EXPERT KNOWLEDGE-AWARE IMAGE DIFFERENCE GRAPH REPRESENTATION LEARNING FOR DIFFERENCE-AWARE MEDICAL VISUAL QUESTION ANSWERING

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ABSTRACT

To contribute to automating the medical vision-language model, we propose a novel Chest-Xray Different Visual Question Answering (VQA) task. Given a pair of main and reference images, this task attempts to answer several questions on both diseases and more importantly, the differences between them. This is consistent with the radiologist's diagnosis practice that compares the current image with the reference before concluding the report. For this task, we propose a new dataset, namely MIMIC-Diff-VQA including 700,821 QA pairs on 109,872 pairs of images. Meanwhile, we also propose a novel expert knowledge-aware graph representation learning model to address this problem. We leveraged the expert knowledge such as anatomical structure prior, semantic and spatial knowledge to construct a multi-relationship graph to represent the image differences between two images for the image difference VQA task. Our dataset and code will be released upon publication. We believe this work would further push forward the medical vision language model.

1 INTRODUCTION

Several recent works focused on extracting text-mined labels from clinical notes and using them to train deep learning models for medical image analysis with several datasets: MIMIC Johnson et al. (2019), NIH14 Wang et al. (2017) and Chexpert Irvin et al. (2019). During this arduous journal on vision-language (VL) modality, the community either mines per-image common disease label (Fig.1. (b)) through Natural Language Processing (NLP), or endeavours on generating report (Fig.1.(c) generated from Nguyen et al. (2021)) or even answer certain pre-defined questions (Fig.1.(d)). Despite significant progress achieved on these tasks, the heterogeneity, systemic biases and subjective nature of the report still pose many technical challenges. For example, the automatically mined labels from reports in Fig.1. (a) is obviously problematic because the rule-based approach did not process all uncertainties and negations well Johnson et al. (2019). Training an automatic radiology report generation system to directly match the report appears to avoid the inevitable bias in the NLP mined common thoracic pathology labels. However, radiologists tend to write more obvious impressions with abstract logic. For example, as shown in Fig.1. (a), a radiology report excludes many diseases (either commonly diagnosed or intended by the physicians) using negation expressions, e.g., no, free of, without, *etc.* However, the artificial report generator could hardly guess which disease is excluded by radiologists.

Instead of thoroughly generating all of the descriptions, VQA is more plausible as it only answers the specific question. As shown in Fig. 1, the question could be raised exactly for "is there any pneumothorax in the image?" in the report while the answer is no doubt "No". However, the questions in the existing VQA dataset ImageCLEF Abacha et al. (2019) concentrates on very few general ones like "is there something wrong in the image? what is the primary abnormality in this image?", lacking the specificity for the heterogeneity and subjective texture. It often decays VQA into classification. While VQA-RAD Lau et al. (2018) has more heterogeneous questions covering 11 question types, its 315 images dataset is relatively too small.

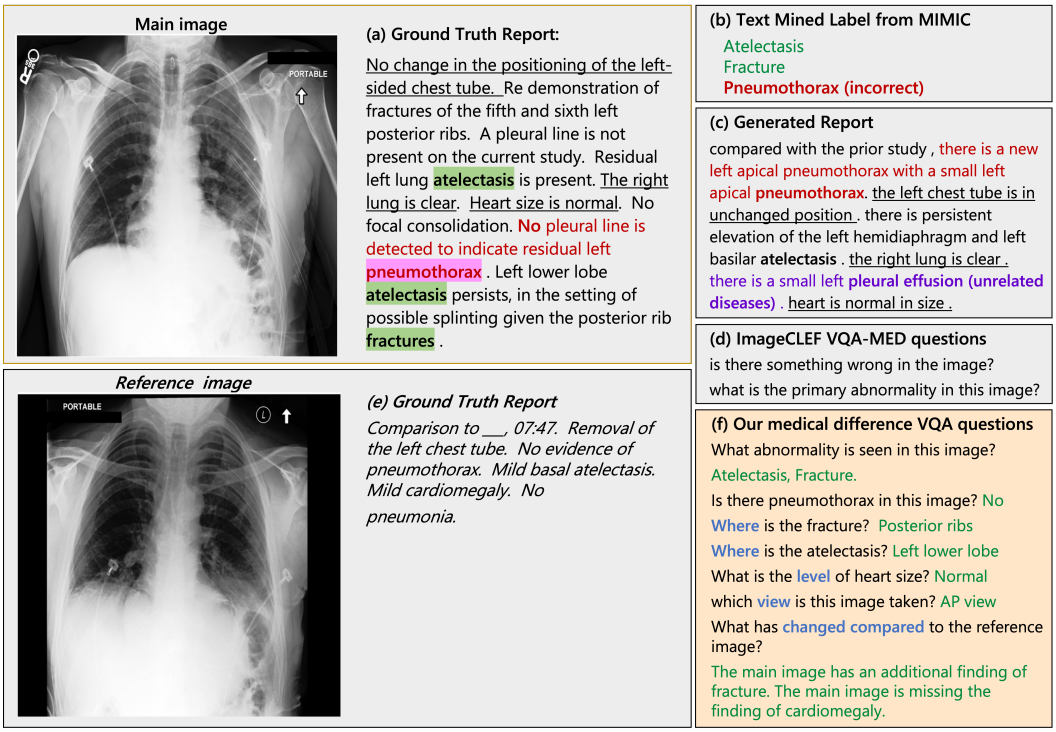


Figure 1: (a) The ground truth report corresponding to the example image. The red text represents labels incorrectly classified by either text mined label or generated report, while the red box marks the misclassified labels. The green box marks the correctly classified ones. The underlined text is correctly generated in the generated report. (b) The label "Pneumothorax" is incorrectly classified because there is NO evidence of pneumothorax from the chest x-ray. (c) "There is a new left apical pneumothorax" $\rightarrow$ This sentence is wrong because the evidence of pneumothorax was mostly improved after treatment. However, the vascular shadow in the left pulmonary apex is not very obvious, so it is understandable why it is misidentified as pneumothorax in the left pulmonary apex. "there is a small left pleural effusion" $\rightarrow$ It is hard for a doctor to tell if the left pleural effusion is present or not. (d) The ImageCLEF VQA-MED questions are designed too simple. (e) The reference image and clinical report. (f) Our medical difference VQA questions are designed to guide the model to focus on and localize important regions.

To bridge the aforementioned gap in the visual language model, we propose a novel medical image difference VQA task which is more consistent with radiologists' practice. When radiologists make a diagnosis, they usually compare the main one with a reference image to find their differences. Therefore, understanding the clinical meaning of what and where has changed on two images is an essential step in the arduous medical vision language journey. Specifically, we present a chest x-ray image difference VQA dataset, MIMIC-Diff-VQA. We create pairs of "main" and "reference" images from the same patient's radiology images at different times from MIMICJohnson et al. (2019) (a large-scale public database of chest radiographs with 227,835 studies, each with a unique report and images). The question and answer pairs are extracted from the MIMIC report for "main" and "reference" images with rule-based techniques. Similar to Abacha et al. (2019); Lau et al. (2018); He et al. (2020), we first collect sets of abnormality names and attributes. Then we extract the abnormality contained in the images and their corresponding attributes using regular expressions. Finally, we compare the abnormalities contained in the two images and ask questions based on the collected information. We designed seven types of questions:1.abnormality, 2.presence, 3.view, 4.location, 5.type, 6.level and, 7.difference. In our MIMIC-Diff-VQA dataset, 700,821 QA pairs are extracted from 109,872 image pairs. Particularly, *difference* questions answer pairs inquiry on the clinic progress and change on the "main image" compared to the "reference one" as shown in Fig. 1.(e).

