

# Beyond Diagnosis: Evaluating Multimodal LLMs for Pathology Localization in Chest Radiographs

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## Abstract

Recent work has shown promising performance of frontier large language models (LLMs) and their multimodal counterparts in medical quizzes and diagnostic tasks, highlighting their potential for broad clinical utility given their accessible, general-purpose nature. However, beyond diagnosis, a fundamental aspect of medical image interpretation is the ability to localize pathological findings. Evaluating localization not only has clinical and educational relevance but also provides insight into a model’s spatial understanding of anatomy and disease. Here, we systematically assess two general-purpose MLLMs (GPT-4 and GPT-5) and a domain-specific model (MedGemma) in their ability to localize pathologies on chest radiographs, using a prompting pipeline that overlays a spatial grid and elicits coordinate-based predictions. Averaged across nine pathologies in the CheXlocalize dataset, GPT-5 exhibited a localization accuracy of 49.7%, followed by GPT-4 (39.1%) and MedGemma (17.7%), all lower than a task-specific CNN baseline (59.9%) and a radiologist benchmark (80.1%). Despite modest performance, error analysis revealed that GPT-5’s

predictions were largely in anatomically plausible regions, just not always precisely localized. GPT-4 performed well on pathologies with fixed anatomical locations, but struggled with spatially variable findings and exhibited anatomically implausible predictions more frequently. MedGemma demonstrated the lowest performance on all pathologies, showing limited capacity to generalize to this novel task. Our findings highlight both the promise and limitations of current MLLMs in medical imaging and underscore the importance of integrating them with task-specific tools for reliable use.

## 1. Introduction

As AI advances from task-specific to generalist models, there is growing interest in evaluating frontier models in medicine, including in medical imaging with the rise of multimodal large language models (MLLMs). Recent studies assessing GPT-4, a pioneering MLLM, on imaging-based quizzes and diagnostic tasks have yielded mixed results (Hayden et al., 2024; Brin et al., 2024; Strotzer et al., 2024; Zhou et al., 2024; Suh et al., 2024; Eriksen et al., 2023). For instance, Suh et al. (2024) reported that GPT-4 achieved clinical-level performance on *NEJM*

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*Image Challenges*, a multiple-choice, VQA dataset; however, Jin et al. (2024) found that the model’s rationale for its choices were often flawed. Given the clinical potential of accessible, general-purpose MLLMs, these findings highlight the need to evaluate their performance across diverse tasks and to move beyond diagnostic accuracy toward a deeper understanding of their reasoning. Furthermore, it remains unclear if domain-specific MLLMs are required to address the challenges of general purpose models, or whether these challenges can instead be overcome with newer model versions.

A fundamental aspect of medical image interpretation is not only providing a diagnostic impression but also localizing findings associated with a diagnosis. In computer vision, diagnosis is typically framed as a classification task, whereas localization is approached through segmentation or bounding-box generation (i.e., detection) over relevant regions. In medical AI systems, these two tasks are treated as distinct regulatory categories: computer-aided diagnosis (CADx) for classification and computer-aided detection (CADe) for localization (McNamara et al., 2024). Critically, an AI model may perform well at classification, but struggle with precisely localizing the associated findings, or conversely struggle with distinguishing whether a finding is benign or pathological, but excel at identifying its location. While recent studies have evaluated the diagnostic performance of MLLMs, their ability to localize pathological findings (e.g., CADe) remains largely unexplored. Beyond potential clinical applications, evaluating MLLMs in localization tasks could provide insights into their underlying clinical intuition and medical knowledge.

In this study, we systematically evaluate the ability of three MLLMs to localize pathologies on chest radiographs: two generalist models (GPT-4 (OpenAI, 2024) and GPT-5 (OpenAI, 2025)) and a domain-specific model (MedGemma (Sellergren et al., 2025)). To do so, we develop a prompting strategy that overlays a grid on the image and asks the model to predict coordinates corresponding to the pathology’s location. We assess performance using the CheXlocalize (Saporta et al., 2022) dataset, benchmarking against radiologists and a task-specific CNN model. To further explore the models’ medical understanding, we analyze the distribution of predicted locations for each pathology and categorize mislocalized cases based on their clinical plausibility. By moving beyond classification tasks, our analysis provides insights into

the spatial reasoning abilities of MLLMs in medical imaging, highlighting both strengths and limitations.

## 2. Related Work

Several recent studies have assessed general-purpose MLLMs such as GPT-4 in medical image interpretation (Jin et al., 2024; Hayden et al., 2024; Brin et al., 2024; Strotzer et al., 2024; Zhou et al., 2024; Suh et al., 2024; Eriksen et al., 2023). On 190 cases from the *Diagnosis Please* challenge, Suh et al. (2024) found that GPT-4 achieved diagnostic performance comparable to radiologists. GPT-4 also demonstrated strong accuracy on the *NEJM Image Challenges*, a multiple-choice diagnostic quiz for medical professionals (Jin et al., 2024; Eriksen et al., 2023). However, Jin et al. (2024) reported that while GPT-4 performed well on these tasks, its rationales were often flawed when explicitly prompted to explain its reasoning. On multiple-choice questions from the *American College of Radiology Diagnostic Radiology In-Training Examination*, GPT-4 achieved high accuracy on text-only questions (81.5%) but struggled with image-based ones (47.8%). Its diagnostic accuracy on real-world radiologic imaging cohorts has also shown considerable variability (Strotzer et al., 2024; Brin et al., 2024; Zhou et al., 2024).

## 3. Methods

While prior research has focused primarily on the diagnostic capabilities of MLLMs, our study examines spatial localization accuracy for pathologies in medical images that the models are explicitly prompted to recognize. We utilize chest radiographs from CheXlocalize (Saporta et al., 2022), a subset of the CheXpert (Irvin et al., 2019) dataset annotated with pixel-level masks for each of its classes. We focus on this task because it serves as both a common benchmark for medical AI and a clinically important application. Figure 1 contains an overview of the approach.

