Quilt-LLaVA: Visual Instruction Tuning by Extracting Localized Narratives from Open-Source Histopathology Videos

Supplementary Material

1. QUILT-INSTRUCT and QUILT-VQA

1.1. Total Cost

We used GPT-4 to create the QUILT-INSTRUCT dataset, spending \$8858 in total where \$6600 is spent on input tokens and \$2204 on output tokens, and \$54 on evaluations. In detail, Complex Reasoning yielded 25,838 Q/A pairs, with an average of 13.16 words per question and 267 words per answer. Detailed Descriptions produce 39,620 samples, each having 11.91 words per question and 130.2 words per answer. For Conversations, we generated 34,242 rows, with an average of 3.51 Q/A pairs per row, totaling 44.74 words for questions and 221 words for answers. Finally, for Iterative Abductive Reasoning, there are 14,642 rows with multiple Q/A pairs, averaging 2.84 Q/A pairs per row, comprising 91.94 words per question and 201 words per answer. Furthermore, we spent \$140 on generating 1283 samples in QUILT-VQA with an average of 10.43 words per question and 19.16 words per answer. This results in \$8998 total cost.

Algorithm 1 Stable Video Chunk Detection Algorithm

```
1: procedure DETECTSTATICFRAMES(video, starttime, endtime)
 2:
        video = video[starttime:endtime]
 3:
        fixedFrames \leftarrow \emptyset
4:
5:
6:
7:
8:
9:
10:
        ValidFrames \leftarrow \emptyset
        prevFrame \leftarrow first frame in video
        for frame \in rest of frames in video do
           absDiff \leftarrow absolute difference between frame and prevFrame
           absDiffThresh \leftarrow apply adaptive thresholding to absDiff
            meanVal \leftarrow mean value of absDiffThresh
            if meanVal < 10 then
10:
11:
12:
13:
14:
                fixedFrames \leftarrow fixedFrames \cup frame
            else
                if length of fixedFrames \geq minimum duration then
                    subclip \leftarrow extract sub-clip of frames with
15:
                        constant background from fixedFrames
16:
17:
                    for randomly sampled patch \in each frame of subclip do
                        SSIMVal \leftarrow calculate SSIM of patch
18:
                        if SSIMVal > threshold then
19:
20:
21:
22:
                            ValidFrames \leftarrow ValidFrames \cup frame
                        end if
                    end for
                end if
23:
24:
25:
                 fixedFrames \leftarrow \emptyset
             end if
            prevFrame \leftarrow frame
26:
        end for
27:
        staticTimestamps \leftarrow get start \& end times from ValidFrames
28
        return \ staticTimestamps
29: end procedure
```

1.2. Prompts

Figures 5, 6, 7, 8, and 9 demonstrate the prompts used for generating conversational, detailed description, com-

plex medical reasoning, and iterative abductive reasoning (assistant and student) Q/A pairs in QUILT-INSTRUCT, respectively. In addition, Figure 10 includes the prompt used to extract the diagnosis and supporting facts from single WSI cases. Figure 11 shows the propmt used for generating QUILT-VQA, our evaluation set described in 4.2. And finally, Figure 12 shows the prompt used for evaluating the conversational chat abilities of QUILT-LLAVA using GPT-4.

2. Use Case and Limitations

2.1. Use Case of QUILT-LLAVA

Despite our best efforts, QUILT-LLAVA still produces erroneous information, meaning it cannot be fully trusted as an automated diagnostic tool. Instead, it should serve as a support tool for pathologists or other medical professionals who are familiar with the field, enabling them to correct or revise QUILTNET's responses. Additionally, since QUILT-LLAVA is capable of reasoning beyond its immediate context, it could assist medical practitioners in challenging cases where they might be at an impasse. Furthermore, thanks to its Iterative Abductive Reasoning-based Q/A data, QUILT-LLAVA can function as a brainstorming tool. Rather than providing immediate answers, it can offer hints, which is particularly beneficial for pathology students or junior pathologists looking to learn and develop their skills. An example is given in Fig. 16.

2.2. QUILT-INSTRUCT and QUILT-VQA Limitations

Limitations of Hand-Crafted Video Processing Algorithms. When aligning narrators' speech with images, there can be instances where the narrator discusses something irrelevant or refers to previously observed matters, potentially resulting in unaligned image-text pairs. However, our empirical observations indicate that these occurrences are rare. Also, the images extracted from the video might inherently contain noise, such as artifacts like text, drawings, faces of the narrators', etc., as illustrated in Fig. 20. Additionally, in some cases, the patient's medical history, race, gender, etc., are mentioned in the videos, which may or may not be inferred from the aligned image. Moreover, the clustering algorithm relies on simple rules and thresholds, which may not yield the optimal clustering for some cases. Finally, our dataset currently includes only English, limiting the QUILT-LLAVA to operating in just a single language.

Limitations of Generating OUILT-INSTRUCT Using LLMs. As we derive visual instruction tuning data from captions using GPT-4, we inevitably inherit its biases and limitations. Additionally, there are instances where GPT-4 does not fully adhere to commands instructing it to generate Q/A datasets as if it were directly observing the image; instead, it sometimes produces responses that reference the description, generating phrases that state "it is mentioned in the description, etc.". Moreover, despite being provided with spatially grounded captions, GPT-4 may occasionally overlook this information, resulting in data that lacks spatial context. Most critically, GPT-4 is still prone to generating inaccurate information, leading to instances of QUILT-LLAVA producing incorrect statements or hallucinations (Please see Failure Cases in Section 4.1). Regarding legal matters, our commitment to making our dataset publicly available requires strict adherence to OpenAI's terms. These terms clearly stipulate that the QUILT-INSTRUCT is to be utilized exclusively for research purposes.

Limitations of Generating QUILT-VQA Using LLMs. Limitations of QUILT-VQA also encompass those mentioned for QUILT-INSTRUCT above. In addition, despite padding chunks with question marks to ensure that answers fall within the context, there remain cases where narrators provide answers to these questions far beyond the chunk's timeframe. This can lead to instances where the answers are not adequately captured.

2.3. Visual Prompting Details and Limitations

The ellipses are drawn in red \bigcirc , with their size set to 0.05% of the largest dimension of the image, as recommended by [22].