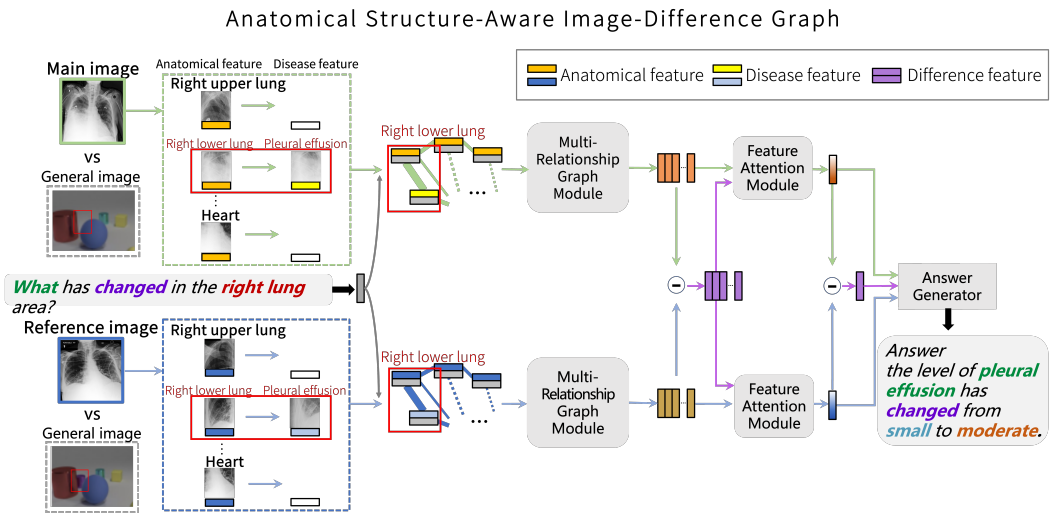


Figure 2: Anatomical structure-aware image-difference graph for medical image difference visual question answering.

While the current state-of-art image difference method can be only applied to synthetic images with small view variations, Jhamtani & Berg-Kirkpatrick (2018); Park et al. (2019); Yao et al. (2022) as shown in Fig. 2. However, real medical image difference comparing is a very challenging task. Even the images from the same patient show large variances in the orientation, scale, range, view, and non-rigid deformation, which are often more significant than the subtle differences caused by diseases as shown in Fig. 2. Since the radiologists examine the anatomical structure to find the progression of diseases, similarly, we proposed an expert knowledge-aware image difference graph representation learning model as shown in Fig. 2. We extracted the features from different anatomical structures (for example, left lower lung, and right upper lung) as nodes in the graph.

Moreover, we constructed three different relationships in the graph to encode expert knowledge: 1) Spatial relationship based on the spatial distance between different anatomical regions, such as "left lower lung", "right costophrenic angle", etc. We construct this graph based on the fact that radiologists prefer to determine the abnormalities based on particular anatomical structures. For example, "Minimal blunting of the left costophrenic angle also suggests a tiny left pleural effusion."; 2) Semantic relationship based on the disease and anatomical structure relationship from knowledge graph Zhang et al. (2020). We construct this graph because of the fact that diseases from the same or nearby regions could affect each other's existence. For example, "the effusions remain moderate and still cause substantial bilateral areas of basilar atelectasis."; 3) Implicit relationship to model potential implicit relationship beside 1) and 2). The graph feature representation for each image is learned as a weighted summation of the graph feature from these three different relationships. The image-difference graph feature representation is constructed by simply subtracting the main image graph feature and reference image graph feature. This graph difference feature is fed into LSTM networks with attention modules for answer generationToutanova et al. (2003). **Our contributions are summarized as:**

1)We firstly proposed the medical imaging difference question answering problem and constructed the first medical image difference question answering dataset, MIMIC-Diff-VQA, containing questions related to various attributes, including abnormality, presence, location, level, type, view, and difference.

2) We proposed an expert knowledge-aware image difference graph model to extract the image differences correlated to changes in diseases and minimize the variances caused by body pose, view, and nonrigid deformations of organs.

3) We developed a multi-relationship image difference graph feature representation learning method to leverage the spatial relationship and knowledge graph to compute image-difference graph feature representation and generate answers.

2 RELATED WORK

Image Difference Captioning. The analysis of different images has been explored by a number of researchers in the general domain. The exploration of Image Difference Captioning(IDC) can be split into three stages. The beginning of the first stage is marked by the "spot-the-diff" dataset Jhamtani & Berg-Kirkpatrick (2018), which consists of different frames of the same video surveillance footage. This is also the very first time that the IDC task has been proposed. In this phase, the researchers only focus on the pixel-level difference in the same view of the same scene. Jhamtani & Berg-Kirkpatrick (2018) use the clusters of differing pixels as a proxy for exposing object-level differences. Tan et al. (2019); Oluwasanmi et al. (2019) propose to employ encoder-decoder architecture with attention modules to find the relationship between two images. In the second phase, the challenge has been upgraded by adding different view angles of the scenes. This demands a higher requirement for the analysis of different regions between images. The iconic dataset in this phase is CLEVR-change dataset Park et al. (2019), which is composed of pictures of a group of objects(cube, sphere, and cylinder) from different views. The attention mechanism is widely employed to address this challenge Park et al. (2019); Shi et al. (2020); Tu et al. (2021); Sun et al.; Kim et al. (2021); Qiu et al. (2021). Hosseinzadeh & Wang (2021) propose to use an auxiliary task to enhance the primary task to generate the captions. Liao et al. (2021) consider 3D information and adopt a scene graph to assist in localizing the changing objects. Kim et al. (2021) also introduces a CLEVR-DC dataset, which is similar to CLEVR-change, but with a larger viewpoint change. In the third phase, more fine-grained visual differences are shown in the image pairs. The Birds-to-Words dataset Forbes et al. (2019) is composed of a variety of bird images and each image pair are captioned by human observers. Since the species, posture, and background of the birds in each picture vary greatly, this desires a new method to solve the problem. Forbes et al. (2019) proposed Neural Naturalist, which is a transformer-based model. Yan et al. (2021) learns to understand the semantic structures while comparing the images. Yao et al. (2022) embrace the pre-training technique to align the visual difference and the text descriptions and achieve state-of-the-art performance.

Medical Visual Question Answering. Medical visual question answering aims to answer clinical questions given medical images. Medical images span a wide spectrum of modalities, including CT/MRI imaging, histopathology images, angiography, characteristic imaging appearance, ultrasound, and radiographs Abacha et al. (2019); Lau et al. (2018); He et al. (2020). Clinical questions mainly ask for modality, plane, organ system, and abnormality Abacha et al. (2019). However, large and well-annotated medical VQA datasets are still in scarcity. Previous MED-VQA methods mostly employ a two-stage procedure: 1) extract visual features on medical images through a detection model like Faster-RCNN Ren et al. (2015), YOLO Redmon et al. (2016), and extract question features via BERT Devlin et al. (2018); 2) attempt to aggregate visual and question features for predicting the final answer Zhan et al. (2020); Abacha et al. (2018); Zhou et al. (2018); Shi et al. (2019); Yan et al. (2019). Lau et al. (2018) deploys existing VQA models, i.e., the stacked attention network (SAN) Yang et al. (2016) and the multimodal compact bilinear pooling (MCB) Fukui et al. (2016), in general domains to solve MED-VQA. Nguyen et al. (2019) proposes to mix enhanced visual features framework with different attention mechanisms such as bilinear attention network (BAN) Kim et al. (2018) and SAN. Zhan et al. (2020) proposes separate reasoning modules for different questions to improve the reasoning on medical questions. Shi et al. (2019) integrates question categories and question topic distributions to assist answer prediction. Yan et al. (2019) improves the CNN feature extractor with global average pooling to boost classification. Zhou et al. (2018) applies some image enhancement methods by reconstructing with small random rotations, offsets, scaling, and clipping to boost classification. However, the MED-VQA problem still suffers from lacking fine-grained annotations on images, massive diversity of medical data types, and medical reasoning skills from professions, and is thus far from practical.