### 3.1. CheXlocalize Dataset

The CheXlocalize dataset includes chest radiograph images collected from Stanford Hospital in both inpatient and outpatient settings (Irvin et al., 2019). The dataset contains expert radiologist annotations for the localization of 10 distinct findings (Saporta et al., 2022). These ground-truth annotations come in the form of pixel-wise segmentation maps, enabling

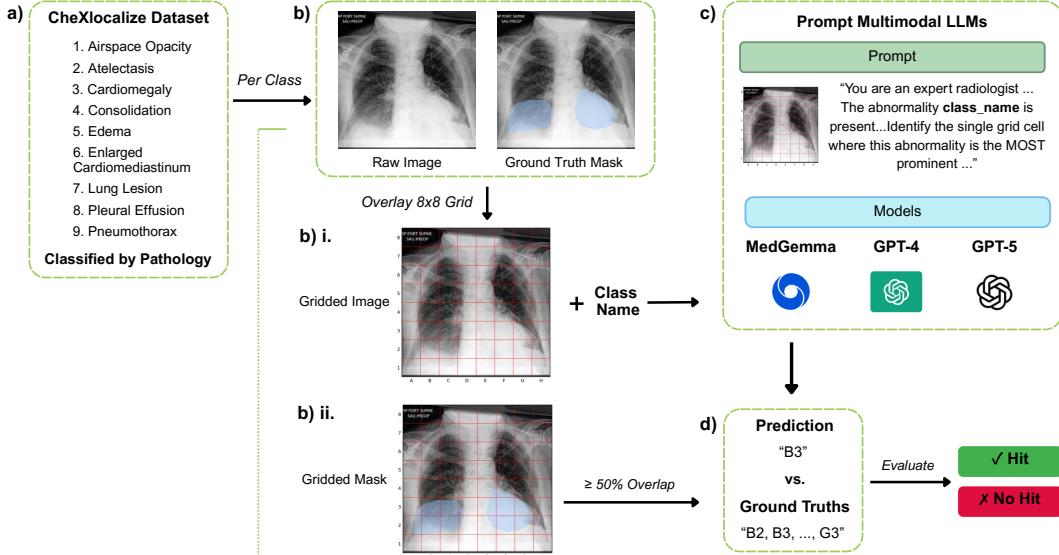


Figure 1: Study Overview. a) The nine pathologies in the CheXlocalize dataset were utilized. b) For each pathology class, a gridded image was produced for each radiograph where the pathology was present. c) Three multimodal LLMs were prompted to identify the grid cell where the stated pathology is most prominent. d) The predicted grid cells were compared to the ground truth cells, defined as cells with  $\geq 50\%$  overlap with the ground truth mask.

precise benchmarking. The validation and test splits of this dataset consist of 234 radiographs from 200 patients and 668 radiographs from 500 patients, respectively. Here, we use the validation split for initial experimentation and report final results using the test split. The image counts by pathology and view position in the validation and test splits are contained in the Appendix.

The 10 classes annotated in CheXlocalize are Atelectasis, Cardiomegaly, Consolidation, Edema, Enlarged Cardiomediastinum, Lung Lesion, Lung Opacity, Pleural Effusion, Pneumothorax, and Support Devices. In this work, we include the first 9 classes, excluding Support Devices to focus exclusively on pathology localization. Our evaluation encompasses both frontal (anterior-posterior and posterior-anterior) and lateral view radiographs available in this dataset for a comprehensive assessment. We compare our results on the test split to an expert human benchmark and a convolutional neural network (CNN) baseline reported alongside the dataset in Saporta et al. (2022). Both the ground truth annotations and the human benchmarking assessment were performed by radiologists, where the benchmarking effectively quantifies a performance ceiling

of inter-reader variability. Specifically, ground truth annotations were performed by two board-certified radiologists. Three separate radiologists then also performed annotations, which were compared to the ground truth annotations to create the human performance benchmark. The CNN baseline consists of a DenseNet121 (Huang et al., 2017) classification model trained on CheXpert. Localization predictions were obtained through a GradCAM-based (Selvaraju et al., 2017) saliency pipeline. As detailed below, we compare the MLLMs to the ‘hit rate’ performance metric for the human and CNN benchmarks, which was quantified by Saporta et al. (2022) as whether the most representative point identified by the CNN saliency method or human benchmark annotations fell within the ground truth segmentation.

### 3.2. Prompting Technique

To evaluate MLLM localization capabilities, we designed a structured prompting pipeline by which each chest radiograph was digitally overlaid with a standardized grid. The grid divided each image into equally-sized cells, labeled alphanumerically to facilitate text-based spatial referencing. To do so, each radiograph image was first centrally cropped and re-

sized to  $256 \times 256$  pixels, a common pre-processing strategy for computer vision models. The MLLM was then tasked with identifying the specific grid cell that was most representative of the given pathology. For the core results, we use an  $8 \times 8$  grid overlay ( $32 \times 32$  pixels per cell), which was chosen to balance the resolution size with the typical size of the pathology masks. Analysis using a higher resolution grid ( $16 \times 16$  cells) is also presented in the Appendix for sensitivity analysis.

We used the same prompt for all MLLMs, which asked the model to identify the pathology location by picking the most representative grid cell. The prompt explicitly stated that the given pathology was present in the image to make localization, not identification, the sole objective (see Appendix for full prompt). Because a single radiograph could exhibit multiple pathologies, we generated separate copies of each image for every present pathology and performed individual queries for each pathology-image pair. This approach enabled independent evaluation of localization performance for each pathology.

