MERJ: Medical Entity-Relation Extraction System for Japanese Clinical Texts

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Abstract Electronic medical records (EMRs) constitute an important resource not only for tracing single patient histories, but also for population studies with clinical and administrative purposes. Medical entity-relation extraction aims to identify named entities and extract relations between them from EMRs. While rich research focused on achieving English medical entity-relation extraction, there are few works that develop Japanese entity-relation extraction systems for EMRs. In this study, we present a pipeline system for Japanese medical entity recognization and relation extraction. We propose a novel medical entity and relation annotation scheme and build a Japanese dataset based on EMRs. The empirical results demonstrate that proposed approaches outperforms previous state-of-the-art entity-relation extraction method on the dataset. We apply the proposed method on real EMRs to transform free–text data into structured patient information. Further analysis of extracted results explores the impact of tumor size and location of early-stage HCC (Hepatocellular carcinoma) on its treatments to help medical decision support.

Key words Medical entity-relation extraction, electronic medical records, text mining, deep learning

1 Introduction

Currently, electronic medical records (EMRs) have been widely used in hospitals for tracing single patient histories. EMRs constitute a lot of information which is valuable for population research with clinical and administrative aims. Since EMRs contain massive free-text data, extracting valuable knowledge from these records is a challenging task. One task of information extraction from EMRs is medical entity-relation extraction. It aims to identify named entities and extract relations between them. This problem can be decomposed into two subtasks: named entity recognition (NER [1,2]) and relation extraction (RE [3,4]). For instance, the text in Figure 1 contains four entities and three relations.

Extracting entities and their relations from unstructured text is a basic problem in information extraction. However, this problem is still not well studied now. Early works [1,5,6] in entity-relation extraction take a pipeline approach. It first

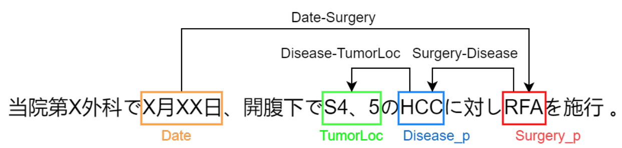

Figure 1: An example of medical entity-relation extraction. Considering privacy, we hide specific date and hospital information.

recognizes all entities in a sentence and then performs relation classification for each entity pair. Such an approach is susceptible to error propagation and exposure bias problems. To tackle these problems, subsequent works propose joint learning of entities and relations. One popular idea is to cast NER and RE as a table filling problem [7–13].

To handle overlapping relation triple cases, some recent works propose decomposition-based models [14–16]. These works regard relation extraction as the extraction of relation triple whose form is (subject, object, relation). Decomposition-based models first distinguish all the candidate subject entities that may be involved with target relations, then label corresponding object entities and relations for each extracted subject. PURE [17] recently re-examines the entity-relation extraction task and showed that with the help of deep pre-training models (e.g., BERT [18]), separating the entity and relation model could surpass existing joint models. They argued that it is crucial to fuse the entity information (both boundary and type) at the input layer of the relation model. PFN [19] is current state-of-the-art work. It developed a partition filter network to model two-way interaction between NER and RE.

In addition to the fact that methods of entity-relation extraction still have a lot of room for development, different languages prevent the direct application of existing methods to Japanese resources. The challenge is lacking Japanese corpora for training and testing of medical entity-relation extraction. Although there have been some works [20,21] release Japanese medical NER dataset, there is no public available medical RE dataset. Based on this reason, there are few works that develop Japanese entity-relation extraction systems for EMRs. As contemporaneous work, JaMIE [22] annotates a Japanese information extraction dataset, but it cannot be released due to the increase of anonymization level. In addition, because JaMIE system is developed based on the traditional pipeline method, the performance of the system relating to entity-relation extraction is limited.

In this study, due to lacking a Japanese medical entity-relation extraction dataset, we propose a novel entity and relation annotation scheme for exploring important concepts and relations that existed in Japanese clinical texts. We intend to explore how surgery decisions are impacted by features of the tumor, such as location or size of the tumor. Therefore, we pay more attention to the information related to tumor characteristics and treatments for tumors. In addition, for event factuality detection, which aims at the assessment of whether a clinical event occurred or not, we set a special attribution for concepts related to disease or surgery. Then, based on the proposed annotation scheme, we build a few-shot dataset for training and testing of medical entity-relation extraction.