3 METHOD

MIMIC-Diff-VQA dataset. We introduce our new MIMIC-Diff-VQA dataset for the medical imaging difference question-answering problem. In MIMIC-Diff-VQA, each entry contains two different chest x-ray images from the same patient with a question-answer pair. Our question design is extended from VQA-RAD, but with an additional question type of "difference". In the end, the

questions can be divided into 7 types: 1) abnormality, 2) presence, 3) view, 4) location, 5) type, 6) level, and 7) difference. Tab. 1 shows the examples of the different question types.

Table 1: Selected examples of the different question types. **See Appendix for the full list.**

Question type	Example
Abnormality	what abnormality is seen in the left lung?
Presence	is there evidence of atelectasis in this image?
View	which view is this image taken?
Location	where in the image is the pleural effusion located?
Type	what type is the opacity?
Level	what level is the cardiomegaly?
Difference	what has changed compared to the reference image?

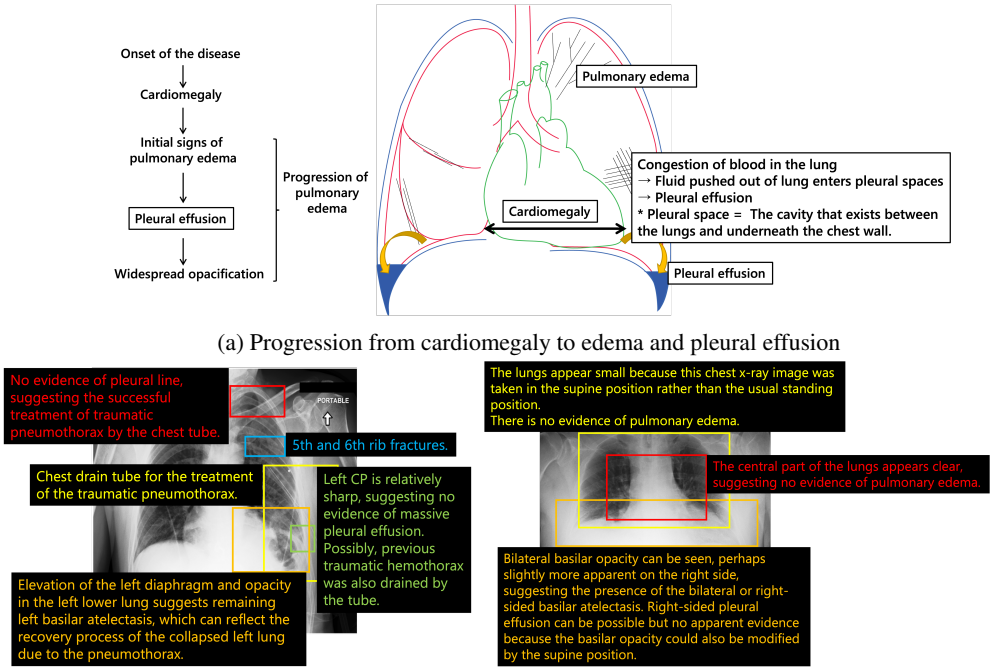
The image pairs are selected from the MIMIC Johnson et al. (2019) dataset, and each image in an image pair is from the same patient. There are 109,872 image pairs are selected from MIMIC, and 700,821 questions are constructed. We also balance the "yes" and "no" answers to avoid possible bias. The statistics regarding each question type can be seen in Fig. 5 in Appendix. The ratio of training, validation, and testing set is 8:1:1. Please refer to Appendix. A.1 for the details on how the dataset is constructed.

Problem Statement. Given an image pair $(\mathbf{I}_m, \mathbf{I}_r)$, consisting of the main image $\mathbf{I}_m$ and the reference image $\mathbf{I}_r$. Also given a question $\mathbf{q}$ which is designed to ask what has been changed comparing the main image to the reference image, our goal is to obtain the answer $\mathbf{a}$ of the question $\mathbf{q}$, based on the information provided by the image pair. In our design of the image pair, the main image and the reference image are coming from the same patient.

Expert Knowledge-Aware Graph Construction and Feature Learning. As shown in the left Fig.2, previous work on image difference question answers in the general image domain. They create paired synthetic images with identical backgrounds and only move or remove the simple objects from the background. The feature of image difference was extracted by simply comparing the feature on the same image coordinates. Unfortunately, even the medical imaging of the same patients shows large variation due to the pose and nonrigid deformation. The change of pose, scale, and range of the main image and reference image in Fig. 2 are strongly different compared to the disease change (pleural effusion changed from small to moderate). If we use the general image difference methods, the computed image differences related to the pose change will dominate and the subtle disease changes will be neglected. To better capture the subtle disease changes and eliminate the pose, orientation, and scale changes, we propose to use an expert knowledge-aware image difference graph learning method by considering each anatomical structure as a node and comparing the image changes in each anatomical structure just as radiologists, which consist of the following parts:

Anatomical Structure, Disease Region Detection and Question Encoding. We first extract the anatomical bounding boxes and their features $\mathbf{f}_a$ from the input images using pre-trained Faster-RCNN on the MIMIC dataset Ren et al. (2015); Karargyris et al. (2020). Then, we train a Faster-RCNN on the VinDr dataset Pham et al. (2021) to detect the diseases. Instead of directly detecting diseases on the given input images, we extract the features $\mathbf{f}_d$ from the same anatomical regions using the extracted anatomical bounding boxes. The questions and answers are processed in the same way as Li et al. (2019); Norcliffe-Brown et al. (2018). Each word is tokenized and embedded with Glove Pennington et al. (2014) embeddings. Then we use a bidirectional RNN with GRU Cho et al. (2014) and self-attention to generate the question embedding $\mathbf{q}$.

Multi-Relationship Graph Module. After extracting the disease and anatomical structure, we constructed an anatomical structure-aware image representation graph for the main and reference image. The multi-relationship graph is defined as $\mathcal{G} = \{\mathbf{V}, \mathcal{E}_{sp}, \mathcal{E}_{se}, \mathcal{E}_{imp}\}$, where each vertex $\mathbf{v}_i \in \mathbf{V}, i = 1, \cdots, 2N$ can be either anatomical node $\mathbf{v}_k = [f_{a,k} \| \mathbf{q}] \in \mathbb{R}^{d_f + d_q}, f_{a,k} \in \mathbf{f}_a$, for $k = 1, \ldots, N$, or disease node $\mathbf{v}_k = [f_{d,k} \| \mathbf{q}] \in \mathbb{R}^{d_f + d_q}, f_{d,k} \in \mathbf{f}_d$, for $k = 1, \ldots, N$, representing anatomical structures or disease regions, respectively. Both of these two types of nodes are embedded with a question feature as shown in Fig. 2. d_f is the dimension of the anatomical and disease features. d_q is the dimension of the question embedding. N represents the number of anatomical structures of one



(a) Progression from cardiomegaly to edema and pleural effusion

(b) Radiologist's annotation example 1

(c) Radiologist's annotation example 2

Figure 3: Illustration of the progression of diseases and two X-ray annotation examples.

image. Because each disease feature is extracted from the same corresponding anatomical region, the total number of the vertex is $2N$.