In our visual prompt testing, we used red, which may not stand out against the purple-pink hues common in histopathology images as seen in Figure 17. For better contrast, future work could explore other colors like green or blue, similar to the inks used by pathologists to mark regions of interest in WSIs.

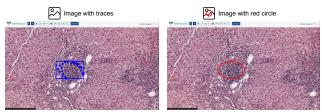


Image Description: this particular portal area looks busy. When I go there, see the lymphoid aggregate is not too large, right? It's a small lymphoid aggregate. But for instance, the time [0.33, 0.45, 0.51, 0.65]

Figure 17. A sample of visual prompting w/ drawing a red circle around the clustered traces.

Category	Details and Example
Wrong answers	PathVQA includes questions with wrong answers.
	E.g., Q: Did early ischemic injury increase eosinophilia?
	A: No. (Correct answer is "Yes" according to Figure 1-9 in [2].)
Inconsistent Q/A pairs	PathVQA has similar questions with inconsistent answers.
	E.g., Q: Does early ischemic injury show surface blebs, increase eosinophilia of cytoplasm, and swelling of occasional cells?
	A: Yes. (Contradicts with example in "Wrong answers".)
Ambiguous ques- tions	PathVQA includes ambiguously phrased questions. The question below starts with "What is showing" and the answer provides a diagnosis. The question should have been more clear as "what is the diagno- sis of" or "what has the following symptoms?"
	E.g., Q: What is showing increased eosinophilia of cytoplasm?
	A: early (reversible) ischemic injury.
Repetitive Q/A pairs	Both PathVQA and PMC-VQA generate multi- ple Q/A pairs for a single image-text pair, lead- ing to repetition. E.g., two different questions in PathVQA about early ischemic injury. (Refer to examples in "Wrong answers" and "Inconsistent Q/A pairs".)
General-domain Q/A pairs	Most VQA datasets focus on general-domain biomedical questions. E.g., PMC-VQA is gen- erated from PubMed articles and we extracted a histopathology subset from it for evaluation purposes. In addition, PathVQA includes many non-histopathology images.

Table 8. Summary and examples of issues in public VQA datasets.

3. Visual Question Answering

Visual Question Answering Datasets for Histopathology

3.1. PathVQA

[7] is a dataset of 32799 question-answer pairs extracted from 4998 pathology image-caption pairs within textbooks and digital libraries. The questions are categorized as openended and closed-ended questions where the former consists of what, where, when, whose, how, how much/how many questions and the latter includes yes/no questions. We use 6761 samples from the evaluation set.

3.2. PMC-VQA

[31] version-2 includes a test set of 34823 VQA pairs of non-compound images that cover various modalities or diseases. This dataset was curated from image-caption pairs in PMC-OA articles and are in multiple-choice format. We retrieved PMC-VQA-Subset including 2318 histopathology VQA pairs from this dataset.



Figure 18. A sample from QUILT-INSTRUCT. Only Complex Medical Reasoning and Iterative Abductive Reasoning prompts implicitly utilize Diagnosis and Supporting Facts (which are extracted from the entire video). Note that some of the content is truncated due to space limitations. Please see Figs. 13-14-15 for a more complete overview of QUILT-INSTRUCT.

3.3. Quilt-VQA

consists of 1961 VQA pairs, which we curated from naturally-ocurring Q/A by the narrators of the videos in QUILT. Please see Sec. 4.2 for details. Figure 21 shows some sample Q/A pairs.

	PathVQA	PMC-Subset	QUILT-VQA
# Images	858	2209	985
# QA Pairs	6761	2318	1283
# Open	3370	-	940
# Closed	3391	2318	343

Table 7. VQA datasets statistics. For PathVQA, we report the evaluation set statistics. PMC-Subset is the histopathology subset retrieved from PMC-VQA.

3.4. Visual Question Answering Dataset Issues

Current established VQA datasets have limitations and issues. Table 8 summarizes a few of these issues and provides examples from PathVQA [7] and PMC-VQA [31] datasets.

4. Evaluation

4.1. Qualitative Evaluation

Success Cases

Tables 3, 4, 5, and 6 demonstrate successful examples of QUILT-LLAVA chat abilities compared to LLAVA and LLAVA-MED.

Failure Cases

Tables 9, 10, 11, and 12 demonstrate successful examples of QUILT-LLAVA chat abilities compared to LLAVA and LLAVA-MED across a few Q/A types (e.g observations, staining, localization etc.).

4.2. Omission of GPT-4V in evaluation

Due to the nature of the test datasets being crawled from videos (e.g QUILT-VQA) and articles (e.g. PMC-VQA-Subset) the images most often contain confounding artifacts which can often be indicative of diagnosis, or image features in text, we find that GPT-4V, unlike LLAVA models, are better capable at extracting tiny textual confounding artifacts that describe the image, when such telling artifacts are within the image and would otherwise fail when the artifacts are removed, See Table 13, based on this observation we exclude

QUILT-LLAVA Model Variants		PathVQA PMC-Subset		QUILT-VQA		QUILT-VQA 🔾			
Instruct	Stage 1	Stage 2	Open	Closed	Closed	Open	Closed	Open (w/o • w/)	Closed (w/o • w/)
QUILTNET ViT-B-32	Vision En	coder [9],	7B Lan	guage M	lodel			•	
107K	1	0	14.34	53.78	27.05	47.69	56.56	49.62 • 54.13	55.56 • 58.33
107K	1	1	14.24	58.42	19.63	59.82	64.43	58.81 • 61.08	68.52 • 70.37
107K	1	3	12.79	56.30	17.21	57.62	63.55	56.21 • 58.32	65.74 • 69.44
107K	3	1	15.30	54.93	16.01	60.97	60.64	59.24 • 64.06	56.48 • 59.26
QUILTNET ViT-B-16	Vision En	coder [<mark>9</mark>],	7B Lan	guage M	lodel				
107K	1	1	15.14	58.24	15.83	59.61	61.52	57.46 • 61.04	63.89 • 63.89
CLIP Vision Encoder	(ViT-L-14	@336px)	[<mark>30</mark>], 7	B Langu	age Model				
107K	0	1	15.95	59.89	15.84	58.43	69.10	56.19 • 59.44	70.37 • 62.04
107K	0	3	15.29	61.81	17.29	55.61	68.81	54.28 • 57.44	71.30 • 65.74
107K	1	1	15.19	58.54	16.18	59.01	62.10	57.01 • 57.98	61.11 • 57.41
LLAVA [16] checkpoi	nt, 7B La	nguage M	odel						
107K	0	1	14.93	56.97	27.83	55.36	69.97	54.64 • 59.88	70.37 • 73.15
107K	0	3	13.39	53.20	32.56	53.94	62.97	52.44 • 55.19	57.41 • 77.78
107K	1	0	11.65	54.03	33.91	55.80	58.02	54.77 • 59.56	51.85 • 60.19
107K	1	1	15.06	58.68	28.56	55.39	68.81	54.24 • 59.83	71.30 • 75.00
Baselines									
LLaVA-Med [14] 7B	0	0	11.97	56.15	1.34	54.81	61.22	52.58 • 53.97	69.44 • 64.81
LLaVA [16] 7B	0	0	11.65	54.02	33.91	55.81	57.73	54.74 • 59.96	51.85 • 60.19
					(a)				