In this paper, we present MERJ (**M**edical **E**ntity-**R**elation **E**xtraction System for **J**apanese Clinical Texts). We treat entity-relation extraction as several turns span extraction problem. The first turn span extraction is for extracting all entities in the text, which doesn't have a noticeable difference from the entity models in pipeline methods. We model relations as functions that map subjects to objects for relation extraction, instead of learning relation classifiers directly. The second span extraction is for extracting all candidate subjects that may be involved with target relations from entities. After extracting candidate subjects, subsequent steps extract corresponding object entities and relations for each extracted candidate subject. We achieve above ideas in our system. It consists of an entity tagging module, an entity-aware subject tagging module and an entity-aware subject-oriented object tagging module. Each module shares a BERT-based [18] encoder and a bidirectional LSTM to capture the sequential information. To encode Japanese characters in clinical texts, we adapt the character-based Japanese bert model as encoder for each module. Experiments on our dataset demonstrate the effectiveness of our method. It outperforms current the best entity-relation extraction model.

In addition, we utilize our system to research real medical problems. The liver is the second most common site of breast cancer metastasis. Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer. Radiofrequency ablation (RFA) and hepatectomy are main treatments for HCC. However, deciding which of RFA and hepatectomy for HCC patients is not simple. In this study, we explore the relation between the feature of liver tumors and their treatment.

The contributions of this paper can be summarized as follows.

- We present a novel annotation schema for medical entity-relation extraction for Japanese Clinical Texts. Based on it, we manually annotate a few-shot dataset to empirically analyze the performance of the system.
- We develop a medical entity-relation extraction system. This system includes entity taggers, subject taggers and entity-aware subject-oriented object taggers.
- We utilize our system to research real medical problems. We mainly explore how features of HCC impact its treatment.

2 Related Work

2.1 Entity-Relation Extraction

Entity-relation extraction is one of the essential tasks of information extraction. Early works [1, 5, 6] take this task in a pipelined manner. Usually, Pipeline methods ignore the relevance of entities and relations, and they suffer from error propagation and exposure bias problems.

To address these problems, a variety of joint extraction of entities and relations are proposed. SPTree [23] introduces an end-to-end approach that extracts entities and their relations using neural network models with shared parameters. Zhang et al. [9] proposes the table-filling approach, which provides an opportunity to incorporate more sophisticated features and algorithms into the model, such as search orders in decoding and global features.

To handle overlapping relation triple cases, a few recent studies proposed decomposition-based methods. There are some works [15, 16] propose cascade methods that first identify all possible subject entities in the input text and then identifies all possible relations and object entities for each subject entity.

PURE [17] showes that with a great method of fusing entity information to relation model, the pipeline method could surpass existing joint models. Their work makes us re-emphasize the multiple steps approach.

Currently, for entity-relation extraction, PFN [19] is current state-of-the-art work which belong to table filling methods. It additionally developed a partition filter network to model two-way interaction between NER and RE.

2.2 Japanese Medical Information Extraction

Most works that focus on Japanese Medical Information Extraction (IE) mainly research how to extract important entities from clinical texts. There are some works [20, 21] release Japanese medical NER dataset and present Japanese clinical IE shared tasks. MedEx/J [24] presents a Japanese medical IE tool that executes entity extraction and event classification simultaneously. Yada et al. [25] presents an annotation guideline aimed at covering medical documents of various types such as radiography interpretation reports and medical records. Their work focuses on general medical entities while our work specifically focuses on medical concepts related to liver tumors. In addition, JaMIE [22] develops a Japanese IE system with three components for recognizing medical entities, classifying entity modalities, and extracting relations. Because their system is developed based on the traditional pipeline method and does not model interaction build different tasks, the performance of the system relating to entity-relation extraction is limited.

3 Annotation and Dataset

In this section, we first define the annotation of medical entity types and relation types. Then we introduce the dataset we build manually which is used to evaluate the performance of our method and achieve data analysis.

3.1 Entity Annotation

In this study, we intend to explore how surgery decisions are impacted by features of liver tumors, such as location or size. Therefore, we pay more attention to the information related to liver tumor characteristics and their treatments. In addition, for event factuality detection, which aims at the assessment of whether a clinical event occurred or not, we set a special attribution for concepts related to disease or surgery. we define seven entity types for our objective: Date, Disease, Tumor Loc, Tumor Size, Surgery, Part, and Inspection. We additionally set certain modalities for Disease and Surgery. To achieve entity modality recognition, we simply perform NER regarding entities with different modalities as different entity types.