We construct three types of relationships in the graph for each image: 1) **spatial relationship**: We construct spatial relationships according to the radiologist's practice of identifying abnormalities based on specific anatomical structures. For example, "the effusions remain moderate and still cause substantial bilateral areas of basilar atelectasis"; "Elevation of the left diaphragm and opacity in the left lower lung suggests remaining left basilar atelectasis" as shown in Fig. 3b; "The central part of the lungs appears clear, suggesting no evidence of pulmonary edema." as shown in Fig. 3c. In our MIMIC-Diff-VQA dataset, questions are designed for the spatial relationship, such as "where in the image is the pleural effusion located?" as shown in Tab. 1. Following previous work Yao et al. (2018), we include 11 types of spatial relations between detected bounding boxes, such as "left lower lung", "right costophrenic angle", etc. The 11 spatial relations includes `inside` (class1), `cover` (class2), `overlap` (class3), and 8 other directional classes. Each class corresponds to a 45-degree of direction. We define the edge between node i and the node j as $a_{ij} = c$, where c is the class of the relationship, $c = 1, 2, \cdots, K$, K is the number of spatial relationship classes, which equals to 11. When $d_{ij} > t$, we set $\mathbf{a}_{ij} = 0$, where d_{ij} is the euclidean distance between the center points of the bounding boxes corresponding to the node i and node j, t is the threshold. The threshold t is defined to be $(l_x + l_y)/3$ by reasoning and imitating the data given by Li et al. (2019).

2) **Semantic relationship**: The semantic relationship is based on two knowledge graphs, including an anatomical knowledge graph from Zhang et al. (2020), as shown in Fig. 7a; and a label occurrence knowledge graph built by ourselves, as shown in Fig. 7b. If there is an edge linking two labels in the Knowledge graph, we connect the nodes having these two labels in our semantic relationship graph. The knowledge graph can include abstracted expert knowledge and depicts the relationships between diseases. These relationships play a crucial role in disease diagnosis. Multiple diseases could be interrelated to each other during the course of a certain disease. For example, in Fig. 3a, a progression from cardiomegaly to edema and pleural effusion is shown. Cardiomegaly, which refers to an enlarged heart, can start with a heart dysfunction that causes congestion of blood in the heart, which eventually leads to the enlargement of the heart. The congested blood can back up into the veins of the lungs. As the pressure of the vessels in the lungs increases, fluid is pushed out of the lungs and enters pleural spaces causing the initial sign of pulmonary edema. Meanwhile,

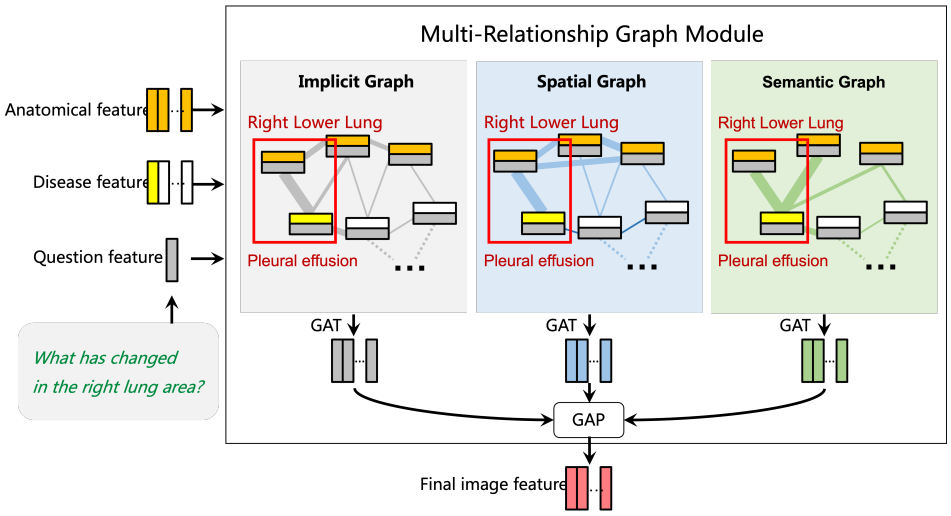


Figure 4: Multi-modal relationship graph module.

the fluid starts to build up between the layers of the pleura outside the lungs, i.e. pleural effusion. Pleural effusion can also cause compression atelectasis. As pulmonary edema continues to progress, widespread opacification in the lung can appear. These can be verified in real diagnostic reports. For example, "the effusions remain moderate and still cause substantial bilateral areas of basilar atelectasis"; "Bilateral basilar opacity can be seen, suggesting the presence of the bilateral or right-sided basilar atelectasis" as shown in Fig. 3c.

3) **Implicit relationship**: a fully connected graph is applied to find the implicit relationships that are not defined by the other two graphs. Among the three types of relationships, spatial relationships and semantic relationships can be grouped as explicit relationships.

Relation-Aware Graph Attention Network. As shown in Fig.4, we construct the multi-relationship graph for both main and reference images and use the relation-aware graph attention network proposed by Li et al. (2019), to learn the graph representation for each image and embed the image into the final latent feature. In a relaiton-aware graph attention network, edge labels are embedded to calculate the attention weights between nodes. Please refer to Appendix. A.2 for details of the calculation. For simplicity, we use $G_{spa}(\cdot)$, $G_{sem}(\cdot)$, and $G_{imp}(\cdot)$ to represent the spatial graph module, the semantic graph module and the implicit graph module, respectively. Given the input feature nodes $\mathbf{V}$ of each image, the final graph feature $\widetilde{V}$ can be represented as:

$$\widetilde{\mathbf{V}} = GAP(G_{spa}(\mathbf{V}) + G_{sem}(\mathbf{V}) + G_{imp}(\mathbf{V})) \tag{1}$$

where $GAP(\cdot)$ means the global average pooling. The image difference graph is constructed by subtracting the node feature and edge feature between the main and reference image:

$$\widetilde{\mathbf{v}}_i^{diff} = \widetilde{\mathbf{v}}_i^{main} - \widetilde{\mathbf{v}}_i^{ref}, i = 1, \cdots, 2N, \tag{2}$$

where $\widetilde{\mathbf{v}}_i^{diff}, \widetilde{\mathbf{v}}_i^{main}, \widetilde{\mathbf{v}}_i^{ref} \in \mathbb{R}^d$ represent the final feature for the i-th node of graphs. Therefore, the final graph features $\widetilde{\mathbf{V}}^{diff}, \widetilde{\mathbf{V}}^{main}, \widetilde{\mathbf{V}}^{ref} \in \mathbb{R}^{2N \times d}$ can be obtained.

Feature Attention and Answer Generation Following previous work Tu et al. (2021), the generated main, reference, and difference features $\widetilde{\mathbf{v}}_i^{main}, \widetilde{\mathbf{v}}_i^{ref}, \widetilde{\mathbf{v}}_i^{diff}$ are then fed into the Feature Attention Module, which first calculate the attention weights of each node, then output the final feature vectors $\mathbf{l}_m$, $\mathbf{l}_r$, and $\mathbf{l}_{diff}$. For details of the calculation, please refer to Appendix A.3. Finally, by feeding the final feature vectors $\mathbf{l}_m$, $\mathbf{l}_r$, and $\mathbf{l}_{diff}$ into the Answer Generation module, the final answer is generated. Same as Tu et al. (2021)'s setting, the Answer Generation module is composed of LSTM networks and attention modules. The Part-Of-Speech (POS) information is also considered to help generate the answers. For the calculation details, please refer to Appendix A.4. We adopt the generative language model because our questions have highly diverse answers. (e.g. the *difference* type question). A simple classification model is not adequate for our task.

