Carcinoma *in situ* of central portion of female breast	C0686300
Secondary malignant neoplasm of central portion of female breast	C0686301
Carcinoma *in situ* of upper inner quadrant of female breast	C0686304

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Appendix 1: Contd...

Term	Code
Secondary malignant neoplasm of upper inner quadrant of female breast	C0686305
Carcinoma *in situ* of lower inner quadrant of female breast	C0686308
Secondary malignant neoplasm of lower inner quadrant of female breast	C0686309
Carcinoma *in situ* of upper outer quadrant of female breast	C0686312
Secondary malignant neoplasm of upper outer quadrant of female breast	C0686313
Carcinoma *in situ* of lower outer quadrant of female breast	C0686316
Secondary malignant neoplasm of lower outer quadrant of female breast	C0686317
Carcinoma *in situ* of axillary tail of female breast	C0686320
Secondary malignant neoplasm of axillary tail of female breast	C0686321
Carcinoma *in situ* of ectopic female breast tissue	C0686324
Primary malignant neoplasm of ectopic female breast tissue	C0686325
Secondary malignant neoplasm of ectopic female breast tissue	C0686326
Carcinoma *in situ* of male breast	C0686328
Secondary malignant neoplasm of male breast	C0686329
Carcinoma *in situ* of nipple of male breast	C0686332
Secondary malignant neoplasm of nipple of male breast	C0686333
Carcinoma *in situ* of areola of male breast	C0686336
Secondary malignant neoplasm of areola of male breast	C0686337
Carcinoma *in situ* of ectopic male breast tissue	C0686340
Primary malignant neoplasm of ectopic male breast tissue	C0686341
Secondary malignant neoplasm of ectopic male breast tissue	C0686342
Invasive breast carcinoma	C0853879
Recurrent inflammatory breast carcinoma	C0853968
Stage IIIB inflammatory breast carcinoma	C0853971
Stage IV inflammatory breast carcinoma	C0853972
Breast cancer aggravated	C0856130
Breast lump (malignant)	C0857005
Slow growing lung and soft tissue metastases from cancer breast	C0857220
Breast adenocarcinoma	C0858252
Malignant nipple neoplasm	C0859086
Colloidal breast carcinoma	C0860579
Medullary breast carcinoma	C0860580
Mucinous breast cancer	C0860581
Lobular neoplasia	C0861352
Breast adenocarcinoma recurrent	C0861355
Colloidal breast carcinoma recurrent	C0861357
Lobular carcinoma recurrent	C0861358
Medullary carcinoma of breast recurrent	C0861359
Mucinous breast cancer recurrent	C0861360
Mucinous ductal breast carcinoma recurrent	C0861361
Breast adenocarcinoma Stage I	C0861362

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Appendix 1: Contd...

Term	Code
Colloidal breast carcinoma Stage I	C0861364
Lobular breast carcinoma Stage I	C0861366
Lobular carcinoma Stage I	C0861367
Medullary carcinoma of breast Stage I	C0861368
Mucinous breast cancer Stage I	C0861369
Mucinous ductal breast carcinoma Stage I	C0861370
Breast adenocarcinoma Stage II	C0861371
Colloidal breast carcinoma Stage II	C0861373
Ductal breast carcinoma Stage II	C0861374
Lobular breast carcinoma Stage II	C0861375
Lobular carcinoma Stage II	C0861376
Medullary carcinoma of breast Stage II	C0861377
Mucinous breast cancer Stage II	C0861378
Mucinous ductal breast carcinoma Stage II	C0861379
Colloidal breast carcinoma Stage III	C0861382
Ductal breast carcinoma Stage III	C0861383
Lobular breast carcinoma Stage III	C0861384
Lobular carcinoma Stage III	C0861385
Medullary carcinoma of breast Stage III	C0861386
Mucinous breast cancer Stage III	C0861387
Mucinous ductal breast carcinoma Stage III	C0861388
Breast adenocarcinoma Stage IV	C0861389
Colloidal breast carcinoma Stage IV	C0861391
Ductal breast carcinoma Stage IV	C0861392
Lobular breast carcinoma Stage IV	C0861393
Lobular carcinoma Stage IV	C0861394
Medullary carcinoma of breast Stage IV	C0861395
Mucinous breast cancer Stage IV	C0861396
Mucinous ductal breast carcinoma Stage IV	C0861397
Breast carcinoma metastatic in the skin	C0935909
Male malignant nipple neoplasm	C0948587
Female malignant nipple neoplasm	C0948966
Contralateral breast cancer	C1096616
Squamous cell breast cancer female	C1112794
Invasive ductal carcinoma, NOS	C1134719
Overlapping malignant neoplasm of female breast	C1263794
Overlapping malignant neoplasm of male breast	C1263804
Carcinoma *in situ* of other site of breast	C1263808
Local recurrence of malignant tumor of breast	C1282471
Primary malignant neoplasm of breast lower outer quadrant	C1298788
Primary malignant neoplasm of breast upper outer quadrant	C1298924
Primary malignant neoplasm of breast upper inner quadrant	C1298925
Primary malignant neoplasm of breast lower inner quadrant	C1298926
Primary malignant neoplasm of axillary tail of breast	C1299235
Secondary malignant neoplasm of axillary tail of breast	C1299236
Primary malignant neoplasm of breast	C1299258
Localized skin involvement by breast carcinoma	C1304482
Primary malignant neoplasm of female breast	C1304708
Primary malignant neoplasm of central portion of female breast	C1305893