- Date: The date when disease was discovered or surgery was performed.
- Disease: Expressions related to diseases and symptoms. Considering its certainty, we set an attribute for this entity type. We use three level to describe whether the disease is confirmed to exist in the patient at the time of EMR writing: positive (Disease_p), suspicious (Disease_s), negative (Disease_n). Specifically, when the annotator confirm the patient had the disease, this disease is labeled as Disease_p. Instead, when the annotator confirm the patient didn't get the disease, it is labeled as Disease_n. When the annotator is not able to identify if the patient have the disease, it is labeled as Disease_s, such as "転移性肝癌" in "転移性肝癌が疑われたため、今回手術目的で入院となる".
- Tumor Loc: Expressions of the specific location of the liver tumor, such as "s2" and "s7".
- Tumor Size: Expressions describe the size of Tumor in detail, such as "10 mm" and "3 cm".
- Surgery: Expressions of surgery. Similar to the disease entity type, we also set an attribute to express its certainty. We use three level to describe whether the surgery is confirmed to perform at the time of EMR writing: positive (Surgery_p), suspicious (Surgery_s), negative (Surgery_n).
- Part: Expressions specify a body part where the disease occurred or the operation was performed.
- Inspection: Expressions specify a medical inspection or test.

3.2 Relation Annotation

In addition to extracting important medical-related concepts in the text, it is also very meaningful to mine the relationships between them. We define eight relation types for our objective: Date-Disease, Date-Surgery, Disease-Surgery, Inspection-Disease, Disease-Part, Disease-TumorLoc, Disease-TumorSize, Disease-Disease.

- Date-Disease: A relationship between the Disease and the date it was discovered.
- Date-Surgery: A relationship between the Surgery and the date it was performed.
- Surgery-Disease: A relationship between the Disease and its treatment surgery.
- Inspection-Disease: A relationship between the Disease and the inspection that discovered it.
- Disease-Part: A relationship between the Disease and the body part where it happened.
- Disease-TumorLoc: A relationship between the Tumor and specific location where it happened.
- Disease-TumorSize: A relationship between the Tumor and specific size of it.

Table 1: The statistics of the entity annotation.

Entity		#num
Date		152
Disease	positive	158
	suspicious	24
	negative	2
	total	184
Tumor Loc		33
Tumor Size		18
Surgery	positive	49
	suspicious	13
	negative	3
	total	65
Part		15
Inspection		59
TOTAL		526

Table 2: The statistics of the relation annotation.

Relation	#num
Date-Disease	114
Date-Surgery	45
Surgery-Disease	53
Inspection-Disease	56
Disease-Part	18
Disease-TumorLoc	35
Disease-TumorSize	21
Disease-Disease	19
TOTAL	361

- Disease-Disease: This is a relationship between the same disease or indicates the recurrence of the disease.

3.3 Dataset

Based on the medical in-hospital experience records (入院までの経歴) from January 2005 to March 2018 stored in electronic medical record system of University of Miyazaki Hopital, we annotate a medical entity-relation extraction dataset manually. We annotate 52 medical record documents include 190 samples. Table 1 shows the statistics of the entity annotation and table 2 shows the statistics of the relation annotation. A total of 160 annotated samples were used as the training set, with 30 samples used for testing.

Our research was approved by the Ethics Review Board of the University of Miyazaki and the Research Ethics Review Committee of the Tokyo Institute of Technology.

4 Methods

In this section, we first formally define the problem of end-to-end entity-relation extraction and then detail the architecture of our system.

4.1 Problem Formalization

The input of the problem is a sentence X consisting of n tokens $x_1, x_2, ..., x_n$ from EMRs. Medical entity-relation extraction aims to identify medical named entities and extract relations between them from the given sentence. Towards this goal, our framework decomposes the problem into three sub-tasks: entity extraction, subject extraction and subject-oriented object extraction. Combining the results of subject extraction and subject-oriented object extraction, we should be able to obtain predicted relations.

4.1.1 Named Entity Recognition

We formulate the named entity recognition task as a sequence labeling problem. As shown in Figure 3, we adopt the BIO tagging scheme [26]. Let E denote a set of predefined entity types and m denotes the number of entity types. However, since there are overlapping entities cases in our datasets, we can not assign $\{B\_e_j, I\_e_j, O\}$ tagging scheme as Lample et al. [27] since this tagging scheme is not able to handle these cases. Therefore, for each words x_i in the sentence and each entity type e_j, we tag them as $y_e(x_i, e_j) \in \{B, I, O\}$ (B: Beginning, I: Inside, O: Others).