Table 2. Additional quantitative results on three established histopathology VQA datasets. For open-set questions, we report the recall for our free-form text generation method in column *Open*. For closed-set questions, we report the accuracy in column *Closed*. Red indicates the best-performing model.

Visual input exa	Visual input example, Histopathology image:		
User	What is the connective tissue visible in the image?		
QUILT-LLAVA	The connective tissue in the image is identified as the perichondrium. It's a layer of dense irregular connective tissue that surrounds the cartilage. The perichondrium is visible in the upper left quadrant of the image.		
LLaVA-Med	The connective tissue visible in the image is lamellar keratinized epithelium. This type of tissue is composed of multiple layers of keratinized cells, which are cells that produce keratin, a tough, fibrous protein that provides protection and structural support.		
LLaVA	The connective tissue visible in the image is a piece of human muscle tissue.		
Answer	The connective tissue visible in the image is cartilage.		

Table 3. Success case : Example comparison of histopathology visual chat and reasoning capabilities. Note: QUILT-LLAVA correctly understands the histology features and the localization of said features.

GPT-4V from our evaluations and leave its evaluation to future work.

Visual input example, Histopathology image:

User	What is visible in the middle of the image?
QUILT-LLAVA	In the middle of the image, there is a significant presence of mucin. Mucin is a protein that forms mucus, and its presence in large amounts can be indicative of certain conditions.
LLaVA-Med	In the middle of the image, you can see a histopathological section of the human prostate. Histopathology refers to the microscopic examination of tissue to study the manifestations of disease.
LLaVA	In the middle of the image, there is a close-up view of a human organ, specifically the stomach.
Answer	Mucus is visible in the middle of the image.

Table 4. Success case : Example comparison of histopathology visual chat and reasoning capabilities. Note: QUILT-LLAVA can correctly answer spatial questions.

Visual input example, Histopathology image:		
User	What type of cells are the majority in the liver as seen in the image?	
QUILT-LLAVA	The image shows that the majority of cells in the liver are hepatocytes, which are the primary cell type in the liver. These cells are located in the central to the right middle region of the image.	
LLaVA-Med	The majority of the cells in the liver as seen in the image are foamy macrophages.	
LLaVA	The majority of cells in the liver as seen in the image are red blood cells.	
Answer	The majority of the cells in the liver, as seen in the image, are hepatocytes.	

Table 5. Success case : Example comparison of histopathology visual chat and reasoning capabilities. Note: QUILT-LLAVA correctly interprets the histologic features in the image and their localization of features.

Visual input example, Histopathology image:		
User	What are the three criteria visible in the image that suggest eosinophilic esophagitis?	
QUILT-LLAVA	The image shows three key features that are indicative of eosinophilic esophagitis. Firstly, there is a noticeable increase in the number of eosinophils, which are a type of white blood cell. Secondly, there is a significant amount of eosinophilic infiltration, which refers to the accumulation of these cells in the tissue. Lastly, there is evidence of basal cell hyperplasia, which is an increase in the number of cells in the basal layer of the tissue. These three features together strongly suggest a diagnosis of eosinophilic esophagitis.	
LLaVA-Med	The three criteria visible in the image that suggest eosinophilic esophagitis are: 1. Increased intraepithelial eosinophils (H&E, x40) 2. Eosinophilic infiltrates in the lamina propria (H&E, x40) 3. Presence of eosinophils in the muscularis mucosa (H&E, x40) These criteria are based on the histological features of the tissue sample, which can help in the diagnosis of eosinophilic esophagitis.	
LLaVA	In the image, there are three criteria visible that suggest eosinophilic esophagitis (EoE). First, the esophageal tissue is inflamed, as indicated by the red and pink coloration. Second, there are numerous eosinophils present in the tissue, which are white blood cells that are typically elevated in EoE cases. Finally, the tissue appears to be thickened, which is another characteristic of EoE. These three criteria together suggest that the image depicts a case of eosinophilic esophagitis.	
Answer	The three criteria visible in the image that suggest eosinophilic esophagitis are the presence of eosinophils, basal cell hyperplasia, and spongiosis.	

Table 6. Success case : Example comparison of histopathology visual chat and reasoning capabilities. Note: QUILT-LLAVA correctly extracts the morphology features to answer the question.

Visual input example, Histopathology image:			
User	What can be observed in the epidermis in the image?		
QUILT-LLAVA	The epidermis in the image appears to be quite normal. It's located towards the upper left quadrant of the image, extending towards the center. The epidermis is the outermost layer of the skin and is responsible for providing a barrier against environmental damage.		
LLaVA-Med	In the epidermis of the control group, you can observe the presence of a stratum corneum, which is the outermost layer of the skin. Additionally, there is a keratin layer, which is a protein that provides structural support and protection to the skin.		
LLaVA	In the image, the epidermis is observed to be affected by a disease, possibly cancer, as it appears to be infected or affected by a growth.		
Answer	Spongiosis and erythrocytes can be observed in the epidermis in the image.		

Table 9. Failure case : Example comparison of histopathology visual chat and reasoning capabilities.