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Appendix 1: Contd...

Term	Code
Primary malignant neoplasm of upper inner quadrant of female breast	C1306024
Primary malignant neoplasm of lower inner quadrant of female breast	C1306025
Primary malignant neoplasm of upper outer quadrant of female breast	C1306026
Primary malignant neoplasm of lower outer quadrant of female breast	C1306027
Primary malignant neoplasm of male breast	C1306469
Tubular breast carcinoma	C1328544
Tubular breast cancer Stage I	C1328545
Tubular breast cancer Stage III	C1328547
Tubular breast cancer Stage IV	C1328548
Tubular breast cancer metastatic	C1328549
Adenoid cystic breast carcinoma	C1332167
Apocrine breast carcinoma *in situ*	C1332315
Apocrine breast carcinoma	C1332316
Breast adenocarcinoma with squamous metaplasia	C1332613
Breast angiosarcoma	C1332614
Breast carcinoma metastatic in the bone	C1332623
Breast carcinoma metastatic in the brain	C1332624
Breast carcinoma metastatic in the liver	C1332625
Breast carcinoma metastatic in the lung	C1332626
Breast fibrosarcoma	C1332630
Breast leiomyosarcoma	C1332631
Breast liposarcoma	C1332632
Breast mucosa-associated lymphoid tissue lymphoma	C1332633
Breast rhabdomyosarcoma	C1332637
Breast small cell carcinoma	C1332638
Ductal breast carcinoma with squamous metaplasia	C1333319
Grade 1 invasive breast carcinoma	C1333832
Grade 2 invasive breast carcinoma	C1333838
Grade 3 invasive breast carcinoma	C1333843
Hereditary female breast carcinoma	C1333986
Hereditary male breast carcinoma	C1333988
High grade ductal breast carcinoma *in situ*	C1334002
High grade mucoepidermoid breast carcinoma	C1334006
Intermediate grade ductal breast carcinoma *in situ*	C1334206
Intraductal cribriform breast adenocarcinoma	C1334248
Intraductal micropapillary breast carcinoma	C1334249
Intraductal noncomedo breast adenocarcinoma	C1334250
Invasive apocrine breast carcinoma	C1334272
Invasive breast carcinoma by histologic grade	C1334273
Invasive cribriform breast carcinoma	C1334275
Invasive ductal and invasive lobular breast carcinoma	C1334276
Invasive ductal and lobular carcinoma	C1334277
Invasive papillary breast carcinoma	C1334280
Low grade ductal breast carcinoma *in situ*	C1334413
Low grade mucoepidermoid breast carcinoma	C1334417
Malignant breast adenomyoepithelioma	C1334564
Malignant breast eccrine spiradenoma	C1334565
Metaplastic breast carcinoma	C1334708
Metastatic signet ring cell breast carcinoma	C1334740
Metastatic squamous cell breast carcinoma	C1334743
Mucinous breast carcinoma	C1334807

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Appendix 1: Contd...