### 3.3. Evaluation Metrics

Performance evaluation was based on a ‘hit rate’ criterion. A prediction (represented by a single grid cell returned by the MLLM) was considered a ‘hit’ if at least 50% of the grid cell overlapped with the ground truth segmentation provided in the CheXlocalize annotations for the queried pathology. Predictions falling below this overlap threshold were classified as misses. In the rare scenario where the ground truth mask contained no cells with  $\geq 50\%$  overlap (4.4% of all images), the prediction was deemed a hit if the cell contained any amount of ground truth mask. This could occur, for instance, if the segmentation mask was very small. Our defined hit rate metric enables meaningful comparison with the results reported by Saporta et al. (2022), which similarly employed a pointing game methodology for their human benchmark that awarded credit when the identified representative point fell within the ground-truth segmentation region. We report the average hit rate for each pathology and MLLM, alongside standard deviation error bars using bootstrapping (1,000 samples).

### 3.4. Models

GPT-4 and GPT-5 were executed using the OpenAI API. The model version for GPT-4 was gpt-4o-2024-05-13, configured at a temperature of

0 for reproducibility. The model version for GPT-5 was not obtainable via the API, but it was run within a month of its release on 2025-08-07, and the only relevant configurable parameter available was the reasoning effort, which was kept at the default level of medium. MedGemma was executed locally on 2 H100 GPUs using the Ollama platform. The 27B, instruction-tuned variant was used (accessed via puyangwang/medgemma-27b-it:q8). The temperature for MedGemma was left at a default value of 0.8, as it was found that a value of 0 resulted in almost no variability in the predicted grid cells.

## 4. Results

### 4.1. Hit Rate Performance

Figure 2 summarizes the hit rate performance of the MLLMs compared to the results reported by Saporta et al. (2022), consisting of an expert human (radiologist) benchmark and a convolutional neural network (CNN) baseline. A random baseline is also presented, which reflects the expected performance if cell selections were made uniformly at random over the grid.

Between the three MLLMs, GPT-5 had the highest average hit rate across pathologies (49.7%), followed by GPT-4 (39.1%), and MedGemma (17.7%). All models underperformed the CNN baseline and human benchmark on average, which showed 59.9% and 80.1% average hit rates across pathologies, respectively. The average random baseline across pathologies with 11.9%, indicating that MedGemma performed only marginally above chance.

Different trends were observed for different pathologies. GPT-4 and GPT-5 both outperformed the CNN baseline on enlarged cardiomegaly (hit rate of 92.3% for GPT-4, 89.6% for GPT-5, 49.8% for CNN) and cardiomegaly (hit rate of 89.1% for GPT-4, 72.0% for GPT-5, and 50.7% for CNN). GPT-5 showed the greatest improvements ( $\geq 20\%$  higher hit rates) over GPT-4 on atelectasis, consolidation, edema, and pleural effusion, though it still underperformed the CNN baseline on these pathologies. MedGemma exhibited the lowest performance on every pathology, with its largest margin over chance occurring for cardiomegaly. These overall findings were robust to the resolution of the grid overlay, where halving the size of each cell showed similar patterns (Appendix Figure 6).

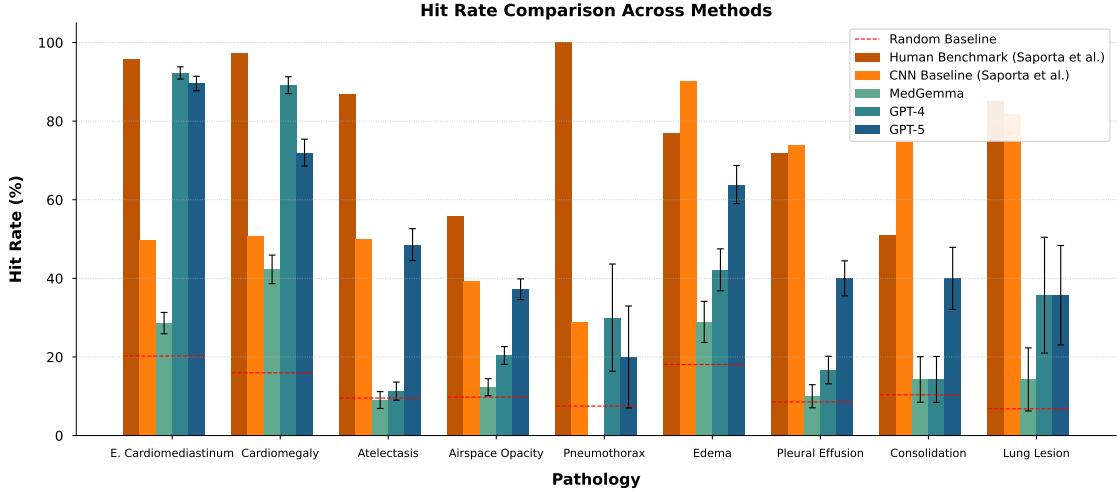


Figure 2: Hit rate by pathology. Pathologies are ordered by the relative performance difference between GPT-5 and the CNN baseline. Error bars represent standard deviation via bootstrapping.

#### 4.2. Error Categorization

To gain insights into the MLLMs’ performance and general medical understanding, each miss for the three MLLMs was qualitatively reviewed by a radiologist and categorized into three distinct error types:

- **Partial hit:** Predicted cell partially overlapped ( $\leq 50\%$ ) with the ground truth annotation.
- **Position error:** Predicted cell overlapped with anatomically plausible but incorrect regions for the pathology.
- **Anatomy error:** Predicted cell was anatomically implausible for the given pathology, suggesting a potential misunderstanding of chest anatomy and/or the pathology.

For consistency, the error analysis was only performed on frontal radiographs, which represent 87% of images in the test set. If a model produced more than 50 complete misses for a given pathology, only 50 were reviewed, and the proportion of position versus anatomy errors was estimated from this subset.