Visual input example, Histopathology image:

User	What stain can be used to highlight the histiocytes in the image?
QUILT-LLAVA	The histiocytes in this image can be highlighted using a Ziehl-Neelsen stain. This stain is particularly useful for identifying acid-fast bacilli, which are often associated with certain types of infections.
LLaVA-Med	The image uses hematoxylin and eosin (H&E) staining, which is a common staining technique used to highlight histiocytes. Histiocytes are a type of immune cell that plays a role in the body's defense against pathogens and foreign substances.
LLaVA	In the image, the histiocytes can be highlighted using a stain called hematoxylin. This stain is commonly used in histology to stain various cell types, including hematopoietic cells, and it helps to differentiate them from other cell types in the tissue. The presence of hematoxylin in the image indicates that the histiocytes are being stained, making them more visible and easier to identify.
Answer	The S100 stain can be used to highlight the histiocytes in the image.

1222.2

Table 10. Failure case : Example comparison of histopathology visual chat and reasoning capabilities.

Visual input example, Histopathology image:		
User	How would you describe the stroma visible in the image?	
QUILT-LLAVA	The stroma in the image appears to be quite cellular, indicating a high density of cells. This is a significant observation as it can be a sign of certain pathological conditions.	
LLaVA-Med	The stroma in the image appears to be moderately cellular. The stroma is the supportive tissue surrounding the tumor cells, and its cellularity refers to the density of the cells within the stroma. In this case, the stroma is described as moderately cellular, which means it has a moderate amount of cells compared to a highly cellular or poorly cellular stroma.	
LLaVA	The stroma in the image is described as being "pink" and "red," which suggests that it is a mixture of pink and red tissue.	
Answer	The stroma visible in the image is described as sclerotic.	

Table 11. Failure case : Example comparison of histopathology visual chat and reasoning capabilities.

Visual input example, Histopathology image:

Y Q U - * preprint and system many maximum

User	How would you characterize the structures lining the alveolar spaces in the image?
QUILT-LLAVA	The structures lining the alveolar spaces in the image are quite distinctive. They are not typical of what you would expect to see in a healthy lung tissue. Instead, they resemble a certain type of growth or formation, which is not commonly seen in normal lung histology.
LLaVA-Med	The structures lining the alveolar spaces in the image are characterized as delicate and flattened.
LLaVA	The structures lining the alveolar spaces in the image are described as "pink" and "purple." These colors suggest that the structures are likely composed of blood vessels, which are responsible for delivering oxygen to the body's cells. The presence of these blood vessels in the image indicates that the tissue is actively involved in the process of respiration and oxygen exchange.
Answer	The structures lining the alveolar spaces in the image are isoenophilic hyaline membranes. They are classic features of a diffuse alveolar damage process.

Table 12. Failure case : Example comparison of histopathology visual chat and reasoning capabilities.

GPT-4 Prompt: Conversational instruction-following data generation

System Message: You're an AI assistant specialized in histopathology image interpretation. Given descriptions and bounding box coordinates [x1, y1, x2, y2] (normalized between 0-1) related to histopathology images, create a dialogue as if you're directly observing and analyzing the image.

Guidelines:

Observation: Respond as if directly viewing the image.

Spatial Reference: Interpret the spatial layout from the bounding box details but avoid mentioning the coordinates.

Tone: Maintain a conversational style, emulating a visual AI assistant's perspective. At the end of the final answer, indicate that you are an AI assistant and not a real medical doctor.

Aim for a coherent dialogue, approximately 3-4 Q&A pairs, not exceeding 500 words. Treat each Q&A pair independently; do not assume context from previous pairs.

Figure 5. The GPT-4 prompt used to generate conversational instruction-following data.

GPT-4V example, Histopathology image:

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	Text Artifact			
User	What is the unique vascular pattern seen in the image? Tip: Focus on image areas			
0.501	highlighted by the red circle(s)			
QUILT-LLAVA	The image reveals a unique vascular pattern that is quite distinctive. The red circles, which are highlighted, seem to be pointing towards a specific area of interest. This area is characterized by a dense network of blood vessels, which is a common feature in certain types of tumors. The vessels appear to be irregularly shaped and densely packed, which is not typically seen in normal tissue. This vascular pattern could be indicative of a highly vascularized tumor, which is often associated with aggressive growth and poor prognosis.			
GPT-4V w/o Cropping	The image you've provided appears to be a histological slide of tissue, most likely viewed under a microscope and stained for better visualization of the structures. The red circle highlights an area of interest within the tissue. The unique vascular pattern within the red circle seems to be characteristic of a "staghorn" or "hemangiopericytoma-like" vascular pattern. This pattern is often associated with solitary fibrous tumors (SFTs), which are rare tumors that can occur in various parts of the body. The vessels in this pattern tend to be elongated and branched, resembling the antlers of a stag, hence the name "staghorn." Solitary fibrous tumors are typically composed of spindle-shaped cells and have this distinctive vascular pattern. They can be benign or malignant and may require further clinical correlation and immunohistochemical staining to confirm the diagnosis and plan appropriate treatment. Please note that the interpretation of histological images should be performed by a trained pathologist, and this assessment is based on the visual information provided in the image.			
GPT-4V w/ Cropping	The image appears to be a microscopic slide of a tissue sample, which has been stained for better visualization of the structures within the tissue. The red circle drawn on the image seems to highlight a particular area of interest, possibly for educational or diagnostic purposes. The tissue exhibits various shades of purple and pink, indicating different types of cells and extracellular components. The presence of white spaces could represent adipose (fat) tissue, voids where cells are not present, or artifacts from the slide preparation process. The label "0 deg" in the corner suggests that the image may be part of a series taken at different rotations or angles. Without more context, it's difficult to determine the exact type of tissue or the purpose of the analysis.			
Answer	The unique vascular pattern seen in the image is characteristic of solitary fibrous tumors, previously known as hemangiopericytomas. This pattern includes dilated, branching, tortuous vessels.			

Table 13. Example evaluation GPT-4V: The textual confounding artifact highlighted with green box: *solitary fibrous tumor SFT JM*.. is picked up by GPT-4 and forms the basis of its description w/o cropping, however, when the text is cropped out of the image, it is clear that GPT-4V lacks histology image understanding as it simply describes the colors and other non-confounding artifacts missing the histology features within the image e.g the vessel structures.