4.1.2 Relation Extraction

We regard relation extraction as relation triple (subject, object, relation) extraction. The subject is the head entity of the relation, while the object is the tail entity of the relation. We model relations as functions that map subjects to objects, instead of learning relation classifiers directly. Therefore, we split relation triple extraction into two subtasks: subject extraction and subject-oriented object extraction.

We formulate the subject extraction task as word pair classification problems. For each word pair (x_i, x_j), we tag them as $y_s(x_i, x_j) \in \{0, 1\}$. When word x_i and word x_j are the start and end position of a subject in any relation triple, $y_s(x_i, x_j)$ will be set as 1, otherwise, it will be 0.

For subject-oriented object extraction, we formulate it as sequence labeling problems. We still adopt the BIO tagging scheme [26], similar to the named entity recognition task. We need perform object extraction for each subject extracted by the previous step. After selecting one candidate subject, we assign tags for each word in the sentence to identify the object arguments (start and end position) and relation type. Let R denote a set of predefined relation types. For each word x_i in the sentence and each relation type r_j, we tag them as $y_r(x_i, r_j) \in \{B, I, O\}$ (B: Beginning, I: Inside, O: Others).

4.2 Our Approach

As shown in Figure 2, our approach consists of entity taggers and entity-aware subject-oriented object taggers. We treat medical entity-relation extraction as several turns sequence labeling. The first turn sequence labeling is for extracting all entities in the text. For relation extraction, we model relations as functions that map subjects to objects.

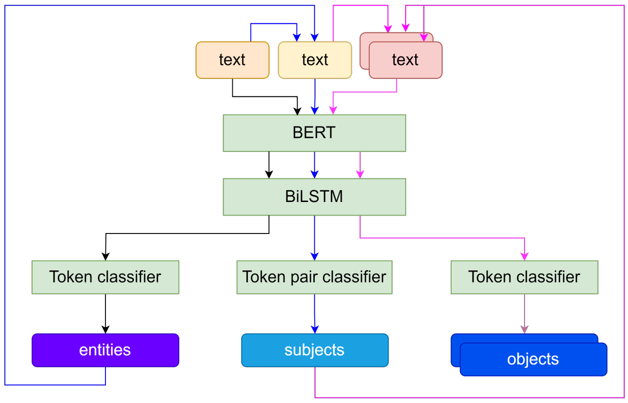

Figure 2: Overview of our models. Connectors of different color represent different steps. Black connectors represent entity extraction. Blue connectors represent subject extraction. Pink connectors represent objects extraction

We select candidate subjects from entities based on their entity type. After extracting entities and selecting candidate subjects, subsequent sequence labeling extracts corresponding object entities and relations for each extracted subject. Figure 3 shows an example of our framework.

4.2.1 Token Encoder

Given a sentence, we use a tokenizer to segment tokens and then feed tokens into the encoder to obtain token representation. For tokenizer, unlike English which mainly uses word level to segment tokens, we use character level as the most basic token. In our pipeline system, we adopt the Japanese pre-trained BERT as the encoder to retrieve token embeddings for each task tagger.

4.2.2 Entity Taggers

The entity taggers are designed to extract all entities in the input text. Firstly, we use a BERT-based model [18] to obtain word representation for each input token x_i. Then we use a bidirectional LSTM to capture the sequential information. Finally, we simply map word representations to the output space with fully connected layers as token classifiers.

4.2.3 Subject Taggers

The subject taggers are designed to extract all entities in the input text. It also includes a pre-trained BERT-based encoder and a bidirectional LSTM. In order to make subject taggers aware of the boundary of the given subject and entity type and boundary, we insert pre-defined text markers into the input text before and after the entities. To highlight the entity with type e_j, we define text markers as *[e_j_S]* and *[e_j_E]* for the start of the entity span and end of the entity span, then insert them before and after the entity span. For word pair (x_i, x_j), we concatenate their feature h_i and h_j, then feeding them into a linear layer to calculate the probability of that word x_i and word x_j are the start and end position of a candidate subject.