Term	Code
Mucoepidermoid breast carcinoma	C1334813
Nipple carcinoma	C1334966
Nipple duct carcinoma	C1334967
Breast extraskeletal osteosarcoma	C1335149
Non-Hodgkin breast lymphoma	C1335489
Breast T-cell Non-Hodgkin lymphoma	C1335493
Signet ring cell breast carcinoma	C1335964
Solid papillary breast carcinoma	C1336027
Sporadic breast carcinoma	C1336076
Squamous cell breast carcinoma	C1336079
Squamous cell carcinoma *in situ* of the nipple	C1336080
Stage IIa breast cancer	C1336156
Stage IIb breast cancer	C1336178
Tubular breast cancer Stage II	C1504470
Adenosquamous breast carcinoma	C1510796
Breast adenocarcinoma with spindle cell metaplasia	C1511281
Breast burkitt lymphoma	C1511286
Breast carcinoma with choriocarcinomatous features	C1511302
Breast carcinoma with melanotic features	C1511303
Breast carcinoma with osteoclastic giant cells	C1511304
Breast columnar cell mucinous carcinoma	C1511305
Breast diffuse large B-cell lymphoma	C1511306
Breast follicular lymphoma	C1511311
Breast large cell neuroendocrine carcinoma	C1511316
Breast mucinous cystadenocarcinoma	C1511318
Glycogen-rich, clear cell breast carcinoma	C1512224
Mixed epithelial/mesenchymal metaplastic breast carcinoma	C1513365
Pleomorphic breast carcinoma	C1514169
Postradiotherapy breast angiosarcoma	C1514246
Synchronous bilateral breast carcinoma	C1515107
Acinic cell breast carcinoma	C1515868
Invasive mixed breast carcinoma	C1517577
Lipid-rich breast carcinoma	C1517894
Low grade adenosquamous breast carcinoma	C1518013
Malignant breast myoepithelioma	C1518167
Oncocytic breast carcinoma	C1518574
Sebaceous breast carcinoma	C1519207
Squamous cell breast carcinoma, acantholytic variant	C1519485
Squamous cell breast carcinoma, large cell keratinizing variant	C1519486
Squamous cell breast carcinoma, spindle cell variant	C1519487
Ductal breast carcinoma	C1527349
Hormone receptor positive malignant neoplasm of breast	C1562029
Breast adenocarcinoma metastatic	C1697918
Paget disease of the nipple	C1704323
Breast carcinoma with chondroid metaplasia	C1707042
Paget disease of the breast without invasive carcinoma	C1709447
Unilateral breast carcinoma	C1710547
Breast carcinoma with osseous metaplasia	C1711312
Atypical medullary breast carcinoma	C1879758
Ductal breast carcinoma *in situ*, solid type	C1880424
Invasive lobular breast carcinoma, signet ring variant	C1883029

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Appendix 1: Contd...

Term	Code
Her2 positive breast carcinoma	C1960398
Stage I breast cancer	C2216695
Malignant neoplasm of breast staging	C2216702
Human epidermal growth factor 2 negative carcinoma of breast	C2316304
Metastatic ductal breast carcinoma	C2698203
Metastatic lobular breast carcinoma	C2698204
Microinvasive breast carcinoma	C2732473
Lobular carcinoma *in situ* with microinvasion	C2733298
Ductal carcinoma *in situ* with microinvasion and involving nipple skin	C2733413
Lobular neoplasia Type A	C2826777
Lobular neoplasia Type B	C2826778
Malignant neoplasm of nipple and areola, female	C2842076
Malignant neoplasm of nipple and areola, right female breast	C2842077
Malignant neoplasm of nipple and areola, left female breast	C2842078
Malignant neoplasm of nipple and areola, unspecified female breast	C2842079
Malignant neoplasm of nipple and areola, male	C2842080
Malignant neoplasm of nipple and areola, right male breast	C2842081
Malignant neoplasm of nipple and areola, left male breast	C2842082
Malignant neoplasm of nipple and areola, unspecified male breast	C2842083
Malignant neoplasm of central portion of right female breast	C2842084
Malignant neoplasm of central portion of left female breast	C2842085
Malignant neoplasm of central portion of unspecified female breast	C2842086
Malignant neoplasm of central portion of breast, male	C2842087
Malignant neoplasm of central portion of right male breast	C2842088
Malignant neoplasm of central portion of left male breast	C2842089
Malignant neoplasm of central portion of unspecified male breast	C2842090
Malignant neoplasm of upper-inner quadrant of right female breast	C2842091
Malignant neoplasm of upper-inner quadrant of left female breast	C2842092
Malignant neoplasm of upper-inner quadrant of unspecified female breast	C2842093
Malignant neoplasm of upper-inner quadrant of breast, male	C2842094
Malignant neoplasm of upper-inner quadrant of right male breast	C2842095
Malignant neoplasm of upper-inner quadrant of left male breast	C2842096
Malignant neoplasm of upper-inner quadrant of unspecified male breast	C2842097
Malignant neoplasm of lower-inner quadrant of right female breast	C2842098
Malignant neoplasm of lower-inner quadrant of left female breast	C2842099

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Appendix 1: Contd...