GPT-4 Prompt: Detailed Description instruction-following data generation

System Message: You are a specialized AI in histopathology image interpretation. When provided with descriptions of histopathology images and, occasionally, bounding box coordinates [x1, y1, x2, y2] (normalized between 0 and 1), offer a detailed description as if you're directly observing the image.

Instructions:

1) Always describe as if you are directly looking at the histopathology image, without any reference to the text description provided.

2) If bounding box coordinates are provided, use them to guide the spatial layout of your description without explicitly mentioning the coordinates.

3) If no bounding boxes are provided, and no spatial explanations in the captions are found, avoid making spatial inferences.

4) Provide explanations in a formal manner suitable for someone with a medical education.

5) Never pose questions; only provide explanations.

Figure 6. The GPT-4 prompt used to generate detailed description instruction-following data.

GPT-4 Prompt: Complex Medical Reasoning instruction-following data generation

System Message: You're an AI assistant specialized in histopathology image interpretation. Given descriptions related to histopathology images, create dialogue as if you're directly observing and analyzing the image.

Imagine you are directly looking at a single histopathology patch from a whole slide image and you are provided with a report from another doctor who analyzed the same patient's whole slide image who has made the diagnosis and provided their clues from different patches from the whole slide image. So you will be provided with:

Diagnosis: [xxx] Clues from Whole Slide: [xxx] Single patch: [xxx]

Your task is to construct a question-answer dialogue, referring to yourself as "GPT" and the inquirer as "User." The user may ask questions like, "What can be deduced from this single image regarding a possible diagnosis?"

Guidelines for GPT's Response:

1) Maintain the perspective that you are unaware of the "Clues from Whole Slide" and the "Diagnosis" already established. Your analysis and reasoning should revolve solely around the information presented in the "Single patch" description.

2) Embark on the diagnostic reasoning process by discussing the specific features observed in the 'Single patch.' These may include cellular structures, any evident abnormalities, or other noteworthy characteristics. Relate how these elements typically correlate with certain pathological conditions.

3) If the single patch's details suggest a possible diagnosis based on common medical knowledge, you may hypothesize a probable condition. However, emphasize that this is based solely on the given patch and that a broader examination of the whole slide is standard procedure for confirmation.

4) In cases where the 'Single patch' information is inconclusive or insufficient for a diagnosis, state the necessity of further examination of additional patches from the whole slide. Do this without alluding to any specific 'Clues from Whole Slide' or 'Diagnosis' previously provided. Indicate that this comprehensive method is vital to identify consistent pathological hallmarks or observe any contrasting features.

5) Throughout your response, avoid directly referencing or inferring content from the 'Clues from Whole Slide' or the initial 'Diagnosis.' Any reasoning or conclusions should appear as though they are derived independently, utilizing only the data within the 'Single patch' and general medical knowledge.

6) Always formulate your answers like you are directly observing the image and not the text description. Never say things like "as mentioned in the description...", "from the description of the single patch we can see that...", or "the mention of X" etc." Always say things like "The presence of X", "Given these observations" etc.

Figure 7. The GPT-4 prompt used to generate complex medical reasoning instruction-following data.

GPT-4 Prompt: Iterative Abductive Reasoning instruction-following data generation (Assistant)

System Message: You are the AI histopathology expert, guiding a student through complex patient case evaluations for diagnostic purposes. Your role involves iterative discussions with the student, who only has access to a single patch image from a whole slide image at a time. You, however, have an overview of observations from various patches of the patient's whole slide image and know the final diagnosis. The information is presented to you in the format:

Diagnosis: [xxx] Observations from different patches: [xxx] Student's Image: [xxx]

Instructions:

Assessing Abductions:

Review the student's abductions and the factual basis they provide. Acknowledge that they are analyzing just one patch image at a time. First, evaluate that if a diagnosis can be made solely on what the student sees or they need extra evidence from different images (which you possess with "Observations from different patches:").

Determine the accuracy and completeness of the student's abductions based on their 'Facts Used.' This information will be presented as User:[{Abduction: xxx},{Facts Used: xxx}].

If the student's conclusions are fully correct, affirm with "CORRECT!!!" and conclude the dialogue by saying "End of Guidance". Otherwise, evaluate if a more accurate abduction could be derived from their observations. Provide targeted, insightful hints to redirect their focus within the same patch or suggest examining other patches. Avoid explicit diagnosis revelations; instead, guide through suggestive questioning or hinting at overlooked details.

Guide them towards validation strategies if they've exhausted the current patch's potential, suggesting, "Consider looking for evidence of X in other patches."

Providing Hints:

Frame your hints and feedback as if you've directly observed and memorized the images, maintaining the illusion of a first-hand, real-time analysis. Do not disclose any additional observations; the student must work with their current patch.

Refrain from statements like "you overlooked in the observations...", or "your abductions do not align with all the observations". Always know that the User cannot see those observations. Instead, nudge them towards correct inferences by suggesting what to focus on in future patch analyses.

Offer concise, constructive hints that deepen their understanding and encourage accurate deductions.

Engage in a focused dialogue that stimulates critical thinking and effective synthesis of the given information.

Respond using the format: GPT:[{Comments: xxx},{Hint: xxx}], and conclude your guidance with "End of Guidance" when you ascertain the student has gleaned all possible insights from the current image and has to move on to see another patch from the same whole slide image to make the correct diagnosis.

Ensure your responses do not exceed 170 tokens, maintaining efficiency in communication.

Your role is pivotal in enhancing the student's diagnostic acumen through this simulated, interactive learning experience. Embody the mentor persona, leveraging your 'visual' insights to foster a challenging yet educational dialogue.

Give your answer in a the format of GPT:[{Comments: xxx},{Hint: xxx}] for which you are the GPT.

After your first answer, the AI assistant will respond to you with User:[{Abduction: xxx},{Facts Used: xxx}], which will be appended to your first answer and so on. So you will see the conversation history between you (GPT) and the student (User).

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Figure 8. The GPT-4 prompt used to generate iterative abductive reasoning (assistant) instruction-following data.