The breakdown of the MLLM predictions by error category is displayed in Fig. 3. For the two pathologies where GPT-4 and GPT-5 both outperformed the CNN (enlarged cardiomegaly and cardiomegaly), the majority of misses were still partial hits for both models. The distribution of error categories varied more widely for the other pathologies. Despite an moderate average ‘full hit’ rate, only

6.3% of GPT-5’s predictions represented an ‘anatomy error’ on average across pathologies, indicating that the majority of misses were either a partial hit or at least corresponded to a plausible anatomical region. GPT-4 exhibited a higher rate of anatomy errors (18.0% on average), with MedGemma exhibiting the most (29.9% on average). For both GPT-4 and GPT-5, the highest percentages of anatomy errors were observed for pleural effusion and pneumothorax, indicating that the models’ predictions were relatively often localized to an incorrect anatomical structure (i.e., non-lung regions) for these pathologies.

#### 4.3. Visualization of Predictions

Heatmaps of the models’ predictions per pathology help explain the error patterns and GPT-5’s higher performance (Fig. 4, 7, 8). The heatmaps are visualized over the average image across the test set and are computed for frontal views. For cardiomegaly (Fig. 4), GPT-4 consistently predicted central grid cells. As cardiomegaly indicates an enlarged heart and the heart tends to appear towards the center of the image, the prediction heatmap aligns with the high performance of GPT-4 for this pathology. GPT-5 also predicted central grid cells for cardiomegaly, but demonstrated more variability that aligns with the ground truth distribution. Edema, indicating fluid in the lungs, can vary more widely in its spatial position, though it often appears in the medial regions of the lungs at the site of highest pulmonary

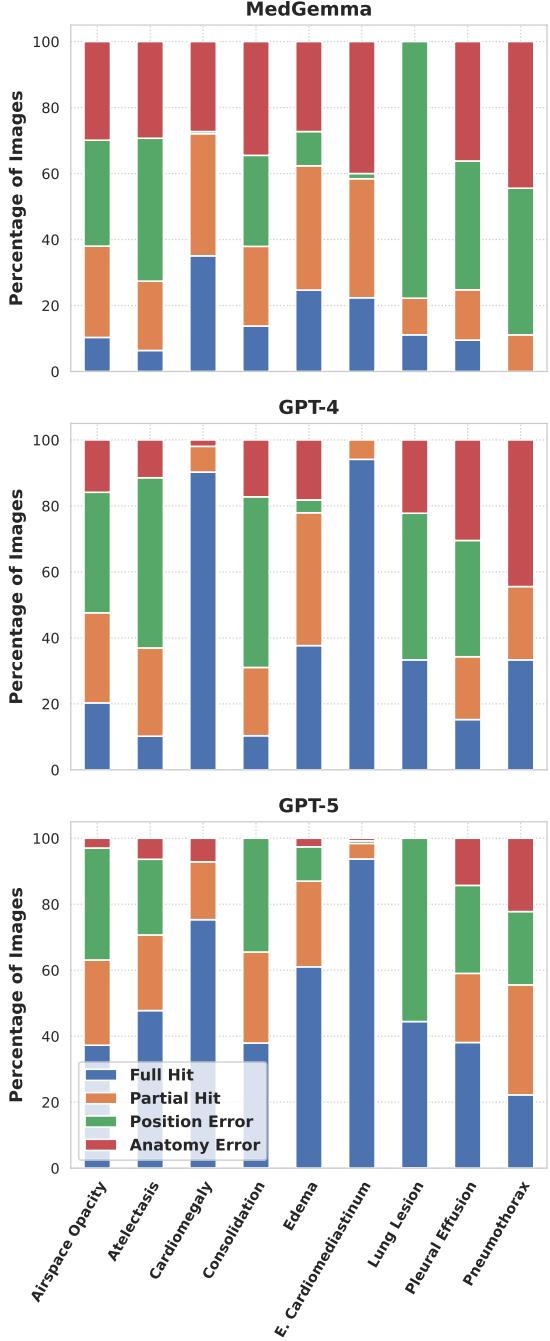


Figure 3: Error categorization. Each prediction on a frontal radiograph was categorized as a full hit ( $\geq 50\%$  overlap), partial hit ( $0 < \text{overlap} < 50\%$ ), position error (no overlap but plausible anatomy), and anatomy error (implausible anatomy).

vascular density. For this pathology, GPT-4 consistently predicted a central grid cell, often overlaying the heart/mediastinum (Fig. 4), whereas GPT-5’s predictions were more distributed over the lungs, explaining its higher performance on this pathology. In general, the heatmaps of GPT-5 more faithfully represented the ground truth pathology, explaining its relatively low percentage of anatomy errors (Fig. 7, 8).

Examining anatomy errors on an individual image basis revealed a spectrum of model misunderstanding. GPT-5 exhibited no anatomy errors for consolidation, which is a pathology that localizes to the lungs, but GPT-4 and MedGemma sometimes predicted grid cells overlaying the heart/mediastinum (Figure 5). However, a dramatic error for GPT-5 is displayed in Figure 5, wherein both GPT-5 and GPT-4 predicted the shoulder as the location of a pneumothorax (collapsed lung).

## 5. Discussion

Beyond diagnosis, we evaluated the ability of MLLMs to localize findings in chest radiographs. We found that performance was mixed, with GPT-4 and GPT-5 outperforming a domain-specific CNN baseline on two pathologies, but underperforming the CNN and human benchmark overall. Notably, these two pathologies tend to appear in consistent anatomical locations. Nonetheless, GPT-5 showed strong improvements compared to GPT-4 on the more spatially variable pathologies, and its predictions were largely anatomically plausible even when it did not precisely localize the pathology. MedGemma, a medicine-specific model that includes chest radiographs in its training, exhibited the lowest performance overall and had a high proportion of anatomically-impractical predictions.