4 EXPERIMENTS

Datasets. *MIMIC-CXR.* The MIMIC-CXR dataset is a large publicly available dataset of chest radiographs with radiology reports, containing 377,110 images corresponding to 227,835 radiograph studies from 65,379 patients Johnson et al. (2019). One patient may have multiple studies, and each study consists of a radiology report and one or more images. Two primary sections of interest in reports are findings: a natural language description of the important aspects of the image, and an impression: a short summary of the most immediately relevant findings. Our MIMIC-Diff-VQA is constructed based on the MIMIC-CXR dataset.

Chest ImaGenome. MIMIC-CXR has been added more annotations by Wu et al.; Goldberger et al. (2000) including the anatomical structure bounding boxes. This new dataset is named Chest ImaGenome Dataset. We trained the faster-RCNN to detect the anatomical structures on their gold standard dataset, which contains 26 anatomical structures.

VinDr. The VinDr dataset consists of 18,000 images manually annotated by 17 experienced radiologists Nguyen et al. (2020). Its images have 22 local labels of boxes surrounding abnormalities and 6 global labels of suspected diseases. We used it to train the pre-trained disease detection model.

Baselines Given that we are the first to propose this medical imaging difference VQA problem, there are no earlier models available for us to compare. Therefore, we chose two baseline models from the traditional medical VQA task and image difference captioning task, respectively. One is Multiple Meta-model Quantifying (MMQ) proposed by Do et al. (2021). The other is Multi-Change Captioning transformers (MCCFormers) proposed by Qiu et al. (2021).

1.*MMQ* is one of the recently proposed methods to perform traditional medical VQA task with excellent results. MMQ adopted Model Agnostic Meta-Learning (MAML) Finn et al. (2017) to handle the problem of the small size of the medical dataset. It also relieves the problem of the difference in visual concepts between general images and medical images when finetuning.

2.*MCCFormers* is proposed to handle image difference captioning task. It achieved state-of-the-art performance on the CLEVR-Change dataset Park et al. (2019), which is a famous image difference captioning dataset. MCCFormers used transformers to capture the region relationships among intra- and inter-image pairs.

Results and Discussion. We implemented the experiments on the PyTorch platform. We used an Adam optimizer with a learning rate of 0.0001 to train our model for 25,000 iterations at a batch size of 64. The bounding box feature dimension is 1024. Each word is represented by a 600-dimensional feature vector including a 300-dimensional Glove Pennington et al. (2014) embedding. We used BLEU Papineni et al. (2002), which is a popular metric for evaluating the generated text, as the metric in our experiments. We obtain the results using Microsoft COCO Caption Evaluation Chen et al. (2015). For the comparison with MMQ, we use accuracy as the metric.

Ablation Study. In Tab. 2 We present quantitative results of ablation studies of our method with different graph settings, including implicit graph-only, spatial graph-only, semantic graph-only, and full model with all three graphs. The studies were performed on our constructed MIMIC-Diff-VQA dataset.

Table 2: Quantitative results of our model with different graph settings perfomrd on the MIMIC-Diff-VQA dataset

Metrics	Implicit	Spatial	Semantic	Full
Bleu-1	0.627	0.616	0.616	**0.630**
Bleu-2	0.543	0.530	0.533	**0.546**
Bleu-3	0.480	0.464	0.469	**0.482**
Bleu-4	0.424	0.408	0.415	**0.426**

Comparison of accuracy. Due to the nature of MMQ being a classification model, MMQ is unable to perform on our *difference* question type because of the diversity of answers. Also, given that the baseline model doesn't have the capability to take in two images at one time, we excluded the

difference type question from this comparison. Therefore, we compare our method with MMQ only on the other six types of questions, including *abnormality, presence, view, location, type*, and *level*. These six types of questions have a limited number of answers. In order to compare with them, we use accuracy as the metric for comparison. Please note that our method is still a text generation model. We count the predicted answer as a True answer only when the prediction is fully matched with the ground truth answer.

The comparison results are shown in Tab. 3. We have refined the comparison more into open-ended question results and closed-ended question (with only 'yes' or 'no' answers) results. It is clear from the results that the current VQA model has difficulty handling our dataset because of the lack of focus on the key regions and the ability to find the relationships between anatomical structures and diseases. Also, even after filtering out the *difference* questions, there are still 9,231 possible answers in total. It is difficult for a classification model to localize the optimal answer from such a huge amount of candidates.

Table 3: Accuracy comparison between our method and MMQ.

Question	Open	Closed	Total
MMQ	11.5	10.8	11.5
Ours	25.59	74.20	49.29

Comparison of quality of text. For the *difference* question, we use the metrics for evaluating the generated text. The comparison results between our method and MCCFormers are shown in Tab. 4 We can see that our method greatly outperformed MCCFormers on every metric. The CIDEr metric even reached 0. This is because the generated answers of MMCFormers are almost identical, which means MMCFormers failed to identify the differences between images. Although MCCFormers is a difference captioning method, it compares patch to patch directly. It may work well in the general domain. However, when it comes to medical images, most of which are not aligned well, the patch-to-patch method has no clue to identify which region corresponds to a specific anatomical structure. And of course, MCCFormers didn't utilize any medical knowledge graphs to find out the relationships between different regions.

Table 4: Comparison results between our method and MCCFormers on *difference* questions of the MIMIC-diff-VQA dataset

Metrics	**MCCFormers**	**Ours**
Bleu-1	0.214	**0.641**
Bleu-2	0.190	**0.564**
Bleu-3	0.170	**0.500**
Bleu-4	0.153	**0.441**

Visualization. Visualized results can be found in Appendix.

5 CONCLUSION

First, We proposed a medical image difference VQA problem and constructed a large-scale MIMIC-Diff-VQA dataset for this task, which is valuable to both the research and medical communities. Also, we designed an anatomical structure-aware multi-relation image difference graph to extract image-difference features. We trained an image difference VQA framework utilizing medical knowledge graphs and compared it to current state-of-the-art methods with improved performances. However, our constructed dataset is currently only focusing on the common cases and ignoring special ones. For example, cases where the same disease appears in more than two places. Our current Key-Info dataset can only take care of at most two locations of one and the same disease. Future work could be extending the dataset to consider more special cases.

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A APPENDIX

A.1 MIMIC-DIFF-VQA DATASET CONSTRUCTION

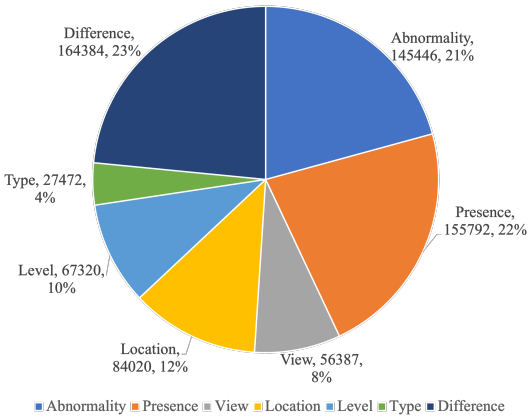


Figure 5: Statistics by question types

Table 5: Full list of examples for each question type.

Question type	example
Abnormality	what abnormalities are seen in this image? what abnormalities are seen in the *[location]*? is there evidence of any abnormalities in this image? is this image normal?
Presence	is there evidence of *[abnormality]* in this image? is there *[abnormality]*? is there *[abnormality]* in the *[location]*?
View	which view is this image taken? is this PA view? is this AP view?
Location	where in the image is the *[abnormality]* located? where is the *[abnormality]*? is the *[abnormality]* located on the left side or right side? is the *[abnormality]* in the *[location]*?
Level	what level is the *[abnormality]*?
Type	what type is the *[abnormality]*?
Difference	what has changed compared to the reference image? what has changed in the *[location]* area?