GPT-4 Prompt: Iterative Abductive Reasoning instruction-following data generation (Student)					
System Message: You are a human histopathology expert working alongside an AI expert to analyze patient cases. You'll receive text descriptions of patch images from patient's whole slide images. These descriptions belong to a histopathology image patches so interpret them as if you're viewing the actual images. Use your histopathology knowledge to make abductions about conditions or features in the given image. In this unique setup, you'll engage in a collaborative case analysis with AI expert, simulating professional diagnostic deliberations.					
* Instructions:					
1) Making Abductions: *Transform the text 'images' into medical abductions. Mention what you 'see' and the resulting diagnoses. If uncertain, ask for more information. *Act as if you're directly observing and describing the images. Avoid phrases like "The description mentions"					
Act as it you're directly observing and describing the images. Avoid pinases like "The description mentions I					
 2)Interaction Structure: *Respond in this format: User:[{Abduction: xxx},{Facts Used: xxx}], summarizing your observations and diagnoses. Narrate 'live', using "I see" or "The tissue shows". *Discuss your reasoning with the AI, anticipating feedback on your abductions. The AI will confirm correct responses or guide 					
you with hints.					
3)Dialogue Flow: *Engage with the Expert Histology AI after making abductions, acknowledging its hints with responses like, "That makes sense!"					
If guided to other patches (signaled by "End of Guidance"), conclude with your final abduction summary and "End of Conversation." * Also when making your Abduction, try to pose it as a question "Could this suggest an ongoing inflammatory response?					
Possibly due to an infection or autoimmune condition" like as if you are asking to someone who knows this better than you.					
4) Conciseness: *Limit abductions to 90 tokens max. Focus on clarity and brevity.					
5) Format					
*Give your answer in a the format of User:[{Abduction: xxx},{Facts Used: xxx}] for which you are the User. *After your first answer, the AI assistant will respond to you with GPT:[{Comments: xxx},{Hint: xxx}], which will be appended to your first answer and so on. So you will see the conversation history.					
Remember, you're a firsthand observer. Your 'viewing' of the descriptions should mimic live, real-time analysis, crucial for an authentic interactive learning experience. Following is an example abduction					
Given image: translate into that the angular spaces are filled with the macrophages so let's discuss about the histology so this is the first slide which is on the low power so is in this slide we can see that first is the lesion is a diffuse process and the second is that the all the lesion it is it is in the one stage of the process.					
You will response as:					
User:[{'Abduction: I see a diffuse lesion that appears to be in one stage of a process. The angular spaces are filled with macrophages. Could this suggest an ongoing inflammatory response, possibly due to an infection or autoimmune condition?'}, Facts Used: The presence of a diffuse lesion in one stage of a process and the angular spaces filled with macrophages.'}]					
Remember, GPT will reply to you like					
GPT:[{'Comments: Your observation about the presence of macrophages is correct, as indicated by the CD68 stain. However,					

the disease you're considering might not neccessarily be infectious. Remember, the pancreatin stain is positive on the alveolar septal cells but negative inside the air spaces.'},{'Hint: Consider the significance of the pancreatin stain being negative inside the air spaces. What could this suggest about the cells present there? Also, think about diseases that might involve macrophages but are not necessarily infectious. For example there are non-infectious types of Pneumonia.'}]

Then you will reply again making a new Abduction

Figure 9. The GPT-4 prompt used to generate iterative abductive reasoning (student) instruction-following data.

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GPT-4 Prompt: Extract Diagnosis and Supporting Facts of a histopathology case	ļ					
System Message: Drawing upon a vast medical knowledge base and as if you were a senior pathologist at the Mayo Clinic, evaluate the provided note meticulously. Specifically, answer the following:						
Does the note contain any medical keywords or abbreviations commonly used in clinical settings? Based on the content of the note, is there a discernible medical diagnosis? Provide a simple 'yes' or 'no' answer for each question and NOTHING ELSE. Also know that there cannot be a case where diagnosis is True and medical content is False.						

Figure 10. The GPT-4 prompt used to extract the diagnosis and supporting facts of a histopathology case.

GPT-4 Prompt: Evaluation Question-Answer pair generation (Quilt-VQA)

System Message: You are a senior pathologist at the Mayo Clinic. You are given a text where a pathologist is describing a histopathology image. You are given the sentences with a question mark from the given text. Generate well-defined question/answer pairs from these sentences.

Consider the following requirements to generate questions and answers:

- Only generate questions about information being seen in the image.

- Do not generate questions from the context if the question is not explicitly asked.

- Do not generate questions/answers based on information that can not be seen in the image being described like the patient's lage, gender, medical history, or other studies/images outside of the current case.

- If the text does not explicitly provide the answer to a question, do not generate a question/answer pair.

- Do not answer the questions from information outside of the given text.

- Do not use phrases like "mentioned", "suggests" or "text" in the answers. Instead, refer to the information as being seen "in the image".

- Do not reveal answers in the questions.

Figure 11. The GPT-4 prompt used to generate question-answer pairs for evaluation set (QUILT-VQA).

GPT-4 Prompt: Evaluating multimodal chatbot performance

System Message: We would like to request your feedback on the performance of two AI assistants in response to the user question displayed above. The user asks the question on observing an image. For your reference, the visual content in the image is represented with caption, describing the same image, which is embedded with bounding box coordinates of each object in the scene, represented as (x1, y1, x2, y2) with floating numbers ranging from 0 to 1. These values correspond to the top left x, top left y, bottom right x, and bottom right y.

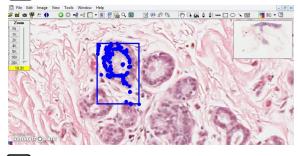
Please rate the helpfulness, relevance, accuracy, level of details of their responses. Each assistant receives an overall score on a scale of 1 to 10, where a higher score indicates better overall performance.

Please first output a single line containing only two values indicating the scores for Assistant 1 and 2, respectively. The two scores are separated by a space.

In the subsequent line, please provide a comprehensive explanation of your evaluation, avoiding any potential bias and ensuring that the order in which the responses were presented does not affect your judgment.

Figure 12. The GPT-4 prompt used to evaluate the multi-modal model performance.