Term	Code
Malignant neoplasm of lower-inner quadrant of unspecified female breast	C2842100
Malignant neoplasm of lower-inner quadrant of breast, male	C2842101
Malignant neoplasm of lower-inner quadrant of right male breast	C2842102
Malignant neoplasm of lower-inner quadrant of left male breast	C2842103
Malignant neoplasm of lower-inner quadrant of unspecified male breast	C2842104
Malignant neoplasm of upper-outer quadrant of right female breast	C2842105
Malignant neoplasm of upper-outer quadrant of left female breast	C2842106
Malignant neoplasm of upper-outer quadrant of unspecified female breast	C2842107
Malignant neoplasm of upper-outer quadrant of breast, male	C2842108
Malignant neoplasm of upper-outer quadrant of right male breast	C2842109
Malignant neoplasm of upper-outer quadrant of left male breast	C2842110
Malignant neoplasm of upper-outer quadrant of unspecified male breast	C2842111
Malignant neoplasm of lower-outer quadrant of right female breast	C2842112
Malignant neoplasm of lower-outer quadrant of left female breast	C2842113
Malignant neoplasm of lower-outer quadrant of unspecified female breast	C2842114
Malignant neoplasm of lower-outer quadrant of breast, male	C2842115
Malignant neoplasm of lower-outer quadrant of right male breast	C2842116
Malignant neoplasm of lower-outer quadrant of left male breast	C2842117
Malignant neoplasm of lower-outer quadrant of unspecified male breast	C2842118
Malignant neoplasm of axillary tail of right female breast	C2842119
Malignant neoplasm of axillary tail of left female breast	C2842120
Malignant neoplasm of axillary tail of unspecified female breast	C2842121
Malignant neoplasm of axillary tail of breast, male	C2842122
Malignant neoplasm of axillary tail of right male breast	C2842123
Malignant neoplasm of axillary tail of left male breast	C2842124
Malignant neoplasm of axillary tail of unspecified male breast	C2842125
Malignant neoplasm of overlapping sites of breast, female	C2842126
Malignant neoplasm of overlapping sites of right female breast	C2842127
Malignant neoplasm of overlapping sites of left female breast	C2842128
Malignant neoplasm of overlapping sites of unspecified female breast	C2842129

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Appendix 1: Contd...

Term	Code
Malignant neoplasm of overlapping sites of breast, male	C2842130
Malignant neoplasm of overlapping sites of right male breast	C2842131
Malignant neoplasm of overlapping sites of left male breast	C2842132
Malignant neoplasm of overlapping sites of unspecified male breast	C2842133
Malignant neoplasm of breast of unspecified site	C2842134
Malignant neoplasm of breast of unspecified site, female	C2842135
Malignant neoplasm of unspecified site of right female breast	C2842136
Malignant neoplasm of unspecified site of left female breast	C2842137
Malignant neoplasm of unspecified site of unspecified female breast	C2842138
Malignant neoplasm of breast of unspecified site, male	C2842139
Malignant neoplasm of unspecified site of right male breast	C2842140
Malignant neoplasm of unspecified site of left male breast	C2842141
Malignant neoplasm of unspecified site of unspecified male breast	C2842142
Lobular carcinoma *in situ* of right breast	C2865371
Lobular carcinoma *in situ* of left breast	C2865372
Intraductal carcinoma *in situ* of right breast	C2865374
Intraductal carcinoma *in situ* of left breast	C2865375
Unspecified type of carcinoma *in situ* of right breast	C2865380
Unspecified type of carcinoma *in situ* of left breast	C2865381
Pleomorphic lobular carcinoma *in situ*	C2919327
Classic lobular carcinoma *in situ*	C2919427
Estrogen receptor positive breast cancer	C2938924
Lobular carcinoma *in situ* of unspecified breast	C2976799
Intraductal carcinoma *in situ* of unspecified breast	C2976800
Other specified type of carcinoma *in situ* of left breast	C2976801
Lobular breast carcinoma *in situ*	C2976802
Other specified type of carcinoma *in situ* of unspecified breast	C2976803
Other specified type of carcinoma *in situ* of right breast	C2976804
Unspecified type of carcinoma *in situ* of unspecified breast	C2976805
Stage IIIC breast cancer	C2980042
Breast carcinoma by AJCC v6 stage	C2983712
Breast carcinoma by AJCC v7 stage	C2984094
Multifocal breast carcinoma	C2986662
Multicentric breast carcinoma	C2986664
Early-stage breast carcinoma	C2986665
Stage III breast cancer	C3146271
Node-positive breast cancer	C3160887
Node-negative breast cancer	C3160889
Sarcoma of axillary tail of female breast	C3163806
Sarcoma lower inner quadrant of female breast	C3163865
Sarcoma of central portion of female breast	C3163866
Sarcoma of male breast	C3164299

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Appendix 1: Contd...