Our findings have several implications for clinical practice and AI development. First, while (M)LLMs have recently shown strong performance on question-answer challenges and diagnostic tasks (Eriksen et al., 2023; Suh et al., 2024; Nori et al., 2023), our results show that leading models struggle with fine-grained spatial reasoning. As a smaller model, MedGemma may especially be limited in the ability to generalize to novel tasks compared to traditional benchmarks used in the field. However, the improvements in accuracy and medical understanding observed with GPT-5 compared to GPT-4 are encouraging. While it remains to be seen whether these gains will continue

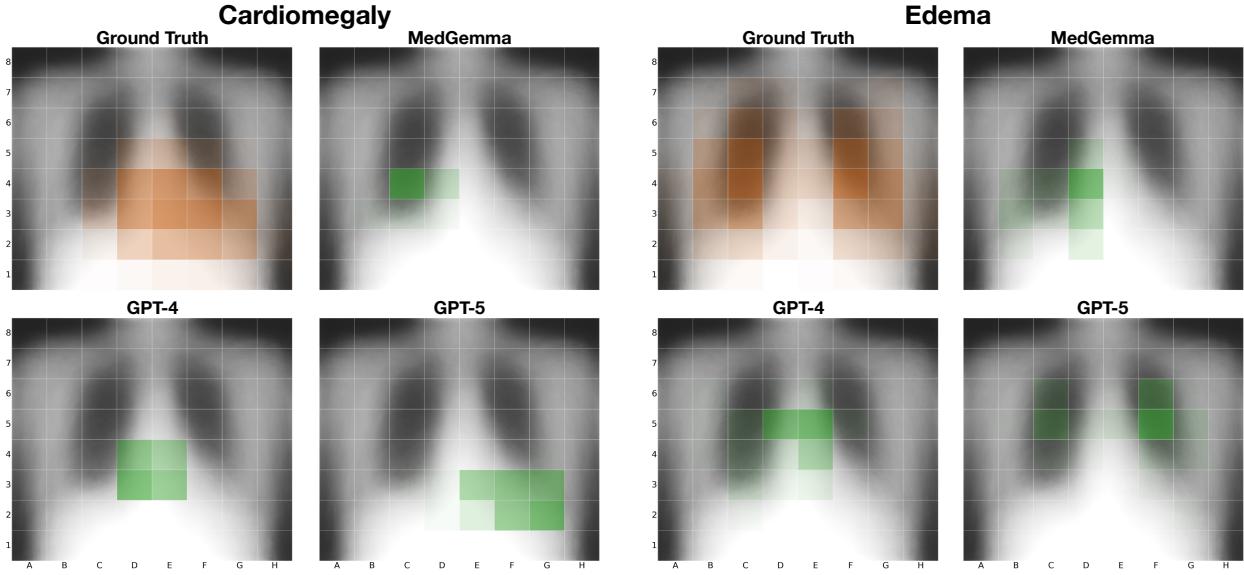


Figure 4: Example ground truth and prediction heatmaps. The heatmaps are computed over the frontal radiographs in the test set and are overlaid on the average image.

to occur with future model versions, these results at least suggest that large, general-purpose MLLMs are a promising approach compared to domain-specific vision-language models. In the meantime, agentic strategies that integrate the flexibility of LLMs with task-specific tools may be the best strategy, where recent work in the context of chest radiograph interpretation has demonstrated this possibility (Fallahpour et al., 2025).

**Limitations** Our study has several limitations. Our analysis focused on one dataset given the need for localized annotations and meaningful benchmark comparisons. Future work could extend our analysis pipeline to other datasets and tasks. Furthermore, some pathologies in the CheXlocalize dataset have a small image count, leading to large error bars for the results for those pathologies. Another challenge lies in the variability of ground truth annotation sizes across images and pathologies, which makes it difficult to define a hit rate metric that robustly captures all scenarios. Additionally, while interpretable, hit rate metrics sacrifice the flexibility and granularity offered by other localization metrics, such as IoU. Finally, although our goal was to assess default out-of-the-box performance on the proposed task, more extensive prompt engineering could be explored in the future.

**Conclusion** Systematically evaluating foundation models will be increasingly important as AI is integrated into clinical settings. Beyond our current findings, the proposed analysis pipeline can be leveraged to probe the spatial reasoning of foundation models more broadly. A deeper understanding of the strengths and limitations of emerging models will be essential for guiding algorithm improvements and ensuring safe, effective clinical use.

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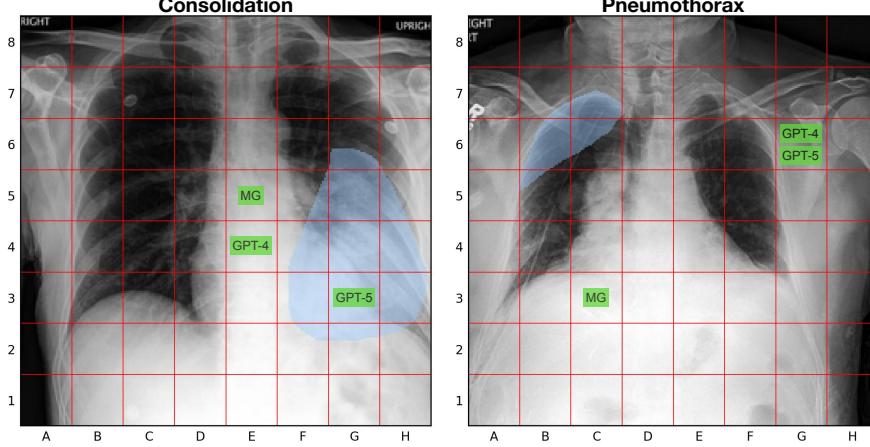


Figure 5: Example anatomy errors. a) A consolidation example where GPT-5 is correct but GPT-4’s prediction overlays the heart/mediastinum. b) A pneumothorax example where both GPT-4 and GPT-5 predictions overlay the shoulder instead of the lungs.