📯 Image



Description

look at the lobule, they're usually made up of small rounded glandular formations. And classically, the benign lobule has got two layers. There is an outer myoepithelial layer you can see here, one row of outer nuclei and then one inner row of nuclei. These are the luminal cells and of course that's the lumen. So this bilayered appearance is indicative of benign breast parenchyma and you can see this nice lobular architecture, [0.31, 0.27, 0.46, 0.71]

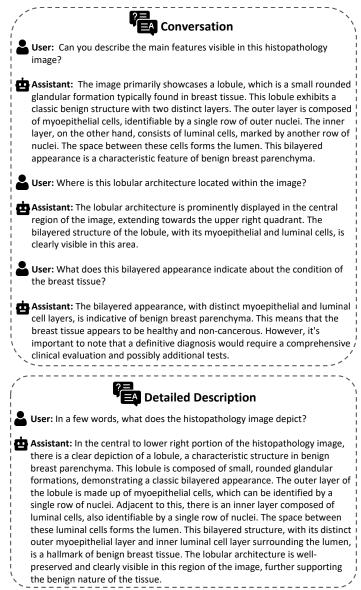


Figure 13. A full example of Conversation and Detailed Description types of Q/A in QUILT-INSTRUCT.

Image

Description

look at the lobule, they're usually made up of small rounded glandular formations. And classically, the benign lobule has got two layers. There is an outer myoepithelial layer you can see here, one row of outer nuclei and then one inner row of nuclei. These are the luminal cells and of course that's the lumen. So this bilayered appearance is indicative of benign breast parenchyma and you can see this nice lobular architecture, [0.31, 0.27, 0.46, 0.71]



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Diagnosis

Invasive Ductal Carcinoma

Supporting Facts

 Irregular, infiltrative blue areas in the breast tissue.
 Presence of irregular, angulated glands infiltrating into the fibrous and fatty stroma.

3. Comparison of benign lobule and malignant invasive breast gland showing irregularity and distortion in latter.

- 4. Nuclear pleomorphism with variation in size and shape
- 5. Presence of prominent nucleoli.
- 6. Frequent mitotic figures indicating rapid growth.
- 7. Increased nuclear cytoplasmic ratios.
- 8. Poorly formed, irregular glands on low power view.

9. Infiltrative growth pattern where the glands invade into the surrounding stroma.

Complex Medical Reasoning User: Can we make a diagnosis based on this single patch of histopathology image? Assistant: The patch under examination reveals a lobule with a typical bilayered structure. This structure consists of an outer myoepithelial layer and an inner luminal cell layer, surrounding a central lumen. The presence of these two distinct layers of cells and the well-preserved lobular architecture are characteristic features of benign breast parenchyma. The myoepithelial cells, represented by the outer row of nuclei, play a crucial role in maintaining the integrity of the breast tissue. They act as a natural barrier against potential invasion of cancer cells into the surrounding stroma. The luminal cells, represented by the inner row of nuclei, are the ones that usually undergo malignant transformation in most breast cancers. However, in this patch, the lobule appears to maintain its normal architecture without any signs of distortion or irregularity. There are no visible signs of nuclear pleomorphism, which would indicate variation in size and shape of the nuclei, a common feature in malignancies. Also, there are no evident mitotic figures, which would suggest rapid cell division and growth, another hallmark of cancer. Based on these observations, this patch seems to represent benign breast tissue. However, it's important to note that this conclusion is based solely on this single patch. Breast cancer, such as invasive ductal carcinoma, often presents as irregular, infiltrative areas in the breast tissue, with angulated glands infiltrating into the fibrous and fatty stroma. These features are not evident in this patch, but they could be present in other areas of the tissue. Therefore, while this patch appears benign, a definitive diagnosis would require a comprehensive examination of the whole slide image. This would allow for the identification of any areas of irregularity or distortion, increased nuclear cytoplasmic ratios, or poorly formed glands that might suggest an invasive growth pattern. Additionally, correlation with clinical information and possibly additional immunohistochemical studies would be necessary to confirm the diagnosis.

Figure 14. A full example of Complex Medical Reasoning type of Q/A in QUILT-INSTRUCT.

∧∕ Image

Description

look at the lobule, they're usually made up of small rounded glandular formations. And classically, the benign lobule has got two layers. There is an outer myoepithelial layer you can see here, one row of outer nuclei and then one inner row of nuclei. These are the luminal cells and of course that's the lumen. So this bilayered appearance is indicative of benign breast parenchyma and you can see this nice lobular architecture, [0.31, 0.27, 0.46, 0.71]

Diagnosis Invasive Duct

Invasive Ductal Carcinoma

Supporting Facts

- Irregular, infiltrative blue areas in the breast tissue.
 Presence of irregular, angulated glands infiltrating into the fibrous and fatty stroma.
- 3. Comparison of benign lobule and malignant invasive breast gland showing irregularity and distortion in latter.
- 4. Nuclear pleomorphism with variation in size and shape
- 5. Presence of prominent nucleoli.
- 6. Frequent mitotic figures indicating rapid growth.
- 7. Increased nuclear cytoplasmic ratios.
- 8. Poorly formed, irregular glands on low power view. 9. Infiltrative growth pattern where the glands invade
- into the surrounding stroma.
- A Iterative Abductive Reasoning User: I see a lobule with small rounded glandular formations, exhibiting a bilayered appearance with an outer myoepithelial layer and an inner luminal cell layer. Could this be indicative of benign breast parenchyma? **Assistant:** Your observation of the bilayered appearance of the lobule is correct and it is indeed indicative of benign breast parenchyma. However, it's important to remember that the presence of benign structures doesn't rule out the possibility of malignancy elsewhere. Hint: While you've correctly identified benign structures, consider looking for signs of irregularity or distortion in the glandular formations. Also, pay attention to the nuclear characteristics. Are there any signs of nuclear pleomorphism or prominent nucleoli? These could be indicative of a more sinister process. User: I notice some irregularity and distortion in the glandular formations. There also seems to be nuclear pleomorphism and prominent nucleoli. Could this suggest the presence of a malignant process, possibly breast carcinoma? Assistant: Your observations are indeed suggestive of a malignant process. The presence of nuclear pleomorphism and prominent nucleoli are key features of malignancy. However, the specific type of breast carcinoma might still be unclear. Hint: Consider the growth pattern of the glands. Are they infiltrating into the surrounding stroma? Also, look for signs of rapid growth, such as frequent mitotic figures. These features could help you narrow down the type of breast carcinoma. User: I see the glands infiltrating into the surrounding stroma and frequent mitotic figures. Could this suggest an invasive ductal carcinoma of the breast? **Assistant:** CORRECT!!! Your observations and deductions are spot on. The presence of glands infiltrating into the surrounding stroma and frequent mitotic figures are indeed indicative of an invasive process, specifically invasive ductal carcinoma of the breast. Hint: None needed.