First, we exclude the lateral view and select only the common PA or AP views for comparison. Patients with only one radiology visit are also excluded because no second image is available for differential comparison.

Next, we collect a set of abnormality names, as well as the sets of important attributes including location, level, and type, from the filtered MIMIC-CXR dataset. The lists of abnormality names and the attribute words are collected by iteratively extracting entities from random reports using ScispaCy Neumann et al. (2019), which is a SpaCy model for biomedical text processing. Then we manually go through all the extracted entities that haven't been added to the collection list and select the common keywords that appear frequently. Then we add these selected keywords to the collection lists of abnormality names and attributes. During this process, different variants that represent the same abnormality are also recorded. Next, for each study, we use regular expressions to localize the abnormality names as well as their variants to detect attribute words near these detected abnor-

malities. (Here, "study" represents a single patient visit. Please refer Section 4 for more context.) Meanwhile, by going through the extracted entities, we manually select the keywords/expressions that are indicating negation information to localize the negative findings, i.e. cases where the abnormality does not exist. After updating the keyword lists, we keep repeating this Extract-Check-Fix cycle until few mistakes are found.

Thereafter, a dataset of single studies can be constructed accordingly. We call this dataset the Key-Info dataset. As shown in Fig. 6, for each study, the Key-Info dataset provides the information of every positive finding and its corresponding attributes as well as the negative findings. The full lists of the selected abnormality names and the attribute words are shown in Tab. 6 and Tab. 7, respectively.

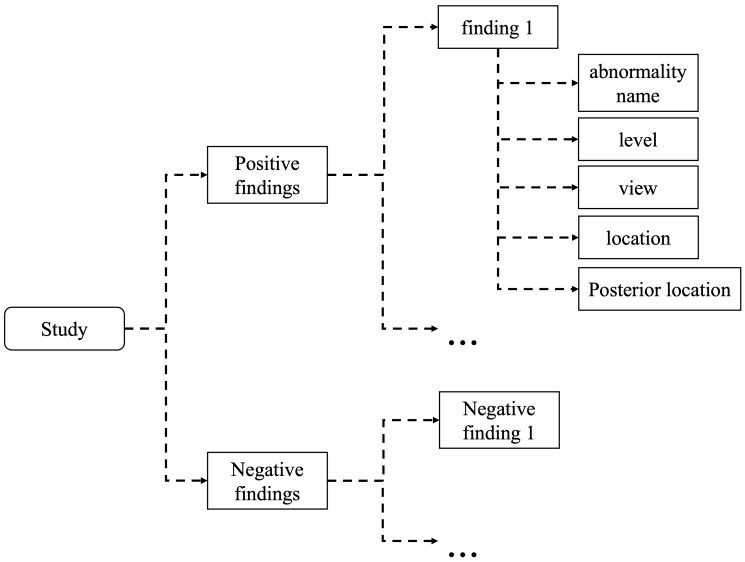


Figure 6: Structure of one study in the Key-Info dataset

Study pairing and question generation

When the abnormality database is constructed, questions for study pairs can be generated accordingly. The examples of each question type are shown in Tab. 1. Each image pair contains a main image and a reference image, which are extracted from different studies. Among all the question types, the first six question types are for the main image only, and the *difference* question is for both images.

A.1.1 Dataset Validation

To further verify the reliability of our constructed dataset, 3 human verifiers were assigned 100 random sampled question-answer pairs along with the reports and evaluated each sample by annotating "correct" or "incorrect". Finally, the accuracy of the evaluation achieved 97%, which is acceptable for training neural networks. Tab. 8 shows the evaluation results of each verifier. It proves that our approach of constructing a dataset in an Extract-Check-Fix cycle works well in ensuring that the constructed dataset has minimum mistakes.

A.2 Relation-Aware Graph Attention Network

For the implicit relationship, each updated node $\widetilde{\mathbf{v}}_i \in \mathbb{R}^d$ in the final graph can be calculated as below:

$$\widetilde{\mathbf{v}}_i = \mathbf{W}^o \cdot (\|_{m=1}^{M} \sigma(\sum_{j \in \mathcal{N}_i} \alpha_{ij} \mathbf{W}^m \mathbf{v}_j)) \tag{3}$$

where $\mathcal{N}_i$ is the neighborhood set of the node i, $\mathbf{W}^m \in \mathbb{R}^{d \times (d_f + d_q)}$ is the projection matrix, d is the dimension of the final node feature, σ is the activation function, $\|_{m=1}^{M}$ represents concatenating

Table 6: Disease Keywords

id	Disease names
1	pleural effusions;pleural effusion;effusion;effusions;pleural fluid
2	volume loss;collapse;atelectasis;atelectases;atelectatic changes;atelectatic change
3	cardiomegaly;heart size is enlarged
4	enlargement of the cardiac silhouette
5	pulmonary edema;edema
6	hiatal hernia;hiatus hernia;hernia
7	pulmonary vascular congestion;vascular congestion
8	hilar congestion
9	pneumothorax
10	cardiac decompensation;congestive heart failure;heart failure
11	lung opacification;airspace opacities;airspace opacity;opacification;opacity;opacities;lung opacity;lung opacities
12	pneumonia
13	tortuosity of the descending aorta
14	infection
15	thoracolumbar scoliosis;scoliosis
16	gastric distention
17	hypoxemia
18	hypertensive heart disease;htn
19	hematoma
20	tortuosity of the thoracic aorta
21	pulmonary contusion;contusion
22	emphysema
23	granulomatous disease;granuloma
24	calcifications;calcification
25	pleural thickening
26	thymoma
27	blunting of the costophrenic angles;blunting of the right costophrenic angle;blunting of the left costophrenic angle
28	consolidation
29	fractures;fracture

the output of the M attention heads, $\mathbf{W}^o \in \mathbb{R}^{d \times Md}$. The attention weights α_{ij} between the node i and node j consider the similarity between node pairs and the relations between the corresponding region locations. The calculation for α_{ij} can be formulated as:

$$\alpha_{ij} = \frac{\alpha_{ij}^b \cdot \exp\left(\alpha_{ij}^v\right)}{\sum_{j=1}^{K} \alpha_{ij}^b \cdot \exp\left(\alpha_{ij}^v\right)} \tag{4}$$

$$\alpha_{ij}^v = \left(\mathbf{U}\mathbf{v}_i\right)^\top \cdot \left(\mathbf{V}\mathbf{v}_j\right) \tag{5}$$

$$\alpha_{ij}^b = \max\left(0, w \cdot f_b(\mathbf{b}_{ij}\right) \tag{6}$$

where $U, V \in \mathbb{R}^{d \times (d_f + d_q)}$ are projection matrices. $\mathbf{b}_{ij}$ is the relative geometry feature between node i and j, and can be calculated by $[\log(\frac{|x_i - x_j|}{w_i}), \log(\frac{|y_i - y_j|}{h_i}), \log(\frac{w_j}{w_i}), \log(\frac{h_j}{h_i})]$, f_b is a function that embeds the 4-dimensional relative geometry feature into d-dimensional,$w \in \mathbb{R}^d$ is a vector that transforms the feature into a scalar weight. The bounding box coordinates, widths, and heights of the node i and j can be represented by $x_i, x_j, y_i, y_j, w_i, w_j, h_i$, and h_j.