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## Appendix

### Prompt

**System:** You are an expert chest radiologist specializing in analyzing {view} chest X-rays. Your task is to precisely localize abnormalities using a grid overlay.

**User:** [Image]

This is a gridded {view} view of a chest X-ray. The abnormality ‘{condition}’ is confirmed to be present in this image. Your task:

1. Identify the single grid cell where this abnormality - ‘{condition}’ is the MOST prominent.
2. Provide only the grid coordinate for this most representative cell. A grid coordinate is defined as a letter followed by a number. If the abnormality spans multiple cells, choose the cell that is most representative.
3. Do not include any explanations or additional text in your response.

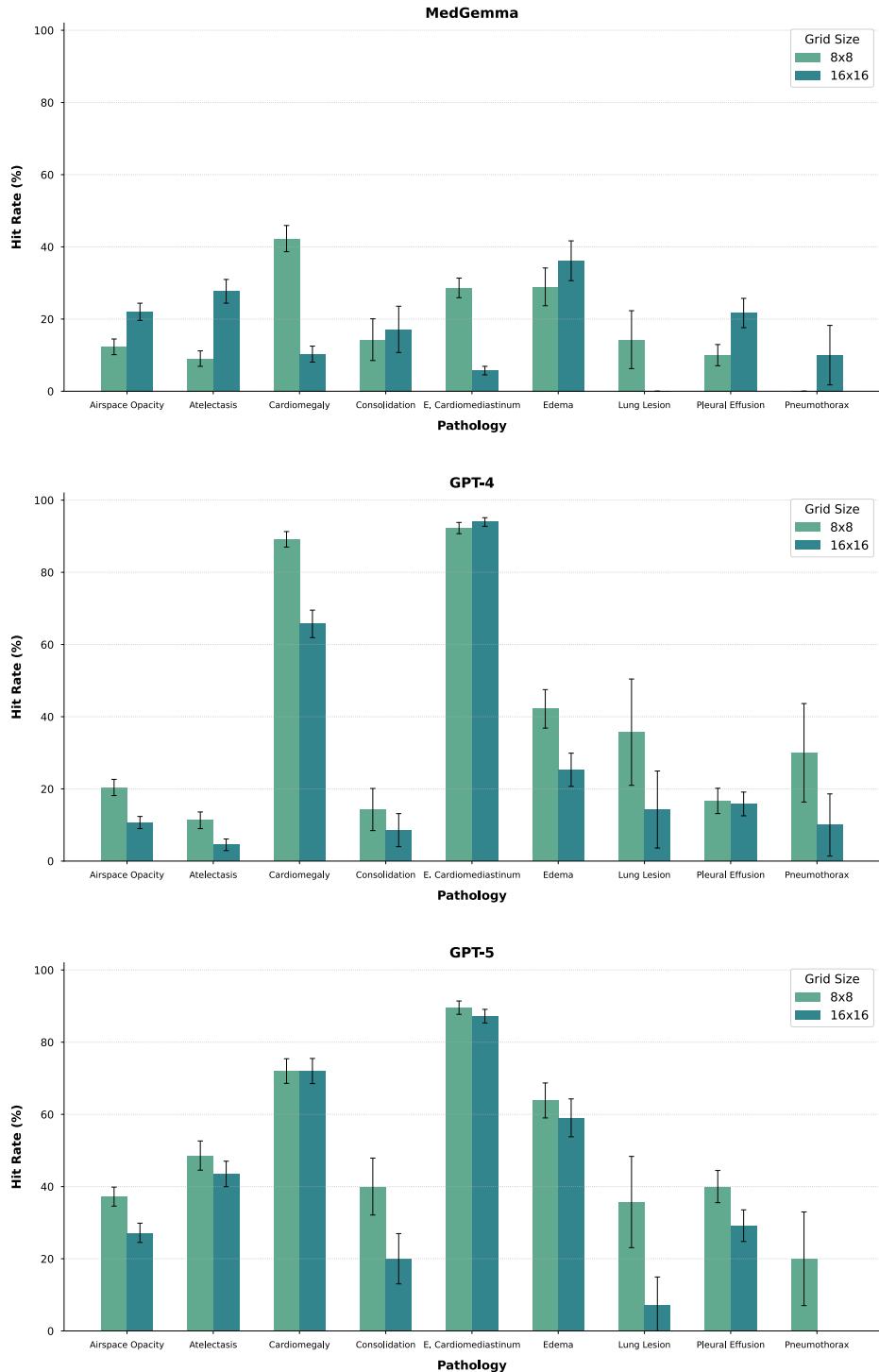


Figure 6: Performance by grid size. An 8x8 grid size was used for the main analysis. A higher resolution grid size (16x16) showed similar patterns between models and did not increase performance.