$$\hat{\mathbf{y}}_s(x_i, x_j) = \sigma(\mathbf{W}_s[\hat{\mathbf{h}}_i, \hat{\mathbf{h}}_j] + \mathbf{b}_{fc,j}) \qquad (1)$$

4.2.4 Object Taggers

As described above, entity-aware subject-oriented object taggers are designed to extract relations between given entities, and we formulate the relation extraction task as a sequence labeling problem. In order to make object taggers aware of the boundary of the given subject and entity type and boundary, we insert pre-defined text markers into the input text before and after the entities. Specifically, to highlight the subject, we define text markers as *[S:S]* and *[S:E]* for the start of the subject and end of the subject, then insert them before and after the subject span. Besides, by inserting pre-defined subject text markers, the model will not be confused by multiple potential subjects in the sentence.

After inserting text markers as special tokens into the input of models, for object taggers, we use the same sequence labeling model architecture as entity taggers. It also includes a pre-trained BERT-based encoder and a bidirectional LSTM. We finetune the BERT-based encoder to make embedding model to learn the representation of these special text markers. We map word representations to the output space with fully connected layers as token classifiers and calculate the probability of the labels of words for each relation types r_j with the softmax function:

$$\hat{\mathbf{y}}_r(x_i, r_j) = \mathrm{softmax}(\mathbf{W}_{fc,j}\hat{\mathbf{h}}_i + \mathbf{b}_{fc,j}) \qquad (2)$$

where $\mathbf{W}_{fc,j}$ and $\mathbf{b}_{fc,j}$ are the trainable parameters of the fully connected layer for relation types r_j.

For training the entity-aware subject-oriented object taggers, we only consider the gold entities $\mathcal{E}$ in the training set and use the gold entity labels as the input of the relation model.

5 Experiments

5.1 Evaluation Metrics

We evaluate our method by using standard micro Precision, Recall and F1-score. For entity extraction, we use a strict matching rule, which means the extracted entity is regarded as correct only if entity border and entity type are recognized correctly. For relation extraction, extracted relation is regraded correct only if two entities are regarded as correct under a strict matching rule and the predicted relation type is also correct.

5.2 Experimental Settings

We develop Japanese entity-relation extraction system based on the proposed entity-relation extraction method.

(注1)：https://huggingface.co/cl-tohoku/bert-base-japanese-char

Figure 3: An example of our framework. Given an input text, entity taggers extract all entities. Then we extract candidate subjects using subject taggers. For each candidate subject, entity-aware subject-oriented object taggers extract all objects related to the given subject. In this example, there are two candidate subjects in the text. We show the result of object taggers when we choose “XX 年 XX 月” as the given subject and we omit the process of choosing ”胆嚢摘出手術” as a given subject for object taggers because of space limits. The input of our subject taggers and object taggers are different text after insert markers (e.g., *Date_S* means start of date entity span, *S:E* means end of subject span).

Table 3: Experiment results (%) for evaluating methods on Japanese dataset.

Model	NER			RE		
	P	R	F1	P	R	F1
PFN [19]	73.61	79.10	76.26	**64.29**	51.43	57.14
MERJ	**73.97**	**80.60**	**77.14**	56.82	**71.43**	**63.29**

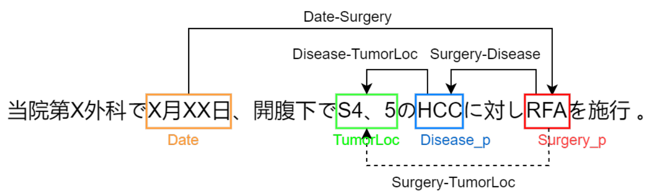

Figure 4: Example of reasoning relation.

For the entity module, subject module, and subject-oriented object module of our system, we adopted the pre-trained BERT base Japanese (character tokenization) model (注1) and finetuned it jointly with other parts of the model. We set the hidden state dimension of the encoder as 128. All of the parameters were optimized by Adam optimizer [28]. All experiments are conducted on one NVIDIA GeForce RTX 2080 Ti GPU.

We compare the Japanese medical entity-relation extraction performance of our methods with the current sota entity-relation extraction method PFN [19]. PFN is a table filling method. Its model consists of a partition filter encoder and two task units. The encoder obtains task-specific features by a model two-way interaction between tasks. Then the features are sent to task units as input for entity and relation extraction. As far as we know, PFN achieves the best performance on most general entity-relation extraction benchmarks. Table 3 shows main performance on Japanese medical entity-relation extraction dataset. We observe that our F1 scores outperform PFN by 1.75% for entity extraction and 4.76% for relation extraction. This proves the effectiveness of our methods.