Spatial and semantic graphs, which can also be called explicit graphs, can be seen as directed graphs. The updating rule considers the relation directions between node pairs and the labels of the edges. The formulation of a single attention head is shown below:

$$\widetilde{\mathbf{v}}_i = \sigma\big(\sum_{j \in \mathcal{N}_i} \alpha_{ij} \mathbf{W}_{dir(i,j)} \mathbf{v}_j + b_{lab(i,j)}\big) \tag{7}$$

$$\alpha_{ij} = \frac{\exp\left((\mathbf{U}\mathbf{v}_i)^\top \cdot \mathbf{V}_{dir(i,j)} \mathbf{v}_j + c_{lab(i,j)}\right)}{\sum_{j \in \mathcal{N}_i} \exp\left((\mathbf{U}\mathbf{v}_i)^\top \cdot \mathbf{V}_{dir(i,j)} \mathbf{v}_j + c_{lab(i,j)}\right)} \tag{8}$$

where $dir(i, j)$ represents the direction goes from node i to j, $lab(i, j)$ is the label assigned to the edge (i, j), $W_{dir(i,j)}, V_{dir(i,j)} \in \mathbb{R}^{d \times (d_f + d_q)}$ are projection matrices, $b_{lab(i,j)}, c_{lab(i,j)} \in \mathbb{R}^d$ are bias terms. The multi-head attention can be calculated similarly by concatenating the output features and adding a projection matrix $\mathbf{W}^o \in \mathbb{R}^{d \times Md}$.

Table 7: Attribute keywords for level, location(pre), location(post), and type.

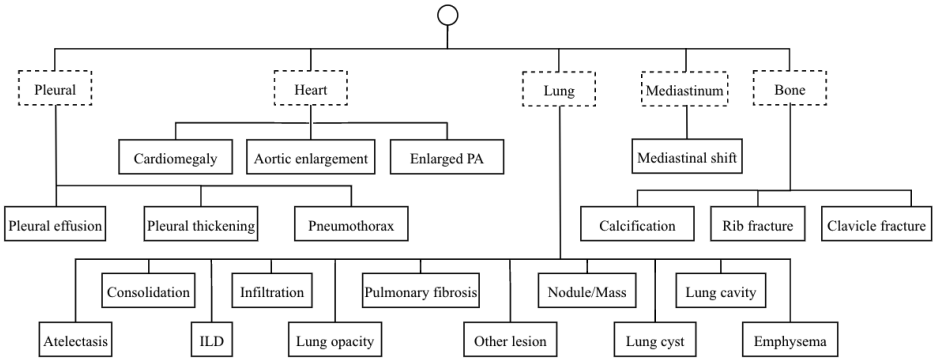
Attribute			
level	location(pre)	location(post)	type
moderate	mid to lower	the lower lobe	interstitial
acute	left	the upper lobe	layering
mild	right	the middle lobe	dense
small	retrocardiac	the left lung base	parenchymal
moderately	pericardial	the right lung base	compressive
severe	bibasilar	the lung bases	obstructive
moderate to large	bilateral	the left base	linear
moderate to severe	basilar	the right base	plate-like
mild to moderate	apicolateral	the right upper lung	patchy
moderate to large	basal	the left upper lung	ground-glass
minimal	left-sided	the right middle lung	calcified
mildly	lobe	the left middle lung	scattered
subtle	lung	the right mid lung	interstitial
	area	the left mid lung	focal
	right-sided	the right lower lung	multifocal
	apical	the left lower lung	multi-focal
	pleural	the right upper lobe	
	upper	the left upper lobe	
	lower	the right middle lobe	
	middle	the left middle lobe	
	mid	the right mid lobe	
	rib	the left mid lobe	
		the right lower lobe	
		the left lower lobe	
		the left apical area	
		the left apical region	
		the right apical area	
		the right apical region	
		the apical region	
		the apical area	
		the right mid to lower lung	
		the left mid to lower lung	
		the medial right lung base	
		the medial left lung base	
		the upper lungs	
		the lower lungs	
		the upper lobes	
		the lower lobes	
		the right mid to lower hemithorax	
		the left mid to lower hemithorax	

A.3 Feature Attention Module

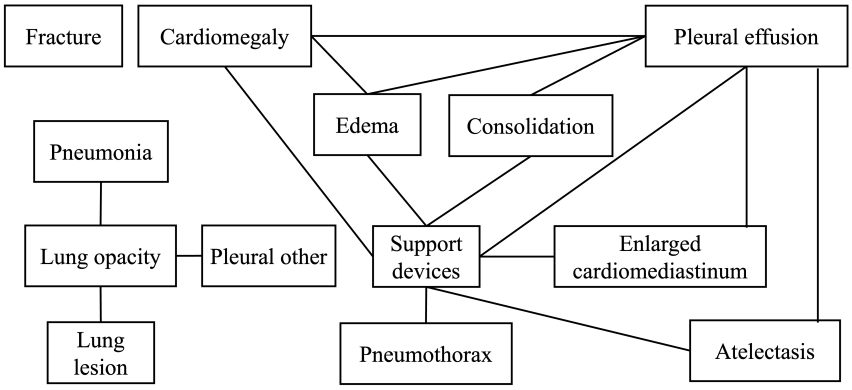
The generated main image features $\widetilde{\mathbf{V}}_i^{main}$, reference image feature$\widetilde{\mathbf{V}}_i^{ref}$ and the difference feature$\widetilde{\mathbf{V}}_i^{diff}$ are then fed into the Feature Attention Module, which is similar to the two modules in Tu et al. (2021) called Cross-semantic Relation Measuring block(CSRM) and Prior Knowledge-guided Change Localizer. In the Feature Attention module, we first calculate the prior knowledge C'_m, and C'_r for the main image and the reference image, respectively. Take C'_m for example, the

Table 8: Evaluation results by human verifiers

Verifier	# of examples	# of correctness	Accuracy
Verifier 1	33	32	96.97%
Verifier 2	33	33	100.00%
Verifier 3	34	32	97.05%
Total	100	97	97.00%



(a) Anatomical knowledge graph



(b) Anatomical knowledge graph

Figure 7: Knowledge graphs

calculation process is shown below.

$$C_m = \phi(\widetilde{\mathbf{V}}^{main} W_q^c + \widetilde{\mathbf{V}}^{main} W_v^c + b^c) \tag{9}$$

$$A_m = \sigma(\widetilde{\mathbf{V}}^{main} W_q^a + \widetilde{\mathbf{V}}^{main} W_v^a + b^a) \tag{10}$$

$$C'_m = A_m \odot C_m \tag{11}$$

where $C_m \in \mathbb{R}^{2N \times d}$ is the "candidate change", $A_m \in \mathbb{R}^{2N \times d}$ is the "attention gate", $W_q^c, W_v^c, W_q^a, W_v^a \in \mathbb{R}^{d \times d}$, $b^c, b^a \in \mathbb{R}^d$, $\odot$ represents the element-wise multiplication, ϕ is the tanh function, σ is the sigmoid function. C'_r can be calculated similarily.

Then, guided by the prior knowledge, we calculate the attention weights a_m and a_r for the main image and the reference image respectively. The formulations are shown below:

$$a_m = \sigma(\text{FC}_2(\text{ReLU}(\text{FC}_1([\widetilde{\mathbf{V}}^{main}; \widetilde{\mathbf{V}}^{diff}; C'_m])))) \tag{12}$$

$$a_r = \sigma(\text{FC}_2(\text{ReLU}(\text{FC}_1([\widetilde{\mathbf{V}}^{ref}; \widetilde{\mathbf{V}}^{diff}; C'_r])))) \tag{13}$$

where $[;]$ represents the concatenation, FC represents fully-connected layer, σ represents the sigmoid function.