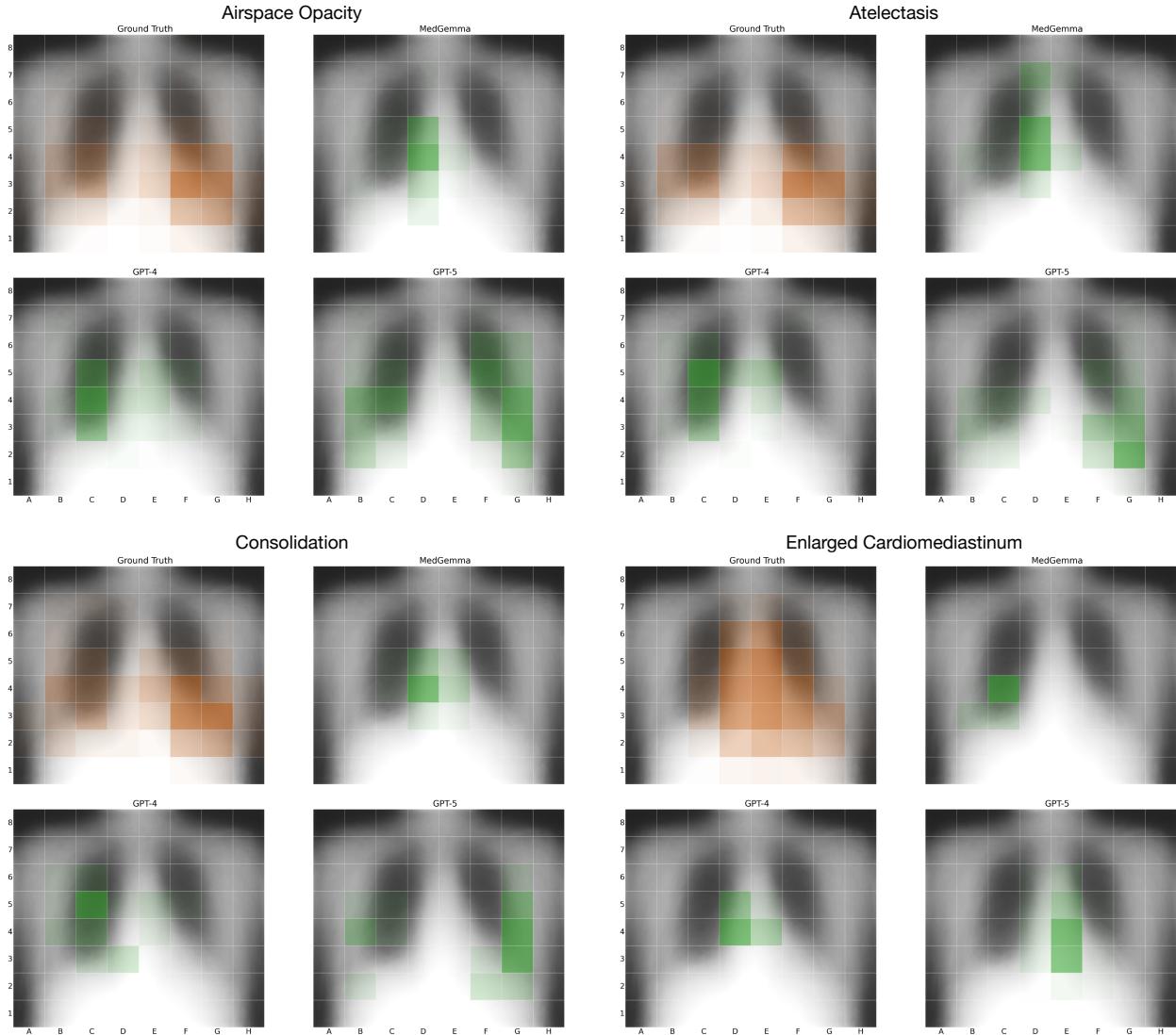


Figure 7: Ground truth and prediction heatmaps. The heatmaps are computed over the frontal radiographs in the test set and are overlaid on the average image.