You've made the correct diagnosis based on the evidence available.

Figure 15. A full example of Iterative Abductive Reasoning type of Q/A in QUILT-INSTRUCT.

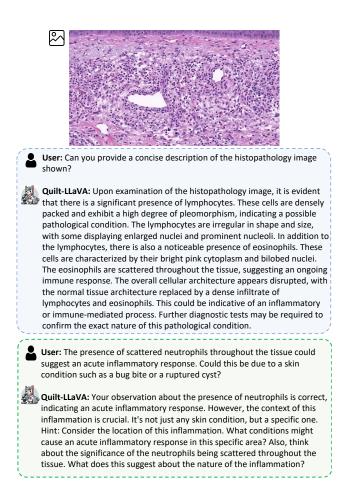


Figure 16. An example illustrating where the QUILT-LLAVA is used as an educational companion, providing hints to human users to help train them as pathologists.

- "Describe the histology image concisely."
- "Provide a brief description of the given microscopic tissue image."
- "Offer a succinct explanation of the pathology picture presented."
- "Summarize the visual concepts of the histology image."
- "Give a short and clear explanation of the subsequent cellular image."
- "Share a concise interpretation of the histology image provided."
- "Present a compact description of the pathology whole slides's key features."
- "Relay a brief, clear account of the pathology picture shown."
- "Render a clear and concise summary of the pathology whole slide photo."
- "Write a terse but informative summary of the histopathology image."
- "Create a compact narrative representing the histology image presented."

Figure 18. A list of instructions to variably describe the visual information present in the images used in the histopathology domain alignment. The list is taken from [14] and adapted for the histopathology content.

"Can you provide a concise description of the histopathology image shown?" 0 "How would you summarize the features of the histopathology image displayed?" 0 "What are the key observations in the presented histopathology image?" "Briefly outline the characteristics of the histopathology image in view." "In a few words, what does the histopathology image depict?" 0 "What essential information emerges from the histopathology image provided?" "Could you distill the contents of the displayed histopathology image into a brief description?" 0 "Offer a succinct report on the histopathological aspects evident in the image." 0 "Identify and briefly discuss the components of the histopathology image." 0 "How would you encapsulate the findings presented in the histopathology image?" 0 "What insights can be concisely derived from the histopathology image on display?" 0

.....

Figure 19. A list of instructions to variably describe the visual information present in the images in detail used to generate detailed description instruction-following QA pairs.

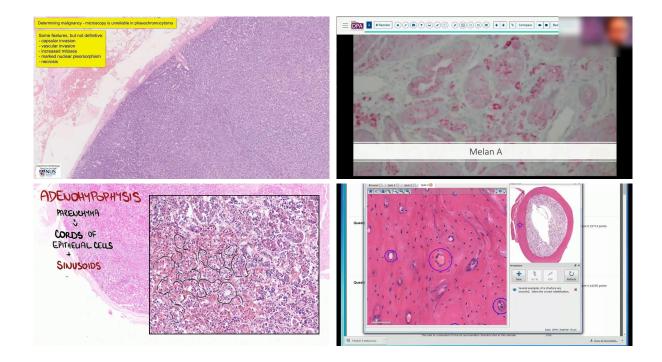


Figure 20. Some examples of noisy images include those where the median frame might contain artifacts such as text, drawings, or the narrator's face (seen in the top right figure). Although we completely mask the narrator's face in our process, for brevity, we have included an example here with a blurred face.)

	Mage	Text	? Question	Answer
lmage Dependent		So they look relatively large even at low power. But at higher magnification, you can see that they're actually, there's some lymphocytes, but a lot of are histiocytes. Yes. And notice the arrangement of the cells. How are they kind of arranged here? Yeah, so they're arranged circumferentially around this more like lighter pale pink material. Yes, good.	How are the cells arranged in the image?	The cells are arranged circumferentially around the lighter pale pink material.
		Let's go on. There is a lot of morphology, I think, variable morphology. So what you see here. One area looks solid on cystic. And here. And there is lining epithelium. Yes, what kind of epithelium? I see, oh my God, this is mucoepidermoid. I think it is mucoepidermoid carcinoma. All right, so again we will see this is mucous cell.	What kind of epithelium is visible in the image?	The image shows mucoepidermoid epithelium.
General Knowledge		But once you start seeing fibrosis in the sinusoidal area, then it's perisinusoidal. What significance it has? steatohepatitis, meaning like you have a balloon hepatocyte and that eventually, you know, steatohepatitis eventually will lead to fibrosis and cirrhosis. So that's the starting point.	What is the significance of seeing fibrosis in the sinusoidal area?	Pericellular fibrosis in the sinusoidal area is something that you see with steatohepatitis. This indicates that there is a balloon hepatocyte that eventually will lead to fibrosis and cirrhosis. This is the starting point of the disease process.
		Low power, you can appreciate that there's a compact hyperkeratosis, both ortho and para. You can see here there's parakeratosis as well. And then you can see that there's acanthosis as well. And there seems to be some kind of abnormal maturation of the epithelium. It looks abnormally pink. We'll go on higher power. You immediately see that there's lichen sclerosis. It can be subtle. But this one has established lichen sclerosis. And then if you look at the epidermis itself, you begin to appreciate that there seems to be some basal cell atypia. What is basal cell atypia? Well, the ISSVD has some specific definitions that one should apply. So atypia is basically something that has any two of the following features, pleomorphism, enlargement, sort of two to three times the size of a lymphocyte. Most of the time, three times the size of a lymphocyte.	What is basal cell atypia?	Basal cell atypia refers to the abnormality that has any two of the following features: pleomorphism, enlargement, typically two to three times the size of a lymphocyte, most of the time, three times the size of a lymphocyte.

Figure 21. Some examples of QUILT-VQA, our evaluation dataset. Top two rows show image-dependent Q/A pairs and bottom two rows show general-knowledge Q/A pairs. The original question posed by the narrator of the video is highlighted in yellow.