After obtaining the attention weights $a_m \in \mathbb{R}^{2N}$ and $a_r \in \mathbb{R}^{2N}$, the final image feature vector $\mathbf{l}_m$ and $\mathbf{l}_r$ for the main image and the reference image can be calculated as follows:

$$\mathbf{l}_m = \sum_{i=1}^{2N} a_{m_i} \widetilde{\mathbf{v}}_i^{main} \tag{14}$$

$$\mathbf{l}_r = \sum_{i=1}^{2N} a_{r_i} \widetilde{\mathbf{v}}_i^{ref} \tag{15}$$

where $a_m \in \mathbb{R}^{2N}$ and $a_r \in \mathbb{R}^{2N}$ are the attention weights. The difference vector is accordingly computed as:

$$\mathbf{l}_{diff} = \mathbf{l}_m - \mathbf{l}_r \tag{16}$$

A.4 Answer Generation

Dynamic Feature Generation

At each time step t, we first calculate the attention weights $\alpha_i^{(t)}$, which is for calculating the intermediate dynamic feature $l_{dyn}^{(t)}$ in the next step. The $\alpha_i(t)$ can be calculated as follows:

$$v = \text{ReLU}(W_{a_1}[l_{bef}; l_{diff}; l_{aft}] + b_{a_1}) \tag{17}$$

$$u^{(t)} = [v; h_c^{(t-1)}] \tag{18}$$

$$h_a^{(t)} = LSTM_a(h_a^{(t)} | u^{(t)}, h_a^{(0:t-1)}) \tag{19}$$

$$\alpha_i^{(t)} \sim Softmax(W_{a_2} h_a^{(t)} + b_{a_2}) \tag{20}$$

where $W_{a_1}, W_{a_2}, b_{a_1}, b_{a_2}$ are learnable parameters, $LSTM_a$ is a LSTM network used as attention weights generator, $h_a^{(t)}$ is the output of the $LSTM_a$ at the time step t, $h_c^{(t-1)}$ is the output of the answer generator $LSTM_c$ at the time step $t-1$, which will be explained in more detail later.

Then, the intermediate dynamic feature $l_{dyn}^{(t)}$ can then be calculated as follows:

$$l_{dyn}^{(t)} = \sum_i \alpha_i^{(t)} l_i \tag{21}$$

where $i \in (bef, diff, aft)$.

Before calculating the final dynamic feature $L_{dyn}^{(t)}$, POS feature $p^{(t)}$ needs to be obtained first. The POS feature is calculated from the hidden embedding of the answer $h_c^{(t-1)}$ from the last time step. The calculation can be formulated as below:

$$h_p^{(t)} = \text{ReLU}(W_{p_1} h_c^{(t-1)} + b_{p_1}) \tag{22}$$

$$w_p^{(t)} = Softmax(W_{p_2} h_p^{(t)} + b_{p_2}) \tag{23}$$

$$p^{(t)} = E_p w_p^{(t)} \tag{24}$$

where $W_{p_1}, W_{p_2}, b_{p_1}, b_{p_2}$ are learnable parameters, E_p is a learnable POS embedding matrix.

With the intermediate dynamic feature $l_{dyn}^{(t)}$ and the POS feature $p^{(t)}$, we can calculated the final dynamic feature $L_{dyn}^{(t)}$.

$$\beta_t = \sigma(W_{c_2}(\text{ReLU}(W_{c_1}[p^{(t)}; h_c^{(t-1)}; l_{dyn}^{(t)}]))) \tag{25}$$

$$L_{dyn}^{(t)} = \beta_t \odot l_{dyn}^{(t)} \tag{26}$$

where the range of β_t is $[0, 1]$, the value of it indicates how much the visual information will be used in the answer generation part.

Answer generator

The answer is generated by an LSTM network word by word. The initial word at time step 0 is the $< start >$ token.

$$c^{(t)} = [E[w^{(t-1)}]; L_{dyn}^{(t)}] \tag{27}$$

$$h_c^{(t)} = \text{LSTM}_c(h_c^{(t)} | c^{(t)}, h_c^{(0:t-1)}) \tag{28}$$

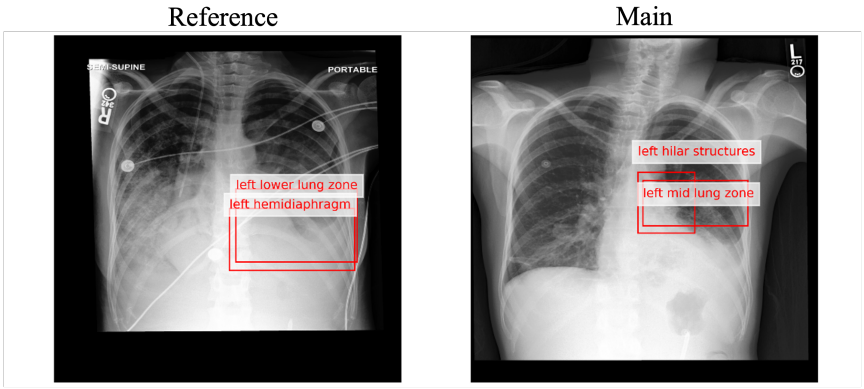
$$w^{(t)} \sim Softmax(W_c h_c^{(t)} + b_c) \tag{29}$$

where E is a word embedding layer, $E[w^{(t-1)}]$ is the word embedding for the word $w^{(t-1)}$, W_c, b_c are learnable parameters.

We adopt the generative language model because our questions have highly diverse answers. (e.g. the *difference* type question). A simple classification model is not adequate for our task.

A.5 VISUALIZATION

As shown in Fig. 8, when asking about pleural effusion, which is an abnormality that happened in the lower lung when there is excess fluid between the layers of the pleura outside the lungs, our method highlighted the corresponding regions (left lower lung). Also, by focusing on these regions, our method can accurately determine the change in the level of pleural effusion between the main and reference image. In Fig. 9, our method also highlighted cardiac silhouette, this could because of the strong semantic relationship between cardiomegaly and pleural effusion as mentioned in Section. 3 and Fig. 3a.

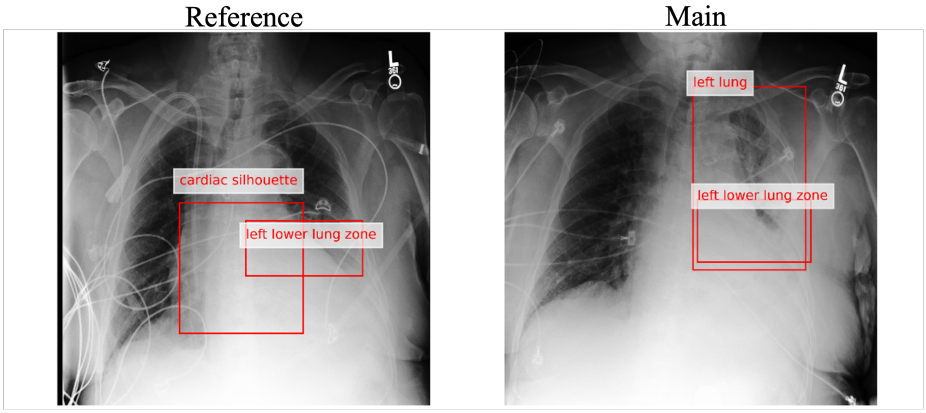


Question: what has changed in the left lung area?

GT Answer: the level of pleural effusion has changed from moderate small to small.

Prediction: the level of pleural effusion has changed from moderate small to small.

Figure 8: Visualization example 1



Question: what has changed in the left lung area?
GT Answer: the level of pleural effusion has changed from moderate to small.
Prediction: the level of pleural effusion has changed from moderate to small.

Figure 9: Visualization example 2