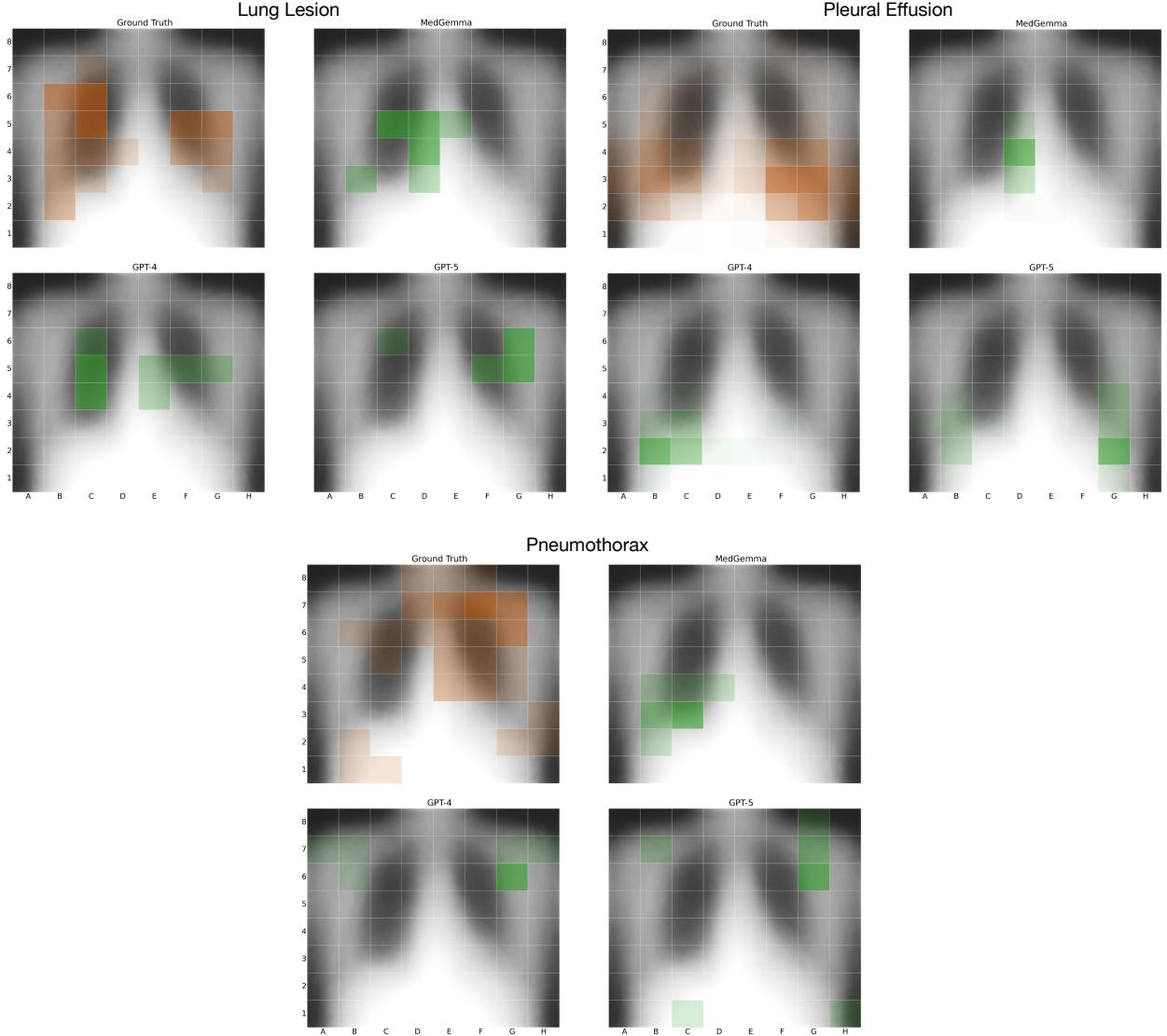


Figure 8: Ground truth and prediction heatmaps. The heatmaps are computed over the frontal radiographs in the test set and are overlaid on the average image.

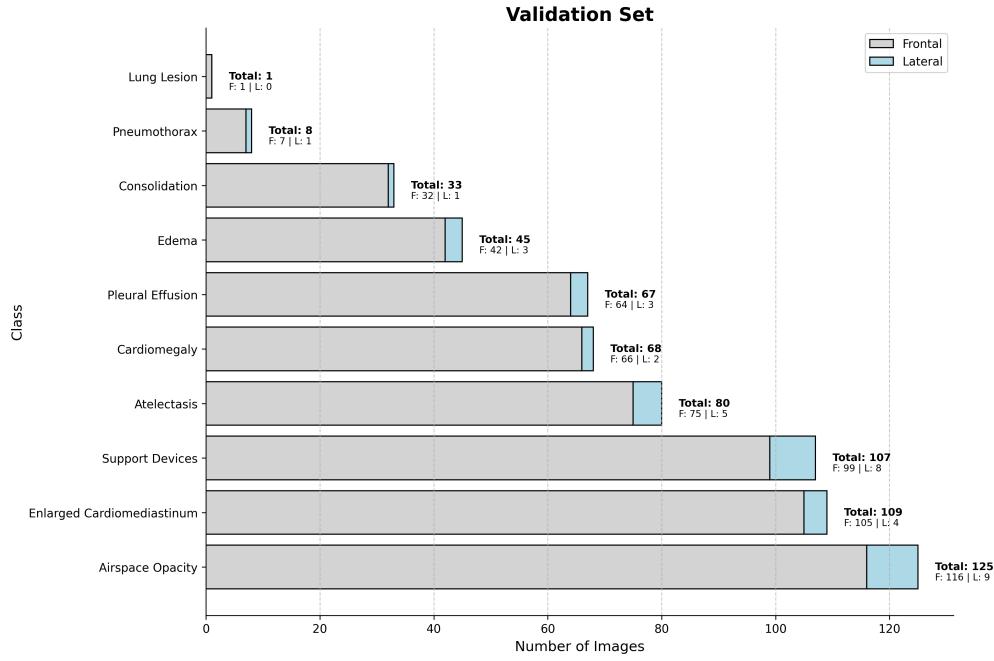


Figure 9: Image counts in CheXlocalize Validation Set.

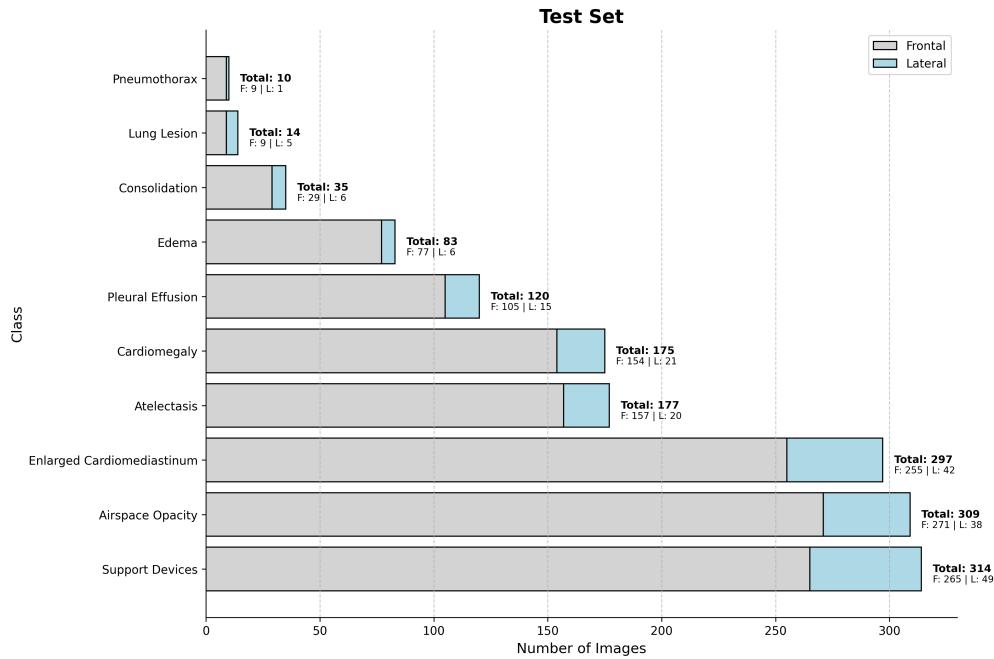


Figure 10: Image counts in CheXlocalize Test Set.