Term	Code
Sarcoma upper outer quadrant of female breast	C3164606
Sarcoma of female breast	C3164849
Sarcoma of upper inner quadrant of female breast	C3164883
Sarcoma of lower outer quadrant of female breast	C3165073
Infiltrating duct carcinoma of female breast	C3165106
Invasive lobular breast carcinoma, alveolar variant	C3273215
Invasive lobular breast carcinoma, pleomorphic variant	C3273216
Invasive lobular breast carcinoma, solid variant	C3273217
Invasive lobular breast carcinoma, tubulolobular variant	C3273218
Breast solid neuroendocrine carcinoma	C3273727
Contralateral breast carcinoma	C3274709
Advanced breast cancer	C3495917
Locally advanced breast cancer	C3495949
Triple-negative breast carcinoma	C3539878
Breast carcinoma by gene expression profile	C3642344
Luminal A breast carcinoma	C3642345
Luminal B breast carcinoma	C3642346
Basal-like breast carcinoma	C3642347
Normal breast-like subtype of breast carcinoma	C3642471
Papillary breast carcinoma	C3812899
Tubulolobular carcinoma	C3838879
Invasive micropapillary breast carcinoma	C3838947
Intraductal papilloma with ductal carcinoma *in situ*	C3839576
Solid papillary carcinoma *in situ*	C3839648
Childhood breast carcinoma	C3897071
Mixed lobular and ductal breast carcinoma	CL007210
Ductal breast carcinoma *in situ* and invasive lobular carcinoma	CL018755
Intraductal and lobular carcinoma	CL028597
Hormone receptor/growth factor receptor-negative breast cancer	CL412277
Hormone receptor/growth factor receptor-positive breast cancer	CL412278
Estrogen receptor-negative breast cancer	CL412279
Progesterone receptor-negative breast cancer	CL412281
progesterone receptor-positive breast cancer	CL412282
HER2-negative breast cancer	CL412283
Hormone-resistant breast cancer	CL412374
Stage IA breast cancer	CL413891
Stage IB breast cancer	CL413892
Invasive lobular breast carcinoma recurrent	CL446964
Mucinous breast carcinoma recurrent	CL446965
Premenopausal breast cancer	CL446988
Mixed ductal lobular breast carcinoma infiltrating	CL453394
Tubular breast cancer	CL497426
Primary malignant neoplasm of female right breast	CL499822
Intraductal carcinoma *in situ* of bilateral breasts	CL500272
Infiltrating duct carcinoma of left female breast	CL500273
Infiltrating duct carcinoma of right female breast	CL500274
Infiltrating duct carcinoma of bilateral female breasts	CL500275
Carcinoma of central portion of breast	CL500661
Mucinous carcinoma of breast	C1334807
Infiltrating ductal carcinoma of breast, Stage 1	C1827104

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Appendix 1: Contd...

Term	Code
infiltrating ductal and lobular carcinoma of breast	C2076522
Infiltrating ductal carcinoma of breast, Stage 3	C1827241
Infiltrating ductal carcinoma of breast, Stage 2	C1827300
Infiltrating ductal carcinoma of breast, Stage 4	C1828351

HER2: Human epidermal growth factor receptor 2, NOS: Not otherwise specified, AJCC: American joint committe on cancer

Appendix 2: The combination list of the terms and National Cancer Institute Metathesaurus codes of "breast" and "cancer"

Term 1	Code 1	Term 2	Code 2
Breast	C0006141	Malignant neoplasm	C0006826
Breast	C0006141	Carcinoma *in situ*	C0007099
Breast	C0006141	Ductal carcinoma	C1176475
Breast	C0006141	Metaplastic carcinoma	C1266089
Breast	C0006141	Invasive carcinoma	C1334274
Breast	C0006141	Mucinous adenocarcinoma	C0007130
Breast	C0006141	Ductal carcinoma *in situ*	C1302731
Breast	C0006141	Papillary carcinoma	C0007133
Breast	C0006141	Tubular adenocarcinoma	C0205645
Breast	C0006141	Medullary carcinoma, NOS	C0206693
Breast	C0006141	Cribriform carcinoma	C0205643
Breast	C0006141	Infiltrating carcinoma with ductal and lobular features	C2732747
Breast	C0006141	Metastatic carcinoma	C1384494

NOS: Not otherwise specified