5.3 Statistic Analysis

In this section, we leveraged our entity-relation extraction system to explore how features of liver tumors impact their surgery decisions, particularly, the choosing of radiofrequency ablation (RFA) or hepatectomy.

Hepatocellular carcinoma (HCC) ranks fifth in the global incidence of malignant tumors. For early-stage HCC, hepatectomy and RFA are the main treatments. However, it is relatively difficult for doctors to decide to take hepatectomy or RFA. Therefore, we selected two important features of HCC: tumor size and tumor location. We researched the relation between these two tumor features with surgery decisions.

Firstly, from the medical in-hospital experience records (入院までの経歴) from January 2005 to March 2018 stored in electronic medical record system of University of Miyazaki Hospital, we extracted In-hospital experiences who record patients took RFA or Hepatectomy. We performed our trained system on these 570 records including 191 RFA patient records and 379 hepatectomy patient records. Then, we collected relation triplets whose relation type belongs to Disease-TumorLoc, Disease-TumorSize, or Disease-Surgery. We filtered part of triplets whose disease entity or surgery entity doesn't have positive attribution. Based on Surgery-Disease relation triplets and Disease-TumorLoc relation triplets, we obtain a reasoning relation: Surgery-TumorLoc relation triplets. Figure 4 shows an example of Surgery-TumorLoc relation. Because "RFA" and "HCC" have Surgery-Disease relation while "HCC" and "S4、5" have Disease-TumorLoc relation, thus we builded Surgery-TumorSize relation for "RFA" and "S4、5". In the same way, we obtain Surgery-TumorSize relation triplets based on Surgery-Disease relation triplets and Disease-TumorSize relation triplets.

After obtaining Surgery-TumorLoc relation triplets and Surgery-TumorSize relation triplets, we performed data analysis on these triplets.

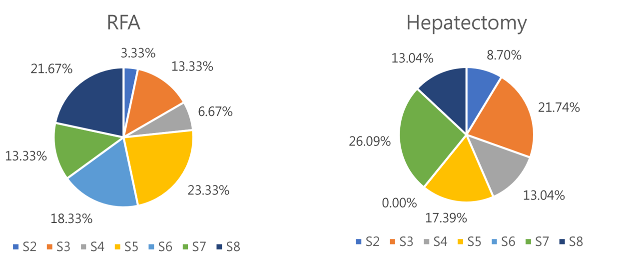

Figure 5: Statistic of Surgery-TumorLoc relation triplets.

Liver segmentation is usually described according to the Couinaud classification, which divides the liver into eight functionally independent segments (S1–S8) based on third-order portal vein distribution. Figure 5 shows the ratio of different segments where tumors appear are treated by RFA and Hepatectomy. We observe that, in our collection data, HCCs arising at the s6 location were all performed by RFA surgery. Additionally, for hepatectomy, it is more common to treat HCC at the s3 and s7 positions.

Table 4: Statistic of Surgery-TumorSize relation triplets

Surgery	Average Tumor Size	Standard Deviation
RFA	14.3 mm	6.28 mm
Hepatectomy	25.2 mm	9.41 mm

As for the relation between tumor size and surgery decision, we calculated the mean size and variance of tumors treated by RFA and Hepatectomy. Table 4 records the calculate results. Results show that the tumor treated by RFA is obviously smaller than Hepatectomy.

Based on statistic results, we state that RFA can be a good alternative to Hepatectomy for patients with small-sized tumors or tumors on S6 liver segmentation. However, as tumor size increases, Hepatectomy tends to be more efficacious. After confirming with medical workers in University of Miyazaki Hospital, this statement is consistency with the medical judgment.

6 Conclusions

In this paper, we present a novel end-to-end pipeline framework for medical entity-relation extraction. Our framework inherits the strength of decomposition-based models that can handle the overlapping relation triple problem, and also consider the importance of fusing the entity information to relation extraction. We present a novel annotation schema for medical entity-relation extraction for Japanese Clinical Texts. Based on it, we manually annotate a few-shot dataset to empirically analyze the performance of the system. Through analyzing extracted results, we explored the impact of tumor size and location of early-stage HCC on its treatments to help medical decision support. In the future, we will build a larger Japanese medical entity-relation extraction dataset and apply our methods to solving other real medical problems.

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